The combination of COM701 + nivolumab demonstrates preliminary antitumor activity in patients with metastatic breast cancer. NCT03667716.

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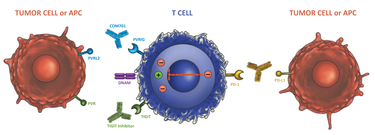
Abstract Number 640

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 metastatic breast cancer who have exhausted standard therapies
- Immune checkpoint inhibitors have limited activity in patients with metastatic breast cancer
- We have previously reported preliminary antitumor activity of COM701 + nivolumab with complete response and partial responses in patients with metastatic solid tumors that have exhausted available standard therapies such as anal squamous cancer[1], MSS-CRC[2,3], high grade platinum resistant ovarian cancer (PROC)[4] and that the combination has a favorable safety profile and is well tolerated
- We have explored preliminary antitumor activity in patients with metastatic breast cancer
- We present preliminary data on safety, tolerability and preliminary antitumor activity in patients with metastatic breast cancer

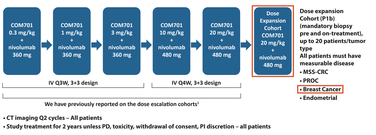
DNAM-1 AXIS PATHWAY

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



In this study we report on the 17 patients enrolled in the breast cancer expansion cohort and treated with the combination.

METHODS

- As part of an expansion cohort, we enrolled 17 patients with metastatic breast cancer
- All patients received COM701 20 mg/kg + 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 v4.03
- All patients received study treatment for 2 years until progressive disease, toxicity, withdrawal of consent or investigator discretion

KEY ELIGIBILITY CRITERIA AND STUDY OBJECTIVES (BREAST CANCER EXPANSION COHORT)

Key Inclusion Criteria:

- Age ≥ 18 years
- Histologically confirmed locally advanced or metastatic breast cancer (regardless of ER/PR andHER2 status)
- Subject must have exhausted standard therapies
- Measurable disease
- Mandatory biopsy: pre and on-treatment
- No limitation on the number of prior lines of therapy
- Prior treatment with anti-PD-(L)-1, anti-CTLA-4 ICI permissible

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

Key Primary Objective:

- Safety and tolerability of profile of the combination

Secondary Objectives:

- Immunogenicity of the combination
- Antitumor activity of the combination

Exploratory Objective:

- Pharmacodynamic activity of the combination

DEMOGRAPHICS

Parameter	COM701 + nivolumab n=17 (%)
Age ≤ 65 years	16 (94)
Prior lines, median (min, max)	6 (2, 10)
Race (white)	9 (53)
Prior anti-PD-(L)1	2 (9)
ECOG (0, 1)	
0	6 (35)

BASELINE CHARACTERISTICS

Parameter	COM701 + nivolumab n=17 (%)
ER or PR Status	
Positive	7 (41)
Negative	7 (41)
Missing	3 (18)
HER-2 status	
Negative	11 (65)
Missing	5 (29)
Positive	1 (6)
Prior anti-PD-(L)1	2 (9)
PD-L1 expression	
Positive/Present	4 (24)
Negative	9 (53)
Missing	4 (24)
Tumor mutation burden	
Low (<10 mut/MB)	12 (71)
Missing/not assessed	5 (29)
BRCA mutation	
No	11 (65)
Missing	5 (29)
Not done	1 (6)

PATIENT DISPOSITION SUMMARY

Parameter	COM701 + nivolumab n=17 (%)
Number of patients treated	17 (100)
Discontinued study treatment	16 (94)
Reasons for study treatment discontinuation	
Progression per RECIST v1.1	13 (76)
Withdrew consent	2 (12)
Adverse event	1 (6)

INVESTIGATOR ASSESSED RESPONSE (RECIST V1.1)

Parameter	20 mg/kg (n=17) n (%)
ORR (CR+PR)	2 (11.8) (95% CI: 5.7, 21.8)
DCR (CR+PR+SD)	5 (29.4) (95% CI: 20.2, 40.5)
Best response	
CR	1 (5.9)
PR	1 (5.9)
SD	3 (17.6)
PD	11 (64.7)
Missing*	1 (5.9)

Data cut off date 05SEP2023.
CR, complete response; DCR, disease control rate; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.
*Patient 7, who withdrew consent.

