#2518: Phase I INSIGHT platform trial: Advanced safety and efficacy data from stratum D evaluating feasibility and safety of eftilagimod alpha (soluble LAG-3 protein) combined with avelumab in advanced stage solid tumors.

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Background

Stratum D of the INSIGHT platform trial evaluates s.c. eftilagimod alpha (efti, IMP321) combined with avelumab in advanced solid tumors. Efti is an MHC class II agonist which activates antigen-presenting cells followed by CD8 T-cell activation. Combination with PD-1/PD-L1 blockade aims at enhanced efficacy.

Figure 1: Study Design

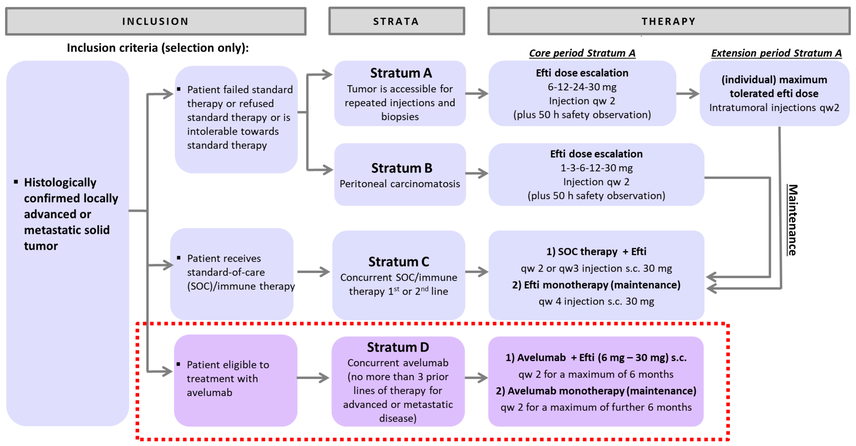

Table 1: Patient overview

Pat-ID	Cohort	Indication	Last prior therapy	PD-L1 staining / MSI / molecular markes	No of cycles	No of efti injections total	No of Avelumab adminin. total	Best response	PFS (months)	OS (months)
001-017	Cohort 1	Adenocarcinoma stomach	1st line FLOT	PD-L1: nk; MSS	5	5	5	PD	1.9	19.4*
001-018	Cohort 1	Adenocarcinoma gallbladder	Gemcitabine / cisplatin additive	PD-L1: CPS 80%, MSS	3	3	3	PD	1.7	1.7
001-019	Cohort 1	Adenocarcinoma right colon	3rd line TAS-102	PD-L1: nk; Pan-RAS wt	4	4	4	PD	1.8	6.1
001-020	Cohort 1	Adenocarcinoma rectum	3rd line TAS-102	PD-L1: nk; Pan-RAS and BRAF wt	4	4	4	PD	2.0	18.4*
001-021**	Cohort 1	Adenocarcinoma right colon	na	**PD-L1: TPS 1%, CPS 2%; MSI high (Lynch-Syndrome)**	24	12	24	PR	17.8*	17.8*
001-022	Cohort 1	Pleural mesothelioma	na	Nk	16	12	16	PR	7.5	15.8*
001-023	Cohort 2	Squamous cell esophageal carcinoma	Def. RCTx carboplatin/ paclitaxel (56 Gy)	PD-L1: CPS 30%	3	3	3	SD	1.5	13.2*
001-024	Cohort 2	Squamous cell anal carcinoma	Def. RCTx (5-FU+ mitomoycin C)	PD-L1: TPS 50%	24	12	24	PR	11.0*	12.4*
001-025	Cohort 2	Adenocarcinoma GEJ Typ III	2nd line paclitaxel / ramucirumab	PD-L1: TPS 30%, CPS 40%	17	12	17	PR	7.4	10.8*
001-026**	Cohort 2	Squamous cell cervical carcinoma	Def. RCTx (cisplatin)	**PD-L1 negative, MSS**	9	9	9	PR	3.9	3.9
001-027	Cohort 2	Adenocarcinoma GEJ Typ II	2nd line FOLFIRI	PD-L1: CPS 80%, MSS	4	4	4	PD	1.8	9.9*
001-028**	Cohort 2	Adenocarcinoma rectum	2nd line FOLFIRI	**PD-L1: nk; MSS, RAS and BRAF wt**	4	4	4	PD	1.9	9.4*

* time to event not yet reached; ** low PD-L1 and MSS stable;
nk = not known; SD = stable disease; PD = progressive disease; PR = partial response; response = acc. RECIST 1.1
TPS = tumor proportion score; CPS = combined positivity score

Methods

This IIT platform trial consists of 5 strata: intratumoral (A) or intraperitoneal efti (B); s.c. efti with SOC (C) or with PD-L1 inhibition (D). Strat E is currently under development and starts soon with a new efti combination. This abstract focuses on preliminary data of Strat D. Patients (pts) received 800mg avelumab i.v. q2w along with s.c. efti: 6mg in cohort 1 (coh 1, 6 pts), 30mg in cohort 2 (coh 2, 6 pts). Primary endpoint: safety.

Results

Recruitment has been completed with 12 pts (coh 1: gastric, gallbladder, colon cancer, pleural mesothelioma; coh 2: gastric, gastroesophageal, anal, rectum, cervix uteri).

