with LN and SLE; despite higher frequency of HZ vs placebo, anifrolumab was well tolerated.

**REFERENCES:**

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**Table 1. Summary of Clinical Efficacy Endpoints**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Anifrolumab</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Combined</strong></td>
<td><strong>Basic</strong></td>
<td><strong>Intensified</strong></td>
</tr>
<tr>
<td><strong>24-hour urine protein–creatinine ratio improvement</strong></td>
<td><strong>W52</strong></td>
<td><strong>N</strong></td>
</tr>
<tr>
<td>CRR rate W52</td>
<td>n/N (%)</td>
<td>n/N (%)</td>
</tr>
<tr>
<td><strong>CRR</strong></td>
<td>0.95 CI</td>
<td>14.34</td>
</tr>
<tr>
<td>W52</td>
<td>−0.08</td>
<td>−14.83</td>
</tr>
<tr>
<td><strong>Glucocorticoid</strong></td>
<td>n/N (%)</td>
<td>n/N (%)</td>
</tr>
<tr>
<td>W24–52</td>
<td>12.94</td>
<td>22.22</td>
</tr>
</tbody>
</table>

**Figure.** Kaplan-Meier plot of time to first CRR vs 24-hour UPCR ≥0.5 mg/mg criteria sustained to Week 52.

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**POS0691**

**EFFECTS OF ANIFROLUMAB ON RENAL DISEASE IN PATIENTS WITH SLE**

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**POS0690**

**RANDOMIZED, CONTROLLED, PHASE 2 TRIAL OF TYPE 1 IFN INHIBITOR ANIFROLUMAB IN PATIENTS WITH ACTIVE PROLIFERATIVE LUPUS NEPHRITIS**

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**Background:** Anifrolumab, a type I interferon receptor antibody, has shown efficacy in patients with systemic lupus erythematosus (SLE), >30% of whom develop lupus nephritis (LN).

**Objectives:** To evaluate the efficacy and safety of anifrolumab vs placebo alongside standard therapy in patients with active proliferative LN.

**Methods:** TULIP-LN (NCT02547922) was a phase 2 double-blind trial in adult patients with active, biopsy-proven LN and 24-hour (h) urine protein–creatinine ratio (UPCR) >1 mg/mg. Patients were randomized (1:1:1) to anifrolumab basic regimen (BR, 300 mg, based on SLE dosing), anifrolumab intensified regimen (IR, 900 mg for 3 doses, 300 mg thereafter), or placebo, intravenously every 4 weeks alongside standard therapy of oral glucocorticoids (GCs; mandatory taper ≤7.5 mg/day by Week [W] 12, ≤7.5 mg/day by W 24) and mycophenolate mofetil (target 2 g/day by Week W8). The primary endpoint was the relative difference in change from baseline to W52 in 24-h UPCR, measured with a geometric mean ratio (GMR) of the change in the combined anifrolumab vs placebo groups (GMR <1 favors anifrolumab). The key secondary endpoint was complete renal response (CRR) at W52 (24-h UPCR ≤0.7 mg/mg, estimated glomerular filtration rate ≥60 mL/min/1.73 m² or no decrease ≥20%, no treatment discontinuation, and no restricted medication use). Sustained GC taper (≤7.5 mg/day, W24–52) was an exploratory endpoint. CRR IR (CRR with UPCR ≤0.5 mg/mg) and time to CRR IR sustained to W52 were analyzed post hoc. Responder rates were calculated with a stratified Cochran–Mantel–Haenszel approach.

**Results:** Patients received anifrolumab BR (n=45) or IR (n=51) or placebo (n=49); demographics and baseline disease characteristics were generally balanced between groups. No difference in change from baseline to W52 in 24-h UPCR was observed for combined anifrolumab vs placebo groups (Table 1). Anifrolumab clearance was higher in patients with LN vs SLE; proteinuria in LN elicited suboptimal anifrolumab serum concentrations (early trough from BR 50%–60% lower than in SLE trials), so anifrolumab IR results are presented. CRR rate at W52 was numerically higher with the IR vs placebo (45.5% vs 31.1%) (Table 1). Time to sustained CRR IR (Figure 1), rate of CRR IR at W52, and rate of sustained GC taper ≤7.5 mg/day (Table 1) were improved with the IR vs placebo. Most adverse events were nonserious, mild, or moderate and did not lead to discontinuation; rates were similar in the combined anifrolumab vs placebo groups (89.8% vs 93.8%). In the combined anifrolumab vs placebo groups, there was a higher incidence of herpes zoster (HZ, 16.7% vs 8.2%); most HZ cases were of mild to moderate intensity, cutaneous, and resolved with treatment.

