SITC 2022

NOVEMBER 8-12 BOSTON MASSACHUSETTS

The Society for Immunotherapy of Cancer 37th Annual Meeting and Pre-Conference Programs

THE LEADING CANCER IMMUNOTHERAPY AND TUMOR IMMUNOLOGY CONFERENCE

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COM701 plus nivolumab demonstrates preliminary antitumor activity and immune modulation of tumor microenvironment in patients with metastatic MSS-CRC and liver metastases.

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Abstract 659 Rasco DW, Dumbrava EE *at al*. Study sponsored by Compugen Ltd. For more information: www.cgen.com

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Disclosure

Introduction

- COM701 is a novel, 1st 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

- We have reported antitumor and pharmacodynamic activity of COM701 monotherapy and in combination in several tumor types[1]

- We present preliminary clinical and translational results of the combination of COM701 + nivolumab in patients with microsatellite stable colorectal cancer [MSS-CRC]

1. Vaena D et al, COM701±nivolumab: Results of an ongoing P1 study of safety, tolerability & preliminaryantitumor activity in pts with advanced solid malig. J Clin Onco 39, 2021 (suppl 15; abst 2504).

MSS-CRC Patients in Urgent Need of New Treatment Options

MSS-CRC represents 95% of metastatic CRC with limited treatment options

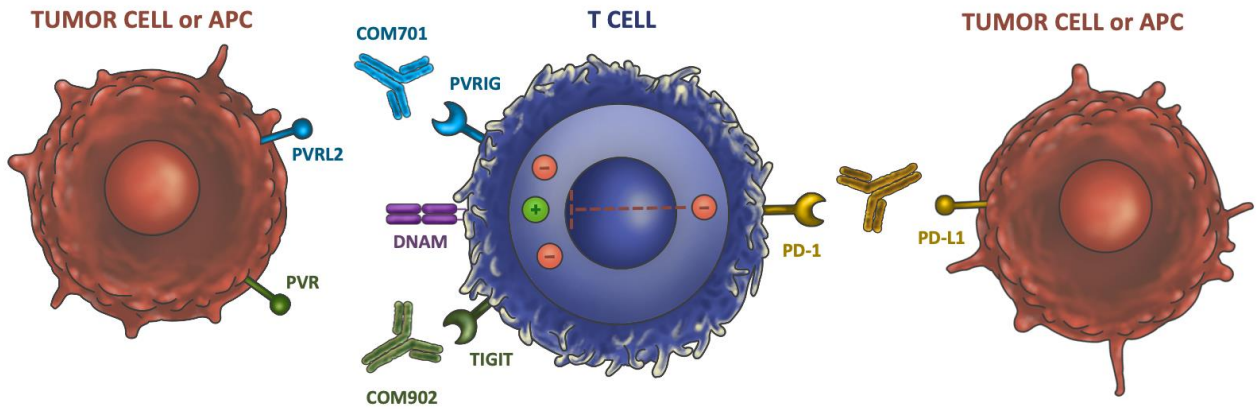
SOC limited efficacy in refractory MSS-CRC[1,2]			
Standard of Care [3L+]	**ORR**	**Median PFS**	**Median OS**
Regorafenib/TAS-102	~1-2%	~2 months	~6-7 months

- Majority of patients with 3L+ MSS-CRC patients have metastases to the liver
  - Presence of liver metastases correlates with lack of response to PD-1/PD-L1 inhibition 0% ORR [n=54][3]
  - Nivolumab + regorafenib showed 0% ORR [n=47][4]
  - Balstilimab [anti-PD-1] + botensilimab [anti-CTLA-4] showed 0% ORR (n=17)[5]

1.Van Cutsem,, 2012, ASCO
2. Mayer et al. N Eng J Med. 2015;372:1909-1919
3.Wang et al, JAMA 2021
4. Fakih et al , 2021, ASCO
5. Bullock AJ et al, 2022 ESMO GI

