Development of an ambulatory infusion protocol for Abatacept

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ABSTRACT

The identification of the genetic causes of Common Variable Immune Deficiency (CVID) has led to recognition of the need for biological medications to treat the autoimmune manifestations that CVID patients with LRBA and CTLA4 deficiency experience. Immunologists have not traditionally used biological medications as treatment in CVID patients and may not be familiar with the use of them. We present the process and protocol as well as a nursing checklist used by the Division of Rheumatology for the use of Abatacept.

Statement of novelty: The methodology used to develop the order set and nursing checklist may be applied to other biologic medications as they become available.

Introduction

The treatment strategies for patients with rheumatological disorders have changed over the past several years with the advent of biologics and the incorporation of treat to target strategies to improve disease outcomes (Consolaro et al. 2012). The increased use of biologics has created a need to develop streamlined order sets and nursing protocols for infusions. Abatacept is a CTLA4 immunoglobulin fusion protein that inhibits T cell responses by competing for co-stimulatory ligands (Bristol-Myers Squibb 2006) and is used in poly-articular juvenile rheumatoid arthritis (JIA). This drug has been approved for use in JIA patients who have had an inadequate response to disease modifying anti-rheumatic drugs and one other immunosuppressive biologic such as a tumor necrosis factor inhibitor or an anti-interleukin 6 agent (Vital and Emery 2006; Ministry of Health and Long-Term Care Exceptional Access Program (EAP) (2017).

Common Variable Immune Deficiency (CVID) is a heterogeneous primary immunodeficiency characterized by antibody deficiency, infections, autoimmunity, and lymphoproliferation (Resnick et al. 2012). Molecular diagnosis of the genetic causes of CVID have identified that mutations in the LRBA gene (encoding the lipopolysaccharide-responsive and beige-like anchor protein) and CTLA4 (cytotoxic T lymphocyte antigen-4) may cause the clinical syndrome of CVID with significant autoimmunity including: type 1 diabetes, severe interstitial lung disease, gastrointestinal disease, and autoimmune cytopenias (Lo et al. 2015).

Increasingly, there are reports that patients with a CVID phenotype and mutations in LRBA or CTLA4 have significant improvement of their autoimmune symptoms following treatment with Abatacept (Orencia) (Lo et al. 2015). Patients were shown to have improvement in their overall clinical well-being, inflammatory markers, and their CT scans and pulmonary

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function tests showed rapid and dramatic improvement. Patients were also shown to have had minimal infectious or autoimmune complications over 5 to 8 years of treatment (Lo et al. 2015).

We present the development of the Abatacept order set and nursing checklist (Appendix 1) that has been used for biologics in pediatric rheumatology patients and propose that this process for protocol development is one that may be applied to immunodeficient patients with autoimmunity, as biologically medications are added to their treatment regimes.

Protocol development

The infusion protocol was developed as a resource for the medical and nursing teams involved with the out-patient infusion clinic at the Hospital for Sick Children, Toronto, Ontario. The infusion orders are embedded within the protocol and were necessary to develop for the out-patient area since drug ordering, access, and funding are different from the in-patient areas. The out-patient infusion centre sees a variety of patients from different departments and relies on updated and accurate information in order to provide safe care. In terms of safety, consideration to work load and patient monitoring were priorities and needed to be vetted by the healthcare teams involved.

The methods used in the development of this protocol included a review of different established infusion protocols already in place and a review of the product monograph from the drug manufacturer. Extensive vetting within the Division of Rheumatology and a review by the hospital's "forms committee" helped to finalize the protocol. Once the protocol was finalized, staff education programs were developed by partnering with representatives from the Abatacept Patient Support Program to provide in-service education opportunities for nurses, physicians and pharmacists prior to the implementation of the protocol (Appendix 1).

Conclusion

The careful review of established protocols for biologics and partnering with the drug manufacturer to provide protocol specific information contributed to a successful launch of the treatment protocol for Abatacept. This protocol is now the standard of care for use in the outpatient area. This protocol has been adopted for use as well by several community colleagues, hospitals and other departments within the hospital, which allows for patients to receive consistency of treatment in multiple settings. The process used for the development of this protocol may be applied to other biologics as they become increasingly recognized as treatment options for immunodeficient patients.

