Table 151 Incidence status for classification of action taken to surveillance drug (total (N=1357))

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Total	68	(5.01)	81	32	(2.36)	40	4	(0.29)	5	16	(1.18)	21	452	(33.31)	856	2	(0.15)	3
Blood and Lymphatic System Disorders	0	(0.00)	0	1	(0.07)	1	1	(0.07)	1	0	(0.00)	0	15	(1.11)	16	0	(0.00)	0
Anaemia	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Iron Deficiency Anaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4	0	(0.00)	0
Leukopenia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(0.37)	5	0	(0.00)	0
Lymphadenitis	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Lymphadenopathy	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Neutropenia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Pancytopenia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Cardiac Disorders	3	(0.22)	3	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(0.37)	5	0	(0.00)	0
Atrial Fibrillation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Cardiac Arrest	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Palpitations	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4	0	(0.00)	0
Ear and Labyrinth Disorders	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4	0	(0.00)	0
Otorrhoea	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Tinnitus	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Vertigo	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Eye Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	10	(0.74)	11	0	(0.00)	0
Blepharitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Dry Eye	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4	0	(0.00)	0
Glaucoma	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Uveitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Vision Blurred	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Visual Acuity Reduced	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Gastrointestinal Disorders	9	(0.66)	9	4	(0.29)	4	1	(0.07)	1	8	(0.59)	8	121	(8.92)	170	0	(0.00)	0
Abdominal Discomfort	1	(0.07)	1	1	(0.07)	1	1	(0.07)	1	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Abdominal Distension	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Abdominal Pain	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	20	(1.47)	28	0	(0.00)	0
Abdominal Pain lower	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Abdominal Pain Upper	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	13	(0.96)	14	0	(0.00)	0
Anal Fistula	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Aphthous Ulcer	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Colitis Ulcerative	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Constipation	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	9	(0.66)	10	0	(0.00)	0
Crohn's Disease	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	3	(0.22)	3	0	(0.00)	0
Diarrhoea	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	19	(1.40)	19	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Dry Mouth	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Dyspepsia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	13	(0.96)	15	0	(0.00)	0
Dysphagia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Enterocutaneous Fistula	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Epigastric Discomfort	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Frequent Bowel Movements	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Gastric Mucosal Lesion	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Gastric Ulcer	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Gastric Ulcer Haemorrhage	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Gastritis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(0.37)	5	0	(0.00)	0
Gastroduodenitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Gastrointestinal Disorder	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Gastrointestinal Inflammation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Gastrooesophageal Reflux Disease	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Haematochezia	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4	2	(0.15)	2	0	(0.00)	0
Ileus	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Intestinal Obstruction	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Large Intestine Polyp	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Melaena	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Mouth Haemorrhage	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Mouth Ulceration	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Nausea	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	18	(1.33)	20	0	(0.00)	0
Proctalgia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Protein-Losing Gastroenteropathy	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Regurgitation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	3	0	(0.00)	0
Small Intestinal Haemorrhage	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Stomatitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Vomiting	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	9	(0.66)	11	0	(0.00)	0
General Disorders and Administration Site Conditions	7	(0.52)	7	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	42	(3.10)	47	1	(0.07)	1
Application Site Haemorrhage	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Asthenia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Chest Discomfort	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Chest Pain	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Chills	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.29)	6	0	(0.00)	0
Disease Progression	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Drug Effect Delayed	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Drug Ineffective	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Face Oedema	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Fatigue	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	6	(0.44)	6	0	(0.00)	0
Generalised Oedema	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Immediate Post-Injection Reaction	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Influenza Like Illness	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Large Intestinal Perforation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Non-Cardiac Chest Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Oedema	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(0.37)	5	0	(0.00)	0
Oedema Peripheral	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Pyrexia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	12	(0.88)	13	1	(0.07)	1
Swelling	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Hepatobiliary Disorders	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0	7	(0.52)	7	0	(0.00)	0
Cholelithiasis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Drug-Induced Liver Injury	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Hepatic Function Abnormal	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Hepatitis	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Hyperbilirubinaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Liver Disorder	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Immune System Disorders	8	(0.59)	8	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Anaphylactic Reaction	4	(0.29)	4	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Anaphylactic Shock	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Hypersensitivity	3	(0.22)	3	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Infections and Infestations	15	(1.11)	15	9	(0.66)	9	1	(0.07)	1	0	(0.00)	0	119	(8.77)	136	1	(0.07)	1
Abdominal Abscess	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Abscess	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Anal Abscess	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Arthritis Bacterial	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Atypical Pneumonia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Body Tinea	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Bronchiolitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Bronchitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	12	(0.88)	12	0	(0.00)	0
Candida Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	2	0	(0.00)	0
Cellulitis	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Clostridium Difficile Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Cystitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Cytomegalovirus Colitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Cytomegalovirus Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Disseminated Tuberculosis	2	(0.15)	2	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Folliculitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4	0	(0.00)	0
Furuncle	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Gastritis Bacterial	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Hepatitis B	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Herpes Simplex	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Herpes Virus Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Herpes Zoster	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	7	(0.52)	7	0	(0.00)	0
Hordeolum	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Influenza	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Lung Abscess	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Nasopharyngitis	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	26	(1.92)	27	0	(0.00)	0
Onychomycosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Oral Candidiasis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Otitis Externa	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	2	0	(0.00)	0
Pharyngitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Pharyngotonsillitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Pneumocystis Jirovecii Pneumonia	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Pneumonia	1	(0.07)	1	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0	6	(0.44)	6	0	(0.00)	0
Pneumonia Bacterial	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Postoperative Wound Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Pseudomembranous Colitis	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Pulmonary Tuberculosis	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Pyelonephritis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Pyelonephritis Acute	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4	0	(0.00)	0
Rhinitis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Sepsis	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Sialoadenitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Sinusitis	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Spleen Tuberculosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Tinea Pedis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Tonsillitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Tuberculosis	3	(0.22)	3	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Tuberculosis Gastrointestinal	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Upper Respiratory Tract Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	24	(1.77)	27	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Ureteritis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Urinary Tract Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	1	(0.07)	1
Vaginal Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Injury, Poisoning and Procedural Complications	3	(0.22)	3	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	13	(0.96)	19	0	(0.00)	0
Ankle Fracture	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Auricular Haematoma	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	3	0	(0.00)	0
Compression Fracture	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Contusion	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Facial Bones Fracture	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Fall	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Foot Fracture	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Fracture	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Hand Fracture	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Infusion Related Reaction	3	(0.22)	3	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Joint Dislocation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Laceration	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Perineal Injury	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Road Traffic Accident	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Investigations	7	(0.52)	7	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	51	(3.76)	65	1	(0.07)	1
Alanine Aminotransferase Increased	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	20	(1.47)	21	0	(0.00)	0
Aspartate Aminotransferase Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	13	(0.96)	13	0	(0.00)	0
Blood Alkaline Phosphatase Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Blood Creatine Phosphokinase Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
C-Reactive Protein Increased	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Eosinophil Count Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Hepatic Enzyme Increased	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4	0	(0.00)	0
Influenza B Virus Test Positive	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Liver Function Test Abnormal	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	6	(0.44)	7	0	(0.00)	0
Occult Blood	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Serum Ferritin Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Transaminases Increased	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Urine Analysis Abnormal	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Weight Decreased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Weight Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(0.37)	5	0	(0.00)	0
White Blood Cell Count Decreased	1	(0.07)	1	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	3	(0.22)	3	1	(0.07)	1

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Metabolism and Nutrition Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	25	(1.84)	26	0	(0.00)	0
Decreased Appetite	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4	0	(0.00)	0
Diabetes Mellitus	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Hypercholesterolaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4	0	(0.00)	0
Hyperglycaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Hyperlipidaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	12	(0.88)	12	0	(0.00)	0
Hypoglycaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4	0	(0.00)	0
Musculoskeletal and Connective Tissue Disorders	3	(0.22)	3	1	(0.07)	1	0	(0.00)	0	8	(0.59)	11	77	(5.67)	103	0	(0.00)	0
Ankylosing Spondylitis	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Arthralgia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4	23	(1.69)	27	0	(0.00)	0
Atlantoaxial Instability	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Back Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	13	(0.96)	14	0	(0.00)	0
Bursal Fluid Accumulation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Fibromyalgia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Flank Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Foot Deformity	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Intervertebral Disc Disorder	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Intervertebral Disc Protrusion	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Joint Swelling	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	6	(0.44)	6	0	(0.00)	0
Lumbar Spinal Stenosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4	0	(0.00)	0
Musculoskeletal Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	5	(0.37)	5	0	(0.00)	0
Musculoskeletal Stiffness	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Myalgia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	8	(0.59)	9	0	(0.00)	0
Osteoarthritis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Osteoporosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Pain in Extremity	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	8	(0.59)	9	0	(0.00)	0
Polyarthritis	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Rheumatoid Arthritis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	2	(0.15)	2	0	(0.00)	0
Rotator Cuff Syndrome	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Spinal Column Stenosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Synovial Cyst	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Synovitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Tendonitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Tenosynovitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps)	4	(0.29)	4	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Colon Adenoma	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Gastric Cancer	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Hypergammaglobulinaemia Benign Monoclonal	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Invasive Ductal Breast Carcinoma	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Nervous System Disorders	0	(0.00)	0	4	(0.29)	4	0	(0.00)	0	1	(0.07)	1	54	(3.98)	65	0	(0.00)	0
Anosmia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Carotid Arteriosclerosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Cerebellar Ataxia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Cerebellar Infarction	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Cerebral Infarction	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Cervical Radiculopathy	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Diabetic Neuropathy	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Dizziness	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	16	(1.18)	16	0	(0.00)	0
Headache	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	11	(0.81)	12	0	(0.00)	0
Hypoaesthesia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	8	(0.59)	8	0	(0.00)	0
Migraine	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Neuropathy Peripheral	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Paraesthesia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	10	(0.74)	11	0	(0.00)	0
Sciatica	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Subarachnoid Haemorrhage	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Syncope	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Tension Headache	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Tremor	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Psychiatric Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	7	(0.52)	8	0	(0.00)	0
Depression	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Insomnia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(0.37)	5	0	(0.00)	0
Tic	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Renal and Urinary Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(0.37)	5	0	(0.00)	0
Calculus Ureteric	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Dysuria	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Pollakiuria	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Proteinuria	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Reproductive System and Breast Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	7	(0.52)	7	0	(0.00)	0
Breast Mass	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Erectile Dysfunction	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Menorrhagia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Pelvic Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Varicocele	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Respiratory, Thoracic and Mediastinal Disorders	4	(0.29)	5	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0	38	(2.80)	43	0	(0.00)	0
Acute Respiratory Distress Syndrome	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Atelectasis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Cough	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	17	(1.25)	18	0	(0.00)	0
Dysphonia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Dyspnoea	1	(0.07)	1	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Dyspnoea Exertional	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Epistaxis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Interstitial Lung Disease	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Laryngeal Oedema	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Nasal Septum Deviation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Oropharyngeal Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Pleural Effusion	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Productive Cough	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	7	(0.52)	7	0	(0.00)	0
Respiratory Distress	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Rhinitis Allergic	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Rhinorrhoea	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Sputum Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Vocal Cord Polyp	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Skin and Subcutaneous Tissue Disorders	14	(1.03)	16	10	(0.74)	14	1	(0.07)	1	0	(0.00)	0	70	(5.16)	92	0	(0.00)	0
Acne	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Alopecia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4	0	(0.00)	0
Androgenetic Alopecia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Decubitus Ulcer	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Dermatitis Acneiform	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Dermatitis Allergic	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Dermatitis Contact	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4	0	(0.00)	0
Diabetic Foot	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Eczema	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Erythema	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Erythema Nodosum	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Hyperhidrosis	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Hyperkeratosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Hypersensitivity Vasculitis	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Pain of Skin	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Papule	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Photosensitivity Reaction	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Pruritus	4	(0.29)	4	4	(0.29)	5	0	(0.00)	0	0	(0.00)	0	21	(1.55)	27	0	(0.00)	0
Pruritus Generalised	1	(0.07)	1	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Pseudofolliculitis Barbae	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Psoriasis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Rash	4	(0.29)	4	3	(0.22)	3	0	(0.00)	0	0	(0.00)	0	12	(0.88)	13	0	(0.00)	0
Rash Generalised	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Seborrhoeic Dermatitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Skin Exfoliation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Skin Lesion	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Swelling Face	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	6	(0.44)	6	0	(0.00)	0
Systemic Lupus Erythematosus Rash	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	2	0	(0.00)	0
Urticaria	3	(0.22)	3	3	(0.22)	4	0	(0.00)	0	0	(0.00)	0	9	(0.66)	9	0	(0.00)	0
Xeroderma	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Social Circumstances	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Andropause	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Surgical and Medical Procedures	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	8	(0.59)	8	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Arthrotomy	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Ileostomy	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	1	(0.07)	1	0	(0.00)	0
Ileostomy Closure	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Intervertebral Disc Operation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Joint Arthroplasty	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Removal of Internal Fixation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Spinal Decompression	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Tooth Extraction	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Vascular Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	15	(1.11)	16	0	(0.00)	0
Arteriosclerosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Deep Vein Thrombosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Flushing	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	6	(0.44)	7	0	(0.00)	0
Hypertension	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3	0	(0.00)	0
Hypotension	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Orthostatic Hypotension	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Renovascular Hypertension	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0

Table 152 Incidence status for classification of action taken to surveillance drug (AS (N=531))

System Organ Class Preferred Term	Permanently Stopped administration	Temporarily Stopped administration	Decreased dosage	Increased dosage	Maintained dosage	Unknown

	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Total	13	(2.45)	14	9	(1.69)	12	2	(0.38)	2	2	(0.38)	4	162	(30.51)	257	0	(0.00)	0
Blood and Lymphatic System Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
Anaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Iron Deficiency Anaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Ear and Labyrinth Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Vertigo	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Eye Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(0.94)	5	0	(0.00)	0
Dry Eye	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
Uveitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.56)	3	0	(0.00)	0
Gastrointestinal Disorders	0	(0.00)	0	1	(0.19)	1	1	(0.19)	1	0	(0.00)	0	24	(4.52)	30	0	(0.00)	0
Abdominal Discomfort	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Abdominal Pain Upper	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	6	(1.13)	6	0	(0.00)	0
Constipation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.75)	4	0	(0.00)	0
Diarrhoea	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	7	(1.32)	7	0	(0.00)	0
Dry Mouth	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Dyspepsia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
Epigastric Discomfort	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Gastric Ulcer Haemorrhage	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Gastritis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Gastroduodenitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Gastrointestinal Disorder	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Large Intestine Polyp	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Mouth Haemorrhage	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Mouth Ulceration	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Nausea	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
General Disorders and Administration Site Conditions	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	11	(2.07)	11	0	(0.00)	0
Chest Discomfort	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Chest Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Fatigue	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.75)	4	0	(0.00)	0
Influenza Like Illness	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Pyrexia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
Swelling	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Hepatobiliary Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
Drug-Induced Liver Injury	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Hepatitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Immune System Disorders	3	(0.56)	3	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Anaphylactic Reaction	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Anaphylactic Shock	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Hypersensitivity	1	(0.19)	1	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Infections and Infestations	3	(0.56)	3	3	(0.56)	3	0	(0.00)	0	0	(0.00)	0	32	(6.03)	40	0	(0.00)	0
Body Tinea	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Bronchiolitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Bronchitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.56)	3	0	(0.00)	0
Cellulitis	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Furuncle	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Gastritis Bacterial	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Hepatitis B	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Herpes Virus Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Herpes Zoster	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.56)	3	0	(0.00)	0
Hordeolum	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Nasopharyngitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	11	(2.07)	12	0	(0.00)	0
Onychomycosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.56)	3	0	(0.00)	0
Pharyngitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Pharyngotonsillitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Pneumonia	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Postoperative Wound Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Pulmonary Tuberculosis	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Sinusitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Tinea Pedis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Tonsillitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Tuberculosis	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Upper Respiratory Tract Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.75)	7	0	(0.00)	0
Injury, Poisoning and Procedural Complications	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(0.94)	9	0	(0.00)	0
Auricular Haematoma	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	3	0	(0.00)	0
Compression Fracture	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Facial Bones Fracture	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Fracture	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Hand Fracture	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Joint Dislocation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Road Traffic Accident	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Investigations	2	(0.38)	2	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	24	(4.52)	34	0	(0.00)	0
Alanine Aminotransferase Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	15	(2.82)	15	0	(0.00)	0
Aspartate Aminotransferase Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	10	(1.88)	10	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Blood Creatine Phosphokinase Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Hepatic Enzyme Increased	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
Liver Function Test Abnormal	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.56)	3	0	(0.00)	0
Transaminases Increased	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
Weight Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Metabolism and Nutrition Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	8	(1.51)	8	0	(0.00)	0
Decreased Appetite	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Diabetes Mellitus	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Hypercholesterolaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.56)	3	0	(0.00)	0
Hyperlipidaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.56)	3	0	(0.00)	0
Musculoskeletal and Connective Tissue Disorders	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	2	(0.38)	4	31	(5.84)	44	0	(0.00)	0
Ankylosing Spondylitis	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
Arthralgia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	10	(1.88)	13	0	(0.00)	0
Back Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	9	(1.69)	9	0	(0.00)	0
Fibromyalgia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Foot Deformity	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Joint Swelling	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	2	(0.38)	2	0	(0.00)	0
Musculoskeletal Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Musculoskeletal Stiffness	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.56)	3	0	(0.00)	0
Myalgia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
Pain in Extremity	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	8	(1.51)	9	0	(0.00)	0
Spinal Column Stenosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Tendonitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Nervous System Disorders	0	(0.00)	0	3	(0.56)	3	0	(0.00)	0	0	(0.00)	0	14	(2.64)	15	0	(0.00)	0
Cerebellar Infarction	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Cervical Radiculopathy	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Dizziness	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
Headache	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	3	(0.56)	3	0	(0.00)	0
Hypoaesthesia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
Migraine	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
Neuropathy Peripheral	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Paraesthesia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
Sciatica	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Syncope	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Psychiatric Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
Depression	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Insomnia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Renal and Urinary Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.75)	4	0	(0.00)	0
Calculus Ureteric	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Dysuria	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Pollakiuria	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Proteinuria	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Reproductive System and Breast Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.75)	4	0	(0.00)	0
Erectile Dysfunction	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Pelvic Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
Varicocele	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Respiratory, Thoracic and Mediastinal Disorders	2	(0.38)	2	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	14	(2.64)	16	0	(0.00)	0
Cough	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	6	(1.13)	6	0	(0.00)	0
Dyspnoea	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Laryngeal Oedema	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Nasal Septum Deviation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Oropharyngeal Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Productive Cough	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(0.94)	5	0	(0.00)	0
Rhinitis Allergic	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Rhinorrhoea	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Sputum Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Skin and Subcutaneous Tissue Disorders	3	(0.56)	3	3	(0.56)	4	1	(0.19)	1	0	(0.00)	0	21	(3.95)	23	0	(0.00)	0
Acne	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Alopecia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Androgenetic Alopecia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Decubitus Ulcer	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Eczema	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Hyperhidrosis	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Hyperkeratosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Hypersensitivity Vasculitis	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Papule	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Pruritus	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	6	(1.13)	6	0	(0.00)	0
Pruritus Generalised	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Psoriasis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0
Rash	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0	0	(0.00)	0	4	(0.75)	4	0	(0.00)	0
Seborrhoeic Dermatitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Swelling Face	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Urticaria	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Xeroderma	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Social Circumstances	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Andropause	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Surgical and Medical Procedures	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Arthrotomy	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Vascular Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.75)	4	0	(0.00)	0
Hypertension	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.56)	3	0	(0.00)	0
Orthostatic Hypotension	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0

Table 153 Incidence status for classification of action taken to surveillance drug (RA/PA/PS (N=409))

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Total	29	(7.09)	39	14	(3.42)	18	0	(0.00)	0	5	(1.22)	7	176	(43.03)	406	1	(0.24)	1
Blood and Lymphatic System Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(1.22)	5	0	(0.00)	0
Iron Deficiency Anaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Lymphadenopathy	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Pancytopenia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Cardiac Disorders	3	(0.73)	3	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Atrial Fibrillation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Cardiac Arrest	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Palpitations	2	(0.49)	2	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3	0	(0.00)	0
Ear and Labyrinth Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3	0	(0.00)	0
Tinnitus	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3	0	(0.00)	0
Eye Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.98)	5	0	(0.00)	0
Blepharitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Dry Eye	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Glaucoma	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Visual Acuity Reduced	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Gastrointestinal Disorders	2	(0.49)	2	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	51	(12.47)	68	0	(0.00)	0
Abdominal Discomfort	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Abdominal Distension	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Abdominal Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4	0	(0.00)	0
Abdominal Pain Upper	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	6	(1.47)	7	0	(0.00)	0
Aphthous Ulcer	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Constipation	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	3	0	(0.00)	0
Diarrhoea	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	7	(1.71)	7	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Dry Mouth	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Dyspepsia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	9	(2.20)	10	0	(0.00)	0
Dysphagia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Gastric Mucosal Lesion	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Gastric Ulcer	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Gastritis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3	0	(0.00)	0
Gastrointestinal Disorder	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Gastrooesophageal Reflux Disease	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Mouth Ulceration	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Nausea	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	11	(2.69)	11	0	(0.00)	0
Proctalgia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Regurgitation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	3	0	(0.00)	0
Stomatitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Vomiting	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4	0	(0.00)	0
General Disorders and Administration Site Conditions	3	(0.73)	3	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	17	(4.16)	21	0	(0.00)	0
Asthenia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Chest Discomfort	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Chest Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Chills	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.98)	6	0	(0.00)	0
Drug Effect Delayed	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Face Oedema	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Fatigue	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Generalised Oedema	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Oedema	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3	0	(0.00)	0
Oedema Peripheral	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3	0	(0.00)	0
Pyrexia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3	0	(0.00)	0
Hepatobiliary Disorders	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3	0	(0.00)	0
Cholelithiasis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Hepatitis	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Liver Disorder	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Immune System Disorders	4	(0.98)	4	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Anaphylactic Reaction	2	(0.49)	2	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Hypersensitivity	2	(0.49)	2	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Infections and Infestations	8	(1.96)	8	3	(0.73)	3	0	(0.00)	0	0	(0.00)	0	56	(13.69)	60	1	(0.24)	1
Abscess	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Arthritis Bacterial	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Body Tinea	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Bronchitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	9	(2.20)	9	0	(0.00)	0
Candida Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	2	0	(0.00)	0
Cystitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Disseminated Tuberculosis	2	(0.49)	2	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Folliculitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Herpes Simplex	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Herpes Zoster	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3	0	(0.00)	0
Influenza	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Nasopharyngitis	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	9	(2.20)	9	0	(0.00)	0
Otitis Externa	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	2	0	(0.00)	0
Pneumonia	1	(0.24)	1	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4	0	(0.00)	0
Pneumonia Bacterial	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Pyelonephritis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Pyelonephritis Acute	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4	0	(0.00)	0
Rhinitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Sepsis	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Sinusitis	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Tinea Pedis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Tuberculosis Gastrointestinal	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Upper Respiratory Tract Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	12	(2.93)	12	0	(0.00)	0
Ureteritis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Urinary Tract Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	1	(0.24)	1
Vaginal Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Injury, Poisoning and Procedural Complications	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	7	(1.71)	9	0	(0.00)	0
Ankle Fracture	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Contusion	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Fall	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Foot Fracture	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Joint Dislocation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Laceration	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Perineal Injury	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Road Traffic Accident	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Investigations	3	(0.73)	3	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	18	(4.40)	20	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Alanine Aminotransferase Increased	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4	0	(0.00)	0
Aspartate Aminotransferase Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Hepatic Enzyme Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Influenza B Virus Test Positive	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Liver Function Test Abnormal	2	(0.49)	2	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	3	0	(0.00)	0
Serum Ferritin Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Urine Analysis Abnormal	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Weight Decreased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Weight Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4	0	(0.00)	0
Metabolism and Nutrition Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	16	(3.91)	17	0	(0.00)	0
Decreased Appetite	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Hypercholesterolaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Hyperglycaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Hyperlipidaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	9	(2.20)	9	0	(0.00)	0
Hypoglycaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4	0	(0.00)	0
Musculoskeletal and Connective Tissue Disorders	1	(0.24)	1	1	(0.24)	1	0	(0.00)	0	5	(1.22)	6	42	(10.27)	55	0	(0.00)	0
Arthralgia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3	12	(2.93)	13	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Atlantoaxial Instability	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Back Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.98)	5	0	(0.00)	0
Bursal Fluid Accumulation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Fibromyalgia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Foot Deformity	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Intervertebral Disc Disorder	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Intervertebral Disc Protrusion	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4	0	(0.00)	0
Joint Swelling	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4	0	(0.00)	0
Lumbar Spinal Stenosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4	0	(0.00)	0
Musculoskeletal Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	3	(0.73)	3	0	(0.00)	0
Myalgia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(1.22)	6	0	(0.00)	0
Osteoarthritis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Osteoporosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3	0	(0.00)	0
Polyarthritis	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Rheumatoid Arthritis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	2	(0.49)	2	0	(0.00)	0
Rotator Cuff Syndrome	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Spinal Column Stenosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Synovial Cyst	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Synovitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Tenosynovitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps)	4	(0.98)	4	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Colon Adenoma	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Gastric Cancer	2	(0.49)	2	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Hypergammaglobulinaemia Benign Monoclonal	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Invasive Ductal Breast Carcinoma	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Nervous System Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	36	(8.80)	46	0	(0.00)	0
Anosmia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Carotid Arteriosclerosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Cerebellar Ataxia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Cerebral Infarction	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Diabetic Neuropathy	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Dizziness	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	11	(2.69)	11	0	(0.00)	0
Headache	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	8	(1.96)	9	0	(0.00)	0
Hypoaesthesia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	5	(1.22)	5	0	(0.00)	0
Migraine	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Neuropathy Peripheral	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Paraesthesia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	8	(1.96)	9	0	(0.00)	0
Subarachnoid Haemorrhage	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Tension Headache	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Tremor	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3	0	(0.00)	0
Psychiatric Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4	0	(0.00)	0
Insomnia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3	0	(0.00)	0
Tic	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Reproductive System and Breast Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3	0	(0.00)	0
Breast Mass	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Erectile Dysfunction	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Menorrhagia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Respiratory, Thoracic and Mediastinal Disorders	1	(0.24)	2	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	18	(4.40)	20	0	(0.00)	0
Acute Respiratory Distress Syndrome	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Atelectasis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Cough	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	9	(2.20)	10	0	(0.00)	0
Dysphonia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Dyspnoea Exertional	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Interstitial Lung Disease	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Oropharyngeal Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Pleural Effusion	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Productive Cough	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Rhinitis Allergic	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Vocal Cord Polyp	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Skin and Subcutaneous Tissue Disorders	7	(1.71)	9	6	(1.47)	9	0	(0.00)	0	0	(0.00)	0	27	(6.60)	47	0	(0.00)	0
Alopecia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3	0	(0.00)	0
Dermatitis Acneiform	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Dermatitis Allergic	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Dermatitis Contact	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4	0	(0.00)	0
Diabetic Foot	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Erythema	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Hyperhidrosis	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Pruritus	2	(0.49)	2	2	(0.49)	3	0	(0.00)	0	0	(0.00)	0	11	(2.69)	17	0	(0.00)	0
Pruritus Generalised	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Pseudofolliculitis Barbae	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Rash	4	(0.98)	4	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	3	(0.73)	4	0	(0.00)	0
Rash Generalised	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Swelling Face	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3	0	(0.00)	0
Systemic Lupus Erythematosus Rash	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	2	0	(0.00)	0
Urticaria	1	(0.24)	1	3	(0.73)	4	0	(0.00)	0	0	(0.00)	0	5	(1.22)	5	0	(0.00)	0
Surgical and Medical Procedures	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(1.22)	5	0	(0.00)	0
Intervertebral Disc Operation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Joint Arthroplasty	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Removal of Internal Fixation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Spinal Decompression	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Tooth Extraction	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Vascular Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	9	(2.20)	10	0	(0.00)	0
Arteriosclerosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Flushing	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	6	(1.47)	7	0	(0.00)	0
Hypotension	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0

Table 154 Incidence status for classification of action taken to surveillance drug (IBD (N=417))

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Total	26	(6.24)	28	9	(2.16)	10	2	(0.48)	3	9	(2.16)	10	114	(27.34)	193	1	(0.24)	2
Blood and Lymphatic System Disorders	0	(0.00)	0	1	(0.07)	1	1	(0.24)	1	0	(0.00)	0	8	(1.92)	9	0	(0.00)	0
Anaemia	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0
Iron Deficiency Anaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Leukopenia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(1.20)	5	0	(0.00)	0
Lymphadenitis	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Neutropenia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Cardiac Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Palpitations	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Ear and Labyrinth Disorders	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Otorrhoea	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Eye Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Vision Blurred	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Gastrointestinal Disorders	7	(1.68)	7	2	(0.48)	2	0	(0.00)	0	8	(1.92)	8	46	(11.03)	72	0	(0.00)	0
Abdominal Discomfort	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Abdominal Pain	2	(0.48)	2	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	16	(3.84)	24	0	(0.00)	0
Abdominal Pain Lower	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Abdominal Pain Upper	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Anal Fistula	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Aphthous Ulcer	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Colitis Ulcerative	2	(0.48)	2	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0
Constipation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.72)	3	0	(0.00)	0
Crohn's Disease	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	3	(0.72)	3	0	(0.00)	0
Diarrhoea	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(1.20)	5	0	(0.00)	0
Dyspepsia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	2	(0.48)	3	0	(0.00)	0
Enterocutaneous Fistula	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Epigastric Discomfort	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0
Frequent Bowel Movements	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Gastritis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Gastrointestinal Inflammation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Haematochezia	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	4	(0.96)	4	2	(0.48)	2	0	(0.00)	0
Ileus	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0
Intestinal Obstruction	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Melaena	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Mouth Ulceration	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Nausea	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(1.20)	7	0	(0.00)	0
Protein-Losing Gastroenteropathy	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Small Intestinal Haemorrhage	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Vomiting	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(1.20)	7	0	(0.00)	0
General Disorders and Administration Site Conditions	4	(0.96)	4	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	14	(3.36)	15	1	(0.24)	1
Application Site Haemorrhage	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Chest Pain	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Disease Progression	2	(0.48)	2	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Drug Ineffective	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Immediate Post-Injection Reaction	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Large Intestinal Perforation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Non-Cardiac Chest Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Oedema	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0
Pyrexia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	7	(1.68)	8	1	(0.24)	1
Hepatobiliary Disorders	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0
Hepatic Function Abnormal	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Hepatitis	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Hyperbilirubinaemia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Immune System Disorders	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Anaphylactic Reaction	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Infections and Infestations	4	(0.96)	4	3	(0.72)	3	1	(0.24)	1	0	(0.00)	0	31	(7.43)	36	0	(0.00)	0
Abdominal Abscess	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Anal Abscess	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.72)	3	0	(0.00)	0
Atypical Pneumonia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Clostridium Difficile Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Cystitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Cytomegalovirus Colitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Cytomegalovirus Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0
Disseminated Tuberculosis	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Folliculitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0
Herpes Virus Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Herpes Zoster	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Lung Abscess	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Nasopharyngitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	6	(1.44)	6	0	(0.00)	0
Oral Candidiasis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Pneumocystis Jirovecii Pneumonia	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Pneumonia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0
Pseudomembranous Colitis	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Rhinitis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Sepsis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Sialoadenitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Spleen Tuberculosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Tuberculosis	2	(0.48)	2	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Upper Respiratory Tract Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	8	(1.92)	8	0	(0.00)	0
Urinary Tract Infection	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0
Injury, Poisoning and Procedural Complications	3	(0.72)	3	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Foot Fracture	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Infusion Related Reaction	3	(0.72)	3	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Investigations	2	(0.48)	2	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	9	(2.16)	11	1	(0.24)	1
Alanine Aminotransferase Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	2	0	(0.00)	0
Aspartate Aminotransferase Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Blood Alkaline Phosphatase Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
C-Reactive Protein Increased	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Eosinophil Count Increased	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Liver Function Test Abnormal	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Occult Blood	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
White Blood Cell Count Decreased	1	(0.24)	1	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	3	(0.72)	3	1	(0.24)	1
Metabolism and Nutrition Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Decreased Appetite	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Musculoskeletal and Connective Tissue Disorders	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	4	(0.96)	4	0	(0.00)	0
Arthralgia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Flank Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Musculoskeletal Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0
Musculoskeletal Stiffness	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Myalgia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Nervous System Disorders	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	4	(0.96)	4	0	(0.00)	0
Dizziness	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	3	(0.72)	3	0	(0.00)	0
Hypoaesthesia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Tremor	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Psychiatric Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	2	0	(0.00)	0
Depression	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Insomnia	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Renal and Urinary Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Calculus Ureteric	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Respiratory, Thoracic and Mediastinal Disorders	1	(0.24)	1	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	6	(1.44)	7	0	(0.00)	0
Cough	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0
Dyspnoea	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	3	(0.72)	3	0	(0.00)	0
Epistaxis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Oropharyngeal Pain	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Rhinitis Distress	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Skin and Subcutaneous Tissue Disorders	4	(0.96)	4	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	22	(5.28)	22	0	(0.00)	0
Acne	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0
Dermatitis Acneiform	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0
Erythema Nodosum	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Pain of Skin	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Photosensitivity Reaction	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Pruritus	2	(0.48)	2	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	4	(0.96)	4	0	(0.00)	0
Rash	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	5	(1.20)	5	0	(0.00)	0
Seborrhoeic Dermatitis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0
Skin Exfoliation	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Skin Lesion	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Swelling Face	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0

System Organ Class Preferred Term	Permanently Stopped administration			Temporarily Stopped administration			Decreased dosage			Increased dosage			Maintained dosage			Unknown		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Urticaria	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0
Surgical and Medical Procedures	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	2	(0.48)	2	0	(0.00)	0
Illeostomy	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	1	(0.24)	1	0	(0.00)	0
Ileostomy Closure	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Vascular Disorders	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2	0	(0.00)	0
Deep Vein Thrombosis	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Renovascular Hypertension	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0

G. Classtification of Treatment

Treatments provided in response to adverse events were categorized in the 3 categories, “No treatment”, “Non-medicinal treatment” and “Treatment with other medication” (multiple choice possible), 558 events of “Treatment with other medication” in 26.09% (354/1357 subjects), 404 events of “No treatment” in 18.94% (257/1357 subjects), and 66 events of “Non-medicinal treatment” in 3.98% (54/1357 subjects) (Table 155).

Adverse event classification of Adverse Event by Treatment in each indication is presented in Table 156, Table 157 and Table 158.

