COM902 (Anti-TIGIT antibody) monotherapy – preliminary evaluation of safety, tolerability, pharmacokinetics and receptor occupancy in patients with advanced solid tumors (NCT04354246)

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Abstract Number 477

BACKGROUND

- COM902 is an IgG4 fully human high-affinity monoclonal antibody, inhibitor of TIGIT (T cell Ig and immunoreceptor tyrosine-based inhibitory motif [ITIM] domain) binding to poliovirus receptor (PVR)
- We have previously demonstrated that COM902 enhance T and NK activity in-vitro and in-vivo[1]
- There is an unmet medical need to develop new treatment options for patients who are refractory to or relapse after treatment with current immune checkpoint inhibitors
- We hypothesized that COM902 as monotherapy will have an acceptable safety and tolerability profile in pts with advanced solid tumors who have exhausted all available standard therapies
- We present preliminary results of pts in dose escalation on safety, tolerability, antitumor activity, pharmacokinetics and immunophenotyping

METHODS

- Using an accelerated titration and 3+3 study design we enrolled 18 patients (pts) with advanced solid tumors who had exhausted all available standard therapies
- Doses of COM902 evaluated were 0.01, 0.03, 0.1, 0.3, 1, 3, 10 [mg/kg IV Q3W]
- Dose-limiting toxicity was evaluated in the 1st 21 days in the 1st cycle of dose escalation
- In the single-patient cohorts [0.01 – 0.3 mg/kg]:
  - If a single toxicity Grade ≥2 at least possibly related to COM902 is reported during the DLT period, 2 additional pts were enrolled
- Other dose cohorts utilized a 3+3 study design
- Antitumor activity was evaluated per RECIST v1.1 with CT imaging every 6 weeks starting from the first dose during the first 6 cycles of the study and every 12 weeks thereafter (or at any time point progressive disease is suspected)
- Safety assessment evaluated per CTCAE v5.0

KEY ELIGIBILITY CRITERIA AND OBJECTIVES

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

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

Primary Objectives:

- Safety and tolerability of COM902 monotherapy (dose escalation for this presentation)
- The MTD and/or recommended dose for expansion of COM902 monotherapy
- PK profile of COM902 monotherapy

Secondary Objectives:

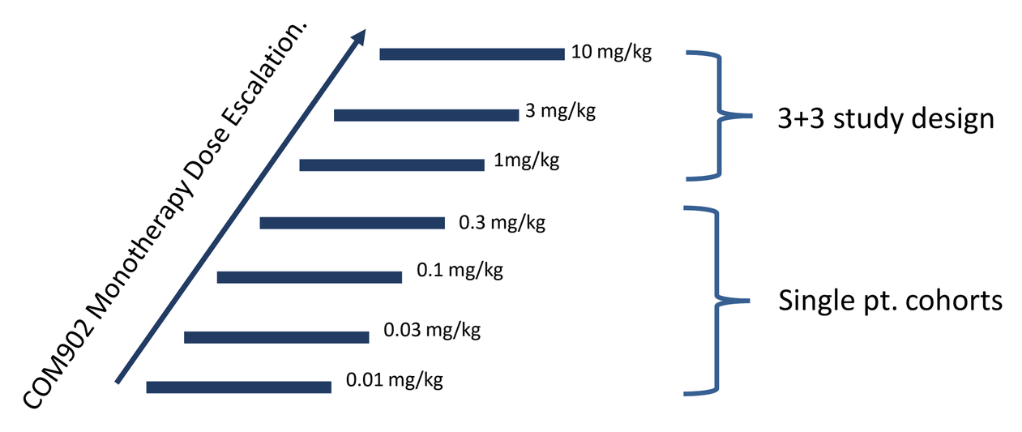
- Immunogenicity of COM902 monotherapy and in combination with COM701

Exploratory Objectives:

- Preliminary antitumor activity of COM902 monotherapy and in combination with COM701
- COM902-mediated pharmacodynamic effect in blood, immune-related changes (cytokines, immunophenotyping)

STUDY DESIGN

COM902 Monotherapy Dose Escalation: Histologically confirmed advanced solid tumors



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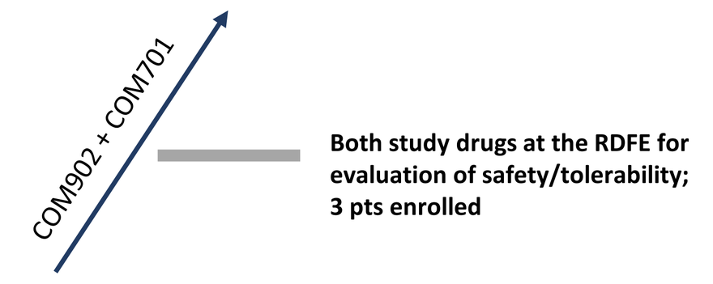
COM902 Monotherapy Expansion (N ~10 total)

