640 THE COMBINATION OF COM701 + NIVOLUMAB DEMONSTRATES PRELIMINARY ANTITUMOR ACTIVITY IN PATIENTS WITH METASTATIC BREAST CANCER

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Background COM701, a novel, first in-class immune checkpoint inhibitor, anti-PVRIG, that leads to activation of T-cells. PVRL2, the ligand of PVRIG, is highly expressed in breast cancer. We have reported preliminary antitumor activity with objective responses [partial responses and a complete response] in patients with solid tumors (MSS-CRC, platinum resistant OVCA, anal squamous CA, MSS-endometrial cancer] who received COM701 +/- nivolumab + BMS-986207 (anti-TIGIT antibody).[1] [2] We present results from the dose expansion cohort with COM701 + nivolumab in patients with metastatic breast cancer (MBC) (NCT03667716).

Methods We enrolled 17 patients with MBC, all received COM701 20 mg/kg + nivolumab 480 mg, both IV Q4 weeks. Primary objectives were to determine safety and tolerability and secondary objective was to evaluate preliminary antitumor activity. Key inclusion criteria: Age $\geq$ 18 years, histologically confirmed locally advanced or MBC (regardless of ER/PR and HER2 status) with measurable disease, who exhausted all available standard treatments. Prior treatment with anti-PD-(L)-1, anti-CTLA-4 ICI was permissible. Key exclusion criteria: history of immune-related events that to immunotherapy treatment discontinuation, history of pneumonitis. Safety was evaluated per CTCAE v4.03 and investigator responses per RECIST v1.1.

Results Treatment related adverse events reported in 12/17 (71%) patients, the majority [11/12 pts] were ≤G2, the most frequent was diarrhoea in 3 pts (all G1). One patient with G3 TRAE of pneumonitis (recovered), no ≥G4 TRAEs. Tumor assessments (by site): PD-L1 negative 9/17 (53%), positive/present 2/17 (12%), missing/not assessed 6/17 (35%); TMB low (<10 mut/MB) in 10/17 (59%), missing/not assessed 7/17 (41%). Objective response rate 2/17 patients (12%) - a CR was achieved in a patient with ER+/PR-, HER2- invasive ductal carcinoma (pretreatment: PD-L1 CPS 3, PVRL2 tumor H-score 300 (both by sponsor assessment), TMB-low (5 Mut/Mb)] who received 3 prior lines of therapy and continues the study treatment (567 days). Another patient with TNBC, PD-L1 negative, TMB-low (1 Mut/Mb), with 4 prior lines of therapy with a PR remained on study treatment (296 days), 3 pts with stable disease, all PDL1 CPS$\leq$1 and low TMB. Disease control rate [CR+PR+SD] 5/17 (29%). Patients with clinical benefit and serum samples available showed increased IFNg at Cycle 2–3 compared to baseline.

Conclusions The combination is well tolerated with no dose-limiting toxicity. Encouraging preliminary antitumor activity with PR and CR reported in heavily pretreated patients with TMB-low MBC. Additional clinical and translational data will be presented at the conference. Data extract 06/09/2023.

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Trial Registration NCT03667716.

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Ethics Approval The study obtained ethics approval from the IRBs below:

1. IntegReview SSU00166554
2. Salus IRB IRB00013027
3. WIRB 20181858
4. IRB at Cleveland Clinic IRB#19–238
5. IRB University of Chicago IRB18–0806
6. OHRS at Dana Farber Institute 18–555
7. Columbia University IRB IRB-AAAR9998
8. UCLA OHRPP IRB#18–001383
9. IRB of MD Anderson 2018–0891
10. Salus IRB IRB00013027
11. Advarra Pro00052320

All participants gave informed consent before taking part.

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