Methods Patients with symptomatic gout and elevated sUA (≥ 6 mg/dL) were treated with fixed doses of pegsiticase (0.2 mg/kg or 0.4 mg/kg) alone or co-administered with SVP-R (0.05, 0.08, or 0.1 mg/kg). SEL-212 was infused in 28 day cycles x3 doses followed by challenge with pegsiticase alone on 28 day cycles x2 doses. Safety, tolerability, sUA, and ADAs were monitored

Results In the SEL-212 Phase 1b study, 70% of patients administered 0.4 mg/kg pegsiticase with a mid-dose of 0.1 mg/kg SVP-R showed low or no ADA formation correlating with sustained low sUA levels for at least 30 days after a single dose, compared to 20% for patients treated with pegsiticase alone. In the ongoing Phase 2 study, the majority of patients receiving 0.1 mg/kg SVP-R administered with either 0.2 or 0.4 mg/kg pegsiticase also showed low or no ADAs and maintained low sUA levels after 3 monthly doses of SEL-212, indicating sustained activity with repeated doses of SEL-212. However after 2 subsequent doses of pegsiticase alone, a drop in activity was noted. These data suggest that either a higher dose of SVP-R or the addition of SVP-R at the 4th and 5th dose may be required to sustain activity through 5 months. Currently patients are being dosed with 0.15 mg/kg SVP-R, a dose level which enabled sustained control of sUA levels in all patients in Phase 1b. SEL-212 was generally well tolerated and associated with a low rate of gout flare rates compared to those treated with pegsiticase alone.

Conclusions SVP-R showed a dose-dependent reduction in ADAs and enabled sustained control of sUA with repeated dosing of SEL-212. SVP-R is a promising approach to prevent the formation of ADAs against immunogenic biologic therapies.

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TOFACITINIB IS ASSOCIATED WITH AN IMPAIRED FUNCTION OF NK CELLS AND A DEFECTIVE IMMUNOSURVEILLANCE AGAINST B-CELL LYMPHOMAS

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Introduction Patients with rheumatoid arthritis (RA) are exposed to an increased risk of lymphoma and the impact of treatments is difficult to assess. Tofacitinib, an oral Janus Kinase (Jak) 3 and 1 inhibitor that has shown positive results in RA patients, may impair NK-cell function due to its inhibitory action on IL2 and IL15 signalling.

Objectives Given the fact that NK cells have been recently shown to participate to anti-lymphoma immunosurveillance, we aimed to assess if tofacitinib might impact NK-cell function and anti-lymphoma activity *in vitro* and *in vivo* in BAFF

transgenic mice (a model of B cell autoimmunity associated with an increased risk of lymphoma).

Methods We have studied the consequences of *in vitro* exposure of NK to tofacitinib (10, 50 and 100 nM) or to DMSO (vehicle) during 6 days in presence of IL-2 (200 UI/ml): phenotype has been studied and then cytotoxicity against 2 non-Hodgkin B-cell lymphoma cell lines [Farage (EBV+) and SU-DHL4 (EBV-)] was assessed. In addition, BAFF transgenic mice were treated for 6 months with tofacitinib (2.25 mg/kg/d n=11; 4.5 mg/kg/d n=10) or vehicle (PEG: DMSO, n=6). Incidence of lymphoma was assessed by histologic examination using a composite score.

Results Firstly, we did not observe difference concerning the survival of NK cells in presence of tofacitinib or vehicle after 6 day culture. Secondly, we observed that culture in presence of tofacitinib was associated with a decreased level of activation with a dose effect. In addition, we observed a decreased expression of activating receptors such as NKp30, NKp44 and NKG2D. Last, we found that tofacitinib blocked NK cell maturation as observed with the significant decreased expression of CD57 on NK cells exposed to tofacitinib at 50 and 100 nM. These phenotypic abnormalities were associated with an impaired function of NK as assessed by co-culture: degranulation and cytotoxicity were significantly decreased after exposure to tofacitinib. In BAFF transgenic mice, the crude mortality and incidence of lymphoma did not differ between the 3 groups of treatment.

Conclusions This study demonstrates that tofacitinib treatment negatively impact the state of activation, maturation and functions of NK cells. These defects were not associated with a higher incidence of lymphoma in BAFF Tg mice after 6 months of exposure. However, this negative impact of tofacitinib on NK cells might participate to the increased risk of herpes zoster infection in patients treated with tofacitinib and suggest to remains cautious about a possible increased risk of lymphoma.

Disclosure of interest None declared

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MESENCHYMAL STEM CELL ENCAPSULATION IN ALGinate MICRO-PARTICLES FOR INTRA-ARTICULAR INJECTION IN OSTEOARTHRITIS

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Introduction Owing to their ability to secrete anti-inflammatory and immuno-modulatory factors Mesenchymal Stromal Cells (MSCs) are an attractive tool for the treatment of osteoarthritis. Considering cell death and the risk of cell leakage upon intra-articular injection, MSCs encapsulation therefore could protect cell from death, avoid cell effusion outside the articular space, and supply a suitable 3D microenvironment supporting the biological activity of MSCs.

Objectives Our objective was to develop a method of MSC encapsulation compatible with their intra-articular injection through a 26G needle.