Original Article

Experience with long-term rituximab use in a multiple sclerosis clinic

Megan E Barra, Dhruy Soni, Khac Huy Vo, Tanuja Chitnis and James M Stankiewicz

Abstract.

Background: Rituximab is a monoclonal antibody directed at CD20 positive B-lymphocytes and a potential therapeutic option in the treatment of multiple sclerosis. The safety of recurrent dosing is not established.

Objectives: The objective of this work was to report the experience of long-term rituximab administration in a comprehensive multiple sclerosis care clinic.

Methods: This was a single-center retrospective observational analysis of patients receiving rituximab for the treatment of multiple sclerosis from 2004 to 2015. Different dosing regimens were reviewed to determine whether frequency or dose may affect safety. CD19 and CD20 counts were collected to evaluate B-cell suppression during therapy. Relapses, magnetic resonance imaging activity and ritux-imab-related adverse events were collected by chart review and prospective database entry.

Results: Of 107 patients included, the average duration of treatment was 33.2 months. Seventy-seven patients received recurrent rituximab dosing after initiation. CD19/20 reconstitution occurred in approximately 20% of patients at 6 months, regardless of dosing strategy. Despite CD19/20 counts of 0, three patients had relapses or magnetic resonance imaging activity. Mostly mild side effects in relation to therapy were seen, with the exception of three patients requiring hospitalization for urinary tract infections.

Conclusions: In our clinic population, rituximab was well tolerated and safe with recurrent administration.

Keywords: Multiple sclerosis, rituximab, safety, long-term

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Introduction

Evidence has accumulated suggesting that B cells are involved either directly or indirectly in the pathophysiology of multiple sclerosis (MS). Rituximab is a monoclonal antibody directed at CD20 positive B-lymphocytes resulting in cell-mediated apoptosis." A phase II double blinded randomized controlled trial of rituximab in a relapsing MS population demonstrated robust efficacy on clinical measures and magnetic resonance imaging (MRI) with an acceptable safety profile.2 Ocrelizamab was recently shown to be effective and safe in two phase III trials conducted in relapsing-remitting patients showing an annualized relapse rate reduction of 46/47%, 43/ 37% risk reduction in confirmed disability progression and 94/95% reduction in total number of gadolinium enhancing lesions in the OPERA I and II studies, respectively.³ Ofatumumab was also successful in phase II.⁴ These monoclonal antibodies all deplete CD20 B cells, but differ in their chimeric (rituximab), humanized (ocrelizamab), or fully human (ofatumumab) molecular composition as well as their ability to stimulate complement and antibody dependent cellular cytotoxic effector mechanisms.

The safety profile of recurrent long-term dosing is not yet established in an MS population. Ritaximabhas been used extensively in many patient populations after its approval in 1997 for non-Hodgkin's lymphoma. Although overall patient exposure is unknown, over 300,000 patients with rheumatoid arthritis are known to have been treated with ritaximab. A recent study demonstrated that ritaximab Multiple Schrous Joannal -Experimental, Franchistorial and Christal

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Multiple Sclerosis Experimental Clinic

Elisabeth Sherman, Jing Tan, Marianne Hrabok

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Multiple Sclerosis Therapeutics Jeffrey A. Cohen, Richard A. Rudick, 2011-10-20 This book comprehensively reviews the current state of clinical trial methods in multiple sclerosis treatment providing investigators sponsors and specialists with current knowledge of outcome measures and study designs for disease and symptom management The status of the rapidly evolving field of disease modifying drugs is presented with emphasis on the most promising therapies currently being tested Experts discuss disease and symptom management for MS subtypes including neuromyelitis optica and pediatric MS In addition key scientific advances in MS pathology genetics immunology and epidemiology are presented The fourth edition has been extensively revised featuring more than 50% new material All chapters have been substantially updated to provide current information on rapidly evolving topics and this volume contains 15 new chapters reflecting the growth of the field in recent years This book is an essential reference for practitioners caring for MS patients investigators planning or conducting clinical trials and clinical trial sponsors Clinical Neuroimmunology Jack Antel, Gary Birnbaum, Hans-Peter Hartung, Angela Vincent, 2005-10-06 Clinical Neurimmunology is the major reference text in the field providing broad and comprehensive coverage of the interaction between the nervous and immune systems in both normal and diseased states Understanding this interaction is fundamental to developing therapeutic approaches to disease and injury of the nervous system that are currently only marginally amenable to therapy Neuroimmunology is a well recognised and growing specialty world wide both at the basic science and clinical level It is a fast moving field and this is the most up to date text available Chapters are dedicated to the role of the immune system in disorders affecting both the central and peripheral nervous systems including important neurodegenerative diseases such as multiple sclerosis and HIV related neural degeneration which cause life long disability Extensive coverage is given to a whole array of immune directed therapies The book has a strong international team of well respected high profile editors and authors The first edition published to extensive and positive reviews and has established itself as the principal reference source in the field This second edition summarizes recent advances in clinical neuroimmunology in a comprehensive and unbiased way Practitioner's Guide to Clinical Neuropsychology Robert M. Anderson Jr., 1994-06-30 The author has written an easily accessible summary of neuropsychological tests neuropsychiatric disorders and the relationships of test performance to disorder and treatment strategy This ready reference provides neuropsychologists with an understanding of the medical context within which neuropsychological evaluation and psychosocial therapy takes place Victims and Survivors of Nazi Human Experiments Paul Weindling, 2014-12-18 While the coerced human experiments are notorious among all the atrocities under National Socialism they have been marginalised by mainstream historians This book seeks to remedy the marginalisation and to place the experiments in the context of the broad history of National Socialism and the Holocaust Paul Weindling bases this study on the reconstruction of a victim group through individual victims life histories and by weaving the victims experiences collectively together in terms of

