COM701 IN COMBINATION with NIVOLUMAB DEMONSTRATES PRELIMINARY ANTITUMOR ACTIVITY in PATIENTS with PLATINUM RESISTANT EPITHELIAL OVARIAN CANCER. (NCT03667716)

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Abstract Number 159P

BACKGROUND

- COM701 is a novel,1st-in-class ICI-blocker that binds to PVRIG, a DNAM-1 axis member, leading to activation of T-and NK-cells
- We have reported that PVRIG pathway is highly expressed in ovarian cancer tumors[1]
- We have reported preliminary anti tumor activity with COM701 ± nivolumab including a confirmed PR with COM701 monotherapy in a patient with OVCA [primary peritoneal cancer][1]
- There is a high unmet medical need for the treatment of patients with platinum resistant epithelial ovarian cancer [PROC] defined as disease recurrence <6 months after completion of platinum-based therapy
- Immune checkpoint inhibitors have limited activity in patients with OVCA
  - Pembrolizumab monotherapy, pembrolizumab + vibostolimab [anti-TIGIT inhibitor] ORR ~8%[3,4]
- We hypothesized that in patients with PROC, dual blockade of PVRIG and PD1 would demonstrate antitumor activity with a favorable safety and tolerability profile
- We present encouraging preliminary results

METHODS

- We enrolled 20 patients with platinum resistant epithelial OVCA, fallopian tube or primary peritoneal cancer; ECOG 0-1
- All patients received COM701 20 mg/kg + nivolumab 480 mg, both IV Q4W
- Antitumor activity (per investigator) was evaluated per RECIST v1.1 with CT imaging every 8 weeks or at any time point progressive disease is suspected
- Study treatment for 2yrs unless PD, toxicity, withdrawal of consent, PI discretion
- Safety assessment evaluated per CTCAE v4.03

ELIGIBILITY CRITERIA AND OBJECTIVES

Key Inclusion Criteria:

- Histologically confirmed locally advanced or metastatic solid malignancy and has exhausted all available standard treatment or is not a candidate for available standard therapy
- Measurable disease
- Mandatory biopsy: pre and on-treatment
- No limitation on the number of prior lines of therapy or prior PD-1/PD-L1 inhibitor

Key Exclusion Criteria:

- Active autoimmune disease requiring systemic treatment
- Prior receipt of anti-PVRIG inhibitor
- History of immune-related toxicities on prior immunotherapy treatment leading to discontinuation

Key Primary Objective:

- Safety and tolerability of COM701 + nivolumab

Key Secondary Objective:

- Antitumor activity of the combination

Key Exploratory Objectives:

- Immunogenicity of COM701
- COM701-mediated pharmacodynamic effect in blood, immune-related changes (cytokines, immunophenotyping)

DEMOGRAPHICS

Characteristics	
Age ≥65 years, n (%)	8 (40)
ECOG (0, 1), n(%)	
0	10 (50)
Histology	
High grade serous	13 (65%)
Clear cell	2 (10%)
Not available	5 (25)
Prior PD-1/PD-L1	4 (20)
Prior bevacizumab/ bevacizumab-regimen	11 (55)
Prior Parp inhibitor	12 (60)

Data cut 23NOV2022

PATIENT DISPOSITION SUMMARY

	n = 20 (%)
Number of patients enrolled and treated - n(%)	20 (100)
#Prior Lines- Median (Min, Max)	6 (2,9)
Discontinued study treatment - n(%)	16(80)
Reasons for study treatment discontinuation (n)	
• Progressive disease per RECIST v1.1/clinical PD	15 (75)
• Adverse event*	1 (5)

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*G3 proteinuria assessed by the PI as related to study drugs

SUMMARY OF TREATMENT RELATED ADVERSE EVENTS

Parameter	All Adverse Events n = 20 (%)
Any TRAE	10 (50)
No TRAE	10 (50)
≤G2	8 (40)
G3	2 (10)
≥G4	-
TRAE leading to study treatment discontinuation	1 (5%)*

Safety analysis set – patients who received ≥1 dose of any of the study drugs. Safety per CTCAE v4.03.
*G3 proteinuria assessed by the PI as related to study drugs.

