1 REPORT SYNOPSIS

Project title: Experiences of using vedolizumab in the East Midlands, United Kingdom: A retrospective observational study
Protocol: PT East Midlands_v3 0_160418 Vedolizumab-5049
Name of sponsor: Takeda UK Limited
Participating centres and clinicians: Dr Gordon Moran (Chief Investigator), Nottingham University Hospitals NHS Trust Dr Jonathan White, NIHR Nottingham Biomedical Research Centre, Nottingham University Hospitals NHS Trust and the University of Nottingham; Nottingham Digestive Diseases Centre, The University of Nottingham; University Hospitals of Derby and Burton NHS Foundation Trust Dr David Elphick, Chesterfield Royal Hospital NHS Foundation Trust Dr Said Din, Derby Teaching Hospitals NHS Foundation Trust Dr Aamir Sajjad, Kettering General Hospital NHS Foundation Trust Dr Stephen Foley, Sherwood Forest Hospitals NHS Foundation Trust Dr Anthony Norman, United Lincolnshire Hospitals NHS Trust Dr Richard Robinson, University Hospitals of Leicester NHS Trust
Number of patients (analysed): 192
Studied period: Patients who were initiated on vedolizumab between 1st November 2014 and 30th November 2016 (the index event) were followed up to the earliest of the following dates: last follow-up, date of death (if applicable) or 31st March 2017. Baseline data captured in the clinical project from the 12-month period before the first dose of vedolizumab were included in the study.

Project objectives:

Primary objective:

To describe corticosteroid-free remission and clinical remission in patients with inflammatory bowel disease (IBD) after initiation of vedolizumab.

Secondary objectives:

To describe:

- Change in disease activity compared with baseline.
- Concomitant drug use after initiation of vedolizumab.
- Mucosal healing after initiation of vedolizumab.
- IBD-related surgical treatment after initiation of vedolizumab.
- IBD-related admissions, including admissions requiring change in treatment after initiation of vedolizumab.
- Adverse events attributed to vedolizumab.

Eligibility criteria:

Patients with IBD who met the following eligibility criteria were included in the study:

Inclusion criteria

- Patients aged ≥18 years at initiation of vedolizumab.
- Patients with clinically confirmed diagnosis of Crohn's disease (CD), ulcerative colitis (UC), or IBD of unclassified type (IBDU), as recorded in medical records.
- Patients who received their first dose of vedolizumab between 1st November 2014 and 30th November 2016 in one of the participating study centres.

Exclusion criteria

- Patients whose hospital medical records were unavailable for review.
- Patients enrolled in an interventional clinical trial of an investigational medicinal product during the observation period.

Project design and methodology:

This was a retrospective observational study with secondary use of patient-level data already collected for a local clinical project in the East Midlands. As the study was non-interventional with no direct patient involvement and used anonymised data only, no patient consent was sought for use of data for this study. All data were extracted and transferred to pH Associates between May and June 2018.

Data analysis methodology:

Both distributions and descriptive statistics of central tendency (medians and arithmetic means) and dispersion (standard deviation, interquartile range) are presented for quantitative variables where possible. Nominal variables are described with frequencies and percentages. Time-dependent variables are presented as Kaplan–Meier plots. Analyses were conducted using only the results of patients with available data; where data were missing, the number of patients included in each analysis is reported.

Summary of key findings:

Of the overall patient population (n=192), 105 (55%) patients had CD/IBDU (mean age at vedolizumab initiation 45.0 [standard deviation (SD) 15.5] years; 63/105 [60%] female; 94/105 [90%] of white ethnicity; 23/91 [25%] current smokers) and 87 (45%) patients had UC (mean age at vedolizumab initiation 44.1 [SD 16.8] years; 34/87 [39%] female; 77/85 [91%] of white ethnicity; 3/76 [4%] current smokers). The median disease duration at vedolizumab initiation was 12.3 (range 0.9 to 45.1) years in patients with CD/IBDU and 5.4 (range 1.5 to 34.9) years in patients with UC. At vedolizumab initiation, 10/105 (10%) patients with CD/IBDU and 40/87 (46%) patients with UC were anti-TNF-naïve.

In the 12 months prior to vedolizumab initiation, 101/105 (96%) patients with CD/IBDU had received corticosteroids, 99/105 (94%) had received at least one immunomodulator and 95/105 (90%) received at least one anti-TNF agent. In the 12 months prior to vedolizumab initiation, 85/87 (98%) patients with UC had received corticosteroids, 81/87 (93%) had received at least one immunomodulator, and 47/87 (54%) had received at least one anti-TNF agent.

