#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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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 followed 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.

Figure 1: Study Design

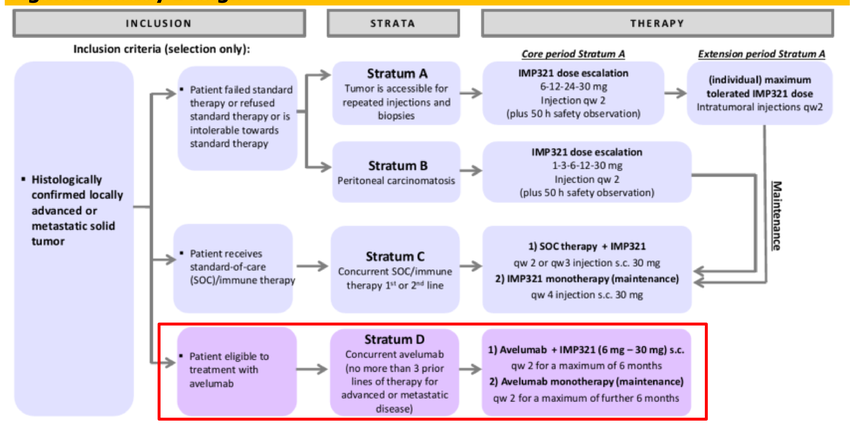

Table 1: Patient overview

Pat-ID	Cohort	Indication	Last prior therapy	PD-L1 staining/ MSI/ molecular markes	No of cycles	Best response	PFS (months)	OS (months)
001-017	Cohort 1	Adenocarcinoma stomach	1st line FLOT	PD-L1: nk, MSS	5	PD	2	11+
001-018	Cohort 1	Adenocarcinoma gallbladder	Gem/Cis additive	PD-L1: CPS 80%, MSS	3	PD	2	2
001-019	Cohort 1	Adenocarcinoma right colon	3rd line TAS-102	PD-L1: nk; Pan-RAS wt	4	PD	2	6
001-020	Cohort 1	Adenocarcinoma rectum	3rd line TAS-102	PD-L1: nk; Pan-RAS and BRAF wt	4	PD	2	9+
001-021	Cohort 1	Adenocarcinoma right colon	na	PD-L1:TPS 1%, CPS 2%; MSI high (Lynch-Syndrome)	16+	PR	7+	7+
001-022	Cohort 1	Pleural mesothelioma	na	Nk	14+	PR	7+	7+
001-023	Cohort 2	Squamous cell esophagus carcinoma	def. RCTx carbo/pacli (56 Gy)	PD-L1: CPS 30%	3	SD	4+	4+
001-024	Cohort 2	Squamous cell anal carcinoma	def. RCTx (5-FU+ mitomoycin C)	PD-L1: TPS 50%	4+	PR	3+	3+
001-025	Cohort 2	Adenocarcinoma GEJ Typ III	2nd line pacli/ram	PD-L1: TPS 30%, CPS 40%	4+	PR	2+	2+
001-026	Cohort 2	Squamous cell cervix carcinoma	def. RCTx (cisplatin)	PD-L1 negative, MSS	2+	nd*	1+	1+
001-027	Cohort 2	Adenocarcinoma GEJ Typ II	2nd line FOLFIRI	PD-L1: CPS 80%, MSS	2+	nd*	1+	1+
001-028	Cohort 2	Adenocarcinoma rectum	2nd line FOLFIRI	PD-L1: nk, MSS, RAS and BRAF wt	1+	nd*	1+	1+

* response assessment not yet performed; + continuing and respective endpoint not yet reached

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 i.v. q2w along with s.c. IMP321 injections (6mg 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 (1 acute kidney injury grade 5 in 1 pt, 2 preileus 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 preileus/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 1-2 were possibly or definitely related to avelumab (nausea 3x in 1 pt; chills; fever; dyspnea; lipohypertrophy, sarcoidosis) (Table 5). The event 'sarcoidosis' was reported as an AE of special interest (AESI) concerning Avelumab . All AEs grade 3-5 were unrelated to any of the study drugs.

Out of the 12 pts enrolled, preliminary data revealed that so far 4 pts showed partial responses acc. to RECIST 1.1 (2 pts of cohort 1 and 2 pts of cohort 2). 5 pts had disease progression (3 progressive diseases acc. to RECIST 1.1 in cohort 1; 1 clinical progression in cohort 1 and 1 clinical progression in cohort 2). 3 pts of cohort 2 have not had tumor assessment yet, but are still under therapy without clinically signs of tumor progression.

Table 2: Summarized SAEs by patients

SAE	Cohort 1 800mg Avelumab + 6mg IMP 321 n=6 (%)	Cohort 2 800mg Avelumab + 30mg IMP 321 n=6 (%)	Total n=12 (%)
Patients with at least one SAE	2 (33%)	2 (33%)	4 (33%)
Patients with at least one SAE with relation to study treatment	0 (0%)	0 (0%)	0 (0%)

Table 3: Serious adverse events

	Cohort 1 800mg Avelumab + 6mg IMP 321 n=6 (%)		Cohort 2 800mg Avelumab + 30mg IMP 321 n=6 (%)	Total n=12 (%)	
Serious adverse event	**G3**	**G5**	**G3**	**G3**	**G5**
Acute kidney injury		1 (17%)			1 (8%)
Preileus	1 (17%)			1 (8%)	
Anal hemorrhage			1 (17%)	1 (8%)	
Gallbladder obstruction			1 (17%)	1 (8%)	
Eye pain			1 (17%)	1 (8%)	

Table 4: Most common adverse events

	Cohort 1 800mg Avelumab + 6mg IMP 321 n=6 (%)	
Most common AEs	**G1/G2**	**G3**
Pain	3 (50%)	
Nausea/Vomiting	2 (33%)	2 (33%)
Agitation	1 (17%)	
Injection site reaction	1 (17%)	
Preileus/ ileus		2 (33%)
Ascites		1 (17%)

Table 5: Adverse reactions in Cohort 1

	Cohort 1 800mg Avelumab + 6mg IMP 321 n=6 (%)					
	G1/G2			G3	G4	G5
Adverse reaction	**Causality IMP321**	**Causality Avelumab**	**Causality IMP321 and Avelumab**			
Fever			1 (17%)			
Lipohypertrophy			1 (17%)			
Injection site reaction	1 (17%)					
Chills		1 (17%)				
Dyspnea		1 (17%)				
Nausea		1 (17%)				
Sarcoidosis (reported as AESI)		1 (17%)				

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.

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