**Identifying features of lymphocytes in newly diagnosed T1D BANDIT participants after treatment with the JAK inhibitor baricitinib**

**Background and aims:** The BANDIT clinical trial (NCT04774224) is a phase 2, randomised, placebo-controlled study which includes a cohort of 90 new-onset type 1 diabetes (T1D) participants. This trial investigates the efficacy of JAK1/JAK2 inhibitor baricitinib in new-onset T1D by collecting clinical endpoints monitoring beta-cell function and immune cell subpopulations. The aim of the current study is to examine NK cell and T-cell populations to understand how inhibiting JAK1 and JAK2 with baricitinib modifies T1D relevant immune cell markers.

**Materials and methods:** Blood samples were collected and processedat baseline and after 24 weeks of treatment with baricitinib. At 24 weeks, samples were collected 2 h and 24 h after baricitinib. The phosphorylation of STAT proteins was measured in response to IFNγ and IL-21 by phosphoflow cytometry as a readout of drug activity. Frequencies of T cells and NK cell subpopulations were analysed using spectral flow cytometry.

**Results:** The frequency of CD56bright NK cells decreased by 30.5% (Wilcoxon test, p=0.0052) and CD56dim NK cellsdecreased by 56.6% (Wilcoxon test, p=<0.0001) after 24 weeks of baricitinib. The frequency of CD8+ effector memory T cells decreased by 28.1% (Wilcoxon test, p=0.0026) after 24 weeks of baricitinib. There was a significant reduction in the pSTAT1 and pSTAT3 gMFI in CD8+ T cells at 24 weeks of treatment when comparing baricitinib and placebo 2 h after drug intake (Komolgorov-Smirnoff test, p<0.001 and p=0.0218 respectively).

**Conclusion:** Advances in the understanding of cytokine signal transduction led to the therapeutic targeting of JAKs to treat autoimmune and inflammatory diseases, including T1D. Baricitinib inhibited cytokine signaling in the immune cells. This led to a reduction of effector memory T cells and NK cell frequencies in recent onset T1D subjects. Future studies will investigate how changes in lymphocyte subsets are linked with beta cell function in BANDIT trial participants.