Myasthenia Gravis Support Group of Central Texas

September 12, 2018

Linda Ann Joslin	Facilitator	Lee Higgins	MGFA Rep	Susan Larkin	Treasurer
Karen Davis	Web Mgr	Rachel Stewart	MGFA Rep	Keith Pflieger	Secretary

Members in Attendance:

Linda Ann Joslin	Larry Joslin	David Renfro	Rachel Higgins	Pauline Estes	Ron Estes
Susan Larkin	Jim Larkin	Richard Armor	Dan McSpadden	Jackie McSpadden	
Joni Kendrick	Kevin Kendrick	Keith Pflieger			

These are notes. Mikaela DeBarba & Danielle Alvarez provided us with the entire briefing which is an attachment to email. This presentation was so informative and educational.

Speaker: Mikaela DeBarba, PharmD: *DRUGS AND MYASTHENIA GRAVIS*

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Shingles Vaccine

- The name of the Shingles Vaccine is Shingrix.
- The vaccine is manufactured in Rixensart Belgium.
- The inactive ingredients each dose of the vaccine contains are sucrose, sodium chloride, potassium phosphate, cholesterol, sodium phosphate, and polysorbate 80.
- The vaccine does not contain preservatives.

Drugs versus Biologics (more expensive than drugs)

- A biologic is manufactured in a living system such as a microorganism, or plant or animal cells. Most biologics are very large, complex molecules or mixtures of molecules. Many biologics are produced using recombinant DNA technology.
- A drug is typically manufactured through chemical synthesis, which means that it is made by combining specific chemical ingredients in an ordered process.
- Drugs generally have well-defined chemical structures, and a finished drug can usually be analyzed to determine all its various components. By contrast it is difficult, and sometimes impossible, to characterize a complex biologic by testing methods available in the laboratory, and some of the components of a finished biologic may be unknown.
- Therefore, for biologics, "the product is the process." Because the finished product cannot be fully characterized in the laboratory, manufacturers must ensure product consistency, quality, and purity by ensuring that the manufacturing process remains substantially the same over time. By contrast, a drug manufacturer can change the manufacturing process extensively and analyze the finished product to establish that it is the same as before the manufacturing change.
- The living systems used to produce biologics can be sensitive to very minor changes in the manufacturing process. Small process differences can significantly affect the nature of the finished biologic and, most importantly, the way it functions in the body. To ensure that a manufacturing process remains the same over time, biologics manufacturers must tightly control the source and nature of starting materials, and consistently employ hundreds of process controls that assure predictable manufacturing outcomes.
- Process controls for biologics are established separately for each unique manufacturing process/product, and are not applicable to a manufacturing process/product created by another manufacturer. These process controls may also be confidential to the original manufacturer. Therefore, it would be difficult or impossible for a second manufacturer to make the "same" biologic without intimate knowledge of and experience with the innovator's process.

Biologics for Myasthenia Gravis tests results

- **Rituxan (rituximab) Phase 2, 3 and 4 Results**
  - Rituximab has been seen in an increasing number of reports claiming success in managing refractory myasthenia gravis (MG). Patients were defined as having refractory MG if they had suboptimal responses to 2+ immunosuppressants, were unable to reduce their dose of corticosteroids without relapse, or required routine treatment with IVIg or PE.
  - Benefits were first described in 2000.
  - More recently, a prospective study of rituximab in 14 patients with refractory MG was published – The Anderson et al study.
    - Primary outcome measure was change in manual muscle test score
    - Secondary measures included change in corticosteroid dose and frequency of IVIg or PE therapy
    - Patients received weekly treatment for 4 weeks and then monthly treatment for 2 months. 11 patients received 1 cycle and 3 received additional cycles.
    - At a follow-up of ~23 months, all patients experienced improvement in clinical status.
    - In the 11 patients treated with 1 cycle:
      - The manual muscle test score fell from 13.1 at baseline to 3.5
      - The average time to peak response was 4.5 months
      - Requirements of prednisone, IVIg and PE fell significantly

