COM701 in combination with COM902 and pembrolizumab demonstrates preliminary antitumor activity in patients with MSS-CRC and liver metastases. NCT04354246.

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Background: There is a high unmet need for the treatment of patients [pts] with metastatic microsatellite stable colorectal cancer [MSS-CRC]. We reported encouraging preliminary antitumor activity with the combination of COM701 + nivolumab in patients with MSS-CRC and liver metastases [12/22(77%)], [ORR 2/17 (12%); disease control rate [DCR] 5/17 (29%)] . COM701 is a novel, 1st-in-class immune checkpoint inhibitor [ICI] that binds to PVRIG, a DNAM-1 axis member, leading to activation of T and NK-cells; COM902 is an ICI of TIGIT. Pembrolizumab is an ICI of PD-1. We hypothesized that in pts with metastatic MSS-CRC, the triple combination by inhibiting the DNAM-1 axis would demonstrate antitumor activity with a favorable safety and tolerability profile. We present encouraging preliminary results.

Methods: We enrolled 20 pts with metastatic MSS-CRC who all received COM701 15 mg/kg + COM902 3 mg/kg + pembrolizumab 200 mg all IV Q3W. Primary objectives were safety/tolerability, with secondary objective of antitumor activity of the combination. Key inclusion criteria: Age ≥ 18 yrs, measurable disease, MSS by IHC or genomic testing, ≤3 prior lines including fluroropyrimidines, irinotecan, and oxaliplatin. Key exclusion criteria: prior receipt of ICI including anti-PVRIG, anti-TIGIT. Investigator assessed responses were per RECIST

v1.1, safety per CTCAE v5.0.

Results: Median age 57.5yrs, 11/20 [F], 15/20 [75%] pts with liver metastases. Median of 3 prior lines of therapy. Objective response rate [ORR] 1/20 [5%] pts; 7 pts with SD. Disease control rate [CR + PR + SD] 8/20 [40%]. In pts with liver mets ORR 1/15 [7%], DCR 6/15 (40%); 6/8 [75%] pts with best response ≥SD had liver mets. Treatment related AEs were reported in 11/20 [55%] pts, the majority were ≤G2 7/20 [35%] with the most frequent TRAE of 4 pts each with ≤G2 fatigue, myalgia, 4/20 pts with G3 TRAE, there were no ≥G4 TRAEs. Strong peripheral IFNɣ induction was observed after treatment. Three pts [1 PR, 2 SD] are ongoing at the time of data cut.

Conclusions: The data further supports the antitumor activity of the combination of COM701 + COM902 + pembrolizumab in pts with MSS-CRC and specifically in patients with liver metastases. Of note the data further reinforces the data previously disclosed in a similar pt population of 22 pts that received COM701 + nivolumab . No new safety signals are reported. Additional clinical and translational data will be presented at the conference. Data cut 01/09/2024.