Table 155 Incidence status for classification of Adverse Event by treatment (total (N=1357))

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Total	257	(18.94)	404	54	(3.98)	66	354	(26.09)	558
Blood and Lymphatic System Disorders	7	(0.52)	7	3	(0.22)	3	9	(0.66)	9
Anaemia*	0	(0.00)	0	2	(0.15)	2	3	(0.22)	3
Iron Deficiency Anaemia	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4
Leukopenia	4	(0.29)	4	1	(0.07)	1	0	(0.00)	0
Lymphadenitis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Lymphadenopathy	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0
Neutropenia	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Pancytopenia	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Cardiac Disorders	6	(0.44)	6	0	(0.00)	0	2	(0.15)	2
Atrial Fibrillation	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Cardiac Arrest	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Palpitations	5	(0.37)	5	0	(0.00)	0	1	(0.07)	1
Ear and Labyrinth Disorders	3	(0.22)	3	0	(0.00)	0	2	(0.15)	2
Otorrhoea	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Tinnitus	2	(0.15)	2	0	(0.00)	0	1	(0.07)	1
Vertigo	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Eye Disorders	6	(0.44)	6	0	(0.00)	0	5	(0.37)	5

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Blepharitis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Dry Eye	2	(0.15)	2	0	(0.00)	0	2	(0.15)	2
Glaucoma	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Uveitis	1	(0.07)	1	0	(0.00)	0	2	(0.15)	2
Vision Blurred	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Visual Acuity Reduced	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Gastrointestinal Disorders	61	(4.50)	75	8	(0.59)	9	84	(6.19)	112
Abdominal Discomfort	2	(0.15)	2	0	(0.00)	0	3	(0.22)	3
Abdominal Distension	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Abdominal Pain	12	(0.88)	14	1	(0.07)	2	12	(0.88)	16
Abdominal Pain Lower	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Abdominal Pain Upper	3	(0.22)	3	0	(0.00)	0	10	(0.74)	11
Anal Fistula*	0	(0.00)	0	1	(0.07)	1	1	(0.07)	1
Aphthous Ulcer	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2
Colitis Ulcerative	0	(0.00)	0	1	(0.07)	1	3	(0.22)	3
Constipation	3	(0.22)	3	0	(0.00)	0	7	(0.52)	8
Crohn's Disease	0	(0.00)	0	1	(0.07)	1	4	(0.29)	4
Diarrhoea	13	(0.96)	13	0	(0.00)	0	6	(0.44)	6
Dry Mouth	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Dyspepsia	5	(0.37)	5	0	(0.00)	0	9	(0.66)	11
Dysphagia	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Enterocutaneous Fistula	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Epigastric Discomfort	3	(0.22)	3	0	(0.00)	0	0	(0.00)	0
Frequent Bowel Movements	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Gastric Mucosal Lesion	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Gastric Ulcer	1	(0.07)	1	0	(0.00)	0	1	(0.07)	1
Gastric Ulcer Haemorrhage*	0	(0.00)	0	1	(0.07)	1	1	(0.07)	1
Gastritis	2	(0.15)	2	0	(0.00)	0	3	(0.22)	3
Gastroduodenitis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Gastrointestinal Disorder	2	(0.15)	2	0	(0.00)	0	2	(0.15)	2
Gastrointestinal Inflammation	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Gastrooesophageal Reflux Disease	1	(0.07)	1	0	(0.00)	0	1	(0.07)	1
Haematochezia	3	(0.22)	3	0	(0.00)	0	4	(0.29)	4
Ileus	1	(0.07)	1	1	(0.07)	1	0	(0.00)	0
Intestinal Obstruction*	0	(0.00)	0	1	(0.07)	1	1	(0.07)	1
Large Intestine Polyp	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Melaena	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Mouth Haemorrhage	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Mouth Ulceration	2	(0.15)	2	0	(0.00)	0	1	(0.07)	1
Nausea	8	(0.59)	8	0	(0.00)	0	11	(0.81)	13
Proctalgia	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Protein-Losing Gastroenteropathy	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Regurgitation	1	(0.07)	1	0	(0.00)	0	1	(0.07)	2
Small Intestinal Haemorrhage*	0	(0.00)	0	1	(0.07)	1	1	(0.07)	1
Stomatitis	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0
Vomiting	4	(0.29)	4	0	(0.00)	0	5	(0.37)	7
General Disorders and Administration Site Conditions	28	(2.06)	28	1	(0.07)	1	22	(1.62)	26
Application Site Haemorrhage	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Asthenia	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Chest Discomfort	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0
Chest Pain	4	(0.29)	4	0	(0.00)	0	0	(0.00)	0
Chills	1	(0.07)	1	0	(0.00)	0	3	(0.22)	5
Disease Progression	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2
Drug Effect Delayed	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Drug Ineffective	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Face Oedema	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Fatigue	6	(0.44)	6	0	(0.00)	0	0	(0.00)	0

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Generalised Oedema	1	(0.07)	1	0	(0.00)	0	1	(0.07)	1
Immediate Post-Injection Reaction	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Influenza Like Illness	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Large Intestinal Perforation	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Non-Cardiac Chest Pain	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Oedema	3	(0.22)	3	0	(0.00)	0	2	(0.15)	2
Oedema Peripheral	2	(0.15)	2	0	(0.00)	0	2	(0.15)	2
Pain	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Pyrexia	3	(0.22)	3	0	(0.00)	0	9	(0.66)	10
Swelling	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Hepatobiliary Disorders	2	(0.15)	2	0	(0.00)	0	7	(0.52)	7
Cholelithiasis	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Drug-Induced Liver Injury	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Hepatic Function Abnormal	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Hepatitis	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4
Hyperbilirubinaemia	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Liver Disorder	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Immune System Disorders	1	(0.07)	1	0	(0.00)	0	9	(0.66)	9
Anaphylactic Reaction	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Anaphylactic Shock	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Hypersensitivity	1	(0.07)	1	0	(0.00)	0	4	(0.29)	4
Infections and Infestations	25	(1.84)	26	7	(0.52)	7	114	(8.40)	132
Abdominal Abscess	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Abscess	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Anal Abscess	0	(0.00)	0	2	(0.15)	2	1	(0.07)	1
Arthritis Bacterial*	0	(0.00)	0	1	(0.07)	1	1	(0.07)	1
Atypical Pneumonia	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Body Tinea	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2
Bronchiolitis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Bronchitis	0	(0.00)	0	0	(0.00)	0	12	(0.88)	12
Candida Infection	0	(0.00)	0	0	(0.00)	0	1	(0.07)	2
Cellulitis	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2
Clostridium Difficile Infection	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Cystitis	1	(0.07)	1	0	(0.00)	0	2	(0.15)	2
Cytomegalovirus Colitis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Cytomegalovirus Infection	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2
Disseminated Tuberculosis	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3
Folliculitis	1	(0.07)	1	0	(0.00)	0	3	(0.22)	3

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Furuncle	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Gastritis Bacterial	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Hepatitis B	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Herpes Simplex	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3
Herpes Virus Infection	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2
Herpes Zoster*	0	(0.00)	0	1	(0.07)	1	7	(0.52)	7
Hordeolum	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Influenza	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Lung Abscess*	0	(0.00)	0	1	(0.07)	1	1	(0.07)	1
Nasopharyngitis	10	(0.74)	11	0	(0.00)	0	17	(1.25)	17
Onychomycosis	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3
Oral Candidiasis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Otitis Externa	1	(0.07)	1	0	(0.00)	0	1	(0.07)	1
Pharyngitis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Pharyngotonsillitis	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Pneumonocystis Jirovecii Pneumonia	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Pneumonia	0	(0.00)	0	0	(0.00)	0	8	(0.59)	9
Pneumonia Bacterial	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Postoperative Wound Infection	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Pseudomembranous Colitis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Pulmonary Tuberculosis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Pyelonephritis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Pyelonephritis Acute	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4
Rhinitis	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2
Sepsis	1	(0.07)	1	0	(0.00)	0	1	(0.07)	1
Sialoadenitis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Sinusitis	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2
Spleen Tuberculosis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Tinea Pedis	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2
Tonsillitis	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Tuberculosis	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4
Tuberculosis Gastrointestinal	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Upper Respiratory Tract Infection	7	(0.52)	7	0	(0.00)	0	17	(1.25)	20
Ureteritis	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Urinary Tract Infection	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4
Vaginal Infection	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Injury, Poisoning and Procedural Complications	4	(0.29)	5	8	(0.59)	13	7	(0.52)	8
Ankle Fracture	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Auricular Haematoma	0	(0.00)	0	1	(0.07)	3	0	(0.00)	0
Compression Fracture	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Contusion	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Facial Bones Fracture	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Fall	1	(0.07)	1	1	(0.07)	1	0	(0.00)	0
Foot Fracture*	0	(0.00)	0	2	(0.15)	2	1	(0.07)	1
Fracture*	0	(0.00)	0	1	(0.07)	1	1	(0.07)	1
Hand Fracture	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Infusion Related Reaction	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3
Joint Dislocation*	0	(0.00)	0	2	(0.15)	2	1	(0.07)	1
Laceration	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Perineal Injury	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Road Traffic Accident	1	(0.07)	1	1	(0.07)	1	0	(0.00)	0
Investigations	43	(3.17)	53	0	(0.00)	0	17	(1.25)	20
Alanine Aminotransferase Increased	17	(1.25)	18	0	(0.00)	0	4	(0.29)	4
Aspartate Aminotransferase Increased	11	(0.81)	11	0	(0.00)	0	2	(0.15)	2
Blood Alkaline Phosphatase Increased	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Blood Creatine Phosphokinase Increased	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
C-Reactive Protein Increased	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0
Eosinophil Count Increased	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Hepatic Enzyme Increased	2	(0.15)	2	0	(0.00)	0	3	(0.22)	3
Influenza B Virus Test Positive	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Liver Function Test Abnormal	3	(0.22)	3	0	(0.00)	0	5	(0.37)	6
Occult Blood	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Serum Ferritin Increased	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Transaminases Increased	2	(0.15)	2	0	(0.00)	0	1	(0.07)	1
Urine Analysis Abnormal	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Weight Decreased	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0
Weight Increased	5	(0.37)	5	0	(0.00)	0	0	(0.00)	0
White Blood Cell Count Decreased	5	(0.37)	5	0	(0.00)	0	0	(0.00)	0
Metabolism and Nutrition Disorders	7	(0.52)	8	1	(0.07)	1	17	(1.25)	17
Decreased Appetite	4	(0.29)	4	0	(0.00)	0	0	(0.00)	0
Diabetes Mellitus	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Hypercholesterolaemia	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4
Hyperglycaemia	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Hyperlipidaemia	0	(0.00)	0	0	(0.00)	0	12	(0.88)	12
Hypoglycaemia	2	(0.15)	2	1	(0.07)	1	1	(0.07)	1

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Musculoskeletal and Connective Tissue Disorders	40	(2.95)	53	14	(1.03)	16	50	(3.68)	58
Ankylosing Spondylitis*	0	(0.00)	0	1	(0.07)	1	3	(0.22)	3
Arthralgia*	11	(0.81)	12	1	(0.07)	1	16	(1.18)	19
Atlantoaxial Instability	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Back Pain*	8	(0.59)	8	3	(0.22)	3	4	(0.29)	4
Bursal Fluid Accumulation	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Fibromyalgia*	1	(0.07)	1	1	(0.07)	1	2	(0.15)	2
Flank Pain	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Foot Deformity	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0
Intervertebral Disc Disorder	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Intervertebral Disc Protrusion*	0	(0.00)	0	3	(0.22)	3	3	(0.22)	3
Joint Swelling	4	(0.29)	4	0	(0.00)	0	3	(0.22)	3
Lumbar Spinal Stenosis	2	(0.15)	2	0	(0.00)	0	2	(0.15)	2
Musculoskeletal Pain	3	(0.22)	3	1	(0.07)	1	3	(0.22)	3
Musculoskeletal Stiffness	4	(0.29)	4	0	(0.00)	0	0	(0.00)	0
Myalgia	6	(0.44)	7	0	(0.00)	0	2	(0.15)	2
Osteoarthritis	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Osteoporosis	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3
Pain in Extremity	7	(0.52)	7	0	(0.00)	0	3	(0.22)	3

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Polyarthritis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Rheumatoid Arthritis	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4
Rotator Cuff Syndrome	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Spinal Column Stenosis*	0	(0.00)	0	2	(0.15)	2	1	(0.07)	1
Synovial Cyst	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Synovitis*	0	(0.00)	0	1	(0.07)	1	1	(0.07)	1
Tendonitis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Tenosynovitis*	0	(0.00)	0	1	(0.07)	1	1	(0.07)	1
Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps)	1	(0.07)	1	4	(0.29)	4	0	(0.00)	0
Colon Adenoma	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Gastric Cancer	0	(0.00)	0	2	(0.15)	2	0	(0.00)	0
Hypergammaglobulinaemia Benign Monoclonal	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Invasive Ductal Breast Carcinoma	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Nervous System Disorders	39	(2.87)	46	1	(0.07)	1	19	(1.40)	23
Anosmia	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Carotid Arteriosclerosis	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Cerebellar Ataxia	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Cerebellar Infarction	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Cerebral Infarction	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Cervical Radiculopathy	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Diabetic Neuropathy	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Dizziness	14	(1.03)	14	0	(0.00)	0	2	(0.15)	3
Headache	11	(0.81)	12	0	(0.00)	0	1	(0.07)	1
Hypoaesthesia	8	(0.59)	8	0	(0.00)	0	1	(0.07)	1
Migraine	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3
Neuropathy Peripheral	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0
Paraesthesia	7	(0.52)	7	0	(0.00)	0	3	(0.22)	4
Sciatica	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Subarachnoid Haemorrhage	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Syncope	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Tension Headache	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Tremor	2	(0.15)	2	0	(0.00)	0	2	(0.15)	2
Psychiatric Disorders	2	(0.15)	2	0	(0.00)	0	5	(0.37)	6
Depression	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2
Insomnia	1	(0.07)	1	0	(0.00)	0	4	(0.29)	4
Tic	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Renal and Urinary Disorders	2	(0.15)	2	1	(0.07)	1	2	(0.15)	2

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Calculus Ureteric	0	(0.00)	0	1	(0.07)	1	1	(0.07)	1
Dysuria	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Pollakiuria	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Proteinuria	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Reproductive System and Breast Disorders	6	(0.44)	6	0	(0.00)	0	1	(0.07)	1
Breast Mass	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Erectile Dysfunction	1	(0.07)	1	0	(0.00)	0	1	(0.07)	1
Menorrhagia	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Pelvic Pain	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0
Varicocele	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Respiratory, Thoracic and Mediastinal Disorders	16	(1.18)	18	1	(0.07)	1	27	(1.99)	31
Acute Respiratory Distress Syndrome	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Atelectasis	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Cough	2	(0.15)	2	0	(0.00)	0	15	(1.11)	16
Dysphonia	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Dyspnoea	2	(0.15)	2	0	(0.00)	0	3	(0.22)	3
Dyspnoea Exertional	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Epistaxis	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Interstitial Lung Disease	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2
Laryngeal Oedema	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Nasal Septum Deviation	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Oropharyngeal Pain	1	(0.07)	1	0	(0.00)	0	2	(0.15)	2
Pleural Effusion	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Productive Cough	5	(0.37)	5	0	(0.00)	0	2	(0.15)	2
Respiratory Distress	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Rhinitis Allergic	1	(0.07)	1	0	(0.00)	0	2	(0.15)	2
Rhinorrhoea	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Sputum Increased	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Vocal Cord Polyp	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Skin and Subcutaneous Tissue Disorders	40	(2.95)	46	2	(0.15)	2	59	(4.35)	75
Acne	3	(0.22)	3	0	(0.00)	0	0	(0.00)	0
Alopecia	3	(0.22)	3	0	(0.00)	0	1	(0.07)	1
Androgenetic Alopecia	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Decubitus Ulcer	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Dermatitis Acneiform	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2
Dermatitis Allergic	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Dermatitis Contact	0	(0.00)	0	0	(0.00)	0	4	(0.29)	4

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Diabetic Foot	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Eczema	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Erythema	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Erythema Nodosum	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Hyperhidrosis	2	(0.15)	2	1	(0.07)	1	0	(0.00)	0
Hyperkeratosis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Hypersensitivity Vasculitis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Pain of Skin	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Papule	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Photosensitivity Reaction	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Pruritus	11	(0.81)	13	0	(0.00)	0	19	(1.40)	23
Pruritus Generalised	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3
Pseudofolliculitis Barbae	1	(0.07)	1	0	(0.00)	0	1	(0.07)	1
Psoriasis	1	(0.07)	1	0	(0.00)	0	1	(0.07)	1
Rash	9	(0.66)	9	0	(0.00)	0	10	(0.74)	11
Rash Generalised	0	(0.00)	0	0	(0.00)	0	2	(0.15)	2
Seborrhoeic Dermatitis	0	(0.00)	0	0	(0.00)	0	3	(0.22)	3
Skin Exfoliation	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Skin Lesion	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Swelling Face	5	(0.37)	5	0	(0.00)	0	1	(0.07)	1
Systemic Lupus Erythematosus Rash	1	(0.07)	1	0	(0.00)	0	1	(0.07)	1
Urticaria	3	(0.22)	3	0	(0.00)	0	12	(0.88)	13
Xeroderma	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Social Circumstances	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Andropause	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Surgical and Medical Procedures	2	(0.15)	2	7	(0.52)	7	4	(0.29)	4
Arthrotomy*	0	(0.00)	0	1	(0.07)	1	1	(0.07)	1
Ileostomy	1	(0.07)	1	1	(0.07)	1	0	(0.00)	0
Ileostomy Closure*	0	(0.00)	0	1	(0.07)	1	1	(0.07)	1
Intervertebral Disc Operation	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Joint Arthroplasty*	0	(0.00)	0	1	(0.07)	1	1	(0.07)	1
Removal of Internal Fixation*	0	(0.00)	0	1	(0.07)	1	1	(0.07)	1
Spinal Decompression	0	(0.00)	0	1	(0.07)	1	0	(0.00)	0
Tooth Extraction	1	(0.07)	1	0	(0.00)	0	0	(0.00)	0
Vascular Disorders	7	(0.52)	7	0	(0.00)	0	8	(0.59)	9
Arteriosclerosis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Deep Vein Thrombosis	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Flushing	4	(0.29)	4	0	(0.00)	0	2	(0.15)	3

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Hypertension	1	(0.07)	1	0	(0.00)	0	2	(0.15)	2
Hypotension	2	(0.15)	2	0	(0.00)	0	0	(0.00)	0
Orthostatic Hypotension	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1
Renovascular Hypertension	0	(0.00)	0	0	(0.00)	0	1	(0.07)	1

* Redundant counting

Table 156 Incidence status for classification of Adverse Event by treatment (AS (N=531))

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Total	81	(15.25)	127	11	(2.07)	15	118	(22.22)	154
Blood and Lymphatic System Disorders	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2
Anaemia*	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Iron Deficiency Anaemia	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Ear and Labyrinth Disorders	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Vertigo	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Eye Disorders	1	(0.19)	1	0	(0.00)	0	4	(0.75)	4
Dry Eye	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2
Uveitis	1	(0.19)	1	0	(0.00)	0	2	(0.38)	2
Gastrointestinal Disorders	12	(2.26)	15	1	(0.19)	1	17	(3.20)	17
Abdominal Discomfort	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Abdominal Pain Upper	2	(0.38)	2	0	(0.00)	0	4	(0.75)	4
Constipation	1	(0.19)	1	0	(0.00)	0	3	(0.56)	3
Diarrhoea	3	(0.56)	3	0	(0.00)	0	4	(0.75)	4
Dry Mouth	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Dyspepsia	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2
Epigastric Discomfort	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Gastric Ulcer Haemorrhage*	0	(0.00)	0	1	(0.19)	1	1	(0.19)	1
Gastritis	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Gastroduodenitis	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Gastrointestinal Disorder	2	(0.38)	2	0	(0.00)	0	0	(0.00)	0
Large Intestine Polyp	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Mouth Haemorrhage	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Mouth Ulceration	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Nausea	1	(0.19)	1	0	(0.00)	0	1	(0.19)	1
General Disorders and Administration Site Conditions	8	(1.51)	8	0	(0.00)	0	3	(0.56)	3
Chest Discomfort	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Chest Pain	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Fatigue	4	(0.75)	4	0	(0.00)	0	0	(0.00)	0
Influenza Like Illness	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Pain	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Pyrexia	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2
Swelling	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Hepatobiliary Disorders	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2
Drug-Induced Liver Injury	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Hepatitis	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Immune System Disorders	1	(0.19)	1	0	(0.00)	0	4	(0.75)	4
Anaphylactic Reaction	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Anaphylactic Shock	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Hypersensitivity	1	(0.19)	1	0	(0.00)	0	2	(0.38)	2
Infections and Infestations	8	(1.51)	9	1	(0.19)	1	30	(5.65)	37
Body Tinea	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Bronchiolitis	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Bronchitis	0	(0.00)	0	0	(0.00)	0	3	(0.56)	3
Cellulitis	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2
Furuncle	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Gastritis Bacterial	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Hepatitis B	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Herpes Virus Infection	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Herpes Zoster*	0	(0.00)	0	1	(0.19)	1	3	(0.56)	3
Hordeolum	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Nasopharyngitis	5	(0.94)	6	0	(0.00)	0	6	(1.13)	6
Onychomycosis	0	(0.00)	0	0	(0.00)	0	3	(0.56)	3
Pharyngitis	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Pharyngotonsillitis	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Pneumonia	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Postoperative Wound Infection	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Pulmonary Tuberculosis	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Sinusitis	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Tinea Pedis	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Tonsillitis	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Tuberculosis	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Upper Respiratory Tract Infection	0	(0.00)	0	0	(0.00)	0	4	(0.75)	7
Injury, Poisoning and Procedural Complications	2	(0.38)	3	2	(0.38)	5	2	(0.38)	3
Auricular Haematoma	0	(0.00)	0	1	(0.19)	3	0	(0.00)	0
Compression Fracture	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Facial Bones Fracture	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Fracture*	0	(0.00)	0	1	(0.19)	1	1	(0.19)	1

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Hand Fracture	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Joint Dislocation*	0	(0.00)	0	1	(0.19)	1	1	(0.19)	1
Road Traffic Accident	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Investigations	19	(3.58)	26	0	(0.00)	0	8	(1.51)	10
Alanine Aminotransferase Increased	13	(2.45)	13	0	(0.00)	0	2	(0.38)	2
Asparate AminoTransferase Increased	8	(1.51)	8	0	(0.00)	0	2	(0.38)	2
Blood Creatine Phosphokinase Increased	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Hepatic Enzyme Increased	0	(0.00)	0	0	(0.00)	0	3	(0.56)	3
Liver Function Test Abnormal	1	(0.19)	1	0	(0.00)	0	2	(0.38)	2
Transaminases Increased	2	(0.38)	2	0	(0.00)	0	1	(0.19)	1
Weight Increased	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Metabolism and Nutrition Disorders	2	(0.38)	2	0	(0.00)	0	6	(1.13)	6
Decreased Appetite	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Diabetes Mellitus	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Hypercholesterolaemia	0	(0.00)	0	0	(0.00)	0	3	(0.56)	3
Hyperlipidaemia	0	(0.00)	0	0	(0.00)	0	3	(0.56)	3
Musculoskeletal and Connective Tissue Disorders	21	(3.95)	30	2	(0.38)	2	16	(3.01)	19

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Ankylosing Spondylitis*	0	(0.00)	0	1	(0.19)	1	3	(0.56)	3
Arthralgia*	7	(1.32)	8	0	(0.00)	0	4	(0.75)	6
Back Pain*	7	(1.32)	7	0	(0.00)	0	2	(0.38)	2
Fibromyalgia*	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Foot Deformity	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Joint Swelling	2	(0.38)	2	0	(0.00)	0	1	(0.19)	1
Musculoskeletal Pain	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Musculoskeletal Stiffness	3	(0.56)	3	0	(0.00)	0	0	(0.00)	0
Myalgia	1	(0.19)	1	0	(0.00)	0	1	(0.19)	1
Pain in Extremity	7	(1.32)	7	0	(0.00)	0	3	(0.56)	3
Spinal Column Stenosis*	0	(0.00)	0	1	(0.19)	1	1	(0.19)	1
Tendonitis	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Nervous System Disorders	7	(1.32)	7	1	(0.19)	1	8	(1.51)	10
Cerebellar Infarction	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Cervical Radiculopathy	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Dizziness	1	(0.19)	1	0	(0.00)	0	1	(0.19)	2
Headache	3	(0.56)	3	0	(0.00)	0	1	(0.19)	1
Hypoaesthesia	1	(0.19)	1	0	(0.00)	0	1	(0.19)	1
Migraine	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Neuropathy Peripheral	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Paraesthesia	1	(0.19)	1	0	(0.00)	0	1	(0.19)	1
Sciatica	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Syncope	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Psychiatric Disorders	0	(0.00)	0	0	(0.00)	0	2	(0.38)	2
Depression	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Insomnia	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Renal and Urinary Disorders	2	(0.38)	2	1	(0.19)	1	1	(0.19)	1
Calculus Ureteric	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Dysuria	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Pollakiuria	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Proteinuria	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Reproductive System and Breast Disorders	3	(0.56)	3	0	(0.00)	0	1	(0.19)	1
Erectile Dysfunction	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Pelvic Pain	2	(0.38)	2	0	(0.00)	0	0	(0.00)	0
Varicocele	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Respiratory, Thoracic and Mediastinal Disorders	6	(1.13)	6	1	(0.19)	1	9	(1.69)	11
Cough	0	(0.00)	0	0	(0.00)	0	6	(1.13)	6

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Dyspnoea	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Laryngeal Oedema	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Nasal Septum Deviation	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Oropharyngeal Pain	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Productive Cough	4	(0.75)	4	0	(0.00)	0	1	(0.19)	1
Rhinitis Allergic	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Rhinorrhoea	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Sputum Increased	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Skin and Subcutaneous Tissue Disorders	10	(1.88)	11	2	(0.38)	2	16	(3.01)	18
Acne	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Alopecia	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Androgenetic Alopecia	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Decubitus Ulcer	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Eczema	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Hyperhidrosis	0	(0.00)	0	1	(0.19)	1	0	(0.00)	0
Hyperkeratosis	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Hypersensitivity Vasculitis	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Papule	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Pruritus	4	(0.75)	4	0	(0.00)	0	3	(0.56)	3

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Pruritus Generalised	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Psoriasis	1	(0.19)	1	0	(0.00)	0	1	(0.19)	1
Rash	2	(0.38)	2	0	(0.00)	0	4	(0.75)	4
Seborrhoeic Dermatitis	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1
Swelling Face	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Urticaria	0	(0.00)	0	0	(0.00)	0	3	(0.56)	3
Xeroderma	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Social Circumstances	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Andropause	1	(0.19)	1	0	(0.00)	0	0	(0.00)	0
Surgical and Medical Procedures	0	(0.00)	0	1	(0.19)	1	1	(0.19)	1
Arthrotomy*	0	(0.00)	0	1	(0.19)	1	1	(0.19)	1
Vascular Disorders	1	(0.19)	1	0	(0.00)	0	3	(0.56)	3
Hypertension	1	(0.19)	1	0	(0.00)	0	2	(0.38)	2
Orthostatic Hypotension	0	(0.00)	0	0	(0.00)	0	1	(0.19)	1

* Redundant counting

Table 157 Incidence status for classification of Adverse Event by treatment (RA/PA/PS (N=409))

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Total	108	(26.41)	187	25	(6.11)	32	147	(35.94)	263

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Blood and Lymphatic System Disorders	2	(0.49)	2	0	(0.00)	0	3	(0.73)	3
Iron Deficiency Anaemia	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2
Lymphadenopathy	2	(0.49)	2	0	(0.00)	0	0	(0.00)	0
Pancytopenia	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Cardiac Disorders	5	(1.22)	5	0	(0.00)	0	2	(0.49)	2
Atrial Fibrillation	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Cardiac Arrest	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Palpitations	4	(0.98)	4	0	(0.00)	0	1	(0.24)	1
Ear and Labyrinth Disorders	2	(0.49)	2	0	(0.00)	0	1	(0.24)	1
Tinnitus	2	(0.49)	2	0	(0.00)	0	1	(0.24)	1
Eye Disorders	4	(0.98)	4	0	(0.00)	0	1	(0.24)	1
Blepharitis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Dry Eye	2	(0.49)	2	0	(0.00)	0	0	(0.00)	0
Glaucoma	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Visual Acuity Reduced	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Gastrointestinal Disorders	23	(5.62)	28	0	(0.00)	0	32	(7.82)	43
Abdominal Discomfort	1	(0.24)	1	0	(0.00)	0	1	(0.24)	1
Abdominal Distension	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Abdominal Pain	2	(0.49)	2	0	(0.00)	0	2	(0.49)	2

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Abdominal Pain Upper	1	(0.24)	1	0	(0.00)	0	5	(1.22)	6
Aphthous Ulcer	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Constipation	1	(0.24)	1	0	(0.00)	0	2	(0.49)	3
Diarrhoea	6	(1.47)	6	0	(0.00)	0	1	(0.24)	1
Dry Mouth	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Dyspepsia	3	(0.73)	3	0	(0.00)	0	6	(1.47)	7
Dysphagia	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Gastric Mucosal Lesion	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Gastric Ulcer	1	(0.24)	1	0	(0.00)	0	1	(0.24)	1
Gastritis	1	(0.24)	1	0	(0.00)	0	2	(0.49)	2
Gastrointestinal Disorder	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2
Gastrooesophageal Reflux Disease	1	(0.24)	1	0	(0.00)	0	1	(0.24)	1
Mouth Ulceration	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Nausea	5	(1.22)	5	0	(0.00)	0	7	(1.71)	7
Proctalgia	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Regurgitation	1	(0.24)	1	0	(0.00)	0	1	(0.24)	2
Stomatitis	2	(0.49)	2	0	(0.00)	0	0	(0.00)	0
Vomiting	1	(0.24)	1	0	(0.00)	0	3	(0.73)	3
General Disorders and Administration Site Conditions	14	(3.42)	14	0	(0.00)	0	8	(1.96)	11

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Asthenia	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Chest Discomfort	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Chest Pain	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Chills	1	(0.24)	1	0	(0.00)	0	3	(0.73)	5
Drug Effect Delayed	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Face Oedema	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Fatigue	2	(0.49)	2	0	(0.00)	0	0	(0.00)	0
Generalised Oedema	1	(0.24)	1	0	(0.00)	0	1	(0.24)	1
Oedema	2	(0.49)	2	0	(0.00)	0	1	(0.24)	1
Oedema Peripheral	2	(0.49)	2	0	(0.00)	0	2	(0.49)	2
Pyrexia	1	(0.24)	1	0	(0.00)	0	2	(0.49)	2
Hepatobiliary Disorders	1	(0.24)	1	0	(0.00)	0	3	(0.73)	3
Cholelithiasis	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Hepatitis	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2
Liver Disorder	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Immune System Disorders	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4
Anaphylactic Reaction	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2
Hypersensitivity	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2
Infections and Infestations	11	(2.69)	11	2	(0.49)	2	56	(13.69)	60

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Abscess	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Arthritis Bacterial*	0	(0.00)	0	1	(0.24)	1	1	(0.24)	1
Body Tinea	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Bronchitis	0	(0.00)	0	0	(0.00)	0	9	(2.20)	9
Candida Infection	0	(0.00)	0	0	(0.00)	0	1	(0.24)	2
Cystitis	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2
Disseminated Tuberculosis	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2
Folliculitis	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2
Herpes Simplex	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3
Herpes Zoster*	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3
Influenza	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Nasopharyngitis	5	(1.22)	5	0	(0.00)	0	5	(1.22)	5
Otitis Externa	1	(0.24)	1	0	(0.00)	0	1	(0.24)	1
Pneumonia	0	(0.00)	0	0	(0.00)	0	5	(1.22)	6
Pneumonia Bacterial	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Pyelonephritis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Pyelonephritis Acute	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4
Rhinitis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Sepsis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Sinusitis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Tinea Pedis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Tuberculosis Gastrointestinal	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Upper Respiratory Tract Infection	4	(0.98)	4	0	(0.00)	0	8	(1.96)	8
Ureteritis	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Urinary Tract Infection	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2
Vaginal Infection	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Injury, Poisoning and Procedural Complications	2	(0.49)	2	5	(1.22)	7	2	(0.49)	2
Ankle Fracture	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Contusion	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Fall	1	(0.24)	1	1	(0.24)	1	0	(0.00)	0
Foot Fracture*	0	(0.00)	0	1	(0.24)	1	1	(0.24)	1
Joint Dislocation*	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Laceration	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Perineal Injury	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Road Traffic Accident	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Investigations	13	(3.18)	14	0	(0.00)	0	8	(1.96)	9
Alanine Aminotransferase Increased	3	(0.73)	3	0	(0.00)	0	2	(0.49)	2

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Aspartate Aminotransferase Increased	2	(0.49)	2	0	(0.00)	0	0	(0.00)	0
Hepatic Enzyme Increased	2	(0.49)	2	0	(0.00)	0	0	(0.00)	0
Influenza B Virus Test Positive	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Liver Function Test Abnormal	1	(0.24)	1	0	(0.00)	0	3	(0.73)	4
Serum Ferritin Increased	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Urine Analysis Abnormal	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Weight Decreased	2	(0.49)	2	0	(0.00)	0	0	(0.00)	0
Weight Increased	4	(0.98)	4	0	(0.00)	0	0	(0.00)	0
Metabolism and Nutrition Disorders	4	(0.98)	5	1	(0.24)	1	11	(2.69)	11
Decreased Appetite	2	(0.49)	2	0	(0.00)	0	0	(0.00)	0
Hypercholesterolaemia	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Hyperglycaemia	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Hyperlipidaemia	0	(0.00)	0	0	(0.00)	0	9	(2.20)	9
Hypoglycaemia	2	(0.49)	2	1	(0.24)	1	1	(0.24)	1
Musculoskeletal and Connective Tissue Disorders	16	(3.91)	20	12	(2.93)	14	31	(7.58)	36
Arthralgia*	3	(0.73)	3	1	(0.24)	1	12	(2.93)	13
Atlantoaxial Instability	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Back Pain*	1	(0.24)	1	3	(0.73)	3	2	(0.49)	2
Bursal Fluid Accumulation	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Fibromyalgia*	0	(0.00)	0	1	(0.24)	1	2	(0.49)	2
Foot Deformity	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Intervertebral Disc Disorder	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Intervertebral Disc Protrusion*	0	(0.00)	0	3	(0.73)	3	3	(0.73)	3
Joint Swelling	2	(0.49)	2	0	(0.00)	0	2	(0.49)	2
Lumbar Spinal Stenosis	2	(0.49)	2	0	(0.00)	0	2	(0.49)	2
Musculoskeletal Pain	3	(0.73)	3	1	(0.24)	1	0	(0.00)	0
Myalgia	5	(1.22)	6	0	(0.00)	0	0	(0.00)	0
Osteoarthritis	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Osteoporosis	0	(0.00)	0	0	(0.00)	0	3	(0.73)	3
Polyarthritis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Rheumatoid Arthritis	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4
Rotator Cuff Syndrome	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Spinal Column Stenosis*	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Synovial Cyst	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Synovitis*	0	(0.00)	0	1	(0.24)	1	1	(0.24)	1
Tenosynovitis*	0	(0.00)	0	1	(0.24)	1	1	(0.24)	1
Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps)	1	(0.24)	1	4	(0.98)	4	0	(0.00)	0
Colon Adenoma	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Gastric Cancer	0	(0.00)	0	2	(0.49)	2	0	(0.00)	0
Hypergammaglobulinaemia Benign Monoclonal	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Invasive Ductal Breast Carcinoma	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Nervous System Disorders	27	(6.60)	34	0	(0.00)	0	11	(2.69)	13
Anosmia	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Carotid Arteriosclerosis	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Cerebellar Ataxia	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Cerebral Infarction	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Diabetic Neuropathy	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Dizziness	10	(2.44)	10	0	(0.00)	0	1	(0.24)	1
Headache	8	(1.96)	9	0	(0.00)	0	0	(0.00)	0
Hypoaesthesia	6	(1.47)	6	0	(0.00)	0	0	(0.00)	0
Migraine	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Neuropathy Peripheral	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Paraesthesia	6	(1.47)	6	0	(0.00)	0	2	(0.49)	3
Subarachnoid Haemorrhage	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Tension Headache	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Tremor	1	(0.24)	1	0	(0.00)	0	2	(0.49)	2
Psychiatric Disorders	2	(0.49)	2	0	(0.00)	0	2	(0.49)	2

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Insomnia	1	(0.24)	1	0	(0.00)	0	2	(0.49)	2
Tic	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Reproductive System and Breast Disorders	3	(0.73)	3	0	(0.00)	0	0	(0.00)	0
Breast Mass	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Erectile Dysfunction	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Menorrhagia	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Respiratory, Thoracic and Mediastinal Disorders	6	(1.47)	7	0	(0.00)	0	14	(3.42)	16
Acute Respiratory Distress Syndrome	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Atelectasis	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Cough	1	(0.24)	1	0	(0.00)	0	8	(1.96)	9
Dysphonia	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Dyspnoea Exertional	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Interstitial Lung Disease	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2
Oropharyngeal Pain	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Pleural Effusion	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Productive Cough	1	(0.24)	1	0	(0.00)	0	1	(0.24)	1
Rhinitis Allergic	1	(0.24)	1	0	(0.00)	0	1	(0.24)	1
Vocal Cord Polyp	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Skin and Subcutaneous Tissue Disorders	20	(4.89)	25	0	(0.00)	0	26	(6.36)	40
Alopecia	2	(0.49)	2	0	(0.00)	0	1	(0.24)	1
Dermatitis Acneiform	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Dermatitis Allergic	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Dermatitis Contact	0	(0.00)	0	0	(0.00)	0	4	(0.98)	4
Diabetic Foot	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Erythema	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Hyperhidrosis	2	(0.49)	2	0	(0.00)	0	0	(0.00)	0
Pruritus	6	(1.47)	8	0	(0.00)	0	10	(2.44)	14
Pruritus Generalised	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2
Pseudofolliculitis Barbae	1	(0.24)	1	0	(0.00)	0	1	(0.24)	1
Rash	6	(1.47)	6	0	(0.00)	0	2	(0.49)	3
Rash Generalised	0	(0.00)	0	0	(0.00)	0	2	(0.49)	2
Swelling Face	2	(0.49)	2	0	(0.00)	0	1	(0.24)	1
Systemic Lupus Erythematosus Rash	1	(0.24)	1	0	(0.00)	0	1	(0.24)	1
Urticaria	2	(0.49)	2	0	(0.00)	0	7	(1.71)	8
Surgical and Medical Procedures	1	(0.24)	1	4	(0.98)	4	2	(0.49)	2
Intervertebral Disc Operation	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Joint Arthroplasty*	0	(0.00)	0	1	(0.24)	1	1	(0.24)	1
Removal of Internal Fixation*	0	(0.00)	0	1	(0.24)	1	1	(0.24)	1
Spinal Decompression	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Tooth Extraction	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Vascular Disorders	6	(1.47)	6	0	(0.00)	0	3	(0.73)	4
Arteriosclerosis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Flushing	4	(0.98)	4	0	(0.00)	0	2	(0.49)	3
Hypotension	2	(0.49)	2	0	(0.00)	0	0	(0.00)	0

* Redundant counting

Table 158 Incidence status for classification of Adverse Event by treatment (IBD (N=417))

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Total	68	(16.31)	90	18	(4.32)	19	89	(21.34)	141
Blood and Lymphatic System Disorders	5	(1.20)	5	3	(0.72)	3	4	(0.96)	4
Anaemia*	0	(0.00)	0	2	(0.48)	2	2	(0.48)	2
Iron Deficiency Anaemia	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Leukopenia	4	(0.96)	4	1	(0.24)	1	0	(0.00)	0
Lymphadenitis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Neutropenia	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Cardiac Disorders	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Palpitations	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Ear and Labyrinth Disorders	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Otorrhoea	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Eye Disorders	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Vision Blurred	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Gastrointestinal Disorders	26	(6.24)	32	7	(1.68)	8	35	(8.39)	52
Abdominal Discomfort	1	(0.24)	1	0	(0.00)	0	1	(0.24)	1
Abdominal Pain	10	(2.40)	12	1	(0.24)	2	10	(2.40)	14
Abdominal Pain Lower	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Abdominal Pain Upper	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Anal Fistula*	0	(0.00)	0	1	(0.24)	1	1	(0.24)	1
Aphthous Ulcer	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Colitis Ulcerative	0	(0.00)	0	1	(0.24)	1	3	(0.72)	3
Constipation	1	(0.24)	1	0	(0.00)	0	2	(0.48)	2
Crohn's Disease	0	(0.00)	0	1	(0.24)	1	4	(0.96)	4
Diarrhoea	4	(0.96)	4	0	(0.00)	0	1	(0.24)	1
Dyspepsia	2	(0.48)	2	0	(0.00)	0	1	(0.24)	2
Enterocutaneous Fistula	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Epigastric Discomfort	2	(0.48)	2	0	(0.00)	0	0	(0.00)	0
Frequent Bowel Movements	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Gastritis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Gastrointestinal Inflammation	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Haematochezia	3	(0.72)	3	0	(0.00)	0	4	(0.96)	4
Ileus	1	(0.24)	1	1	(0.24)	1	0	(0.00)	0
Intestinal Obstruction*	0	(0.00)	0	1	(0.24)	1	1	(0.24)	1
Melaena	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Mouth Ulceration	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Nausea	2	(0.48)	2	0	(0.00)	0	3	(0.72)	5
Protein-Losing Gastroenteropathy	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Small Intestinal Haemorrhage*	0	(0.00)	0	1	(0.24)	1	1	(0.24)	1
Vomiting	3	(0.72)	3	0	(0.00)	0	2	(0.48)	4
General Disorders and Administration Site Conditions	6	(1.44)	6	1	(0.24)	1	11	(2.64)	12
Application Site Haemorrhage	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Chest Pain	2	(0.48)	2	0	(0.00)	0	0	(0.00)	0
Disease progression	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2
Drug Ineffective	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Immediate Post-Injection Reaction	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Large Intestinal Perforation	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Non-Cardiac Chest Pain	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Oedema	1	(0.24)	1	0	(0.00)	0	1	(0.24)	1
Pyrexia	2	(0.48)	2	0	(0.00)	0	5	(1.20)	6
Hepatobiliary Disorders	1	(0.24)	1	0	(0.00)	0	2	(0.48)	2
Hepatic Function Abnormal	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Hepatitis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Hyperbilirubinaemia	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Immune System Disorders	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Anaphylactic Reaction	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Infections and Infestations	6	(1.44)	6	4	(0.96)	4	28	(6.71)	35
Abdominal Abscess	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Anal Abscess	0	(0.00)	0	2	(0.48)	2	1	(0.24)	1
Atypical Pneumonia	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Clostridium Difficile Infection	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Cystitis	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Cytomegalovirus Colitis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Cytomegalovirus Infection	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2
Disseminated Tuberculosis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Folliculitis	1	(0.24)	1	0	(0.00)	0	1	(0.24)	1
Herpes Virus Infection	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Herpes Zoster*	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Lung Abscess*	0	(0.00)	0	1	(0.24)	1	1	(0.24)	1
Nasopharyngitis	0	(0.00)	0	0	(0.00)	0	6	(1.44)	6
Oral Candidiasis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Pneumocystis Jirovecii Pneumonia	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Pneumonia	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2
Pseudomembranous Colitis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Rhinitis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Sepsis	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Sialoadenitis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Spleen Tuberculosis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Tuberculosis	0	(0.00)	0	0	(0.00)	0	3	(0.72)	3
Upper Respiratory Tract Infection	3	(0.72)	3	0	(0.00)	0	5	(1.20)	5
Urinary Tract Infection	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2
Injury, Poisoning and Procedural Complications	0	(0.00)	0	1	(0.24)	1	3	(0.72)	3
Foot Fracture*	0	(0.00)	0	1	(0.24)	1	0	(0.00)	0
Infusion Related Reaction	0	(0.00)	0	0	(0.00)	0	3	(0.72)	3

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Investigations	11	(2.64)	13	0	(0.00)	0	1	(0.24)	1
Alanine Aminotransferase Increased	1	(0.24)	2	0	(0.00)	0	0	(0.00)	0
Aspartate Aminotransferase Increased	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Blood Alkaline Phosphatase Increased	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
C-Reactive Protein Increased	2	(0.48)	2	0	(0.00)	0	0	(0.00)	0
Eosinophil Count Increased	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Liver Function Test Abnormal	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Occult Blood	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
White Blood Cell Count Decreased	5	(1.20)	5	0	(0.00)	0	0	(0.00)	0
Metabolism and Nutrition Disorders	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Decreased Appetite	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Musculoskeletal and Connective Tissue Disorders	3	(0.72)	3	0	(0.00)	0	3	(0.72)	3
Arthralgia*	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Flank Pain	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Musculoskeletal Pain	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2
Musculoskeletal Stiffness	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Myalgia	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Nervous System Disorders	5	(1.20)	5	0	(0.00)	0	0	(0.00)	0
Dizziness	3	(0.72)	3	0	(0.00)	0	0	(0.00)	0
Hypoaesthesia	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Tremor	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Psychiatric Disorders	0	(0.00)	0	0	(0.00)	0	1	(0.24)	2
Depression	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Insomnia	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Renal and Urinary Disorders	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Calculus Ureteric	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Respiratory, Thoracic and Mediastinal Disorders	4	(0.96)	5	0	(0.00)	0	4	(0.96)	4
Cough	1	(0.24)	1	0	(0.00)	0	1	(0.24)	1
Dyspnoea	1	(0.24)	1	0	(0.00)	0	3	(0.72)	3
Epistaxis	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Oropharyngeal Pain	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Respiratory Distress	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Skin and Subcutaneous Tissue Disorders	10	(2.40)	10	0	(0.00)	0	17	(4.08)	17
Acne	2	(0.48)	2	0	(0.00)	0	0	(0.00)	0
Dermatitis Acneiform	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1

System Organ Class Preferred Term	No treatment			Non-medicinal treatment			Treatment with other medication		
	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events	No. of Subjects	(%)	No. of Events
Erythema Nodosum	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Pain of Skin	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Photosensitivity Reaction	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Pruritus	1	(0.24)	1	0	(0.00)	0	6	(1.44)	6
Rash	1	(0.24)	1	0	(0.00)	0	4	(0.96)	4
Seborrhoeic Dermatitis	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2
Skin Exfoliation	1	(0.24)	1	0	(0.00)	0	0	(0.00)	0
Skin Lesion	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Swelling Face	2	(0.48)	2	0	(0.00)	0	0	(0.00)	0
Urticaria	1	(0.24)	1	0	(0.00)	0	2	(0.48)	2
Surgical and Medical Procedures	1	(0.24)	1	2	(0.48)	2	1	(0.24)	1
Ileostomy	1	(0.24)	1	1	(0.24)	1	0	(0.00)	0
Ileostomy Closure*	0	(0.00)	0	1	(0.24)	1	1	(0.24)	1
Vascular Disorders	0	(0.00)	0	0	(0.00)	0	2	(0.48)	2
Deep Vein Thrombosis	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1
Renovascular Hypertension	0	(0.00)	0	0	(0.00)	0	1	(0.24)	1

* Redundant counting

3.1.7 Adverse events in special population

A. Elderly

122 out of 1357 subjects were geriatric, aged ≥65 years, incidence of adverse events in the geriatric was 54.92% (67/122 subjects, 169 events); compared to subjects aged <65 years, there was a statistically significant difference (p=0.0002, Table 159). Incidence of adverse events in Elderly aged ≥65 years by indication are shown in Table 160.