Mandatory biopsy: pretreatment and on treatment
Measurable disease
- COM902 Recommended dose for expansion
- Patients with advanced solid malignancies including pts with multiple myeloma

COM902 + COM701 Safety/Tolerability Histologically confirmed advanced solid tumors



COM902 + COM701 Expansion (N ~60 total)

- Mandatory biopsy: pretreatment and on treatment
- Measurable disease per RECIST 1.1
- Approximately 20 evaluable pts each with:
  - Colorectal cancer (microsatellite stable)
  - Head and neck squamous cell cancer
  - Non small cell lung cancer

- CT imaging every 6 weeks starting from the first dose during the first 6 cycles of the study and every 12 weeks thereafter (or at any time point progressive disease is suspected).
- Study treatment for 2yrs unless PD, toxicity, withdrawal of consent, PI discretion –All pts.

RESULTS

- A total of 18 pts were treated and MTD of COM902 was not reached, COM902 was well tolerated and has a favorable safety profile
  - A pt in a single pt dose cohort [0.01 mg/kg] reported DLT of G2 vomiting and a pt [1 mg/kg] with DLT of G3 atrial fibrillation; these were assessed by the investigator as possibly related to study drug
- No DLTs were reported at any other COM902 doses including higher doses [3 mg/kg, 10 mg/kg]
- Best response of stable disease in 9 pts (50%) with 6 pts (67%) with confirmed SD and 3 pts (17%) with SD ≥6 months [includes 1pt (#08)with SD ≥6 months within the datacut date, data entry delayed]
- The most frequent TEAE was fatigue ≤2 7 pts (39%)
- Serious adverse events reported in 2 pts (11%) – G3 atrial fibrillation assessed by the investigator as possibly related to study drug; a pt with G3 acute pulmonary failure, spinal cord compression and urinary retention with widely metastatic rectal cancer (pulmonary metastases, spinal cord compression), assessed by the investigator as related to disease progression, not related to study drug
- Median (min, max) 7 (2, 16) number of prior therapies
- COM902 peripheral receptor occupancy was above 90% at doses ≥0.1 mg/kg
- Preliminary PK profiles of COM902 were generally dose proportional
- No depletion of major lymphocyte populations expressing TIGIT (NK, CD4 and CD8 T cells)

DEMOGRAPHICS

DATA CUT DATE 03SEP2021

Parameter	All Patients N=18
Sex, n (%) F M	 9 (50%) 9 (50%)
Age, n (%) ≤ 65 yrs ≥ 65 yrs	 8 (44%) 10 (56%)
Median prior therapies (range)	7 (2, 16)
ECOG (0, 1) 0 1	 5 (28%) 13 72%)
Cancer type at study entry (n)	CRC (3), Prostate (2), 1 each: Adenoid cystic carcinoma of the trachea, Atypical carcinoid lung CA, Appendiceal CA, Chordoma, Esophageal CA, Mesothelioma, Ovarian CA, Pancreatic CA, Primary peritoneal CA, Rectal CA, Renal cell CA, Small cell lung CA, Uterine leiomyosarcoma,

DLT evaluable population   CRC – colorectal cancer

PATIENT DISPOSITION SUMMARY

DATA CUT DATE 03SEP2021

	0.01 mg/kg n = 3	0.03 mg/kg n = 1	0.1 mg/kg n = 1	0.3 mg/kg n = 1	1 mg/kg n = 6	3 mg/kg n = 3	10 mg/kg n = 3	All patients n = 18 (%)
Number of patient enrolled and treated – n (%)	3 (100)	1 (100)	1 (100)	1 (100)	6 (100)	3 (100)	3 (100)	18 (100)
Dose limiting toxicity – n (%)	1*	-	-	-	1**	-	-	2 (11)
Median (Min, Max) #Prior Therapies	7 (3, 8)	7 (7)	10 (10)	9 (9)	8 (2,16)	6 (6,16)	6 (2,13)	7 (2,16)
Discontinued study treatment – n (%)	3 (100)	1 (100)	1 (100)	1 (100)	5 (83)	3 (100)	3 (100)	17 (94)
Reasons for study treatment discontinuation (n)								
• Progressive disease per RECIST v1.1	3 (100)	1 (100)	1 (100)	1 (100)	3 (60)	1 (33)	1 (33)	11 (64)
• Clinical PD/PI decision	-	-	-	-	1 (20)	2 (67)	1 (33)	4 (24)
• Adverse event	-	-	-	-	1 (20)**	-	-	1 (6)
• Withdrew consent	-	-	-	-	-	-	1 (33)	1 (6)

DLT evaluable population.