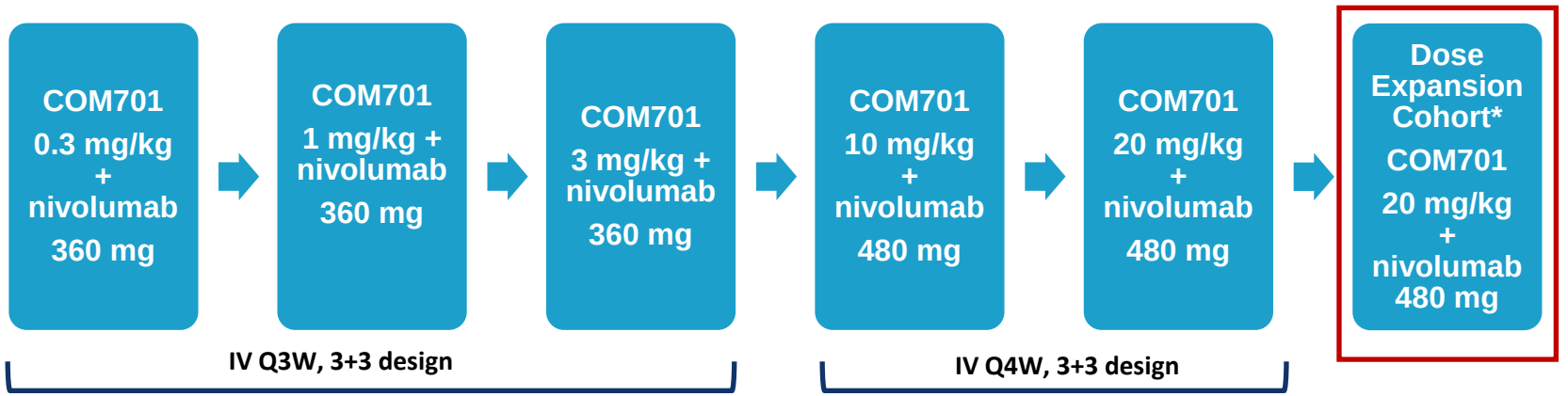
DNAM Axis Pathway

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 Schema – Combination Dose Escalation and Expansion



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

- **MSS-CRC**
- **OVCA**
- **Breast**
- **Endometrial**

- **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 22 patients:

- Combination dose escalation - 2 pts [COM701 0.3,1mg/kg + nivolumab 360 mg both IV Q3W]
- Combination dose expansion - 20 pts cohort [COM701 20mg/kg + nivolumab 480mg both IV Q4W]

Key Eligibility Criteria and Study Objectives

- Key Inclusion Criteria [MSS-CRC]:
  - Histologically confirmed adenocarcinoma of the colon/rectum; Stage IV disease
  - Prior PD-1/PD-L1 permissible
  - Documented MSS status by an FDA approved test e.g. genomic testing, IHC for mismatch repair proficient
  - Disease progression with ≥2 prior systemic therapies for metastatic CRC that must have included the following: fluoropyrimidines, irinotecan, and oxaliplatin
  - Measurable disease
- Key Exclusion Criteria:
  - Active autoimmune disease requiring systemic treatment
  - History of immune-related toxicities on prior immunotherapy treatment leading to discontinuation
- Key Primary Objective:
  - Safety and tolerability of profile of COM701 ± nivolumab
- Secondary Objectives:
  - Immunogenicity of COM701 ± nivolumab
  - Antitumor activity of COM701 + nivolumab [combination expansion cohort]
- Exploratory Objective:
  - COM701-mediated pharmacodynamic effect in blood [COM701 ± nivolumab], immune-related changes [cytokines, immunophenotyping]

Demographics

Parameter	COM701 + Nivolumab n = 22 [%]
Sex, M	16/22 [73]
Age ≤ 65 yrs	17/22, [77]
Median prior therapies [range]	3 [2, 10]
Race [white]	18 [82]
Prior anti-PD1/PD-L1	2 [9]
Liver metastases	17/22 [77]
ECOG [0, 1] 0	 10 [45]
Prior regorafenib or TAS-102	7 [32]
KRAS mutation Mutated Wildtype Missing	 13 [59] 6 [27] 3 [14]