Table 159 Incidence of adverse events in special population (geriatric)

Geriatric classification		Incidence Rate			No. of events	95% Confidence Interval (lower limit, upper limit)	p-value
		No. of Subjects	Total Subjects	(%)			
Total	<65 years	463	1235	(37.49)	837	(34.83,40.22)	0.0002[1)]
	≥65 years	67	122	(54.92)	169	(46.07,63.46)	
Total		530	1357	(39.06)	1006	(36.50,41.68)	
AS	<65 years	176	511	(34.44)	277	(30.45,38.66)	0.9589[1)]
	≥65 years	7	20	(35.00)	12	(18.12,56.71)	
Total		183	531	(34.46)	289	(30.55,38.60)	
RA/PA/PS	<65 years	154	326	(47.24)	349	(41.88,52.66)	0.0849[1)]
	≥65 years	48	83	(57.83)	122	(47.09,67.88)	
Total		202	409	(49.39)	471	(44.57,54.22)	
IBD	<65 years	133	398	(33.42)	211	(28.96,38.19)	0.0078[1)]
	≥65 years	12	19	(63.16)	35	(41.04,80.85)	
Total		145	417	(34.77)	246	(30.36,39.46)	

[1)] Chi-square test

B. Children

12 out of 1357 subjects were children, aged <12 years, incidence of adverse event in the children was 25.00% (3/12 subjects, 3 events); compared to subjects aged ≥12 years, there was no statistically significant difference (p=0.3859, Table 159). Incidence of adverse events in children aged <12 years by indication are shown in Table 159

Table 160 Incidence of adverse events in special population (children)

Children classification	Incidence Rate	No. of	95% Confidence	p-value

		No. of Subjects	Total Subjects	(%)	events	Interval (lower limit, upper limit)	
Total	<12 years	3	12	(25.00)	3	(8.89,53.23)	0.3859[1)]
	≥12 years	527	1345	(39.18)	1003	(36.61,41.82)	
Total		530	1357	(39.06)	1006	(36.50,41.68)	
AS	<12 years	0	0	N/A	-	-	-
	≥12 years	183	531	(34.46)	289	(30.55,38.60)	
Total		183	531	(34.46)	289	(30.55,38.60)	
RA/PA/PS	<12 years	0	0	N/A	-	-	-
	≥12 years	202	409	(49.39)	471	(44.57,54.22)	
Total		202	409	(49.39)	471	(44.57,54.22)	
IBD	<12 years	3	12	(25.00)	3	(8.89,53.23)	0.5547[1)]
	≥12 years	142	405	(35.06)	243	(30.57,39.46)	
Total		145	417	(34.77)	246	(30.36,39.46)	

[1)] Fisher's exact test

C. Pregnant women

There were no pregnant women in the surveillance.

D. Hepatic impairment

39 out of 1357 subjects had history of hepatic impairment, incidence of adverse event in subjects with history hepatic impairment was 38.46% (15/39 subjects, 22 events); compared to those with no hepatic impairment, there was no statistically significant difference (p=0.9384, Table 161). Incidence of adverse events in subjects with history of hepatic impairment in shown in Table 161 by indication.

Table 161 Incidence of adverse events in special population (hepatic impairment)

Hepatic impairment classification		Incidence Rate			No. of events	95% Confidence Interval (lower limit, upper limit)	p-value
		No. of Subjects	Total Subjects	(%)			
Total	Yes	15	39	(38.46)	22	(24.89,54.10)	0.9384[1)]
	No	515	1318	(39.07)	984	(36.48,41.74)	
Total		530	1357	(39.06)	1006	(36.50,41.68)	

Hepatic impairment classification		Incidence Rate			No. of events	95% Confidence Interval (lower limit, upper limit)	p-value
		No. of Subjects	Total Subjects	(%)			
AS	Yes	5	17	(29.41)	5	(13.28,53.13)	0.6560[1)]
	No	178	514	(34.63)	284	(30.64,38.84)	
Total		183	531	(34.46)	289	(30.55,38.60)	
RA/PA/PS	Yes	5	9	(55.56)	5	(26.67,81.12)	0.7485[2)]
	No	197	400	(49.25)	466	(44.38,54.13)	
Total		202	409	(49.39)	471	(44.57,54.22)	
IBD	Yes	5	13	(38.46)	12	(17.71,64.48)	0.7735[2)]
	No	140	404	(34.65)	234	(30.18,39.42)	
Total		145	417	(34.77)	246	(30.36,39.46)	

[1)] Chi-square test / [2)] Fisher's exact test

E. Renal impairment

16 out of 1357 subjects had history of renal impairment, incidence of adverse events in subjects with history of renal impairment was 50.00% (8/16 subjects, 27 events); compared to those with no renal impairment, there was no statistically significant difference (p=0.3668, Table 162). Incidence of adverse events in subjects with history of renal impairment is shown in Table 162 by indication.

Table 162 Incidence of adverse events in special population (renal impairment)

Renal impairment Classification		Incidence Rate			No. of events	95% Confidence Interval (lower limit, upper limit)	p-value
		No. of Subjects	Total Subjects	(%)			
Total	Yes	8	16	(50.00)	27	(28.00,72.00)	0.3668[1)]
	No	522	1341	(38.93)	979	(36.35,41.56)	
Total		530	1357	(39.06)	1006	(36.50,41.68)	
AS	Yes	5	6	(83.33)	11	(43.65,96.99)	0.0202[2)]
	No	178	525	(33.90)	278	(29.99,38.06)	
Total		183	531	(34.46)	289	(30.55,38.60)	
RA/PA/PS	Yes	1	3	(33.33)	11	(6.15,79.23)	1.0000[2)]

Renal impairment Classification		Incidence Rate			No. of events	95% Confidence Interval (lower limit, upper limit)	p-value
		No. of Subjects	Total Subjects	(%)			
	No	201	406	(49.51)	460	(44.67,54.35)	
Total		202	409	(49.39)	471	(44.57,54.22)	
IBD	Yes	2	7	(28.57)	5	(8.22,64.11)	1.0000[2)]
	No	143	410	(34.88)	241	(30.42,39.61)	
Total		145	417	(34.77)	246	(30.36,39.46)	

[1)] Chi-square test / [2)] Fisher's exact test

F. Long-term use

Long-term users are those who received the surveillance drug until the point of long-term efficacy assessment and otherwise, they were categorized as short-term user. Incidence of adverse event was 40.78% (407/998 subjects, 790 events) in long-term users and 34.26% (123/359 subjects, 216 events) in short-term users, with no statistically significant difference with the short-term users (p=0.0299, Table 163). Incidence of adverse events in subjcets with long-term users is shown in Table 163 by indication.

Table 163 Incidence of adverse events by duration of use

Short- and Long-term use Classification		Incidence Rate			No. of events	95% Confidence Interval (lower limit, upper limit)	p-value
		No. of Subjects	Total Subjects	(%)			
Total	Short-term	123	359	(34.26)	216	(29.54,39.31)	0.0299[1)]
	Long-term	407	998	(40.78)	790	(37.77,43.86)	
Total		530	1357	(39.06)	1006	(36.50,41.68)	
AS	Short-term	27	83	(32.53)	40	(23.42,43.19)	0.6866[1)]
	Long-term	156	448	(34.82)	249	(30.56,39.35)	
Total		183	531	(34.46)	289	(30.55,38.60)	
RA/PA/PS	Short-term	42	102	(41.18)	86	(32.12,50.88)	0.0555[1)]
	Long-term	160	307	(52.12)	385	(46.54,57.64)	
Total		202	409	(49.39)	471	(44.57,54.22)	
IBD	Short-term	54	174	(31.03)	90	(24.63,38.26)	0.1750[1)]
	Long-term	91	243	(37.45)	156	(31.60,43.68)	

Short- and Long-term use Classification	Incidence Rate			No. of events	95% Confidence Interval (lower limit, upper limit)	p-value
	No. of Subjects	Total Subjects	(%)			
Total	145	417	(34.77)	246	(30.36,39.46)	

[1)] Chi-square test

3.1.8 Factors that are thought to affect the adverse event occurrence

In this surveillance, in relation to safety, the adverse event incidence was surveyed by sex, age, height, body weight, previous treatment, medical history, concomitant medication and status of surveillance drug administration condition.
From analysis of the adverse events occurrence status by factor in the entire subjects, a statistically significant difference was detected for sex ($p<0.0001$), age ($p<0.0001$), type of visit ($p=0.0008$), body weight ($p=0.0046$), concurrent disease ($p<0.0001$), tuberculosis and other severe infection ($p=0.0384$), concomitant medication ($p=0.0091$) and long-term use ($p=0.02999$). A statistically significant difference was observed for sex ($p=0.0445$), concurrent disease ($p=0.0015$), tuberculosis and other severe infection ($p=0.1008$), average dose per administration of the surveillance drug ($p=0.0305$) and concomitant medication ($p=0.0453$) in ankylosing spondylitis; age ($p=0.0181$), type of visit ($p=0.0002$), concurrent disease ($p<0.0001$) and average administration duration (rheumatoid arthritis only, $p<0.0001$) in rheumatoid arthritis/active progressive psoriatic arthritis (in adults)/moderate to severe plaque psoriasis (in adults); and age ($p=0.0043$), concurrent disease ($p<0.0001$) and tuberculosis and other severe infection ($p=0.0003$) in fistulizing active Crohn's disease (in adults)/moderate to severe active Crohn's disease (in adults)/severe active Crohn's disease (children and adolescents)/moderate to severe ulcerative colitis (in adults)/ moderate to severe ulcerative colitis (children and adolescents).

Logistic regression analysis was conducted for background factors ($p<0.2$) that may affect adverse event occurrence, as suggested from analysis by factor.

Results were statistically significant for sex ($p=0.0416$), age ($p=0.0021$), type of visit (inpatient vs outpatient, $p=0.0007$, inpatient ↔ outpatient vs outpatient, $p=0.0095$), long-term use ($p=0.0416$), concurrent disease ($p<0.0001$) and hypersensitivity history for treatment of the indication (No vs Yes, $p=0.0462$); odds of adverse event occurrence increased 0.750-fold in male compared to female, 1.013-fold with every 1 year increase in age, 1.742-fold in inpatient compared to outpatient, 1.632-fold in inpatient ↔ outpatient compared to outpatient, 1.323-fold in long-term users compared to short-term users and 2.002-fold in subjects with concurrent disease compared with subjects with no concurrent disease (Table 164).

Results are shown in Table 165, Table 166 and Table 167 by indication.

Table 164 Logistic regression analysis (factors that affect safety) (Total)

Background factor		p-value	Odds ratio	95% Confidence Interval	
				Lower limit	Upper limit
Sex	M vs F*	0.0416	0.750	0.57	0.99
Age (year)	Continuous (year)	0.0021	1.013	1.00	1.02
Type of visit	Inpatient vs Outpatient*	0.0007	1.742	1.27	2.40
	Inpatient ↔ Outpatient vs Outpatient*	0.0095	1.632	1.13	2.36
Body weight (kg)	Continuous (kg)	0.9048	1.001	0.99	1.01
Long-term user	Long-term vs Short-term*	0.0416	1.323	1.01	1.73

Background factor		p-value	Odds ratio	95% Confidence Interval	
				Lower limit	Upper limit
Concurrent disease	Yes vs No*	<0.0001	2.002	1.56	2.57
Complication	Yes vs No	0.2284	1.545	0.76	3.14
Tuberculosis and other severe infection	Yes vs No*	0.0648	1.425	0.98	2.08
Treatment history for the indication	No vs Yes*	0.4667	0.911	0.71	1.17
	Unknown vs Yes*	0.0637	0.134	0.02	1.12
Hypersensitivity history for treatment of the indication	No vs Yes*	0.0462	0.578	0.34	0.99
	Unknown vs Yes*	0.2730	0.661	0.32	1.39
Concomitant medication	Yes vs No*	0.0684	2.754	0.93	8.19

*Reference level
Note) This logistic analysis was conducted after selecting variables by considering the following items.
* Specific variables were excluded due to multicollinearity.
* In case of the p-value<0.2 for both the medical history and the sub-variable, only the sub-variable was included in the model.
* Excluded in case the p-value is not <0.2 for the treatment-related variable for all indications in the subgroup (other than subgroup 2) analysis of safety analysis

Table 165 Logistic regression analysis (factors that affect safety) (AS)

Background factor		p-value	Odds ratio	95% CI	
				Lower limit	Upper limit
Sex	M vs F*	0.0036	0.469	0.28	0.78
Body weight (kg)	Continuous (kg)	0.0014	1.032	1.01	1.05
Renal impairment	Yes vs No*	0.0409	10.462	1.10	99.28
Concurrent disease	Yes vs No*	0.0094	1.674	1.13	2.47
Complication	Yes vs No*	0.1939	2.088	0.69	6.34
Tuberculosis and other severe infection	Yes vs No*	0.0549	1.656	0.99	2.77
Concomitant medication	Yes vs No*	0.2084	2.627	0.58	11.82
Average dose (mg/kg)	Continuous (mg/kg)	0.0115	1.359	1.07	1.72

*Reference level
Note) This logistic analysis was conducted after selecting variables by considering the following items.
* Specific variables were excluded due to multicollinearity.
* In case of the p-value<0.2 for both the medical history and the sub-variable, only the sub-variable was included in the model.
* Excluded in case the p-value is not <0.2 for the treatment-related variable for all indications in the subgroup (other than subgroup 2) analysis of safety analysis

Table 166 Logistic regression analysis (factors that affect safety) (RA/PA/PS)

Background factor		p-value	Odds Ratio	95% CI	
				Lower limit	Upper limit
Age (year)	Continuous (year)	0.0465	1.018	1.00	1.04
Inpatient/Outpatient classification	Inpatient vs Outpatient*	0.0032	2.547	1.37	4.75

Background factor		p-value	Odds Ratio	95% CI	
				Lower limit	Upper limit
	Inpatient ↔ Outpatient vs Outpatient*	0.0021	2.868	1.46	5.62
Long-term user	Long-term vs Short-term*	0.1832	1.396	0.85	2.28
Concurrent disease	Yes vs No*	0.0002	2.447	1.52	3.94
Complication	Yes vs No*	0.9894	+∞+∞	0.00	+∞
Previous treatment for the indication	No vs Yes*	0.0359	0.625	0.40	0.97
	Unknown vs Yes*	0.9913	<0.001	0.00	+∞

*Reference level

Note) This logistic analysis was conducted after selecting variables by considering the following items.

* Specific variables were excluded due to multicollinearity.

* In case of the p-value<0.2 for both the medical history and the sub-variable, only the sub-variable was included in the model.

* Excluded in case the p-value is not <0.2 for the treatment-related variable for all indications in the subgroup (other than subgroup 2) analysis of safety analysis

Table 167 Logistic regression analysis (factors that affect safety) (IBD)

Background factor		p-value	Odds ratio	95% CI	
				Lower limit	Upper limit
Age (year)	Continuous (year)	0.058	1.013	1.00	1.03
Body weight (kg)	Continuous (kg)	0.0767	0.985	0.97	1.00
Long-term user	Long-term vs Short-term*	0.1819	1.343	0.87	2.07
Concurrent disease	Yes vs No*	0.0007	2.271	1.41	3.65
Tuberculosis and other severe infection	Yes vs No*	0.01	4.128	1.40	12.15

*Reference level

Note 1) This logistic analysis was conducted after selecting variables by considering the following items.

* Specific variables were excluded due to multicollinearity.

* In case of the p-value<0.2 for both the medical history and the sub-variable, only the sub-variable was included in the model.

* Excluded in case the p-value is not <0.2 for the treatment-related variable for all indications in the subgroup (other than subgroup 2) analysis of safety analysis

3.2 Efficacy assessment results

Among 1357 subjects in the Safety Analysis Set, 113 subjects who did not achieve efficacy assessment and 7 subject who received temporary Remicade (comparator) during surveillance drug treatment were excluded. Data from remaining 1237 subjects were included in efficacy assessment.

Number of subjects in efficacy analysis set by indication was as follows: 502 subjects for ankylosing spondylitis, 355 subjects for rheumatoid arthritis, 2 subjects for active progressive psoriatic arthritis(in adults), 6 subject for moderate to severe plaque psoriasis (in adults), 21 subjects for fistulizing active Crohn's disease (in adults), 159 subjects for moderate to severe active Crohn's disease (in adults), 47 subjects for severe active Crohn's disease (children and adolescents), 123 subjects for moderate to severe ulcerative colitis, and 22 subjects for moderate to severe ulcerative colitis (children and adolescents) (Table 168).

Table 168 Number of subjects for efficacy analysis set by indication

Classification		Efficacy Analysis Set	Short-term subject*	Long-term subject*
Indication	Patient classification			
Total		1237	946	703
AS	All	502	468	340
	Naïve subject	292	283	202
	Switched subject	210	185	138
RA	All	355	134	183
	Naïve subject	260	75	140
	Switched subject	95	59	43
PA	All	2	1	2
	Naïve subject	2	1	2
	Switched subject	0	0	0
PS	All	6	0	4
	Naïve subject	4	0	2
	Switched subject	2	0	2
FC	All	21	17	14
	Naïve subject	13	10	10
	Switched subject	8	7	4
SC	All	159	158	86
	Naïve subject	84	84	44
	Switched subject	75	74	42
PC	All	47	47	17
	Naïve subject	25	25	4

Classification		Efficacy Analysis Set	Short-term subject*	Long-term subject*
Indication	Patient classification			
	Switched subject	22	22	13
UC	All	123	100	50
	Naïve subject	94	79	38
	Switched subject	29	21	12
PU	All	22	21	7
	Naïve subject	15	14	2
	Switched subject	7	7	5

*Number of short-term and long-term subjects includes all subjects evaluated as Responder / Non-responder / Not evaluable.

Efficacy assessment was classified into naïve subjects and switched subjects, and was conducted according to the timing and criteria specified for each indication. If data was missing at the point of efficacy assessment, data from the nearest subsequent point were used. However, if efficacy assessment results was absent between short-term efficacy assessment point and long-term efficacy assessment point, short-term efficacy data was considered missing.
Subjects for whom the surveillance drug was their first anti-TNF agent were classified as naïve subjects, and subjects who had received anti-TNF prior to the surveillance drug were classified as switched subjects.Switched subjects were classified as responder if efficacy was maintained.

This subjects were applied following criteria to each indication for efficacy assessment.

Ankylosing spondylitis

Efficacy was evaluated pre-dose as well as Week 6 (42 ±14 days) and at Week 24-30 (168-210 ±14 days) after administration.

① Naïve subjects who met following criteria compared to pre-dose were considered responders. Otherwise, they were considered non-responders. The BASDAI has been reduced by 50% or more; and/or
② The BASDAI has been reduced by 2 or more points (on scale 0-10)

Switched subjects who met following criteria compared to pre-dose were considered to have maintained efficacy.

① The BASDAI has not been increased by 2 times or more compared with baseline value; and/or
② The BASDAI has not been increased by 2 or more points (on scale 0-10)

Main efficacy assessment used the results from Week 6 (42 ±14 days). For long-term (24-30 weeks [168 ~ 210 ±14 days]) subjects, difference between short-term and long-term results was analyzed.

Rheumatoid arthritis

Efficacy assessment based on ACR 3 criteria was conducted pre-dose as well as Week 14 (98 ± 14 days) and Week 38 (266 ± 14 days) after administration, while efficacy assessment based on DAS28 was conducted pre-dose and Week 30 (210 ± 14 days) after administraion.

Naïve subjects who met following criteria when post-dose results were compared to pre-dose results were considered responders. Otherwise, they were considered non-responders.

<ACR 3 criteria>

① The tender joint count has been reduced by 50% or more; and
② The swollen joint count has been reduced by 50% or more; and
③ The ESR is equal to or less than 28 mm/hr or the CRP is equal to or less than 2.0 mg/dl; OR the value (ESR or CRP) has decreased by 20% or more compared with baseline value.

<DAS28 criteria>

① The DAS28 has been reduced by 1.2 points or more points

Switched subjects who met following criteria when post-dose results were compared to pre-dose results were considered to have maintained efficacy.

<ACR 3 criteria>

① The tender and swollen joint count have not been increased by 2 times or more; and
② The ESR is equal to or less than 28 mm/hr or the CRP is equal to or less than 2.0 mg/dl; OR the value (ESR or CRP) has not been increased by 20% or more compared with baseline value.

<DAS28 criteria>

① The DAS28 has not been increased by 1.2 points or more points compared with baseline value

Main efficacy assessment used the results from Week 14 (98 ±14 days). For long-term (Week 38 [266 ±14 days]) subjects, difference between short-term and long-term results was analyzed. When DAS28 is used, short-term and long-term results were not analyzed since single long-term efficacy assessment was carried out at Week 30 (210 ±14 days).

Fistulizing active Crohn's disease (in adults)

Efficacy was evaluated pre-dose as well as Week 14 (98 ±14 days) and at Week 30 (210 ±14 days) after administration.

Naïve subjects who met following criteria when post-dose results were compared to pre-dose results were considered responders. Otherwise, they were considered non-responders.

① The number of fistulas has been reduced by 50% or more

Switched subjects who met following criteria when post-dose results were compared to pre-dose results were considered to have maintained efficacy.

① The number of fistulas has not been increased by 2 times or more compared with baseline value

Main efficacy assessment used the results from Week 14 (98 ±14 days). For long-term (30 weeks [210 ±14 days]) subjects, difference between short-term and long-term results was analyzed.

Moderate to severe active Crohn's disease (in adults)

Efficacy was evaluated pre-dose as well as Week 2 (14 ±14 days) and at Week 30 (210 ±14 days) after administration.

Naïve subjects who met following criteria when post-dose results were compared to pre-dose results were considered responders. Otherwise, they were considered non-responders.

① The CDAI has been reduced by 70 or more points; and/or

② The total CDAI score has decreased by 25% or more

Switched subjects who met following criteria when post-dose results were compared to pre-dose results were considered to have maintained efficacy.

① The CDAI has not been increased by 70 or more points compared with baseline value

Main efficacy assessment used the results from Week 2 (14 ±14 days). For long-term (30 weeks [210 ±14 days]) subjects, difference between short-term and long-term results was analyzed.

Children and adolescence (6-17 years of age) Crohn's disease

Efficacy was evaluated pre-dose as well as Week 2 (14 ±14 days) and at Week 30 (210 ±14 days) after administration.

Naïve subjects who met following criteria when post-dose results were compared to pre-dose results were considered responders. Otherwise, they were considered non-responders.

① The PCDAI has been reduced by 12.5 or more points; and/or

② The total PCDAI score has decreased by 25% or more

Switched subjects who met following criteria when post-dose results were compared to pre-dose results were considered to have maintained efficacy.

① The PCDAI has not been increased by 12.5 or more points compared with baseline value

Main efficacy assessment used the results from Week 2 (14 ±14 days). For long-term (30 weeks [210 ±14 days]) subjects, difference between short-term and long-term results was analyzed.

Moderate to severe ulcerative colitis

Efficacy was evaluated pre-dose as well as Week 14 (98 ±14 days) and at Week 30 (210 ±14 days) after

administration.

Naïve subjects who met following criteria when post-dose results were compared to pre-dose results were considered responders. Otherwise, they were considered non-responders.

① The MSS has been reduced by 30% or more and 3 or more points compared with baseline value; and
② The rectal bleeding sub-score is 0 or 1 point or has dropped by one or more points

Switched subjects who met following criteria when post-dose results were compared to pre-dose results were considered to have maintained efficacy.

① The MSS has not been increased by 1.43 times or more and 3 or more points compared with baseline value; and
② The rectal bleeding sub-score has not been increased by 1 or more points or the rectal bleeding sub-score is not more than 2 points

Main efficacy assessment used the results from Week 14 (98 ±14 days). For long-term (30 weeks [210 ±14 days]) subjects, difference between short-term and long-term results was analyzed.

Children and adolescence (6-17 years of age) ulcerative colitis

Efficacy was evaluated pre-dose as well as Week 14 (98 ±14 days) and at Week 30 (210 ±14 days) after administration.

Naïve subjects who met following criteria when post-dose results were compared to pre-dose results were considered responders. Otherwise, they were considered non-responders.

① The PUCAI has been reduced by 20 or more points compared with baseline value

Switched subjects who met following criteria when post-dose results were compared to pre-dose results were considered to have maintained efficacy.

① The PUCAI has not been increased by 20 or more points compared with baseline value

Main efficacy assessment used the results from Week 14 (98 ±14 days). For long-term (30 weeks [210 ±14 days]) subjects, difference between short-term and long-term results was analyzed.

Active progressive psoriatic arthritis (in adults)

Efficacy was evaluated pre-dose as well as Week 14 (98 ±14 days) and at Week 30 (210 ±14 days) after administration.

Naïve subjects who met following criteria when post-dose results were compared to pre-dose results were considered responders. Otherwise, they were considered non-responders.

① The active joint count (tender joint count and swollen joint count) has been reduced by 30% or more compared with baseline value rst dose

Switched subjects who met following criteria when post-dose results were compared to pre-dose results were considered to have maintained efficacy.

① The active joint count (tender joint count and swollen joint count) has not been increased by 1.43 times or more compared with baseline value

Main efficacy assessment used the results from Week 14 (98 ±14 days). For long-term (30 weeks [210 ±14 days]) subjects, difference between short-term and long-term results was analyzed.

Moderate to severe plaque psoriasis (in adults)

Efficacy was evaluated pre-dose as well as Week 22 (154 ±14 days) after administration.

Naïve subjects who met following criteria when post-dose results were compared to pre-dose results were considered responders. Otherwise, they were considered non-responders.

① The PASI has been reduced by 85% or more

Switched subjects who met following criteria when post-dose results were compared to pre-dose results were considered to have maintained efficacy.

① The PASI has not been increased by 4 times or more compared with baseline value

3.2.1 Effective Ratio for Each Indication

Among subjects who received the surveillance drug for ankylosing spondylitis, 502 subjects were included in the efficacy evaluation. Among these subjects, 468 and 340 were assessed for short-term and long-term efficacy, respectively; of these, 193 naïve subjects and 112 switched subjects had both short-term and long-term efficacy assessment results. Response rate was 96.79% (453/468subjects) for short-term, and 96.47% (328/340subjects) for long-term. Short-term and long-term efficacy assessment results for naïve subjects showed changes of "responder → non-responder" 3.63% (7/193 subjects) and "non-responder → responder" 0.52% (1/193 subjects) which were statistically significant (p=0.0339), and while the efficacy assessment results for switched subjects showed changes of "responder → non-responder" 0.89% (1/112 subjects) and "non-responder → responder" 4.46% (5/112 subjects), although statistically not significant (p=0.1025, Table 169 and Table 170).

Among subjects who received the surveillance drug for rheumatoid arthritis, 355 subjects were included in the efficacy evaluation. Among these subjects, 134 and 183 were assessed for short-term and long-term efficacy, respectively. For 110 subjects, Long-term efficacy assessment was conducted using the DAS28. 48 naïve subjects and 23 switched subjects had both short-term and long-term efficacy assessment results. Response rate was 76.12% (102/134 subjects) for short-term, and 87.98% (161/183 subjects) for long-term. Short-term and long-term efficacy assessment results for naïve subjects showed changes of "responder → non-responder" 6.25% (3/48 subjects) and "non-responder → responder" 2.08% (1/48 subjects), although statistically not significant (p=0.3173), short-term and long-term efficacy assessment results for switched subjects showed changes of "responder → non-responder" 8.70% (2/23 subjects) and "non-responder → responder" 8.70% (2/23 subjects), although statistically not significant (p=1.0000, Table 169 and Table 170).

Among subjects who received the surveillance drug for active progressive psoriatic arthritis (in adults), 2 subjects were included in efficacy evaluation. Among these subjects, 1 and 2 were assessed for short-term and long-term efficacy, respectively. 1 naïve subject had both short-term and long-term efficacy results. Response rate was 100.00% (1/1 subject) for both short-term and long-term, indicating no change in efficacy results (Table 169 and Table 170).

Among subjects who received the surveillance drug for moderate to severe plaque psoriasis (in adults), 6 subjects were included in efficacy evaluation. Among these subjects, 4 were assessed for long-term efficacy. Response rate was 75.00% (3/4 subject) for long-term.

Among subjects who received the surveillance drug for fistulizing active Crohn's disease (in adults), 21 subjects were included in efficacy evaluation. Among these subjects, 17 and 14 were assessed for short-term and long-term efficacy, respectively. of these, 8 naïve subjects and 4 switched subjects had both short-term and long-term efficacy results. Response rate was short-term 82.35% (14/17 subjects) and long-term 78.57% (11/14 subjects), indicating no change in efficacy results (Table 169 and Table 170).

Among subjects who received the surveillance drug for moderate to severe active Crohn's disease (in adults), 159 subjects were included in efficacy evaluation. 158 and 86 were assessed for the short-term and long-term efficacy, respectively; of these, 40 naïve subjects and 41 switched subjects had both short-term and long-term efficacy results. Response rate was 91.77% (145/158 subjects) for short-term

and 93.02% (80/86 subjects) for long-term. Short-term and long-term efficacy assessment results for naïve subjects showed a change of "non-responder → responder" 2.50% (1/40 subjects), although statistically not significant (p=0.3173), and short-term and long-term efficacy assessment results for switched subjects showed changes of "responder → non-responder" 2.44% (1/41 subjects) and "non-responder → responder" 2.44% (1/41 subjects), although statistically not significant (P=1.0000, Table 169 and Table 170).

Among subjects who received the surveillance drug for severe active Crohn's disease (children and adolescents), 47 subjects were included in efficacy evaluation. Among these subjects, 47 and 17 were assessed for short-term and long-term efficacy, respectively; of these, 4 naïve subjects and 13 switched subjects had both short-term and long-term efficacyresults. . Response rate was short-term 78.72% (37/47 subjects) for short-term and 100.0% (17/17 subjects) for long-term, indicating no change in efficacy results for naïve subjects (Table 163 and Table 164).

Among subjects who received the surveillance drug for moderate to severe ulcerative colitis, 123 subjects were included in efficacy evaluation. Among these subjects, 100 and 50 were assessed for short-term and long-term efficacy, respectively; of these, 20 naïve subjects and 1 switched subject had both short-term and long-term efficacy results. Response rate was 64.00% (64/100 subjects) for short-term and 46.00% (23/50 subjects) for long-term. Short-term and long-term efficacy assessment results for naïve subjects showed changes of "responder → non-responder" 5.00% (1/20 subjects) and "non-responder → responder" 5.00% (1/20 subjects), although statistically not significant (p=1.0000), indicating no change in efficacy results for switched subjects (Table 169 and Table 170).

Among subjects who received the surveillance drug for moderate to severe ulcerative colitis (children and adolescents), 22 subjects were included in efficacy evaluation.Among these subjects, 21 and 7 were included in the short-term and long-term efficacy, respectively; of these, 4 naïve subjects and 5 switched subjects had both short-term and long-term efficacy results. Response rate was 33.33% (7/21 subjects) for short-term, and 71.43% (5/7 subjects) for long-term. Short-term and long-term efficacy assessment results for switched subjects showed a change of "responder → non-responder" 20.00% (1/5 subjects), indicating no change in efficacy results (P=0.3173, Table 169 and Table 170).

Table 169 Short-term and long-term response rate by indication and subject (naïve/switched)

			Responder		Non-responder		Not evaluable[1)]	
			n	(%)	n	(%)	n	(%)
AS	Total	Short (N=468)	453	(96.79)	14	(2.99)	1	(0.21)
		Long (N=340)	328	(96.47)	10	(2.94)	2	(0.59)
	Naïve subject	Short (N=283)	276	(97.53)	7	(2.47)	0	(0.00)
		Long (N=202)	192	(95.05)	9	(4.46)	1	(0.50)
	Switched subject	Short (N=185)	177	(95.68)	7	(3.78)	1	(0.54)
		Long (N=138)	136	(98.55)	1	(0.72)	1	(0.72)
RA[2)]	Total	Short (N=134)	102	(76.12)	32	(23.88)	0	(0.00)
		Long (N=183)	161	(87.98)	19	(10.38)	3	(1.64)

			Responder		Non-responder		Not evaluable[1)]	
			n	(%)	n	(%)	n	(%)
	Naïve subject	Short (N=75)	50	(66.67)	25	(33.33)	0	(0.00)
		Long (N=140)	122	(87.14)	16	(11.43)	2	(1.43)
	Switched subject	Short (N=59)	52	(88.14)	7	(11.86)	0	(0.00)
		Long (N=43)	39	(90.70)	3	(6.98)	1	(2.33)
PA	Total	Short (N=1)	1	(100.0)	0	(0.00)	0	(0.00)
		Long (N=2)	2	(100.0)	0	(0.00)	0	(0.00)
	Naïve subject	Short (N=1)	1	(100.0)	0	(0.00)	0	(0.00)
		Long (N=2)	2	(100.0)	0	(0.00)	0	(0.00)
	Switched subject	Short (N=0)	0	(NA)	0	(NA)	0	(NA)
		Long (N=0)	0	(NA)	0	(NA)	0	(NA)
PS[3)]	Total	Long (N=4)	3	(75.00)	1	(25.00)	0	(0.00)
	Naïve subject	Long (N=2)	1	(50.00)	1	(50.00)	0	(0.00)
	switched subject	Long (N=2)	2	(100.0)	0	(0.00)	0	(0.00)
FC	Switched subject	Short (N=17)	14	(82.35)	3	(17.65)	0	(0.00)
		Long (N=14)	11	(78.57)	3	(21.43)	0	(0.00)
	Naïve subject	Short (N=10)	7	(70.00)	3	(3.00)	0	(0.00)
		Long (N=10)	7	(70.00)	3	(3.00)	0	(0.00)
	Switched subject	Short (N=7)	7	(100.0)	0	(0.00)	0	(0.00)
		Long (N=4)	4	(100.0)	0	(0.00)	0	(0.00)
SC	Total	Short (N=158)	145	(91.77)	10	(6.33)	3	(1.90)
		Long (N=86)	80	(93.02)	4	(4.65)	2	(2.33)
	Naïve subject	Short (N=84)	74	(88.10)	7	(8.33)	3	(3.57)
		Long (N=44)	39	(88.64)	3	(6.82)	2	(4.55)
	Switched subject	Short (N=74)	71	(95.95)	3	(4.05)	0	(0.00)
		Long (N=42)	41	(97.62)	1	(2.38)	0	(0.00)
PC	Total	Short (N=47)	37	(78.72)	9	(19.15)	1	(2.13)
		Long (N=17)	17	(100.0)	0	(0.00)	0	(0.00)
	Naïve subject	Short (N=25)	15	(60.00)	9	(36.00)	1	(4.00)
		Long (N=4)	4	(100.0)	0	(0.00)	0	(0.00)
	Switched	Short (N=22)	22	(100.0)	0	(0.00)	0	(0.00)

			Responder		Non-responder		Not evaluable[1)]	
			n	(%)	n	(%)	n	(%)
	subject	Long (N=13)	13	(100.0)	0	(0.00)	0	(0.00)
UC	Total	Short (N=100)	64	(64.00)	12	(12.00)	24	(24.00)
		Long (N=50)	23	(46.00)	5	(10.00)	22	(44.00)
	Naïve subject	Short (N=79)	57	(72.15)	9	(11.39)	13	(16.46)
		Long (N=38)	20	(52.63)	5	(13.16)	13	(34.21)
	Switched subject	Short (N=21)	7	(33.33)	3	(14.29)	11	(52.38)
		Long (N=12)	3	(25.00)	0	(0.00)	9	(75.00)
PU	Total	Short (N=21)	7	(33.33)	14	(66.67)	0	(0.00)
		Long (N=7)	5	(71.43)	2	(28.57)	0	(0.00)
	Naïve subject	Short (N=14)	0	(0.00)	14	(100.0)	0	(0.00)
		Long (N=2)	0	(0.00)	2	(100.0)	0	(0.00)
	Switched subject	Short (N=7)	7	(100.0)	0	(0.00)	0	(0.00)
		Long (N=5)	5	(100.0)	0	(0.00)	0	(0.00)

[1)] Not evaluable due to some missing efficacy assessment items

[2)] Of Long-term efficacy assessment patients, 110 subjects were assessed using the DAS28 Criteria

[3)] For moderate to severe plaque psoriasis (in adults), efficacy assessment was conducted at posttreatment 22 weeks (154±14 days), and short- and Long-term result analysis was not performed.

