Table 1. Primary Efficacy Endpoint.

<table>
<thead>
<tr>
<th></th>
<th>DISESSL I</th>
<th>DISESSL II</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>(36)</td>
<td>(37)</td>
</tr>
<tr>
<td>High dose</td>
<td>56</td>
<td>48</td>
</tr>
<tr>
<td>Low dose</td>
<td>48</td>
<td>4</td>
</tr>
<tr>
<td>Placebo</td>
<td>4</td>
<td>47</td>
</tr>
<tr>
<td>High dose</td>
<td>41</td>
<td>41</td>
</tr>
<tr>
<td>Low dose</td>
<td>40</td>
<td>12</td>
</tr>
<tr>
<td>Placebo</td>
<td>39</td>
<td></td>
</tr>
</tbody>
</table>

Response rate %
Risk Difference
p-value

1 p-value vs placebo (Mantel-Haenszel test)

Acknowledgments: We would like to acknowledge all participants, investigators, and study staff involved in the DISESSL phase III clinical studies. Writing support provided by Michael Wilson, PhD, of Swedish Orphan Biovitrum.


DOI: 10.1136/annrheumdis-2023-eular.7084

Figure 1. Adjusted Mean Change from Baseline in ESSPRI Score. Dashed line represents the MCID. Data analyzed using MMRM. ESSPRI, EULAR Sjögren’s Syndrome Patient Reported Index; LS, least squares; MCID, minimal clinically important difference; SE, standard error.

REFERENCES: NIL.

Acknowledgments: Medical writing support provided by Brendan Lujan, PhD, of Horizon Therapeutics.


DOI: 10.1136/annrheumdis-2023-eular.7074

Keywords: Safety, Randomized control trial, Sjögren syndrome


Methods: This was a randomized, double-blind, placebo-controlled, crossover study of DAZ in adult Sjögren’s subjects with an unacceptable symptom burden but limited systemic organ involvement. Methods: This was a randomized, double-blind, placebo-controlled, crossover study of DAZ in adult Sjögren’s subjects with an unacceptable symptom burden but limited systemic organ involvement. As assessed using EULAR Sjögren’s Syndrome Patient Reported Index, a statistically significant and clinically meaningful improvement in the key subjective symptoms of Sjögren’s relative to PBO as measured by the improvement in ESSPRI and associated responder analysis. DAZ therapy was generally safe and well tolerated. Larger trials of DAZ therapy for Sjögren’s are warranted to further explore its safety profile and confirm its clinical efficacy.

BACKGROUND: Sjögren’s is a systemic autoimmune disease associated with marked morbidity and poor health-related quality of life, generally driven by the cardinal symptoms of the disease: dryness, pain, and fatigue (assessed via EULAR Sjögren’s Syndrome Patient Reported Index (ESSPRI). The population of Sjögren’s patients with unacceptable symptom burden independent of systemic involvement represents a substantial proportion of Sjögren’s patients who have largely been excluded from recent trials despite significant disease burden and overall unacceptable health status.

OBJECTIVES: The objective of this study (NCT04129164) was to evaluate the efficacy and safety of dazodalibep (DAZ), a non-antibody biologic antagonist of CD40L, in adult Sjögren’s subjects with an unacceptable symptom burden but limited systemic organ involvement.

RESULTS: A total of 109 subjects were randomized and received ≥1 dose of study medication (DAZ, N=54; PBO, N=55). The mean (standard deviation) age of subjects was 49.9 (12.1) years and most were female (94.5%). The change from baseline to Day 169 in ESSPRI (LS mean ± SE) was −1.80 ± 0.23 in the DAZ group compared to −0.53 ± 0.23 in the PBO group, a difference of −1.27 ± 0.33 (p = 0.0002). The change from baseline to Day 169 in each of the three domains of ESSPRI was significantly greater in the DAZ group compared to PBO (dryness: p = 0.0066; fatigue: p = 0.0022; pain: p = 0.0010). At Day 169, a significantly larger proportion of DAZ-treated subjects achieved a ≥1 point or ≥15% reduction in ESSPRI relative to PBO (66.7% vs 32.7%; p = 0.008). The improvement from baseline to day 169 in the Functional Assessment of Chronic Illness Therapy-Fatigue score (LS mean ± SE) was significantly greater in the DAZ group (8.1 ± 1.4) relative to PBO (2.8 ± 1.4; p = 0.0095). Greater numerical improvement in DAZ-treated subjects was observed for the Ocular Surface Disease Index (−14.0 ± 3.0 vs −8.5 ± 2.9; p = 0.1936) and Patient’s Global Impression of Severity (−0.6 ± 0.1 vs −0.4 ± 0.1; p = 0.1781) at Day 169 relative to PBO. Through Day 169, a total of 75 subjects reported an adverse event (AE; DAZ: 37 [66.5%]; PBO: 38 [69.1%]) and the majority were mild/moderate in severity. The most frequently reported AEs occurring in ≥5% of DAZ-treated subjects were COVID-19, nasopharyngitis, anemia, and diarrhea. There were three serious AEs in the DAZ group (pneumonia influenza, post-acute COVID-19 syndrome, and gammopathy) and one in the PBO group (neutropenia). All serious AEs were deemed by investigators to be unrelated to study medication. One subject in the DAZ group discontinued the study due to an AE compared to two subjects in the PBO group.

Conclusion: In this study of Sjögren’s subjects with an unacceptable symptom burden but limited systemic organ involvement, the primary endpoint was achieved. DAZ-treated subjects experienced a statistically significant and clinically meaningful improvement in the key subjective symptoms of Sjögren’s relative to PBO as measured by the improvement in ESSPRI and associated responder analysis. DAZ therapy was generally safe and well tolerated. Larger trials of DAZ therapy for Sjögren’s are warranted to further explore its safety profile and confirm its clinical efficacy.

REFERENCES: NIL.

Acknowledgments: Medical writing support provided by Brendan Lujan, PhD, of Horizon Therapeutics.


DOI: 10.1136/annrheumdis-2023-eular.7074

Keywords: Safety, Randomized control trial, Sjögren syndrome


Methods: This was a randomized, double-blind, placebo-controlled, crossover study of DAZ in adult Sjögren’s subjects with an unacceptable symptom burden but limited systemic organ involvement, as defined by having an ESSPRI score ≥5 and EULAR Sjögren’s Syndrome Disease Activity Index (ESSDAI) score <5. Eligible subjects were randomized 1:1 to receive intravenous DAZ 1500 mg or placebo (PBO) Q2W x 3 doses, then Q4W x 4 additional doses. Starting on Day 169, subjects initially ran- domized to DAZ received PBO Q4W x 5 doses and subjects randomized to PBO received DAZ Q4W x 5 doses and were then followed for 12 weeks. The primary end- point was the change from baseline in ESSPRI at Day 169. Safety was also evaluated.

RESULTS: A total of 109 subjects were randomized and received ≥1 dose of study med- ication (DAZ, N=54; PBO, N=55). The mean (standard deviation) age of subjects was