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Appendix 1

Abatacept (Orencia™) Infusion Protocol

Infuse Abatacept (Orencia™) (_____mg/kg)_____in 100 mL 0.9% Sodium Chloride over 30 minutes. Dose may be rounded up or down to the closest 250 mg to avoid wastage (e.g., 400 mg give 500 mg). **Recommended dose: 10 mg/kg for patients under 75 kg. For patients over 75 kg–100 kg, give 750 mg (3 vials) and for patients over 100 kg give 1 gram (4 vials)**.

Procedure:

Patient must be seen by MD/Practitioner to assess suitability for Orencia™

Patient appropriate for nursing checklist

1. Assess patient for signs of infection, fever, known sensitivities to Orencia™
2. Ensure previous lab results are reviewed by physician or delegate (i.e., practitioner, resident)
3. Notify responsible physician or delegate on service of patient's arrival on the unit and if not suitable for infusion (based on checklist and previous labs)
4. Routine labs with IV start:

Standard Labs: CBC & Differential, ESR, Creatinine, AST, ALT, CRP, Albumin. **Please send CBC & Diff STAT if previous results are unavailable.**

Additional labs: _____

No Labs required

5. **Infusion schedule for the first 3 doses are week 0, 2, 4 and then every 4 weeks.**
6. Measure and record baseline weight, height, Blood Pressure (BP), Heart Rate (HR), Respirations (RR), and Temperature (T); Vital Signs are to be assessed before, during, and after the infusion as well as at the end of the 30 minute Observation Period.

Notify MD if systolic BP is · 120% × baseline or diastolic BP · 120% × baseline; if Temperature is >37.5 °C, if HR is 30 beats/min > baseline; if RR 10/min > baseline

7. **Observe for infusion and adverse reactions:** headaches, hypotension, nausea, fever, dizziness, and allergic response such as urticaria, itching, hives, flu-like symptoms, transient

fevers, gastrointestinal symptoms, skin rash, and anaphylaxis such as bronchospasm, wheezing. **Stop infusion and notify physician immediately if reaction occurs.**

8. **Keep anaphylaxis kit at bedside and emergency equipment available.**

9. **Give one or more of the following in the event of a reaction:**

    ♦ Diphenhydramine (Benadryl®) 1 mg/kg IV/PO **(Max. dose 50 mg)**____mg

    ♦ Acetaminophen (Tylenol®) PO 15 mg/kg _____mg

    ♦ **If previous reaction give:**

    Prednisone 1 mg/kg PO (Max. dose 40 mg)_____mg

    OR

    Hydrocortisone 5 mg/kg/dose/IV _____mg

Abatacept (Orencia™) Infusion Protocol (continued)

Payment:

Cash

Section 16 (Trillium/ASCD/ODSP/Ontario Works) Section 16 Expiry date _____

Private Insurance

Other (specify)_____

Infusion booking date and time: _____

MD Signature: _____

Date & Time: _____

Nursing Checklist:

This form is to be completed prior to the infusion of the following biologics:

infliximab (REMICADE®) abatacept (ORENCIA®)

tocilizumab (ACTEMRA®) adalimumab (HUMIRA®)

Have you/your child had any of the following symptoms in the last week?

Fever Y□ N □ Cough Y□ N □ Runny Nose Y□ N □ Mouth or Lip Sores Y□ N □ Ear Pain Y□ N □ Eye Discharge Y□ N □ Sore Throat Y□ N □ Breathing Problems Y□ N □	Chest Pain Y□ N □ Vomiting Y□ N □ Diarrhea Y□ N □ Frequency/Pain/Burning with Urination Y□ N □ Rash or Unusual Bruising Y□ N □ Any redness, pain or swelling around nails Y□ N □ Other Y□ N □

If YES, additional details:

_____

- Exposure to TB – Does anyone in your home have a cough? Y□ N □
- Prior TB Y□ N □
- Exposure to Chicken Pox Y□ N □
- Is there any possibility that you could be pregnant? Y□ N □
- Are you currently being treated with antibiotics? Y□ N □
- Any recent or upcoming surgical procedures (including eye, dental)? Y□ N □

Type of Surgery and Date:

(details)_____

Rheumatology Directives (Rheumatology to complete and attach to orders):

- Prior bloodwork reviewed. If patient/parent answers “no” to the above questions, the patient can proceed with infusion. If patient/parent answers “yes” to any of the above questions please review with the Rheumatology MD

OR

- Must wait for labs today and review with Rheumatology MD before proceeding with infusion