Table 170 Change in response rate between short-term and long-term by indication and subject (naïve/switched)

Short-term[2)] \ Long-term		Responder		Non-responder		p-value[1)]
		n	(%)	n	(%)	
AS naïve subject (N=193)	Responder	183	(94.82)	7	(3.63)	0.0339
	Non-responder	1	(0.52)	2	(1.04)	
AS switched subject (N=112)	Responder	106	(94.64)	1	(0.89)	0.1025
	Non-responder	5	(4.46)	0	(0.00)	
RA naïve subject (N=48)	Responder	34	(70.83)	3	(6.25)	0.3173
	Non-responder	1	(2.08)	10	(20.83)	
RA switched subject[3)] (N=23)	Responder	18	(78.26)	2	(8.70)	1.0000
	Non-responder	2	(8.70)	1	(4.35)	

Short-term[2] \ Long-term		Responder		Non-responder		p-value[1]
		n	(%)	n	(%)	
PA naïve subject (N=1)	Responder	1	(100.0)	0	(0.00)	-
	Non-responder	0	(0.00)	0	(0.00)	
PA switched subject (N=0)	Responder	0	(NA)	0	(NA)	-
	Non-responder	0	(NA)	0	(NA)	
FC naïve subject (N=8)	Responder	6	(75.00)	0	(0.00)	--
	Non-responder	0	(0.00)	2	(25.00)	
FC switched subject (N=4)	Responder	4	(100.0)	0	(0.00)	--
	Non-responder	0	(0.00)	0	(0.00)	
SC naïve subject (N=40)	Responder	36	(90.00)	0	(0.00)	0.3173
	Non-responder	1	(2.50)	3	(7.50)	
SC switched subject (N=41)	Responder	39	(95.12)	1	(2.44)	1.0000
	Non-responder	1	(2.44)	0	(0.00)	
PC naïve subject (N=4)	Responder	4	(100.0)	0	(0.00)	--
	Non-responder	0	(0.00)	0	(0.00)	
PC switched subject (N=13)	Responder	13	(100.0)	0	(0.00)	--
	Non-responder	0	(0.00)	0	(0.00)	
UC naïve subject (N=20)	Responder	16	(80.00)	1	(5.00)	1.0000
	Non-responder	1	(5.00)	2	(10.00)	
UC switched subject (N=1)	Responder	1	(100.0)	0	(0.00)	-
	Non-responder	0	(0.00)	0	(0.00)	
PU naïve subject (N=4)	Responder	2	(0.00)	0	(0.00)	--
	Non-responder	0	(0.00)	0	(0.00)	
PU switched subject (N=5)	Responder	4	(80.00)	1	(20.00)	0.3173

Short-term[2] \ Long-term		Responder		Non-responder		p-value[1]
		n	(%)	n	(%)	
	Non-responder	0	(0.00)	0	(0.00)	

[1] McNemar's test
[2] Number of subjects in each indication is the number of subjects who completed short-term and long-term efficacy assessment.
[3] Only subjects assessed using the ACR 3 were included in Short-term and Long-term effective rate change analysis.

3.2.2 Efficacy assessment by factor

Of indications, active progressive psoriatic arthritis (in adults) cases were all surveyed as effective, so that the efficacy assessment by factor was not separately described.

Efficacy was analyzed as responder and non-responder for Short-term according to the main efficacy assessment criteria; however, as only long-term assessment was performed for rheumatoid arthritis subjects using the DAS28 and main efficacy assessment for moderate to severe plaque psoriasis (in adults), long-term efficacy assessment results were reflected in analysis by factor.

1) Sex

From response rate analysis by sex, in ankylosing spondylitis naïve subjects, it was female 98.44% (63/64 subjects) and male 97.26% (213/219 subjects), and in switched subjects, it was male 97.10% (134/138 subjects) and female 93.48% (43/46 subjects). In RA naïve subjects, it was male 85.71% (30/35 subjects) and female 82.31% (107/130 subjects), and in switched subjects, it was female 90.91% (60/66 subjects) and male 90.00% (9/10 subjects). In moderate to severe plaque psoriasis (in adults) naïve subjects, it was female 50.00% (1/2 subjects) and in switched subjects, it was all effective in female and male. In fistulizing active Crohn's disease (in adults) naïve subjects, it was female 50.00% (1/2 subjects) and male 75.00% (6/8 subjects), and in switched subjects, it was male 100.0% (6/6 subjects) and female 100.0% (1/1 subject). In moderate to severe active Crohn's disease (in adults) naïve subjects, it was female 94.74% (18/19 subjects) and male 90.32% (56/62 subjects), and in switched subjects, it was male 96.23% (51/53 subjects) and female 95.24% (20/21 subjects). In moderate to severe active Crohn's disease (children and adolescents) naïve subjects, it was female 53.85% (7/13 subjects) and male 72.73% (8/11 subjects), and in switched subjects, it was all responder in male and female. In moderate to severe naïve ulcerative colitis patients, it was male 83.33% (35/42 subjects) and female 91.67% (22/24 subjects), and in switched subjects, it was female 80.00% (4/5 subjects) and male 60.00% (3/5 subjects). In moderate to severe ulcerative colitis (children and adolescents) naïve subjects, it was non-responder in both male and female, and in switched subjects, it was all responder in male and female, and of these, there was no indication showing a statistically significant difference (Table 171).

Table 171 Efficacy assessment by sex

Sex		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	Male	213	(97.26)	6	(2.74)	219	(77.39)	1.0000[2)]
	Female	63	(98.44)	1	(1.56)	64	(22.61)	
Total		276	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	Male	134	(97.10)	4	(2.90)	138	(75.00)	0.3690[2)]
	Female	43	(93.48)	3	(6.52)	46	(25.00)	
Total		177	(96.20)	7	(3.80)	184	(100.0)	
RA naïve subject	Male	30	(85.71)	5	(14.29)	35	(21.21)	0.6337[1)]
	Female	107	(82.31)	23	(17.69)	130	(78.79)	
Total		137	(83.03)	28	(16.97)	165	(100.0)	

Sex		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
RA switched subject	Male	9	(90.00)	1	(10.00)	10	(13.16)	1.0000[2)]
	Female	60	(90.91)	6	(9.09)	66	(86.84)	
Total		69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	Male	1	(100.0)	0	(0.00)	1	(100.0)	-
	Female	0	(NA)	0	(NA)	0	(NA)	
Total		1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	Male	0	(NA)	0	(NA)	0	(NA)	-
	Female	0	(NA)	0	(NA)	0	(NA)	
Total		0	(NA)	0	(NA)	0	(NA)	
PS naïve subject	Male	0	(NA)	0	(NA)	0	(NA)	-
	Female	1	(50.00)	1	(50.00)	2	(100.0)	
Total		1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	Male	1	(100.0)	0	(0.00)	1	(50.00)	-
	Female	1	(100.0)	0	(0.00)	1	(50.00)	
Total		2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	Male	6	(75.00)	2	(25.00)	8	(80.00)	1.0000[2)]
	Female	1	(50.00)	1	(50.00)	2	(20.00)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	Male	6	(100.0)	0	(0.00)	6	(85.71)	-
	Female	1	(100.0)	0	(0.00)	1	(14.29)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	Male	56	(90.32)	6	(9.68)	62	(76.54)	1.0000[2)]
	Female	18	(94.74)	1	(5.26)	19	(23.46)	
Total		74	(91.36)	7	(8.64)	81	(100.0)	
SC switched subject	Male	51	(96.23)	2	(3.77)	53	(71.62)	1.0000[2)]
	Female	20	(95.24)	1	(4.76)	21	(28.38)	
Total		71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	Male	8	(72.73)	3	(27.27)	11	(45.83)	0.4225[2)]
	Female	7	(53.85)	6	(46.15)	13	(54.17)	
Total		15	(62.50)	9	(37.50)	24	(100.0)	
PC	Male	12	(100.0)	0	(0.00)	12	(54.55)	-

Sex		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
switched subject	Female	10	(100.0)	0	(0.00)	10	(45.45)	
Total		22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	Male	35	(83.33)	7	(16.67)	42	(63.64)	0.4689[2)]
	Female	22	(91.67)	2	(8.33)	24	(36.36)	
Total		57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	Male	3	(60.00)	2	(40.00)	5	(50.00)	1.0000[2)]
	Female	4	(80.00)	1	(20.00)	5	(50.00)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
PU naïve subject	Male	0	(0.00)	8	(100.0)	8	(57.14)	-
	Female	0	(0.00)	6	(100.0)	6	(42.86)	
Total		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	Male	2	(100.0)	0	(0.00)	2	(28.57)	-
	Female	5	(100.0)	0	(0.00)	5	(71.43)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Chi-square test / [2)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

2) Age

From response rate analysis by age, the maximum and minimum responder rates were as follows: in AS naïve subjects, 100.0% (17/17 subjects, 8/8 subjects and 1/1 subject, respectively) in 60 to <70 years, 18 to <20 years and ≥70 years and 95.00% (38/40 subjects) in 50 to <60 years; in AS switched subjects, 100.0% (30/30 subjects, 8/8 subjects and 2/2 subjects, respectively) in 50 to <60 years, 60 to <70 years, 18 to <20 years and 94.59% (35/37 subjects) in 40 to <50 years; in RA naïve subjects, 93.10% (27/29 subjects) in 60 to <70 years and 66.67% (10/15 subjects) in ≥70 years; in RA switched subjects, 100.0% (9/9 subjects, 6/6 subjects, 4/4 subjects and 1/1 subject, respectively) in ≥70 years, 30 to <40 years, 20 to <30 years, 18 to <20 years and 80.00% (8/10 subjects) in 40 to <50 years; in PS naïve subjects, 100.0% (1/1 subject) in 50 to <60 years and 0% (0/1 subject) in 40 to <50 years; in PS switched subjects, 100.0% (1/1 subject and 1.1 subject, respectively) in 50 to <60 years and20 to <30 years; in FC naïve subjects, 100.0% (3/3 subjects, 2/2 subjects and 1/1 subject, respectively) in 18 to <20 years, 20 to <30 years and 40 to <50 years and 0.00% (0/2 subjects) in 30 to <40 years; in SC naïve subjects, 100.0% (23/23 subjects and 2/2 subjects, respectively) in 30 to <40 years and 60 to <70 years and 50% (1/2 subjects) in ≥70 years; in SC switched subjects, 100.0% (12/12 subjects, 10/10 subjects, 2/2 subjects and 1/1 subject, respectively) in 30 to <40 years, 40 to <50 years, 50 to <60 years and 60 to <70 years and 91.67% (11/12 subjects) in 18 to <20 years; in PC naïve subjects, 62.50% (15/24 subjects) in <20 years; in PC switched subjects, 100.0% (22/22 subjects) in <20 years; in UC naïve subjects, 100.0% (3/3 subjects) in 18 to <20 years and 77.78% (7/9 subjects) in 30 to <40 years; and in UC switched subjects, 100.0% (2/2 subjects, 1/1 subject and 1/1 subject, respectively) in 50 to <60 years, 20 to <30 years and ≥70 years and 50% (1/2 subjects, 1/2 subjects and 1/2 subjects, respectively) in 60 to <70 years, 40 to <50 and 30 to <40; in PU naïve subjects, 0.00% (0/14 subjects) in <20 years; and in PU switched subjects, 100.0%

(7/7 subjects) in <20 years, and there was no indication with a statistically significant difference (Table 172).

Table 172 Efficacy assessment by age

Age (unit: year)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	18 to <20	8	(100.0)	0	(0.00)	8	(2.83)	0.8867[1)]
	20 to <30	72	(97.30)	2	(2.70)	74	(26.15)	
	30 to <40	76	(97.44)	2	(2.56)	78	(27.56)	
	40 to <50	64	(98.46)	1	(1.54)	65	(22.97)	
	50 to <60	38	(95.00)	2	(5.00)	40	(14.13)	
	60 to <70	17	(100.0)	0	(0.00)	17	(6.01)	
	≥70	1	(100.0)	0	(0.00)	1	(0.35)	
Total		276	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	18 to <20	2	(100.0)	0	(0.00)	2	(1.09)	0.5526[1)]
	20 to <30	39	(97.50)	1	(2.50)	40	(21.74)	
	30 to <40	56	(94.94)	3	(5.08)	59	(32.07)	
	40 to <50	35	(94.59)	2	(5.41)	37	(20.11)	
	50 to <60	30	(100.0)	0	(0.00)	30	(16.30)	
	60 to <70	8	(100.0)	0	(0.00)	8	(4.35)	
	≥70	7	(87.50)	1	(12.50)	8	(4.35)	
Total		177	(96.20)	7	(3.80)	184	(100.0)	
RA naïve subject	18 to <20	0	(NA)	0	(NA)	0	(NA)	0.3275[1)]
	20 to <30	4	(80.00)	1	(20.00)	5	(3.03)	
	30 to <40	11	(78.57)	3	(21.43)	14	(8.48)	
	40 to <50	27	(84.38)	5	(15.63)	32	(19.39)	
	50 to <60	58	(82.86)	12	(17.14)	70	(42.42)	
	60 to <70	27	(93.10)	2	(6.90)	29	(17.58)	
	≥70	10	(66.67)	5	(33.33)	15	(9.09)	
Total		137	(83.03)	28	(16.97)	165	(100.0)	
RA switched subject	18 to <20	1	(100.0)	0	(0.00)	1	(1.32)	0.7976[1)]
	20 to <30	4	(100.0)	0	(0.00)	4	(5.26)	
	30 to <40	6	(100.0)	0	(0.00)	6	(7.89)	
	40 to <50	8	(80.00)	2	(20.00)	10	(13.16)	
	50 to <60	28	(90.32)	3	(9.68)	31	(40.79)	

Age (unit: year)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
	60 to <70	13	(86.67)	2	(13.33)	15	(19.74)	
	≥70	9	(100.0)	0	(0.00)	9	(11.84)	
Total		69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	18 to <20	0	(NA)	0	(NA)	0	(NA)	-
	20 to <30	0	(NA)	0	(NA)	0	(NA)	
	30 to <40	0	(NA)	0	(NA)	0	(NA)	
	40 to <50	0	(NA)	0	(NA)	0	(NA)	
	50 to <60	1	(100.0)	0	(0.00)	1	(100.0)	
	60 to <70	0	(NA)	0	(NA)	0	(NA)	
	≥70	0	(NA)	0	(NA)	0	(NA)	
Total		1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	18 to <20	0	(NA)	0	(NA)	0	(NA)	-
	20 to <30	0	(NA)	0	(NA)	0	(NA)	
	30 to <40	0	(NA)	0	(NA)	0	(NA)	
	40 to <50	0	(NA)	0	(NA)	0	(NA)	
	50 to <60	0	(NA)	0	(NA)	0	(NA)	
	60 to <70	0	(NA)	0	(NA)	0	(NA)	
	≥70	0	(NA)	0	(NA)	0	(NA)	
Total		0	(NA)	0	(NA)	0	(NA)	
PS naïve subject	18 to <20	0	(NA)	0	(NA)	0	(NA)	1.0000[1)]
	20 to <30	0	(NA)	0	(NA)	0	(NA)	
	30 to <40	0	(NA)	0	(NA)	0	(NA)	
	40 to <50	0	(0.00)	1	(100.0)	1	(50.00)	
	50 to <60	1	(100.0)	0	(0.00)	1	(50.00)	
	60 to <70	0	(NA)	0	(NA)	0	(NA)	
	≥70	0	(NA)	0	(NA)	0	(NA)	
Total		1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	18 to <20	0	(NA)	0	(NA)	0	(NA)	-
	20 to <30	1	(100.0)	0	(0.00)	1	(50.00)	
	30 to <40	0	(NA)	0	(NA)	0	(NA)	
	40 to <50	0	(NA)	0	(NA)	0	(NA)	

Age (unit: year)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
	50 to <60	1	(100.0)	0	(0.00)	1	(50.00)	
	60 to <70	0	(NA)	0	(NA)	0	(NA)	
	≥70	0	(NA)	0	(NA)	0	(NA)	
Total		2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	18 to <20	3	(100.0)	0	(0.00)	3	(30.00)	
	20 to <30	2	(100.0)	0	(0.00)	2	(20.00)	
	30 to <40	0	(0.00)	2	(100.0)	2	(20.00)	
	40 to <50	1	(100.0)	0	(0.00)	1	(10.00)	0.1333[1)]
	50 to <60	1	(50.00)	1	(50.00)	2	(20.00)	
	60 to <70	0	(NA)	0	(NA)	0	(NA)	
	≥70	0	(NA)	0	(NA)	0	(NA)	
Total		7	(70.00)	3	(30.00)	6	(100.0)	
FC switched subject	18 to <20	0	(NA)	0	(NA)	0	(NA)	
	20 to <30	4	(100.0)	0	(0.00)	4	(57.14)	
	30 to <40	0	(NA)	0	(NA)	0	(NA)	
	40 to <50	2	(100.0)	0	(0.00)	2	(28.57)	-
	50 to <60	1	(100.0)	0	(0.00)	1	(14.29)	
	60 to <70	0	(NA)	0	(NA)	0	(NA)	
	≥70	0	(NA)	0	(NA)	0	(NA)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	18 to <20	7	(87.50)	1	(12.50)	8	(9.88)	
	20 to <30	31	(91.18)	3	(8.82)	34	(41.98)	
	30 to <40	23	(100.0)	0	(0.00)	23	(28.40)	
	40 to <50	8	(88.89)	1	(11.11)	9	(11.11)	0.0838[1)]
	50 to <60	2	(66.67)	1	(33.33)	3	(3.70)	
	60 to <70	2	(100.0)	0	(0.00)	2	(2.47)	
	≥70	1	(50.00)	1	(50.00)	2	(2.47)	
Total		74	(91.36)	7	(8.64)	81	(100.0)	
SC switched subject	18 to <20	11	(91.67)	1	(8.33)	12	(16.22)	
	20 to <30	35	(94.59)	2	(5.41)	37	(50.00)	1.0000[1)]
	30 to <40	12	(100.0)	0	(0.00)	12	(16.22)	

Age (unit: year)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
	40 to <50	10	(100.0)	0	(0.00)	10	(13.51)	
	50 to <60	2	(100.0)	0	(0.00)	2	(2.70)	
	60 to <70	1	(100.0)	0	(0.00)	1	(1.35)	
	≥70	0	(NA)	0	(NA)	0	(NA)	
Total		71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	<20	15	(62.50)	9	(37.50)	24	(100.0)	-
	20 to <30	0	(NA)	0	(NA)	0	(NA)	
	30 to <40	0	(NA)	0	(NA)	0	(NA)	
	40 to <50	0	(NA)	0	(NA)	0	(NA)	
	50 to <60	0	(NA)	0	(NA)	0	(NA)	
	60 to <70	0	(NA)	0	(NA)	0	(NA)	
	≥70	0	(NA)	0	(NA)	0	(NA)	
Total		15	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	<20	22	(100.0)	0	(0.00)	22	(100.0)	-
	20 to <30	0	(NA)	0	(NA)	0	(NA)	
	30 to <40	0	(NA)	0	(NA)	0	(NA)	
	40 to <50	0	(NA)	0	(NA)	0	(NA)	
	50 to <60	0	(NA)	0	(NA)	0	(NA)	
	60 to <70	0	(NA)	0	(NA)	0	(NA)	
	≥70	0	(NA)	0	(NA)	0	(NA)	
Total		22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	18 to <20	3	(100.0)	0	(0.00)	3	(4.55)	0.9832[1)]
	20 to <30	9	(81.82)	2	(18.18)	11	(16.67)	
	30 to <40	7	(77.78)	2	(22.22)	9	(13.64)	
	40 to <50	15	(88.24)	2	(11.76)	17	(25.76)	
	50 to <60	10	(90.91)	1	(9.09)	11	(16.67)	
	60 to <70	7	(87.50)	1	(12.50)	8	(12.12)	
	≥70	6	(85.71)	1	(14.29)	7	(10.61)	
Total		57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	18 to <20	0	(NA)	0	(NA)	0	(NA)	1.0000[1)]
	20 to <30	1	(100.0)	0	(0.00)	1	(10.00)	

Age (unit: year)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
	30 to <40	1	(50.00)	1	(50.00)	2	(20.00)	
	40 to <50	1	(50.00)	1	(50.00)	2	(20.00)	
	50 to <60	2	(100.0)	0	(0.00)	2	(20.00)	
	60 to <70	1	(50.00)	1	(50.00)	2	(20.00)	
	≥70	1	(100.0)	0	(0.00)	1	(10.00)	
Total		7	(70.00)	3	(33.33)	10	(100.0)	
PU naïve subject	<20	0	(0.00)	14	(100.0)	14	(100.0)	-
	20 to <30	0	(NA)	0	(NA)	0	(NA)	
	30 to <40	0	(NA)	0	(NA)	0	(NA)	
	40 to <50	0	(NA)	0	(NA)	0	(NA)	
	50 to <60	0	(NA)	0	(NA)	0	(NA)	
	60 to <70	0	(NA)	0	(NA)	0	(NA)	
	≥70	0	(NA)	0	(NA)	0	(NA)	
Total		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	<20	7	(100.0)	0	(0.00)	7	(100.0)	-
	20 to <30	0	(NA)	0	(NA)	0	(NA)	
	30 to <40	0	(NA)	0	(NA)	0	(NA)	
	40 to <50	0	(NA)	0	(NA)	0	(NA)	
	50 to <60	0	(NA)	0	(NA)	0	(NA)	
	60 to <70	0	(NA)	0	(NA)	0	(NA)	
	≥70	0	(NA)	0	(NA)	0	(NA)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

3) Inpatient/outpatient classification

From response rate analysis by inpatient, outpatient, inpatient ↔ outpatient classification, the result was as follows: in AS naïve subjects, 94.74% (18/19 subjects), 97.84% (226/231 subjects) and 96.97% (32/33 subjects), respectively; in AS switched subjects, 100.0% (3/3 subjects), 95.93% (165/172 subjects) and 100.0% (9/9 subjects), respectively; in RA naïve subjects, 88.46% (23/26 subjects), 85.98% (92/107 subjects) and 68.75% (22/32 subjects), respectively; in RA switched subjects, 100.0% (4/4 subjects), 89.39% (59/66 subjects) and 100.0% (6/6 subjects), respectively; in PA naïve subjects, outpatient 100.0% (1/1 subject); in PS naïve subjects, outpatient 50.00% (1/2 subjects); in PS switched

subjects, outpatient 100% (2/2 subjects); in FC naïve subjects, inpatient 77.78% (7/9 subjects), outpatient 0.00% (1/2 subjects); in FC switched subjects, inpatient 100.0% (1/1 subject), outpatient 100.0% (6/6 subjects); in SC naïve subjects 86.67% (26/30 subjects), 97.14% (34/35 subjects) and 87.50% (14/16 subjects), respectively; in SC switched subjects, 100.0% (13/13 subjects), 96.49% (55/57 subjects) and 75.00% (3/4 subjects), respectively; in PC naïve subjects, 62.50% (10/16 subjects), 25.00% (1/4 subjects) and 100.0% (4/4 subjects), respectively; in PC switched subjects, 100.0% (4/4 subjects), 100.0% (15/15 subjects) and 100.0% (3/3 subjects), respectively; in UC naïve subjects, 78.26% (18/23 subjects), 88.24% (30/34 subjects) and 100.0% (9/9 subjects), respectively; in UC switched subjects, 66.67% (2/3 subjects), 66.67% (4/6 subjects) and 100.0% (1/1 subject), respectively; in PU naïve subjects, inpatient 0.00% (0/14 subjects); and in PU switched subjects, 100.0% (1/1 subject), 100.0% (4/4 subjects) and 100.0% (2/2 subjects), respectively, and there was no indication with a statistically significant difference (Table 173).

Table 173 Efficacy assessment by inpatient/outpatient classification

Inpatient/Outpatient classification		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	Inpatient	18	(94.74)	1	(5.26)	19	(6.71)	0.3787[2)]
	Outpatient	226	(97.84)	5	(2.16)	231	(81.63)	
	Inpatient ↔ Outpatient	32	(96.97)	1	(3.03)	33	(11.66)	
Total		276	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	Inpatient	3	(100.0)	0	(0.00)	3	(1.63)	1.0000[2)]
	Outpatient	165	(95.93)	7	(4.07)	172	(93.48)	
	Inpatient ↔ Outpatient	9	(100.0)	0	(0.00)	9	(4.89)	
Total		177	(96.20)	7	(3.80)	184	(100.0)	
RA naïve subject	Inpatient	23	(88.46)	3	(11.54)	26	(15.76)	0.0540[1)]
	Outpatient	92	(85.98)	15	(14.02)	107	(64.85)	
	Inpatient ↔ Outpatient	22	(68.75)	10	(31.25)	32	(19.39)	
Total		137	(83.03)	28	(16.97)	165	(100.0)	
RA switched subject	Inpatient	4	(100.0)	0	(0.00)	4	(5.26)	1.0000[2)]
	Outpatient	59	(89.39)	7	(10.61)	66	(86.84)	
	Inpatient ↔ Outpatient	6	(100.0)	0	(0.00)	6	(7.89)	
Total		69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	Inpatient	0	(NA)	0	(NA)	0	(NA)	-
	Outpatient	1	(100.0)	0	(0.00)	1	(100.0)	
	Inpatient ↔ Outpatient	0	(NA)	0	(NA)	0	(NA)	
Total		1	(100.0)	0	(0.00)	1	(100.0)	

Inpatient/Outpatient classification		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
PA switched subject	Inpatient	0	(NA)	0	(NA)	0	(NA)	-
	Outpatient	0	(NA)	0	(NA)	0	(NA)	
	Inpatient ↔ Outpatient	0	(NA)	0	(NA)	0	(NA)	
Total		0	(NA)	0	(NA)	0	(NA)	
PS naïve subject	Inpatient	0	(NA)	0	(NA)	0	(NA)	-
	Outpatient	1	(50.00)	1	(50.00)	2	(100.0)	
	Inpatient ↔ Outpatient	0	(NA)	0	(NA)	0	(NA)	
Total		1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	Inpatient	0	(NA)	0	(NA)	0	(NA)	-
	Outpatient	2	(100.0)	0	(0.00)	2	(100.0)	
	Inpatient ↔ Outpatient	0	(NA)	0	(NA)	0	(NA)	
Total		2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	Inpatient	7	(77.78)	2	(22.22)	9	(90.00)	0.3000[2)]
	Outpatient	0	(0.00)	1	(100.0)	1	(10.00)	
	Inpatient ↔ Outpatient	0	(NA)	0	(NA)	0	(NA)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	Inpatient	1	(100.0)	0	(0.00)	1	(14.29)	-
	Outpatient	6	(100.0)	0	(0.00)	6	(85.71)	
	Inpatient ↔ Outpatient	0	(NA)	0	(NA)	0	(NA)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	Inpatient	26	(86.67)	4	(13.33)	30	(37.04)	0.2222[2)]
	Outpatient	34	(97.14)	1	(2.86)	35	(43.21)	
	Inpatient ↔ Outpatient	14	(87.50)	2	(12.50)	16	(19.75)	
Total		74	(91.36)	7	(8.64)	81	(100.0)	
SC switched subject	Inpatient	13	(100.0)	0	(0.00)	13	(17.57)	0.2286[2)]
	Outpatient	55	(96.49)	2	(3.51)	57	(77.03)	
	Inpatient ↔ Outpatient	3	(75.00)	1	(25.00)	4	(5.41)	
Total		71	(95.95)	3	(4.05)	74	(100.0)	
PC	Inpatient	10	(62.50)	6	(37.50)	16	(66.67)	0.0883[2)]

Inpatient/Outpatient classification		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
naïve subject	Outpatient	1	(25.00)	3	(75.00)	4	(16.67)	
	Inpatient ↔ Outpatient	4	(100.0)	0	(0.00)	4	(16.67)	
Total		16	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	Inpatient	4	(100.0)	0	(0.00)	4	(18.18)	-
	Outpatient	15	(100.0)	0	(0.00)	15	(68.18)	
	Inpatient ↔ Outpatient	3	(100.0)	0	(0.00)	3	(13.64)	
Total		22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	Inpatient	18	(78.26)	5	(21.74)	23	(34.85)	0.3178[2)]
	Outpatient	30	(88.24)	4	(11.76)	34	(51.52)	
	Inpatient ↔ Outpatient	9	(100.0)	0	(0.00)	9	(13.64)	
Total		57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	Inpatient	2	(66.67)	1	(33.33)	3	(30.00)	1.0000[2)]
	Outpatient	4	(66.67)	2	(33.33)	6	(60.00)	
	Inpatient ↔ Outpatient	1	(100.0)	0	(0..00)	1	(10.00)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
PU naïve subject	Inpatient	0	(0.00)	14	(100.0)	14	(100.0)	-
	Outpatient	0	(NA)	0	(NA)	0	(NA)	
	Inpatient ↔ Outpatient	0	(NA)	0	(NA)	0	(NA)	
Total		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	Inpatient	1	(100.0)	0	(0.00)	1	(14.29)	-
	Outpatient	4	(100.0)	0	(0.00)	4	(57.14)	
	Inpatient ↔ Outpatient	2	(100.0)	0	(0.00)	2	(28.57)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Chi-square test / [2)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

4) Body weight

From response rate analysis by body weight, the maximum and minimum responder rates were as follows; in AS naïve subjects, 100.0% (80/80 subjects, 14/14 subjects, 13/13 subjects and 1/1 subject, respectively) in 70 to <80kg, 40 to <50kg, ≥90kg, 30 to <40kg and 60 to <70kg 94.32% (83/88 subjects); in AS switched subjects, 100.0% (21/21 subjects, 8/8 subjects and 6/6 subjects, respectively) in 80 to

<90kg, 40 to <50kg, ≥90kg and 93.02% (40/43 subjects) in 70 to <80kg; in RA naïve subjects, 88.24% (30/34 subjects) in 60 to <70kg and 73.33% (22/30 subjects and 11/15 subjects, respectively) in 40 to <50kg and 70 to <80kg; in RA switched subjects, 100.0% (3/3 subjects and 2/2 subjects, respectively) in 30 to <40kg and 80 to <90kg and 83.33% (5/6 subjects) in 70 to <80kg; in PS naïve subjects, 50.00% (1/2 subjects) in 50 to <60kg; in PS switched subjects, 100.0% (1/1 subject and 1/1 subject, respectively) in 50 to <60kg and 70 to <80kg; in FC naïve subjects, 100.0% (2/2 subjects and 1/1 subject, respectively) in 70 to <80kg and 90kg; in FC switched subjects, 100.0% (4/4 subjects, 2/2 subjects and 1/1 subject, respectively) in 60 to <70kg, 50 to <60kg and 70 to <80kg; in SC naïve subjects, 100.0% (16/16 subjects, 13/13 subjects, 2/2 subjects and 2/2 subjects, respectively) in 70 to <80kg, 40 to <50kg, 80 to <90kg and ≥90kg and 66.67% (2/3 subjects) in 30 to <40kg; in SC switched subjects, 100.0% (22/22 subjects, 9/9 subjects, 3/3 subjects and 3/3 subjects, respectively) in 50 to <60kg, 70 to <80kg, ≥90kg and 30 to <40kg and 80.00% (4/5 subjects) in 80 to <90kg; in PC naïve subjects, 85.71% (6/7 subjects) in 40 to <50kg and 33.33% (1/3 subjects) in 60 to <70kg; in PC switched subjects, all 100.0%; in UC naïve subjects, 100.0% (9/9 subjects and 2/2 subjects, respectively) in 70 to <80kg and 30 to <40kg and 0.00% (0/2 subjects and 0/1 subject, respectively) in 80 to <90kg and ≥90kg; in UC switched subjects, 62.50% (5/8 subjects) in 50 to <60kg and 100% for all other subjects; in PU naïve subjects, all 0.00%; in PU switched subjects, all 100.0%, and the indication with a statistically significant difference was UC naïve subjects with a p-value of 0.0161 (Table 174).

