#2632: Phase 1 dose escalation study of DSP107, a first-in-class CD47 and 4-1BB targeting fusion protein, in combination with atezolizumab in patients with advanced solid tumors

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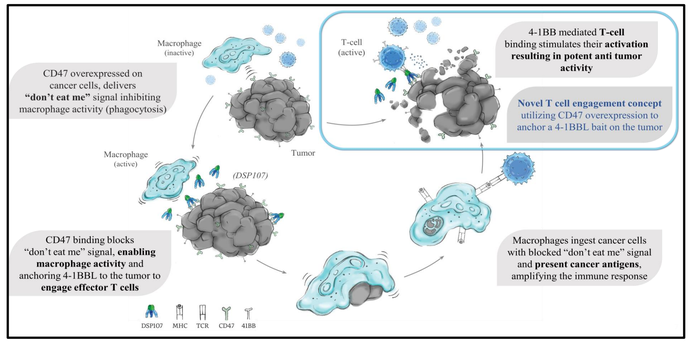
Introduction:

- DSP107 is a bi-functional, trimeric, fusion protein targeting CD47 and 4-1BB
- Phase 1 monotherapy dose escalation data demonstrated an excellent safety profile with no binding to red blood cells and no dose limiting toxicities (DLTs), hematological or hepato-toxicities

Figure 1: DSP107 Designed for Synergistic Innate & Adaptive Immune Activation



Methods:

- Adult patients with advanced solid tumors treated QW with IV DSP107 infusions (1, 3 or 10 mg/kg; N = 6-7 /dose cohort) and atezolizumab (1200 mg) Q3W during 3-week treatment cycles
- **Study objectives:**
- **Primary**: Determine the safety and tolerability of DSP107 in combination with atezolizumab.
- **Secondary**: Assess preliminary efficacy of DSP107 in combination with atezolizumab. CT scans performed after cycles 2 and 4 and then every 2 months and evaluated according to RECIST v1.1
- Here we report data from the completed DSP107 dose escalation in combination with atezolizumab portion of study NCT04440735

Results:

Safety:

- DSP107 doses up to and including 10 mg/kg were safe and well tolerated in combination with atezolizumab
- No DLTs and no treatment-related SAEs
- No binding to RBCs, no hematological toxicities, and no hepato-toxicities

Treatment-Related Adverse Events

- Grade 1-2 treatment-related AEs were observed in 68% of patients (13/19)
- Two Grade 3 AEs – myalgia and transient neutropenia that recovered spontaneously within 7 days and did not recur with subsequent dosing

Pharmacokinetics and Target Engagement:

- No effect of atezolizumab combination therapy on DSP107 exposure and target engagement

Table 1: Patient Baseline Characteristics

Characteristics	
Total number of patients	N = 19
Sex	7 (37%) ♀; 12 (63%) ♂
Age	Median 58 (Range 32-75)
Previous lines of therapy	Median 3 (Range 1-7)
PD1/PD-L1 experienced	5 (26%)

Table 2: DSP107 Related AEs

Treatment-Related AEs in ≥ 2 Patients Total No. of Patients N = 19	Treatment-related AEs (any grade) n (%)	1 mg/kg	3 mg/kg	10 mg/kg
Any	13 (68)			
Diarrhea	4 (21)	0	2	2
Fatigue	4 (21)	1	1	2
IRR*	3 (16)	0	0	3
Nausea	3 (16)	1	1	0
Anemia	2 (11)	0	1	1
Decreased Appetite	2 (11)	0	1	1
Myalgia	2 (11)	1	1	0

*IRRs Grade 1-2 in severity. Easily abrogated in subsequent infusions by reduced rate of infusion and concomitant IV fluids

Response:

Best Overall Response After DSP107 combination therapy with atezolizumab

- In MSS-CRC patients, 57% Disease Control Rate (DCR; 4/7 with SD or better at 3 months) across all dose levels
- Patient with parotid gland tumor stable on treatment for > 12 months at 3 mg/kg
- In 10 mg/kg + atezolizumab combination cohort 57% DCR (4/7 patients with SD or better at 3 months), including:
  - Deep and durable objective response in 2/3 MSS-CRC patients (target lesion shrinkage of -73% and -83%) with current DOR of 10 and 9 months, respectively.
  - Third MSS-CRC patient with SD (-16% target lesion shrinkage)

