Durable responses with triple blockade of the DNAM-1 axis with COM701 + BMS-986207 + nivolumab in patients with platinum resistant ovarian cancer. NCT04570839.

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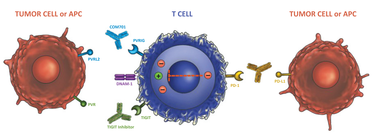
BACKGROUND

- COM701 is a novel 1st in-class immune checkpoint inhibitor (ICI) that binds to poliovirus receptor related immunoglobulin domain containing (PVRIG) leading to enhanced activation of T and NK-cells
- There is a high unmet medical need for the treatment of patients with platinum resistant high grade epithelial ovarian cancer (PROC) who have exhausted standard therapies
- Standard therapies for platinum-resistant or refractory ovarian cancer, including pegylated liposomal doxorubicin, weekly paclitaxel, and topotecan, provide limited benefits and with accompanying high level of toxic effects[1,2]
- Immune checkpoints, eg, PD-1/PD-L1 inhibitors as monotherapy or combined with a TIGIT inhibitor, have reported response rates ~10%[3-5]
- We have previously reported that blocking the DNAM-1 axis with the triplet combination of COM701 + anti-TIGIT antibody (BMS-986207) and nivolumab is very well tolerated, has a favorable safety profile and demonstrates preliminary antitumor activity[6]
- We present encouraging follow up data demonstrating long term durable responses in these patients with PROC treated with the COM701 triplet combination

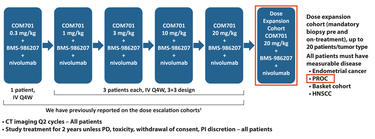
DNAM-1 AXIS PATHWAY

PVRIG may be the missing piece when current checkpoint inhibitors fail



- Two parallel and complementary inhibitory pathways (PVRIG & TIGIT) – discovered by Compugen's computational discovery platform
- Potential intersection between PVRIG/TIGIT and PD-1 pathway

STUDY DESIGN



- CT imaging Q2 cycles – All patients
- Study treatment for 2 years unless PD, toxicity, withdrawal of consent, PI discretion – all patients

In this study we report on long term follow up of PROC expansion cohort.

METHODS

- As part of an expansion cohort, we enrolled 20 patients with platinum resistant high grade epithelial ovarian cancer, primary peritoneal cancer, fallopian tube cancer
- All patients received COM701 20 mg/kg + BMS-986207 480 mg + nivolumab 480 mg. All study drugs IV Q4W
- Investigator assessment of antitumor activity evaluated per RECIST v1.1 with CT imaging every 8 weeks starting from the first dose during the first 6 cycles of the study and every 16 weeks thereafter (or at any time point progressive disease is suspected)
- Safety per CTCAE v5.0
- All patients received study treatment for 2 years until progressive disease, toxicity, withdrawal of consent or investigator discretion

KEY ELIGIBILITY CRITERIA AND STUDY OBJECTIVES (PROC EXPANSION COHORT)

Key Inclusion Criteria:

- Age ≥ 18 years
- Histologically confirmed high grade epithelial ovarian cancer
- Subject must have platinum refractory/resistant ovarian cancer defined as refractoriness to platinum-containing regimen or disease recurrence <6 months after completion of a platinum-containing regimen
- Prior PARP inhibitor therapy permissible
- Measurable disease
- Mandatory biopsy: pre and on-treatment
- No limitation on the number of prior lines of therapy

Key Exclusion Criteria:

- Active autoimmune disease requiring systemic treatment
- History of immune-related toxicities on prior immunotherapy treatment leading to discontinuation
- Prior receipt of anti-PVRIG antibody, anti-TIGIT antibody, PD-1/PD-L1 inhibitor, anti-CTLA-4 antibody, anti-OX-40 antibody, anti-CD137 antibody

Key Primary Objective:

- Safety and tolerability profile of the triplet combination

Secondary Objectives:

- Immunogenicity of the triplet
- Antitumor activity of the triplet

Exploratory Objective:

- Pharmacodynamic activity of the triplet

DEMOGRAPHICS

Characteristics	
Age, n (%)	
≤ 65 years	10 (50)
ECOG (0, 1)	
1	14 (70)
Histology	
High grade serous	11 (55%)
Clear cell	3 (15%)
Not available	6 (30%)
Prior bevacizumab-containing regiment	16 (80%)
Prior PARP inhibitor	6 (30%)
Median (min, max) number of prior lines of therapy	4 (1, 10)

PATIENT DISPOSITION SUMMARY

Parameter	COM701 + BMS-986207 + nivolumab n=20 (%)
Number of patients treated	20 (100)
Discontinued study treatment	17 (85)
Reasons for study treatment discontinuation	
PD per RECIST v1.1	12 (71)
PD (clinical evaluation)	2 (12)
Withdrew consent	1 (6)
Adverse event*	1 (6)
Death (due to progressive disease)	1 (6)

Data cut off date 05SEP2023.
*G3/G2 AST/ALT increased.