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INCIDENCE OF TRAEs (10% OF PATIENTS)

PREFERRED TERM (PT)	Grade 1/2 n [%]	Grade 3** n [%]	Grade 4 n [%]	Grade 5 n [%]	All Grades n [%]
Any TRAE	8 (40)	2 (10)	-	-	10 (50)
Fatigue	4 (20)	-	-	-	4 (20)
Nausea	3 (15)	-	-	-	3 (15)
Aspartate Aminotransferase Increased	2 (10)	-	-	-	2 (10)
Hypothyroidism	2 (10)	-	-	-	2 (10)
Influenza Like Illness	2 (10)	-	-	-	2 (10)

**Grade 3 TRAE: 1 patient with hyperkalemia and 1 patient with proteinuria.
Safety analysis set – patients who received ≥1 dose of any of the study drugs. AEs reported within 30 days of last dose of study treatment. Safety per CTCAE v4.03.

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INCIDENCE OF RELATED SERIOUS ADVERSE EVENTS - ALL PATIENTS

PREFERRED TERM (PT)	Grade 1/2 n [%]	Grade 3 n [%]	Grade 4 n [%]	Grade 5 n [%]	All Grades n [%]
Any Serious	-	1 (5)	-	-	1 (5)
Hyperkalaemia	-	1 (5)	-	-	1 (5)

Safety analysis set – patients who received ≥1 dose of any of the study drugs. AEs reported within 30 days of last dose of study treatment. Safety per CTCAE v4.03.

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SUMMARY OF INVESTIGATOR ASSESSED RESPONSE (RECIST V1.1)

Parameter	All patients n = 20 (%)
ORR (CR+PR)	2 (10); (95% CI: 1-32%)
Disease control rate (CR+PR+SD)	9 (45); (95%CI: 23-68%)
Best response	
CR	-
PR	2 (10)
SD	7 (35)
PD	11 (55)

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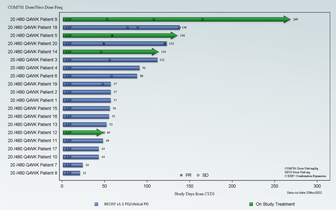
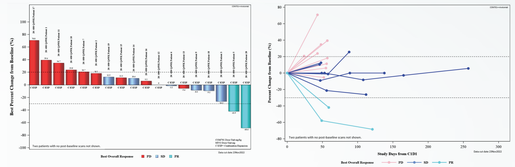
SWIMMER PLOT



Patients who received prior PD-1/PD-L1 inhibitor (best response to prior parp inhibitor): Patient: 4 (SD), 14 (unk), 17 (PR), 20 (PD).

WATERFALL and SWIMMER PLOTS



CHARACTERISTICS OF RESPONDERS

Patient ID	Histology	Ongoing study treatment Y/N	PR confirmed Y/N	Number of prior lines
Patient 5	High grade serous adenocarcinoma of the fallopian tube	Y	Y*	4
Patient 20	High grade serous adenocarcinoma, OVCA	N	Y	7 [including PD to nivolumab/lucitanib]

*Outside data cut date, confirmed by PI.

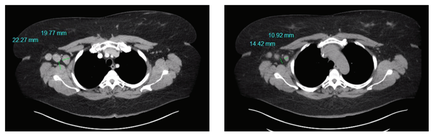
Data cut 23NOV2022

CLINICAL VIGNETTE – Patient 20

53yr old female with OVCA, histology - high grade serous adenocarcinoma.

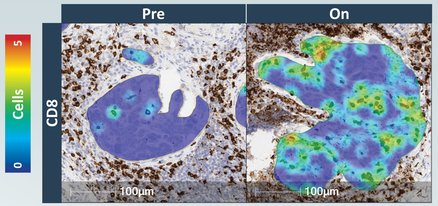
Received 7 prior lines: adjuvant carboplatin/paclitaxel [2017]. 1st line metastatic [2019]: carboplatin/ paclitaxel/bevacizumab, bevacizumab maintenance, 2nd line: carboplatin/pegylated liposomal doxorubicin, [PLD stopped for PD] and switched to carboplatin/gemcitabine, maintenance niraparib. 3rd line: pemetrexed [best response PD]. 4th line: nivolumab/ˡlucitanib (TKI) [best response PD]. 5th line: cyclophosphamide [best response SD]. 6th line [2022]: bevacizumab/cyclophosphamide [best response SD]

ˡLucitanib, is an investigational angiogenesis inhibitor, which inhibits vascular endothelial growth factor receptors 1 through 3 (VEGFR 1-3), platelet-derived growth factor receptors alpha and beta (PDGFRα/β) and fibroblast growth factor receptors 1 through 3 (FGFR 1-3).