different groupings especially gender ethnicity and religion age and nationality. The timing of the experiments where they occurred how many victims there were and who they were is analysed as are hitherto under researched aspects such as Nazi anatomy and executions The experiments are also linked more broadly to major elements in the dynamic and fluid Nazi power structure and the implementation of racial policies. The approach is informed by social history from below exploring both the rationales and motives of perpetrators but assessing these critically in the light of victim narratives Clinical Neuropsychology [oel E. Morgan, Joseph H. Ricker, 2016-02-26 Containing 50 chapters by some of the most prominent clinical neuropsychologists the Textbook of Clinical Neuropsychology sets a new standard in the field in its scope breadth and scholarship Unlike most other books in neuropsychology the Textbook is organized primarily around syndromes disorders and related clinical phenomena Written for the clinician at all levels of training from the beginner to the journeyman the Textbook presents contemporary clinical neuropsychology in a comprehensive volume Chapters are rich with reviews of the literature and clinical case material spanning a range from pediatric to adult and geriatric disorders Chapter authors are among the most respected in their field leaders of American Neuropsychology known for their scholarship and professional leadership Rarely have so many distinguished members of one discipline been in one volume This is essential reading for students of neuropsychology and all others preparing for careers in the field The Molecular and Clinical Pathology of Neurodegenerative Disease Patrick A. Lewis, Jennifer E. Spillane, 2018-11-16 The Molecular and Clinical Pathology of Neurodegenerative Disease brings together in one volume our current understanding of the molecular basis of neurodegeneration in humans targeted at neuroscientists and graduate students in neuroscience and the biomedical and biological sciences Bringing together up to date molecular biology data with clinical evidence this book sheds a light on common molecular mechanisms that underlie many different neurodegenerative diseases and addresses the molecular pathologies in each The combined research and clinical background of the authors provides a unique perspective in relating clinical experiences with the molecular understanding needed to examine these diseases and is a must read for anyone who wants to learn more about neurodegeneration Provides an up to date summary of neurodegeneration at a molecular cellular and tissue level for the most common human disorders Describes the clinical background and underlying molecular processes for Alzheimer's disease Parkinson's Prion Motor Neuron Huntington's and Multiple Sclerosis Highlights the state of the art treatment options for each disorder Details examples of relevant cutting edge experimental systems including genome editing and human pluripotent stem cell derived neuronal models An Overview and Management of Multiple **Chronic Conditions** Sevgi Akarsu, 2020-11-26 Multiple chronic conditions also known as multimorbidity is a special situation frequently encountered by global healthcare professionals especially internists primary care physicians neurologists respiratory pulmonologists pain specialists and oncologists who spend more than three quarters of their time in the treatment of chronic diseases and direct patient care Thus the increasing need for multidisciplinary approaches in the

