The Landscape of Real-world Evidence of Rituximab Utilization and Clinical Outcomes in Patients with Cancer, Rheumatoid Arthritis, and Multiple Sclerosis: A Scoping Review

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BACKGROUND

- Rituximab is a CD-20 directed monoclonal antibody with broad treatment use in oncology and rheumatoid arthritis (RA), as well as regular off-label use in multiple sclerosis (MS)[1,2]
- Since its approval in 1997, three biosimilars have entered the market but many barriers (e.g., cost and coverage) to patient access still exist[3]
- Rituximab's real-world utilization and effectiveness is unclear

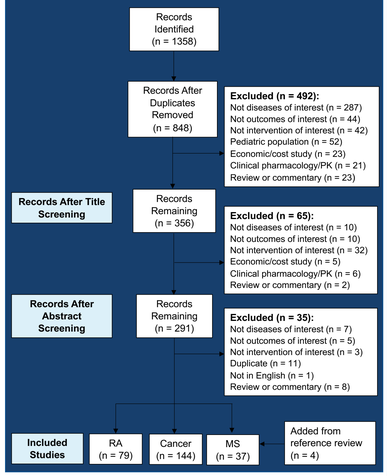
OBJECTIVE

- To describe the state of observational research and real-world evidence (RWE) evaluating rituximab in oncology, RA, and off-label use in MS

METHODS

- Scoping review conducted according to the PRISMA-ScR framework (Figure 1)
- Peer-reviewed articles published in English between 1 January 2010 and 14 June 2022 were included
- Included studies were observational (prospective or retrospective) and included patients aged 18 years or older treated with rituximab for an oncologic indication, RA, or MS
- 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

Characteristic	Cancer (n = 144)	MS (n = 37)	RA (n = 79)
Study Design, n (%)			
Prospective	34 (23.6)	5 (13.5)	29 (36.7)
Retrospective	109 (75.7)	31 (83.8)	49 (62.0)
Both	1 (0.7)	1 (2.7)	1 (1.3)
Centers, n (%)			
Monocentric	51 (35.4)	19 (51.4)	29 (36.7)
Multicentric	93 (64.6)	18 (48.6)	50 (63.3)
Mean (range)	24.8 (1, 400)	2.2 (1, 9)	50.7 (1, 1624)
Location, n (%)*			
NA	36 (25)	10 (27.0)	11 (13.9)
EMEA	65 (45.1)	28 (75.7)	59 (74.7)
LATAM	2 (1.4)	0	2 (2.5)
APAC	42 (29.2)	1 (2.7)	7 (8.9)
Data Source, n (%)*			
Hospital/EHR	105 (72.9)	25 (67.6)	41 (51.9)
Registry	24 (16.7)	12 (32.4)	29 (36.7)
Claims	12 (8.3)	0	4 (5.1)
Other†	3 (2.1)	2 (5.4)	5 (6.3)
Sample Size, n			
Mean (range)	757 (7, 9333)	3,129 (12, 100921†)	11,291 (19, 409706†)
Study Follow-up, mo			
Mean (range)	44.6 (2.5, 156)	25.7 (9.6, 40)	24.8 (3, 108)
Funding, n (%)			
Grant	41 (28.5)	13 (35.1)	24 (30.4)
Industry	39 (27.1)	0	18 (22.8)
Both	6 (4.2)	0	3 (3.8)
No funding	23 (16.0)	16 (43.2)	21 (26.6)
Unspecified	35 (24.3)	8 (21.6)	13 (16.5)

Abbreviations: MS = multiple sclerosis; RA = rheumatoid arthritis; NA = North America; EMEA = Europe, Middle East, Africa; LATAM = Latin America; APAC = Asia Pacific; EHR = electronic health record; RMS = relapsing multiple sclerosis
*Studies may have been counted twice (e.g., study conducted in multiple location or utilized multiple data sources)
†Other includes governmental databases (e.g., Medicare, FDA) which attribute to large sample sizes
^Studies include lymphoma and leukemia patients alongside other hematologic cancers

Characteristic	Cancer (n = 144)	MS (n = 37)	RA (n = 79)
Primary Diagnosis, n (%)			
Lymphomas	100 (69.4)		
Leukemias	27 (18.8)		
Any hematologic cancers^	10 (6.9)		
Any cancer type	7 (4.9)		
RMS		12 (32.4)	
Non-RMS		2 (5.4)	
Any MS subtype		23 (62.2)	
RA			64 (81.0)
Any rheumatic disease			15 (19.0)
Treatment, n (%)			
Monotherapy	11 (7.6)	37 (100)	78 (98.7)
Combination therapy	133 (92.4)	0	1 (1.3)
Comparator, n (%)			
Yes	44 (30.6)	18 (48.6)	60 (75.9)
No	100 (69.4)	19 (51.4)	19 (24.1)
Primary Outcome, n (%)			
Efficacy	83 (57.6)	27 (73.0)	43 (54.4)
Safety	25 (17.4)	9 (24.3)	26 (32.9)
Descriptive	11 (7.6)	0	5 (6.3)
Treatment patterns	26 (18.1)	1 (2.7)	5 (6.3)
Safety Measure, n (%)			
Yes	77 (53.5)	21 (56.8)	47 (59.5)
No	67 (46.5)	16 (43.2)	32 (40.5)
Conclusion, n (%)			
Positive benefit	66 (45.8)	30 (81.1)	29 (36.7)
Neutral benefit	17 (11.8)	5 (13.5)	10 (12.7)
Negative benefit	6 (4.2)	1 (2.7)	11 (13.9)
Unspecified or no relation	55 (38.2)	1 (2.7)	29 (36.7)
Study Evaluation			
Common strengths	large sample size, length of follow up period, real-world, high external validity, multiple study outcomes		
Common limitations	retrospective study design, small sample size, heterogeneous population, selection bias, and lack of direct comparators and control groups		

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

ACKNOWLEDGEMENTS

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CONCLUSIONS

- Most RWE studies assessing rituximab are designed retrospectively and primarily conducted in the **EMEA region**
- While data sources varied, the majority of studies derived their data from either **hospital databases** or **registries**
- Rituximab is primarily used as part of a **combination therapy** for cancer indications and **monotherapy** for RA and MS
- Majority of studies focused on **efficacy as the primary outcomes** across all three disease states
- Within all disease states, rituximab was more often reported to have a **positive benefit** than neutral or negative benefit

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