Background
Stratum D of the INSIGHT platform trial investigates the feasibility and safety of s.c. application of IMP321 (eftilagimod alpha) combined with the PD-L1 inhibitor avelumab in advanced stage solid tumors. The MHC class II agonist IMP321 activates antigen-presenting cells by CD8 T-cell activation. The addition of avelumab aims at enhancing activity by combining IMP321’s activating effects on immune cells with the release of immune inhibitory effects caused by interruption of the PD-1/PD-L1 axis.

Methods
This investigator-initiated phase I trial consists of four strata: intratumoral (A) or intraperitoneal IMP321 (B); s.c. IMP321 with SOC (C) or with PD-L1 inhibition (D). This poster focuses on Stratum D. Patients (pts) receive 800mg avelumab 0.5q2w along with s.c. IMP321 injections (5mg IMP321 in cohort 1 and 30mg IMP321 in cohort 2). 12 pts were planned to be enrolled in stratum D: 6 pts in cohort 1 and 6 pts in cohort 2. Primary endpoint is safety.

Results
Recruitment of Stratum D was completed in April 2020 with 12 enrolled pts (6 in cohort 1 and 6 in cohort 2). Pts were/are treated for different tumor indications (Table 1). So far, no dose limiting toxicities (DLTs) occurred. 6 serious adverse events (SAEs) were reported in Stratum D, none of them related to any of the study drugs: 3 SAEs in 2 pts of cohort 1 (acute kidney injury grade 5 in 1 pt, 2 pleural grade 3 in 1 pt) and 3 SAEs in 2 pts of cohort 2 (1 anal hemorrhage and 1 gallbladder obstruction in 1 pt, 1 eye pain in 1 pt, each of them grade 3) (Table 2 and Table 3).

Regarding safety data in cohort 1, 43 adverse events (AEs; grade 1-2; 26; grade 3, 15; grade 4, 1; grade 5, 1) have been documented in 5 pts so far. Most common grade 1-2 AEs were pain, nausea, agitation, and injection site reaction in 50%, 33%, 17% and 17% of the pts. Most common grade 3 AEs were pleural/ileus, nausea/vomiting, and ascites in 33%, 33%, and 17% of the pts (Table 4). One AE grade 4 (sepsis) and one AE grade 5 (acute kidney injury) were reported. 4 AEs grade 1-2 were possibly or definitely related to IMP321 (injection site reaction 2x in 1 pt; fever; lipohypertrophy), 8 AEs grade 3,5 were possibly or definitely related to avelumab (nausea 3x in 1 pt; chills; fever; dyspea; lipohypertrophy, sarcoidosis) (Table 5).

Conclusion
Combination treatment with avelumab 800mg and IMP321 6mg is safe and well tolerated. Safety data of cohort 2 will be presented at a later timepoint. Individual patients displayed responses which will be further evaluated. 

Table 1: Patient overview

Table 2: Summarized SAEs by patients

Table 3: Serious adverse events

Table 4: Most common adverse events

Table 5: Adverse reactions in Cohort 1

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#3099: Open-label, phase I study evaluating feasibility and safety of subcutaneous IMP321 (a soluble LAG-3 protein, eftilagimod alpha) combined with avelumab in advanced stage solid tumor entities: results from stratum D of the INSIGHT platform trial

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