2021 ASCO ANNUAL MEETING

compugen
FROM CODE TO CURE®

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).

Daniel A. Vaena, MD

West Cancer Center and Research Institute Memphis, TN.

June 7, 2021

DANIEL A. VAENA[1], GINI F. FLEMING[2], BARTOSZ CHMIELOWSKI[3], MANISH SHARMA[4], ERIKA P. HAMILTON[5], RYAN J. SULLIVAN[6], DALE RANDALL SHEPARD[7], KYRIAKOS P. PAPADOPOULOS[8], AMITA PATNAIK[8], ADAM ELNAGGAR[1], ADEBOYE H. ADEWOYE[9], ROBINA SMITH[9], EMERSON A. LIM[10], ECATERINA E DUMBRAVA[11], DREW W. RASCO[8].

[1]WEST CANCER CENTER AND RESEARCH INSTITUTE., MEMPHIS, TN; [2]UNIVERSITY OF CHICAGO MEDICINE, CHICAGO, IL; [3]UCLA JONSSON COMPREHENSIVE CANCER CENTER, LOS ANGELES, CA; [4]START-MIDWEST, GRAND RAPIDS, MI; [5]SARAH CANNON RESEARCH INSTITUTE AND TENNESSEE ONCOLOGY, PLLC, NASHVILLE, TN; [6]MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MA; [7]CLEVELAND CLINIC TAUSSIG CANCER INSTITUTE, CLEVELAND, OH; [8]START-SAN ANTONIO, SAN ANTONIO, TX; START, SAN ANTONIO, TX; [1]WEST CANCER CENTER, MEMPHIS, TN; [9]COMPUGEN USA INC., SOUTH SAN FRANCISCO, CA; [10]COLUMBIA UNIVERSITY-HERBERT IRVING COMPREHENSIVE CANCER CENTER, NEW YORK, NY; [11]THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER, HOUSTON, TX.

Disclosures

Introduction

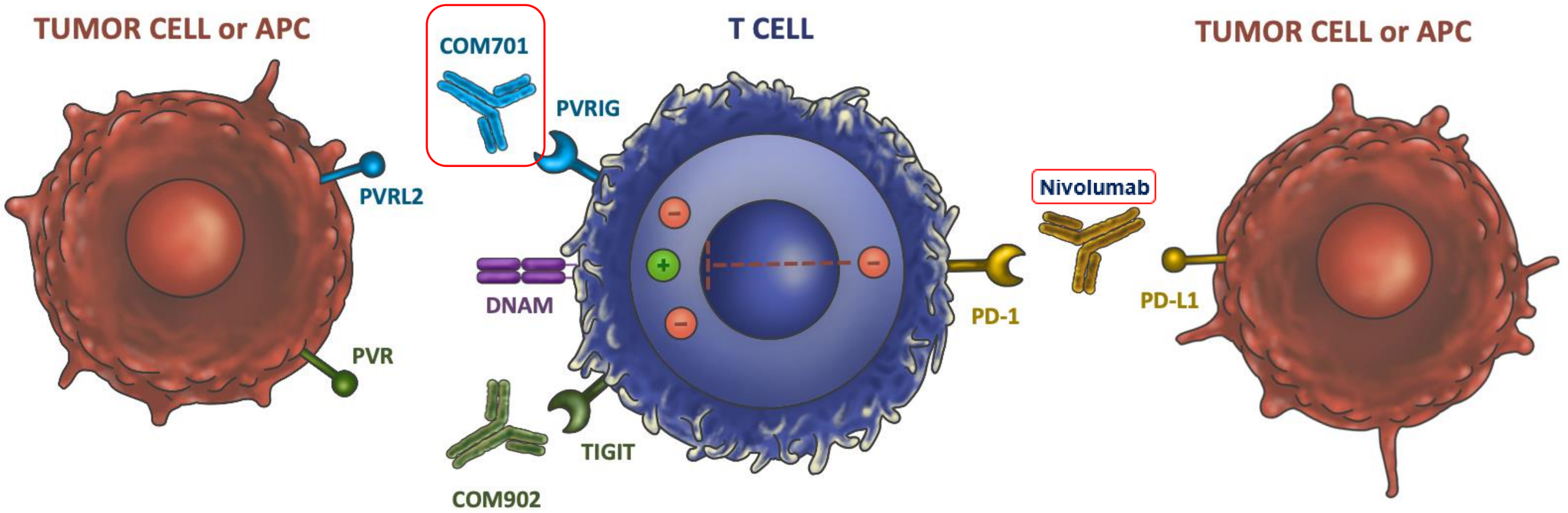
- PVRIG (poliovirus receptor related immunoglobulin domain containing) is a coinhibitory receptor expressed on T and NK cells and is part of an immune checkpoint pathway which is parallel to the TIGIT pathway and part of the DNAM-1 Axis

- COM701 is a novel first in class humanized IgG4 monoclonal antibody that binds with high affinity to PVRIG, blocking its interaction with its natural ligand PVRL2 expressed in tumor cells and antigen presenting cells and increases T and NK cell activation

- In pre-clinical models, inhibition of PVRIG leads to enhanced activation of T and NK cells, and results in tumor growth inhibition, in combination but also independent of αPD-1 treatment