*G2 vomiting assessed by the investigator as possibly related to study drug.
**G3 Atrial fibrillation assessed by the investigator as possibly related to study drug.

SUMMARY OF ADVERSE EVENTS

DATA CUT DATE 03SEP2021

	0.01 mg/kg n = 3	0.03 mg/kg n = 1	0.1 mg/kg n = 1	0.3 mg/kg n = 1	1 mg/kg n = 6	3 mg/kg n = 3	10 mg/kg n = 3	All patients n (%)
Any TEAE	3 (100)	1 (100)	1 (100)	1 (100)	6 (100)	2 (67)	3 (100)	17 (94)
No TEAE	-	-	-	-	-	1 (33)	-	1 (6)
Grade 1	1 (33)	-	1 (100)	1 (100)	2 (33)	-	1 (33)	6 (33)
Grade 2	2 (67)	-	-	-	3 (50)	-	1 (33)	6 (33)
Grade 3	-	1 (100)	-	-	1 (17)	2 (67)	1 (33)	5 (28)
Grade ≥4	-	-	-	-	-	-	-	-
TEAE resulting in treatment discontinuation	-	-	-	-	1 (17)*	-	-	1 (6)
Any serious AE	-	-	-	-	1 (17)	1 (33)	-	2 (11)
Grade ≤2	-	-	-	-	-	-	-	-
Grade 3	-	-	-	-	1 (17)	1 (33)	-	2 (11)
Grade ≥4	-	-	-	-	-	-	-	-
Serious AE resulting in treatment discontinuation	-	-	-	-	1 (17)*	-	-	1 (6)

Safety analysis set – patients who received ≥1 dose of study drug. Safety per CTCAE v5.0.
*Patient with prostate cancer, G3 Atrial Fibrillation assessed by the investigator as possibly related to study drug.

INCIDENCE OF TREATMENT EMERGENT ADVERSE EVENTS IN ≥2 PATIENTS

DATACUT 03SEP2021

PREFERRED TERM (PT)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)	All Grades n (%)
ANY TEAE	6 (33)	6 (33)	5 (28)	-	-	17 (94)
FATIGUE	5 (28)	2 (11)	-	-	-	7 (39)
DIARRHOEA	3 (17)	-	-	-	-	3 (17)
ANAEMIA	-	-	2 (11)	-	-	2 (11)
BLOOD CREATININE INCREASED	2 (11)	-	-	-	-	2 (11)
DECREASED APPETITE	-	2 (11)	-	-	-	2 (11)
DEHYDRATION	-	2 (11)	-	-	-	2 (11)
INSOMNIA	2 (11)	-	-	-	-	2 (11)
NAUSEA	2 (11)	-	-	-	-	2 (11)
URINARY TRACT INFECTION	-	2 (11)	-	-	-	2 (11)
VOMITING	1 (6)	1 (6)	-	-	-	2 (11)

Safety analysis set – patients who received ≥1 dose of study drug. Safety per CTCAE v5.0.

INCIDENCE OF SERIOUS ADVERSE EVENTS (ALL CAUSALITY) - ALL PATIENTS

DATACUT 03SEP2021

PREFERRED TERM (PT)	Grade 1/2 n (%)	Grade 3 n (%)	Grade ≥4 n (%)	All Grades n (%)
ANY SERIOUS	-	2 (11)	-	2 (11)
ACUTE RESPIRATORY FAILURE*	-	1 (6)*		1 (6)
ATRIAL FIBRILLATION**	-	1 (6)**		1 (6)
SPINAL CORD COMPRESSION*	-	1 (6)*		1 (6)
URINARY RETENTION*	-	1 (6)*		1 (6)

Safety analysis set – patients who received ≥1 dose of study drugs. AEs reported within 30 days of last dose of study treatment. Safety per CTCAE v5.0.

*Patient with widely metastatic rectal cancer, bilateral pulmonary metastatic disease and spinal cord compression. The SAEs were assessed as related to disease progression and not related to study drug.

