The Global Landscape of Real-world Utilization and Clinical Outcomes in Patients Treated with Adalimumab: A Scoping Review

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BACKGROUND

- Adalimumab is a fully human monoclonal antibody and is a tumor necrosis factor alpha (TNFα) inhibitor indicated for use in the treatment of rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), Crohn's disease (CD), psoriasis (PsO), juvenile idiopathic arthritis (JIA), ulcerative colitis (UC), hidradenitis suppurativa (HS), and uveitis (UV) [1]
- Since its initial approval in 2002, 10 biosimilars have entered the market but many barriers to patient access still exist [2]
- There is a lack of real-world utilization and effectiveness outcomes for adalimumab products

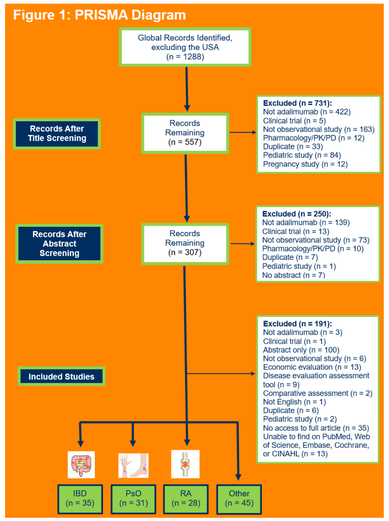
OBJECTIVE

- To develop a comprehensive understanding of observational research and real-world evidence (RWE) evaluating adalimumab use and its biosimilars

METHODS

- Scoping review conducted according to the PRISMA-ScR framework (Figure 1)
- Peer-reviewed articles published in English anytime up to July 4th, 2023, were included
- Included studies were observational (prospective or retrospective), conducted globally except the United States as it was previously reviewed, and included patients aged 18 years or older treated with adalimumab for any approved or off-label indication
- Data were descriptively analyzed and summarized based on overall trends, similarities, and differences across included studies and stratified by disease state

Figure 1: PRISMA Diagram



RESULTS

A previous review of studies conducted in the United States (US) yielded 11 results. The observed trends are described below:

- Most common studied disease states were psoriasis (n = 5), rheumatoid arthritis (n = 5), and Crohn's disease (n = 1)
- The average sample size across all 11 studies was 3,528 (434, 8643), with the smallest sample size being for a rheumatoid arthritis study and the largest for a psoriasis study
- 54.5% of the studies utilized claims data as their data source
- Safety and efficacy were the primary outcomes in most of the studies, with some descriptive analyses of treatment patterns
- Compared to other tumor necrosis factor inhibitors, patients on adalimumab were more likely to undergo dose escalations or to use the medication above label, increasing the risk of infections, which on average, first occurred around 12 months from start of therapy
- Time to treatment discontinuation was about 12 months, and persistence past 12 months was around 50%
- Majority of studies were funded by pharmaceutical manufacturers

Overall, 127 global studies are included in the current scoping, with respect to the 11 previously identified US studies. The observed trends are described below:

- The average sample size across all inflammatory bowel disease studies was 602 (16, 5003), 30,057 (11, 874549) for psoriasis studies, and 1,238 (52, 7052) for rheumatoid arthritis studies
- Most studies were conducted in Japan (n = 20), followed by Italy (n = 16), as well as South Korea (n = 11), and the US (n = 11)
- The primary outcome of interest is treatment patterns across inflammatory bowel diseases (Crohn's disease and ulcerative colitis), psoriasis, and rheumatoid arthritis; while the primary outcome of interest in the less-frequently studied disease states is efficacy
- Common strengths are large sample size, multicentric approach, real-world, direct comparators, and multiple study outcomes
- Common limitations are small sample size, observational and retrospective study design, heterogeneous population, and lack of control groups
- Majority of studies are funded by pharmaceutical manufacturers

Characteristic	IBD (n = 35)	PsO (n = 31)	RA (n = 28)	Other (n = 45)*†
Study Design, n (%)				
Prospective	6 (17.1)	8 (25.8)	5 (17.9)	15 (33.3)
Retrospective	21 (60.0)	18 (58.1)	13 (46.4)	19 (42.2)
Both	3 (8.6)	0 (0.0)	1 (3.6)	0 (0.0)
Other/Unspecified*	5 (14.3)	5 (16.1)	9 (32.1)	11 (24.5)
Centers, n (%)				
Monocentric	4 (11.4)	10 (32.3)	4 (14.3)	15 (33.3)
Multicentric	31 (88.6)	21 (67.7)	24 (85.7)	30 (66.7)
Location, n (%)*				
NA	2 (5.7)	7 (22.6)	6 (21.4)	2 (4.4)
EMEA	20 (57.1)	17 (54.8)	14 (50.0)	25 (55.6)
LATAM	1 (2.9)	0 (0.0)	0 (0.0)	2 (4.4)
APAC	12 (34.3)	7 (22.6)	8 (28.6)	16 (35.6)
Data Source, n (%)*				
Hospital/EHR	8 (22.9)	11 (35.5)	5 (17.9)	16 (35.6)
Registry	4 (11.4)	10 (32.3)	12 (42.9)	6 (13.3)
Claims	10 (28.6)	3 (9.7)	5 (17.9)	3 (6.7)
Other^	21 (60.0)	13 (41.9)	10 (35.7)	21 (46.7)
Primary Outcome, n (%)				
Efficacy	12 (34.3)	6 (19.4)	9 (32.1)	20 (44.4)
Safety	1 (2.9)	0 (0.0)	2 (7.1)	1 (2.2)
Both	5 (14.3)	4 (12.9)	3 (10.7)	3 (6.7)
Descriptive	3 (8.5)	1 (3.2)	4 (14.4)	4 (8.9)
Treatment patterns	14 (40.0)	20 (64.5)	10 (35.7)	17 (37.8)

Abbreviations: IBD = inflammatory bowel disease (including Crohn's disease, CD, and ulcerative colitis, UC); PsO = psoriasis; RA = rheumatoid arthritis; NA = North America; EMEA = Europe, Middle East, Africa; LATAM = Latin America; APAC = Asia Pacific; EHR = electronic health record
*Studies may have been counted twice (e.g., study conducted in multiple locations, study consisted of multiple disease states, or utilized multiple data sources)
†Other disease states include psoriatic arthritis (PsA), ankylosing spondylitis (AS), hidradenitis suppurativa (HS), uveitis (UV), spondyloarthritis (SpA), axial spondyloarthritis (axSpA), sarcoidosis, Behçet's disease, immune-mediated inflammatory diseases (IMIDs), and other rheumatic diseases.
^Other includes routine encounters databases, supplemental databases, or governmental databases (e.g., Medicare, FDA) which attribute to large sample sizes

REFERENCES

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A complete list of studies that were included in this research may be found via this QR code.

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CONCLUSIONS

- Most studied disease states are inflammatory bowel diseases (Crohn's disease and ulcerative colitis), psoriasis, and rheumatoid arthritis; most RWE studies are designed retrospectively and are used to assess adherence, persistence, discontinuation, switching, and restarting of adalimumab products using a combination of data sources, but predominantly encounters databases and medical charts
- In general, studies found that adalimumab was more likely than other products to require dose escalation or to be used above label, and the real-world effectiveness of adalimumab biosimilars is comparable to the originator
- Time to treatment discontinuation is around 12 months, and reasons for discontinuing treatment, switching to a biosimilar, or switching to an alternative agent were due to inadequate response and/or increased risk of infections, usually occurring close to 12 months following the initiation of therapy; retention rate past 12 months was around 50%
- These findings will help identify potential gaps in literature which can inform future studies

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