        - In the 3 patients treated with additional cycles:
            - Treatment response was meaningful clinically but less robust
    - Robeson et al study
        - Retrospectively reported on durability of rituximab's treatment response in 16 patients with AChR autoantibody-positive MG.
        - Previous study (Zebardast et al) reported 2 retrospective series totaling 20 patients with refractory MG, each of whom responded favorably to rituximab.
        - Current study focuses on long-term effects of rituximab in refractory MG.
            - Refractory: inability to lower immunotherapy does without clinical relapse, poor control with existing immunotherapy, severe adverse effects of that therapy.
        - Patients received 2-4 cycles of rituximab, where each cycle lasted approximately 4 weeks.
            - Number of cycles was based on achievement of a symptom-free state and the ability to taper or withdraw other immunotherapies.
        - After 1st cycle
            - 13 patients were able to discontinue all other forms of immunotherapy at an average of 8 months after last rituximab cycle
            - 9/16 patients had relapse at an average of 36 months after last cycle but all improved with further immunosuppressive therapy. Remaining 7 patients had stable control up to 81 months follow-up.
            - Levels of AChR antibody declined significantly and remained low in patients without relapse
    - Well tolerated by most patients
        - Adverse effects commonly reported relate to infusions
            - Fever
            - Chills
            - Hypotension
            - Dyspnea
        - Development of progressive multifocal leukoencephalopathy remains a potential risk
    - Dosing regimens have varied
    - Mechanism of Action
        - Monoclonal antibody directed against antigen on B-lymphocytes
        - Binds to the antigen on the cell surface and activates destruction of the B cells believed to play a role in MG
    - Not cheap - $30,000 for 1 treatment cycle
        - Other options for refractory MG such as maintenance IVIg or PE provide benefits that last only a few weeks per cycle and require repeated administration for years.
        - 1-2 cycles of rituximab appear to produce persistent improvement lasting for months-years
        - Benefit-cost ratio is favorable.
    - Patients with MG achieve good outcomes with conventional approaches. Effective and safe alternatives are needed for the significant number with refractory disease, whether defined by poor response to therapy, an inability to taper immunotherapies that convey long-term risks, or poor tolerance.
    - Robeson study adds to growing literature that sines a bright light on the use of rituximab in MG. There is a need for repeated treatment cycles and their effect. There is another randomized clinical trial with enrollment completed. If results from Roberson trial are duplicated, rituximab will progress as a go-to intervention for refractory MG.
    - Currently approved for 6 diseases
        - Non-Hodgkin's Lymphoma
        - Chronic Lymphocytic Leukemia
        - Rheumatoid Arthritis
        - Granulomatosis with Polyangitis
        - Microscopic Polyangitis
        - Pemphigus Vulgaris
    - Off-label use for MG (refractory)
        - Patients unresponsive to first-line prednisone and other second-line immunosuppressants suggest rituximab may be useful in management of refractory MG, particularly in patients who are MuSK antibody-positive.
- **Soliris (eculizumab)**
    - Approved for use in the US in treatment of generalized myasthenia gravis in adults who are anti-AChR antibody positive.
        - Approved in the EU for adults with anti-AChR antibody-positive refractory gMG
        - Approved in Japan for patients with anti-AChR antibody-positive gMG whose symptoms are difficult to control with high-dose IVIg therapy or PLEX
    - Binds to C5 complement protein and inhibits the activation of terminal complement, thereby protecting the neuromuscular junction from the destructive effects of antibody-mediated complement activation
    - Significantly improved the ADL, muscle strength and HR-QOL relative to placebo in secondary analyses of the pivotal REGAIN study in patients with refractory disease, but did not achieve statistical significance in the prespecified primary endpoint analysis
    - Treatment benefits maintained for up to at least 52 weeks in an ongoing extension study
    - Generally well tolerated, with most adverse events of mild or moderate severity. The most common adverse event reported with gMG patients is musculoskeletal pain. Infusion reactions are also possible.
    - Through its mechanism of action, it causes patients to have increased susceptibility to infections, especially with encapsulated bacteria. Aspergillus infections have also occurred in immunocompromised and neutropenic patients.
    - Warning for serious meningococcal infections

        - Meningococcal immunization should be administered at least two weeks prior to first dose of eculizumab unless risks of delaying drug outweigh risk of developing meningococcal infection
    - Cost-effectiveness is important to consider. There are currently no pharmacoeconomic analyses of eculizumab in patients with gMG. Studies are needed
    - Available only through a restricted REMS program

Antibiotics to Avoid

Blackbox Warning – Fluoroquinolones

- Drugs in this class may exacerbate the signs of myasthenia gravis and lead to life-threatening weakening of the respiratory muscles. Serious post-marketing events including deaths and the requirement for ventilatory support, have been associated with quinolone use in patients with myasthenia gravis. Because of the risk for serious and potentially permanent side effects, quinolones should only be used for the treatment of uncomplicated urinary tract infection, acute bacterial exacerbation of chronic bronchitis, or acute bacterial sinusitis in cases where alternative treatment options cannot be used.
- Drugs in this class include:
    - Ciprofloxacin
    - Moxifloxacin
    - Levofloxacin
    - Delafloxacin