**Patient with prostate cancer, G3 atrial fibrillation assessed by the investigator as possibly related to study drug.

SUMMARY OF INVESTIGATOR ASSESSED RESPONSE (RECIST V1.1)

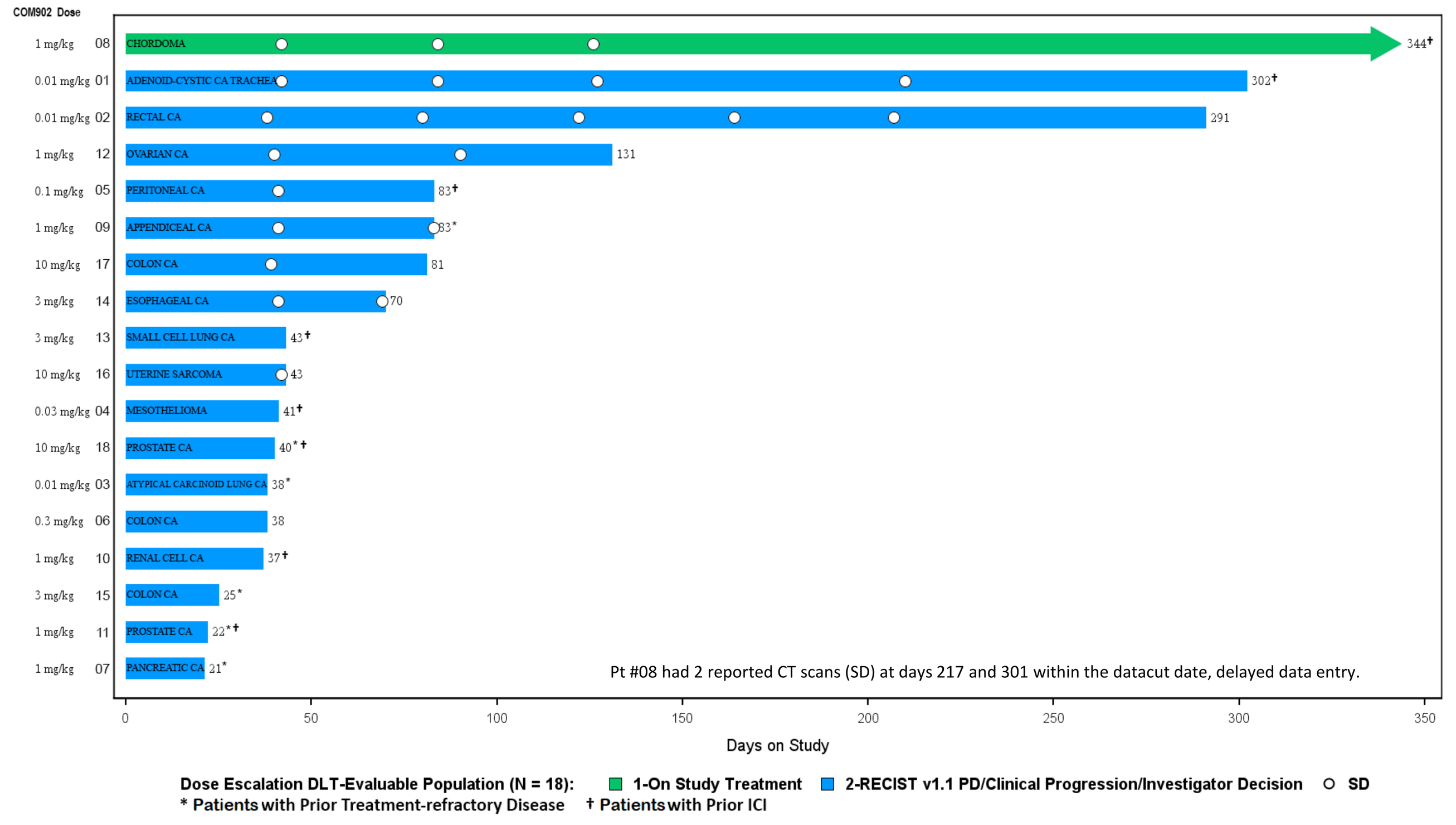
DATACUT 03SEP2021

Parameter	All patients n = 18 (%)
ORR (CR+PR)	-
Disease control rate (CR+PR+SD) Confirmed SD	9 (50) 6 (67)
Best response of at least SD ≥6 months+	3 (17)
Best response	
CR	-
PR	-
SD	9 (50)
PD	8 (44)
Not Assessed*	1 (6)

DLT evaluable population.