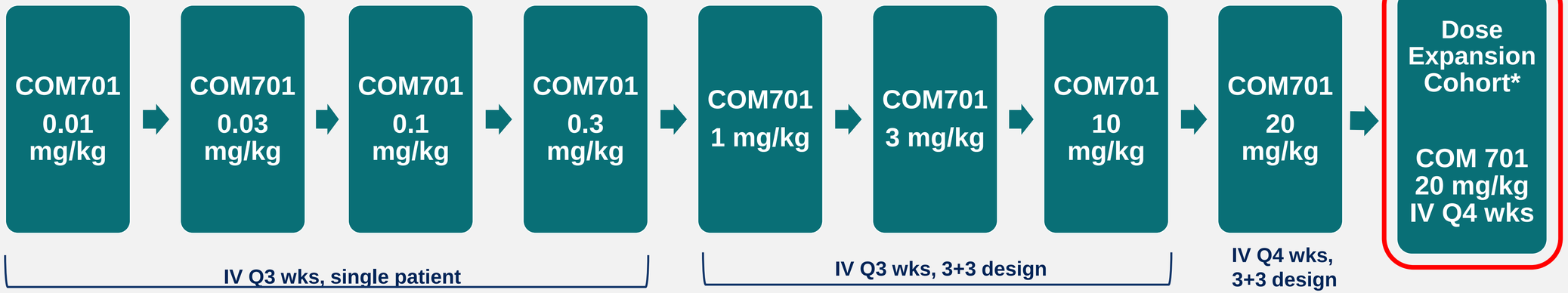
- We report updated data on the ongoing phase 1 study

PVRIG pathway in the DNAM axis



Study design

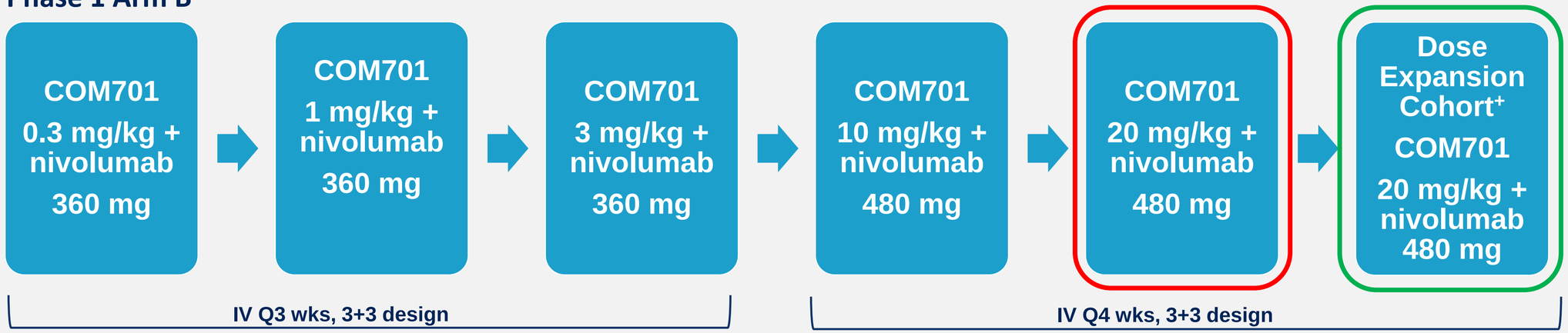
Phase 1 Arm A



*Dose expansion Cohort (mandatory biopsy pre and on-treatment) – Total 20 patients
All patients must have measurable disease

- NSCLC
- OVCA
- Breast
- Endometrial
- CRC (MSS)

Phase 1 Arm B



+Dose expansion Cohort (P1b) (mandatory biopsy pre and on-treatment) – 20 patients/tumor type
All patients must have measurable disease

- OVCA
- Breast
- Endometrial
- CRC (MSS)

- DLT evaluated in Cycle 1 Dose Escalation – Arm A and Arm B

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

Study design

- **Key Inclusion Criteria:**
  - Age ≥18 yrs
  - Histologically confirmed locally advanced or metastatic solid malignancy
  - Has exhausted all available standard treatment or is not a candidate for available standard therapy
  - ECOG 0-1
  - Measurable disease not required in dose escalation
- **Key Exclusion Criteria:**
  - Active autoimmune disease requiring systemic treatment
  - History of inflammatory pneumonitis or interstitial lung disease
  - History of immune-related toxicities on prior immunotherapy treatment leading to discontinuation
- **Key Primary Objectives:**
  - Safety and tolerability of profile of COM701 ± nivolumab
  - To identify the MTD and/or recommended dose for expansion of COM701 ± nivolumab
  - PK profile of COM701 ± nivolumab
- **Secondary Objectives:**
  - Immunogenicity of COM701 ± nivolumab
  - Antitumor activity of COM701 + nivolumab (Phase 1b only)
- **Exploratory Objectives:**
  - Antitumor activity of COM701 ± nivolumab (Phase 1a only)
  - COM701-mediated pharmacodynamic effect in blood (COM701 ± nivolumab), immune-related changes (cytokines, immunophenotyping)

Demographics

Parameter	COM701 Monotherapy n = 36 (%)	Combination n = 15 (%)
Sex, F	26 (72)	11 (73)
Age ≤ 65 yrs	22 (61)	8 (53)
Median prior therapies (range)	6 (2, 19)	5 (2, 10)
Prior immune checkpoint inhibitor (ICI) Prior ICI: COM701 monotherapy expansion cohort only	11 (31) 7 (35)	7 (47) -
Prior treatment refractory disease*	15 (42)	6 (40)
ECOG (0, 1) 0	14 (39)	4 (27)
Cancer Type	CRC (10), Pancreatic (2), Ovarian/Primary peritoneal (6), NSCLC (1), Adenoid cystic (1), melanoma (1), mesothelioma (1), Cancer of unknown primary (1), Gall bladder (1), Endometrial (4), NSCLC (4), Breast (4)	Endometrial (3), CRC (2), NSCLC (2), Neuroendocrine lung (1), Anal SCC (1), RCC (1), Mesothelioma (1), Cervical (2), Breast (1), GEJ (1)

DLT-evaluable set: patients enrolled into dose escalation, patients in COM701 monotherapy expansion cohort.

Datacut 15Apr2021

*Patients with best response of PD to last therapy immediately prior to enrollment on this study.

