Previously unknown gastro-intestinal adverse drug reactions attributed to etanercept

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Background

Although an increased risk of inflammatory bowel disease (IBD) during etanercept (ETN) use is included in the product information of ETN, no other gastro-intestinal adverse drug reactions (GI ADRs) are described. This is in contrast with other TNFα-inhibitors such as adalimumab (ADA) and infliximab, as these are associated with various GI-ADRs such as nausea and abdominal pain.

Objective

To describe patient-reported and health care professional (HCP)- reported ETN associated GI-ADRs and to identify the proportion of these ADRs and compare this with ADA associated GI-ADRs.

Method

Patient-reported data on ADRs attributed to biologics were collected from the Dutch Biologic Monitor (DBM) [1] from 1 Jan 2017 until 1 Nov 2019. HCP-reported data on ADRs attributed to biologics were collected from the Dutch Rheumatic Arthritis Monitoring Registry and the Dutch Registry for Spondyloarthritis from 22 Jun 2004 until 1 Nov 2019. GI-ADRs were defined by MedDRA [2] System Organ Class 'Gastrointestinal disorders'. All reported GI-ADRs attributed to ETN and ADA for patients with inflammatory rheumatic diseases (IRDs) were selected. Proportion of GI-ADRs for ETN and ADA in patient and HCP reports was defined as the number of patients with at least one GI-ADR per total number of patients using ETN or ADA. Patient-reported burden and actions taken after GI-ADRs were compared between ETN and ADA.

Results

Table 1. Proportion of patient- and healthcare professional-reported gastro-intestinal adverse drug reactions attributed to etanercept and adalimumab

	Proportion etanercept	Top 3 reported ADRs	Proportion adalimumab	Top 3 reported ADRs	p-value*
DBM (n=755; ETN: 415, ADA: 358)	6.3% (26 pt)	1. Nausea: 6 2. Diarrhea: 5 3. Abdominal pain: 5	5.9% (21 pt)	1. Nausea: 8 2. Diarrhea: 3 3. Oral aphthous ulcer: 2	0.9
Registries (n=1,343; ETN: 804, ADA: 796)	1.6% (13 pt)	1. Diarrhea: 6 2. Nausea: 2 3. Abdominal pain: 2	3.4% (25 pt)	1. Nausea: 7 2. Abdominal pain: 6 3. Diarrhea: 5	0.049

* Differences between etanercept (ETN) and adalimumab (ADA) were tested using Fisher's exact
DMB: Dutch Biologic Monitor

Table 2. Actions following patient-reported gastro-intestinal adverse drug reactions attributed to etanercept and adalimumab in the Dutch Biologic Monitor

	Etanercept (n=38)	Adalimumab (n=22)
ADR burden* (mean±SD)	2.9 ± 1.0	2.5 ± 0.9
Contact HCP	23 (61%)	10 (45%)
Specialist doctor	10 (43%)	3 (30%)
General practitioner	10 (43%)	8 (80%)
Nurse	6 (26%)	2 (20%)
Other	7 (30%)	2 (20%)
Action of HCP		
Discontinuation	1 (4%)	1 (10%)
Dose adjustment	2 (9%)	1 (10%)
Treatment	4 (17%)	3 (30%)
Referral	3 (13%)	2 (20%)
Mentioned, no action	12 (52%)	5 (50%)
Other	3 (13%)	2 (20%)
* Burden was measured on a five point Likert-type scale (5: very high burden)		

We included 755 patients from the DBM using ETN (415) and ADA (358) for IRDs, of which 47 patients reported 60 GI-ADRs. The proportion of patient-reported GI-ADRs was 6.3% for ETN and 5.9% for ADA (Table 1). We included 1343 patients using ETN (804) or ADA (796) from the registries, with 43 HCP-reported GI-ADRs in 38 patients. The proportion of HCP-reported GI-ADRs was 1.6% for ETN, which was significantly lower than 3.4% for ADA (p=0.049). Patients experienced ETN associated GI-ADRs more burdensome than ADA associated GI-ADRs (p=0.05 using Mann-Whitney U) (Table 2). The ADR required action in 34% of patient-reported GI-ADRs attributed to ETN and 41% of GI-ADRs attributed to ADA, including biologic discontinuation. No hospitalisation following a GI-ADR was reported.

Conclusion

Although GI-ADRs other than IBD are not included in the product information of ETN, they are often reported by both patients and HCPs. The type of patient-reported GI-ADRs attributed to ETN and ADA is comparable. However, patients regard GI-ADRs attributed to ETN as more burdensome.

1. Van Lint JA, *et al*. Patient-reported burden of adverse drug reactions attributed to biologics used for immune-mediated inflammatory diseases. *Drug Saf.* 2020
2. Brown EG, Wood L, Wood S. The medical dictionary for regulatory activities (MedDRA). *Drug Saf.* 1999;20(2):109–17

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