PATIENT INCIDENCE OF TREATMENT-RELATED ADVERSE EVENTS – ALL PATIENTS

	All TRAE (n=17)
Any TRAE	12 (71)
No TRAEs	1 (6)
Grade 1	5 (29)
Grade 2	6 (35)
Grade 3	1 (6)
Grade 4	-
Grade 5	-
TRAE resulting in study treatment discontinuation	2 (12)*
Any serious TRAE	1 (6)
Grade 1	-
Grade 2	-
Grade 3	1 (6)[‡]
Grade 4	-
Grade 5	-
Serious TRAE resulting in study treatment discontinuation	-

Data cut off date 05SEP2023.
Treatment related adverse events include any AE with start date on or after first dose date.
*G2 infusion related reaction, G2 pneumonia.
‡G3 pneumonitis.

INCIDENCE OF SERIOUS TRAE BY MAXIMUM SEVERITY (N=1)

Preferred Term	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4/5 n (%)	All Grades n (%)
Any TRAE	–	-	1 (100)	-	1 (100)
Pneumonitis	-	-	1 (100)	-	1 (100)

Data cut off date 05SEP2023.

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	5 (41.7)	6 (50.0)	1 (8.3)	–	12 (100)
Diarrhoea	2 (16.7)	–	–	–	2 (16.7)
Dyspnoea	2 (16.7)	–	–	–	2 (16.7)
Hypokalaemia	2 (16.7)	–	–	–	2 (16.7)
Infusion related reaction	–	2 (16.7)	–	–	2 (16.7)
Pyrexia	1 (8.3)	1 (8.3)	–	–	2 (16.7)

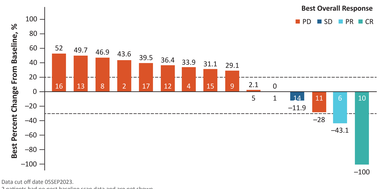
Data cut off date 05SEP2023.
Treatment related adverse events include any AE with start date on or after first dose date.
Preferred terms are sorted in descending frequency of All Grades column then alphabetically.
A patient with multiple occurrences of a AE under one treatment is counted only once in the AE category for that treatment.
A patient with multiple adverse events is count only once in All Grades. MedDRA version 23.0

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 TRAE	–	–	1 (100)	–	1 (100)
Pneumonitis	–	–	1 (100)	–	1 (100)

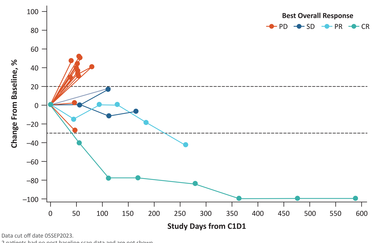
Data cut off date 05SEP2023.
Treatment related adverse events include any AE with start date on or after first dose date.
Preferred terms are sorted in descending frequency of All Grades column then alphabetically.
A patient with multiple occurrences of a AE under one treatment is counted only once in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

WATERFALL PLOT



Data cut off date 05SEP2023.
2 patients had no post baseline scan data and are not shown.

SPIDER PLOT

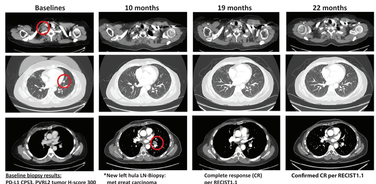


Data cut off date 05SEP2023.
2 patients had no post baseline scan data and are not shown.

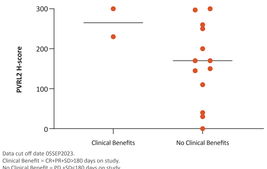
CLINICAL VIGNETTE – PATIENT 10 WITH COMPLETE RESPONSE

- **2017: Diagnosed with invasive ductal carcinoma of the right breast** (2.2 cm, high histologic grade, 0/5 LN, ER 88%, PR 0%, HER2 negative)
  - s/p R mastectomy and elective L prophylactic mastectomy, TAHBSO
  - Adj doxorubicin, cyclophosphamide, paclitaxel, followed by tamoxifen
- **2020: Recurrence in right chest wall**- 3.2 cm, high-grade, 2/12 lymph nodes (10 mm and 9 mm) ER 70%, PR 0, HER-2 non amplified
  - Docetaxel, doxorubicin, cyclophosphamide (switched to gemcitabine and carboplatin because of tolerance)
  - Chest wall resection with no residual carcinoma; followed by radiation
  - Adj Capecitabine, followed by Abemaciclib and Fulvestrant
- **2021: Metastatic recurrence in lungs and supraclavicular and hilar lymph nodes** in 2021, biopsy supraclavicular LN: ER 60% PR 0, HER2 0. PD-L1 CPS 50, TMB-low (5 Mut/Mb)]
  - Nov 2021: Fresh Biopsy supraclavicular LN at inclusion: PD-L1 CPS 50, PVRL2 tumor H-score 300;
  - Started COM701 + nivolumab
  - Aug 2022: New left hilar LN; on-treatment biopsy: met breast carcinoma ER< 2%, HER2 0, PD-L1 CPS 60
  - March 2023: Complete response (CR) per RECIST1.1 and the patient continues treatment with COM701 + nivolumab.

