VIEWPOINT OPEN ACCESS

Rituximab for Multiple Sclerosis

Hiding in Plain Sight

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In February 2023, following extensive discussions with stakeholders and data review, the Institute for Clinical and Economic Review issued final policy recommendations for treatment of relapsing multiple sclerosis (RMS)[1]: "All stakeholders have a responsibility and an important role to play in ensuring that all effective treatment options for patients with RMS, including off-label use of rituximab, are utilized in ways to help improve affordability and access and reduce health inequities." The report calls on payers to remove barriers to rituximab coverage, the American Academy of Neurology and the National MS Society to publicly endorse rituximab for RMS, and clinicians to advocate for coverage of rituximab and its biosimilars. In July 2023, the World Health Organization listed rituximab as an essential medicine for MS.[2] Yet not much has changed. Food and Drug Administration (FDA)-approved MS disease-modifying therapies continue to generate enormous profits for pharma, and rituximab remains hidden in plain sight.

Rituximab, an anti-CD20 monoclonal antibody (mAb), has led to dramatic strides in improving disease control and pathophysiologic understanding of MS. In 2007, Roche/Genentech announced the phase II randomized controlled trial (RCT) results of rituximab in RMS, stunning and delighting the MS community because B cells were not believed to play an important role in MS pathophysiology. These results indicated that anti-CD20 mAb therapy would be a game changer in the treatment of RMS. However, further development of rituximab was halted to prioritize development of a similar anti-CD20 mAb, ocrelizumab. Not surprisingly, ocrelizumab, FDA-approved in late 2017, is sold at a much higher annual price ($75,000) than brand rituximab and its biosimilars ($2,000–$14,000). The continued underutilization of rituximab and this delay in widespread availability of anti-CD20 mAb treatment have been a huge loss for persons with MS.

Most insurance carriers in the United States and Europe limited access to rituximab for MS, citing lack of regulatory approval. Kaiser Permanente and Sweden, however, authorized use, enabling evidence to satisfy FDA criteria for drug approval to be generated. Rituximab's staying power (a combined measure of efficacy, compliance, safety, and tolerability) outlasts natalizumab, fingolimod, and dimethyl fumarate.[3] A phase III RCT demonstrated significant superiority in controlling relapses and inflammatory disease activity compared with dimethyl fumarate.[4] Increasing use of rituximab and its biosimilars over the past 12 years has resulted in dramatically improved quality and affordability of MS care.[5] Rituximab's staying power and low cost are particularly advantageous for patients with high inflammatory disease activity, unstable health insurance or unaffordable co-pays, many of whom are young, Black, and/or Hispanic in the United States. Yet FDA-approval remains elusive because only Roche/Genentech can request rituximab approval for MS; without this, biosimilars cannot be granted an MS indication (Section 351[a], Public Health Services Act).

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Rituximab use presents a unique opportunity to lower the cost of MS care without loss of benefit. We urge the American Academy of Neurology and the National MS Society to support the use of rituximab for MS, Medicare to approve its coverage, and neurologists to prescribe it. It is time for us all to bring rituximab out of hiding.

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A. Langer-Gould is a site principal investigator for clinical trials in MS sponsored by Atara Biotherapeutics and a former Genentech employee (assistant medical director, rituximab and ocrelizumab MS development programs 2006–2007). E. Sotirchos reports scientific advisory boards and/or consulting for Alexion, Horizon Therapeutics, Roche/Genentech, and Ad Scientiam; receives speaking honoraria from Alexion; and is a site principal investigator for clinical trials in myelin oligodendrocyte glycoprotein antibody associated disease funded by Roche/Genentech and UCB. D. Bourdette is a consultant for Best Doctors/Teladoc and Magellan Health and a co-inventor of thyromimetic drugs for multiple sclerosis with founder stock shares for Autobahn Therapeutics. Go to Neurology.org/N for full disclosures.

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Elias S. Sotirchos	Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD	Drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data
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