The combination of COM701 + BMS-986207 + nivolumab demonstrates preliminary anti-tumor activity in patients with recurrent, metastatic MSS endometrial cancer. NCT04570839.

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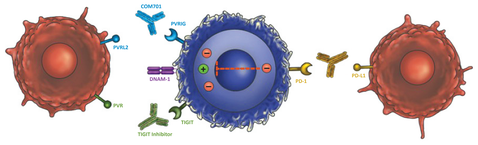
Abstract Number 5595

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
- BMS-986207 is an ICI and anti-TIGIT antibody
- Nivolumab is an ICI that has been well described
- We have previously reported that the triplet [COM701 + BMS-986207 + nivolumab] is very well tolerated, has a favorable safety profile and demonstrates preliminary anti-tumor activity[1,2]
- There is a high unmet medical need for the treatment of patients with microsatellite stable [MSS], recurrent, metastatic, endometrial cancer.
- We hypothesized that in patients with MSS-endometrial cancer blocking the DNAM-1 axis with a triplet combination consisting of COM701, nivolumab and BMS-986207 will have an acceptable safety/tolerability profile and also demonstrate anti-tumor activity
- We present preliminary results on safety, tolerability, translational pharmacodynamic readouts and anti-tumor activity

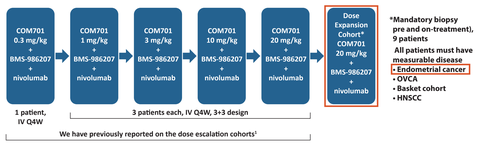
DNAM-1 Axis Pathway

Blocking 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 synergy between PVRIG/TIGIT and PD-1 pathway

STUDY DESIGN



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

In this study we report on 9 patients [red boxes above]:

- Combination dose expansion - in addition to COM701; all patients received BMS-986207 + nivolumab both 480mg all study treatment IV Q4W

METHODS

- As part of an expansion cohort, we enrolled 9 patients with MSS, recurrent, metastatic endometrial cancer
- All pts received COM701 20 mg/kg + BMS-986207 480 mg + nivolumab 480 mg. All IV Q4W
- Anti-tumor activity (per investigator) was 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
- Study treatment for 2yrs unless PD, toxicity, withdrawal of consent, PI discretion

KEY ELIGIBILITY CRITERIA AND STUDY OBJECTIVES [MSS-EC COHORT]

Key Inclusion Criteria:

- Age ≥ 18 yrs
- Histologically confirmed endometrial cancer
- Documented MSS status by an FDA approved test e.g. genomic testing or IHC
- Disease progression with ≤2 prior systemic cytotoxic therapies
- Prior PD-1/PD-L1 permissible
- Measurable disease

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
- Prior receipt of Anti-TIGIT antibody

Key Primary Objective:

- Safety and tolerability of profile of the triplet combination

Secondary Objectives:

- Immunogenicity of the triplet
- Anti-tumor activity of the triplet

Exploratory Objective:

- Pharmacodynamic activity of the triplet

DEMOGRAPHICS

	COM701 + BMS-986207 + nivolumab N=9 [%]
Sex, Female	9 [100]
Age [yr], ≥65	6 [67]
ECOG [0, 1]	
0	3 [33]
Race [white]	8 [89]
Median prior lines of therapy [range]	2 [1, 3]
Prior cytotoxic therapy	9 [100]
Prior anti-PD1/PD-L1	3 [33]

Data cut date 04/10/2023.

PATIENT DISPOSITION SUMMARY

Parameter	COM701 + BMS-986207 + nivolumab N=9 (%)
Number of patients treated	9 [100]
Discontinued study treatment	9 [100]
Reasons for study treatment discontinuation	
PD per RECIST v1.1	5 [56]
PD [clinical evaluation]	1 [11]
Withdrew consent	1 [11]
Adverse event	1 [11]
Death [due to progressive disease]	1 [11]

Data cut date 04/10/2023.

SUMMARY OF INVESTIGATOR-ASSESSED RESPONSE [RECIST V1.1]

Parameter	COM701 + BMS-986207 + nivolumab n=9 [%]
ORR [CR+PR]	2 [22] [95% CI: 3, 60]
Disease control rate [CR+PR+SD]	4 [44] [95% CI: 14, 79]
Best response	
CR	-
PR [confirmed]	2 [22]
SD	2 [22]
PD	5 [56]

Patient 003 with confirmed PR, delayed data entry. Data cut date 04/10/2023.

