659 **COM701 PLUS NIVOLUMAB DEMONSTRATES PRELIMINARY ANTITUMOR ACTIVITY AND IMMUNE MODULATION OF TUMOR MICROENVIRONMENT IN PATIENTS WITH METASTATIC MSS-CRC AND LIVER METASTASES**

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Background COM701 a novel, 1st in-class, humanized IgG4 monoclonal antibody binds with high affinity to PVRIG, blocking its interaction with its natural ligand PVRL2 expressed in tumor cells and antigen-presenting-cells. We have reported antitumor and pharmacodynamic activity of COM701.[1] Anti-PD1/L1 therapies have limited to no activity in MSS-CRC. Therefore, novel ICI are urgently needed for the treatment of pts with MSS-CRC particularly pts with liver metastasis. We present preliminary clinical and translational results of the combination in pts with MSS-CRC.

Methods This is a phase I clinical trial of COM701 and nivolumab. Key objectives were safety/tolerability [primary], preliminary antitumor activity, immune-related changes [secondary/exploratory]. Key inclusion criteria: Age ≥18 yrs, histologically/cytologically confirmed advanced malignancy who have exhausted all available standard therapy or not a candidate for standard therapy, MSS-CRC determination per local testing. Pre- and on-treatment biopsies were obtained and analyzed by IHC for PDL1, CD8 expression and omics profiling.

Results Twenty two pts were enrolled: 2 pts combination dose-escalation [COM701 0.3,1mg/kg + nivolumab 360 mg] both IV Q3W and 20 pts dose-expansion cohort [COM701 20mg/kg + nivolumab 480mg IV Q4W]. Age ≤65 17/22, [77%], male 16/22 [73%], median [Min, Max] of 3 (2, 10) prior lines of therapy, 17/22 [77%] had liver metastases. Overall, ORR 9% (2/22 pts, PRs]; ORR 12% [2/17] in pts with liver metastases [1 PR, PFS 44 weeks; 1 PR, PFS 16 weeks due to brain metastasis, however, response of target and non-target lesions still maintained]; DCR (CR+PR+SD) 27% (6/22). No new safety findings are reported. In 13 paired biopsy samples, 9 demonstrated induction in PD-L1 expression (mean 16.3+/-7% PD-L1 CPS-score increase, $p<0.05$), suggesting TME immune-modulation following treatment. In pts with PR or SD >6months greater induction in PD-L1 expression was seen (49.7+/-14.9%). CD8 T-cell quantification was available in 12 paired biopsies with increase >1% in 8 pts (mean% CD8 increase of 9.1+/-4.4% , $p=0.08$), with substantial increases in responders (36.5% and 44.7%%CD8 increase). In responding pts IFNγ signature up-regulation, increased T-cell clonality and specific clonal expansion, were demonstrated between baseline and on-treatment biopsies.

Conclusions COM701 + nivolumab demonstrates preliminary antitumor activity in pts with heavily pretreated metastatic MSS-CRC with 12% ORR in pts with liver metastases [typically unresponsive to ICI]. TME immune modulation observed in the majority of pts, substantial in responders, suggests unique potential of COM701 in less inflamed tumors such as MSS-CRC. The combination warrants further development. Datacut June 17, 2022.

Acknowledgements The study is sponsored by Compugen Ltd and is in collaboration with Bristol Myers Squibb.

Trial Registration NCT03667716

REFERENCE

1. Vaena, DA, Fleming, GF, Chmielowski B *et al* COM701 with or without nivolumab: Results of an ongoing phase 1 study of safety, tolerability, and preliminary antitumor activity in patients with advanced solid malignancies (NCT03667716). *Journal of Clinical Oncology* 2021;**39**:15_suppl, 2504–2504.

Ethics Approval The study obtained ethics approval from all participating clinical trial sites. All study participants gave informed consent before taking part.

- o 0001: M0D00985865 [SCRI]
- o 0002: START2018.06 [START-San Antonio]
- o 0003: 20181858 [West Cancer Center]
- o 0004: 19-238 [Cleveland Clinic]
- o 0005: 18-0806-CR003 [Uni Chicago]
- o 0006: 18-555 [MGH]
- o 0007: CUMC-AAAR9998 [Columbia University]
- o 0010: 18-001383 [UCLA]
- o 0012: 2018-0891 [MDACC]
- o 0013: STMW2019.01 [Florida Cancer Center]

http://dx.doi.org/10.1136/jitc-2022-SITC2022.0659