Incidence of Infusion-Associated Reactions Decreases With Subsequent Courses of Alemtuzumab: 5-Year Data From the CARE-MS Extension Study

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OBJECTIVE

To report on infusion-associated reactions (IARs) associated with alemtuzumab during 3 years of the ongoing CARE-MS extension study (5-year total follow-up).

INTRODUCTION

Alemtuzumab is a humanized anti-CD52 monoclonal antibody approved for the treatment of RMS in >50 countries. Alemtuzumab demonstrated greater improvements in clinical and MRI efficacy outcomes over SC IFNB-1a, with a consistent safety profile across clinical trials, in patients with active RMS who were either treatment-naive (CARE-MS-I: NCT00305340) or had an inadequate response (11356) to prior therapy at baseline (CARE-MS-II: NCT00304443).1 In an ongoing extension study (NCT00305345), alemtuzumab showed durable efficacy on clinical and MRI outcomes through 2 years, and further recruitment of inflammatory cells2,3 with alemtuzumab 12-mg infusion, and were mostly mild to moderate.4,5 Most frequent adverse events (AEs) with alemtuzumab were IARs.

METHODS

Study Design

CARE-MS I and II were phase 3, randomized, head-to-head, rater-blinded, 2-year studies of alemtuzumab versus SC IFNB-1a (44 mg twice weekly).6–10 CARE-MS I and II consisted of a 3-year treatment phase followed by a 2-year extension.11 Among patients who completed CARE-MS I or II, 742 (91.5%) entered the extension study (CARE-MS extension).12

RESULTS

Patients

A total of 811 patients received alemtuzumab 12 mg in the core study.13 Patients received the initial 2 courses of alemtuzumab in the core study and no retreatment.14

Statistical Analyses

In the extension study, patients continued to receive alemtuzumab every 3 to 4 years, with an ongoing subset of patients receiving IAR prophylaxis.15

IAR Incidence, Severity, and Type During Alemtuzumab Treatment Courses

In the CARE-MS extension, patients received a third course of alemtuzumab in 36.1% (n=292), a fourth course in 20.9% (n=169), and a fifth course in 11.9% (n=98). The incidence of IARs through Years 0–5 was low (3.2%) and stable over time

TABLE 1. IARs Were Mostly Mild to Moderate

<table>
<thead>
<tr>
<th>Course</th>
<th>Grade</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Course 1</td>
<td>1</td>
<td>808 (99.3)</td>
</tr>
<tr>
<td>Course 2</td>
<td>2</td>
<td>808 (99.3)</td>
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<tr>
<td>Course 3</td>
<td>3</td>
<td>808 (99.3)</td>
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<tr>
<td>Course 4</td>
<td>4</td>
<td>808 (99.3)</td>
</tr>
<tr>
<td>Course 5</td>
<td>5</td>
<td>808 (99.3)</td>
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Notes: aAngioedema (n=1) and atrial fibrillation (n=1); bNon-cardiac chest pain and dyspnea in the same patient.

Statistical Analyses

The most common types of IARs were headache, rash, and pyrexia (Table 2).

figure 2

IARs were managed with pretreatment, patient education, appropriate symptomatic medication, monitoring, and adjustment of rate of infusion.

Among patients who received a third course, the incidence of IARs was 62.6% (5.0%) serious in those who received Course 3 during Year 3 (n=43), 71.4% (6.4%) serious in those who received Course 3 during Year 4 (n=44), and 51.5% (5.0%) serious in those who received Course 4 during Year 4 (n=33).

Most IAR types decreased in incidence from Course 1 to Courses 4 and 5.

Serious IARs through Year 5 included pyrexia (n=3 [0.4%]), urticaria (n=3 [0.4%]), anaphylaxis, nausea, chest discomfort, incorrect dose administered, headache, and hypertension (all n=2 [0.2%]).

Adverse Events:

Most AEs were investigator-assessed headache, nausea, pyrexia, and rash (all n=411). The incidence of serious AEs was 4.2% (n=33) during Year 3, 4.4% (n=35) during Year 4, and 4.0% (n=32) during Year 5.

Common AEs in the extension study included headache, nausea, pyrexia, and rash (all n=411).

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REFERENCES


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Figure 1. Management of IARs in the Alemtuzumab Clinical Trials

Figure 2. Incidence of Infusion-Associated Reactions Decreases With Subsequent Courses of Alemtuzumab: 5-Year Data From the CARE-MS Extension Study

Figure 3. Frequency of IARs per Patient Was Highest With Initial Alemtuzumab Exposure

Figure 4. A Minority of Patients Required Infusion Interruption or Adjustment

Figure 5.