Data cut 09/02/2022

Patient Disposition Summary

Parameter	COM701 + Nivolumab n = 22 (%)
Number of cycles of study drug[s]; Median (Min, Max)	2.0 (1, 16)
Discontinued study treatment	22 (100)
Reasons for study treatment discontinuation • PD per RECIST v1.1 • Physician decision/clinical PD/loss of clin benefit • Adverse event	 17 [77] 3 [14] 2 [9]*

Data cut 09/02/2022

***Grade 3 blood bilirubin increased, assessed by the investigator as related to disease, not related to study drugs**

Incidence of Treatment Emergent Adverse Events in ≥15% of Patients

PREFERRED TERM (PT)	Grade 1/2 n [%]	Grade 3 n [%]	Grade 4 n [%]	Grade 5 n [%]	All Grades n [%]
Any TEAE	11 (50)	10 (46)	-	-	21 [96]
Anaemia	7 [32]	1 [5]	-	-	8 [36]
Hypoalbuminaemia	5 [23]	-	-	-	5 [23]
Fatigue	5 [23]	-	-	-	5 [23]
Ascites	3 [14]	1 [5]	-	-	4 [18]
Vomiting	3 [14]	1 [5]	-	-	4 [18]
Aspartate aminotransferase increased	4 [18]	-	-	-	4 [18]
Oedema peripheral	4 [18]	-	-	-	4 [18]

Safety analysis set – patients who received ≥1 dose of any of the study drugs, includes adverse events deemed related or not related to study drug[s] by the investigator. Safety per CTCAE v4.03.

Data cut 09/02/2022

Incidence of All Serious Adverse Events*

PREFERRED TERM (PT)	Grade 1/2 n [%]	Grade 3 n [%]	Grade 4 n [%]	Grade 5 n [%]	All Grades n [%]
Any SAE	2 [9]	7 [32]	-	-	9 [41]
Abdominal distension	-	1 [4]	-	-	1 [4]
Abdominal pain	-	1 [4]	-	-	1 [4]
Small intestinal obstruction	-	1 [4]	-	-	1 [4]
Blood bilirubin increased	-	2 [9]	-	-	2 [9]
Troponin increased	1 [4]		-	-	1 [4]
Device related infection	-	1 [4]	-	-	1 [4]
Sepsis	-	1 [4]	-	-	1 [4]
Hyperbilirubinaemia	-	1 [4]	-	-	1 [4]
Hypokalaemia	-	1 [4]	-	-	1 [4]
Back pain	1 [4]	-	-	-	1 [4]
Cancer pain	-	1 [4]	-	-	1 [4]
Device dislocation	-	1 [4]	-	-	1 [4]
Dyspnoea	1 [4]	-	-	-	1 [4]