Patient disposition summary

Parameter	COM701 Monotherapy n = 36 (%)	Combination n = 15 (%)
Number of DLTs	-	-
Number of patients continuing study treatment	1 (3)	2 (13)
Discontinued study treatment	35 (97)	13 (87)
Reasons for study treatment discontinuation • PD per RECIST v1.1 • Physician decision/Clin PD • Adverse event • Death	 25 (69) 9 (25) - 1** (3)	 11 (73) 1 (7) 1* (7) -

DLT-evaluable set: patients enrolled into dose escalation, patients in COM701 monotherapy expansion cohort.

Datacut 15Apr2021

*G2 maculopapular rash COM701 1 mg/kg + nivolumab 360mg both IV Q3 wks.

**Progressive disease (breast cancer). COM701 monotherapy expansion COM701 20 mg/kg IV Q4 wks.

Summary of adverse events

Parameter	COM701 Monotherapy n = 38 (%)	Combination n = 16 (%)
Any TEAE	33 (87)	14 (88)
No TEAE	5 (13)	2 (13)
≤G2	19 (50)	6 (38)
G3	11 (29)	7 (44)
G4	2 (5)	-
Grade 5	1* (3)	1** (6)

Safety analysis set – patients who received ≥1 dose of any of the study drugs. Safety per CTCAE v4.03.

Datacut 15Apr2021

*Cardiac arrest. Assessed by investigator as related to disease (pancreatic cancer), not related to COM701. COM701 20 mg/kg IV Q4 wks (monotherapy dose escalation). Patient had progressive disease.

**Malignant neoplasm progression (PT), breast cancer. Dose escalation (COM701 3 mg//kg + nivolumab 360 mg, both IV Q3 wks). Assessed by investigator as related to disease, not related to any of the study drugs.

Incidence of TEAEs in ≥4 patients - monotherapy

PREFERRED TERM (PT)	Grade 1/2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)	All Grades n (%)
ANY TEAE	19 (50)	11 (29)	2* (5)	1** (3)	33 (87)
FATIGUE	12 (32)	-	-	-	12 (32)
NAUSEA	8 (21)	1 (3)	-	-	9 (24)
DIARRHOEA	6 (16)	1 (3)	-	-	7 (19)
VOMITING	6 (16)	1 (3)	-	-	7 (19)
DYSPNOEA	4 (11)	2 (5)	-	-	6 (16)
CONSTIPATION	5 (13)	-	-	-	5 (13)
ABDOMINAL PAIN	3 (8)	1 (3)	-	-	4 (11)
ANXIETY	4 (11)	-	-	-	4 (11)
ASCITES	1 (3)	3 (8)	-	-	4 (11)
HYPOMAGNESAEMIA	4 (11)	-	-	-	4 (11)
PYREXIA	4 (11)	-	-	-	4 (11)

Safety analysis set – patients who received ≥1 dose of any of the study drugs. Safety per CTCAE v4.03.

Datacut 15Apr2021

*Blood bilirubin increased (PT), Aspartate aminotransferase increased (PT) – same patient. Assessed by investigator as related to disease (Breast cancer), not related to COM701. COM701 20 mg/kg IV Q4 wks (monotherapy expansion cohort).

**Cardiac arrest. Assessed by investigator as related to disease (pancreatic cancer), patient had progressive disease, not related to COM701. COM701 20 mg/kg IV Q4 wks (monotherapy dose escalation).

Incidence of TEAEs ≥ 3 patients - combination

PREFERRED TERM (PT)	Grade 1/2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)	All Grades n (%)
ANY TEAE	6 (38)	7 (44)	-	1* (6)	14 (88)
FATIGUE	6 (38)	-	-	-	6 (38)
ANAEMIA	3 (19)	2 (13)	-	-	5 (32)
ASPARTATE AMINOTRANSFERASE INCREASED	4 (25)	-	-	-	4 (25)
NAUSEA	3 (19)	1 (6)	-	-	4 (25)
BACK PAIN	2 (13)	1 (6)	-	-	3 (19)
COUGH	3 (19)	-	-	-	3 (19)
OEDEMA PERIPHERAL	3 (19)	-	-	-	3 (19)
VOMITING	3 (19)	-	-	-	3 (19)

Safety analysis set – all patients who received ≥1 dose of any of the study drugs CTCAE v4.03.

Datacut 15Apr2021

*Malignant neoplasm progression (PT). Assessed by investigator as related to disease, not related to any of the study drugs.

Summary of investigator assessed response (RECIST v1.1)

Parameter	COM701 Monotherapy n = 36 (%)	Combination n = 15 (%)
ORR (CR+PR)	1 (3)	2 (13)
Disease control rate (CR+PR+SD)	17 (47)	10 (67)
Best response of CR, PR or SD (≥ 6 months)	5 (14)	5 (33)
Patients who received prior treatment with ICI Best response of CR, PR or SD in pts with prior treatment with ICI	11 (31) 7 (19)	7 (47) 6* (40)
Prior treatment-refractory disease Best response of CR, PR or SD in patients with prior treatment-refractory disease	15 (42) 7 (19)	6 (40) 4** (27)
Best response		
CR	-	1 (7)
PR	1 (3)	1 (7)
SD	16 (44)	8 (53)
PD	13 (36)	4 (27)
Not Assessed per RECIST v1.1 (clin PD prior to 1st imaging assessment)	6 (17)	1 (7)

