Alemtuzumab Infusion Experience

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Introduction and Purpose

- Alemtuzumab is a humanized monoclonal antibody that selectively targets CD52 [1] approved for treatment of relapsing Multiple Sclerosis (MS)
- Alemtuzumab 12 mg had superior efficacy compared with subcutaneous interferon beta-1a, as demonstrated in the CARE-MSIand CARE-MS II clinical trials [2,3]
- In the CARE-MS core studies, infusion adverse reactions (IARs) occurred in 90% of patients with alemtuzumab 12 mg infusions; 3% were categorized as serious [2,3]
- Alemtuzumab associated IARs are mainly attributed to cytokine-release syndrome involving target cell lysis and further recruitment of inflammatory cells
- We present the incidence and severity of alemtuzumab-associated IARs in our practice at the Multiple Sclerosis Center of Excellence in Oklahoma City

Methods

We identified 11 patients with multiple sclerosis that received alemtuzumab at our center from February 2015 through December 2015. The patients were all females between 33 and 55 years of age and had an inadequate response to at least 2 disease-modifying therapies.
The infusion protocol included premedication with H1/ H2 antagonists and antipyretics daily 2 days before treatment initiation and each day prior to alemtuzumab infusion. Methylprednisolone was administered intravenously prior to the first 3 infusion days. Symptomatic medication was available as needed during or after infusions. Patients were monitored for IARs during and 2 hours after completion of each alemtuzumab infusion.
All patients underwent the following protocol:

Pre-infusion:
1. Hydroxyzine: 50 mg PO daily starting 2 days prior to infusion
2. Ranitidine: 150 mg PO daily starting 2 days prior to infusion

Infusion :
Pre – medication:
1. Hydroxyzine: 50 mg PO prior to infusion
2. Ranitidine: 150 mg PO prior to infusion
3. Methylprednisolone 1000 mg IV prior to infusion for the first 3 days

Infusion:
1. Alemtuzumab 12 mg IV over 4 hours
2. Vital Signs monitoring hourly

Other
1. Acyclovir 400 mg PO twice daily starting on infusion day 1

Post- infusion:
1. Continue acyclovir 400 mg BID for a minimum of 2 months
2. Use effective contraception measures up to at least 4 months following treatment with alemtuzumab
3. Avoid or adequately heat foods that are potential sources for Listeria (raw foods, unpasteurized milk and cheeses)
4. Obtain blood test and urinalysis monthly for 48 months after the last dose of alemtuzumab
5. Yearly skin survey by dermatology and HPV screening
6. Avoid live viral vaccines
7. Notify clinic if there is appearance of:
   - Skin rash, lesions or bleeding
   - Infections, cough, shortness of breath, wheezing, chest pain or tightness

Results

- All patients completed the 5 days of treatment without interruptions
- Five patients (45%) had no IARs
- IARs observed:
  - Rash was observed in 4 patients
  - Headache in 3 patients
  - Back ache in 2 patients
  - Itching in one patient
  - Transient tight feeling in the chest in one patient
- All IARs were mild and resolved with symptomatic medication prior to discharge
- Infusion rate adjustments occurred in 5 patients

Discussion

Alemtuzumab is an effective alternative for the management of relapsing forms of multiple sclerosis. Adverse events can limit the utilization of medications. In the case of alemtuzumab there are potential adverse events related to the infusion itself in addition to the known increased risk for other autoimmune conditions such as dysthyroidism, immune thrombocytopenic purpura, and glomerulonephritis. IARs have been reported and can be severe in some cases. In our experience, applying a specific protocol, the IARs were mild to moderate and successfully managed with symptomatic medications.
Patient education and close monitoring remain paramount in the management of these patients.

Conclusions

- Alemtuzumab infusions were generally well tolerated.
- The most common IARs were rash, headache, back pain, and itching.
- IARs were effectively managed with symptomatic medications.
- All patients completed the 5 day course of the initial cycle without interruptions.

References

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3. Coles AJ, Twyman CL, Arnold DL, et al. Lancet 2012;380:1829-39

Disclosures

Tania Reyna – speaker for Teva, Biogen, Genzyme, Novarits and Acorda
Gabriel Pardo– consultant/speaker for Biogen, EMD Serono, Genentech, Genzyme, Novartis, and Teva
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Anthony Sharp – advisory board for Novartis and EMD Serono
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