PATIENT INCIDENCE OF TREATMENT-RELATED ADVERSE EVENTS – ALL PATIENTS

Preferred Term (PT)	Grade 1/2 n [%]	Grade 3 n [%]	Grade 4/5 n [%]	All Grades n [%]
Any TRAE	5 [56]	2 [22]		7 [78]
Arthritis	1 [11]	-	-	1 [11]
Backpain	1 [11]	-	-	1 [11]
Chills	1 [11]	-	-	1 [11]
Headache	1 [11]	-	-	1 [11]
Lipase increased	1 [11]	-	-	1 [11]
Myalgia	1 [11]	-	-	1 [11]
Pneumonitis	-	1 [11]	-	1 [11]
Pruritus	1 [11]	-	-	1 [11]
Pyrexia	1 [11]	-	-	1 [11]
Small intestinal obstruction	-	1 [11]	-	1 [11]

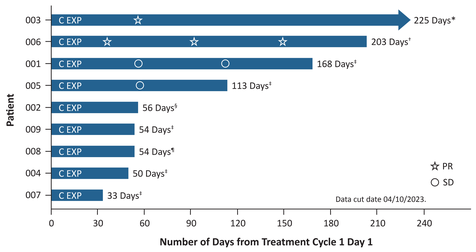
Data cut date 04/10/2023.

PATIENT INCIDENCE OF SERIOUS TRAE – ALL PATIENTS

Preferred Term (PT)	Grade 1/2 n [%]	Grade 3 n [%]	Grade 4/5 n [%]	All Grades n [%]
Any serious TRAE	-	2 [22]		2 [22]
Pneumonitis	-	1 [11]	-	1 [11]
Small intestinal obstruction	-	1 [11]	-	1 [11]

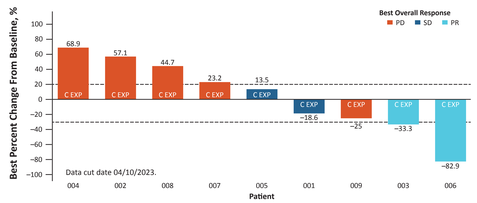
Data cut date 04/10/2023.

SWIMMER PLOT



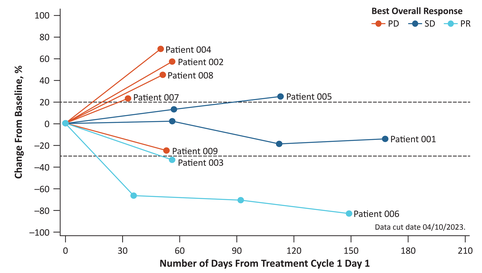
Patient 003 had additional imaging assessments for confirmation of PR prior to data cut date. However delayed data entry at data cut date.
All patients received COM701 20 mg/kg + BMS-986207 480 mg + nivolumab 480 mg. All IV Q4W.
C EXP: combination expansion.
*Discontinued study treatment due to AE [pneumonitis]. PR maintained at time of AE. Patient off study treatment, but ongoing study imaging assessments. †Death [due to progressive disease] ‡PD [RECIST v1.1] §Consent Withdrawn ¶PD [clinical evaluation]

WATERFALL PLOT



All patients received COM701 20 mg/kg + BMS-986207 480 mg + nivolumab 480 mg. All IV Q4W. C EXP: combination expansion.

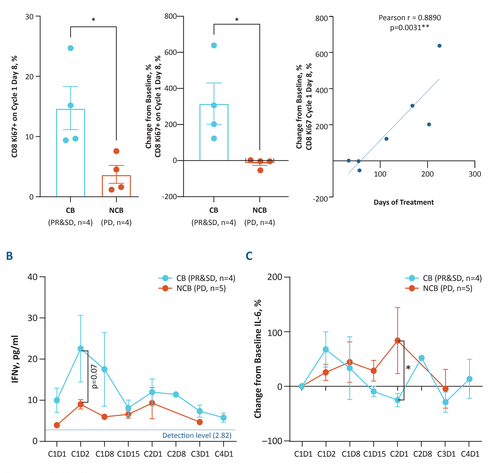
SPIDER PLOT



All patients received COM701 20 mg/kg + BMS-986207 480 mg + nivolumab 480 mg. All IV Q4W. C EXP: combination expansion.