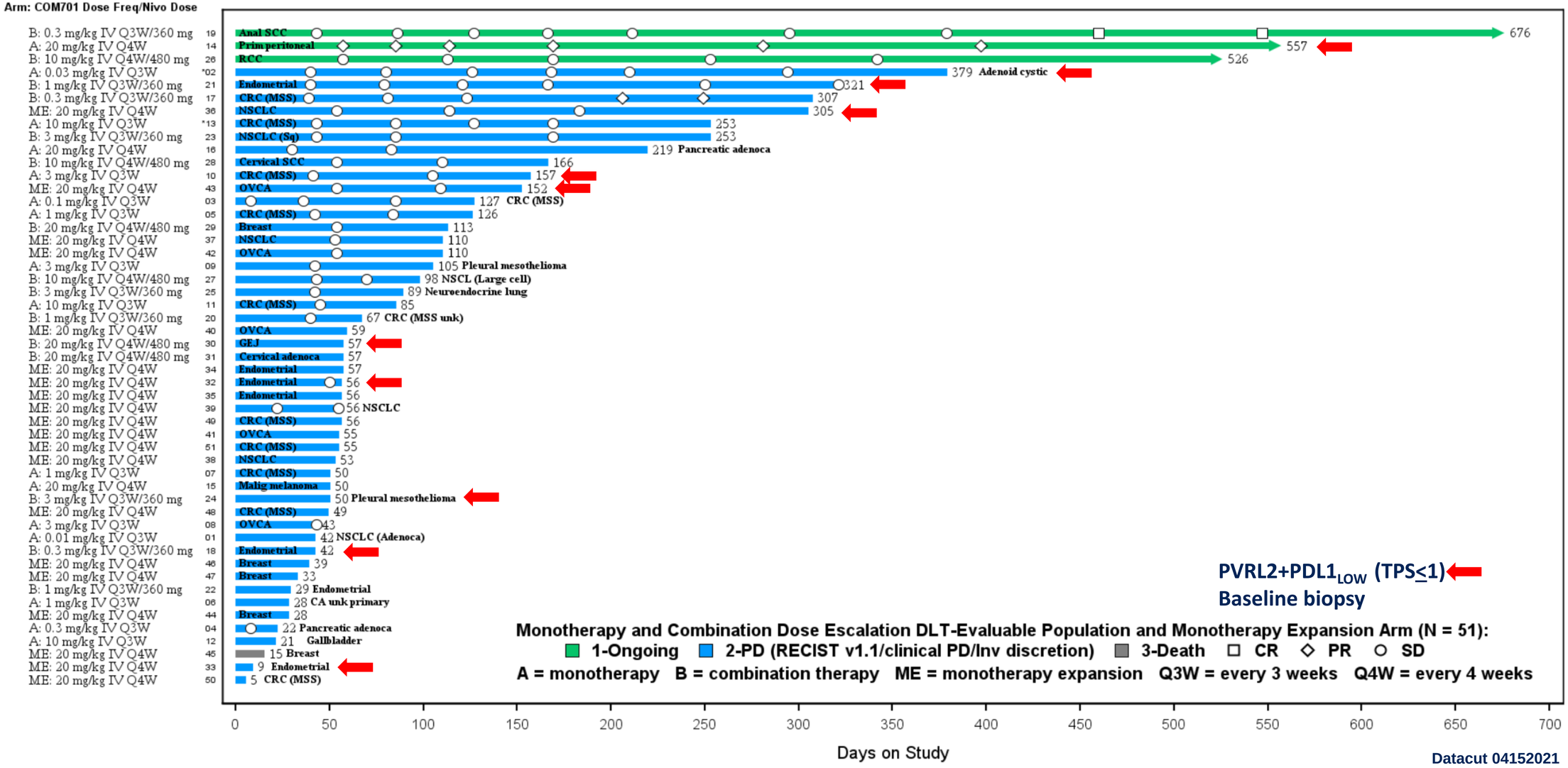
DLT-evaluable set: patients enrolled into dose escalation, patients in COM701 monotherapy expansion cohort.

- Prior treatment refractory disease: Best response of PD to last therapy prior to enrollment into this study.
- Patients who received prior treatment with ICI: Any line of therapy that includes an ICI prior to enrollment into this study.

*Includes a patient with anal SCC with confirmed CR.

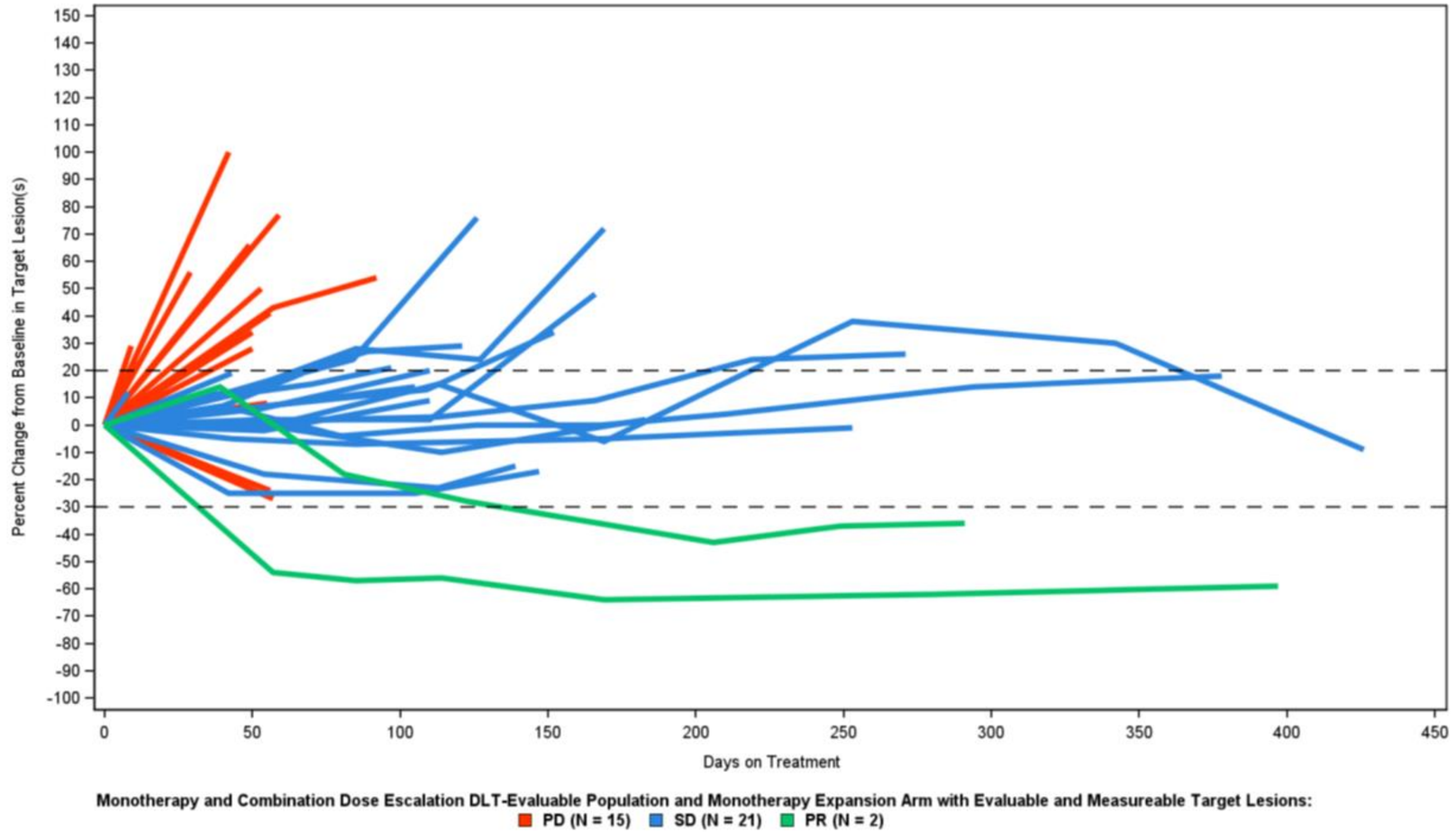
**Includes a patient with CRC (MSS) with confirmed PR.