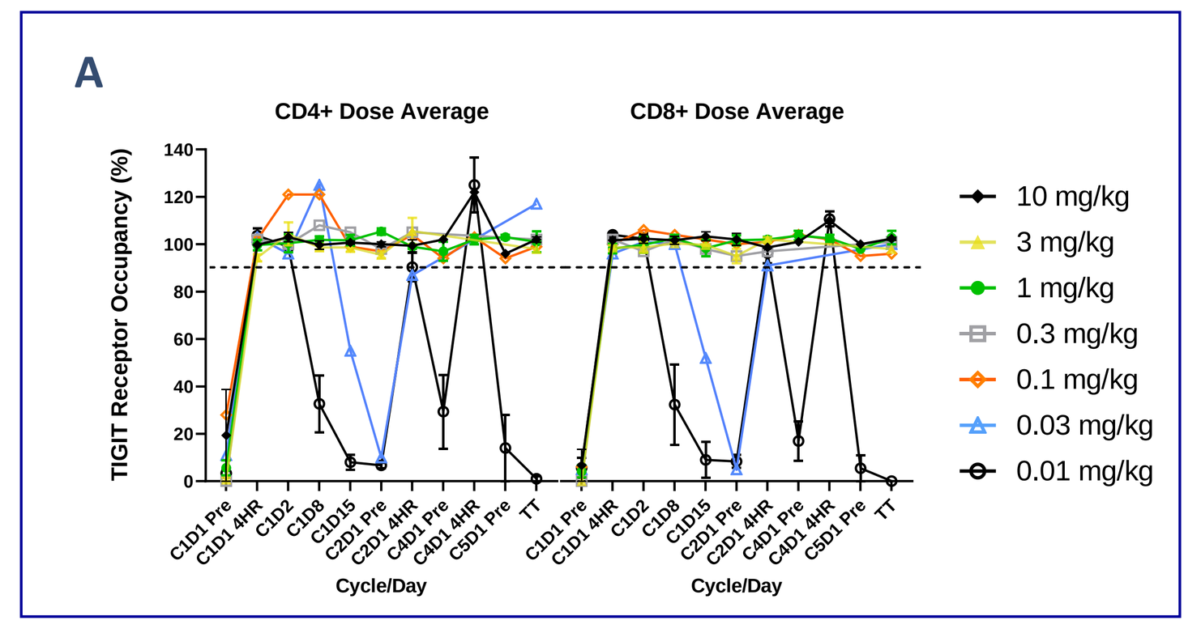
*Pt discontinued study treatment in the 1st cycle of dose escalation due to G3 Atrial fibrillation.
+Includes 1pt (#08) with SD ≥6 months within the datacut date, delayed data entry.

SWIMMER PLOT

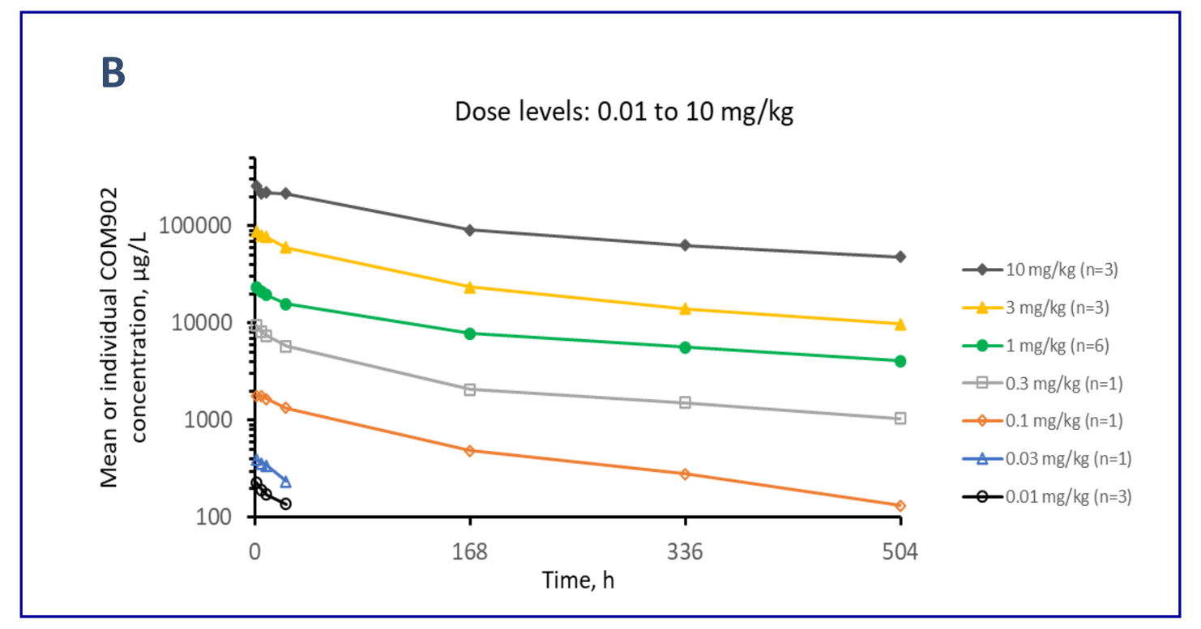


- Prior treatment refractory disease: Best response of PD to last therapy prior to enrollment into this study.
- Patients who received prior treatment with ICI: Any line of therapy that includes an ICI prior to enrollment into this study