TRANSLATIONAL PHARMACODYNAMIC READOUTS

- Translational assessment of peripheral blood, including profiling of cytokines and circulating immune cells, clearly showed a positive pharmacodynamic activation of the immune system following PD1/TIGIT/PVRIG blockade, which correlates with days of treatment and clinical benefit (CB), ie PR and SD>100 days.
  - (A) Increased proliferation of CD8 T cells, as reflected by increase in Ki67, 8 days post first treatment (C1D8), both by raw values and percent of change compared to baseline, among patients with clinical benefit compared to patients with progressive disease as best response, which also positively correlates to days of treatment.
  - (B) Overall increase in serum IFNγ (C1D2, C1D8) compared to baseline, which trends to be higher among patients with clinical benefit.
  - (C) Serum IL-6 reduction at D28 post first treatment (C2D1), among patients with clinical benefit compared to patients with progressive disease.

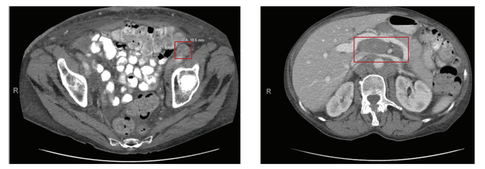


Data cut date 04/10/2023.

CLINICAL VIGNETTE - PATIENT 006 WITH CONFIRMED PARTIAL RESPONSE

- 71yr old female, ECOG 0 with stage III endometrial cancer [histology - endometrial carcinosarcoma] initially diagnosed 2020, diagnosed stage IV 2022. MSS by IHC. Received 2 prior lines: adjuvant carboplatin/paclitaxel [2020]. 1st line metastatic [2021]: pembrolizumab + lenvatinib [best response PD]

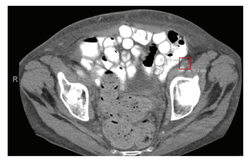
Pre-treatment Imaging Assessment



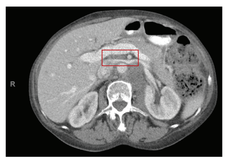
B: 21.3 mm; A: 18.6 mm

B: 25.9 mm; A: 51 mm

1st Post-treatment Imaging Assessment



B: 10.0 mm; A: 11.3 mm



B: 28 mm; A: 6.7 mm

CONCLUSIONS

- The triplet combination of COM701 with nivolumab and BMS-986207 is well tolerated and has a favorable safety and toxicity profile with no new safety signal
- The triplet combination demonstrates encouraging preliminary signal of anti-tumor activity in pts with microsatellite stable recurrent, metastatic endometrial cancer
  - Confirmed partial responses in 2/9 [ORR 22%] patients
  - Disease control rate 4/9 [44%] patients
  - Patients with clinical benefit (PR+SD>100 days) had early pharmacodynamic activation as shown by peripheral IFNγ and CD8 T cell proliferation increase at first cycle and IL-6 decrease at cycle 2 compared to patients with progressive disease
- Confirmed partial response reported with the triplet combination in a patient with endometrial carcinosarcoma and prior treatment refractory disease to standard of care treatment with lenvatinib + pembrolizumab
  - On study treatment with the triplet combination for 203 days
- The data adds to prior disclosures on anti-tumor activity in multiple tumor types [anal SCC, NSCLC, MSS-CRC with liver metastases, OVCA] of COM701 in combination with nivolumab +/- BMS-986207 in patients with prior treatment refractory disease or PD after prior exposure to ICI[2-7]
- This data supports Compugen's DNAM-1 axis hypothesis and strengthens the need for further development as cancer immunotherapy

REFERENCES

1. Dumbrava E E, et al., SITC 2021 **2.** Moroney J, et al., ESMO-IO 2022 **3.** Yeku O, et al., ESMO-IO 2022 **4.** Sullivan R, et al., ESMO-IO, 2022 **5.** Overman M J, et al., SITC 2022 **6.** Vaena D A, et al., ASCO 2021 **7.** Sullivan R, et al., AACR, 2020

ACKNOWLEDGMENTS

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