JOURNAL OF DRY EYE AND OCULAR SURFACE DISEASE

Conference Review
DOI: 10.22374/jded.v2i1.16

AAO 2018 ANTERIOR SEGMENT SECTION SYMPOSIUM: BIOLOGIC THERAPY: APPLICATIONS IN ANTERIOR SEGMENT DISEASE

Casey L Hogan, OD, FAAO[1], Laura M Periman, MD[2], David Scales, MD[3]

[1]Owner, Advanced Eye Care Professionals, Oak Lawn, IL

[2]Director of DryEye Services and Clinical Research, Evergreen Eye Center, Seattle WA

[3]Founder and Opthalmologist, Specialty Surgery Centre, San Antonio, TX

Corresponding Author: lauraperiman@yahoo.com

Submitted: January 24, 2019. Published: February X, 2019.

The esteemed American Academy of Optometry held their 97th annual meeting, Academy 2018 San Antonio, during the month of November at the Henry B. Gonzalez Convention Center in San Antonio Texas. The goal of the annual meeting that attracts eye-care providers globally, is to maintain and enhance excellence in optometric practice, by both promoting research and the dissemination of knowledge. This year the Anterior Segment Section hosted a novel symposium highlighting biologic therapy, "Biologic Therapy: Applications in Anterior Segment Disease."

Biotherapeutics (or biologics), the fastest-growing sector in the pharmaceutical industry, are transforming medicine. These agents are instrumental in the management of autoimmune disorders and certain cancers, but also have multiple and increasing applications in eye care. The course provided an orientation to this class of medications, a discussion of the most commonly prescribed agents in medicine, and applications in ocular disease with an emphasis on disorders of the anterior segment. Moderated by Walt Whitley, OD, FAAO and Katherine M. Mastrota, OD, FAAO the panel included speakers: Casey Hogan, OD, FAAO, FSLS, Diplomate, American Board of Optometry, Laura M. Periman, MD, and David Scales, MD.

BACKGROUND ON BIOLOGICS AND BIOSIMILARS

Dr. Hogan set the stage by reviewing the basics and background of biologic medicines. The Food and Drug Administration (FDA) defines a biologic as a product that can be a "virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product or analogous product applicable to the prevention, treatment, or cure of a disease or condition of human beings." The FDA definition of biosimilars was also discussed, noting that they are defined by the FDA as biologic products that are "highly similar to an FDA-approved biologic product known as a reference product notwithstanding minor differences in clinically inactive components, and that there can be no clinically meaningful differences between the biologic product and the reference product in terms of safety, purity, and potency." The differences between biologics and conventional drugs were reviewed. Biologics are macromolecules that are more complex in structure, identical copies are not reproducible, and they are highly sensitive to external conditions and environmental changes. Immunogenicity was discussed. Biologics have a higher immunogenic potential, and this is critical for clinicians to consider when prescribing biotherapeutics for their patients.

THE ROLE OF BIOLOGIC THERAPY IN THE MANAGEMENT OF PRIMARY SJÖGREN'S SYNDROME

The Sjögren's Syndrome Foundation (SSF) developed the first U.S. Rheumatology Clinical Practice Guidelines for Sjögren's to aid clinicians in the consistency and care of their patients with systemic disease. Eye-care providers are often the first line of help that undiagnosed Sjögren's patients seek for care. Ocular manifestations of primary Sjögren's (pSS) are well established, and SSF Guidelines also provide guidance for ocular management. Biologic therapies, such as rituximab (RTX) and others, may continue to play a vital role in the management of pSS as more research continues. At the present time, biologic therapies such as RTX should only be considered in patients with serious organ manifestations who fail other conservative treatments. The SSF Rheumatology Clinical Practice Guidelines state RTX may be considered as a therapeutic option in adults with pSS with any or all of the associated systemic manifestations including pulmonary disease, inflammatory arthritis, cryoglobulinemia associated with vasculitis, peripheral neuropathy, and severe parotid swelling. RTX may be considered as a therapeutic option for keratoconjunctivitis sicca in patients with pSS when all other conservative treatments have failed; however, this is considered a weak recommendation per the consensus expert panel. The value of RTX treatment in pSS is predicated on the well-established role of B-cell hyperactivity in the immunopathogenesis of the disease. Inconsistency has been shown between studies in the clinical outcomes of RTX use, with some studies not meeting primary endpoints, and others showing beneficial effects. The positive effects that are seen, no doubt, will lead to better study designs, response predictors, and continued emphasis on understanding the role biologics play in reducing morbidity of disease.