Swimmer plot



Datacut 04152021

Spider plot

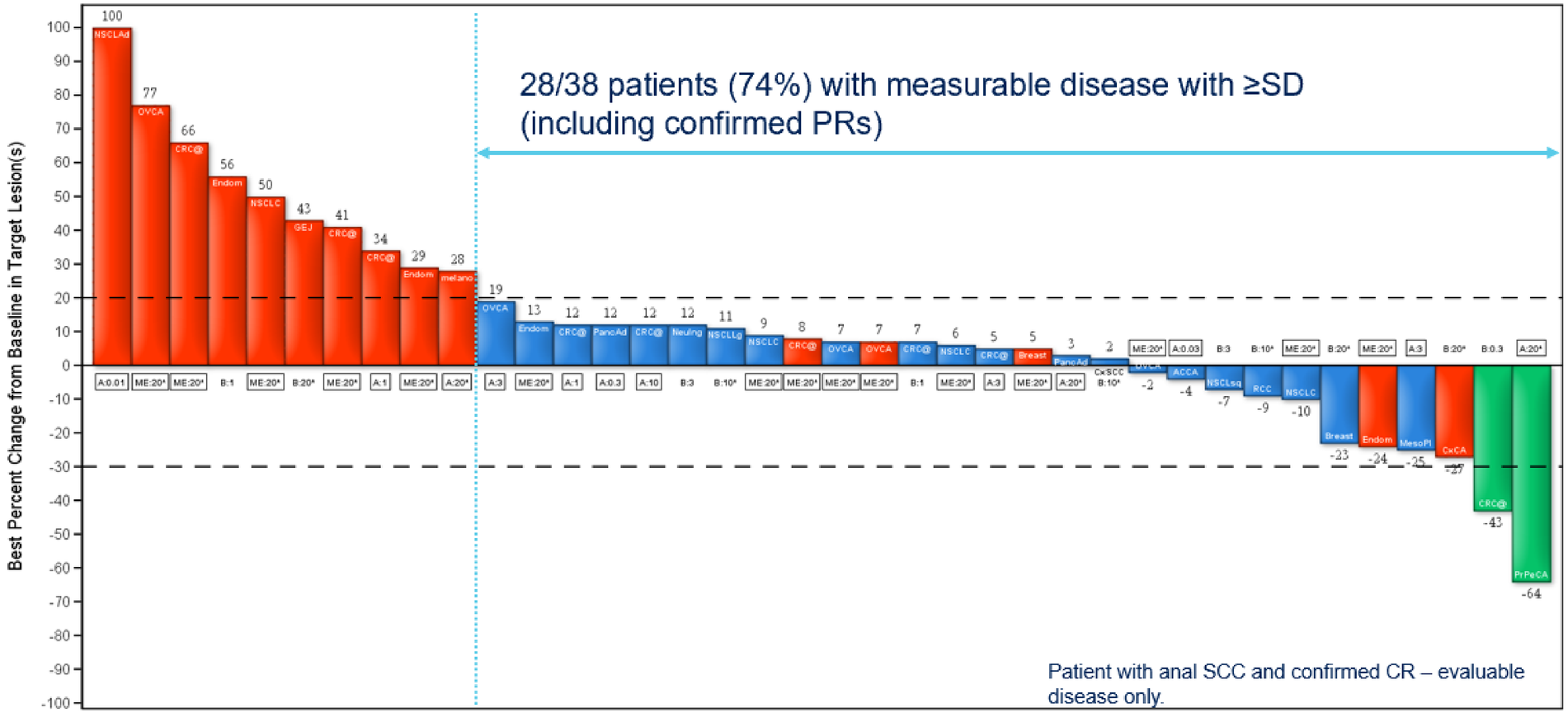


Datacut 15Apr2021

DLT-evaluable set: patients with measurable disease enrolled into dose escalation, patients in COM701 monotherapy expansion cohort.

Patient with anal SCC and confirmed CR – evaluable disease only.