management of multiple chronic medical problems rather than focusing on individual diseases should be borne in mind by global healthcare professionals public health professionals healthcare providers health policymakers and pharmaceutical industries This book is an up to date source of information for physicians residents and advanced medical students seeking a broader understanding of managing chronic disease clusters **Advances In ME/CFS Research and Clinical Care** Kenneth J. Friedman, Lucinda Bateman, Alison Bested, Zaher Nahle, 2019-11-25 In 2015 the Institute of Medicine USA issued a report critical of the research effort and clinical care for ME CFS Myalgic Encephalomyelitis Chronic Fatigue Syndrome formerly known as Chronic Fatique Syndrome CFS and Chronic Fatique Immune Deficiency Syndrome CFIDS While worldwide investigation into the cause and nature of ME CFS remains disproportionately small and treatment remains symptomatic and controversial modest research continues in all aspects of this disease epidemiology possible infectious origins and other triggers possible involvement of genetics metabolism and microbiome influence of co morbid conditions and more Treatment of patients consists of providing symptomatic relief Guidance in doing so is provided for the clinician School age children require not only treatment but as revealed in a 25 year retrospective study continued engagement with peers and social activity This e book explores the breadth and depth of current ME CFS research and clinical care Its impact and Neuromedical Disorders Igor Grant, Kenneth Adams, 2009-03-10 This is a major revision of a standard reference work for neuropsychologists psychiatrists and neurologists About one half of the book contains entirely new work by new contributors New topics not covered in the previous editions include consideration of common sources of neurocognitive morbidity such as multiple sclerosis diabetes and exposure to heavy metals psychiatric and behavioral disorders associated wtih traumatic brain injury neuropsychology in relation to everyday functioning the effects of cognitive impairment on driving skills and adherence to medical treatments The Third Edition aims to reflect the enormous developments in neuropsychology in terms of research clinical applications and growth of the discipline during the past decade At one time focused on mapping the cognitive and related consequences of brain injuries research in neuropsychology has now expanded to much broader considerations of the effects of systemic disease infection medications and inflammatory processes on neurocognition and emotion The Third Edition attemtps to capture these developments while continuing to adhere to the objective of presenting them in a concise manner in a single volume A Compendium of Neuropsychological Tests Elisabeth Sherman, Jing Tan, Marianne Hrabok, 2023-04-25 The Compendium is an essential guidebook for selecting the right test for specific clinical situations and for helping clinicians make empirically supported test interpretations BL Revised and updated BL Over 85 test reviews of well known neuropsychological tests and scales for adults BL Includes tests of premorbid estimation dementia screening IQ attention executive functioning memory language visuospatial skills sensory function motor skills performance validity and symptom validity BL Covers basic and advanced aspects of neuropsychological

assessment including psychometric principles reliability test validity and performance symptom validity testing Multiple Sclerosis New York Academy of Sciences, 1984 Functional Neuroimaging in Clinical Populations Frank G. Hillary, John DeLuca, 2007-06-06 Bringing together leading experts this volume reviews cutting edge applications of neuroimaging techniques in the study of brain injury brain disease and normal aging It provides up to date descriptions of EEG MEG PET and fMRI discusses salient methodological issues and presents significant clinical advances that have been brought about through the use of these procedures Specific disorders addressed include epilepsy aphasia traumatic brain injury multiple sclerosis alcoholism autism schizophrenia and stroke Analyzing what functional imaging has revealed about the causes and mechanisms of sensory motor and cognitive disturbances associated with these conditions the book also explores implications for improving cognitive rehabilitation More than 60 illustrations including 24 in full color Naturopathic Medicine Leah Hechtman, 2018-09-19 New chapters Diagnostics Case taking and treatment and Nutritional medicine Dietary Rigorously researched with over 10 000 references from the latest scientific papers and historical texts Every section chapter system and condition has been expanded and updated to the latest recommendations Black Book of Neuropsychology Mike R. Schoenberg, James G. Scott, 2011-01-11 From translating the patient's medical records and test results to providing recommendations the neuropsychological evaluation incorporates the science and practice of neuropsychology neurology and psychological sciences The Little Black Book of Neuropsychology brings the practice and study of neuropsychology into concise step by step focus without skimping on scientific quality This one of a kind assessment reference complements standard textbooks by outlining signs symptoms and complaints according to neuropsychological domain such as memory language or executive function with descriptions of possible deficits involved inpatient and outpatient assessment methods and possible etiologies Additional chapters offer a more traditional approach to evaluation discussing specific neurological disorders and diseases in terms of their clinical features neuroanatomical correlates and assessment and treatment considerations Chapters in psychometrics provide for initial understanding of brain behavior interpretation as well as more advanced principals for neuropsychology practice including new diagnostic concepts and analysis of change in performance over time For the trainee beginning clinician or seasoned expert this user friendly presentation incorporating guick reference guides throughout which will add to the practice armentarium of beginning and seasoned clinicians alike Key features of The Black Book of Neuropsychology Concise framework for understanding the neuropsychological referral Symptoms syndromes presented in a handy outline format with dozens of charts and tables Review of basic neurobehavioral examination procedure Attention to professional issues including advances in psychometrics and diagnoses including tables for reliable change for many commonly used tests Special Writing Reports like You Mean It section and guidelines for answering referral questions Includes appendices of practical information including neuropsychological formulary The Little Black Book of Neuropsychology is an indispensable resource for the range of

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Immunology Manuela Berto Pucca, Bryan Fry, Wuelton Monteiro, Steve Peigneur, Marco Aurelio Sartim, 2021-08-26 **Medicus**, 1922

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