PR – 35% reduction in target lesion at 1st post imaging assessment.

TME modulation in partial responding PATIENT [patient 20]

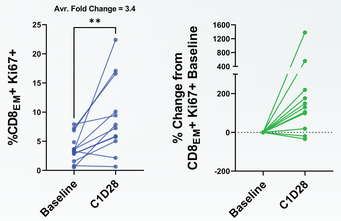


	Pre	On
% CD8 Positive in tumor area	15.7%	25.7%
Average CD8 Density (CD8/µm²)	8.5×10^{-4}	16×10^{-4}

CD8 IHC staining of patient with HGSC treated with COM701 and nivolumab, who received 7 prior lines of anti-cancer therapy (including nivolumab). The biopsy taken from lymph node shows extensive CD8 staining as expected. Focusing only on tumor nests in the pre-treatment biopsy, there are very few CD8 cells infiltrating into and between the tumor cells while in the on-treatment biopsy there is a clear infiltration of CD8 into the tumor, demonstrated by both precent of positive CD8 stain in the tumor areas and CD8 density.

CD8 cell density was calculated, using HALO Density Heatmap Algorithm, for tumor region only (blue background, selected manually) biopsy site lymph node both for PRE and ON treatment

PHARMACODYNAMIC ACTIVATION OF THE IMMUNE SYSTEM WITH STUDY TREATMENT



Translational assessment of circulating immune cells showed a positive pharmacodynamic activation of the immune system following PD1 and PVRIG blockade

With Increased proliferation of CD8+CD45RA-CCR7- effector memory (EM) T cells as reflected by increase in Ki67

REFERENCE:

1. Whelan S, Ophir E, et al. PVRIG and PVRL2 Are Induced in Cancer and Inhibit CD8+ T-cell Function. Cancer Immunol Res. 2019 Feb;7(2):257-268. **2.** Vaena, DA, Fleming GF 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). J Clin Oncol 39, 2021 (suppl 15; abstr 2504). **3.** Ursula M, Shapira-Frommer R et al. Antitumor activity and safety of pembrolizumab in patients with advanced recurrent OVCA: Final results from the P2 KEYNOTE-100 study. **4.** Ruth, P, Gutierrez, M et al. Safety and efficacy of vibostolimab (vibo) plus pembrolizumab (pembro) and coformulation of vibo/pembro in ovarian cancer naive to PD-1/PD-L1 inhibitors. In: Proceedings of the American Association for Cancer Research Annual Meeting 2022; 2022 Apr 8-13. Philadelphia (PA): AACR; Cancer Res 2022;82(12_Suppl):Abstract nr CT180 ASCO Annual Meeting 2020.

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DISCLOSURES

Oladapo Yeku, MD, PhD reports consultant payments from GIMV NV, and TigaTx Inc, and Advisory Board positions at Celldex and hC Bioscience. Massachusetts General Hospital has contracts with Ascendis Pharma A/S, Avant Immunotherapeutics, Instil Bio, Inc, and Merck Sharp & Dohme Corp, for trials where he is the local PI.

Conclusion

The combination of COM701 with nivolumab is well tolerated and has a favorable safety and toxicity profile. Encouraging preliminary antitumor activity with: ORR of 10%, DCR 45% In a heavily pretreated and heterogenous patient population. Antitumor activity in diverse histology – high-grade serous (a histological type that is typically unresponsive to checkpoint inhibitors), clear cell. A confirmed partial response in a patient previously treated with nivolumab/lucitanib [with best response of progressive disease]. Increased effector memory T cell proliferation was observed, confirming the expected immune activation induced by COM701 given in combination with nivolumab. The combination deserves further evaluation.