The landscape of real-world research of rituximab utilization and clinical outcomes in patients with multiple sclerosis treated with rituximab: a scoping review

Mohammad Nasir Kaker, PharmD Candidate[1]; Catherine Lockhart, PharmD, PhD[2]

[1]Shenandoah University, Fairfax, VA; [2]Biologics and Biosimilar Collective Intelligence Consortium, Alexandria, VA

INTRODUCTION

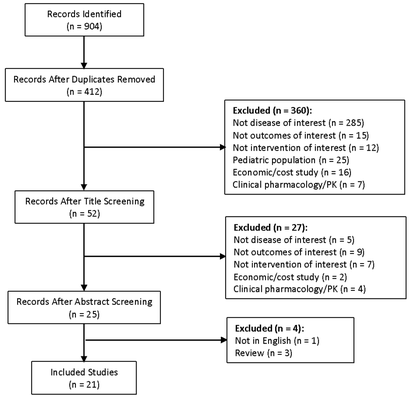
- Multiple Sclerosis (MS) is the most common immune-mediated, demyelinating, neurological degenerative disease affecting the central nervous system[1]
- It is estimated that 400,000 individuals in the US and 2.1 million individuals worldwide are affected with MS[2]
- Treatment options have significantly increased over the last couple of years; however, many patients continue to suffer from persistent disease activity[1]
- Rituximab (RTX) is a chimeric CD20 monoclonal antibody that has shown efficacy in the treatment of MS[1,3,4]

OBJECTIVE

- To better understand the landscape pf observational research of rituximab utilization and clinical outcomes in patients with MS, and to identify gaps in the available literature regarding observational studies that have been done with rituximab originator and biosimilar products in this disease setting

METHODS

- Scoping review conducted to the PRISMA-ScR framework
- Peer-reviewed, observational (retrospective or prospective) studies of adults (≥ 18 years of age) with MS treated with RTX between January 2010 and December 2020 were included
- Literature indexed in Medline (PubMed), EMBASE, and CINAHL was included in the search strategy, as well as a search of the grey literature identified via Google Scholar



