

Disease-specific adverse drug reaction profiles of adalimumab and etanercept as reported by immune-mediated inflammatory disease patients

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Background

Information on adverse drug reactions (ADRs) is generally clustered for all indications of a drug in the patient information leaflet. However, previous research has shown that participants of the Dutch Biologic Monitor (DBM) that use a biologic for their immune-mediated inflammatory disease (IMID) prefer to receive ADR information tailored to their own biologic and IMID (1). Currently, it is unclear whether the ADR profile of a specific biologic may differ between patients with different IMIDs, which would be vital information for health care providers (HCPs) in their patient guidance.

Table 1. Respondent characteristics

Characteristics	ADA		ETN	
	n=218	%	n=185	%
Female gender, n (%)	140	64.2	129	69.7
Median age (IQR), years	56.0 (46.0-64.0)		58.0 (48.0-66.0)	
ADR reports	572	100.0	450	100.0
Indication for biologic therapy				
Rheumatoid arthritis	90	41.3	127	68.6
Psoriatic arthritis	46	21.1	35	18.9
Ankylosing spondylitis/axSpA	32	14.7	23	12.4
IBD ^a	50	22.9	0	0.0
Combination therapy ^b				
Methotrexate	63	30.3	70	40.2
Corticosteroids	25	12.0	21	12.1
Thiopurines	18	8.7	1	0.6
No combination therapy	87	41.8	59	33.9
Other	31	14.9	48	28.2

IQR: interquartile range; IBD: inflammatory bowel disease; axSpA: axial spondyloarthritis. **a.** IBD includes Crohn's disease and ulcerative colitis. **b.** The overall percentage exceeds 100% since patients can have a combination therapy consisting of one or more drugs.

Objective

To determine whether the profiles of ADRs attributed to adalimumab (ADA) and etanercept (ETN) reported by patients in the DBM differs between IMIDs.

Method

The DBM is a prospective cohort event monitoring system for patient-reported ADRs attributed to biologics (2). Study data was extracted from the DBM for the period Jan 2017 – Oct 2020. ADRs were coded according to their corresponding Preferred Term (PT) following MedDRA terminology. Unique PTs were selected per participant and grouped under System Organ Classes (SOCs) (Figure 1) for ADA and ETN. SOC's contributing for <1% to the total number of reported ADRs were grouped as 'other'. Participants with more than one of the included IMIDs, i.e. Psoriatic Arthritis (PsA), Inflammatory Bowel Disease (IBD, i.e. Crohn's disease and ulcerative colitis), rheumatoid arthritis (RA), and axial spondyloarthritis (axSpA) including Ankylosing Spondylitis (AS), were excluded. Differences in ADR profiles between IMIDs were tested using the Fisher-Freeman-Halton's Exact Test with Monte Carlo simulation. SOC's of interest were separately tested with the Fisher-Freeman-Halton's Exact Test (no simulation) and subsequently corrected for multiple comparisons using the Benjamini-Hochberg (BH) correction.

Results

A total of 572 ADR reports from 218 participants using ADA and 450 ADR reports from 185 participants using ETN were analyzed (Table 1). Overall, a statistically significant difference in patient-reported ADR profile between the assessed indications was found for ADA ($p=0.011$), but not for ETN ($p=0.057$). The following separate tests for selected SOC's of interest showed a significant difference in the frequencies of 'respiratory, thoracic and mediastinal disorders' and 'musculoskeletal and connective tissue disorders' between the different IMIDs for ADA after BH correction, but none for ETN.