**Conclusion:** Although the primary endpoint was not met, the anifrolumab IR was associated with numeric improvements across clinical endpoints vs placebo; thus, intensified dosing may be required to reach clinical efficacy in LN vs SLE without active renal disease. Anifrolumab had a similar safety profile in patients

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Background: The type I interferon (IFN) receptor antibody anifrolumab has shown efficacy in patients with systemic lupus erythematosus (SLE) in the phase 3 TULIP-1 and TULIP-2 trials. Type I IFN dysregulation is associated with lupus nephritis (LN) pathogenesis.3

Methods: Objectives: 3 TULIP-1 and TULIP-2 trials.1,2 Type I IFN dysregulation is associated with lupus shown efficacy in patients with systemic lupus erythematosus (SLE) in the phase Background:

Scientific Abstracts

Table 1. Renal Endpoints in TULIP-1 and TULIP-2

Endpoint (baseline to Week 52) Placebo Anifrolumab 300 mg

UPCR AUCA

n 54 45
LS mean (SE) 271.8 (54.8) 217.7 (60.0)
LS mean difference (SE), 95% CI −54.1 (54.3), −161.9, 53.6

 Improvement from >0.5 to <0.5 mg/mg UPCR2

n 33 24
Patients with improvement (%) 36.3 41.2
Difference, % (SE), 95% CI 4.9 (13.3), −21.1, 30.9
Glucocorticoid AUC

n 54 45
LS mean (SE) 3524.5 (339.0) 3314.2 (365.2)
LS mean difference (SE), 95% CI −210.3 (332.6), −870.7, 450.1

Change in C3/C4 (%)3

C3 n 31 21
Mean (SE) 20.3 (6.2) 26.6 (5.0)
C4 n 19 14
Mean (SE) 29.1 (12.0) 38.7 (13.8)

AUC, area under the curve; CI, confidence interval; LS, least squares; UPCR, urine protein–creatinine ratio; SE, standard error, number satisfying baseline inclusion criteria for subgroup;4Patients with baseline renal involvement; analysis of covariance.5Stratified Cochran–Mantel–Haenszel.6Patients with renal involvement and abnormal C3/C4 at baseline.

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POS0692

JANIALUMAB (VAY736) SAFETY AND EFFICACY IN PATIENTS WITH SJOGEREN’S SYNDROME; 52 WEEK RESULTS FROM A RANDOMISED, PLACEBO-CONTROLLED, PHASE 2B DOSE-RANGING TRIAL


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Background: Sjogren’s syndrome (SS) is an autoimmune disease affecting excretory glands and characterised by B-cell hyperactivity. Janialumab (VAY736) is a human monoclonal antibody to B-cell activating factor receptor, engineered for direct ADCC-mediated B-cell depletion. A Phase 2b study evaluated the dose-response of VAY736 vs placebo (PBO) in EULAR SS Disease Activity Index (ESSDAI) change from baseline (CHB) and other secondary endpoints.

Objectives: Primary results at Week (Wk) 24 were reported previously1. Here we report 52 Wk safety and efficacy from extended blinded treatment period 2 (TP2).

Methods: 190 patients (pts) were randomised equally to receive s.c. doses of VAY736 (5, 50, 300 mg) or PBO every 4 Wks (q4w). Eligible pts fulfilled American European Consensus Group (AECG) criteria, were anti-Ro/SSA+, had ESSDAI ≥6 and EULAR SS Patient Reported Index (ESSPRI) ≥5. At Wk 24, after completion of the first blinded TP (TP1), PBO-treated pts were switched to VAY736 150 mg, and pts on 300 mg were re-randomised to continue 300 mg or PBO for 28 Wks in TP2. Pts were followed post-treatment for ≥20 Wks. Safety was assessed for all periods. Due to lack of PBO-control in TP2, descriptive efficacy analysis was performed for ESSDAI, ESSPRI, Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F), Physician’s (PhGA) and Patient’s Global Assessments (PaGA), SF-36, and SS symptom diary (SSSD).

Results: Overall, there was no dose dependency of treatment emergent adverse events (TEAEs) except for injection site reactions, which were mostly mild to moderate in severity. Lymphopenia and neutropenia were mostly grade (G1) and G2, no G4. Most common TEAEs were infections and infestations in exposure-adjusted analysis of incidence rates. Nasopharyngitis and upper