Safety and Efficacy of Rituximab For Multiple Sclerosis and NMO

Experience of a single MS center

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Objective

To assess the long term safety and efficacy profile of rituximab (RTX) in patients with multiple sclerosis (MS) and neuromyelitis optica (NMO).

Introduction

- The B cell has been implicated in the pathology of multiple sclerosis since the report of Kabat et al. on immunoglobulin production in the central nervous system in the 1940s. [1]
- Immunoglobulin transcripts are elevated 125 fold in acute or active MS lesions as compared to chronic lesions, suggesting B cell activation plays an active role in an MS relapse. [2]
- Numerous B cell depleting anti-CD20 drugs are under development and demonstrate efficacy in treating MS. The first of these, rituximab remains a viable off-label treatment option since its potential utility was first demonstrated in 2005. [3]
- Rituximab is an antibody mediated intravenous medication, whose mechanism of action is inducing cell death through apoptosis by binding to the CD20 antigen on B cells.
- A recent retrospective observational study in Sweden illustrated the safety and efficacy of rituximab in MS patients up to two years. [4] Our current data extends this observational period to seven years, with similar results.
- This observational data becomes more relevant with the recent FDA approval of ocrelizumab, a humanized CD20 monoclonal antibody with proven benefit in both primary progressive (PPMS) and relapsing remitting multiple sclerosis (RRMS). [5,6]

Methods

- In this retrospective, uncontrolled, observational, single center study, patients with MS and NMO using rituximab as disease modifying therapy were identified through The Ohio State University infusion center data base.
- Patients were treated with a single infusion of 1,000mg rituximab IV subdivided into 2 infusions given two weeks apart. This protocol was repeated every 6 months.
- Clinical exams were performed every 6-12 months, or if clinically indicated otherwise.
- Outcome data (EDSS, relapse events) and adverse events were collected from the patient's electronic medical record. Specific adverse events of interest included infection, malignancy, and autoimmune events.
- Subjects included in the study met the following criteria: age 18 years or older, received RTX from 2005 to December 2016, had been taking the drug for longer than one year, and were diagnosed with either MS based on the McDonald Criteria, or NMO based on the 2006 criteria, or NMO spectrum disorder (see table 1).

Table 1: Descriptive characteristics of patients on Rituximab

	RRMS	PPMS	NMO	Total
Individuals studied (n)	23	17	24	64
Average age at start of drug (years)	40.78	47.12	50.33	45.91
Average disease duration prior to drug start (years)	6.58	3.28	1.55	
Average initial EDSS	4.20	5.73	4.60	
Female gender, n (%)	18 (78)	10 (59)	20 (83)	48 (75)

Results

- In the RRMS cohort, there was an annual relapse rate (ARR) of 0.005 and 87% were reported as clinically stable at the end of the chart review period (see table 2).
- In the PPMS cohort, 47% were reported as clinically stable at the end of the chart review period.
- In the NMO cohort, there was an ARR of 0.0074 and 79% were reported as clinically stable at the end of the chart review period.
- A total of 33 adverse events were recorded during the observation period. Twenty two out of 64 total patients (34% of the total population) reported an adverse event.
- Thirty two of 33 events may be classified as grade II, based on the common terminology criteria for adverse events, and were treated with either diphenhydramine or methylprednisilone.
- The most common reported event was skin irritation, either erythema, hives, or itching (70%).

Table 2: Overview of clinical progression of patients on rituximab

	RRMS	PPMS	NMO	Total
Individuals studied (n)	23	17	24	64
Individuals with clinical relapse on rituximab, n (%)	7 (30)	1 (17)	6 (25)	14 (22)
Total clinical relapses reported on rituximab per cohort, n	7	1	13	21
Annual relapse rate	0.005	NA	.177	
Mean EDSS change	-0.22*	0.12	-0.08	
Average time on the drug (years)	2.5	3.28	3.06	

* An improvement in EDSS, that is a lower score, is noted by (-)

Conclusions

- In this retrospective chart review analysis, rituximab was well tolerated and efficacious as measured by relapse rate, EDSS scores, and contemporary clinical evaluation.
- In addition to confirming the effectiveness of rituximab under these conditions, this study extends previous findings by demonstrating effectiveness in patients in a real world setting and with treatment duration up to seven years.
- Limitations inherent to this study include uncontrolled and unblinded surveillance.

References

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