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We confirmed an increased surface expression of Sialic acid-bind-
ing Ig-like lectin-1 (Siglec-1) on CD14+ monocytes and further showed increased Siglec-1 expression also on CD14+CD16+ non-classical monocytes and con-

ventional dendritic cells in anti-Ro/La-exposed compared to healthy control neo-
nates. We did not observe any major differences in general populations such as

CD4+, CD8+ or gamma delta T cells. However, we found a decreased frequency of regulatory CD4+ FoxP3+ T cells in the autoantibody-exposed newborns. In line with this, we observed an increase in conventional CD4+ FoxP3- T cells and that these cells have less of a naïve phenotype with significantly lower frequency of CD62L- and more CD69-expressing cells in the CD4+ FoxP3- population. Interestingly, Ro/La-exposed newborns also had less CD5-expressing CD19+ B cells compared to healthy newborns, while the frequency of CD19+CD5- B cells was not affected. Further, we noted a decreased surface expression of CD19 and Siglec-1 expression also on CD14-CD16+ non-classical monocytes and con-

Background: Together, our data provide valuable insight into the effects of Ro/La autoantibody exposure in utero on immune activation of both innate and adaptive immune cell populations in exposed fetuses, enhancing our understanding of the immunological basis of neonatal lupus.

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**Disclosure of Interests:** None Declared.

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**POS1432 CAR-TREGS FOR SYSTEMIC LUPUS ERYTHEMATOSUS**

**Keywords:** Systemic lupus erythematosus, Adaptive immunity, Animal models

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**Objectives:** We aimed at developing a CAR-Treg based product to be employed in SLE.

**Methods:** We isolated Tregs from Healthy Donors Peripheral Blood Mononuclear Cells (PBMCs) and expanded them with IL-2 and rapamycin. We transduced Tregs with a Lentiviral Vector encoding for a second-generation anti-CD19 CAR, considering the relevant role of autoreactive B cells and auto-antibodies in SLE.

**Results:** Engineered cells retained their immune suppressive capabilities upon polyclonal stimulation. Noticeably, they acquired new antigen-specific suppressive capacities, being able to block autologous B cell proliferation. We set up a humanized mouse model of SLE. In vivo, CAR-Tregs delayed the occurrence of B cell lymphopenia, producing immunomodulatory cytokines and without showing toxicity or reprogramming towards Th17 pro-inflammatory cells. In inflamed organs, CAR-Tregs restored the normal composition of the immune system.

**Conclusion:** In conclusion, we efficiently generated anti-CD19 CAR-Tregs and proved their efficacy both in vitro and in an in vivo humanized mouse model of lupus.

**Acknowledgements:** NIL.

**Disclosure of Interests:** None Declared.

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**POS1433 RELATIONSHIP BETWEEN THE EFFECT OF BELUMUMAB ON IMMUNOPHENOTYPE AND THE DISCONTINUATION OF GLUCOCORTICOIDS IN PATIENTS WITH SLE: LOOPS REGISTRY, FLOW STUDY**

**Keywords:** Systemic lupus erythematosus, Real-world evidence

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**Background:** The efficacy of belimumab (BEL) for maintenance therapy in patients with systemic lupus erythematosus (SLE) remains unclear. Furthermore, the effects of BEL on the peripheral blood immunophenotype in patients with SLE are unknown.

**Objectives:** Patients with SLE in the maintenance phase were analyzed to determine the differences in the efficacy of BEL and peripheral immunophenotypes. This study aimed to identify patients with SLE for whom belimumab was optimal by clinical findings and peripheral immunophenotypes.

**Methods:** In this retrospective observational study, patients with SLE (n=110) in the maintenance phase (SELENA-SLEDAI ≤ 10, glucocorticoid [GC] dose ≤ 0.2mg/kg/day) were assessed. Based on the standard human immune cell subset classification protocol by NIH/FICIS, peripheral immunophenotypes were analyzed in SLE patients and age/gender-matched healthy controls (n=76), and compared. The efficacy of BEL combined with standard-of-care (BEL+SoC group, n=64) was compared with SoC alone (SoC group, patients using either mycophenolate mofetil or hydroxychloroquine, n=46). Selection bias was adjusted by propensity score-based inverse probability of treatment weighting (PS-IPTW).

**Results:** The proportion of naïve-CD4 T-, CD8 T-, and B cells were lower, and that of the memory CD4 T-, memory CD8 T-, class-switched memory B-, and IgD CD27 B cells, and plasmocytes was higher in the SLE patients than in controls. No significant difference was observed in the patient background between the two groups after adjustment by PS-IPTW. Compared with the SoC group, the GC dose after one year was significantly lower (BEL+SoC group, 1.7±2.3 vs. SoC, 5.4±4.8mg/day, p<0.0001) in the BEL+SoC group. In the BEL+SoC group, 31.3% (20/64) of patients discontinued GC, significantly more than the SoC group (BEL+SoC, 31.3% vs. SoC, 5.0%, p=0.0012). The relapse rate (BEL+SoC, 6.1% vs. SoC, 22.4%, p=0.0128) was significantly lower in the BEL+SoC group than in the SoC group. The incidence of infections was significantly lower in the BEL+SoC group compared to the SoC group before and after PS-IPTW. No significant difference between the two groups was observed in peripheral immunophenotypes at baseline. The proportion of activated Tfh cells (p=0.0323), IgD CD27 B cells (p<0.0001), and plasmocytes (p=0.0370) was significantly decreased six months after BLM introduction. In the BEL+SoC group, 18 (28.1%) who discontinued GC had no relapse for one year and showed a significantly lower proportion of IgD CD27 B cells six months after BLM introduction (p=0.0387). These changes were not observed in the SoC group.

**Conclusion:** In maintenance-phase SLE, administration of BLM was able to achieve a reduction or discontinuation of GC dose while suppressing flare-ups. A reduction in IgD CD27 B cells due to BLM may help to control disease activity and enable the reduction/discontinuation of GC in SLE patients in the mainte-
nance phase.

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