Waterfall plot



Monotherapy and Combination Dose Escalation DLT-Evaluable Population and Monotherapy Expansion Arm with Evaluable and Measureable Target Lesions (N = 38):
PD SD PR @ CRC-MSS

Treatment regimen (ARM:COM701 dose (mg/kg)) is displayed along the x-axis. A = monotherapy, ME = monotherapy expansion, B = combination therapy (Nivolumab 360 mg for COM701 doses < 10 mg/kg, Nivolumab 480 mg for higher COM701 doses), * = Q4W.

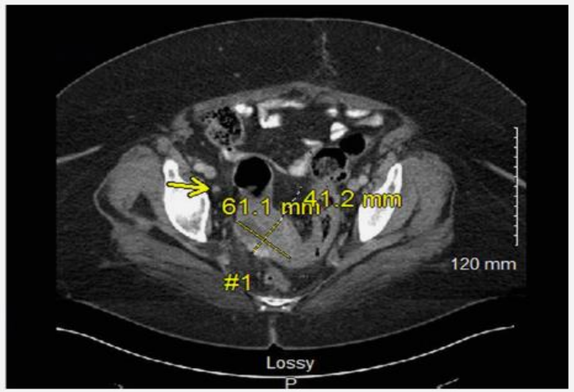
Datacut 15Apr2021

Example (1) of patient with response ongoing study treatment

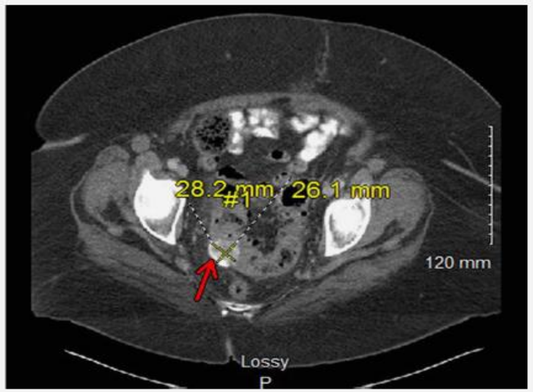
Patient with primary peritoneal cancer (platinum resistant, MSS). Confirmed PR ongoing study treatment 18 months.

Had 3 prior lines of SOC treatment (1st line carboplatin/paclitaxel SD (best response), carboplatin/paclitaxel PD (best response), Doxorubicin/Bevacizumab, PR (best response, d/c due to toxicity) and enrolled into Arm A dose escalation (COM701 20 mg/kg IV Q4 wks).

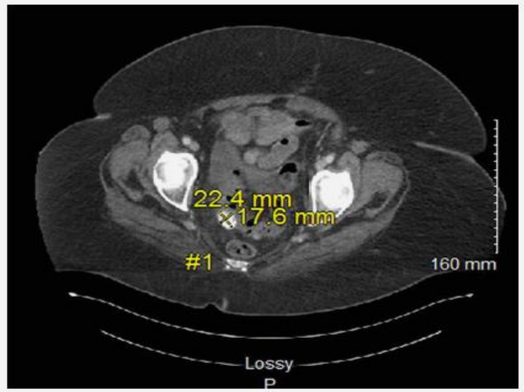
63 year old female with microsatellite stable platinum resistant primary peritoneal cancer.
PDL1 negative, MRE11 mutation; 3 prior lines of chemotherapy
Study Treatment: COM701 20 mg/kg IV Q 4 wks



Baseline: 9/11/19



C2D28: 12/2/19 (PR)



C6D28: 3/23/20 (PR)

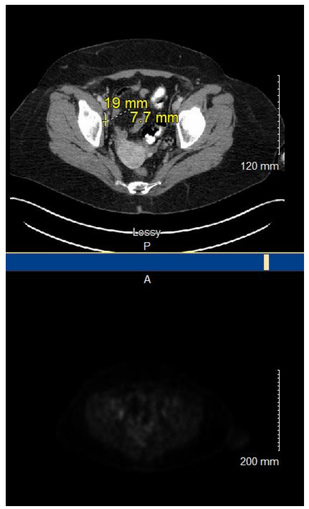
Example (2) of patient with response ongoing study treatment

57-year-old female patient with anal SCC, HPV+. Patient had evaluable disease but not measurable per RECIST v1.1 at study entry (not mandatory in dose escalation). Increasing adenopathy and SUV uptake at study entry.

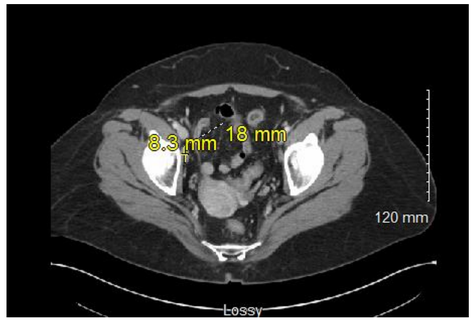
Confirmed CR ongoing study treatment 22 months. Node stable and felt to be reactive/resolved.

Had 3 prior lines of chemotherapy (5-FU/mitomycin, SD (best response), 5-FU/platinum, PR (best response for 8 months), nivolumab monotherapy, CR (best response for 9 months). Enrolled (within 1 month after progression on nivolumab monotherapy) to combination dose escalation arm: COM701 0.3 mg/kg + nivolumab 360 mg both IV Q3 wks.