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RESULTS

Study (PMID)	MS Subtype	Data Source	Country and N	Study Outcomes	Key findings
Arias 2020 (32066031)	RRMS, SPMS, PPMS	EHR	Finland (N=72)	EDSS, ARR, CEL, BCC	Reduction in ARR and CEH
Alcalá 2019 (30661133)	RRMS	GITEM registry	Spain (N=55)	EDSS, ARR, NEDA, disability, IA, safety	RTX vs ALM. No difference in EDSS, ARR and safety. Longer mean disease duration with RTX
Alcalá 2018 (29785523)	RRMS, PPMS	GITEM registry	Spain (N=90)	EDSS, ARR, DA, NEDA, safety	88% reduction in ARR, 90% relapse free, 70% NEDA, safe and effective
Barra 2016 (2860773)	RRMS, SPMS, PPMS	EHR	US (N=107)	EDSS, relapse, CD19/20, CEL, safety	Reduction in EDSS, 3% T1 CEL and 11% T2 CEH in RRMS, 20% above zero for CD19/20 count at 6 months
Barrenguer 2016 (27046661)	RRMS	EHR	Spain (N=12)	EDSS, new relapses, MRI activity, EQ VAS	Reduction in EDSS, improved EQ VAS, no relapses
Durozard 2019 (29722639)	RRMS	EHR and OFSEP register	France (N=50)	EDSS, ARR, CEL, safety	Reduction in EDSS and ARR, 20% relapses, 53.6% new CEL
Hellgren 2020 (31990978)	RRMS, PPMS	EHR	Sweden (N=83)	AEE, new CEL, clinical disability, safety	Reduction in ARR and CEL, mild non-infusion related reactions
Juto 2020 (31683231)	RRMS	EHR	Sweden (N=92)	Relapses, safety, cause for D/C	3% relapses, pregnancy and ADRs most common cause for D/C
Maarouf 2020 (32587103)	RRMS	EHR	France (N=33)	EDSS, ARR, $CD19^+$ count	Reduction in EDSS and ARR, $CD19^+$ >1% in 10 patients
Naser 2019 (31586800)	RRMS, SPMS, PMS	EHR	Iran (N=100)	EDSS, ARR, disease duration, disease duration prior to RTX	Reduction in EDSS in RRMS, Reduction in ARR in all subtypes, avg disease duration 10 years, ADRS (limb, pain, fatigue, UTI)
Oshima 2019 (29985084)	Not specified	FAERS database	US & Japan N=100,921	Development of PML, time to onset of PML	0.78% developed PML, onset of PML 178 days, PML higher in Japan compared to US (2.4% vs 0.24%)
Rommer 2016 (26589235)	RRMS, SPMS, PMS	Registry	Germany (N=56)	Safety	Infusion reactions (4), infections (3)
Salzer 2016 (27760868)	RRMS, SPMS, PMS	EHR and MS registry	Sweden (N=822)	Safety (ADR grade 2-5), efficacy	80 non-infusion ADRs grade 2-5 (76 infections), 94% drug survival, safe and effective up to 2 years
Scotti 2018 (29758075)	RRMS, PMS	MS Registry	Switzerland (N=82)	Drug comparison, NTZ: EDA, EDSS, safety, effectiveness, relapses	RTX and NTZ similar in time to EDA (HR 1.6), similar in effectiveness, infections more frequent in PMS
Sotirchos 2020 (30741108)	RRMS	EHR	US (N=78)	Drug comparison, inf-β and glatiramer: EDSS, disease duration	RTX had slower atrophy, higher EDSS (3.0 vs 2.0), no difference in disease activity
Yamout 2018 (30539030)	RRMS, PMS	EHR	Lebanon (N=89)	EDSS. ARR, safety, efficacy, CEL	EDSS, unchanged, ARR decreased, increased MRI CEL (18.6% to 92.6%
Boremalm 2019 (30762259)	RRMS	MS registry	Sweden (N=241)	ARR, ADDR	Lower ARR and ADDR, decreased disease activity when switching to RTX from fingolimod
D'Amico 2019 (30471585)	RRMS, SPMS, PPMS	EHR	Italy (N=11)	Relapses, safety, disease progression, new lesions	Relapses (8 RRMS, 2 SPMS, 1 PPMS), no disease progression or new T1/T2 lesions
He 2020 (32199096)	RRMS	MS registry	Sweden + 35 more (N=466)	EDSS, disability progression	Lower EDSS (2.2 vs 2.9) and disability progression in early RTX intervention group
Leonidou 2019 (31353999)	RRMS, SPMS, PPMS	EHR	Cypriot	EDSS, relapses, safety	Significant reduction in relapses in SPMS (none in RRMS), reduction in EDSS (avg 6.25 to 5.5)
Spelman 2018 (28649912)	RRMS	MS Registry	Sweden (N=461)	Drug compactor, ING-β: EDSS, ARR, time to first relapse	Greater reduction in EDSS and ARR In RTX, 87% reduction in relapses

Abbreviations: RRMS: relapsing remitting MS, SPMS: secondary progressive MS, PPMS: primary progressive MS, PMS: progressive MS, EDSS: expanded disability status scale, ARR: annualized relapse rate, CEL: contrasting enhancing lesions, BCC: b-cell counts, NEDA: no evidence of disease activity, IA: inflammatory activity, ALM: alemtuzumab, DA: disease activity, EQ VAS: euroqol visual analog scale score, D/C: discontinue, ADR: adverse drug reactions, NTZ: natalizumab, EDA: evidence of disease activity, ADDR: annualized drug discontinuation rate, GITEM: Grup d'Investigació i Tractament de l'Esclerosi Múltiple, OFSEP: French Observatory of Multiple Sclerosis

CONCLUSIONS

- Rituximab was studied in all MS subtypes, however, RRMS was the most represented subtype in all the studies
- Expanded disability status scale (EDSS), annualized relapse rate (ARR) and safety were the most common outcomes studied
- Common limitations: small sample size, retrospective design and lack of control group
- Common strengths: real world data, multiple study outcomes, and multiple MS subtypes studied
- While these studies are promising, more prospective studies with larger sample sizes are needed
- These findings will help identify potential gaps in literature which can inform future studies