Tolerability of oral cetirizine and dexamethasone vs oral diphenhydramine and IV dexamethasone in patients treated with ocrelizumab.

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Background

Ocrelizumab (OCR) is a humanized monoclonal anti-CD20 antibody approved for treatment of relapsing (RMS) and primary progressive multiple sclerosis (PPMS). Infusion-related reactions (IRRs) are thought to occur from cytokines and chemokines released by lysed B-cells. Typical IRRs include flushing, pruritis, hives, and sore throat, with serious IRRs (hypotension and anaphylaxis) being extremely uncommon. In the pivotal trials of OCR, IRRs ranged from 34.3%-39.9%[1,2].

The FDA OCR label recommends pre-treatment with antihistamines and intravenous (IV) corticosteroids (100mg of methylprednisolone or its equivalent) with an optional antipyretic to reduce the incidence of IRRs. These premedications can cause side effects during the infusion (drowsiness and metallic taste) and 24 hours post-infusion (insomnia, increased appetite, and malaise). In addition, administration of IV corticosteroids (as opposed to oral steroids) can lengthen the patients' treatment and increase the nursing burden and time in the infusion chair.

Premedication with nonsedating antihistamines and oral steroids may have fewer side effects, improve ease of administration, and shorten overall treatment time.

Objectives

We sought to compare two premedication regimens: Oral (PO) diphenhydramine 50mg, IV dexamethasone 20mg, PO famotidine 20mg (D-IV) vs. PO cetirizine 10mg, PO dexamethasone 20mg, PO famotidine 20mg (C-PO) in patients treated with OCR to determine the frequency of drowsiness and treatment-related symptoms (TRSs) during and post infusion.

Methods

We enrolled 50 patients with MS currently receiving OCR 600mg and premedication D-IV without a history of IRRs. Patients received OCR 600mg with premedication D-IV for one cycle, then received OCR 600mg with premedication C-PO at the subsequent cycle. Subjects were given a survey immediately following and 24 hours post-infusion.

They surveys evaluated drowsiness and TRSs. Survey responses were scored as none (0), mild (1), moderate (2), or severe (3). If patients scored on any of the five TRSs questions (itching, sore throat, flushing, rash and runny nose), then they were considered positive for TRSs. Preliminary analysis was qualitative and focused on binary results (presence vs absence).

Results

Table 1: Treatment-Related Symptom (TRS) Subscores

	D-IV	C-PO	D-IV	C-PO
	During Infusion (n=50)	During Infusion (n=45)	Within 24 Hours (n=50)	Within 24 Hours (n=44)
Itching	19	14	7	12
Sore Throat	16	15	14	11
Flushing	8	3	14	2
Rash	2	1	0	6
Runny Nose	8	7	9	16

Figure 1: Treatment-Related Symptoms (TRSs) During and Post Infusion

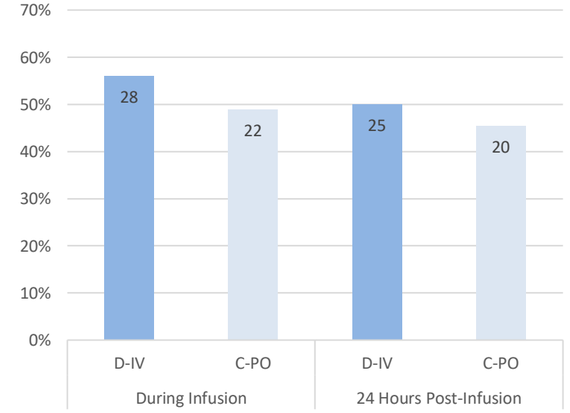
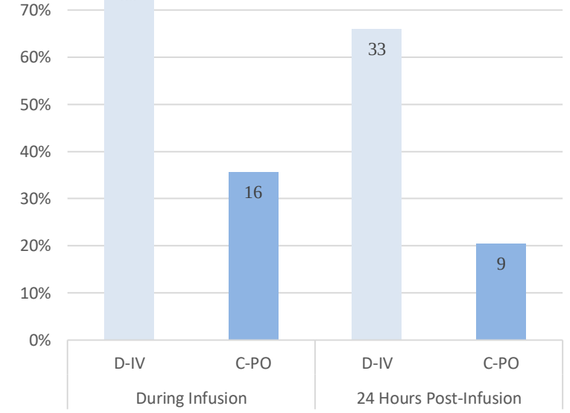
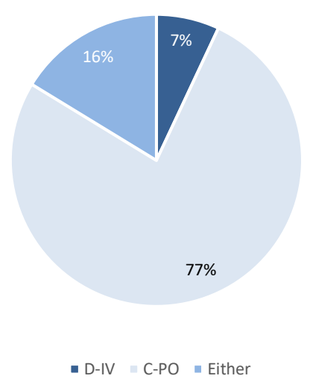


Figure 2: Drowsiness During and Post Infusion



- 68% of patients reported TRSs with D-IV during and/or 24 hours post-infusion compared to 55% with C-PO.
- 20% of patients reported one or more moderate to severe TRSs with both D-IV and C-PO.
- 86% of patients reported being less alert with D-IV compared to 45% with C-PO.
- 48% experienced moderate to severe decreased alertness with D-IV compared to 19% with C-PO.
- One patient was administered a rescue dose of diphenhydramine for TRSs with C-PO.

Figure 3: Pre-Medication Patient Preference (*n*=44)



Summary

- Patients on OCR receiving C-PO had a similar frequency and severity of TRSs, but less sedation than patients receiving D-IV.
- C-PO appears to be a safe and effective premedication regimen for OCR.
- C-PO can ease administration and potentially shorten overall treatment time.

NOTE: Patient-reported TRSs are different than clinically significant IRRs. *Though a majority of patients reported at least one or more moderate or severe TRS, only one patient given C-PO required a rescue dose of diphenhydramine. No patients required slowing or interruption of their infusions.*

References:

1. Hauser SL, Bar-Or A, Comi G et al. Ocrelizumab versus Interferon Beta-1a in Relapsing Multiple Sclerosis. New England Journal zof Medicine, 2017 Jan 19; 376:221-234

2. Montalban X, Hauser SL, Kappos L et al. Ocrelizumab versus Placebo in Primary Progressive Multiple Sclerosis. New England Journal of Medicine, 2017 Jan 19; 376:209-220