Data cut 09/02/2022

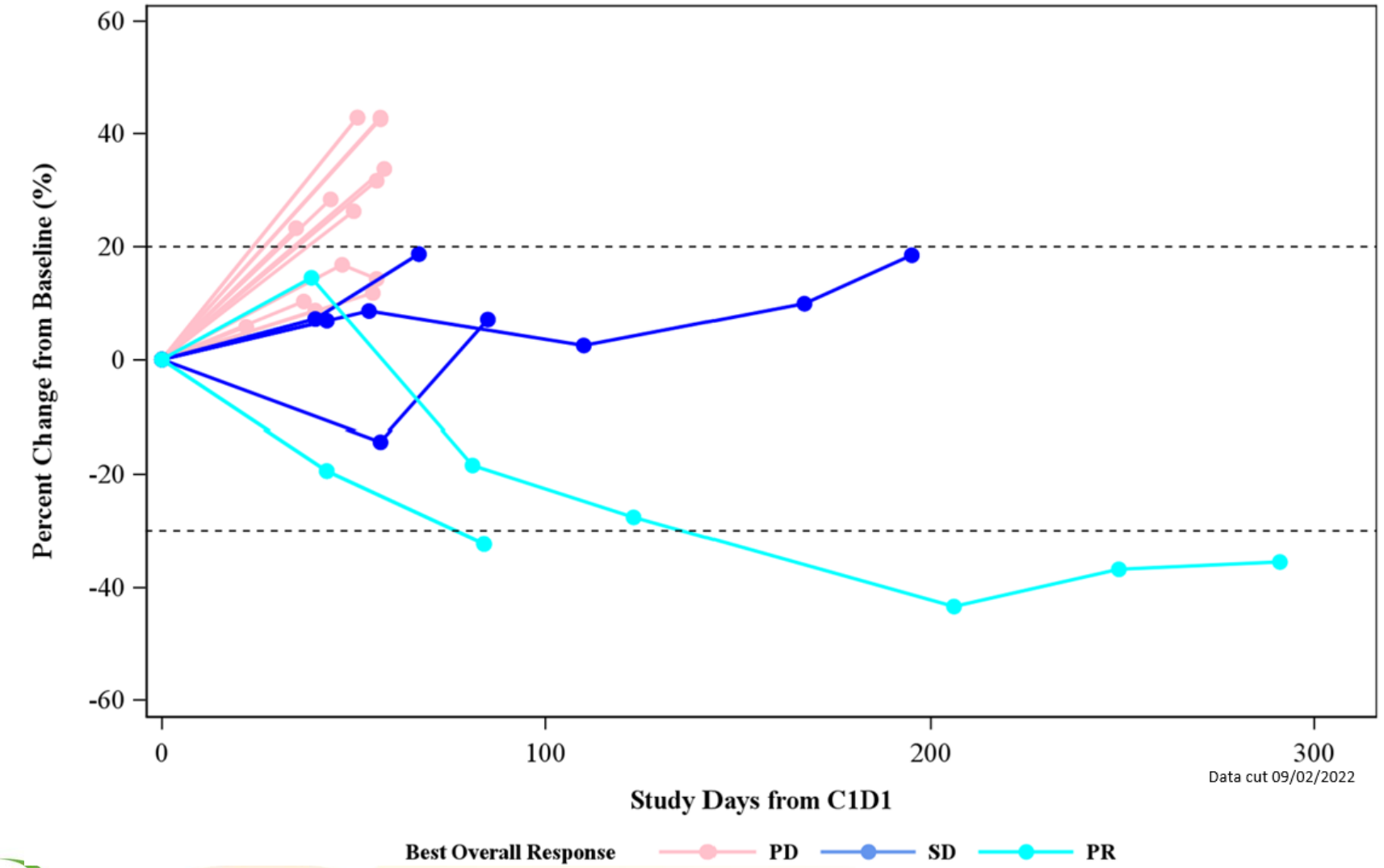
Safety analysis set – patients who received ≥1 dose of any of the study drugs. Safety per CTCAE v4.03.