Table 174 Efficacy assessment by body weight

Body weight (unit: kg)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	30 to < 40	1	(100.0)	0	(0.00)	1	(0.36)	0.3001[1)]
	40 to < 50	14	(100.0)	0	(0.00)	14	(5.05)	
	50 to < 60	42	(97.67)	1	(2.33)	43	(15.52)	
	60 to <70	83	(94.32)	5	(5.68)	88	(31.77)	
	70 to <80	80	(100.0)	0	(0.00)	80	(28.88)	
	80 to <90	37	(97.37)	1	(2.63)	38	(13.72)	
	≥ 90	13	(100.0)	0	(0.00)	13	(4.69)	
Total		270	(97.47)	7	(2.53)	277	(100.0)	
AS switched subject	30 to < 40	0	(NA)	0	(NA)	0	(NA)	0.8195[1)]
	40 to < 50	8	(100.0)	0	(0.00)	8	(4.60)	
	50 to < 60	34	(97.14)	1	(2.86)	35	(20.11)	
	60 to <70	59	(96.72)	2	(3.28)	61	(35.06)	
	70 to <80	40	(93.02)	3	(6.98)	43	(24.71)	
	80 to <90	21	(100.0)	0	(0.00)	21	(12.07)	
	≥ 90	6	(100.0)	0	(0.00)	6	(3.45)	
Total		168	(96.55)	6	(3.45)	174	(100.0)	
RA	30 to < 40	0	(NA)	0	(NA)	0	(NA)	0.2304[1)]

Body weight (unit: kg)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
naïve subject	40 to < 50	22	(73.33)	8	(26.67)	30	(18.75)	
	50 to < 60	67	(87.01)	10	(12.99)	77	(48.13)	
	60 to <70	30	(88.24)	4	(11.76)	34	(21.25)	
	70 to <80	11	(73.33)	4	(26.67)	15	(9.38)	
	80 to <90	3	(75.00)	1	(25.00)	4	(2.50)	
	≥ 90	0	(NA)	0	(NA)	0	(NA)	
Total		133	(83.13)	27	(16.88)	160	(100.0)	
RA switched subject	30 to < 40	3	(100.0)	0	(0.00)	3	(3.95)	0.9221[1)]
	40 to < 50	11	(91.67)	1	(8.33)	12	(15.79)	
	50 to < 60	28	(90.32)	3	(9.68)	31	(40.79)	
	60 to <70	20	(90.91)	2	(9.09)	22	(28.95)	
	70 to <80	5	(83.33)	1	(16.67)	6	(7.89)	
	80 to <90	2	(100.0)	0	(0.00)	2	(2.63)	
	≥90	0	(NA)	0	(NA)	0	(NA)	
Total		69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	30 to < 40	0	(NA)	0	(NA)	0	(NA)	-
	40 to < 50	0	(NA)	0	(NA)	0	(NA)	
	50 to < 60	1	(100.0)	0	(0.00)	1	(100.0)	
	60 to <70	0	(NA)	0	(NA)	0	(NA)	
	70 to <80	0	(NA)	0	(NA)	0	(NA)	
	80 to <90	0	(NA)	0	(NA)	0	(NA)	
	≥90	0	(NA)	0	(NA)	0	(NA)	
Total		1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	30 to < 40	0	(NA)	0	(NA)	0	(NA)	-
	40 to < 50	0	(NA)	0	(NA)	0	(NA)	
	50 to < 60	0	(NA)	0	(NA)	0	(NA)	
	60 to <70	0	(NA)	0	(NA)	0	(NA)	
	70 to <80	0	(NA)	0	(NA)	0	(NA)	
	80 to <90	0	(NA)	0	(NA)	0	(NA)	
	≥90	0	(NA)	0	(NA)	0	(NA)	
Total		0	(NA)	0	(NA)	0	(NA)	

Body weight (unit: kg)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
PS naïve subject	30 to < 40	0	(NA)	0	(NA)	0	(NA)	-
	40 to < 50	0	(NA)	0	(NA)	0	(NA)	
	50 to < 60	1	(50.00)	1	(50.00)	2	(100.0)	
	60 to <70	0	(NA)	0	(NA)	0	(NA)	
	70 to <80	0	(NA)	0	(NA)	0	(NA)	
	80 to <90	0	(NA)	0	(NA)	0	(NA)	
	≥90	0	(NA)	0	(NA)	0	(NA)	
Total		1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	30 to < 40	0	(NA)	0	(NA)	0	(NA)	-
	40 to < 50	0	(NA)	0	(NA)	0	(NA)	
	50 to < 60	1	(100.0)	0	(0.00)	1	(50.00)	
	60 to <70	0	(NA)	0	(NA)	0	(NA)	
	70 to <80	1	(100.0)	0	(0.00)	1	(50.00)	
	80 to <90	0	(NA)	0	(NA)	0	(NA)	
	≥90	0	(NA)	0	(NA)	0	(NA)	
Total		2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	30 to < 40	0	(0.00)	1	(100.0)	1	(10.00)	0.6667[1)]
	40 to < 50	0	(NA)	0	(NA)	0	(NA)	
	50 to < 60	1	(50.00)	1	(50.00)	2	(20.00)	
	60 to <70	3	(75.00)	1	(25.00)	4	(40.00)	
	70 to <80	2	(100.0)	0	(0.00)	2	(20.00)	
	80 to <90	0	(NA)	0	(NA)	0	(NA)	
	≥90	1	(100.0)	0	(0.00)	1	(10.00)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	30 to < 40	0	(NA)	0	(NA)	0	(NA)	-
	40 to < 50	0	(NA)	0	(NA)	0	(NA)	
	50 to < 60	2	(100.0)	0	(0.00)	2	(28.57)	
	60 to <70	4	(100.0)	0	(0.00)	4	(57.14)	
	70 to <80	1	(100.0)	0	(0.00)	1	(14.29)	
	80 to <90	0	(NA)	0	(NA)	0	(NA)	
	≥90	0	(NA)	0	(NA)	0	(NA)	

Body weight (unit: kg)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	30 to < 40	2	(66.67)	1	(33.33)	3	(3.70)	0.2729[1)]
	40 to < 50	13	(100.0)	0	(0.00)	13	(16.05)	
	50 to < 60	22	(84.62)	4	(16.38)	26	(32.10)	
	60 to <70	17	(89.47)	2	(10.53)	19	(23.46)	
	70 to <80	16	(100.0)	0	(0.00)	16	(19.75)	
	80 to <90	2	(100.0)	0	(0.00)	2	(2.47)	
	≥90	2	(100.0)	0	(0.00)	2	(2.47)	
Total		74	(91.36)	7	(8.64)	81	(100.0)	
SC switched subject	30 to < 40	3	(100.0)	0	(0.00)	3	(4.05)	0.3396[1)]
	40 to < 50	9	(90.00)	1	(10.00)	10	(13.51)	
	50 to < 60	22	(100.0)	0	(0.00)	22	(29.73)	
	60 to <70	21	(95.45)	1	(4.55)	22	(29.73)	
	70 to <80	9	(100.0)	0	(0.00)	9	(12.16)	
	80 to <90	4	(80.00)	1	(20.00)	5	(6.76)	
	≥90	3	(100.0)	0	(0.00)	3	(4.05)	
Total		71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	30 to < 40	5	(71.43)	2	(28.57)	7	(29.17)	0.3931[1)]
	40 to < 50	6	(85.71)	1	(14.29)	7	(29.17)	
	50 to < 60	2	(40.00)	3	(60.00)	5	(20.83)	
	60 to <70	1	(33.33)	2	(66.67)	3	(12.50)	
	70 to <80	1	(50.00)	1	(50.00)	2	(8.33)	
	80 to <90	0	(NA)	0	(NA)	0	(NA)	
	≥90	0	(NA)	0	(NA)	0	(NA)	
Total		15	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	<30	3	(100.0)	0	(0.00)	3	(13.64)	-
	30 to < 40	1	(100.0)	0	(0.00)	1	(4.55)	
	40 to < 50	6	(100.0)	0	(0.00)	6	(27.27)	
	50 to < 60	6	(100.0)	0	(0.00)	6	(27.27)	
	60 to <70	2	(100.0)	0	(0.00)	2	(9.09)	
	70 to <80	2	(100.0)	0	(0.00)	2	(9.09)	

Body weight (unit: kg)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
	80 to <90	1	(100.0)	0	(0.00)	1	(4.55)	
	≥90	1	(100.0)	0	(0.00)	1	(4.55)	
Total		22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	30 to < 40	2	(100.0)	0	(0.00)	2	(3.03)	0.0161[1)]
	40 to < 50	13	(92.86)	1	(7.14)	14	(21.21)	
	50 to < 60	17	(89.47)	2	(10.53)	19	(28.79)	
	60 to <70	16	(84.21)	3	(15.79)	19	(28.79)	
	70 to <80	9	(100.0)	0	(0.00)	9	(13.64)	
	80 to <90	0	(0.00)	2	(100.0)	2	(3.03)	
	≥90	0	(0.00)	1	(100.0)	1	(1.52)	
Total		57	(8.36)	9	(13.64)	66	(100.0)	
UC switched subject	30 to < 40	0	(NA)	0	(NA)	0	(NA)	1.0000[1)]
	40 to < 50	0	(NA)	0	(NA)	0	(NA)	
	50 to < 60	5	(62.50)	3	(37.50)	8	(80.00)	
	60 to <70	1	(100.0)	0	(0.00)	1	(10.00)	
	70 to <80	1	(100.0)	0	(0.00)	1	(10.00)	
	80 to <90	0	(NA)	0	(NA)	0	(NA)	
	≥90	0	(NA)	0	(NA)	0	(NA)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
PU naïve subject	<30	0	(0.00)	4	(100.0)	4	(28.57)	-
	30 to < 40	0	(0.00)	1	(100.0)	1	(7.14)	
	40 to < 50	0	(0.00)	4	(100.0)	4	(28.57)	
	50 to < 60	0	(0.00)	4	(100.0)	4	(28.57)	
	60 to <70	0	(NA)	0	(NA)	0	(NA)	
	70 to <80	0	(0.00)	1	(100.0)	1	(7.14)	
	80 to <90	0	(NA)	0	(NA)	0	(NA)	
	≥90	0	(NA)	0	(NA)	0	(NA)	
Total		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	30 to < 40	2	(100.0)	0	(0.00)	2	(28.57)	-
	40 to < 50	2	(100.0)	0	(0.00)	2	(28.57)	
	50 to < 60	3	(100.0)	0	(0.00)	3	(42.86)	

Body weight (unit: kg)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
	60 to <70	0	(NA)	0	(NA)	0	(NA)	
	70 to <80	0	(NA)	0	(NA)	0	(NA)	
	80 to <90	0	(NA)	0	(NA)	0	(NA)	
	≥90	0	(NA)	0	(NA)	0	(NA)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

5) Medical history and previous treatment

A. History of the target disease and previous treatment

A.1. Duration of target disease

From response rate analysis by duration of target disease of <5 years, 5 to <10 years and ≥10 years, the result was as follows: in AS naïve subjects, 97.27% (214/220 subjects), 96.77% (30/31 subjects) and 100.0% (26/26 subjects), respectively; in AS switched subjects, 97.33% (73/75 subjects), 90.74% (49/54 subjects) and 100.0% (49/49 subjects), respectively; in RA naïve subjects, 86.73% (85/98 subjects), 78.57% (22/28 subjects) and 80.65% (25/31 subjects), respectively; in RA switched subjects, 92.59% (25/27 subjects), 90.91% (20/22 subjects) and 92.00% (23/25 subjects), respectively; in PS naïve subjects, 50.00% (1/2 subjects) for ≥10 years, and there were no subjects for <5 years or 5 to <10 years; in PS switched subjects, 100.0% (1/1 subject and 1/1 subject, respectively) for 5 to <10 years and ≥10 years, and there were no subjects for <5 years; in FC naïve subjects, 75.00% (6/8 subjects) for <5 years, 50.00% (1/2 subjects) for 5 to <10 years, and there were no subjects for ≥10 years; in FC switched subjects, 100.0% (2/2 subjects and 5/5 subjects, respectively) for 5 to <10 years and ≥10 years, and there were no subjects for <5 years; in SC naïve subjects, 89.13% (41/46 subjects), 94.44% (17/18 subjects) and 91.67% (11/12 subjects), respectively; in SC switched subjects, 96.16% (25/26 subjects), 93.33% (28/30 subjects) and 100.0% (18/18 subjects), respectively; in PC naïve subjects, 62.50% (15/24 subjects) for <5 years, and there were no subjects for 5 to <10 years or ≥10 years; in PC switched subjects, 100.0% (18/18 subjects and 3/3 subjects, respectively) for <5 years and 5 to <10 years, and there were no subjects for ≥10 years; in UC naïve subjects, 87.18% (34/39 subjects), 85.71% (12/14 subjects) and 90.91% (10/11 subjects), respectively; in UC switched subjects, 71.43% (5/7 subjects), 100.0% (2/2 subjects) and 0.00% (0/1 subject), respectively; in PU naïve subjects, 0.00% (0/13 subjects and 0/1 subject, respectively) for <5 years and ≥10 years and there were no subjects for 5 to <10 years; in PU switched subjects, 100.0% (6/6 subjects and 1/1 subject, respectively) for <5 years and 5 to <10 years and there were no subjects for ≥10 years, and the indication with a statistically significant difference was AS switched subjects, with a p-value of 0.0467 (Table 175).

Table 175 Efficacy assessment by duration of target disease

Illness duration (unit: year)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	<5	214	(97.27)	6	(2.73)	220	(79.42)	1.0000[2)]
	5 to <10	30	(96.77)	1	(3.23)	31	(11.19)	

Illness duration (unit: year)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
	≥10	26	(100.0)	0	(0.00)	26	(9.39)	
Total		270	(97.47)	7	(2.53)	277	(100.0)	
AS switched subject	<5	73	(97.33)	2	(2.67)	75	(42.13)	
	5 to <10	49	(90.74)	5	(9.26)	54	(30.34)	0.0467[2)]
	≥10	49	(100.0)	0	(0.00)	49	(27.53)	
Total		171	(96.07)	7	(3.93)	178	(100.0)	
RA naïve subject	<5	85	(86.73)	13	(13.27)	98	(62.42)	
	5 to <10	22	(78.57)	6	(21.43)	28	(17.83)	0.4470[2)]
	≥10	25	(80.65)	6	(19.325)	31	(19.75)	
Total		132		25		157		
RA switched subject	<5	25	(92.59)	2	(7.41)	27	(36.49)	
	5 to <10	20	(90.91)	2	(9.09)	22	(29.73)	1.0000[2)]
	≥10	23	(92.00)	2	(8.00)	25	(33.78)	
Total		68	(91.89)	6	(8.11)	74	(100.0)	
PA naïve subject	<5	1	(100.0)	0	(0.00)	1	(100.0)	
	5 to <10	0	(NA)	0	(NA)	0	0	-
	≥10	0	(NA)	0	(NA)	0	(NA)	
Total		1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	<5	0	(NA)	0	(NA)	0	(NA)	
	5 to <10	0	(NA)	0	(NA)	0	(NA)	-
	≥10	0	(NA)	0	(NA)	0	(NA)	
Total		0	(NA)	0	(NA)	0	(NA)	
PS naïve subject	<5	0	(NA)	0	(NA)	0	(NA)	
	5 to <10	0	(NA)	0	(NA)	0	(NA)	-
	≥10	1	(50.00)	1	(50.00)	1	(100.0)	
Total		1	(50.00)	1	(50.00)	1	(100.0)	
PS switched subject	<5	0	(NA)	0	(NA)	0	(NA)	
	5 to <10	1	(100.0)	0	(0.00)	1	(50.00)	-
	≥10	1	(100.0)	0	(0.00)	1	(50.00)	
Total		2	(100.0)	0	(0.00)	2	(100.0)	
FC	<5	6	(75.00)	2	(25.00)	8	(80.00)	1.0000[2)]

Illness duration (unit: year)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
naïve subject	5 to <10	1	(50.00)	1	(50.00)	2	(20.00)	
	≥10	0	(NA)	0	(NA)	0	(NA)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	<5	0	(NA)	0	(NA)	0	(NA)	
	5 to <10	2	(100.0)	0	(0.00)	2	(28.57)	-
	≥10	5	(100.0)	0	(0.00)	5	(71.43)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	<5	41	(89.13)	5	(10.87)	46	(60.53)	
	5 to <10	17	(94.44)	1	(5.56)	18	(23.68)	0.8630[2)]
	≥10	11	(91.67)	1	(8.33)	12	(15.79)	
Total		69	(90.79)	7	(9.21)	76	(100.0)	
SC switched subject	<5	25	(96.15)	1	(3.85)	26	(35.14)	
	5 to <10	28	(93.33)	2	(6.67)	30	(40.54)	0.7834[2)]
	≥10	18	(100.0)	0	(0.00)	18	(24.32)	
Total		71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	<5	15	(62.50)	9	(37.50)	24	(100.0)	
	5 to <10	0	(NA)	0	(NA)	0	(NA)	-
	≥10	0	(NA)	0	(NA)	0	(NA)	
Total		15	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	<5	18	(100.0)	0	(0.00)	18	(85.71)	
	5 to <10	3	(100.0)	0	(0.00)	3	(14.29)	-
	≥10	0	(NA)	0	(NA)	0	(NA)	
Total		21	(100.0)	0	(0.00)	21	(100.0)	
UC naïve subject	<5	34	(87.18)	5	(12.82)	39	(60.94)	
	5 to <10	12	(85.71)	2	(14.29)	14	(21.88)	1.0000[2)]
	≥10	10	(90.91)	1	(9.09)	11	(17.19)	
Total		56	(87.50)	8	(12.50)	64	(100.0)	
UC switched subject	<5	5	(71.43)	2	(28.57)	7	(70.00)	
	5 to <10	2	(100.0)	0	(0.00)	2	(20.00)	0.3583[2)]
	≥10	0	(0.00)	1	(100.0)	1	(10.00)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	

Illness duration (unit: year)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
PU naïve subject	<5	0	(0.00)	13	(100.0)	13	(92.86)	-
	5 to <10	0	(NA)	0	(NA)	0	(NA)	
	≥10	0	(0.00)	1	(100.0)	1	(7.14)	
Total		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	<5	6	(100.0)	0	(0.00)	6	(85.71)	-
	5 to <10	1	(100.0)	0	(0.00)	1	(14.29)	
	≥10	0	(NA)	0	(NA)	0	(NA)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Chi-square test/ [2)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

A.2. Treatment history for the indication

From response rate analysis by treatment history for the indication of 'Yes, No, Unknown', the result was as follows: in AS naïve subjects, it was 98.08% (102/104 subjects), 97.14% (170/175 subjects) and 100.0% (4/4 subjects), respectively; in AS switched subjects, all subjects were 'Yes' and the response rate was 96.20% (177/184 subjects); in RA naïve subjects, it was 81.25% (39/48 subjects) and 83.76% (98/117 subjects) respectively, with no 'Unknown'; in RA switched subjects, all subjects were 'Yes' and the response rate was 90.79% (69/76 subjects); in PS naïve subjects, all subjects were 'Yes' and the response rate was 50.00% (1/2 subjects); in PS switched subjects, all subjects were 'Yes' and the response rate was 100.0% (2/2 subjects); in FC naïve subjects, it was 60.00% (3/5 subjects) and 80.00% (4/5 subjects) respectively, with no 'Unknown'; in FC switched subjects, all subjects were 'Yes' and the response rate was 100.0% (7/7 subjects); in SC naïve subjects, it was 87.76% (43/49 subjects), 96.77% (30/31 subjects) and 100.0% (1/1 subject), respectively; in SC switched subjects, all subjects were 'Yes' and the response rate was 95.95% (71/74 subjects); in PC naïve subjects, it was 63.64% (7/11 subjects) and 61.54% (8/13 subjects), respectively, and there weas no 'Unknown'; in PC switched subjects, all subjects were 'Yes' and the response rate was 100.0% (22/22 subjects); in UC naïve subjects, it was 82.76% (24/29 subjects), 88.57% (31/35 subjects) and 100.0% (2/2 subjects), respectively; in UC switched subjects, all subjects were 'Yes' and the response rate was 70.00% (7/10 subjects); in PU naïve subjects, it was 0.00% (0/9 subjects) and 0.00% (0/7 subjects), respectively, and there was no 'Unknown'; in PU switched subjects, all subjects were 'Yes' and the response rate was 100.0% (7/7 subjects), there was no 'Unknown', and there was no indication with a statistically significant difference (Table 176).

Table 176 Efficacy assessment by treatment history for the indication

Treatment history		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS	Yes	102	(98.08)	2	(1.92)	104	(36.75)	1.0000[2)]

Treatment history		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
naïve subject	No	170	(97.14)	5	(2.86)	175	(61.84)	
	Unknown	4	(100.0)	0	(0.00)	4	(1.41)	
Total		276	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	Yes	177	(96.20)	7	(3.80)	184	(100.0)	
	No	0	(NA)	0	(NA)	0	(NA)	-
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		177	(96.20)	7	(3.80)	184	(100.0)	
RA naïve subject	Yes	39	(81.25)	9	(18.75)	48	(29.09)	
	No	98	(83.76)	19	(16.24)	117	(70.91)	0.6964[1)]
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		137	(83.03)	28	(16.97)	165	(100.0)	
RA switched subject	Yes	69	(90.79)	7	(9.21)	76	(100.0)	
	No	0	(NA)	0	(NA)	0	(NA)	-
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	
	No	1	(100.0)	0	(0.00)	1	(100.0)	-
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	
	No	0	(NA)	0	(NA)	0	(NA)	-
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		0	(NA)	0	(NA)	0	(NA)	
PS naïve subject	Yes	1	(50.00)	1	(50.00)	2	(100.0)	
	No	0	(NA)	0	(NA)	0	(NA)	-
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	Yes	2	(100.0)	0	(0.00)	2	(100.0)	
	No	0	(NA)	0	(NA)	0	(NA)	-
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		2	(100.0)	0	(0.00)	2	(100.0)	

Treatment history		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
FC naïve subject	Yes	3	(60.00)	2	(40.00)	5	(50.00)	1.0000[2)]
	No	4	(80.00)	1	(20.00)	5	(50.00)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	Yes	7	(100.0)	0	(0.00)	7	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	Yes	43	(87.76)	6	(12.24)	49	(60.49)	0.3044[2)]
	No	30	(96.77)	1	(3.23)	31	(38.27)	
	Unknown	1	(100.0)	0	(0.00)	1	(1.23)	
Total		74	(91.36)	7	(8.64)	81	(100.0)	
SC switched subject	Yes	71	(95.95)	3	(4.05)	74	(100.0)	
	No	0	(NA)	0	(NA)	0	(NA)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	Yes	7	(63.64)	4	(36.36)	11	(45.83)	1.0000[2)]
	No	8	(61.54)	5	(38.46)	13	(54.17)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		15	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	Yes	22	(100.0)	0	(0.00)	22	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	Yes	24	(82.76)	5	(17.24)	29	(43.94)	0.7917[2)]
	No	31	(88.57)	4	(11.43)	35	(53.03)	
	Unknown	2	(100.0)	0	(0.00)	2	(3.03)	
Total		57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	Yes	7	(70.00)	3	(30.00)	10	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	

Treatment history		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
PU naïve subject	Yes	0	(0.00)	9	(100.0)	9	(64.29)	-
	No	0	(0.00)	5	(100.0)	5	(35.71)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	Yes	7	(100.0)	0	(0.00)	7	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Chi-square test / [2)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

A.3. Hypersensitivity history for treatment of the indication

From response rate analysis by hypersensitivity history for treatment of the indication, in FC naïve subjects, UC switched subjects and PU naïve subjects, there were no subjects who had the hypersensitivity history for treatment of the indication; for other indications, the responder rate for 'Yes, No, Unknown' was as follows; in AS naïve subjects, 100.0% (1/1 subject), 97.44% (266/273 subjects) and 100.0% (9/9 subjects), respectively; in AS switched subjects, 100.0% (16/16 subjects), 96.05% (146/152 subjects) and 93.75% (15/16 subjects), respectively; in RA naïve subjects, 100.0% (2/2 subjects), 82.80% (130/157 subjects) and 83.55% (5/6 subjects), respectively; in RA switched subjects, 83.33% (5/6 subjects), 93.75% (60/64 subjects) and 66.67% (4/6 subjects), respectively; in PS naïve subjects, 50.00% (1/2 subjects) only in subjects for 'Yes'; in PS switched subjects, 100.0% (1/1 subject) and 100.0% (1/1 subject), respectively, and there were no subjects for 'Unknown'; in FC naïve subjects, 100.0% (7/7 subjects) only in subjects for 'No'; in FC switched subjects, 100.0% (1/1 subject) and 100.0% (6/6 subjects), respectively, with no subjects for 'Unknown'; in SC naïve subjects, 100.0% (3/3 subjects), 90.79% (69/76 subjects) and 100.0% (2/2 subjects), respectively; in SC switched subjects, 100.0% (8/8 subjects) and 95.45% (63/66 subjects), respectively, and there were no subjects for 'Unknown'; in PC naïve subjects, 100.0% (1/1 subject) and 60.87% (14/23 subjects), respectively, and there were no subjects for 'Unknown'; in PC switched subjects, 100.0% (5/5 subjects), 100.0% (16/16 subjects) and 100.0% (1/1 subject), respectively; in UC naïve subjects, 100.0% (2/2 subjects), 85.48% (53/62 subjects) and 100.0% (2/2 subjects), respectively; in UC switched subjects, 70.00% (7/10 subjects) only in subjects for 'No'; in PU naïve subjects, 0.00% (0/14 subjects) only in subjects for 'No'; in PU switched subjects, 100.0% (1/1 subject) and 100.0% (6/6 subjects), respectively, and there were no subjects for 'Unknown', and there was no indication with a statistically significant difference (Table 177).

Table 177 Efficacy assessment by hypersensitivity history for treatment of the indication

Hypersensitivity history	Responder	Non-responder	Total	p-value

		N	(%)	N	(%)	N	(%)	
AS naïve subject	Yes	1	(100.0)	0	(0.00)	1	(0.35)	1.0000[1)]
	No	266	(97.44)	7	(2.56)	273	(96.47)	
	Unknown	9	(100.0)	0	(0.00)	9	(3.18)	
	Total	276	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	Yes	16	(100.0)	0	(0.00)	16	(8.70)	0.7439[1)]
	No	146	(96.05)	6	(3.95)	152	(82.61)	
	Unknown	15	(93.75)	1	(6.25)	16	(8.70)	
	Total	177	(96.20)	7	(3.80)	184	(100.0)	
RA naïve subject	Yes	2	(100.0)	0	(0.00)	2	(1.21)	1.0000[1)]
	No	130	(82.80)	27	(17.20)	157	(95.15)	
	Unknown	5	(83.33)	1	(16.67)	6	(3.64)	
	Total	137	(83.03)	28	(16.97)	165	(100.0)	
RA switched subject	Yes	5	(83.33)	1	(16.67)	6	(7.89)	0.0741[1)]
	No	60	(93.75)	4	(6.25)	64	(84.21)	
	Unknown	4	(66.67)	2	(33.33)	6	(7.89)	
	Total	69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	1	(100.0)	0	(0.00)	1	(100.0)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
	Total	1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
	Total	0	(NA)	0	(NA)	0	(NA)	
PS naïve subject	Yes	1	(50.00)	1	(50.00)	2	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
	Total	1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	Yes	1	(100.0)	0	(0.00)	1	(50.00)	-
	No	1	(100.0)	0	(0.00)	1	(50.00)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
	Total	2	(100.0)	0	(0.00)	2	(100.0)	

Hypersensitivity history		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
FC naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(70.00)	3	(30.00)	10	(100.0)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	Yes	1	(100.0)	0	(0.00)	1	(14.29)	-
	No	6	(100.0)	0	(0.00)	6	(85.71)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	Yes	3	(100.0)	0	(0.00)	3	(3.70)	1.0000[1)]
	No	69	(90.79)	7	(9.21)	76	(93.83)	
	Unknown	2	(100.0)	0	(0.00)	2	(2.47)	
Total		74	(91.36)	7	(9.21)	81	(100.0)	
SC switched subject	Yes	8	(100.0)	0	(0.00)	8	(10.81)	1.0000[1)]
	No	63	(95.45)	3	(4.55)	66	(89.19)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		71	(95.95)	3	(4.55)	74	(100.0)	
PC naïve subject	Yes	1	(100.0)	0	(0.00)	1	(4.17)	1.0000[1)]
	No	14	(60.87)	9	(39.13)	23	(95.83)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		15	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	Yes	5	(100.0)	0	(0.00)	5	(22.73)	-
	No	16	(100.0)	0	(0.00)	16	(72.73)	
	Unknown	1	(100.0)	0	(0.00)	1	(4.55)	
Total		22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	Yes	2	(100.0)	0	(0.00)	2	(3.03)	1.0000[1)]
	No	53	(85.48)	9	(14.52)	62	(93.94)	
	Unknown	2	(100.0)	0	(0.00)	2	(3.03)	
Total		57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(70.00)	3	(30.00)	10	(100.0)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	

Hypersensitivity history		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
PU naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	0	(0.00)	14	(100.0)	14	(100.0)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	Yes	1	(100.0)	0	(0.00)	1	(14.29)	-
	No	6	(100.0)	0	(0.00)	6	(85.71)	
	Unknown	0	(NA)	0	(NA)	0	(NA)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

B. Current disease

B.1. Total

From response rate analysis by medical history for 'Yes' or 'No', the result was as follows: in AS naïve subjects, 95.63% (153/160 subjects) and 100.0% (123/123 subjects), respectively; in AS switched subjects, 94.50% (103/109 subjects) and 98.67% (74/75 subjects), respectively; in RA naïve subjects, 81.82% (90/110 subjects) and 85.45% (47/55 subjects), respectively; in RA switched subjects, 91.67% (55/60 subjects) and 87.50% (14/16 subjects), respectively; in PS naïve subjects, 50.00% (1/2 subjects) only in subjects for 'Yes'; in PS switched subjects, 100.0% (2/2 subjects) only in subjects for 'Yes'; in FC naïve subjects, 100.0% (3/3 subjects) and 57.14% (7/4 subjects), respectively; in FC switched subjects, 100.0% (4/4 subjects) and 100.0% (3/3 subjects), respectively; in SC naïve subjects, 96.77% (30/31 subjects) and 88.00% (44/60 subjects), respectively; in SC switched subjects, 95.24% (20/21 subjects) and 96.23% (51/553 subjects), respectively; in PC naïve subjects, 75.00% (3/4 subjects) and 60.00% (12/20 subjects), respectively; in PC switched subjects 100.0% (4/4 subjects) and 100.0% (18/18 subjects), respectively; in UC naïve subjects, 77.27% (17/22 subjects) and 90.91% (40/44 subjects), respectively; in UC switched subjects, 60.00% (3/5 subjects) and 80.00% (4/5 subjects), respectively; in PU naïve subjects, 0.00% (0/2 subjects) and 0.00% (0/14), respectively; in PU switched subjects, 100.0% (1/1 subject) and 100.0% (6/6 subjects), respectively. The indication with a statistically significant difference was AS naïve subjects, with a p-value of 0.0201 (Table 178).

Table 178 Efficacy assessment by current disease

Current disease		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	Yes	153	(95.63)	7	(4.38)	160	(56.54)	0.0201[2)]
	No	123	(100.0)	0	(0.00)	123	(43.46)	

Current disease		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
Total		276	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	Yes	103	(94.50)	6	(5.50)	109	(59.24)	0.2434[2)]
	No	74	(98.67)	1	(1.33)	75	(40.76)	
	Total	177	(96.20)	7	(3.80)	184	(100.0)	
RA naïve subject	Yes	90	(81.82)	20	(18.18)	110	(66.67)	0.5575[1)]
	No	47	(85.45)	8	(14.55)	55	(33.33)	
	Total	137	(83.03)	28	(16.97)	165	(100.0)	
RA switched subject	Yes	55	(91.67)	5	(8.33)	60	(78.95)	0.6336[2)]
	No	14	(87.50)	2	(12.50)	16	(21.05)	
	Total	69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	Yes	1	(100.0)	0	(0.00)	1	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Total	1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Total	0	(NA)	0	(NA)	0	(NA)	
PS naïve subject	Yes	1	(50.00)	1	(50.00)	2	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Total	1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	Yes	2	(100.0)	0	(0.00)	2	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Total	2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	Yes	3	(100.0)	0	(0.00)	3	(30.00)	0.4750[2)]
	No	4	(57.14)	3	(42.86)	7	(70.00)	
	Total	7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	Yes	4	(100.0)	0	(0.00)	4	(57.14)	-
	No	3	(100.0)	0	(0.00)	3	(42.86)	
	Total	7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	Yes	30	(96.77)	1	(3.23)	31	(38.27)	0.2416[2)]
	No	44	(88.00)	6	(12.00)	50	(61.73)	
	Total	74	(91.36)	7	(8.64)	81	(100.0)	

Current disease		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
SC switched subject	Yes	20	(95.24)	1	(4.76)	21	(28.38)	1.0000[2)]
	No	51	(96.23)	2	(3.77)	53	(71.62)	
	Total	71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	Yes	3	(75.00)	1	(25.00)	4	(16.67)	1.0000[2)]
	No	12	(60.00)	8	(40.00)	20	(83.33)	
	Total	16	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	Yes	4	(100.0)	0	(0.00)	4	(18.18)	-
	No	18	(100.0)	0	(0.00)	18	(81.82)	
	Total	22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	Yes	17	(77.27)	5	(22.73)	22	(33.33)	0.1472[2)]
	No	40	(90.91)	4	(9.09)	44	(66.67)	
	Total	57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	Yes	3	(60.00)	2	(40.00)	5	(50.00)	1.0000[2)]
	No	4	(80.00)	1	(20.00)	5	(50.00)	
	Total	7	(70.00)	3	(30.00)	10	(100.0)	
PU naïve subject	Yes	0	(0.00)	2	(100.0)	2	(14.29)	-
	No	0	(0.00)	12	(100.0)	14	(85.71)	
	Total	0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	Yes	1	(100.0)	0	(0.00)	1	(14.29)	-
	No	6	(100.0)	0	(0.00)	6	(85.71)	
	Total	7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Chi-square test / [2)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

B.2. History of allergy

From response rate analysis by history of allergy, there were no subjects with the history of allergy in PS naïve and switched subjects, FC naïve and switched subjects, PC switched subjects, UC naïve and switched subjects and PU naïve and switched subjects; for other indications, the response rate for 'Yes' or 'No' was as follows; in AS naïve subjects, 0.00% (0/2 subjects) and 98.22% (276/281 subjects), respectively; in AS switched subjects, 100.0% (2/2 subjects) and 96.15% (175/182 subjects), respectively; in RA naïve subjects, 100.0% (2/2 subjects) and 82.82% (135/163 subjects), respectively; in RA switched subjects, 100.0% (2/2 subjects) and 90.54% (67/74 subjects), respectively; in SC naïve subjects, 100.0% (2/2 subjects) and 91.14% (72/79 subjects), respectively; in SC switched subjects,

100.0% (1/1 subject) and 95.89% (70/73 subjects), respectively; in PC naïve subjects, 100.0% (1/1 subject) and 60.87% (14/23 subjects), respectively, and the indication with a statistically significant difference was AS naïve subjects, with a p-value of 0.0005 (Table 179).

Table 179 Efficacy assessment by current disease (history of allergy)

History of allergy		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	Yes	0	(0.00)	2	(100.0)	2	(0.71)	0.0005[1)]
	No	276	(98.22)	5	(1.78)	281	(99.29)	
	Total	276	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	Yes	2	(100.0)	0	(0.00)	2	(1.09)	1.0000[1)]
	No	175	(96.15)	7	(3.85)	182	(98.91)	
	Total	177	(96.20)	7	(3.80)	184	(100.0)	
RA naïve subject	Yes	2	(100.0)	0	(0.00)	2	(1.21)	1.0000[1)]
	No	135	(82.82)	28	(17.18)	163	(98.79)	
	Total	137	(83.03)	28	(16.97)	165	(100.0)	
RA switched subject	Yes	2	(100.0)	0	(0.00)	2	(2.78)	1.0000[1)]
	No	67	(90.54)	7	(9.45)	74	(97.37)	
	Total	69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	1	(100.0)	0	(0.00)	1	(100.0)	
	Total	1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Total	0	(NA)	0	(NA)	0	(NA)	
PS naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	1	(50.00)	1	(50.00)	2	(100.0)	
	Total	1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	2	(100.0)	0	(0.00)	2	(100.0)	
	Total	2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(70.00)	3	(30.00)	10	(100.0)	
	Total	7	(70.00)	3	(30.00)	10	(100.0)	

History of allergy		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
FC switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(100.0)	0	(0.00)	7	(100.0)	
	Total	7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	Yes	2	(100.0)	0	(0.00)	2	(2.47)	1.0000[1)]
	No	72	(91.14)	7	(8.86)	79	(97.53)	
	Total	74	(91.36)	7	(8.64)	81	(100.0)	
SC switched subject	Yes	1	(100.0)	0	(0.00)	1	(1.35)	1.0000[1)]
	No	70	(95.89)	3	(4.11)	73	(98.65)	
	Total	71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	Yes	1	(100.0)	0	(0.00)	1	(4.17)	1.0000[1)]
	No	14	(60.87)	9	(39.13)	23	(95.83)	
	Total	15	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	22	(100.0)	0	(0.00)	22	(100.0)	
	Total	22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	57	(86.36)	9	(13.64)	66	(100.0)	
	Total	57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(70.00)	3	(30.00)	10	(100.0)	
	Total	7	(70.00)	3	(30.00)	10	(100.0)	
PU naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	0	(0.00)	14	(100.0)	14	(100.0)	
	Total	0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(100.0)	0	(0.00)	7	(100.0)	
	Total	7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

B.3. Concurrent disease

From response rate analysis by concurrent disease, the response rate for 'Yes' or 'No' was as follows; in AS naïve subjects, 96.18% (126/131 subjects) and 98.68% (150/152 subjects), respectively; in AS switched subjects, 93.88% (92/98 subjects) and 98.84% (85/86 subjects), respectively; in RA naïve subjects, 80.39% (82/102 subjects) and 87.30% (55/63 subjects), respectively; in RA switched subjects, 91.53% (54/59 subjects) and 88.24% (15/17 subjects), respectively; in PS naïve subjects, 50.00% (1/2 subjects) only in subjects for 'Yes'; in PS switched subjects, 100.0% (2/2 subjects) only in subjects for 'Yes'; in FC naïve subjects, 100.0% (3/3 subjects) and 57.14% (4/7 subjects), respectively; in FC switched subjects, 100.0% (4/4 subjects) and 100.0% (3/3 subjects), respectively; in SC naïve subjects, 100.0% (24/24 subjects) and 87.72% (80/57 subjects), respectively; in SC switched subjects, 93.33% (14/15 subjects) and 96.61% (57/59 subjects), respectively; in PC naïve subjects, 66.67% (2/3) and 61.90% (13/21 subjects), respectively; in PC switched subjects, 100.0% (4/4 subjects) and 100.0% (18/18 subjects), respectively in UC naïve subjects, 80.00% (16/20 subjects) and 89.13% (41/46 subjects), respectively; in UC switched subjects, 50.00% (2/4 subjects) and 83.33% (5/6 subjects), respectively; in PU naïve subjects, 0.00% (0/2 subjects) and 0.00% (0/14 subjects), respectively; in PU switched subjects, 100.0% (1/1 subject) and 100.0% (6/6 subjects), respectively, and there was no indication with a statistically significant difference (Table 180).

Table 180 Efficacy assessment by current disease (concurrent disease)

Concurrent disease		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	Yes	126	(96.18)	5	(3.82)	131	(46.29)	0.2552[2)]
	No	150	(98.68)	2	(1.32)	152	(53.71)	
	Total	276	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	Yes	92	(93.88)	6	(6.12)	98	(53.26)	0.1234[2)]
	No	85	(98.84)	1	(1.16)	86	(46.74)	
	Total	177	(96.20)	7	(3.80)	184	(100.0)	
RA naïve subject	Yes	82	(80.39)	20	(19.61)	102	(61.82)	0.2507[1)]
	No	55	(87.30)	8	(12.70)	63	(38.18)	
	Total	137	(83.03)	28	(16.97)	165	(100.0)	
RA switched subject	Yes	54	(91.53)	5	(8.47)	59	(77.63)	0.6496[2)]
	No	15	(88.24)	2	(11.76)	17	(22.37)	
	Total	69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	Yes	1	(100.0)	0	(0.00)	1	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Total	1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Total	0	(NA)	0	(NA)	0	(NA)	

Concurrent disease		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
PS naïve subject	Yes	1	(50.00)	1	(50.00)	2	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Total	1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	Yes	2	(100.0)	0	(0.00)	2	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Total	2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	Yes	3	(100.0)	0	(0.00)	3	(30.00)	0.4750[2)]
	No	4	(57.14)	3	(42.86)	7	(70.00)	
	Total	7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	Yes	4	(100.0)	0	(0.00)	4	(57.14)	-
	No	3	(100.0)	0	(0.00)	3	(42.86)	
	Total	7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	Yes	24	(100.0)	0	(0.00)	24	(29.63)	0.0978[2)]
	No	50	(87.72)	7	(12.08)	57	(70.37)	
	Total	74	(91.36)	7	(8.64)	81	(100.0)	
SC switched subject	Yes	14	(93.33)	1	(6.67)	15	(20.27)	0.4985[2)]
	No	57	(96.61)	2	(3.39)	59	(79.73)	
	Total	71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	Yes	2	(66.67)	1	(33.33)	3	(12.50)	1.0000[2)]
	No	13	(61.90)	8	(38.10)	21	(87.50)	
	Total	15	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	Yes	4	(100.0)	0	(0.00)	4	(18.18)	-
	No	18	(100.0)	0	(0.00)	18	(81.82)	
	Total	22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	Yes	16	(80.00)	4	(20.00)	20	(30.30)	0.4368[2)]
	No	41	(89.13)	5	(10.87)	46	(69.70)	
	Total	57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	Yes	2	(50.00)	2	(50.00)	4	(40.00)	0.5000[2)]
	No	5	(83.33)	1	(16.67)	6	(60.00)	
	Total	7	(70.00)	3	(30.00)	10	(100.0)	

Concurrent disease		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
PU naïve subject	Yes	0	(0.00)	2	(100.0)	2	(14.29)	-
	No	0	(0.00)	12	(100.0)	14	(85.71)	
Total		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	Yes	1	(100.0)	0	(0.00)	1	(14.29)	-
	No	6	(100.0)	0	(0.00)	6	(85.71)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Chi-square test / [2)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

B.4. Complication

From response rate analysis by complication, after excluding PS naïve and switched subjects, FC switched subjects, PC naïve and switched subjects, UC switched subjects and PU naïve and switched subjects as there were no relevant subjects, the response rate by complication was as follows: in AS naïve subjects, 100.0% (6/6 subjects) and 97.47% (270/277 subjects), respectively; in AS switched subjects, 100.0% (8/8 subjects) and 96.02% (169/176 subjects), respectively; in RA naïve subjects, 100.0% (1/1 subject) and 82.93% (136/164 subjects), respectively; in RA switched subjects, 100.0% (1/1 subject) and 90.67% (68/75 subjects), respectively; in FC naïve subjects, 100.0% (1/1 subject) and 66.67% (6/9 subjects), respectively; in SC naïve subjects, 100.0% (6/6 subjects) and 90.67% (68/75 subjects), respectively; in SC switched subjects, 100.0% (4/4 subjects) and 95.71% (67/70 subjects), respectively; in UC naïve subjects, 66.67% (2/3 subjects) and 87.30% (55/63 subjects), respectively, and there was no indication with a statistically significant difference (Table 181).