The median observation period following vedolizumab initiation was 36.3 (range 3.0 to 78.3) weeks in patients with CD/IBDU and 40.4 (range 4.9 to 80.1) weeks in patients with UC. Corticosteroid-free remission following vedolizumab initiation was achieved by 27/60 (45%) patients with CD/IBDU and 18/39 (46%) patients with UC. The median time to achieve corticosteroid-free remission was 14.1 (Interquartile range [IQR] 6.0 to 21.7) weeks in patients with CD/IBDU and 17.6 (IQR 8.7 to 29.6) weeks in patients with UC. In patients who were anti-TNF-naïve, corticosteroid-free remission was achieved in 3/3 patients with CD/IBDU and 10/25 (40%) patients with UC. In patients who were anti-TNF-experienced, corticosteroid-free remission was achieved in 24/57 (42%) of patients with CD/IBDU and 8/14 (57%) patients with UC.

At vedolizumab initiation, 28/105 (27%) patients with CD/IBDU were treated with corticosteroids, 27/105 (26%) were treated with immunomodulators and 24/105 (23%) were treated with aminosalicylates;

54/105 (51%) patients did not receive concomitant therapy at vedolizumab initiation. At vedolizumab initiation; 42/87 (48%) patients with UC were treated with corticosteroids, 36/87 (41%) were treated with immunomodulators and 58/87 (67%) were treated with aminosalicylates; 26/87 (30%) patients did not receive concomitant therapy at vedolizumab initiation.

Thirty-six (34%) patients with CD/IBDU and 24 (28%) patients with UC had discontinued vedolizumab at the end of the study observation period. The most common reasons for discontinuing vedolizumab in patients with CD/IBDU were primary non-response (28/36 [78%]) and intolerance (5/36 [14%]); the most common reasons in patients with UC were primary non-response (20/24 [83%]) and secondary loss of response (3/24 [13%]). The median vedolizumab treatment duration (including the 8-week wash-out period following final dose) in patients with CD/IBDU and UC was 30.9 (IQR 21.3 to 49.6) and 38.0 (23.7 to 56.7) weeks, respectively.

Clinical remission was achieved after vedolizumab initiation in 31/70 (44%) patients with CD/IBDU and 25/48 (52%) patients with UC. The median time to clinical remission following vedolizumab initiation in patients with CD/IBDU and UC was 10.1 (IQR 3.1 to 21.0) and 15.1 (IQR 7.4 to 24.9) weeks, respectively.

A clinical response (≥3-point decrease in Harvey-Bradshaw Index [HBI] score from baseline) was achieved in 16/30 (53%) patients with CD/IBDU in a median of 9.5 (IQR 6.1 to 18.2) weeks. A clinical response (≥2-point decrease in partial Mayo score from baseline) was achieved in 17/35 (49%) patients with UC in a median of 9.4 (IQR 5.7 to 15.4) weeks.

In patients with CD/IBDU, 10/105 (10%) had one IBD-related surgical procedure and 2/105 (2%) had two IBD-related surgical procedures following vedolizumab initiation. In patients with UC, 12/87 (14%) had one IBD-related surgical procedure and 2/87 (2%) had IBD-related two surgical procedures following vedolizumab initiation.

Patients with CD/IBDU had a median of 1.0 (interquartile range [IQR] 0.0–2.0; range 0.0–8.0 [mean 0.9 (SD 1.2)]) IBD-related admissions/patient/year in the 12 months preceding vedolizumab initiation and a median of 0.0 (IQR 0.0–1.0; range 0.0–18.1 [mean 1.3 (SD 3.0)]) IBD-related admissions/patient/year following vedolizumab initiation. Patients with UC had a median of 1.0 (IQR 0.0–1.0; range 0.0–14.0 [mean 1.0 (SD 1.7)]) IBD-related admissions/patient/year in the 12 months preceding vedolizumab initiation and a median of 0.0 (IQR 0.0–1.0; range 0.0–11.6 [mean 1.2 (SD 2.5)]) IBD-related admissions/patient/year following vedolizumab initiation.

A total of 12 AEs attributed to vedolizumab were recorded in 10 (5%) patients during the study observation period; 9 AEs were recorded in 7 (7%) patients with CD/IBDU (mean 0.1 [SD 0.4] per patient) and 3 AEs were recorded in 3 (3%) patients with UC (mean <0.1 [SD 0.2] per patient).

Conclusions:

These results, in a predominantly anti-TNF-experienced complex patient cohort, mirror other published clinical data and demonstrate good clinical effectiveness and an acceptable safety profile.