such as autoantibody-related nephritides. ALPN-303 is an Fc fusion protein of a variant, engineered TACI domain which mediates significantly more potent inhibitory activity than WT TACI-Fc or BAFF- or APRIL-specific monoclonal antibodies, with enhanced pharmacokinetic (PK) and immunomodulatory properties versus WT TACI-Fc in preclinical studies. ALPN-303 may therefore significantly improve clinical outcomes in SLE and other B-cell-related diseases.

**Purpose**
To evaluate the safety, tolerability, PK, and pharmacodynamics (PD) of ALPN-303 in adult healthy volunteers (HV).

**Methods**
In this first-in-human study (NCT05034484), adult HVs are enrolled in single ascending dose cohorts of intravenously (IV) or subcutaneously (SC) administered ALPN-303. For each IV cohort, the first 2 subjects are randomized 1:1 to receive ALPN-303 or placebo, followed by the remaining 4 subjects randomized 3:1 to receive ALPN-303 or placebo. For each SC cohort, HVs are randomized 2:1 to receive a single SC dose of ALPN-303 or placebo. For each SC cohort, HVs are randomized 4:2 to receive a single SC dose of ALPN-303 or placebo. All subjects are followed to assess safety and PK of ALPN-303, to measure levels of circulating immunoglobulins (Ig), and to characterize leukocyte populations in peripheral blood by flow cytometry.

**Results**
ALPN-303 has been well tolerated in all IV and SC cohorts evaluated to date, and overall exhibits dose-related PK and expected PD effects on circulating Ig levels, including reductions in serum Ig (Figure 1). To date there have been no treatment-related serious adverse events, no infusion-related reactions, and no adverse trends in safety laboratory parameters reported in any of the dosed cohorts. The remainder of dose escalation is expected to be completed by the time of the meeting; the presentation will include all available safety, PK, and PD (circulating Ig and B-cell population) data.

**Conclusion**
In this first-in-human study, ALPN-303 to date demonstrates acceptable preliminary safety and tolerability, and exhibits expected PD effects on circulating Ig. These findings support future clinical development of ALPN-303 in patients with SLE and/or other B-cell- and/or autoantibody-related diseases.

**REFERENCES**
clinically meaningful (Figure 1), tapering of CS therapy to reduce placebo responses, and ongoing review by a panel of lupus trial experts to ensure accuracy and consistency of patient data.

Conclusions Afimetoran is a novel, oral, potent, selective inhibitor of TLR 7/8. Using insights from past lupus clinical trial designs, a phase 2b clinical trial design was optimized to test whether inhibition of TLR7/8 is beneficial for the treatment of SLE. This study is currently enrolling patients globally (EudraCT 2019–004021-25; NCT04895696).

### DYNAMICAL TRAJECTORY OF GLUCOCORTICOID TAPERING AND DISCONTINUATION IN REAL-WORLD PATIENTS WITH NEWLY DIAGNOSED SYSTEMIC LUPUS ERYTHEMATOSUS: THE GULP STUDY

**P0.6.133**

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**Purpose** Glucocorticoids (GCs) are recommended in patients with systemic lupus erythematosus (SLE), in combination with hydroxychloroquine (HCQ) or immunosuppressant, but should be tapered or discontinued in the medium to long-term to minimize detrimental effects. A sub-analysis of the multicenter Early Lupus inception cohort was performed to investigate the real-world trajectory of Glucocorticoids (GCs) Use in newly diagnosed SLE Patients (the GULP study) and the associated outcomes.

**Methods** The GULP study enrolled patients starting prednisone (PDN) ≥5mg/day and concomitant HCQ or immunosuppressant within 12 months of SLE classification. SLE core set variables were recorded at baseline and then every six months for 2 years, including changes in PDN dose, ECLAM and BILAG active domains. The SLICC/ACR Damage Index (SDI) and a 0–10 global health visual analog scale (GH-VAS) were also recorded. Regression models analyzed the damage accrual and GH-VAS in different GCs tapering and discontinuation trajectories.

**Results** Overall, 127 SLE patients with a mean age of 36.7 (±13.4) years and a median disease duration of 6.1 (1.3 - 11.5) months were included. At baseline 98 (77.2%) patients received HCQ, 81 (63.8%) received conventional immunosuppressants, and 57 (44.9%) received a combination of them. The median daily dose of PDN at baseline was 12.5 (6.3–25.0) mg/day and significantly decreased to 5.4 (4.3–9.4) mg/day at 12-month and 4.9 (2.5–6.6) mg/day at 24-month (p<0.001). At the end of follow-up, 73 (57.5%) successfully tapered PDN doses below 5 mg/day, and 17 (13.4%) discontinued GCs within a 2-year follow-up (Figure 1). Overall, 99 (78%) patients tapered the PDN dose below 5 mg/day: 34 (26.8%) within 6 months, 35 (27.6%) within 12 months, 22 (17.3%) within 18 months and 8 (6.3%) within 24 months of follow-up; 42.4% of patients who tapered PDN and 46.4% of those who never tapered PDN below 5mg/day required to increase the PDN dose within the end of the 2-year follow-up. A higher daily dose of PDN resulted in a greater probability (OR 1.4 per mg/day; 95%CI 1.3–1.5; p<0.001) of GCs tapering regardless of disease activity, whereas ECLAM (OR 1.6; 95%CI 1.2–2.3; p=0.004) and BILAG (OR 1.9; 95%CI 1.3–3.0; p=0.004) were independently associated with the risk of increasing GCs dose. In patients taking PDN <5mg/day, ECLAM (OR 1.5; 95%CI 1.3–1.7; p<0.001) and BILAG (OR 2.3; p=0.004) were independently associated with the risk of tapering GCs regardless of disease activity, whereas ECLAM (OR 1.6; 95%CI 1.2–2.3; p=0.004) and BILAG (OR 1.9; 95%CI 1.3–3.0; p=0.004) were independently associated with the risk of increasing GCs dose. In patients taking PDN <5mg/day, sustained GCs were 17 (13.4%) patients.

**Abstract P0.6.133 Figure 1** Heatmap of the mean daily prednisone dose interval during the 24 months follow-up since diagnosis.