Individuals with low endogenous IgG antibodies against C. difficile have been shown to be at increased risk for rCDI.

Advanced age, a characteristic that is a known risk factor for rCDI, did not appear to be a predictor of low eAb-B titer.

The characteristics of participants based on baseline eAb-B titer are shown in Table 1.

The lack of correlation between eAb-A titers and rCDI is consistent with the lack of efficacy of actoxumab in the prevention of rCDI observed in the MODIFY I trial.

There was no evident correlation between low eAb-A titers and the proportion of participants experiencing CDI at any time point (Figure 3A).

The rise in eAb-A and eAb-B titers over time is consistent with a convalescent humoral immune response to toxins A and B following CDI.

There is no clearly defined immunological surrogate of efficacy for rCDI tied to a specific eAb-A or eAb-B level, as the proportion of participants with low eAb-B titers was similar in participants 2605 years of age and participants >65 years of age.

The rise in eAb-A and eAb-B titers over time is consistent with a convalescent humoral immune response to toxins A and B following CDI.

The lack of correlation between eAb-A titers and rCDI is consistent with the lack of efficacy of actoxumab in the prevention of CDI observed in the MODIFY I trial.

Conversely, higher eAb-B titers are associated with lower risk for rCDI, consistent with the efficacy of both toxins. 

Although there was an inverse correlation between low eAb-B titers and rCDI rate, there was a fairly high proportion of participants with high eAb-B titers on Day 1 who experienced rCDI (22.7%). Therefore, eAb-B titers measured by an electrochemiluminescence immunoassay may have marginal utility as a biomarker for rCDI risk and are not likely to improve predictive value over clinical and demographic characteristics such as advanced age, compromised immunity, and rCDI history.

endogenous IgG antibodies against C. difficile toxin B (eAb-B) are associated with protection against C. difficile infection recurrence.

METHODS

MODIFY I and MODIFY II were randomized, double-blind, placebo-controlled, multicenter, trials that were conducted from November 1, 2011, through May 25, 2012 at 322 sites in 30 countries (Figure 1).

Participants were treated with antibacterial drug treatment for CDI for 10 to 14 days, during which time they received a single infusion of bezlotoxumab alone, bezlotoxumab alone (MODIFY I only), bezlotoxumab + actoxumab, or placebo – Only participants randomized to the placebo groups of MODIFY I or MODIFY II were included in this analysis.

Initial clinical cure was defined as receipt of a ≤14-day regimen of antibacterial drug treatment for CDI and no diarrhea during the subsequent 2 consecutive days following completion of antibacterial drug treatment for CDI.

rCDI was defined as a new episode of diarrhea associated with a positive stool test for toxigenic C. difficile and did not improve efficacy.

Our aim was to explore the correlation of eAb-A and eAb-B with rCDI risk by measuring the titers of these antibodies in the participants receiving placebo in the MODIFY trials and to evaluate the utility of assays for these antibodies as potential biomarkers to predict which patients may benefit from monomeric antibody treatment.

The characteristics of participants based on baseline eAb-B titer are shown in Table 1.

Previous rCDI episodes ever

The rise in eAb-A and eAb-B titers over time is consistent with a convalescent humoral immune response to toxins A and B following CDI.

The lack of correlation between eAb-A titers and rCDI is consistent with the lack of efficacy of actoxumab in the prevention of CDI observed in the MODIFY I trial by eAb-A Titer and (B) by eAb-B Titer Measured on Day 1 and at Weeks 4 and 12 (Clinical Cure Population)

Table 1. Demographics and Characteristics by Day 1 eAb-B Titer

<table>
<thead>
<tr>
<th>Titer Level</th>
<th>Low</th>
<th>Medium</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (% of population)</td>
<td>202 (29.9%)</td>
<td>51.5 (48.2%)</td>
<td>40.2 (21.5%)</td>
</tr>
<tr>
<td>Median age (years)</td>
<td>65 (30.7%)</td>
<td>69 (48.6%)</td>
<td>62 (20.7%)</td>
</tr>
<tr>
<td>30 years of age</td>
<td>34 (19.3%)</td>
<td>56 (50.4%)</td>
<td>40 (19.3%)</td>
</tr>
<tr>
<td>≥65 years of age</td>
<td>20 (19.7%)</td>
<td>45 (43.6%)</td>
<td>48 (26.7%)</td>
</tr>
</tbody>
</table>

Limitations

• The assays employed in this analysis measured polyclonal antibodies to C. difficile toxins A and B and did not discriminate between neutralizing antibodies and nonneutralizing antibodies. Therefore, some participants categorized in the medium- or high-titer categories may have had a low proportion of neutralizing antibodies.