Study Endpoints

- Primary efficacy endpoint: At Week 52, the proportion of patients achieving sustained complete remission (CR) without experiencing treatment failure
  - Sustained CR was defined as Pemphigus Disease Area Index (PDAI) activity score of 0 and mg/day prednisone or equivalent for at least 16 consecutive weeks (i.e., sustained CR predosine >16 weeks), during the 52-week treatment period

- Secondary efficacy endpoints (ranked):
  - Cumulative oral CS dose (prednison equivalent) or equivalent over the treatment period
  - Total number of disease flares during the treatment period
  - Time to sustained CR
  - Time to disease flare
  - Change in health-related quality of life, as measured by the Dermatology Life Quality Index (DLQI) score, from baseline to Week 52

Primary Efficacy Endpoint at Week 52

- Rituximab was superior to MMF, in combination with a tapering course of oral prednisolone (or equivalent):
  - At Week 52, a significantly higher proportion of patients in the rituximab arm achieved sustained CR >16 weeks than in the MMF arm (Figure 3)

Secondary Efficacy Endpoints

Corticosteroid Exposure

- Patients in the rituximab arm had a significantly lower cumulative oral CS dose prednison or equivalents equivalent over the 52-week treatment than in the MMF arm
  - The median (min, max) cumulative dose was 2775 mg (450, 22180) in the rituximab arm compared to 4045 mg (800, 19035) in the MMF arm (P = 0.0005)

Disease Flare

- Total number of disease flares: significantly fewer number of flares occurred in patients treated with rituximab compared to MMF (8 vs. 44, P = 0.0001) (Figure 4)
- Number of patients with disease flare: fewer rituximab-treated patients experienced ≥1 disease flare, 5 rituximab patients (8.1%) vs. 26 MMF patients (41.3%) (P < 0.0001)
- The likelyhood of achieving sustained CR on rituximab was 5 times greater than on MMF (hazard ratio [HR] = 4.83 [95% CI, 1.97 to 11.81], P = 0.0003)
- 5 patients (8.1%) experienced ≥1 disease flare, 26 patients (41.3%) experienced ≥1 disease flare
- The median time to disease flare was not estimable in either arm
- Patients treated with rituximab experienced ≥1 disease flare in 5 patients (8.1%), while patients treated with MMF experienced ≥1 disease flare in 26 patients (41.3%)
- The most common AEs in ≥ 10% of patients treated with rituximab were diarrhea (10 patients, 14.7%), and nasopharyngitis (9 patients, 11.8%)
- The most common AEs in ≥ 10% of patients treated with MMF were, in patient each, pneumonia and influenza (same patient), herpes zoster, urinary retention, and chronic obstructive pulmonary disease and skin ulcer

Safety

Table 2. Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>Rituximab (N = 62)</th>
<th>MMF (N = 63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths, n (%)</td>
<td>0 (0)</td>
<td>1 (1.5)†</td>
</tr>
<tr>
<td>Patients with SAEs, n (%)</td>
<td>15 (24.2)</td>
<td>10 (14.7)</td>
</tr>
<tr>
<td>Patients with SAEs related to the study drug, n (%)</td>
<td>6 (9.7)</td>
<td>5 (7.4)</td>
</tr>
<tr>
<td>Patients with serious infections, n (%)</td>
<td>6 (9.7)</td>
<td>4 (5.9)</td>
</tr>
<tr>
<td>Total number of serious infections</td>
<td>2 (3.2)</td>
<td>5 (7.4)</td>
</tr>
<tr>
<td>Total number of serious infections related to study drug, n (%)</td>
<td>2 (3.2)</td>
<td>5 (7.4)</td>
</tr>
<tr>
<td>Patients with opportunistic infections, n (%)</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Patients with Grade 3 or higher CS-related AEs, n (%)</td>
<td>1 (1.6)</td>
<td>2 (2.9)</td>
</tr>
</tbody>
</table>

*Newly diagnosed = diagnosis of PV of < 6 months or no prior treatments for PV; established disease = PV for ≥6 months and treated prior therapies for PV before study entry.
**SAEs related as assessed by the investigator.
¶IRRs reported from placebo infusion.

REFERENCES


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AUTHOR DISCLOSURES

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2. Pascal Joly, MD, PhD was consultant for Genentech, Roche, and Merck Sharp & Dohme. He also received research support from the International Pemphigus and Pemphigoid Foundation.