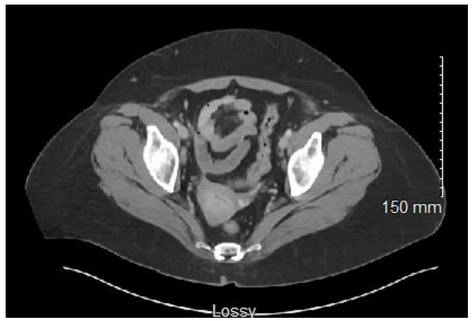
Pre-study



Baseline

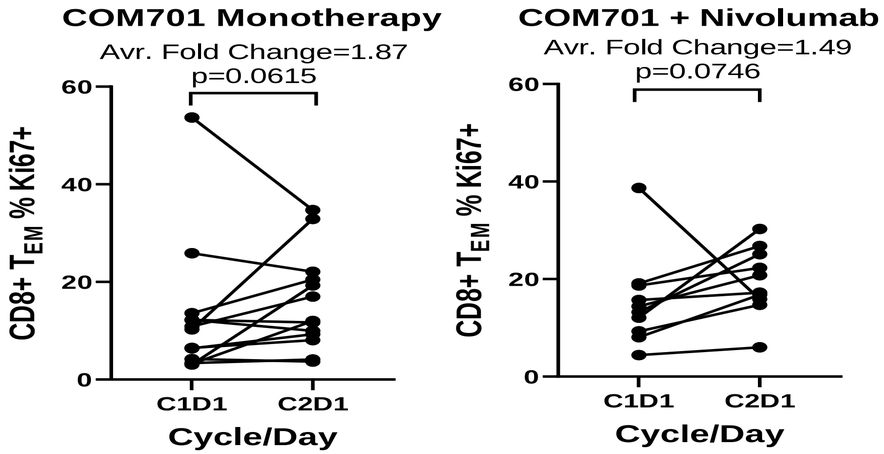


96 weeks

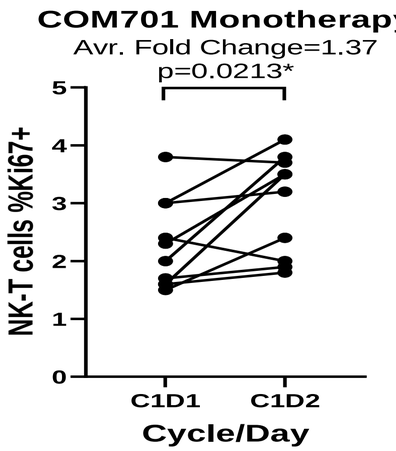


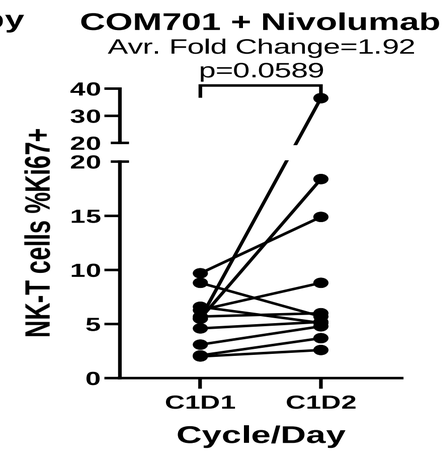
A trend of increasing proliferation of CD8+ T_{EM} (effector memory T cells) and NK-T cells in peripheral blood of both COM701 monotherapy and combination therapy patients

