potential explanations are incomplete B-cell depletion in relation to substantial surges in B-cell activating factor (BAFF). To improve B-cell targeting strategies, we conducted the first study in SLE patients aimed at investigating immunological effects and feasibility of combining rituximab (anti-CD20) and belimumab (anti-BAFF).

Methods Reported is the long-term follow-up of a phase 2 proof-of-concept study in 15 patients with SLE including 12 (80%) with lupus nephritis (LN).

Results In 10/15 (67%) patients a clinical response was observed by achievement of lupus low disease activity state (LLDAS) of which 8 (53%) continued treatment (belimumab +≤7.5 mg prednisolone) during the complete 2 years of follow-up. Five patients (33%) were referred to as ‘non-responders’ due to persistent LN, major flare or repeated minor flare. Out of 12 LN patients 9 (75%) showed a renal response including 8 (67%) complete renal responders. All anti-dsDNA+ patients converted to negative and both anti-C1q and extractable nuclear antigen autoantibodies (ENAs) showed significant reductions. CD19+B-cells showed a median decrease from baseline of 97% at 24 weeks, with a persistent reduction of 84% up to 104 weeks. When comparing responders to non-responders, CD20+B-cells were depleted significantly less in non-responders and double negative (DN) B-cells repopulated significantly earlier.

Conclusion Combined B-cell targeted therapy with rituximab (RTX) and belimumab (BLM) prevented full B-cell repopulation including DN B-cells, with concomitant specific reduction of SLE-relevant autoantibodies. The observed clinical and immunological benefits in a therapy-refractory SLE population prompt further studies on RTX+BLM.

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Abstract P128

Efficacy of Intravenous Belimumab in Children with Systemic Lupus Erythematosus with Markers of High Disease Activity: Across-Trial Comparison with Adult Belimumab Studies

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Background Belimumab is approved as add-on therapy for patients ≥5 years with active, autoantibody-positive systemic lupus erythematosus (SLE).1 The PLUTO trial (NCT01649765) demonstrated safety and efficacy of belimumab in children with SLE as generally consistent with adult studies. The current analysis assessed the efficacy of belimumab 10 mg/kg given intravenously (IV) to patient subgroups with baseline markers of high disease activity in PLUTO versus pooled BLISS-52 (NCT00424476) and BLISS-76 (NCT00410384) SLE trials.

Methods Patients 5–17 years (PLUTO) and ≥18 years (BLISS-52 and BLISS-76) with active SLE were randomised to IV belimumab 10 mg/kg or placebo, plus standard of care (SoC) (PLUTO);2 and IV belimumab 10 mg/kg, or
Results In PLUTO, belimumab demonstrated higher SRI4 response versus placebo; this response was similar for patients with baseline SELENA-SLEDAI scores of ≥10 and ≤9, and for those receiving steroids, but greater in those with scores ≥13, low anti-dsDNA, or normal/high C3/C4 (Table 1). Subgroup analyses from the BLISS adult studies demonstrated similar findings with the exception of patients with high anti-dsDNA or low C3/C4 (Table 1).

Table 1

<table>
<thead>
<tr>
<th>Subgroup Analysis</th>
<th>Response, n (%)</th>
<th>OR (95% CI)</th>
<th>P (Fisher's exact test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline normal/high C3</td>
<td>28 (33)</td>
<td>0.91 (0.47, 1.76)</td>
<td>0.82 (0.42, 1.60)</td>
</tr>
<tr>
<td>Baseline low C4</td>
<td>5 (8)</td>
<td>1.31 (0.27, 6.52)</td>
<td>0.72 (0.18, 2.78)</td>
</tr>
<tr>
<td>Baseline normal/high C4</td>
<td>25 (32)</td>
<td>1.19 (0.82, 1.72)</td>
<td>0.38 (0.14, 1.02)</td>
</tr>
<tr>
<td>Baseline steroids*</td>
<td>No</td>
<td>2 (3)</td>
<td>0.91 (0.47, 1.76)</td>
</tr>
</tbody>
</table>

*Post hoc analyses; †Low C3 defined as <90 mg/dL; ‡Low C4 defined as <10 mg/dL; BEL, belimumab; C, complement; CI, confidence interval; OR, odds ratio; PBO, placebo

Disclosures DLB, MO, AH, BJ, DR and HQ are employees of GSK. BJ and DLB hold stocks and shares in GSK; MO, AH, DR and HQ hold shares in GSK.

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REFERENCES