Table 181 Efficacy assessment by current disease (complication)

Complication		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	Yes	6	(100.0)	0	(0.00)	6	(2.12)	1.0000[1)]
	No	270	(97.47)	7	(2.53)	277	(97.88)	
Total		276	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	Yes	8	(100.0)	0	(0.00)	8	(4.35)	1.0000[1)]
	No	169	(96.02)	7	(3.98)	176	(95.65)	
Total		177	(96.20)	7	(3.80)	184	(100.0)	
RA naïve subject	Yes	1	(100.0)	0	(0.00)	1	(0.61)	1.0000[1)]
	No	136	(82.93)	28	(17.07)	164	(99.39)	
Total		137	(83.03)	28	(16.97)	165	(100.0)	

Complication		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
RA switched subject	Yes	1	(100.0)	0	(0.00)	1	(1.32)	1.0000[1)]
	No	68	(90.67)	7	(9.33)	75	(98.68)	
	Total	69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	1	(100.0)	0	(0.00)	1	(100.0)	
	Total	1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Total	0	(NA)	0	(NA)	0	(NA)	
PS naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	1	(50.00)	1	(50.00)	2	(100.0)	
	Total	1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	2	(100.0)	0	(0.00)	2	(100.0)	
	Total	2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	Yes	1	(100.0)	0	(0.00)	1	(10.00)	1.0000[1)]
	No	6	(66.67)	3	(33.33)	9	(90.00)	
	Total	7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(100.0)	0	(0.00)	7	(100.0)	
	Total	7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	Yes	6	(100.0)	0	(0.00)	6	(7.41)	1.0000[1)]
	No	68	(90.67)	7	(9.33)	75	(92.59)	
	Total	74	(91.36)	7	(8.64)	81	(100.0)	
SC switched subject	Yes	4	(100.0)	0	(0.00)	4	(5.41)	1.0000[1)]
	No	67	(95.71)	3	(4.29)	70	(94.59)	
	Total	71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	15	(62.50)	9	(37.50)	24	(100.0)	
	Total	15	(62.50)	9	(37.50)	24	(100.0)	

Complication		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
PC switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	22	(100.0)	0	(0.00)	22	(100.0)	
Total		22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	Yes	2	(66.67)	1	(33.33)	3	(4.55)	0.3606[1)]
	No	55	(87.30)	8	(12.70)	63	(95.45)	
Total		57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(70.00)	3	(30.00)	10	(100.0)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
PU naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	0	(0.00)	14	(100.0)	14	(100.0)	
Total		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(100.0)	0	(0.00)	7	(100.0)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

B.5. Tuberculosis and other severe infection

From response rate analysis by tuberculosis and other severe infection, after excluding PS naïve and switched subjects, FC switched subjects, PC naïve and switched subjects and PU naïve and switched subjects as there were no relevant subjects, the response rate for 'Yes' or 'No' was as follows: in AS naïve subjects, 95.08% (58/61 subjects) and 98.20% (218/222 subjects), respectively; in AS switched subjects, 100.0% (10/10 subjects) and 95.98% (167/174 subjects), respectively; in RA naïve subjects, 82.61% (19/23 subjects) and 83.10% (118/142 subjects), respectively; in RA switched subjects, 50.00% (1/2 subjects) and 91.89% (68/74 subjects), respectively; in SC naïve subjects, 100.0% (5/5 subjects) and 90.79% (69/76 subjects), respectively; in SC switched subjects, 100.0% (1/1 subject) and 95.89% (70/73 subjects), respectively; in UC naïve subjects, 66.67% (2/3 subjects) and 87.30% (55/63 subjects), respectively; in UC switched subjects, 100.0% (1/1 subject) and 66.67% (6/9 subjects) respectively, and there was no indication with a statistically significant difference (Table 182).

Table 182 Efficacy assessment by current disease (tuberculosis and other severe infection)

Tuberculosis and other severe infection	Responder		Non-responder		Total		p-value
	N	(%)	N	(%)	N	(%)	

Tuberculosis and other severe infection		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	Yes	58	(95.08)	3	(4.92)	61	(21.55)	0.1734[1)]
	No	218	(98.20)	4	(1.80)	222	(78.45)	
	Total	276	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	Yes	10	(100.0)	0	(0.00)	10	(5.43)	1.0000[1)]
	No	167	(95.98)	7	(4.02)	174	(94.57)	
	Total	177	(96.20)	7	(3.80)	184	(100.0)	
RA naïve subject	Yes	19	(82.61)	4	(17.39)	23	(13.94)	1.0000[1)]
	No	118	(83.10)	24	(16.90)	142	(86.06)	
	Total	137	(83.03)	28	(16.97)	165	(100.0)	
RA switched subject	Yes	1	(50.00)	1	(50.00)	2	(2.63)	0.1768[1)]
	No	68	(91.89)	6	(8.11)	74	(97.37)	
	Total	69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	1	(100.0)	0	(0.00)	1	(100.0)	
	Total	1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Total	0	(NA)	0	(NA)	0	(NA)	
PS naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	1	(50.00)	1	(50.00)	2	(100.0)	
	Total	1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	2	(100.0)	0	(0.00)	2	(100.0)	
	Total	2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(70.00)	3	(30.00)	10	(100.0)	
	Total	7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(100.0)	0	(0.00)	7	(100.0)	
	Total	7	(100.0)	0	(0.00)	7	(100.0)	

Tuberculosis and other severe infection		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
SC naïve subject	Yes	5	(100.0)	0	(0.00)	5	(6.17)	1.0000[1)]
	No	69	(90.79)	7	(9.21)	76	(93.83)	
	Total	74	(91.36	7	(8.64)	81	(100.0)	
SC switched subject	Yes	1	(100.0)	0	(0.00)	1	(1.35)	1.0000[1)]
	No	70	(95.89)	3	(4.11)	73	(98.65)	
	Total	71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	15	(62.50)	9	(37.50)	24	(100.0)	
	Total	15	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	22	(100.0)	0	(0.00)	22	(100.0)	
	Total	22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	Yes	2	(66.67)	1	(33.33)	3	(4.55)	0.3606[1)]
	No	55	(87.30)	8	(12.70)	63	(95.45)	
	Total	57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	Yes	1	(100.0)	0	(0.00)	1	(10.00)	1.0000[1)]
	No	6	(66.67)	3	(33.33)	9	(90.00)	
	Total	7	(70.00)	3	(30.00)	10	(100.0)	
PU naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	0	(0.00)	14	(100.0)	14	(100.0)	
	Total	0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(100.0)	0	(0.00)	7	(100.0)	
	Total	7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

B.6. Opportunistic infection

There were no subjects with opportunistic infection.

B.7. Moderate to severe heart failure

There were no subjects with moderate to severe heart failure.

6) Status of surveillance drug treatment

A. Average dose per administration

From response rate analysis by average dose per administration of the surveillance drug, the response rate was as follows: in AS naïve subjects, 96.50% (193/200 subjects), 100% (73/73 subjects) and 100% (4/4 subjects) for <5 mg/kg, ≥5 ~ <6 mg/kg and ≥6 mg/kg, respectively; in AS switched subjects, 95.54% (107/112 subjects), 98.28% (57/58 subjects) and 100% (4/4 subjects) for <5 mg/kg, ≥5 ~ <6 mg/kg and ≥6 mg/kg, respectively; in RA naïve subjects, 83.33% (10/12 subjects), 81.88% (113/138 subjects) and 100.0% (10/10 subjects) for <3 mg/kg, ≥3 ~ <4.5 mg/kg and ≥4.5 ~ <6 mg/kg, respectively; in RA switched subjects, 100.0% (9/9 subjects), 88.89% (32/36 subjects), 89.29% (25/28 subjects) and 100.0% (3/3 subjects) for <3 mg/kg, ≥3 ~ <4.5 mg/kg, ≥4.5 ~ <6 mg/kg and ≥6 mg/kg, respectively; in PS naïve subjects, 50.00% (1/2 subjects) only for <5 mg/kg; in PS switched subjects, 100.0% (1/1 subject) and 100.0% (1/1 subject) for <5 mg/kg and ≥5 ~ <6 mg/kg, respectively; in FC naïve subjects, 66.67% (4/6 subjects) and 75.00% (3/4 subjects) for <5 mg/kg and ≥5 ~ <7.5 mg/kg, respectively; in FC switched subjects, 100.0% (1/1 subject), 100.0% (5/5 subjects) and 100.0% (1/1 subject) for <5 mg/kg, ≥5 ~ <7.5 mg/kg and ≥10 mg/kg, respectively; in SC naïve subjects, 93.75% (15/16 subjects), 90.48% (57/63 subjects) and 100.0% (2/2 subjects) for <5 mg/kg, ≥5 ~ <7.5 mg/kg and ≥7.5 ~ <10 mg/kg, respectively; in SC switched subjects, 100.0% (14/14 subjects), 97.83% (45/46 subjects), 100.0% (8/8 subjects) and 66.67% (4/6 subjects) for <5 mg/kg, ≥5 ~ <7.5 mg/kg, ≥7.5 ~ <10 mg/kg ≥10 mg/kg, respectively; in PC naïve subjects, 66.67% (2/3 subjects) and 61.90% (13/21 subjects) for <5 mg/kg and ≥5 ~ <7.5 mg/kg, respectively; in PC switched subjects, 100.0% (3/3 subjects), 100.0% (13/13 subjects) and 100.0% (4/4 subjects) for <5 mg/kg, ≥5 ~ <7.5 mg/kg and ≥7.5 ~ <10 mg/kg, respectively; in UC naïve subjects, 80.00% (12/15 subjects), 90.24% (37/41 subjects) and 80.00% (8/10 subjects) for <5 mg/kg, ≥5 ~ <6 mg/kg and ≥6 mg/kg, respectively; in UC switched subjects, 100.0% (2/2 subjects) and 62.50% (5/8 subjects) for <5 mg/kg and ≥5 ~ <6 mg/kg, respectively; in PU naïve subjects, 0.00% (0/2 subjects), 0.00% (0/2 subjects) and 0.00% (0/10 subjects) for <5 mg/kg, ≥5 ~ <7.5 mg/kg and ≥7.5 ~ <10 mg/kg, respectively; and in PU switched subjects, 100.0% (3/3 subjects) and 100.0% (4/4 subjects) for ≥5 ~ <7.5 mg/kg and ≥7.5 ~ <10 mg/kg, respectively, and an indication with a statistically significant difference was SC switched subjects with a p-value of 0.0500 (Table 183).

Table 183 Efficacy assessment by average dose per administration

Average dose per administration (unit: mg/kg)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	<5	193	(96.50)	7	(3.50)	200	(72.20)	0.2738[1)]
	≥5 ~ <6	73	(100.0)	0	(0.00)	73	(26.35)	
	≥6	4	(100.0)	0	(0.00)	4	(1.44)	
Total		270	(97.47)	7	(2.53)	277	(100.0)	
AS switched subject	<5	107	(95.54)	5	(4.46)	112	(64.37)	0.7094[1)]
	≥5 ~ <6	57	(98.28)	1	(1.72)	58	(33.33)	
	≥6	4	(100.0)	0	(0.00)	4	(2.30)	

Average dose per administration (unit: mg/kg)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
Total		168	(96.55)	6	(3.45)	174	(100.0)	
RA naïve subject	<3	10	(83.33)	2	(16.67)	12	(7.50)	0.4634[1)]
	≥3 ~ <4.5	113	(81.88)	25	(18.12)	138	(86.25)	
	≥4.5 ~ <6	10	(100.0)	0	(0.00)	10	(6.25)	
	≥6	0	(NA)	0	(NA)	0	(NA)	
Total		133	(83.13)	27	(16.88)	160	(100.0)	
RA switched subject	<3	9	(100.0)	0	(0.00)	9	(11.84)	0.8120[1)]
	≥3 ~ <4.5	32	(88.89)	4	(11.11)	36	(47.37)	
	≥4.5 ~ <6	25	(89.29)	3	(10.71)	28	(36.84)	
	≥6	3	(100.0)	0	(0.00)	3	(3.95)	
Total		69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	<5	1	(100.0)	0	(0.00)	1	(100.0)	-
	≥5 ~ <6	0	(NA)	0	(NA)	0	(NA)	
	≥6	0	(NA)	0	(NA)	0	(NA)	
Total		1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	<5	0	(NA)	0	(NA)	0	(NA)	-
	≥5 ~ <6	0	(NA)	0	(NA)	0	(NA)	
	≥6	0	(NA)	0	(NA)	0	(NA)	
Total		0	(NA)	0	(NA)	0	(NA)	
PS naïve subject	<5	1	(50.00)	1	(50.00)	2	(100.0)	-
	≥5 ~ <6	0	(NA)	0	(NA)	0	(NA)	
	≥6	0	(NA)	0	(NA)	0	(NA)	
Total		1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	<5	1	(100.0)	0	(0.00)	1	(50.00)	-
	≥5 ~ <6	1	(100.0)	0	(0.00)	1	(50.00)	
	≥6	0	(NA)	0	(NA)	0	(NA)	
Total		2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	<5	4	(66.67)	2	(33.33)	6	(60.00)	1.0000[1)]
	≥5 ~ <7.5	3	(75.00)	1	(25.00)	4	(40.00)	
	≥7.5 ~ <10	0	(NA)	0	(NA)	0	(NA)	
	≥10	0	(NA)	0	(NA)	0	(NA)	

Average dose per administration (unit: mg/kg)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	<5	1	(100.0)	0	(0.00)	1	(14.29)	-
	≥5 ~ <7.5	5	(100.0)	0	(0.00)	5	(71.43)	
	≥7.5 ~ <10	0	(NA)	0	(NA)	0	(NA)	
	≥10	1	(100.0)	0	(0.00)	1	(14.29)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	<5	15	(93.75)	1	(6.25)	16	(19.75)	1.0000[1)]
	≥5 ~ <7.5	57	(90.48)	6	(9.52)	63	(77.78)	
	≥7.5 ~ <10	2	(100.0)	0	(0.00)	2	(2.47)	
	≥10	0	(NA)	0	(NA)	0	(NA)	
Total		74	(91.36)	7	(8.64)	81	(100.0)	
SC switched subject	<5	14	(100.0)	0	(0.00)	14	(18.92)	0.0500[1)]
	≥5 ~ <7.5	45	(97.83)	1	(2.17)	46	(62.16)	
	≥7.5 ~ <10	8	(100.0)	0	(0.00)	8	(10.81)	
	≥10	4	(66.67)	2	(33.33)	6	(8.11)	
Total		71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	<5	2	66.67	1	33.33	3	12.50	1.0000[1)]
	≥5 ~ <7.5	13	61.90	8	38.10	21	87.50	
	≥7.5 ~ <10	0	(NA)	0	(NA)	0	(NA)	
	≥10	0	(NA)	0	(NA)	0	(NA)	
Total		15	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	<5	2	66.67	1	33.33	3	12.50	-
	≥5 ~ <7.5	13	61.90	8	38.10	21	87.50	
	≥7.5 ~ <10	0	(NA)	0	(NA)	0	(NA)	
	≥10	0	(NA)	0	(NA)	0	(NA)	
Total		22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	<5	12	(80.00)	3	(20.00)	15	(22.73)	0.4478[1)]
	≥5 ~ <6	37	(90.24)	4	(9.76)	41	(62.12)	
	≥6	8	(80.00)	2	(20.00)	10	(15.15)	
Total		57	(86.36)	9	(13.64)	66	(100.0)	
UC	<5	2	(100.0)	0	(0.00)	2	(20.00)	1.0000[1)]

Average dose per administration (unit: mg/kg)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
switched subject	≥5 ~ <6	5	(62.50)	3	(37.50)	8	(80.00)	
	≥6	0	(NA)	0	(NA)	0	(NA)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
PU naïve subject	<5	0	(0.00)	2	(100.0)	2	(14.29)	
	≥5 ~ <7.5	0	(0.00)	2	(100.0)	2	(14.29)	-
	≥7.5 ~ <10	0	(0.00)	10	(100.0)	10	(71.43)	
Total		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	<5	0	(NA)	0	(NA)	0	(NA)	
	≥5 ~ <7.5	3	(100.0)	0	(0.00)	3	(42.86)	-
	≥7.5 ~ <10	4	(100.0)	0	(0.00)	4	(57.14)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	

1) Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

B. Total administration number

From response rate analysis by total administration number, the response rate was as follows: in AS naïve subjects, 33.33% (1/3 subjects), 96.67% (29/30 subjects) and 98.40% (246/250 subjects) for 1~2, 3~4 and 5~6, respectively; in AS switched subjects, 90.91% (10/11 subjects), 94.74% (18/19 subjects) and 96.75% (149/154 subjects) for 1~2, 3~4 and 5~6, respectively; in RA naïve subjects, 25.00% (1/4 subjects), 42.86% (3/7 subjects) and 86.36% (133/154 subjects) for 1~3, 4~5 and 6~7, respectively; in RA switched subjects, 50.00% (2/4 subjects), 100.0% (2/2 subjects) and 92.86% (65/70 subjects) for 1~3, 4~5 and 6~7, respectively; in PS naïve subjects, 50.00% (1/2 subjects) for 5~6; in PS switched subjects, 100.0% (1/1 subject) and 100.0% (1/1 subject) for 1~4 and 5~6, respectively; in FC naïve subjects, 70.00% (7/10 subjects) for 4~6; in FC switched subjects, 100.0% (7/7 subjects) for 4~6; in SC naïve subjects, 100.0% (2/2 subjects), 100.0% (12/12 subjects) and 89.55% (60/67 subjects) for 1~2, 3~4 and 5~6, respectively; in SC switched subjects, 77.78% (7/9 subjects), 100.0% (15/15 subjects) and 98.00% (49/50 subjects) for 1~2, 3~4 and 5~6, respectively; in PC naïve subjects, 69.23% (9/13 subjects) and 54.55% (3/11 subjects) for 3~4 and 5~6, respectively; in PC switched subjects, 100.0% (1/1 subject), 100.0% (5/5 subjects) and 100.0% (16/16 subjects) for 1~2, 3~4 and 5~6, respectively; in UC naïve subjects, 40.00% (2/5 subjects) and 90.16% (55/61 subjects) for 1~3 and 4~6, respectively; in UC switched subjects, 0% (0/3 subjects) and 100.0% (7/7 subjects) for 1~3 and 4~6, respectively; in PU naïve subjects, 0.00% (0/14 subjects) for 4~6; in PU switched subjects, 100.0% (7/7 subjects) in 4~6; items with a statistically significant difference were AS naïve subjects, RA naïve subjects, RA switched subjects, UC naïve subjects and UC switched subjects, and the p-value was 0.0010, 0.0006, 0.0475, 0.0158 and 0.0083, respectively (Table 184).

Table 184 Efficacy assessment by total administration number

Total administration number		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	1~2	1	(33.33)	2	(66.67)	3	(1.06)	0.0010[1)]
	3~4	29	(96.67)	1	(3.33)	30	(10.60)	
	5~6	246	(98.40)	4	(1.60)	250	(88.34)	
Total		276	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	1~2	10	(90.91)	1	(9.09)	11	(5.98)	0.3198[1)]
	3~4	18	(94.74)	1	(5.26)	19	(10.33)	
	5~6	149	(96.75)	5	(3.25)	154	(83.70)	
Total		177	(96.20)	7	(3.80)	184	(100.0)	
RA naïve subject	1~3	1	(25.00)	3	(75.00)	4	(2.42)	0.0006[1)]
	4~5	3	(42.86)	4	(57.14)	7	(4.24)	
	6~7	133	(86.36)	21	(13.64)	154	(93.33)	
Total		137	(83.03)	28	(16.97)	165	(100.0)	
RA switched subject	1~3	2	(50.00)	2	(50.00)	4	(5.26)	0.0475[1)]
	4~5	2	(100.0)	0	(0.00)	2	(2.63)	
	6~7	65	(92.86)	5	(7.14)	70	(92.11)	
Total		69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	1~3	0	(NA)	0	(NA)	0	(NA)	-
	4~6	1	(100.0)	0	(NA)	1	(100.0)	
Total		1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	1~3	0	(NA)	0	(NA)	0	(NA)	-
	4~6	0	(NA)	0	(NA)	0	(NA)	
Total		0	(NA)	0	(NA)	0	(NA)	
PS naïve subject	1~4	0	(NA)	0	(NA)	0	(NA)	-
	5~6	1	(50.00)	1	(50.00)	2	(100.0)	
Total		1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	1~4	1	(100.0)	0	(0.00)	1	(50.00)	-
	5~6	1	(100.0)	0	(0.00)	1	(50.00)	
Total		2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	1~3	0	(NA)	0	(NA)	0	(NA)	-
	4~6	7	(70.00)	3	(30.00)	10	(100.0)	

Total administration number		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	1~3	0	(NA)	0	(NA)	0	(NA)	-
	4~6	7	(100.0)	0	(0.00)	7	(100.0)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	1~2	2	(100.0)	0	(0.00)	2	(2.47)	0.6556[1)]
	3~4	12	(100.0)	0	(0.00)	12	(14.81)	
	5~6	60	(89.55)	7	(10.45)	67	(82.72)	
Total		74	(91.36	7	(8.64)	81	(100.0)	
SC switched subject	1~2	7	(77.78)	2	(22.22)	9	(12.16)	0.0590[1)]
	3~4	15	(100.0)	0	(0.00)	15	(20.27)	
	5~6	49	(98.00)	1	(2.00)	50	(67.57)	
Total		71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	1~2	0	(NA)	0	(NA)	0	(NA)	0.6752[1)]
	3~4	9	(69.23)	4	(30.77)	13	(54.17)	
	5~6	6	(54.55)	5	(45.45)	11	(45.83)	
Total		15	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	1~2	1	(100.0)	0	(0.00)	1	(4.55)	-
	3~4	5	(100.0)	0	(0.00)	5	(22.73)	
	5~6	16	(100.0)	0	(0.00)	16	(72.73)	
Total		22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	1~3	2	(40.00)	3	(60.00)	5	(7.58)	0.0158[1)]
	4~6	55	(90.16)	6	(9.84)	61	(92.42)	
Total		57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	1~3	0	(0.00)	3	(100.0)	3	(30.00)	0.0083[1)]
	4~6	7	(100.0)	0	(0.00)	7	(70.00)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
PU naïve subject	1~3	0	(NA)	0	(NA)	0	(NA)	-
	4~6	0	(0.00)	14	(100.0)	14	(100.0)	
Total		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	1~3	0	(NA)	0	(NA)	0	(NA)	-
	4~6	7	(100.0)	0	(0.00)	7	(100.0)	

Total administration number	Responder		Non-responder		Total		p-value
	N	(%)	N	(%)	N	(%)	
Total	7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

C. Average administration duration

From response rate analysis by average administration duration, the response rate was as follows: in AS naïve subjects, 100.0% (31/31 subjects), 97.44% (228/234 subjects) and 94.44% (17/18 subjects) for <120 min, ≥120 ~ <180 min and ≥180 min, respectively; in AS switched subjects, 100.0% (26/26 subjects), 95.21% (139/146 subjects) and 100.0% (12/12 subjects) for <120 min, ≥120 ~ <180 min and ≥180 min, respectively; in RA naïve subjects, 78.95% (45/57 subjects), 84.38% (81/96 subjects) and 91.67% (11/12 subjects) for <120 min, ≥120 ~ <180 min and ≥180 min, respectively; in RA switched subjects, 96.88% (31/32 subjects), 89.19% (33/37 subjects) and 71.43% (5/7 subjects) for <120 min, ≥120 ~ <180 min and ≥180 min, respectively; in PS naïve subjects, 50.00% (1/2 subjects) for ≥120 ~ <180 min; in PS switched subjects, 100.0% (2/2 subjects) for ≥120 ~ <180 min; in FC naïve subjects, 70.00% (7/10 subjects) for ≥20 ~ <180 min; in FC switched subjects, 100.0% (1/1 subject) and 100.0% (6/6 subjects) for <120 min, ≥120 ~ <180 min, respectively; in SC naïve subjects, 93.75% (15/16 subjects), 91.80% (56/61 subjects) and 75.00% (3/4 subjects) for <120 min, ≥120 ~ <180 min and ≥180 min, respectively; in SC switched subjects, 100.0% (17/17 subjects), 93.75% (45/48 subjects) and 100.0% (9/9 subjects) for <120 min, ≥120 ~ <180 min and ≥180 min, respectively; in PC naïve subjects, 71.43% (10/14 subjects) and 50.00% (5/10 subjects) for ≥120 ~ <180 min and ≥180 min, respectively; in PC switched subjects, 100.0% (16/16 subjects) and 100.0% (6/6 subjects) for ≥120 ~ <180 min and ≥180 min, respectively; in UC naïve subjects, 100.0% (11/11 subjects), 83.02% (44/53 subjects) and 100.0% (2/2 subjects) for <120 min, ≥120 ~ <180 min and ≥180 min, respectively; in UC switched subjects, 50% (1/2 subjects) and 75.00% (6/8 subjects) for <120 min and ≥120 ~ <180 min, respectively; in PU naïve subjects, 0.00% (0/10 subjects) and 0.00% (0/4 subjects) for ≥120 ~ <180 min and ≥180 min, respectively; in PU switched subjects, 100.0% (6/6 subjects) and 100.0% (1/1 subject) for ≥120 ~ <180 min and ≥180 min, respectively, and there was no indication with a statistically significant difference (Table 185).

Table 185 Efficacy assessment by average administration duration

Average administration duration (unit: min)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	<120	31	(100.0)	0	(0.00)	31	(10.95)	0.4923[2)]
	≥120 ~ <180	228	(97.44)	6	(2.56)	234	(82.69)	
	≥180	17	(94.44)	1	(5.56)	18	(6.36)	
Total		276	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	<120	26	(100.0)	0	(0.00)	26	(14.13)	0.7503[2)]
	≥120 ~ <180	139	(95.21)	7	(4.79)	146	(79.35)	
	≥180	12	(100.0)	0	(0.00)	12	(6.52)	
Total		177	(96.20)	7	(3.80)	184	(100.0)	

Average administration duration (unit: min)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
RA naïve subject	<120	45	(78.95)	12	(21.05)	57	(34.55)	0.4885[1)]
	≥120 ~ <180	81	(84.38)	15	(15.63)	96	(58.18)	
	≥180	11	(91.67)	1	(8.33)	12	(7.27)	
Total		137	(83.03)	28	(16.97)	165	(100.0)	
RA switched subject	<120	31	(96.88)	1	(3.13)	32	(42.11)	0.0858[2)]
	≥120 ~ <180	33	(89.19)	4	(10.81)	37	(48.68)	
	≥180	5	(71.43)	2	(28.57)	7	(9.21)	
Total		69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	<120	0	(NA)	0	(NA)	0	(NA)	-
	≥120 ~ <180	1	(100.0)	0	(0.00)	1	(100.0)	
	≥180	0	(NA)	0	(NA)	0	(NA)	
Total		1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	<120	0	(NA)	0	(NA)	0	(NA)	-
	≥120 ~ <180	0	(NA)	0	(NA)	0	(NA)	
	≥180	0	(NA)	0	(NA)	0	(NA)	
Total		0	(NA)	0	(NA)	0	(NA)	
PS naïve subject	<120	0	(NA)	0	(NA)	0	(NA)	-
	≥120 ~ <180	1	(50.00)	1	(50.00)	2	(100.0)	
	≥180	0	(NA)	0	(NA)	0	(NA)	
Total		1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	<120	0	(NA)	0	(NA)	0	(NA)	-
	≥120 ~ <180	2	(100.0)	0	(0.00)	2	(100.0)	
	≥180	0	(NA)	0	(NA)	0	(NA)	
Total		2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	<120	0	(NA)	0	(NA)	0	(NA)	-
	≥120 ~ <180	7	(70.00)	3	(30.00)	10	(100.0)	
	≥180	0	(NA)	0	(NA)	0	(NA)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	<120	1	(100.0)	0	(0.00)	1	(14.29)	-
	≥120 ~ <180	6	(100.0)	0	(0.00)	6	(85.71)	
	≥180	0	(NA)	0	(NA)	0	(NA)	

Average administration duration (unit: min)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	<120	15	(93.75)	1	(6.25)	16	(19.75)	0.4137[2)]
	≥120 ~ <180	56	(91.80)	5	(8.20)	61	(75.31)	
	≥180	3	(75.00)	1	(25.00)	4	(4.94)	
Total		74	(91.36	7	(8.64)	81	(100.0)	
SC switched subject	<120	17	(100.0)	0	(0.00)	17	(22.97)	0.7042[2)]
	≥120 ~ <180	45	(93.75)	3	(6.25)	48	(64.86)	
	≥180	9	(100.0)	0	(0.00)	9	(12.16)	
Total		71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	<120	0	(NA)	0	(NA)	0	(NA)	0.4028[2)]
	≥120 ~ <180	10	(71.43)	4	(28.57)	14	(58.33)	
	≥180	5	(50.00)	5	(50.00)	10	(41.67)	
Total		15	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	<120	0	(NA)	0	(NA)	0	(NA)	-
	≥120 ~ <180	16	(100.0)	0	(0.00)	16	(72.73)	
	≥180	6	(100.0)	0	(0.00)	6	(27.27)	
Total		22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	<120	11	(100.0)	0	(0.00)	11	(16.67)	0.5076[2)]
	≥120 ~ <180	44	(83.02)	9	(16.98)	53	(80.30)	
	≥180	2	(100.0)	0	(0.00)	2	(3.03)	
Total		57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	<120	1	(50.00)	1	(50.00)	2	(20.00)	1.0000[2)]
	≥120 ~ <180	6	(75.00)	2	(25.00)	8	(80.00)	
	≥180	0	(NA)	0	(NA)	0	(NA)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
PU naïve subject	<120	0	(NA)	0	(NA)	0	(NA)	-
	≥120 ~ <180	0	(0.00)	10	(100.0)	10	(71.43)	
	≥180	0	(0.00)	4	(100.0)	4	(28.57)	
Total		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	<120	0	(NA)	0	(NA)	0	(NA)	-
	≥120 ~ <180	6	(100.0)	0	(0.00)	6	(85.71)	

Average administration duration (unit: min)		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
	≥180	1	(100.0)	0	(0.00)	1	(14.29)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Chi-square test / [2)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

7) Concomitant medication

From response rate analysis by use of concomitant medication, after excluding RA switched subjects, PS naïve and switched subjects, FC naïve and switched subjects, PC switched subjects, UC switched subjects and PU naïve and switched subjects as there were no subjects not using the concomitant medication, the response rate for 'Yes' or 'No' was as follows: in AS naïve subjects, 97.50% (273/280 subjects) and 100.0% (3/3 subjects), respectively; in AS switched subjects, 95.93% (165/172 subjects) and 100.0% (12/12 subjects), respectively; in RA naïve subjects, 82.93% (136/164 subjects) and 100.0% (1/1 subject), respectively; in SC naïve subjects, 91.25% (73/80 subjects) and 100.0% (1/1 subject), respectively; in SC switched subjects, 95.83% (69/72 subjects) and 100.0% (2/2 subjects), respectively; in PC naïve subjects, 60.87% (14/23 subjects) and 100.0% (1/1 subject), respectively; in UC naïve subjects, 86.15% (56/65 subjects) and 100.0% (1/1 subject) respectively, and there was no indication with a statistically significant difference (Table 186).

Table 186 Efficacy assessment by use of concomitant medication

Use of concomitant medication		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	Yes	273	(97.50)	7	(2.50)	280	(98.94)	1.0000[1)]
	No	3	(100.0)	0	(0.00)	3	(1.06)	
Total		276	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	Yes	165	(95.93)	7	(4.07)	172	(93.48)	1.0000[1)]
	No	12	(100.0)	0	(0.00)	12	(6.52)	
Total		177	(96.20)	7	(3.80)	184	(100.0)	
RA naïve subject	Yes	136	(82.93)	28	(17.07)	164	(99.39)	1.0000[1)]
	No	1	(100.0)	0	(0.00)	1	(0.61)	
Total		137	(83.03)	28	(16.97)	165	(100.0)	
RA switched subject	Yes	69	(90.79)	7	(9.21)	76	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
Total		69	(90.79)	7	(9.21)	76	(100.0)	
PA	Yes	1	(100.0)	0	(0.00)	1	(100.0)	-

Use of concomitant medication		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
naïve subject	No	0	(NA)	0	(NA)	0	(NA)	
Total		1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	0	(NA)	0	(NA)	0	(NA)	
Total		0	(NA)	0	(NA)	0	(NA)	
PS naïve subject	Yes	1	(50.00)	1	(50.00)	2	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
Total		1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	Yes	2	(100.0)	0	(0.00)	2	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
Total		2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	Yes	7	(70.00)	3	(30.00)	10	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	Yes	7	(100.0)	0	(0.00)	7	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	Yes	73	(91.25)	7	(8.75)	80	(98.77)	1.0000[1)]
	No	1	(100.0)	0	(0.00)	1	(1.23)	
Total		74	(91.36)	7	(8.64)	81	(100.0)	
SC switched subject	Yes	69	(95.83)	3	(4.17)	72	(97.30)	1.0000[1)]
	No	2	(100.0)	0	(0.00)	2	(2.70)	
Total		71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	Yes	14	(60.87)	9	(39.13)	23	(95.83)	1.0000[1)]
	No	1	(100.0)	(0.00)	(0.00)	1	(4.17)	
Total		15	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	Yes	22	(100.0)	0	(0.00)	22	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
Total		22	(100.0)	0	(0.00)	22	(100.0)	
UC	Yes	56	(86.15)	9	(13.85)	65	(98.48)	1.0000[1)]

Use of concomitant medication		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
naïve subject	No	1	(100.0)	0	(0.00)	1	(1.52)	
Total		57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	Yes	7	(70.00)	3	(30.00)	10	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
PU naïve subject	Yes	0	(0.00)	14	(100.0)	14	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
Total		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	Yes	7	(100.0)	0	(0.00)	7	(100.0)	-
	No	0	(NA)	0	(NA)	0	(NA)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

3.2.3 Efficacy assessment in special population

A. Elderly

From response rate analysis after classifying subjects aged ≥65 years as the Elderly, PS naïve and switched subjects, FC naïve and switched subjects, SC switched subjects, PC naïve and switched subjects and PU naïve and switched subjects included no Elderly aged ≥65 years, and the response rate by elderly classification was as follows: in AS naïve subjects, <65 years 97.48% (271/278 subjects), ≥65 years 100.0% (5/5 subjects); in AS switched subjects, <65 years 96.51% (166/172 subjects), ≥65 years 91.67% (11/12 subjects); in RA naïve subjects, <65 years 83.46% (111/133 subjects), ≥65 years 81.25% (26/32 subjects); in RA switched subjects, <65 years 88.52% (54/61 subjects), ≥65 years 100.0% (15/15 subjects); in SC naïve subjects, <65 years 92.31% (72/78 subjects), ≥65 years 66.67% (2/3 subjects); in UC naïve subjects, <65 years 87.50% (49/56 subjects), ≥65 years 80.00% (8/10 subjects); in UC switched subjects, <65 years 62.50% (5/8 subjects), ≥65 years 100.0% (2/2 subjects), and there was no indication with a statistically significant difference (Table 187).

Table 187 Efficacy assessment by Elderly classification

Elderly classification		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	<65 years	271	(97.48)	7	(2.52)	278	(98.23)	1.0000[2)]
	≥65 years	5	(100.0)	0	(0.00)	5	(1.77)	
	Total	276	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	<65 years	166	(96.51)	6	(3.49)	172	(93.48)	0.3814[2)]
	≥65 years	11	(91.67)	1	(8.33)	12	(6.52)	
	Total	177	(96.20)	7	(3.80)	184	(100.0)	
RA naïve subject	<65 years	111	(83.46)	22	(16.54)	133	(80.61)	0.7651[1)]
	≥65 years	26	(81.25)	6	(18.75)	32	(19.39)	
	Total	137	(83.03)	28	(16.97)	165	(100.0)	
RA switched subject	<65 years	54	(88.52)	7	(11.48)	61	(80.26)	0.3333[2)]
	≥65 years	15	(100.0)	0	(0.00)	15	(19.74)	
	Total	69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	<65 years	1	(100.0)	0	(0.00)	1	(100.0)	-
	≥65 years	0	(NA)	0	(NA)	0	(NA)	
	Total	1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	<65 years	0	(NA)	0	(NA)	0	(NA)	-
	≥65 years	0	(NA)	0	(NA)	0	(NA)	
	Total	0	(NA)	0	(NA)	0	(NA)	
PS	<65 years	1	(50.00)	1	(50.00)	2	(100.0)	

Elderly classification		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
naïve subject	≥65 years	0	(NA)	0	(NA)	0	(NA)	
	Total	1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	<65 years	2	(100.0)	0	(0.00)	2	(100.0)	-
	≥65 years	0	(NA)	0	(NA)	0	(NA)	
	Total	2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	<65 years	7	(70.00)	3	(30.00)	10	(100.0)	-
	≥65 years	0	(NA)	0	(NA)	0	(NA)	
	Total	7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	<65 years	7	(100.0)	0	(0.00)	7	(100.0)	-
	≥65 years	0	(NA)	0	(NA)	0	(NA)	
	Total	7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	<65 years	72	(92.31)	6	(7369)	78	(96.30)	0.2402[2)]
	≥65 years	2	(66.67)	1	(33.33)	3	(3.70)	
	Total	74	(91.36)	7	(8.64)	81	(100.0)	
SC switched subject	<65 years	71	(95.95)	3	(4.05)	74	(100.0)	-
	≥65 years	0	(NA)	0	(NA)	0	(NA)	
	Total	71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	<65 years	15	(62.50)	9	(37.50)	24	(100.0)	-
	≥65 years	0	(NA)	0	(NA)	0	(NA)	
	Total	15	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	<65 years	22	(100.0)	0	(0.00)	22	(100.0)	-
	≥65 years	0	(NA)	0	(NA)	0	(NA)	
	Total	22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	<65 years	49	(87.50)	7	(12.50)	56	(84.85)	0.6162[2)]
	≥65 years	8	(80.00)	2	(20.00)	10	(15.15)	
	Total	57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	<65 years	5	(62.50)	3	(37.50)	8	(80.00)	1.0000[2)]
	≥65 years	2	(100.0)	0	(0.00)	2	(20.00)	
	Total	7	(70.00)	3	(30.00)	10	(100.0)	

Elderly classification		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
PU naïve subject	<65 years	0	(0.00)	14	(100.0)	14	(100.0)	-
	≥65 years	0	(NA)	0	(NA)	0	(NA)	
Total		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	<65 years	7	(100.0)	0	(0.00)	7	(100.0)	-
	≥65 years	0	(NA)	0	(NA)	0	(NA)	
		7	(100.0)	0	(0.00)	7	(100.0)	

[1] Chi-square test / [2] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

B. Children

From response rate analysis after classifying subjects aged <12 years as children, the response rate by children classification was as follows: in PC naïve subjects, <12 years 50.00% (1/2 subjects), ≥12 years 63.64% (14/24 subjects); in PC switched subjects, <12 years 100.0% (4/4 subjects), ≥12 years 100.0% (18/18 subjects); in PU naïve subjects, <12 years 0.00% (0/4 subjects), ≥12 years 0.00% (0/10 subjects); in PU switched subjects, <12 years 100.0% (2/2 subjects), ≥12 years 100.0% (5/5 subjects). For other indications, there were no children aged <12 years, and there was no indication with a statistically significant difference (Table 188).