CD8+ T_{EM}

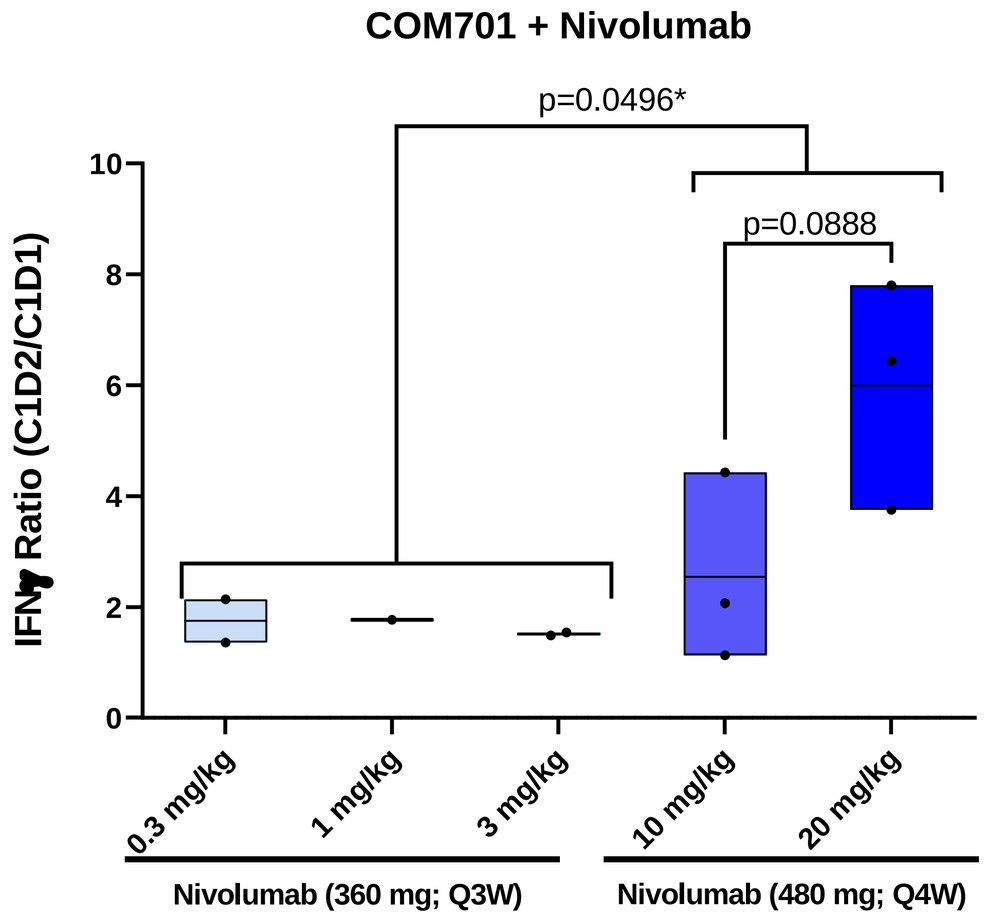


NK-T



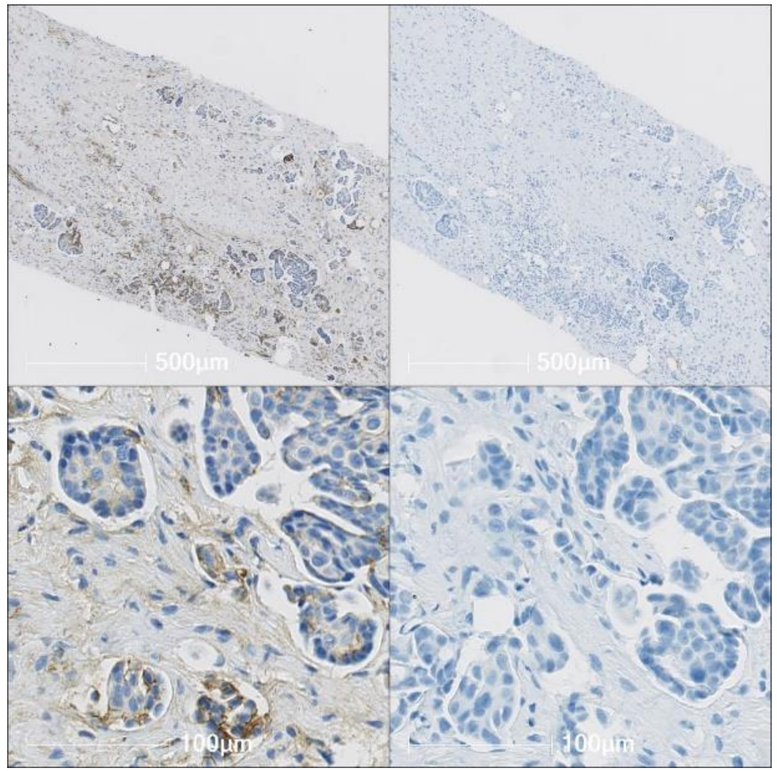


Increase in serum IFNγ upon COM701 and Nivolumab treatment with a trend for COM701 dose dependency



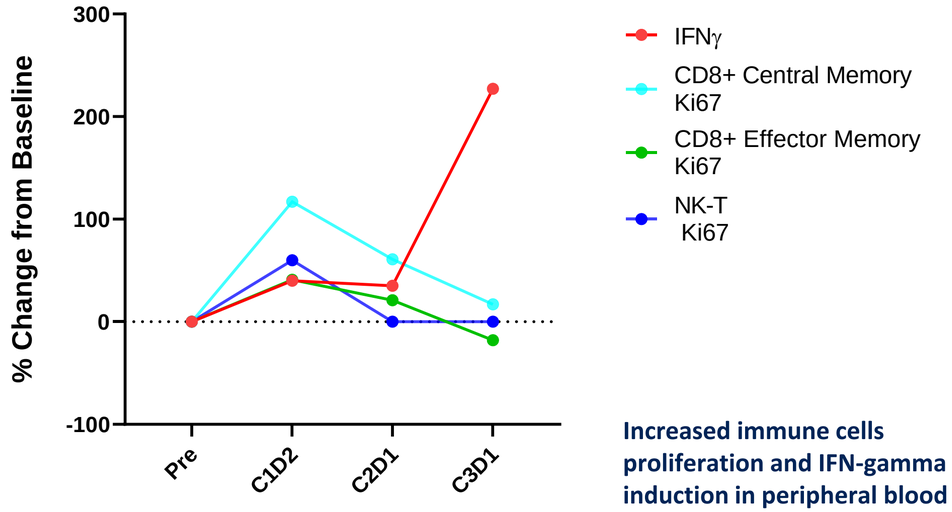
Confirmed partial response: Patient with primary peritoneal cancer (Platinum Resistant), MSS, PD-L1 Negative - COM701 20 mg/kg IV Q 4 WKS

PVRL2 | PDL1



- Pre-treatment Archival biopsy (>1 year)
- Negative PDL1 staining
- PVRL2 expression found on tumor and endothelial cells
- Immune “desert”: no immune cells detected in biopsy

Peripheral blood assessment



Increased immune cells proliferation and IFN-gamma induction in peripheral blood

PR in patient with non inflamed TME demonstrating immune activation in the blood following COM701 monotherapy treatment

Conclusions

- COM701 ± nivolumab has an acceptable safety profile and was well tolerated with no DLTs at the maximum administered doses evaluated (COM701 20 mg/kg IV Q4 wks monotherapy, COM701 20 mg/kg + nivolumab 480 mg both IV Q4 wks)
- COM701 ± nivolumab demonstrated durable antitumor activity in extensively pretreated patient population
  - CR, PR or SD ≥ 6 months in 10/51 (19%) patients
  - Best response of CR, PR or SD in 11/21 (52%) patients with prior treatment refractory disease
  - Best response of CR, PR or SD in 13/18 (72%) patients with prior treatment with immune checkpoint inhibitor
- Highlights of responding patients:
  - Confirmed CR - ongoing study treatment 22 months in a patient with anal SCC (non-measurable disease at study entry) and prior progression on nivolumab
  - Confirmed PR (ongoing study treatment 18 months in a patient with primary peritoneal cancer (platinum resistant, MSS)
  - Confirmed PR in a patient with CRC (MSS) (was on study treatment for 44 wks)
- Evidence of immune activation
  - Preliminary indication for antitumor activity in patients with $PVRL2^{+}PD\text{-}L1_{low}$ tumors
  - A trend of increasing peripheral immune cell proliferation and in serum IFNγ, suggesting immune activation by COM701
- The results of this phase 1 trial support further clinical development of COM701

Acknowledgment

- We thank the patients for participating in this clinical trial and their families, the investigators and their staff at the clinical trial sites
- Inbal Barbiro, Ilan Vaknin, Gady Cojocaru and Eran Ophir (Compugen Ltd, for analyses of biomarkers)
- Study Sponsor - Compugen Ltd in collaboration with Bristol Myers Squibb