Figure 2: CT Scans

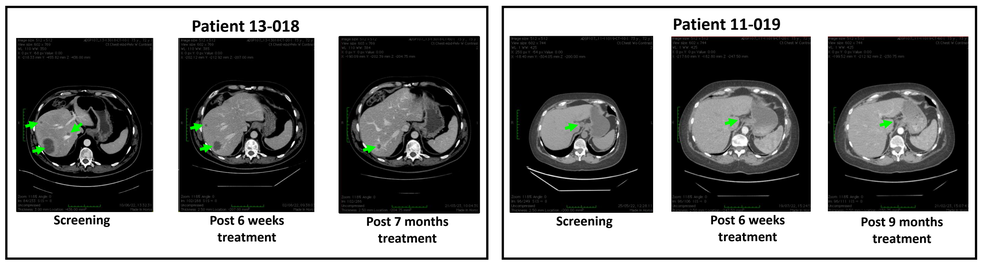


Figure 3: 57% DCR in MSS-CRC patients across all dose levels

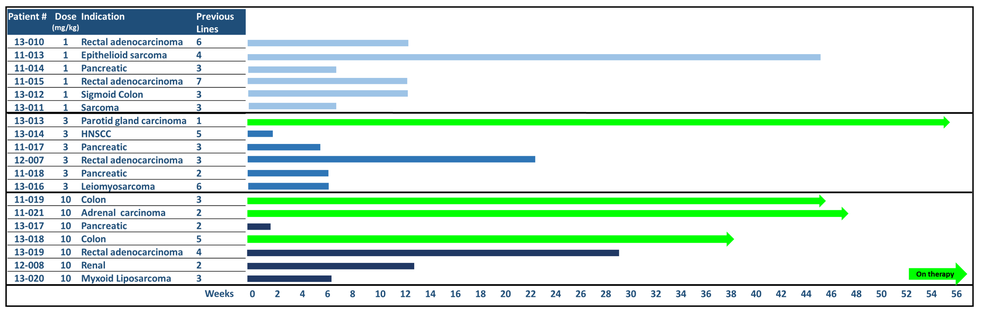
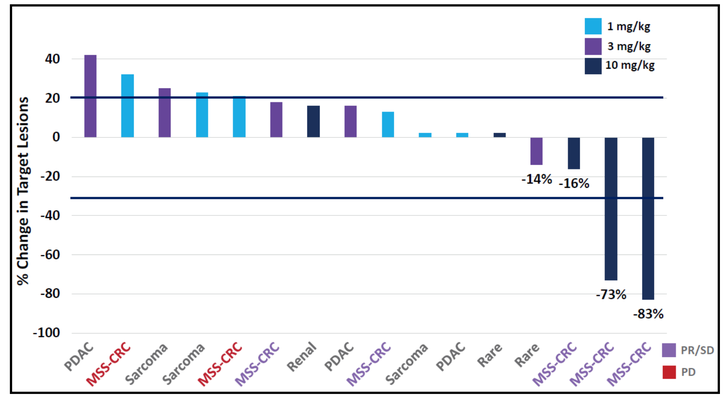


Figure 4: Objective response in 2/3 MSS-CRC patients at 10 mg/kg



Summary:

- DSP107 in combination with atezolizumab was well tolerated with no DLTs and no hematological or hepato-toxicities
- Combination therapy did not affect DSP107 PK or CD47 occupancy
- **Stable disease** (SD) or better at 3 months in **7/19 (37%)** patients across dose levels with treatment duration currently standing at more than 12 months

10 mg/kg DSP107 + Atezolizumab combination cohort:

- 57% DCR (4/7 patients with SD or better at 3 months)
- Deep, **durable objective responses in 2/3 MSS-CRC patients** (target lesion shrinkage by **73% and 83%**) with current DOR of 10 and 9 months, respectively. Third patient with SD (16% target lesion shrinkage, 6.5 months until progression)
- Responses observed in patients with KRAS / BRAF mutations and liver and lung metastases

Conclusion:

- DSP107 in combination with atezolizumab appears to be safe and efficacious in cold tumors such as MSS-CRC
- DSP107 dose of 10 mg/kg selected for ongoing Phase 2 expansion cohorts in 3rd line MSS-CRC and 2nd/3rd line NSCLC

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