***All SAEs were assessed by the investigator as related to disease, not related to study drugs**

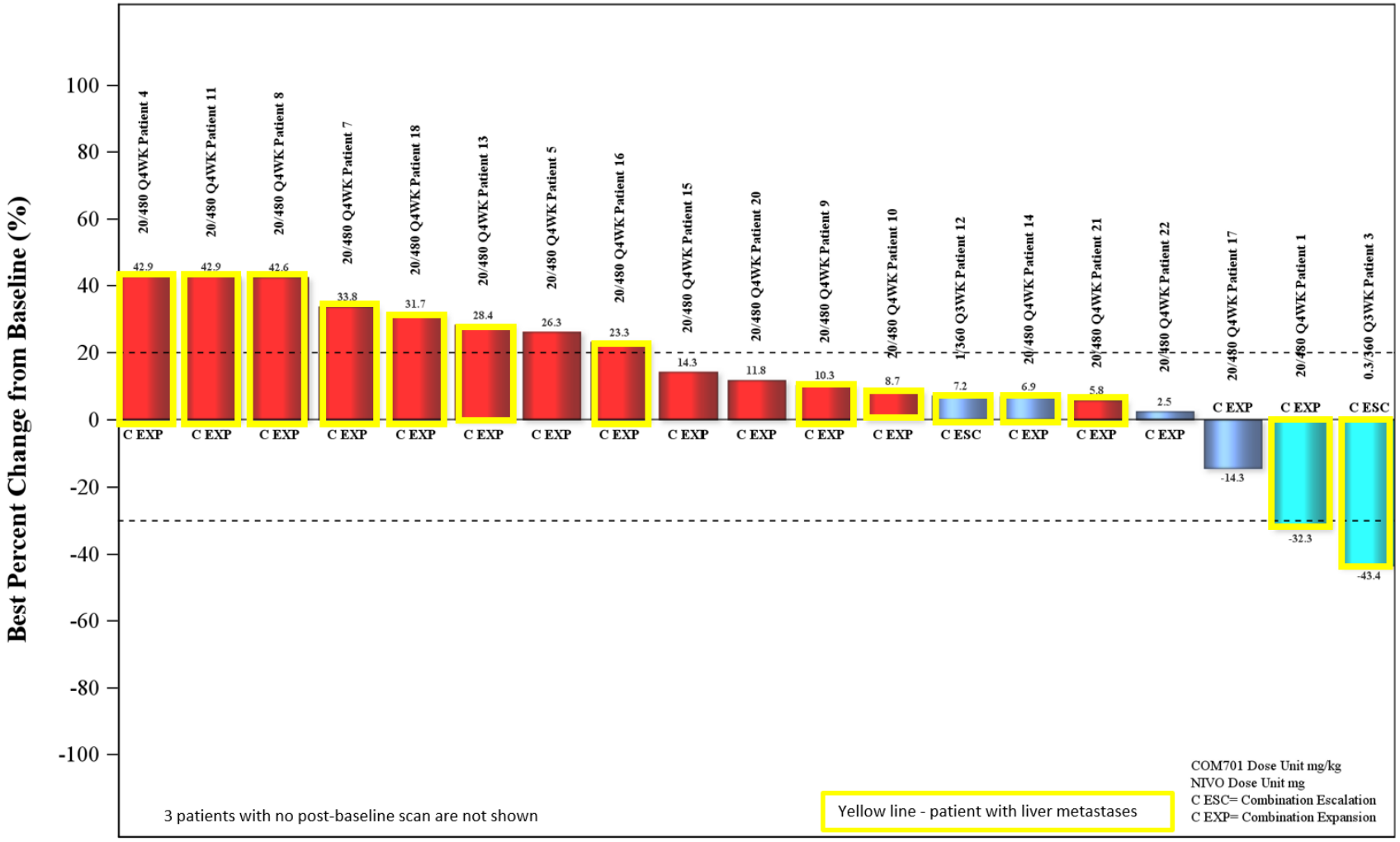
Summary of Investigator Assessed Response [RECIST v1.1]

Parameter	COM701 + Nivolumab n = 22 [%]
ORR [CR+PR]	2 [9]
Disease control rate (CR+PR+SD)	6 [27]
Best response of CR, PR or SD [≥ 6 months]	2 [9]
Liver metastases PR SD Disease control rate [CR+PR+SD]	17 [77] 2 [12] 3 [18] 5 [29]
Best response	
CR	-
PR	2 [9]
SD	4 [18]
PD	13 [59]
Clinical PD/lack of clinical benefit	3 [13]

Spider Plot


60
40
20
0
-20
-40
-60
Percent Change from Baseline (%)
0
100
200
300
Data cut 09/02/2022
Study Days from C1D1
Best Overall Response
PD
SD
PR