Strong Warning - Macrolides

- Exacerbation of symptoms of myasthenia gravis and new onset of myasthenic syndrome have been reported in patients.
- Drugs in this class include:
    - Erythromycin
    - Azithromycin
    - Clarithromycin

Whole Biologics study attached to email. Also attached: Generic vs Name Brands

References

- http://www.antibodysociety.org/wordpress/wp-content/uploads/2015/12/Carter-IBC-INN-talk-Dec-2015-FINAL.pdf
- Clinical Pharmacology
- https://jamanetwork.com/journals/jamaneurology/fullarticle/2586253
- http://online.lexi.com.ezproxy.lib.utexas.edu/lco/action/doc/retrieve/docid/patch_f/7634#pha
- https://www.ncbi.nlm.nih.gov/pubmed/29435915
- http://alexion.com/Products/Soliris/Soliris-Generalized-Myasthenia-Gravis

You all might want to read China RX by Sharyl Attkison or watch
https://m.youtube.com/watch?v=KgJydT6lwLA

A note from MGFA. If you are not registered – Please contact MGFA

We need your help with a project that matters to all of us! Currently the MG patient registry has 2550 individuals registered. To increase the value and accuracy of our data, we want to continue to grow. We have attached a chart that gives you a breakdown of how many people in each individual state have registered for the registry.

The MGFA has brochures on the Patient Registry! The brochure explains the goals and purpose of the registry, its confidentiality and privacy policies (not even MGFA has the names or any personal information from the registry) and how to sign-up. Please discuss the patient registry at each of your support group events. We need your help to make this registry more complete and we all know there is strength in numbers.

You are welcome to submit an order for brochures electronically via the attached Literature Order Form or contact national office at MGFA@myasthenia.org 1-800-541-5454. Also please encourage individuals to contact the national office if they would like some brochures to take to their doctor's offices.

Stretching & Stronger upper body for MG'ers

Increases blood flow to your muscles. It can improve flexibility and may decrease risk of injury. Learn more about the benefits of stretching. http://mayocl.in/1RMcGVg

Having a strong upper body is important for posture and everyday activities. Here are some good exercises to help. http://wb.md/29Xqz6T

Support Groups in Texas **------ LET'S GO TEXAS!!!!!!!!!!!!**

Central Texas MG Support Group meets every 2nd Wed. Spicewood Springs Library 8637 Spicewood Springs Rd Austin 78759
Linda Ann & Larry Joslin, Facilitators Started in February 2007 ***www.mg-centraltexas.org***

Alamo MG Support Group meets in San Antonio on the 2nd Health Link Fitness Center, 288 W. Bitters Rd San Antonio 78216
Elroy and Gail Tschirhart, Facilitators Started in February 2007 ***www.mgsouthtexas.org***

Houston MG Support meets in Houston every 2nd Saturday. Trini Mendenhall Community Center, 1414 Wirt Rd. Houston 77055
Meena Outlaw or Sarah Ricks, Facilitators Started January 2017 ***https://mghoustontx.org/***

Northwest TX/DFW Support meets in Dallas Every 2nd Sat contact Facilitator to confirm location
Karon & Jerry Faught, Facilitator ***Facebook: DFW Myasthenia Gravis Support Group***

Southeast Texas MG Support (also servicing Southwest Louisiana) 2nd Thurs in Beaumont - Howell's Furniture Community Rm
Tracey Young, Facilitator Started November ***Facebook Page***

Corpus Christi Texas MG Support Meets 3rd Saturday confirm location Robert Harvey, Facilitator Started January 2017
https://www.facebook.com/Myasthenia-Gravis-Support-Group-of-Corpus-Christi-Texas-630868910390981/?ref=page_internal&gsefr=1

Deep South Texas MG Support Harlingen Karen Mau
San Angelo Texas MG Support Ralph Rumph ***https://www.facebook.com/ sanangelomg/***

Linda Ann Joslin, Facilitator, MG Support Central Texas **www.mg-centraltexas.org**

October 10 Carla at EK Creations – MG specific Ki Gong class

November 14 Round Robin and Final Planning for **The Walk**

November 18 **Walk** **2018 Austin MG Walk**

Register For The 2018 Austin MG Walk

Sunday, November 18, 2018
East Metro Park (Manor, TX) Check-In begins at 9:00 AM