Abstract

Title

Linaclotide Utilization Study in Selected European Populations

Keywords

Linaclotide, Irritable Bowel Syndrome, Drug Utilization, Treatment Patterns, Off-label Use

Rationale and Background

Linaclotide (Constella ©) has been approved for the treatment of moderate-to-severe irritable bowel syndrome (IBS) with constipation (IBS-C) in adults in the European Union (EU). This drug utilization study (DUS) aims to describe the characteristics of patients prescribed linaclotide, as well as their treatment patterns.

Research Question and Objectives

The primary research questions were:

- What are the characteristics of patients prescribed linaclotide?
- What is the extent of linaclotide off-label use with regards to its indication?

And secondarily:

- What are the linaclotide prescription patterns?

Study Design

Cohort study using administrative healthcare databases in three countries: the UK, Spain and Sweden.

Setting

The study period was determined by the launch date of linaclotide in each of the three contributing countries: from May 2013 (UK), September 2014 (Spain), or February 2013 (Sweden) until 31 December 2017.

Subjects and Study Size, Including Dropouts

1,319, 1,981 and 5,081 patients prescribed/dispensed linaclotide from the UK, Spain and Sweden respectively were included.

Variables and Data Sources

Two primary care databases: the Clinical Practice Research DataLink (CPRD) in the UK and the Information System for the Development of Primary Care Research (SIDIAP) database in Spain; and one secondary care data source: the linked patient, prescription and causes of death registries in Sweden, were used. Patients with IBS-C were identified with diagnostic codes (Read in the UK and ICD-10 in Spain and Sweden) using an algorithm.

Results

The median (interquartile range [IQR]) age of linaclotide users in the UK, Spain and Sweden was 45 (34- 58), 57 (44- 69) and 51 years (36- 65) respectively, and most were female (86.3%, 85.7% and 81.1%. in the UK, Spain and Sweden). Having no record of an IBS diagnosis was common in all countries (41%, 40% and 69% in the UK, Spain and Sweden), however, among those patients with a known IBS diagnosis, the majority of patients were classified as IBS-C in all countries (68.8% in the UK, 62.0% in Spain and 92.7% in Sweden).

The largest subgroup of patients not sufficiently documented in the clinical program were patients with hypertension in all countries (25.2%, 30.2% and 26.5% in the UK, Spain and Sweden). The largest group of patients with potential off-label use was those with potential for excessive or abusive use in the UK and Spain (17.1% and 31.3%), however, in Sweden this group was small (1.7%), and the largest patient group with potential off label use were patients with inflammatory bowel disease or mechanical gastrointestinal obstruction (5.8%).

Over the follow-up period, 449 (36.0%) UK users discontinued treatment and 606 (48.6%) switched. In Spanish users, 1,294 (69.8%) discontinued and 134 (7.2%) patients switched; and in Swedish users 2,261 (46.2%) discontinued and 2,099 (42.9%) switched. In a meta-analysis, factors associated with linaclotide discontinuation were having another type of IBS than IBS-C (HR: 1.20, 95%CI: 1.07-1.34) and having no diagnosis of IBS recorded (HR: 1.11, 95%CI: 1.03-1.19). Variables associated with an increased risk of switching were being 65 or older (vs. 18-64 years old; HR = 1.52, 95%CI: 1.38-1.68), concomitant use of antidepressants (HR: 1.49, 95%CI: 1.13-1.97), laxatives (HR: 1.23, 95%CI: 1.12-1.36) or prokinetics (HR: 1.15, 95%CI: 1.03-1.28).

Discussion

Linaclotide users in the UK, Spain and Sweden were mostly female and aged over 40. Having no recorded diagnosis of IBS was common, however, of patients who had an IBS diagnosis, the

majority were classified as IBS-C. Both discontinuations and switches from linaclotide were common events, however, patients who were classified as IBS-C were less likely to discontinue treatment compared to those who were classified as having another type of IBS, or those without an IBS diagnosis. Potential off-label use appeared limited as demonstrated by the small subgroups sizes, with the exception of those with a possible risk of abuse or excessive use (as defined by the presence of a diagnosed eating disorder [<1.5% of patients in this group] or a particularly high or low BMI [>98.5% of patients in this group].

Marketing Authorization Holder(s)

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