COM902 PERIPHERAL RECEPTOR OCCUPANCY AND COM902 PK PROFILE

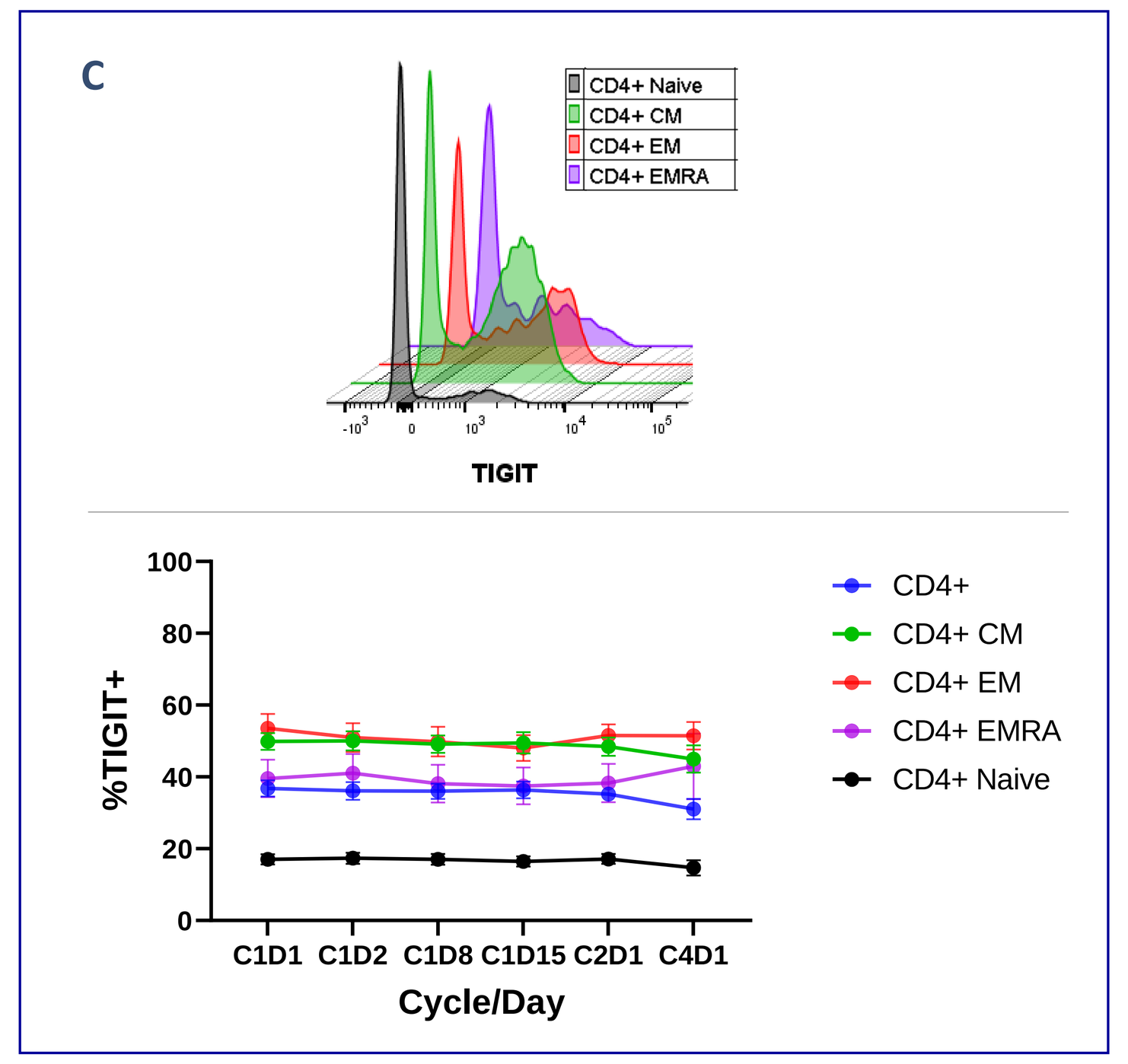