IMMUNOPATHOPHYSIOLOGY AND BIOLOGIC THERAPY: APPLICATIONS IN ANTERIOR SEGMENT DISEASE

Dr. Laura Periman, globally recognized as an expert in immunology and ocular surface disease, reviewed the immunopathology behind anterior segment disease. She described the immune system as an exquisitely complex, dynamic and finely tuned arrangement of checks and balances, detailing the important role of innate and adaptive immunity in ocular surface disease. The immunological basis of dry eye disease and treatment options was classified into four stages: (1) Initiation with proinflammatory cytokine release; (2) amplification with T-cell differentiation and proliferation; (3) reactivation and recruitment of T-cells; and (4) resolution and immunoregulation. Loss of homeostatic and immunoregulatory control ultimately leads to ocular tissue destruction in the patient suffering from pSS and dry eye disease (DED).

SPECIFIC THERAPEUTIC STRATEGIES: HOW BIOLOGICS WORK

In general terms, Dr. Periman reviewed how biologic therapies work by interfering with cytokine function, production, and signal transduction, general suppression and limiting cell proliferation and T-cell activation, and B-cell depletion. Specific therapeutic strategies reviewed were interference with cytokines via TNF (tumour necrosis factor) inhibitors like etanercept or infliximab, limiting T-cell activation with biologic agents including abatacept, or B-cell depletion by biologic agents such as RTX or belimumab.

THE ROLE OF THE IMMUNE SYSTEM AND DED IN PRIMARY SJÖGREN'S SYNDROME

Loss of homeostasis and regulatory control of the immune system is the key driver behind DED in the pSS patient. CD4+ TH1 and TH17 cells are the primary CD4+ T-cells implicated in DED and pSS. CD8+ cells suppress the Th17 response and suppress Th17-induced barrier disruption. CD8+ are decreased in DED. T reg cells may be defective in function or insufficient in quantity in patients with DED and pSS.

The immune response involves a complex interaction between innate and adaptive immunity and the cells unique to each. Lymphocytes (T and B cells) play critical roles in shaping immune responses in both healthy individuals, healthy response to injury and people with pSS. Advancements in the fields of DED and pSS have expanded the immunotherapeutic options for patients with DED and pSS. Eye care

J Dry Eye Ocul Sur Dis 2(1):e1-e3; February 4, 2019

will see more impacts from commonly prescribed immunobiological therapies.

BIOLOGICS IN THE TREATMENT OF NON-INFECTIOUS UVEITIS (NIU)

Dr. David Scales presented on the use of biologics in the treatment of non-infectious uveitis (NIU). Dr. Scales practices at Retina and Uveitis Consultants of Texas in San Antonio, known by his colleagues as a specialist in the management of recalcitrant NIU cases often seen in the autoimmune patient. Biologics were originally considered second or third-line treatment options, but for Dr. Scales and others, they are a first-line choice (following steroid pulse to control active inflammation). There is a need for immune modulating agents in the management of NIU. NIU is a group of ocular inflammatory end-organ diseases resulting from immune-mediated processes and cytokine-mediated disease modulated by the CD20 molecule, IL-17, IL-23, and TNF-a. The immunomodulating biologic drugs considered in the treatment of NIU would include TFN-alpha inhibitors such as adalimumab, infliximab, or abatacept. Anti-CD20 monoclonal antibodies such as RTX are also employed. Traditionally, corticosteroids have been standard therapy for NIU due to their efficacy, rapid onset of action, and they are titratable. However, Dr. Scales emphasized that all clinicians are familiar with the high incidence of local ocular side effects and systemic complications from chronic steroid therapy, which pushes biologic therapies to the first-line option.

A typical course of action utilizing biologic agents in the treatment of NIU would include suppression of inflammation with oral steroid while starting the biologic agent. Most cases would include the initiation of 1 mg/kg initial dose, followed by a 4–6-week taper. Most immunomodulating agents including biologic therapy need 4–6 weeks onset of action.

MANAGEMENT CONSIDERATIONS IN BIOLOGICS AND NIU

Management considerations in biologics and NIU would include testing for tuberculosis and hepatitis (exclude), rule out multiple sclerosis and history of optic neuritis, and if in doubt obtain magnetic resonance imaging of the brain/neurology consult. It is important for clinicians to understand the risk of heart failure development or worsening, and always coordinate care with internal medicine, rheumatology, hematology, and others.

Complications of biologics used in NIU could include the following:

• Rash/allergic reaction
• Immune reactions (lupus like)
• Development of severe infections
• Liver dysfunction
• Blood dyscrasias
• Heart Failure development or worsening
• Activation /reactivation of tuberculosis
• Multiple sclerosis activation/reactivation
• Immunosuppression and increased risk of infection
• Risk of developing malignancy

In conclusion, biologics are an important class of medications to treat pSS and DED, NIU, and other anterior segment diseases. Adalimumab is now FDA approved for the treatment of NIU. Look for new studies to expand treatment modalities, including novel B-cell depletion therapies. Active research is ongoing to evaluate new alternative treatments and to improve study designs with the end goal to improve the quality of life of patients who suffer from these often challenging to treat and recalcitrant diseases.

J Dry Eye Ocul Sur Dis 2(1):e1-e3; February 4, 2019