No dose limiting toxicities (DLTs) occurred. With data cut off from 22-Jan-2021, 10 serious adverse events (SAEs) were reported, none of them considered causally related (4 in 3 pts of coh 1 [1 acute renal insufficiency grade 5 in 1 pt, 2 preileus grade 3 in 1 pt, hearing impaired grade 4 in 1 pt] and 6 in 4 pts of coh 2 [1 anal hemorrhage and 1 gallbladder obstruction in 1 pt, 1 eye pain and 1 feeding tube dislocation in 1 pt, each grade 3, 1 skin infection grade 2, 1 diffuse myocardial fibrosis grade 5]. 1 AE of special interest (AESI) possibly related with avelumab (sarcoidosis grade 1) occurred in coh 1. 2 pts completed max treatment duration with 24 cycles.

In coh 1, 47 adverse events (AEs; grade 1-2, 29; grade 3, 14; grade 4, 3; grade 5, 1) occurred in 5 pts. Most common grade 1-2 AEs were nausea, pain in 33%, 33% of the pts. Most common grade 3 AEs were ileus, vomiting in 33%, 33% of the pts. 2 AEs grade 4 (hearing impaired, sepsis) and 1 AE grade 5 (acute renal insufficiency) were reported. All AEs grade 3-5 were considered causally unrelated.

In coh 2, 51 adverse events (AEs; grade 1-2, 29; grade 3, 19; grade 4, 2; grade 5, 1) occurred in 5 pts. The most common grade 1-2 AE was hypothyroidism in 33% of the pts. 1 AE grade 5 (diffuse myocardial fibrosis) was reported. Only 1 AE grade 3-5 was considered causally related (urinary tract infection grade 3 related with avelumab).

5 pts showed partial response as best response (2 coh 1: colon, pleural mesothelioma; 3 coh 2: gastric, anal, cervical), 1 stable disease with clinical progression (coh 2) (all but one of these pts still alive), 5 disease progressions acc. to RECIST 1.1 (3 coh 1, 2 coh 2), 1 clinical progression (coh 1). Signals of activity were also observed in pre-treated *MSS/PD-L1$_{low}$* pts.

Table 2: Summarized SAEs by patients

SAE	Cohort 1 800mg avelumab + 6mg efti n=6 (%)	Cohort 2 800mg evelumab + 30mg efti n=6 (%)	Total n=12 (%)
Patients with at least one SAE	3 (50%)	4 (67%)	7 (58%)
Patients with at least one SAE with relation to study treatment	0 (0%)	0 (0%)	0 (0%)

First author conflicts of interest

TOG had an advisory role for Lilly, MSD Oncology, Bayer, SERVIER, BMS and Roche, served as speaker for Lilly, MSD, Servier, and received research funding from Deutsche Forschungsgemeinschaft, Deutsche Krebshilfe, Gemeinsamer Bundesausschuss and AstraZeneca

Table 3: Serious adverse events (irrespective of relationship to study drug)

	Cohort 1 800mg avelumab + 6mg efti n=6 (%)			Cohort 2 800mg avelumab + 30mg efti n=6 (%)			Total n=12 (%)			
Serious adverse event	**G3**	**G4**	**G5**	**G2**	**G3**	**G5**	**G2**	**G3**	**G4**	**G5**
Acute renal insufficiency			1 (17%)							1 (8%)
Ileus	1 (17%)							1 (8%)		
Anal hemorrhage					1 (17%)			1 (8%)		
Diffuse myocardial fibrosis						1 (17%)				1 (8%)
Gallbladder obstruction					1 (17%)			1 (8%)		
Eye pain					1 (17%)			1 (8%)		
Hearing impaired		1 (17%)							1 (8%)	
Feeding tube dislocation					1 (17%)			1 (8%)		
Skin infection				1 (17%)			1 (8%)			

Table 4: Most common adverse events (irrespective of relationship to study drug)

	Cohort 1 800mg avelumab + 6mg efti n=6 (%)		Cohort 2 800mg avelumab + 30mg efti n=6 (%)	
Most common AEs	**G1/G2**	**G3**	**G1/G2**	**G3**
Pain	3 (50%)	1 (17%)		2 (33%)
Nausea/Vomiting	2 (33%)	2 (33%)	1 (17%)	
Injection site reaction	1 (17%)		1 (17%)	
Ileus		2 (33%)		
Chills	1 (17%)		1 (17%)	
Fever	1 (17%)		1 (17%)	
Hypokalemia	1 (17%)			1 (17%)
CRP increased	1 (17%)		1 (17%)	
Dysphagia			1 (17%)	1 (17%)
Hypothyroidism			2 (33%)	

Table 5: Treatment related AEs

	Cohort 1 800mg avelumab + 6mg efti n=6 (%)						Cohort 2 800mg avelumab + 30mg efti n=6 (%)							
	G1/G2			G3	G4	G5	G1/G2			G3			G4	G5
Adverse reaction	**Causality efti**	**Causality avelumab**	**Causality efti and avelumab**				**Causality efti**	**Causality avelumab**	**Causality efti and avelumab**	**Causality efti**	**Causality avelumab**	**Causality efti and avelumab**		
Chills		1 (17%)						1 (17%)						
CRP increased							1 (17%)							
Dry eye		1 (17%)												
Dyspnea		1 (17%)												
Fever			1 (17%)					1 (17%)						
Hypotension								1 (17%)						
Hypothyroidism								2 (33%)						
Injection site reaction	1 (17%)						1 (17%)							
Lipohypertrophy			1 (17%)											
Nausea		1 (17%)												
Sarcoidosis		1 (17%)												
Urinary tract infection											1 (17%)			

Conclusion

Combined treatment with avelumab 800mg and efti 6mg (coh 1) or 30 mg efti (coh 2) seems feasible and safe. No unexpected AEs occurred. Signals of efficacy with CPI-combination were seen (DCR 50.0%)

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