INVESTIGATOR ASSESSED RESPONSE (RECIST V1.1)

Parameter	(n=20)
ORR (CR+PR)*	4 (20.0) (95% CI: 12.8, 29.6)
DCR (CR+PR+SD)†	9 (45.0) (95% CI: 35.4, 55.0)
Best response	
PR	4 (20.0)
SD	5 (25.0)
PD	9 (45.0)

Data cut off date 05SEP2023. Patient 3 and Patient 6 deceased before reaching the assessment.
DCR, disease control rate; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.
*ORR is defined as confirmed CR or PR.
†DCR includes BOR as CR, PR, or SD.

SUMMARY OF TREATMENT RELATED ADVERSE EVENTS

	All TRAE (n=20)
Any TRAE	9 (45.0)
No TRAEs	11 (55.0)
Grade 1	1 (5.0)
Grade 2	2 (10.0)
Grade 3	6 (30.0)
Grade 4	-
Grade 5	-
TRAE resulting in study treatment discontinuation	1 (5.0)*
Any serious TRAE	2 (10.0)
Grade 1	-
Grade 2	1 (5.0)
Grade 3	1 (5.0)
Grade 4	-
Grade 5	-
Serious TRAE resulting in study treatment discontinuation	-

Treatment related adverse events include any AE with start date on or after first dose date and up to data cut off date 05SEP2023.
*G3: ALT/AST increased.

INCIDENCE OF TREATMENT RELATED AEs (AT LEAST 2 PATIENTS)

Preferred Term	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4/5 n (%)	All Grades n (%)
Any TRAE	1 (5.0)	2 (10.0)	6 (30.0)	-	9 (45.0)
Diarrhoea	2 (10.0)	1 (5.0)	1 (5.0)	-	4 (20.0)
Nausea	3 (15.0)	1 (5.0)	-	-	4 (20.0)
Anaemia	-	2 (10.0)	1 (5.0)	-	3 (15.0)
Alanine aminotransferase increased	-	1 (5.0)	1 (5.0)	-	2 (10.0)
Aspartate aminotransferase increased	-	1 (5.0)	1 (5.0)	-	2 (10.0)
Dry mouth	2 (10.0)	-	-	-	2 (10.0)
Fatigue	1 (5.0)	1 (5.0)	-	-	2 (10.0)
Hyponatraemia	2 (10.0)	-	-	-	2 (10.0)
Pyrexia	-	1 (5.0)	-	-	2 (10.0)

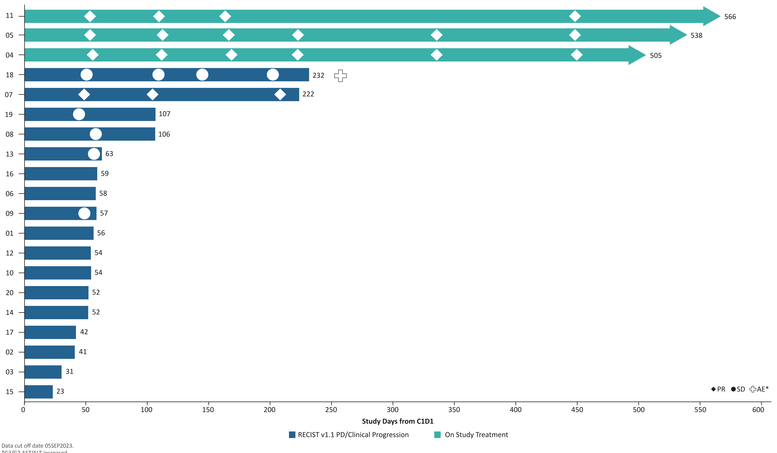
Treatment related adverse events include any AE with start date on or after first dose date and up to data cut off date 05SEP2023 (inclusive).
Preferred terms are sorted in descending frequency of All Grades column then alphabetically.
A patient with multiple occurrences of a AE under one arm is counted only once in the AE category for that arm.