Waterfall Plot



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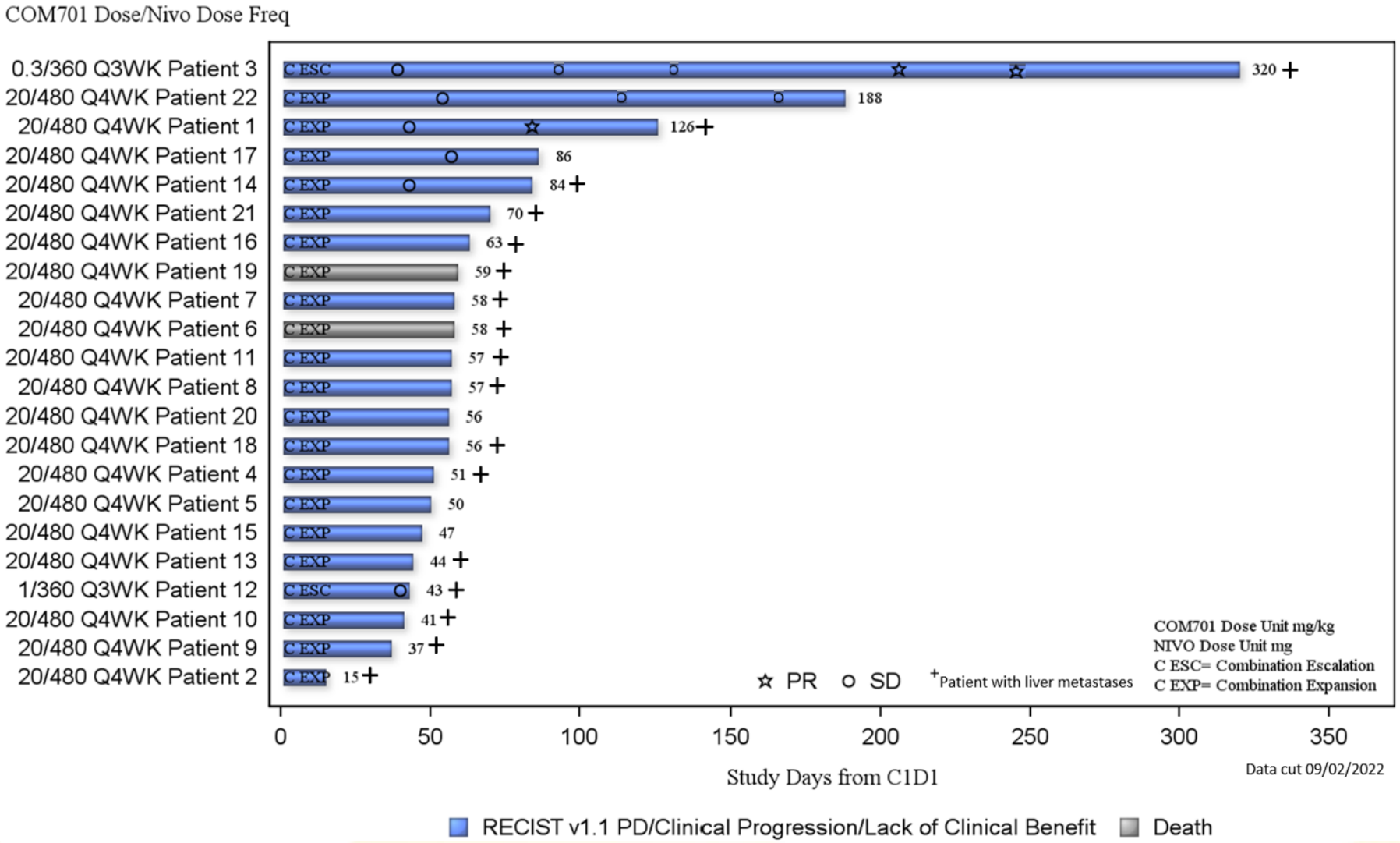
Swimmer Plot