Conclusion

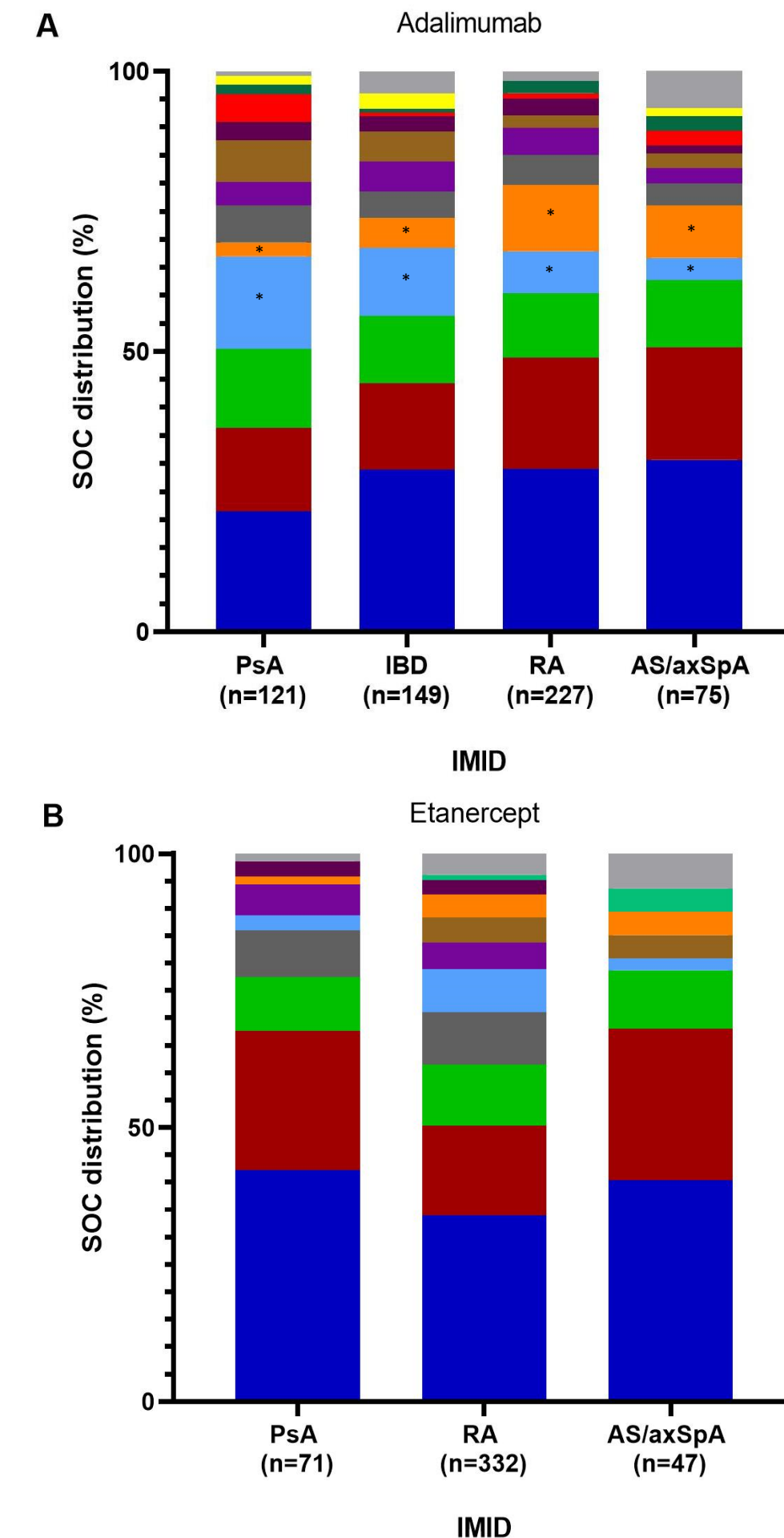
Although only ADA shows a statistically significant difference in ADR profile between different IMIDs, more research with a larger sample size might show similar results for ETN. Furthermore, explanations for the differences found, like disease-drug interactions, must be examined. This would help HCPs in providing disease-specific information and patient guidance.

Legend

- Other
- Cardiac disorders
- Investigations
- Psychiatric disorders
- Vascular disorders
- Eye disorders
- Nervous system disorders
- Gastrointestinal disorders
- Respiratory, thoracic and mediastinal disorders *
- Musculoskeletal and connective tissue disorders *
- Skin and subcutaneous tissue disorders
- Infections and infestations
- General disorders and administration site conditions
- Neoplasms benign, malignant and unspecified (incl cysts and polyps)

- SOC = System organ class
- IMID = Immune-mediated inflammatory disease
- PsA = Psoriatic arthritis
- RA = Rheumatoid arthritis
- IBD = Inflammatory bowel disease
- AS/axSpA = Ankylosing spondylitis / axial spondyloarthritis
- n = Number of reported adverse drug reactions
- * = $p < 0.05$ after Benjamini-Hochberg correction

Figure 1: The disease-specific patient-reported ADR profile of ADA (A) and ETN (B) in IMID patients resulting from the Dutch Biologic Monitor



References:

Kosse LJ et al.; *Expert Opin Drug Saf.* 2020;19(8):1045-1054.
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