Pre-treatment Imaging Assessment



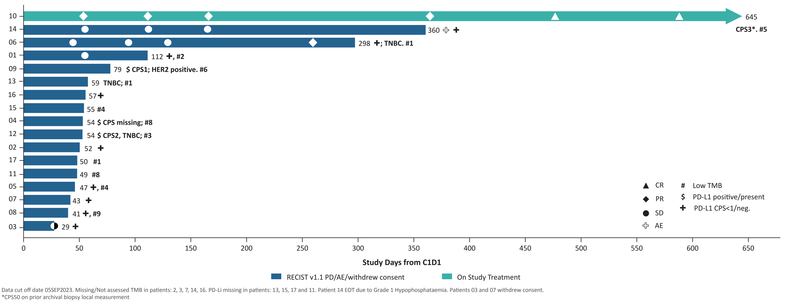
PVRL2 BASELINE LEVELS CORRELATE WITH CLINICAL BENEFIT IN BREAST CANCER PATIENTS TREATED WITH COM701 + NIVOLUMAB



IHC staining of baseline biopsies of breast cancer patients treated with COM701 + nivolumab using antiPVRL2 IHC mAb (clone 181H1L2), tumor H-score (sum of IHC intensity multiplied by precent of positive cells in each intensity), shows a trend higher expression in patients with clinical benefit as defined by RECIST 1.1

Data cut off date 05SEP2023.
Clinical Benefit = CR+PR+SD>180 days on study.
No Clinical Benefit = PD +SD<180 days on study.

SWIMMER PLOT



Data cut off date 05SEP2023. Missing/Not assessed TMB in patients: 2, 3, 7, 14, 16. PD-L1 missing in patients: 13, 15, 17 and 11. Patient 14 EOT due to Grade 1 Hypophosphataemia. Patients 03 and 07 withdrew consent.
*CPS50 on prior archival biopsy local measurement

CONCLUSIONS

- The combination of COM701 + nivolumab demonstrates preliminary antitumor activity in heavily pretreated patients with metastatic breast cancer regardless of ER/PR, HER2 status
- Investigator assessed response [CR + PR] 2/17 [12%]; disease control rate [CR + PR + SD] 5/17 [29%]
  - A complete response in a patient with ER+/PR-, low TMB [5 mut/MB] and low PD-L1 expression [CPS 3] (by sponsor central testing), refractory to last prior therapy who continues study treatment for 645 days [21 months]
  - A partial response in a patient with TNBC who received 4 prior lines of treatment, refractory to treatment [carboplatinum + gemcitabine], at study screening: PD-L1 negative, low TMB [1 mut/MB] who remained on study treatment for 298 days [~10 months]
  - All 3 patients with stable disease were PD-L1 CPS<1 and with low TMB
- The combination is well tolerated and has a favorable safety and toxicity profile with no new safety signals
- This preliminary data adds to prior promising antitumor activity of COM701 + nivolumab +/- BMS-986207 in pts with multiple tumor types, patients with prior treatment refractory disease or PD after prior exposure to ICI[1-6]
- Baseline PVRL2 expression levels are higher in patients with clinical benefit
  - This observation is in line with our finding that baseline PVRL2 expression in PROC patients treated with COM701 + nivolumab +/- BMS-986207, is associated with clinical benefit[7]
- This data supports Compugen's DNAM-1 axis hypothesis and strengthens the need for further development of COM701 drug combinations as cancer immunotherapy

REFERENCES
1. Vaena D.A. et al., ASCO, 2021 2. Sullivan, R.J. et al., AACR, 2020 3. Overman, M.J. et al., SITC 2022 4. Yeku, O, et al., ESMO-IO 2022 5. Moroney J, et al., ESMO-IO 2022 6. Sullivan R, et al., ESMO-IO, 2022 7. Cojocaru G, et al. SITC, 2023

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Some data included for completeness due to delayed data entry after the datacut date.

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