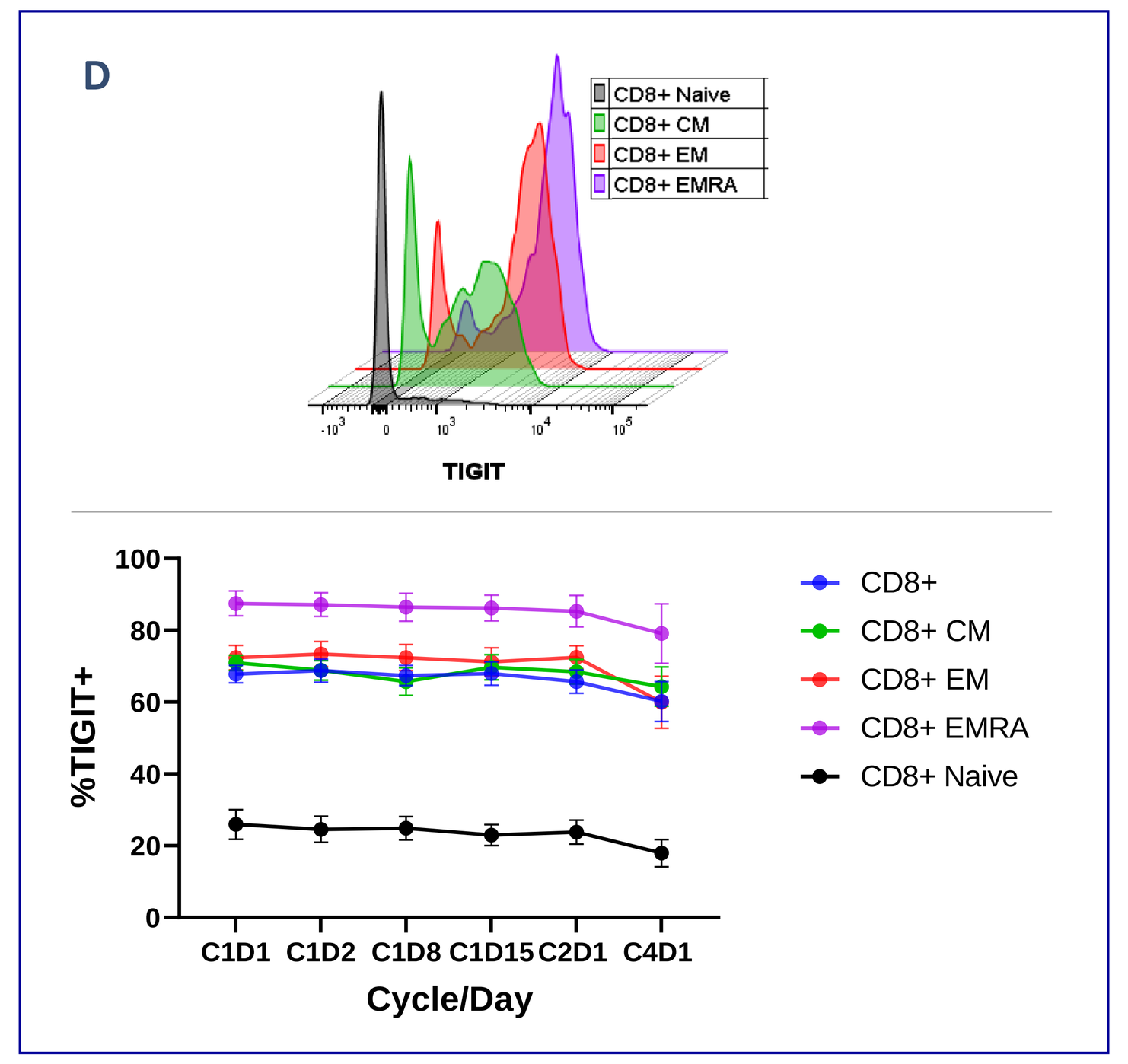
COM902 peripheral RO >90% of TIGIT from 0.1 mg/kg dose level