Table 188 Efficacy assessment by children classification

Children classification		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
PC naïve subject	<12 years	1	(50.00)	1	(50.00)	2	(8.33)	1.0000[2]
	≥12 years	14	(63.64)	8	(36.36)	22	(91.67)	
Total		15	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	<12 years	4	(100.0)	0	(0.00)	4	(18.18)	-
	≥12 years	18	(100.0)	0	(0.00)	18	(81.82)	
Total		22	(100.0)	0	(0.00)	22	(100.0)	
PU naïve subject	<12 years	0	(0.00)	4	(100.0)	4	(28.57)	-
	≥12 years	0	(0.00)	10	(100.0)	10	(71.43)	
Total		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	<12 years	2	(100.0)	0	(0.00)	2	(28.57)	-
	≥12 years	5	(100.0)	0	(0.00)	5	(71.43)	

Children classification	Responder		Non-responder		Total		p-value
	N	(%)	N	(%)	N	(%)	
Total	7	(100.0)	0	(0.00)	7	(100.0)	

[1] Chi-square test / [2] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

C. Pregnant women

There were no pregnant women among subjects.

D. Hepatic impairment

From response rate analysis by hepatic impairment, there were no subjects with hepatic impairment in PS naïve and switched subjects, FC naïve subjects, PC naïve and switched subjects, PU naïve and switched subjects, and the response rate for other indications was as follows: in AS naïve subjects, 100.0% (4/4 subjects) for subjects with hepatic impairment and 97.49% (272/279 subjects) for subjects without hepatic impairment; in AS switched subjects, 100.0% (11/11 subjects) for subjects with hepatic impairment and 95.95% (166/173 subjects) for subjects without hepatic impairment; in RA naïve subjects, 100.0% (3/3 subjects) for subjects with hepatic impairment and 82.72% (134/162 subjects) for subjects without hepatic impairment; in RA switched subjects, 50.00% (1/2 subjects) for subjects with hepatic impairment and 91.89% (68/74 subjects) for subjects without hepatic impairment; in SC naïve subjects, 75.00% (3/4 subjects) for subjects with hepatic impairment and 92.21% (71/77 subjects) for subjects without hepatic impairment; in SC switched subjects, 100.0% (2/2 subjects) for subjects with hepatic impairment and 95.83% (69/72 subjects) for subjects without hepatic impairment; in UC naïve subjects, 0.00% (0/1 subject) for subjects with hepatic impairment and 87.69% (57/65 subjects) for subjects without hepatic impairment; in UC switched subjects, 0.00% (0/1 subject) for subjects with hepatic impairment and 77.78% (7/9 subjects) for subjects without hepatic impairment, and there was no indication with a statistically significant difference (Table 189).

Table 189 Efficacy assessment by hepatic impairment classification

Hepatic impairment		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	Yes	4	(100.0)	0	(0.00)	4	(1.41)	1.0000[1]
	Yes	272	(97.49)	7	(2.51)	279	(98.59)	
Total		No	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	Yes	11	(100.0)	0	(0.00)	11	(5.98)	1.0000[1]
	No	166	(95.95)	7	(4.05)	173	(94.02)	
Total		177	(96.20)	7	(3.80)	184	(100.0)	
RA naïve subject	Yes	3	(100.0)	0	(0.00)	3	(1.82)	1.0000[1]
	No	134	(82.72)	28	(17.28)	162	(98.18)	
Total		137	(83.03)	28	(16.97)	165	(100.0)	

Hepatic impairment		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
RA switched subject	Yes	1	(50.00)	1	(50.00)	2	(2.63)	0.1768[1)]
	No	68	(91.89)	6	(8.11)	74	(97.37)	
	Total	69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	1	(100.0)	0	(0.00)	1	(100.0)	
	Total	1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Total	0	(NA)	0	(NA)	0	(NA)	
PS naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	1	(50.00)	1	(50.00)	2	(100.0)	
	Total	1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	2	(100.0)	0	(0.00)	2	(100.0)	
	Total	2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(70.00)	3	(30.00)	10	(100.0)	
	Total	7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	Yes	1	(100.0)	0	(0.00)	1	(14.29)	-
	No	6	(100.0)	0	(0.00)	6	(85.71)	
	Total	7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	Yes	3	(75.00)	1	(25.00)	4	(4.94)	0.3084[1)]
	No	71	(92.21)	6	(7.79)	77	(95.06)	
	Total	74	(91.36)	7	(8.64)	81	(100.0)	
SC switched subject	Yes	2	(100.0)	0	(0.00)	2	(2.70)	1.0000[1)]
	No	69	(95.83)	3	(4.17)	72	(97.30)	
	Total	71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	15	(62.50)	9	(37.50)	24	(100.0)	
	Total	15	(62.50)	9	(37.50)	24	(100.0)	

Hepatic impairment		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
PC switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	22	(100.0)	0	(0.00)	22	(100.0)	
Total		22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	Yes	0	(0.00)	1	(100.0)	1	(1.52)	0.1364[1)]
	No	57	(87.69)	8	(12.31)	65	(98.48)	
Total		57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	Yes	0	(0.00)	1	(100.0)	1	(10.00)	0.3000[1)]
	No	7	(77.78)	2	(22.22)	9	(90.00)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
PU naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	0	(0.00)	14	(100.0)	14	(100.0)	
Total		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(100.0)	0	(0.00)	7	(100.0)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

E. Renal impairment

From response rate analysis by renal impairment, there were no subjects with renal impairment in PS naïve and switched subjects, FC naïve and switched subjects, SC switched subjects, PC naïve and switched subjects, UC switched subjects and PU naïve and switched subjects, and the response rate for other indications was as follows: in AS naïve subjects, 100.0% (4/4 subjects) for subjects with renal impairment and 97/49% (272/279 subjects) for subjects without renal impairment; in AS switched subjects, 100.0% (2/2 subjects) for subjects with renal impairment and 96.15% (175/182 subjects) for subjects without renal impairment; in RA naïve subjects, 100.0% (1/1 subject) for subjects with renal impairment and 82.93% (136/164 subjects) for subjects without renal impairment; in RA switched subjects, 100.0% (1/1 subject) for subjects with renal impairment and 90.67% (68/75 subjects) for subjects without renal impairment; in SC naïve subjects, 100.0% (2/2 subjects) for subjects with renal impairment and 91.14% (72/79 subjects) for subjects without renal impairment; in UC naïve subjects, 0.00% (0/2 subjects) for subjects with renal impairment and 89.06% (57/64 subjects) for subjects without renal impairment, and the item with a statistically significant difference was UC naïve subjects, with a p-value of .0168 (Table 190).

Table 190 Efficacy assessment by renal impairment classification

Renal impairment	Responder	Non-responder	Total	p-value

		N	(%)	N	(%)	N	(%)	
AS naïve subject	Yes	4	(100.0)	0	(0.00)	4	(1.41)	1.0000[1)]
	No	272	(97.49)	7	(2.51)	279	(98.59)	
	Total	276	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	Yes	2	(100.0)	0	(0.00)	2	(1.09)	1.0000[1)]
	No	175	(96.15)	7	(3.85)	182	(98.91)	
	Total	177	(96.20)	7	(3.80)	184	(100.0)	
RA naïve subject	Yes	1	(100.0)	0	(0.00)	1	(0.61)	1.0000[1)]
	No	136	(82.93)	28	(17.07)	164	(99.39)	
	Total	137	(83.03)	28	(16.97)	165	(100.0)	
RA switched subject	Yes	1	(100.0)	0	(0.00)	1	(1.32)	1.0000[1)]
	No	68	(90.67)	7	(9.33)	75	(98.68)	
	Total	69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	1	(100.0)	0	(0.00)	1	(100.0)	
	Total	1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	0	(NA)	0	(NA)	0	(NA)	
	Total	0	(NA)	0	(NA)	0	(NA)	
PS naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	1	(50.00)	1	(50.00)	2	(100.0)	
	Total	1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	2	(100.0)	0	(0.00)	2	(100.0)	
	Total	2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(70.00)	3	(30.00)	10	(100.0)	
	Total	7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(100.0)	0	(0.00)	7	(100.0)	
	Total	7	(100.0)	0	(0.00)	7	(100.0)	
SC	Yes	2	(100.0)	0	(0.00)	2	(2.47)	1.0000[1)]

Renal impairment		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
naïve subject	No	72	(91.14)	7	(8.86)	79	(97.53)	
	Total	74	(91.36	7	(8.64)	81	(100.0)	
SC switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	71	(95.95)	3	(4.05)	74	(100.0)	
	Total	71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	15	(62.50)	9	(37.50)	24	(100.0)	
	Total	15	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	22	(100.0)	0	(0.00)	22	(100.0)	
	Total	22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	Yes	0	(0.00)	2	(100.0)	2	(3.03)	0.0168[1)]
	No	57	(89.06)	7	(10.94)	64	(96.97)	
	Total	57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(70.00)	3	(30.00)	10	(100.0)	
	Total	7	(70.00)	3	(30.00)	10	(100.0)	
PU naïve subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	0	(0.00)	14	(100.0)	14	(100.0)	
	Total	0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	Yes	0	(NA)	0	(NA)	0	(NA)	-
	No	7	(100.0)	0	(0.00)	7	(100.0)	
	Total	7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

F. Long-term use

From response rate analysis by Long-term use, the response rate was as follows: in AS naïve subjects, 91.18% (31/34 subjects) for non Long-term users and 98.39% (245/249 subjects) for Long-term users; in AS switched subjects, 96.15% (25/26 subjects) for non Long-term users and 96.20% (152/158 subjects) for Long-term users; in RA naïve subjects, 42.11% (8/19 subjects) for non Long-term users

and 88.36% (129/146 subjects) for Long-term users; in RA switched subjects, 75.00% (6/8 subjects) for non Long-term users and 92.65% (63/68 subjects) for Long-term users; in PS naïve subjects, 50.00% (1/2 subjects) for non Long-term users; in PS switched subjects, 100.0% (2/2 subjects) for non Long-term users; in FC naïve subjects, 50.00% (1/2 subjects) for non Long-term users and 75.00% (6/8 subjects) for Long-term users; in FC switched subjects, 100.0% (2/2 subjects) for non Long-term users and 10.00% (5/5 subjects) for Long-term users; in SC naïve subjects, 95.65% (22/23 subjects) for non Long-term users and 89.66% (52/58 subjects) for Long-term users; in SC switched subjects, 92.31% (24/26 subjects) for non Long-term users and 97.92% (47/48 subjects) for Long-term users; in PC naïve subjects, 68.42% (13/19 subjects) for non Long-term users and 40.00% (2/5 subjects) for Long-term users; in PC switched subjects, 100.0% (9/9 subjects) for non Long-term users and 100.0% (13/13 subjects) for Long-term users; in UC naïve subjects, 84.00% (21/25 subjects) for non Long-term users and 87.80% (36/41 subjects) for Long-term users; in UC switched subjects, 40.00% (2/5 subjects) for non Long-term users and 100.0% (5/5 subjects) for Long-term users; in PU naïve subjects, 0.00% (0/11 subjects) for non Long-term users and 0.00% (0/3 subjects) for Long-term users; in PU switched subjects, 100.0% (1/1 subject) for non Long-term users and 100.0% (6/6 subjects) for Long-term users, and indications with a statistically significant difference were AS naïve subjects and RA naïve subjects, with a p-value of 0.0397 and <0.0001, respectively (Table 191).

Table 191 Efficacy assessment by Long-term use

Classification		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
AS naïve subject	Short-term	31	(91.18)	3	(8.82)	34	(12.01)	0.0397[1)]
	Long-term	245	(98.39)	4	(1.61)	249	(87.99)	
Total		276	(97.53)	7	(2.47)	283	(100.0)	
AS switched subject	Short-term	25	(96.15)	1	(3.85)	26	(14.13)	1.0000[1)]
	Long-term	152	(96.20)	6	(3.80)	158	(85.87)	
Total		177	(96.20)	7	(3.80)	184	(100.0)	
RA naïve subject	Short-term	8	(42.11)	11	(57.89)	19	(11.52)	<.0001[1)]
	Long-term	129	(88.36)	17	(11.64)	146	(88.48)	
Total		137	(83.03)	28	(16.97)	165	(100.0)	
RA switched subject	Short-term	6	(75.00)	2	(25.00)	8	(10.53)	0.1560[1)]
	Long-term	63	(92.65)	5	(7.35)	68	(89.47)	
Total		69	(90.79)	7	(9.21)	76	(100.0)	
PA naïve subject	Short-term	0	(NA)	0	(NA)	0	(NA)	-
	Long-term	1	(100.0)	0	(0.00)	1	(100.0)	
		1	(100.0)	0	(0.00)	1	(100.0)	
PA switched subject	Short-term	0	(NA)	0	(NA)	0	(NA)	-
	Long-term	0	(NA)	0	(NA)	0	(NA)	
Total		0	(NA)	0	(NA)	0	(NA)	

Classification		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
PS naïve subject	Short-term	0	(NA)	0	(NA)	0	(NA)	-
	Long-term	1	(50.00)	1	(50.00)	2	(100.0)	
Total		1	(50.00)	1	(50.00)	2	(100.0)	
PS switched subject	Short-term	0	(NA)	0	(NA)	0	(NA)	-
	Long-term	2	(100.0)	0	(0.00)	2	(100.0)	
Total		2	(100.0)	0	(0.00)	2	(100.0)	
FC naïve subject	Short-term	1	(50.00)	1	(50.00)	2	(20.00)	1.0000[1)]
	Long-term	6	(75.00)	2	(25.00)	8	(80.00)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	
FC switched subject	Short-term	2	(100.0)	0	(0.00)	2	(28.57)	-
	Long-term	5	(100.0)	0	(0.00)	5	(71.43)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	
SC naïve subject	Short-term	22	(95.65)	1	(4.35)	23	(28.40)	0.6666[1)]
	Long-term	52	(89.66)	6	(10.34)	58	(71.60)	
Total		74	(91.36)	7	(8.64)	81	(100.0)	
SC switched subject	Short-term	24	(92.31)	2	(7.69)	26	(35.14)	0.2808[1)]
	Long-term	47	(97.92)	1	(2.08)	48	(64.86)	
Total		71	(95.95)	3	(4.05)	74	(100.0)	
PC naïve subject	Short-term	13	(68.42)	6	(31.58)	19	(79.17)	0.3256[1)]
	Long-term	2	(40.00)	3	(60.00)	5	(20.83)	
Total		15	(62.50)	9	(37.50)	24	(100.0)	
PC switched subject	Short-term	9	(100.0)	0	(0.00)	9	(40.91)	-
	Long-term	13	(100.0)	0	(0.00)	13	(59.09)	
Total		22	(100.0)	0	(0.00)	22	(100.0)	
UC naïve subject	Short-term	21	(84.00)	4	(16.00)	25	(37.88)	0.7206[1)]
	Long-term	36	(87.80)	5	(12.20)	41	(62.12)	
Total		57	(86.36)	9	(13.64)	66	(100.0)	
UC switched subject	Short-term	2	(40.00)	3	(60.00)	5	(50.00)	0.1667[1)]
	Long-term	5	(100.0)	0	(0.00)	5	(50.00)	
Total		7	(70.00)	3	(30.00)	10	(100.0)	

Classification		Responder		Non-responder		Total		p-value
		N	(%)	N	(%)	N	(%)	
PU naïve subject	Short-term	0	(0.00)	11	(100.0)	11	(78.57)	-
	Long-term	0	(0.00)	3	(100.0)	3	(21.43)	
		0	(0.00)	14	(100.0)	14	(100.0)	
PU switched subject	Short-term	1	(100.0)	0	(0.00)	1	(14.29)	-
	Long-term	6	(100.0)	0	(0.00)	6	(85.71)	
Total		7	(100.0)	0	(0.00)	7	(100.0)	

[1)] Fisher's exact test
NA: Not applicable
Responder and non-responder percentages were calculated by using Total of the relevant category as a denominator, and the percentage for each Total was calculated by using Total number of subjects as a denominator.

3.2.4 Factors that are thought to affect efficacy

In this surveillance, in relation to efficacy, the response rate was surveyed by baseline demographics, duration of target disease, previous treatment, medical history, concomitant medication and status of surveillance drug treatment.

From efficacy analysis by factor, after excluding Medical history, a statistically significant difference in the response rate ($p<0.05$) was observed for Long-term use ($p=0.0397$), Allergy history ($p=0.0005$), Total administration number of the surveillance drug ($p=0.0001$), and Current disease ($p=0.0201$) in naïve subjects with ankylosing spondylitis; Long-term use ($p<0.0001$) and Total administration number of the surveillance drug ($p=0.0006$) in naïve subjects with RA; Total administration number of the surveillance drug ($p=0.0475$) in switched subjects with RA; Body weight ($p=0.0161$), Renal impairment ($p=0.0168$), and Total administration number of the surveillance drug ($p=0.0158$) in naïve subjects with UC; Total administration number of the surveillance drug ($p=0.0083$) in switched subjects with UC; and Duration of target disease ($p=0.0467$) in switched subjects with ankylosing spondylitis. There was no item showing a statistically significant difference in naïve and switched subjects with moderate to severe plaque psoriasis (in adults), naïve subjects with SC(in adults), and naïve and switched subjects with UC (children and adolescents).

Logistic regression analysis was conducted for background factors ($p<0.2$) that may affect the response rate, as suggested from analysis by factor. However, in case of logistic regression analyses of naïve and switched subjects with UC and naïve subjects with SC, it was not possible to estimate correlation due to inappropriate distribution of clinical outcomes. Therefore, these analyses were excluded from TLF.

Results of logistic regression analysis was statistically significant for Long-term use ($p=0.0329$) and Total administration number ($p=0.0050$) in naïve subjects with ankylosing spondylitis; Odds increased 0.001-fold for Long-term use of the surveillance drug compared to Short-term use, and 15.161-fold with 1 more dose of the surveillance drug(Table 192). In naïve subjects with RA, Type of visit (Inpatient ↔ Outpatient vs Outpatient, $p=0.0052$) and Long-term use ($p=0.0061$) showed statistically significant results; Odds increased 0.222-fold for Inpatient ↔ Outpatient compared to Outpatient, and 9.055-fold for Long-term use of the surveillance drug compared to Short-term use(Table 194). In switched subjects with moderate to severe active Crohn's disease, Average dose per administration ($p=0.0496$) and Total administration number ($p=0.0497$) showed statistically significant results; Odds increased 0.593-fold with every 1 mg/kg increase of Average dose per administration, and 2.704-fold with 1 more dose of the surveillance drug(Table 196). Results were not statistically significant for any item in case of switched subjects with ankylosing spondylitis, switched subjects with RA, naïve subjects with UC, and switched subjects with UC.

Table 192 Logistic regression analysis (factors that affect efficacy) (AS_naïve subjects)

Background factor		p-value	Odds ratio	95% CI	
				Lower limit	Upper limit
Long-term user	Long-term vs Short-term*	0.0329	0.001	0.00	0.58
History of allergy	Yes vs No*	1.0000	<0.001	0.00	+∞
Tuberculosis and other severe infection	Yes vs No*	0.1953	0.274	0.02	1.94
Total administration number (dose)	Continuous (dose)	0.0050	15.161	2.27	101.28

*Reference level

Note 1) This logistic analysis was conducted after selecting variables by considering the following items.

* In case of the p-value<0.2 for both the medical history and the sub-variable, only the sub-variable was included in the model.

Table 193 Logistic regression analysis (factors that affect efficacy) (AS_switched subjects)

Background factor		p-value	Odds ratio	95% CI	
				Lower limit	Upper limit
Illness duration (year)	Continuous (year)	0.6978	1.029	0.89	1.19
Concurrent disease	Yes vs No*	0.1162	0.180	0.02	1.53

*Reference level

Note 1) This logistic analysis was conducted after selecting variables by considering the following items.

* In case of the p-value<0.2 for both the medical history and the sub-variable, only the sub-variable was included in the model.

Table 194 Logistic regression analysis (factors that affect efficacy) (RA_naïve subjects)

Background factor		p-value	Odds ratio	95% CI	
				Lower limit	Upper limit
Inpatient/Outpatient classification	Inpatient vs Outpatient*	0.8116	1.197	0.27	5.24
	Inpatient ↔ Outpatient vs Outpatient*	0.0052	0.222	0.08	0.64
Long-term user	Long-term vs Short-term*	0.0061	9.055	1.88	43.66
Total administration number(dose)	Continuous (dose)	0.3815	1.325	0.71	2.49

*Reference level

Note 1) This logistic analysis was conducted after selecting variables by considering the following items.

* In case of the p-value<0.2 for both the medical history and the sub-variable, only the sub-variable was included in the model.

Table 195 Logistic regression analysis (factors that affect efficacy) (RA_switched subjects)

Background factor		p-value	Odds ratio	95% CI	
				Lower limit	Upper limit
Long-term user	Long-term vs Short-term*	0.8357	0.571	0.00	114.59
Hepatic impairment	No vs Yes*	0.6462	0.305	0.00	48.39
Tuberculosis and other severe infection	No vs Yes*	0.0591	0.045	0.00	1.13
Hypersensitivity history of treatment for indication	No vs Yes*	0.8903	1.366	0.02	115.16
	Unknown vs Yes*	0.3601	0.117	0.00	11.63
Total administration number (dose)	Continuous (dose)	0.2236	2.349	0.59	9.29

Background factor		p-value	Odds ratio	95% CI	
				Lower limit	Upper limit
Average dose per administration (min)	Continuous (min)	0.6582	0.994	0.97	1.02

*Reference level

Note 1) This logistic analysis was conducted after selecting variables by considering the following items.

* In case of the p-value<0.2 for both the medical history and the sub-variable, only the sub-variable was included in the model.

Table 196 Logistic regression analysis (factors that affect efficacy) (SC_switched subjects)

Background factor		p-value	Odds ratio	95% CI	
				Lower limit	Upper limit
Average dose per administration (mg/kg)	Continuous (kg)	0.0496	0.593	0.35	1.00
Total administration number (dose)	Continuous (dose)	0.0497	2.704	1.00	7.30

*Reference level

Note 1) This logistic analysis was conducted after selecting variables by considering the following items.

* In case of the p-value<0.2 for both the medical history and the sub-variable, only the sub-variable was included in the model.

IV. Listings of adverse events

Listings of adverse events

Appendix 3-1	Listings of adverse drug reactions incidence status during post marketing surveillance
Appendix 3-2	Listings of serious adverse events • adverse drug reactions incidence status in post marketing surveillance • special surveillance • post marketing clinical study
Appendix 4	Listings of adverse event incidence status
Appendix 5	Adverse event case report table

V. Discussion of Surveillance Results and the Future Plan

Discussion of Surveillance Results and the Future Plan

This surveillance was conducted in subjects who had not been previously treated with the surveillance drug for on-label indications, including ankylosing spondylitis, rheumatoid arthritis, fistulizing active Crohn's disease (in adults), moderate to severe Crohn's disease (in adults), children and adolescence (6-17 years of age) Crohn's disease, moderate to severe ulcerative colitis, children and adolescence (6-17 years of age) ulcerative colitis, active progressive psoriatic arthritis (in adults), and moderate to severe plaque psoriasis. This surveillance was intended to identify any unexpected adverse event and serious adverse event and frequency and pattern of occurrence of adverse events under the condition of general clinical practice and determine any factor that may affect the safety and efficacy.

During the surveillance period, CRF for 1362 subjects who received Remsima Inj. 100 mg (infliximab) (monoclonal antibody, recombinant) for ankylosing spondylitis, rheumatoid arthritis, moderate to severe active Crohn's disease (in adults), moderate to severe ulcerative colitis, fistulizing active Crohn's disease (in adults), active progressive psoriatic arthritis (in adults), moderate to severe plaque psoriasis (in adults), children and adolescence (6-17 years of age) Crohn's disease and children and adolescence (6-17 years of age) ulcerative colitis were collected.

Among 1362 subjects for whose CRFs were collected, 2 subjects who were registered before the contract date, 1 subject for lost to adverse event follow-up, 1 subject for double enrollment even if not at the same site, and 1 subject for off-label prescription were excluded and data from remaining 1357subjects were included in the safety assessment. Among those in the safety analysis set, 113 subjects who did not achieve efficacy assessment, and 7 subjects who received temporary Remicade (comparator) treatment were excluded, and data from remaining 1237 subjects were included in efficacy assessment.

Among 1357 subjects in the safety analysis set, the surveillance drug was administered to treat ankylosing spondylitis (AS) in 39.13% (531/1357 subjects), rheumatoid arthritis/plaque psoriasis/psoriatic arthritis in 30.14% (409/1357 subjects), and Crohn's disease/ulcerative colitis in 30.73% (417/1357 subjects). Rheumatoid arthritis/plaque psoriasis/psoriatic arthritis included rheumatoid arthritis (RA) in 29.48% (400/1357 subjects), active progressive psoriatic arthritis (in adults) (PA) in 0.22% (3/1357 subjects), and Plaque psoriasis (in adults) (PS) in 0.44% (6/1357 subjects). Crohn's disease/ulcerative colitis (IBD) included fistulizing active Crohn's disease (in adults) (FC) in 1.77% (24/1357 subjects), moderate to severe active Crohn's disease (in adults) (SC) in 13.26% (180/1357 subjects), moderate to severe ulcerative colitis (UC) in 10.24% (139/1357 subjects), children and adolescence (6-17 years of age) Crohn's disease(Pediatric Crohn's disease, PC) in 3.76% (51/1357 subjects), and children and adolescence (6-17 years of age) ulcerative colitis(Pediatric ulcerative colitis, PU) in 1.69% (23/1357 subjects).

1006 AEs occurred in 530 out of 1357 subjects (39.06%) in the safety analysis set. 261 ADRs, defined as AEs for which causal relationship to the surveillance drug cannot be excluded, occurred in 181 out of 1357 subjects (13.34%) in the safety analysis set.

Most common incidences of AEs by system organ class were as following order: 10.46% (142/1357 subjects, 192 events) for Gastrointestinal Disorders occurred, 10.24% (139/1357 subjects, 162 events) for Infections And Infestations, and 6.48% (88/1357 subjects, 118 events) for Musculoskeletal And Connective Tissue Disorders. At preferred term level, most common events included Pruritus occurred in 2.14% (29/1357 subjects, 36 events), Arthralgia in 1.99% (27/1357 subjects, 31 events) and Nasopharyngitis in 1.99% (27/1357 subjects, 28 events),.
Most common incidences of ADRs by system organ class were as following order: 4.27% (58/1357 subjects, 76 events) for Skin And Subcutaneous Tissue Disorders occurred, 3.98% (54/1357 subjects, 64

events) for Infections And Infestations, and 1.33% (18/1357 subjects, 25 events) for Investigations. At preferred term level, most common reactions included Pruritus in 1.47% (20/1357 subjects, 24 events), Urticaria 1.11% (15/1357 subjects, 16 events), and Nasopharyngitis 0.74% (10/1357 subjects, 10 events)

During the surveillance period, 148 SAEs developed in 102 out of 1357 subjects (7.52%), and 44 serious ADRs developed in 32 out of 1357 subjects (2.36%) in the safety analysis set. Most common incidences of SAEs by system organ class were as following order: 2.65% (37/1357 subjects, 45 events) for Infections And Infestations, 1.40% (19/1357 subjects, 31 events) for Gastrointestinal Disorders and 1.11% (15/1357 subjects, 16 events) for Musculoskeletal And Connective Tissue Disorders. Most common incidences of serious ADRs by system organ class were as following order: 1.84% (25/1357subjects, 31 events) for Infections And Infestations, 0.15% (2/1357 subjects, 3 events) for Gastrointestinal Disorders, and 0.15% (2/1357 subjects, 2 events) for Immune System Disorders.

Unexpected adverse events were adverse events not listed in the Precautions for Use; 279 events occurred in 205 subjects (15.11%). Most common incidence of unexpected adverse event by system organ class was Gastrointestinal Disorders 3.39% (46/1357 subjects, 51 events), followed by Musculoskeletal and Connective Tissue Disorders 3.17% (43/1357 subjects, 47 events), and Respiratory, Thoracic and Mediastinal Disorders 2.36% (32/1357 subjects, 36 events). As unexpected ADR, 27 events occurred in 22 subjects (1.62%), and incidence by system organ class was Skin and Subcutaneous Tissue Disorders 0.44% (6/1357 subjects, 6 events), followed by Respiratory, Thoracic and Mediastinal Disorders 0.29% (4/1357 subjects, 6 events), General Disorders and Administration Site Conditions 0.22% (3/1357 subjects, 3 events), Gastrointestinal Disorders, Musculoskeletal and Connective Tissue Disorders and Nervous System Disorders, each at 0.15% (2/1357 subjects, 2 events).

For special subject population, incidence of AE was 54.92% (67/122 subjects, 169 events) in 122 elderly subjects aged ≥ 65 years, 25.00% (3/12 subjects, 3 events) in 12 children aged <12 years, 38.46% (15/39 subjects, 22 events) in 39 subjects with history of hepatic impairment, and 50.00% (8/16 subjects, 27 events) in 16 subjects with history of renal impairment, and 40.78% (407/998 subjects, 790 events) in 998 long-term subjects who administered the surveillance drug until the long-term efficacy assessment time. There was no pregnant subject.

From analysis of the adverse event occurrence status by factor in the entire subjects, a statistically significant difference was detected for Sex ($p<0.0001$), Age ($p<0.0001$), Type of visit ($p=0.0008$), Body weight ($p=0.0046$), concurrent disease ($p<0.0001$), Tuberculosis and other severe infection ($p=0.0384$), Concomitant medication ($p=0.0091$), and Long-term use ($p=0.0299$). A statistically significant difference was observed for Sex ($p=0.0445$), concurrent disease ($p=0.0015$), Average dose per administration of the surveillance drug ($p=0.0305$), and Concomitant medication ($p=0.0453$) in ankylosing spondylitis; Age ($p=0.0181$), Type of visit ($p=0.0002$), Concurrent disease ($p<0.0001$), and Average administration duration (RA only, $p<0.0001$) in RA and active and PA (in adults); and Age ($p=0.0043$), Concurrent disease ($p<0.0001$), and Tuberculosis and other severe infection ($p=0.0003$) in FC(in adults)/SC(in adults)/UC.

Logistic regression analysis was conducted for background factors ($p<0.2$) that may affect adverse event occurrence, as suggested from analysis by factor. Results were statistically significant for Sex ($p=0.0416$), Age ($p=0.0021$), Type of visit (Inpatient vs Outpatient, $p=0.0007$, Inpatient ↔ Outpatient vs Outpatient. $p=0.0095$), Long-term use ($p=0.0416$), Concurrent disease ($p<0.0001$), and Hypersensitivity history for treatment of the indication (No vs Yes, $p=0.0462$); Odds of the adverse event occurrence increased 0.750-fold in Male compared to Female, 1.013-fold with every 1 year increase in Age, 1.742-fold in Inpatient compared to Outpatient, 1.632-fold in Inpatient ↔ Outpatient compared to Outpatient, 1.323-fold in Long-term users compared to Shor-term users, and 2.002-fold in subjects with Concurrent disease compared with subjects with no Concurrent disease

Long-term and short-term efficacy was analyzed for each indication in 1237 subjects in the efficacy set. Response rate was 96.79% (453/468 subjects) in short-term and 96.47% (328/340 subjects) in long-term for ankylosing spondylitis; 76.12% (102/134 subjects) in short-term and 87.98% (161/183 subjects) in long-term for RA; 100.0% (1/1 subject and 2/2 subjects, respectively) in short-term and long-term for PA (in adults); 75.00% (3/4 subjects) in long-term for moderate to severe plaque psoriasis (no short-term user), 82.35% (14/17 subjects) in short-term and 78.57% (11/14 subjects) in long-term for FC(in adults); 91.77% (145/158 subjects) in short-term and 93.02% (80/86 subjects) in long-term for SC(in adults); 78.72% (37/47 subjects) in short-term and 100.0% (17/17 subjects) in long-term for children and adolescence (6-17 years of age) Crohn's disease ; 64.00% (64/100 subjects) in short-term and 46.00% (23/50 subjects) in long-term for UC; and 33.33% (7/21 subjects) in short-term and 71.43% (5/7 subjects) in long-term for children and adolescence (6-17 years of age) UC.

From efficacy analysis by factor, after excluding Medical history, a statistically significant difference in the response rate ($p<0.05$) was observed for Long-term use ($p=0.0397$), Allergy history ($p=0.0005$), Total administration number of the surveillance drug ($p=0.0001$), and Current disease ($p=0.0201$) in naïve subjects with ankylosing spondylitis; Long-term use ($p<0.0001$) and Total administration number of the surveillance drug ($p=0.0006$) in naïve subjects with RA; Total administration number of the surveillance drug ($p=0.0475$) in switched subjects with RA; Body weight ($p=0.0161$), Renal impairment ($p=0.0168$), and Total administration number of the surveillance drug ($p=0.0158$) in naïve subjects with UC; Total administration number of the surveillance drug ($p=0.0083$) in switched subjects with UC; and Duration of target disease ($p=0.0467$) in switched subjects with ankylosing spondylitis. There was no item showing a statistically significant difference in naïve and switched subjects with moderate to severe plaque psoriasis (in adults), naïve subjects with SC(in adults), and naïve and switched subjects with UC (children and adolescents).

Logistic regression analysis was conducted for background factors ($p<0.2$) that may affect the response rate, as suggested from analysis by factor. However, in case of logistic regression analyses of naïve and switched subjects with UC and naïve subjects with SC, it was not possible to estimate correlation due to inappropriate distribution of clinical outcomes. Therefore, these analyses were excluded from TLF.

Results of logistic regression analysis was statistically significant for Long-term use ($p=0.0329$) and Total administration number ($p=0.0050$) in naïve subjects with ankylosing spondylitis; Odds increased 0.001-fold for Long-term use of the surveillance drug compared to Short-term use, and 15.161-fold with 1 more dose of the surveillance drug. In naïve subjects with RA, Type of visit (Inpatient ↔ Outpatient *vs* Outpatient, $p=0.0052$) and Long-term use ($p=0.0061$) showed statistically significant results; Odds increased 0.222-fold for Inpatient ↔ Outpatient compared to Outpatient, and 9.055-fold for Long-term use of the surveillance drug compared to Short-term use. In switched subjects with moderate to severe active Crohn's disease, Average dose per administration ($p=0.0496$) and Total administration number ($p=0.0497$) showed statistically significant results; Odds increased 0.593-fold with every 1 mg/kg increase of Average dose per administration, and 2.704-fold with 1 more dose of the surveillance drug. Results were not statistically significant for any item in case of switched subjects with ankylosing spondylitis, switched subjects with RA, naïve subjects with UC, and switched subjects with UC.

Overall, no special finding for safety and efficacy was reported from the domestic Post Marketing Surveillance of Remsima Inj.100mg (Infliximab) (monoclonal antibody, recombinant); subsequently, safety and efficacy information will be updated and managed by continuously collecting adverse events and adverse event-related items with domestic and overseas spontaneous reporting.

VI. Sales Volumes

Production/Sales Volumes

(Unit: vial)

Period	Production volumes [1]		Sales volumes in korea
	For internal use	For exports[2]	
2012-07-20 ~ 2013-01-19	184,478	0	3,234
2013-01-20 ~ 2013-07-19	0	19,152[3]	6,988
2013-07-20 ~ 2014-01-19	0	256	7,297
2014-01-20 ~ 2014-07-19	0	7,560	9,885
2014-07-20 ~ 2015-07-19	0	30,273	29,222
2015-07-20 ~ 2016-07-19	0	67,934	39,332
Total	184,478	125,175	95,958

[1] Production performance was calculated based on the volume of finished products manufactured and reported to the Ministry of Food and Drug Safety according to the "Regulations for performance report on production and import of pharmaceutical product"(Definition of finished product is specified in the "Good Manufacturing Practice ").

[2] Products for exports may be supplied as brite stock, skipping the final assembly procedure including labeling and secondary packaging according to the applicable regulations in the regions and agreements made with local importers. Production volumes as brite stock were not included in this report.

[3] According to the regulations for performance report on production of finished product applied as of the third quarter of 2013, the volume of products supplied as brite stock for export were included in production volumes.

VII. Safety Data from Korea and overseas countries

7.1 Reported Adverse Events in Korea from other sources apart from the PMS

7.1.1 Data collected from outside the planned data collection systems(Unsolicited sources)

A. Spontaneous reporting

During the re-examination period, a total of 32 adverse events were received spontaneous reports in Korea. Details are shown below.