PATIENT INCIDENCE OF SERIOUS TRAE – ALL PATIENTS

Preferred Term	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4/5 n (%)	All Grades n (%)
Any serious TRAE	-	1 (5.0)	1 (5.0)	-	2 (10.0)
Hypercalcaemia	-	-	1 (5.0)	-	1 (5.0)
Pyrexia	-	1 (5.0)	1 (100)	-	1 (5.0)

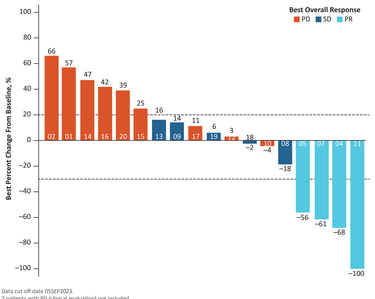
Treatment related adverse events include any AE with start date on or after first dose date and up to data cut off date 05SEP2023 (inclusive).
Preferred terms are sorted in descending frequency of All Grades column.
A patient with multiple occurrences of a AE under one treatment is counted only once in the AE category for that treatment.
A patient with multiple adverse events is counted only once in All Grades.

SWIMMER PLOT



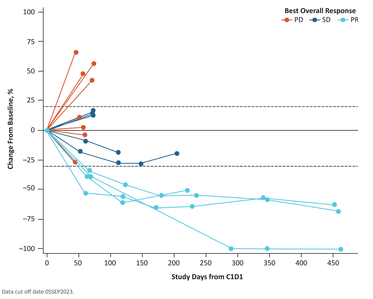
Data cut off date 05SEP2023.
*G3/G2 AST/ALT increased.

WATERFALL PLOT



Data cut off date 05SEP2023.
2 patients with PD (clinical evaluation) not included.

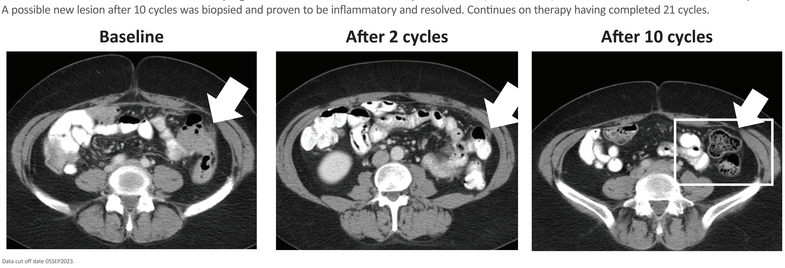
SPIDER PLOT



Data cut off date 05SEP2023.

CLINICAL VIGNETTE – PATIENT 11 WITH PARTIAL RESPONSE

51F with ovarian clear cell carcinoma previously treated with surgery followed by 6 cycles adjuvant carboplatin, paclitaxel, bevacizumab and continued on maintenance bevacizumab for 3 months until progression of disease. Started on study with COM701, BMS-986207, nivolumab. Noted to have PR after 10 cycles. A possible new lesion after 10 cycles was biopsied and proven to be inflammatory and resolved. Continues on therapy having completed 21 cycles.



Data cut off date 05SEP2023.

CONCLUSIONS

- We report durable partial responses in patients with high grade epithelial PROC treated with the combination of COM701 with nivolumab and BMS-986207 is well tolerated and has a favorable safety and toxicity profile with no new safety signals
- Investigator assessed partial response 4/20 [20%]
- Median duration of response not reached in the 4 subjects with partial responses
- There are 3 patients continuing on study treatment:
  - 505 days (16.6 months)
  - 538 days (17.7 months)
  - 566 days (18.6 months)
- While the dataset are small, the duration of response compares favorably to median DOR [6.9 months] recently reported with mirvetuximab[7]
- The data adds to prior disclosures on antitumor activity in multiple tumor types [anal SCC, NSCLC, MSS-CRC with liver metastases, PROC] of COM701 in combination with nivolumab +/- BMS-986207 in patients with prior treatment refractory disease or PD after prior exposure to ICI[6,8-12]
- Baseline PVRL2 expression levels in PROC patients treated with COM701 + nivolumab +/- BMS-986207 is associated with clinical benefit[13]
- This data supports Compugen's DNAM-1 axis hypothesis and strengthens the need for further development of this drug combination as cancer immunotherapy

REFERENCES

1. Pujade-Lauraine et al., JCI 2014 **2.** Secord et al., JCO 2007 **3.** Matulonis et al., ASCO 2022 **4.** Holmes et al., JCO-ASCO 2022 **5.** Pereira et al ACCR 2022 **6.** Mooney J, et al., ESMO-IO 2022 **7.** Elahare Prescribing information **8.** Vaena D.A. et al., ASCO, 2021 **9.** Sullivan, R.J. et al., AACR, 2020. **10.** Overman, M. J. et al., SITC 2022. **11.** Yeku, O, et al., ESMO-IO 2022 **12.** Sullivan R, et al., ESMO-IO, 2022 **13.** Cojocaru G, et al., SITC 2023

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