Preliminary COM902 PK profiles with a dose-proportional increase

NO SIGNIFICANT CHANGES IN TIGIT+ CD4 AND TIGIT+ CD8 T CELL SUBSETS

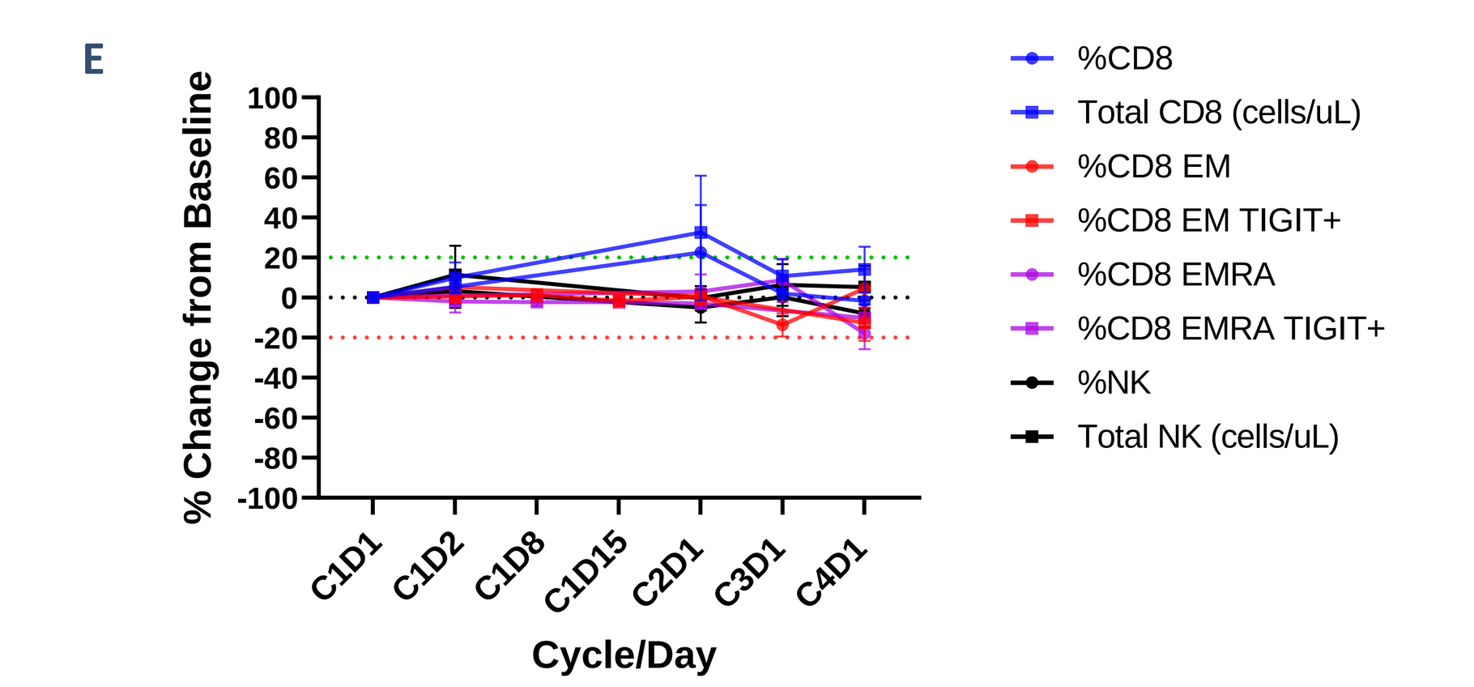




Legend

Flow cytometry analysis of %TIGIT positive cells out of CD4 (C) and CD8 (D) T cell subsets. Shown in each panel are representative histograms of TIGIT+ T cell subsets and the average of all patients for each subset. TIGIT detection was carried out by labeled secondary antibody (anti-hIgG4) following blood samples saturation by COM902, T cell subsets were defined by CD45RA and CCR7 staining (CM: CD45RA-CCR7+ ; EM: CD45RA-CCR7- ; EMRA: CD45RA+ CCR7- ; Naïve: CD45RA+CCR7+).

NO SIGNIFICANT CHANGES IN CD8 T CELL SUBSETS AND NK CELLS



Legend

Flow cytometry analysis of %TIGIT positive cells out of CD4 (C) and CD8 (D) T cell subsets. Shown in each panel are representative histograms of TIGIT+ T cell subsets and the average of all patients for each subset. TIGIT detection was carried out by labeled secondary antibody (anti-hIgG4) following blood samples saturation by COM902, T cell subsets were defined by CD45RA and CCR7 staining (CM: CD45RA-CCR7+ ; EM: CD45RA-CCR7- ; EMRA: CD45RA+ CCR7- ; Naïve: CD45RA+CCR7+).

CONCLUSION

- COM902 monotherapy has a favorable safety and toxicity profile and is well tolerated
- Encouraging signal of antitumor activity with SD 9 pts (50%) and 6 pts (67%) with confirmed SD; 3 pts (17%) with SD ≥6 months [includes an additional pt with SD ≥6 months within the datacut date, data entry delayed] in a heavily pretreated and heterogenous pt population with median (min, max) 7 (2, 16) prior therapies
- COM902 peripheral receptor occupancy >90% from 0.1 mg/kg dose
- Preliminary PK profiles of COM902 were generally dose proportional
- COM902 3 mg/kg IV Q3W has been selected as the RDFE
- COM902 did not deplete major TIGIT+ expressing lymphocytes (CD4, CD8, NK cells)
- The COM902 monotherapy expansion cohort is enrolling pts
- A PD-L(1)-free regimen (COM902 in combination with COM701) is part of the expansion cohort evaluating pts with relapsed/refractory colorectal cancer, non small cell lung cancer, head and neck squamous cell cancer

REFERENCE

1. Hansen, et al. Cancer Immunol Immunother 2021.

ACKNOWLEDGEMENT

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Compugen Ltd. SITC November 2021; www.cgen.com