MFDSNo.	Adverse event term	Symptom onset date	Symptom stop date/death	Outcome	Seriousness	Causal relationship to surveillance drug	Action taken for the surveillance drug	Specified in product label
20130081976/ 20130098890	Abdominal pain	2012-12-16	2012-12-19	Resolved	Serious	Unlikely	Not applicable	Specified
20130083356/ 20130098894	Abdominal pain	2013-02-12	Not applicable[1)]	UK[1)]	Non-Serious	Possible	Temporary interruption	Specified
201420060030000071/ 201420060030000070	Hypoaesthesia	2014-10-27	UK	Resolved	Serious	Possible	Discontinuation	Specified
	Infusion related reaction	2014-10-27	UK	Resolved	Serious	Possible	Discontinuation	Specified
	Paraesthesia	2014-10-27	UK	Resolved	Serious	Possible	Discontinuation	Specified
	Respiratory distress	2014-10-27	UK	Resolved	Serious	Possible	Discontinuation	Not Specified
201520060030000100/ 201520060030000083	Pruritus	2014-11-27	UK	Resolved	Non-Serious	Possible	Not applicable	Specified
	Pyrexia	2014-11-27	2014-11-27	Resolved	Non-Serious	Possible	Not applicable	Specified
	Infusion related reaction	2014-11-27	2014-11-27	Resolved	Non-Serious	Possible	Not applicable	Specified
20150073166/ 20150127701	Exposure during pregnancy	UK	UK	Persisted	Non-Serious	Not evaluable	UK	Not Specified
20150147036	Arthralgia	UK	UK	Resolved	Non-Serious	Possible	Discontinuation	Specified
201520060030000216	Leukopenia	UK	UK	UK	Serious	Not evaluable	UK	Specified
	Pyrexia	UK	UK	UK	Serious	Not evaluable	UK	Specified
201520060030000225	Dermatitis psoriasiform	2015-05-05	UK	UK	Serious	Possible	UK	Specified
20150177296 20150190859	Colitis	2015-05-05	UK	Resolved	Serious	Possible	Not applicable	Not Specified
20150226836 20150250630	Interstitial lung disease	2013-08-31	2013-10-25	Resolved	Serious	Possible	UK	Specified
	Still's disease adult onset	UK	UK	UK	Serious	Unlikely	UK	Not Specified
	Off label use	UK	UK	UK	Non-Serious	Unassessible/ unclassifiable	UK	Not Specified
20150245205 20150268208	Anaphylactic shock	2015-11-04	2014-11-05	Resolved	Serious	Probably	Discontinuation	Specified

20160011424	Sarcoidosis	UK	UK	Resolved	Non-Serious	Possible	UK	Specified
20160003128	Pyrexia	2015-12-14	UK	UK	Non-Serious	Possible	UK	Specified
	Rash	2015-12-14	UK	UK	Non-Serious	Possible	UK	Specified
20160056222	Abdominal pain	2015-09-07	UK	UK	Serious	Unassessible/ unclassifiable	UK	Specified
20160169344	Chest pain	2016-03-28	UK	UK	Non-Serious	Unassessible/ unclassifiable	UK	Specified
	Rash	2016-03-28	UK	UK	Non-Serious	Unassessible/ unclassifiable	UK	Specified
20160169393	Pruritus	UK	UK	UK	Non-Serious	Unassessible/ unclassifiable	UK	Specified
20160169356	Pruritus	UK	UK	UK	Non-Serious	Unassessible/ unclassifiable	UK	Specified
20160169397	Pruritus	UK	UK	UK	Non-Serious	Unassessible/ unclassifiable	UK	Specified
20160091790	Vasculitis	2016-04-11	UK	UK	Serious	Unassessible/ unclassifiable	UK	Specified
20160170476	Psoriasis	UK	UK	Persisted	Non-Serious	Unassessible/ unclassifiable	UK	Specified
201607033055 20160166769 20160166857	Pneumonia	2015-12-28	2016-01-14	Resolved	Serious	Unlikely	Not applicable	Specified
20160165185	Intervertebral disc operation	2016-06-30	2016-07-14	Resolved	Serious	Unassessible/ unclassifiable	UK	Not Specified

[1)] While follow-up was requested to the investigator for adverse event resolution and outcome for the relevant patient, it was not possible to collect further information so that follow-up was completed.

UK: Unknown

B. Scientific Documents Including Research Journals

During the re-examination period, there was no adverse event report from the scientific documents such as research papers etc. collected in Korea.

C. Other Sources(Broadcasting media, Publication, communication media, etc.)

During the re-examination period, there was no adverse event report from other sources in Korea.

7.1.2 Data collected from the planned data collection systems(Solicited sources)

During the the re-examination period, following SAEs were identified from phase 4 clinical studies (Protocol No. CT-P13.4.1, CT-P13.4.2, CT-P13.4.3 and CT-P13.4.4). Non-serious AEs will be reported upon completion of relevant studies.

Adverse event term	Symptom onset date	Symptom stop date/death	Outcome	Seriousness	Causal relationship to surveillance drug	Action taken for the surveillance drug	Specified in product label
Gastritis	2013-07-22	2013-07-25	Resolved	Serious	Possible	No change	Not Specified

Adverse event term	Symptom onset date	Symptom stop date/death	Outcome	Seriousness	Causal relationship to surveillance drug	Action taken for the surveillance drug	Specified in product label
Abdominal distension	2013-07-22	2013-07-25	Resolved	Serious	Possible	No change	Not Specified
Abdominal pain upper	2013-07-22	2013-07-25	Resolved	Serious	Possible	No change	Specified
Nausea	2013-07-22	2013-07-25	Resolved	Serious	Possible	No change	Specified
Colitis ulcerative	2014-06-30	(NA)	Persisted	Serious	Unlikely	No change	Not Specified
Surgery	2014-06-02	2014-06-03	Resolved	Serious	Unlikely	No change	Not Specified
Colitis ulcerative	2014-06-28	2014-07-07	Resolved	Serious	Unlikely	UK	Not Specified
Pain	2014-01-01	2014-01-15	Resolved	Serious	Unlikely	No change	Specified
Myalgia	2014-02-06	2014-02-22	Resolved	Serious	Unlikely	No change	Specified
Arthralgia	2014-03-03	2014-04-04	Resolved	Serious	Unlikely	No change	Specified
Joint swelling	2014-03-03	2014-04-04	Resolved	Serious	Possible	No change	Not Specified
Drug ineffective	2014-03-03	2014-04-04	Resolved	Serious	Possible	No change	Not Specified
Pruritus	2014-03-03	2014-04-04	Resolved	Serious	Possible	No change	Specified
Rash pruritic	2014-04-05	(NA)	Persisted	Serious	Possible	No change	Specified
Pneumonia	2014-06-11	(NA)	Persisted	Serious	Possible	Not applicable	Specified
Dyspnoea	2014-06-19	(NA)	Persisted	Serious	Possible	No change	Specified
Chest discomfort	2014-06-19	(NA)	Persisted	Serious	Possible	Discontinuation	Not Specified
Haemorrhoids	2015-03-18	(NA)	Persisted	Serious	Unlikely	Not applicable	Not Specified
Pneumothorax	2014-11-22	2014-11-29	Resolved	Serious	Unlikely	Not applicable	Not Specified
Infusion related reaction	2014-09-01	2014-09-03	Resolved	Serious	Possible	Not applicable	Specified
Lobar pneumonia	2014-09-17	2014-10-08	Resolved	Serious	Unlikely	Not applicable	Specified
Intentional overdose	2014-10-05	2014-10-07	Resolved	Serious	Unlikely	Not applicable	Not Specified
Asthma	2014-10-13	2014-10-18	Resolved	Serious	Possible	Not applicable	Not Specified
Pyelonephritis acute	2014-12-28	2015-01-04	Resolved	Serious	Possible	Discontinuation	Specified
Renal cell carcinoma	2014-12-28	2015-01-22	Resolved	Serious	Possible	Discontinuation	Not Specified
fall	2015-04-17	(NA)	Persisted	Serious	Unlikely	Not applicable	Not Specified

Adverse event term	Symptom onset date	Symptom stop date/death	Outcome	Seriousness	Causal relationship to surveillance drug	Action taken for the surveillance drug	Specified in product label
injury	2015-04-17	(NA)	Persisted	Serious	Unlikely	Not applicable	Not Specified
Multiple fractures	2015-04-17	(NA)	Persisted	Serious	Unlikely	Not applicable	Not Specified
Pneumonia	2015-06-29	2015-07-10	Resolved	Serious	Possible	Discontinuation	Specified
Ileus	2015-04-25	2015-05-07	Resolved	Serious	Unlikely	Not applicable	Not Specified
Urethral stenosis	2015-05-21	2015-05-23	Resolved	Serious	Unlikely	Not applicable	Not Specified
Hepatitis toxic	2015-01-12	2015-02-10	Resolved	Serious	Unlikely	Not applicable	Specified
Pulmonary tuberculosis	2015-05-25	(NA)	Persisted	Serious	Probably	Discontinuation	Specified
Herpes zoster	2015-07-11	2015-07-18	Resolved	Serious	Possible	Dose maintained	Specified
Intervertebral disc protrusion	2014-10-08	2014-11-01	Resolved	Serious	Unlikely	Not applicable	Not Specified
Pyrexia	2015-08-19	2015-08-24	Resolved	Serious	Unlikely	Not applicable	Specified
Myalgia	2015-08-19	2015-08-24	Resolved	Serious	Unlikely	Not applicable	Specified
Procedural intestinal perforation	2015-12-14	2015-12-18	Resolved	Serious	Unrelated	Not applicable	Not Specified
Anaemia	2016-03-02	2016-03-14	Resolved	Serious	Unlikely	Not applicable	Specified
Rotavirus infection	2016-02-27	2016-03-02	Resolved	Serious	Related	Not applicable	Specified
Osteoporosis	2016-03-21	Not applicable	Persisted	Serious	Unlikely	Not applicable	Not Specified
Otitis media Chronic	2016-01-20	2016-01-23	Resolved	Serious	Unrelated	Not applicable	Specified
Death	2016-03-28	2016-03-28	Resolved	Serious	Unlikely	Not applicable	Not Specified
Colon neoplasm	2016-04-26	2016-05-04	Resolved	Serious	Unrelated	Not applicable	Not Specified
Pancytopenia	2016-05-18	2016-06-20	Resolved	Serious	Unlikely	Not applicable	Specified
Anaemia	2016-06-24	2016-06-29	Resolved	Serious	Unlikely	Not applicable	Specified
Calculus ureteric	2016-06-17	2016-06-18	Resolved	Serious	Unlikely	Not applicable	Not Specified
Peritonitis	2016-06-16	2016-06-28	Resolved	Serious	Unrelated	Not applicable	Not Specified
Hip fracture	2015-09-22	2015-11-20	Resolved	Serious	Unlikely	Discontinuation	Not Specified

Adverse event term	Symptom onset date	Symptom stop date/death	Outcome	Seriousness	Causal relationship to surveillance drug	Action taken for the surveillance drug	Specified in product label
Meniscus injury	2015/11/09	UK	Persisted	Serious	Unlikely	Discontinuation	Not Specified
Arthritis bacterial	2016/02/22	UK	Persisted	Serious	Possible	Discontinuation	Specified
Urticaria	2015-10-08	2015-10-20	Resolved	Serious	Possible	Not applicable	Specified
Arthralgia	2015-12-15	2016-04-23	Resolved	Serious	Unlikely	Not applicable	Specified
Patella fracture	2016-02-21	UK	Resolved	Serious	Unlikely	Dose maintained	Not Specified
Fall	2016-02-21	UK	Resolved	Serious	Unlikely	Dose maintained	Not Specified
Bronchitis	2016-02-20	2016-03-05	Resolved	Serious	Unlikely	Not applicable	Specified
Pneumonia	2016-02-20	2016-03-05	Resolved	Serious	Unlikely	Not applicable	Specified
Intervertebral disc protrusion	2016-02-25	UK	Resolved	Serious	Unlikely	Dose maintained	Not Specified
Myocardial infarction	2015-12-29	2016-01-01	Resolved	Serious	Unlikely	Dose maintained	Not Specified
Vasculitis	2016-04-16	2016-04-26	Resolved	Serious	Possible	Discontinuation	Specified
Otitis media Chronic	2016-06-15	UK	Persisted	Serious	Possible	Dose maintained	Specified
Femoral neck fracture	2015-07-31	2015-08-17	Resolved	Serious	Unlikely	Not applicable	Not Specified
Pulmonary tuberculosis	2015-08-21	UK	Persisted	Serious	Probably	Discontinuation	Specified
Chest pain	2015-10-02	UK	Persisted	Serious	Unlikely	Discontinuation	Specified
Sudden death	2015-10-16	2015-10-16	Resolved	Serious	Unlikely	Discontinuation	Not Specified
Diverticulitis	2015-11-12	2015-11-23	Resolved	Serious	Unlikely	Dose maintained	Specified
Tuberculosis	2015-11-05	UK	Persisted	Serious	Probably	Discontinuation	Specified
Muscle strain	2015-12-21	2016-01-08	Resolved	Serious	Unlikely	UK	Not Specified
Ligament sprain	2015-12-21	2016-01-08	Resolved	Serious	Unlikely	UK	Not Specified

NA: Not Applicable

UK: Unknown

7.2 Safety information form overseas

7.2.1 Assessment data of adverse drug reaction of the surveillance drug collected in overseas

A. PSUR summary - 1st PERIODIC SAFETY UPDATE REPORT FOR ACTIVE SUBSTANCE: Infliximab (Annex 2)

(1) Reporting period

10 Sep 2013 ~ 09 Mar 2014

(2) Executive summary

- This is the first Periodic Safety Update Report (PSUR) of Infliximab (CT-P13) and was completed for regulatory authorities according to the current Guideline on Good Pharmacovigilance Practices Module VII. This report summarizes all adverse drug reaction (ADR) reports and other safety data collected from worldwide sources from 10 Sep 2013 to 09 Mar 2014 by Celltrion Inc.
- For Infliximab:
  - ATC (Anatomical Therapeutic Chemical) code: L04AB02 (tumor necrosis factor alpha [TNF-α] inhibitor)
  - Mechanism of action: Infliximab is a chimeric human-mouse monoclonal antibody that binds with both soluble and transmembrane TNF-α with high affinity.
  - Indications: Approved for indications of rheumatoid arthritis in adults, Crohn's disease in adults, Crohn's disease in children (≥6 years) and adolescents, ulcerative colitis in adults, ulcerative colitis in children (≥6 years) and adolescents, ankylosing spondylitis, psoriatic arthritis, psoriasis in adults
  - Formulation: Lyophilised powder
  - Dose: For RA, initial dose 3 mg/kg; for other indications, initial dose 5 mg/kg
  - Route of administration: Intravenous injection
- Infliximab was first approved in Korea on 20 Jul 2012 with the brand name of Remsima. To date[1], Infliximab has been registered in 48 countries and is marketed in 20 countries (Korea, Georgia, Azerbaijan Republic, Philippines, Belarus, Kazakhstan, Panama, Portugal, Iceland, Ireland, Malta, Czech Republic, Rumania, Poland, Finland, Norway, Bulgaria, Slovak Republic, Latvia and Lithuania).
- After marketing authorization, 10 clinical studies (CT-P13 1.1, CT-P13 1.2, CT-P13 1.3, CT-P13 1.4, CT-P13 3.1, CT-P13 3.2, CT-P13 3.3, CT-P13 4.1 and CT-P13 4.2 [RA registered] and CT-P13 post-marketing study [PMS] Korea) were conducted by Celltrion Inc. to reflect the effectiveness and efficacy of Infliximab. Of these. 3 clinical studies (CT-P13 1.2, CT-P13 1.3 and CT-P13 3.2) were completed[2] and 5 clinical studies (CT-P13 1.4, CT-P13 3.3, CT-P13 4.1, CT-P13 4.2 and PMS Korea) were ongoing during the reporting period. Additionally, 2 clinical studies (B1P13101 and B2P13111) were sponsored by Nippon Kayaku in Japan and of these, B2P13111 was ongoing during the reporting period. A total of 1553 subjects were exposed to Remsima® in these 12 studies. Additionally, 15 subjects were enrolled in an ongoing blind Remsima®/Remicade® clinical study (CT-P13 3.3).

1 The relevant time refers to up to 09 Mar 2014, the reporting period of the PSUR attached to this report.
2 Clinical studies completed during the PSUR reporting period

- In Korea, Philippines, Azerbaijan Republic, Bulgaria, Belarus, Czech Republic, Georgia, Kazakhstan, Latvia, Slovak Republic, Poland and Lithuania, the post-marketing exposure to Infliximab is estimated as follows:
  - Surveillance period: 704 patients
  - Accumulated period: 1237 patients
- During Oct 2013 ~ Mar 2014, the post-marketing exposure to Infliximab in Finland and Norway is estimated as 33733 patient-days.
- During the reporting period, safety information was updated for consistency of the Reference Safety Information (RSI) with Remicade® RSI.
- During the reporting period, a total of 21 cases were collected. Of these, 18 events for 13 cases were reported from PMS (12 events were ADRs). Three cases involved the elderly (>65 years). Use of Infliximab in children were not reported. Age was unknown for 5 cases. There were no individual case reports associated with Infliximab overdose or drug abuse/misuse and there were no cases coded as drug-drug interactions. For off-label indication (pustular psoriasis), there was a voluntary report of Infliximab use case which was an infusion-related reaction.
- No new and clinically important safety and efficacy information was collected from Infliximab clinical studies that were ongoing during the reporting period. Safety profile from completed clinical studies was consistent with what were expected based on previous literatures and prior data on Infliximab (Remicade®).
- Based on assessment of available information included in this PSUR, there is no recommended or implemented action to Celltrion Healthcare Hungary Kft for the approved Infliximab formulation.
- In conclusion, the evaluated safety data were consistent with the established overall safety profile of Infliximab as described in RSI. No significant and new safety information was identified that requires revision of Infliximab RSI from the review of global safety data during the reporting period. The benefit-risk ratio of Infliximab remains favorable.

B. PBRER summary - PERIODIC BENEFIT-RISK EVALUATION REPORT (Celltrion Infliximab, 20JUL2014 to 20JAN2015) (Annex 3)

(1) Reporting period

20 Jul 2014 ~ 20 Jan 2015

(2) Executive summary

- This Periodic Benefit-Risk Evaluation Report (PBRER) of Infliximab was completed for regulatory authorities according to the current Guideline on Good Pharmacovigilance Practices Module VII. This document summarizes all adverse drug reaction (ADR) reports and other safety data collected from worldwide sources from 20 Jul 2014 to 20 Jan 2015 by Celltrion Inc. (Celltrion Healthcare Philippines Inc., Celltrion Healthcare Co. Ltd., Celltrion Healthcare Hungary Kft. and Celltrion Healthcare Turkey), OLIMED CV, Hikma Pharmaceuticals Co., Ltd. and Nippon Kayaku and their vendors/distributors. Data in the PBRER are collected from the International Birth Date (IBD), 20 Jul 2012.

- For Infliximab:
  - ATC (Anatomical Therapeutic Chemical) code: L04AB02 (tumor necrosis factor alpha [TNF-α] inhibitor)
  - Mechanism of action: Infliximab is a chimeric human-mouse monoclonal antibody that binds with both soluble and transmembrane TNF-α with high affinity.
  - Indications: Approved for indications of rheumatoid arthritis in adults, Crohn's disease in adults, Crohn's disease in children (≥6 years) and adolescents, ulcerative colitis in adults, ulcerative colitis in children (≥6 years) and adolescents, ankylosing spondylitis, psoriatic arthritis, psoriasis in adults
  - Formulation: Lyophilised powder
  - Dose: For RA, initial dose 3 mg/kg; for other indications, initial dose 5 mg/kg
  - Route of administration: Intravenous injection
- Infliximab was first approved on 20 Jul 2012 in Korea with the brand name Remsima®. To date, Infliximab was registered in 56 countries.
- As of the database lock point, a total of 846 subjects were exposed to Infliximab in clinical studies during the CT-P13 clinical development program. In the CT-P13 clinical development program, 1 clinical study (CT-P13 3.3) was completed during the PBRER reporting period. During the reporting period, 3 clinical studies were ongoing, and one of them (B2P13111) was sponsored by Nippon Kayaku in Japan. From completed and ongoing clinical studies, no important new study results on efficacy and safety were identified.
- During the PBRER reporting period, 4 non-interventional studies (3 registry studies and 1 PMS study) were ongoing. Based on data review from these studies, no new information was identified that potentially affect benefit-risk assessment.
- Infliximab was launched in 32 countries. In launched countries, the post-marketing exposure to Infliximab is estimated as follows:
  - Surveillance period: Approximately 3,063 patient-years
  - Accumulated period: Approximately 5,037 patient-years
- In Moldova, Guatemala, Ecuador, El Salvador, Canada, Jordan, Malta and Paraguay, there was no Infliximab exposure during the accumulated period and surveillance period (i.e., no Sales Records).
- During the PBRER reporting period, no immediate safety restriction or other regulatory safety action was taken for Infliximab. The Marketing Authorization Holder (MAH) issued a Defective Product Report Form to the European Medicines Agency (EMA) to inform the translation error in the product information in Iceland and Netherlands. The erroneous text in the product information for Iceland and Netherlands will be corrected during the next text update. Revision for this outcome was submitted to EMA by MAH on 19 Feb 2015. The revision was approved by EMA on 11 Mar 2015.
- Summary of Product Characteristics (SmPC) of the European Union (EU) currently serves as the Reference Safety Information (RSI). As of the reporting period completion, the current EU SmPC Version is Version 5.1 dated 09 Dec 2014. Nevertheless, the Version 5.0 EU SmPC dated 05 Dec 2014 serves as the RSI for this PBRER. During the PBRER reporting period, the safety sections (Section 4.4 and 4.8) in RSI were updated to be consistent with the product information of the 'developer'. Section 4.4 was updated to mention that there is no evidence that Infliximab worsens

or causes fibrotic stenosis. Section 4.8 was updated to include leukemia, Merkel cell carcinoma, melanoma, pediatric malignancy and sarcoidosis/sarcoid-like reactions as the most serious ADRs related to Infliximab use.

- National/local SmPC in EU was updated for consistency with Remicade® SmPC. SmPC in Azerbaijan Republic, Turkey and Armenia was updated for the shelf-life and other logistical revision.
- During the accumulated period, a total of 201 serious adverse events (131 events from patients who administered CT-P13, 66 events from patients who administered the active comparator, and 4 blind SAE) were reported in the CT-P13 clinical development program.
- During the current reporting period, a total of 236 ADRs were reported during the accumulated period, including 179 events obtained from the post-marketing data sources (voluntary reports including unsolicited cases reported directly to Celltrion/vendor from a medical professional or consumer or through regulatory authorities and post-marketing study sources including cases of 3 registry studies [CT-P13 4.2, CT-P13 4.3 and CT-P13 4.4] and CT-P13 Korea PMS study). During the reporting period, 2 off-label use cases and 1 overdose case were reported. During the PBRER reporting period, no cases related to drug abuse or misuse, drug-drug interactions and body weight gain were collected. There were no cases of reporting a fatal outcome.
- During the PBRER reporting period, 2 cases of lack of efficacy (Medical Dictionary for Regulatory Affairs Preferred Term: No drug effect) were collected from the post-marketing data source. As the underlying disease is a chronic disease characterized by the flare and remission period, it may have been a contributing factor to the lack of efficacy.
- During the PBRER reporting period, no new, ongoing or closed signal was identified for Infliximab. During this reporting period, no new information was collected for the previously identified or potential risk and no missing information was updated. There was no action taken or proposed risk minimization activity for any safety reason.
- During the reporting period, a review of 7 clinical studies and clinical efficacy was published that report new information on efficacy in the approved indications or efficacy of Remsima®/ Flammegis®. These studies confirm efficacy of Infliximab. They do not suggest that the benefit of Infliximab treatment is greater or less than previously considered.
- According to the review of safety data in literature published during the period included in this report, there were no clinically significant and new safety results requiring an immediate revision of RSI.
- According to the assessment result of available information include in this PBRER, there is no recommended or implemented action to Celltrion Inc. (Celltrion Healthcare Philippines Inc., Celltrion Healthcare Co. Ltd., Celltrion Healthcare Hungrary Kft. and Celltrion Healthcare Turkey), OLIMED CV, Hikma Pharmaceuticals Co., Ltd. and Nippon Kayaku for the approved Infliximab formulation.
- In conclusion, the evaluated safety data were consistent with the established overall safety profile of Infliximab as described in RSI. No significant and new safety information was identified that requires revision of Infliximab RSI from the review of global safety data during the PBRER reporting period. The benefit-risk ratio of Infliximab remains favorable.

C. PBRER summary - PERIODIC BENEFIT-RISK EVALUATION REPORT (Celltrion Infliximab, 21JAN2015 to 20JUL2015) (Annex 4)

(1) Reporting period

21 Jan 2015 ~ 20 Jul 2015

(2) Executive summary

- This document is a Periodic Benefit-Risk Evaluation Report (PBRER) of Infliximab for submission to regulatory authorities according to the current Guideline on Good Pharmacovigilance Practices Module VII. This document summarizes all adverse drug reaction (ADR) reports and other safety data collected from worldwide sources from 21 Jan 2015 to 20 Jul 2015 by Celltrion Inc. Celltrion Healthcare Philippines Inc., Celltrion Healthcare Co. Ltd., Celltrion Healthcare Malaysia, Celltrion Healthcare Hungary Kft., Celltrion Healthcare Turkey and Celltrion Healthcare Distribuição de Produtos Farmacêuticos do Brasil Ltda., OLIMED CV, Oktal Pharma, Hikma Pharmaceuticals Co., Ltd and Nippon Kayaku and their vendors/distributors. Data in the PBRER are collected from the International Birth Date (IBD), 20 Jul 2012.
- For Infliximab,
  - ATC (Anatomical Therapeutic Chemical) code: L04AB02 (tumor necrosis factor alpha [TNF-α] inhibitor)
  - Mechanism of action: TNF-α inhibitor
  - Approved for indications of rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis and psoriasis in adults; Crohn's disease (CD) and ulcerative colitis (UC) in adults and children
  - Formulation: Lyophilised powder
  - Dose: For RA, initial dose 3 mg/kg; for other indications, initial dose 5 mg/kg
  - Route of administration: Intravenous injection
- Infliximab was first approved on 20 Jul 2012 in Korea with the brand name Remsima®. To date, Infliximab was registered in 61 countries.
- As of the database lock point, a total of 846 subjects were exposed to Infliximab in clinical studies during the CT-P13 clinical development program. During the PBRER reporting period, 1 clinical study (B2P13111) in the CT-P13 clinical development program was completed. This clinical study was sponsored by Nippon Kayaku of Japan. During the reporting period, 2 clinical studies (CT-P13 3.4 and CT-P13 4.1) were ongoing. No study results on important new efficacy and safety were identified from completed and ongoing clinical studies.
- During the PBRER reporting period, 6 non-interventional studies (5 registry studies and 1 PMS) were ongoing. Based on the review of these study data, no new information was identified that may affect the benefit-risk assessment.
- Infliximab was launched in market in 44 countries. In launched countries, the post-marketing exposure to Infliximab is estimated as follows:
  - Surveillance period: Approximately 11, 647 patient-years
  - Accumulated period: Approximately 16, 434 patient-years
- Infliximab was also launched in Moldova, Guatemala, Luxembourg and El Salvador. In these countries, there was no Infliximab exposure during the accumulated period and surveillance

period (i.e., no Sales Records). While Infliximab was launched in Azerbaijan Republic, Malta and Panama, there were no Sales Records during the reporting period in these countries.

- During the PBRER reporting period, the indication of inflammatory bowel disease was not approved in Malaysia by the Malaysian public health authorities. Approved indications were RA, AS, PsA and psoriasis. To enhance understanding of investigators and emphasize the previous contents of the European Union (EU) Summary of Product Characteristics (SmPC) section 4.4 (Special warnings and precautions for use), the description to strengthen the tuberculosis monitoring procedure was added in the protocols (CT-P13 4.2, CT-P13 4.3 and CT-P13 4.4 registry).
- Marketing Authorization Holder (MAH) conducted a survey of all other EU SmPCs and it was found out that a similar error was present in the Dutch SmPC in addition to the Iceland SmPC. MAH contacted Dutch authorities and proposed an action for the translation issue and subsequently, the Dutch authorities consented to this.
- EU SmPC currently serves as the reference safety information (RSI). As of completion of the reporting period, the current EU SmPC Version was Version 6.0 dated 11 Mar 2015. Nevertheless, for this PBRER, EU SmPC Version 5.0 dated 05 Dec 2014 serves as the RSI. There was no safety-related revision during the reporting period.
- In EU, the national/local SmPC was updated to be consistent with Remicade® SmPC.
- During the accumulated period, a total of 210 serious adverse events were reported in the CT-P13 clinical development program (132 patient who administered CT-P13, 66 patients who administered the active comparator and 12 blind SAEs).
- During the accumulated period, a total of 416 ADRs were reported including 230 events during the current reporting period from post-marketing data sources (voluntary reports including unsolicited cases directly reported to Celltrion/vendor by a medical professional or consumer or through regulatory authorities and PMS sources including cases of 5 registry studies [CT-P13 4.2, CT-P13 4.3, CT-P13 4.4, BSRBR registry (UK registry) and RABBIT registry (Germany registry)] and CT-P13 Korea PMS study). During the reporting period, 1 off-label use case and 1 intentional overdose were reported. During the PBRER reporting period, no drug abuse or misuse, drug-drug interactions and weight gain cases were collected. Four cases with a fatal outcome were reported.
- During the PBRER reporting period, 7 cases were found for SMQ (narrow) “Lack of efficacy/effect” and the following Low Level Term (LLT) from post-marketing data sources: ‘Rheumatoid arthritis aggravated’, ‘Crohn’s aggravated’, ‘Colitis ulcerative aggravated’, ‘Psoriasis aggravated’, ‘Psoriatic arthritis aggravated’, ‘Psoriatic arthropathy aggravated’, ‘Rheumatoid arthritis flare up’, ‘Psoriasis flare up’ and ‘Flare up of arthritis’. Based on a review of these cases, no safety findings were identified that suggest quality or efficacy-related concerns.
- During the PBRER reporting period, no new, ongoing or closed signal was identified for Infliximab. During this reporting period, no new information was collected for previously identified or potential risks and there was no update for missing information. There was no action taken or proposed risk minimization activity for a safety reason.
- Four published papers during the reporting period provide significant new information on the effect or efficacy of Remsima®/Flammegis® in approved indications. These studies confirm the effect of Infliximab. They do not suggest that benefits of Infliximab treatment are greater or less than previously considered.
- According to the safety data review of literatures published during the period for this report, there were no clinically significant and new safety results requiring RSI revision.

- There is no recommend or implemented action to Celltrion Inc. Celltrion Healthcare Philippines Inc., Celltrion Healthcare Co. Ltd., Celltrion Healthcare Malaysia, Celltrion Healthcare Hungary Kft., Celltrion Healthcare Turkey and Celltrion Healthcare Distribuição de Produtos Farmacêuticos do Brasil Ltda., OLIMED CV, Oktal Pharma, Hikma Pharmaceuticals Co., Ltd and Nippon Kayaku for the approved Infliximab formulation as the result of assessment of available information included in this PBRER.
- In conclusion, the evaluated safety data were consistent with the established overall safety profile of Infliximab as described in RSI. No significant and new safety information was identified that requires revision of Infliximab RSI from the review of global safety data during the PBRER reporting period. The benefit-risk ratio of Infliximab remains favorable.

D. PBRER summary - PERIODIC BENEFIT-RISK EVALUATION REPORT (Celltrion Infliximab, 21JUL2015 to 20JAN2016) (Annex 5)

(1) Reporting period

21 Jul 2015 ~ 20 Jan 2016

(2) Executive summary

- This document is a Periodic Benefit-Risk Evaluation Report (PBRER) of Infliximab for submission to regulatory authorities according to the current Guideline on Good Pharmacovigilance Practices Module VII. This document summarizes all adverse drug reaction (ADR) reports and other safety data collected from worldwide sources from 21 Jul 2015 to 20 Jan 2016 by the marketing authorization holder (MAH), Celltrion Inc., Celltrion Healthcare Philippines Inc., Celltrion Healthcare Co. Ltd., Celltrion Healthcare Malaysia Sdn Bhd, Celltrion Healthcare Hungary Kft., Celltrion Healthcare Turkey, Celltrion Healthcare Distribuição de Produtos Farmacêuticos do Brasil Ltd., OLIMED CV, Oktal Pharma, Hikma Pharmaceuticals Co., Ltd, Pharmbio Pty. Ltd, iQone Healthcare Switzerland Sarl, Celltrion Healthcare Israel Ltd, Promopharm, Celltrion Healthcare (Thailand) Ltd. and Nippon Kayaku and their vendors/distributors. Data in the PBRER are collected from the International Birth Date (IBD), 20 Jul 2012.
- For Infliximab,
  - ATC (Anatomical Therapeutic Chemical) code: L04AB02 (tumor necrosis factor alpha [TNF-α] inhibitor)
  - Mechanism of action: TNF-α inhibitor
  - Approved for indications of rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis and psoriasis in adults; Crohn's disease (CD) and ulcerative colitis (UC) in adults and children
  - Formulation: Lyophilised powder
  - Dose: For RA, initial dose 3 mg/kg; for other indications, initial dose 5 mg/kg
  - Route of administration: Intravenous injection
- Infliximab was first approved on 20 Jul 2012 in Korea with the brand name Remsima®. To date,

Infliximab was registered in 65 countries.

- As of the database lock point (DLP), a total of 846 subjects were exposed to Infliximab in clinical studies during the CT-P13 clinical development program. In addition, approximately 110 subjects are estimated to have been exposed to CT-P13 in the ongoing clinical study CT-P13 3.4. During the reporting period, 2 clinical studies (CT-P13 3.4 and CT-P13 4.1) were ongoing. From ongoing clinical studies, no important new study results on efficacy and safety were identified.
- During the PBRER reporting period, 6 non-interventional studies (5 registry studies and 1 PMS study) were ongoing. Based on the review of data from these studies, no new information was identified that may have a potential impact on the benefit-risk assessment.
- Infliximab was launched in 49 countries. In launched countries, the post-marketing exposure to Infliximab is estimated as follows:
  - Surveillance period: Approximately 16, 990 patient-years
  - Accumulated period: Approximately 36, 086 patient-years

  Infliximab was also launched in Moldova, Guatemala, Luxembourg, El Salvador, Brazil and Russia. In these countries, there were no Infliximab exposure during the accumulated period and surveillance period (i.e., no Sales Records). Infliximab was launched in Armenia, Azerbaijan Republic, Belarus, Malta, Panama and Paraguay but in these countries, there were no Sales Records during the reporting period.
- European Union Summary of Product Characteristics (EU SmPC) Version 6.0 dated 10 Mar 2015 served as the reference safety information (RSI) and was effective as of the end of the reporting period. During the reporting period, EU SmPC was being updated to be consistent with Remicade® SmPC. In Nov 2015, EU SmPC Version 7.0 was submitted to the European Medicines Agency (EMA) and on 08 Jan 2016, EU SmPC Version 7.1 was submitted to the EMA. Both versions were approved after DLP.
- In the EU, the national/local SmPC was updated to be consistent with the innovative new drug Remicade® SmPC.
- During the accumulated period, a total of 220 serious adverse events were reported from the CT-P13 clinical development program. Of these, 134 SAEs were reported from patients who administered CT-P13 and 66 SAEs were reported from patients who administered the active comparator, and 20 events were blind SAEs.
- During the accumulated period, a total of 1045 ADR were reported, including 661 events during the current reporting period from post-marketing data sources (voluntary reports including unsolicited cases reported directly to Celltrion/vendor by a medical professional or consumer or through regulatory authorities and PMS sources including cases from 5 registry studies [CT-P13 4.2, CT-P13 4.3, CT-P13 4.4, BSRBR registry (UK registry) and RABBIT registry (Germany registry)] and CT-P13 Korea PMS study). During the reporting period, 10 off-label use cases and 6 unintentional drug misuse cases were reported. During the PBRER reporting period, no overdose or drug-drug interaction cases were collected. During the current reporting period, a fatal outcome was reported from 7 cases from post-marketing data sources (5 initial reports and 2 follow-up reports). In accumulation, 10 cases with a fatal outcome were reported since 20 Jul 2012.
- During the PBRER reporting period, 45 cases were retrieved for the standardized MedDRA query (narrow) “Lack of efficacy/effect” or the following Low-Level Term): Arthritis rheumatoid aggravated or rheumatoid arthritis aggravated or Arthritis aggravated or Crohn’s aggravated or

Crohn's disease aggravated or Crohns disease aggravated or Colitis aggravated or UC aggravated or Colitis ulcerative aggravated or Psoriasis aggravated or Psoriatic arthritis aggravated or Psoriatic arthropathy aggravated or Spondylitis ankylosing aggravated or Progression of rheumatoid arthritis or progression of psoriatic arthritis or rheumatoid arthritis flare up or Arthritis flare up or Psoriasis flare up or Flare up of arthritis or Exacerbation of psoriasis from post-marketing data sources. Based on the review of these cases, no safety finding was identified that suggests the quality or efficacy-related concern.

- During the PBRER reporting period, no new, ongoing or closed signal was identified for Infliximab (Remsima®/Flammegis™). The 3 newly identified major risks were included in important safety concerns during the current reporting period: acute hypersensitivity [anaphylactic shock included], Merkel cell carcinoma and melanoma. To exclude specific disease conditions, 2 important potential risks (malignancy and skin cancer) were updated, and for consistency with the Remicade® Risk Management Plan (RMP), 1 important potential risk (bowel stenosis, stricture and occlusion [in CD]) was deleted. Hypersensitivity was moved to the section of identified important risks in the section of missing information on important safety concerns. Lack of efficacy was deleted from the section for missing information for consistency of the revision in the reference drug Remicade® RMP and Remsima® RMP. Other than the routine pharmacovigilance activity and planned additional risk minimization activity, there was no other action taken or proposed risk minimization activity for a safety reason.
- Seven papers published during the reporting period provide significant new information on effect or efficacy of Remsima®/Flammegis® in approved indications. These studies confirm efficacy of Infliximab.
- According to the review of safety data from literatures published during the period for this report, there were no clinically significant and new safety results requiring RSI revision.
- There is no recommended or implemented action taken to Celltrion Inc., Celltrion Healthcare Philippines Inc., Celltrion Healthcare Co. Ltd., Celltrion Healthcare Malaysia Sdn Bhd, Celltrion Healthcare Hungary Kft., Celltrion Healthcare Turkey, Celltrion Healthcare Distribuição de Produtos Farmacêuticos do Brasil Ltd., OLIMED CV, Oktal Pharma, Hikma Pharmaceuticals Co., Ltd, Pharmbio Pty. Ltd, iQone Healthcare Switzerland Sàrl, Celltrion Healthcare Israel Ltd, Promopharm, Celltrion Healthcare (Thailand) Ltd. and Nippon Kayaku for the approved Infliximab formulation based on results of assessment of available information included in this PBRER.
- In conclusion, the evaluated safety data were consistent with the established overall safety profile of Infliximab as described in RSI. No significant and new safety information was identified that requires revision of Infliximab RSI from the review of global safety data during the PBRER reporting period. The benefit-risk ratio of Infliximab remains effective within approved indications.

7.2.2 Safety Data reported from the literature and academic information in overseas

Safety reporting data such as overseas literature and academic conference information of the surveillance drug collected during the re-examination period are described in Appendix 8 and 9.

7.2.3 Sales and approval status in overseas

Surveillance drug is currently approved in 72 countries (excluding Republic of Korea) and marketed in 59 countries (excluding Republic of Korea) (see Appendix 6).