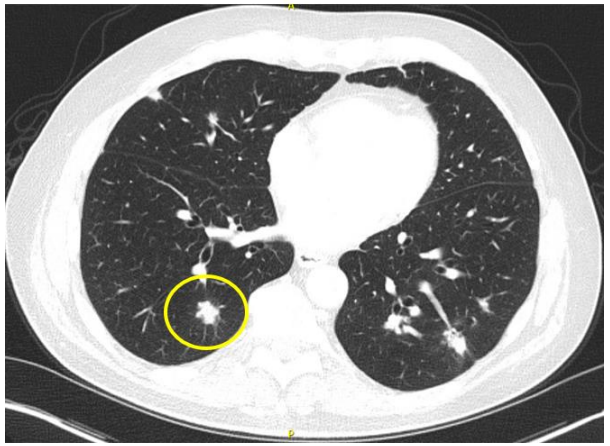


Clinical Vignette – Patient with Partial Response

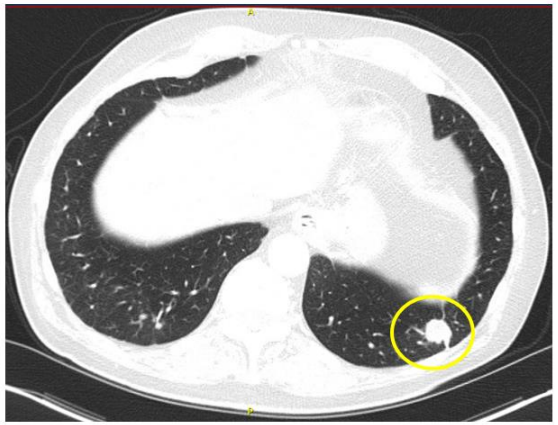
72yr old w/m, MSS-CRC stage IV diagnosed 2015; metastases to liver. Had 2 prior lines in the metastatic setting FOLFOX [2016; best response CR]; FOLFIRI [2020; best response SD]. Mutations: positive TP53 AND APC, KRAS mutated. Tumor marker: CEA 36.38 U/mL [screening]; 8.16 U/mL on 11/03/21 [partial response]

At time of PD [12/2021] due to brain metastases – RECIST v1.1 [partial response] target lesion response maintained with 32% reduction in target lesions [below] and non-target lesions, liver metastases present but not measurable

Screening – target lesions

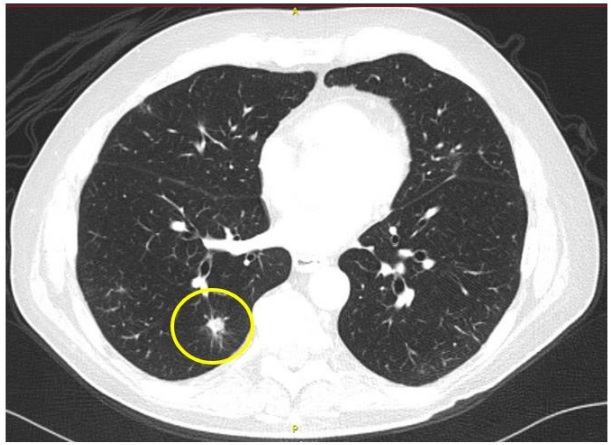


Screening Target Lesion 1 [15 mm; RECIST v1.1] - 8/03/21

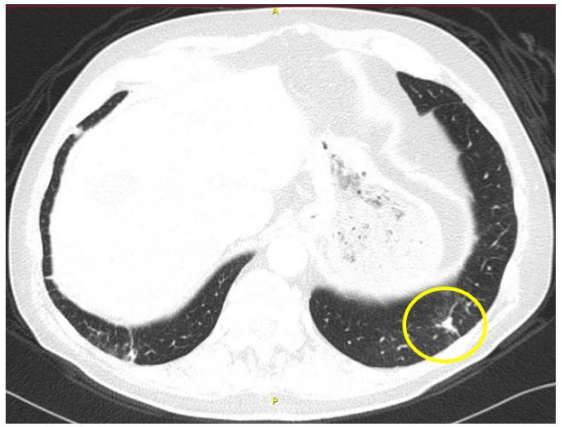


Screening Target Lesion 2 [16 mm; RECIST v1.1] - 8/03/21

2nd post screening – target lesions



2nd post Screening Target Lesion 1 [10 mm; RECIST v1.1] - 11/03/21

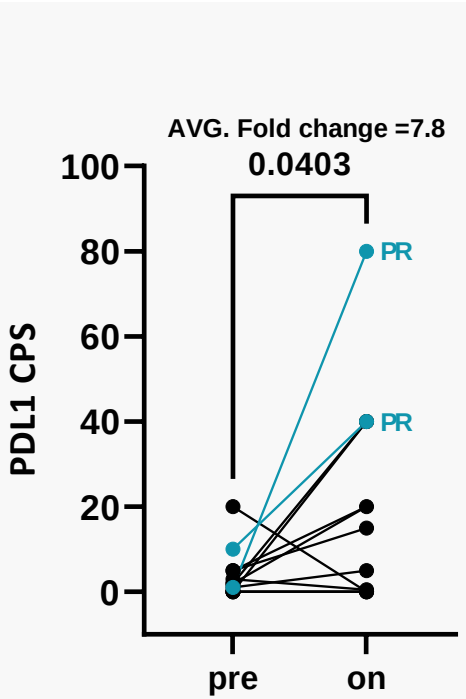


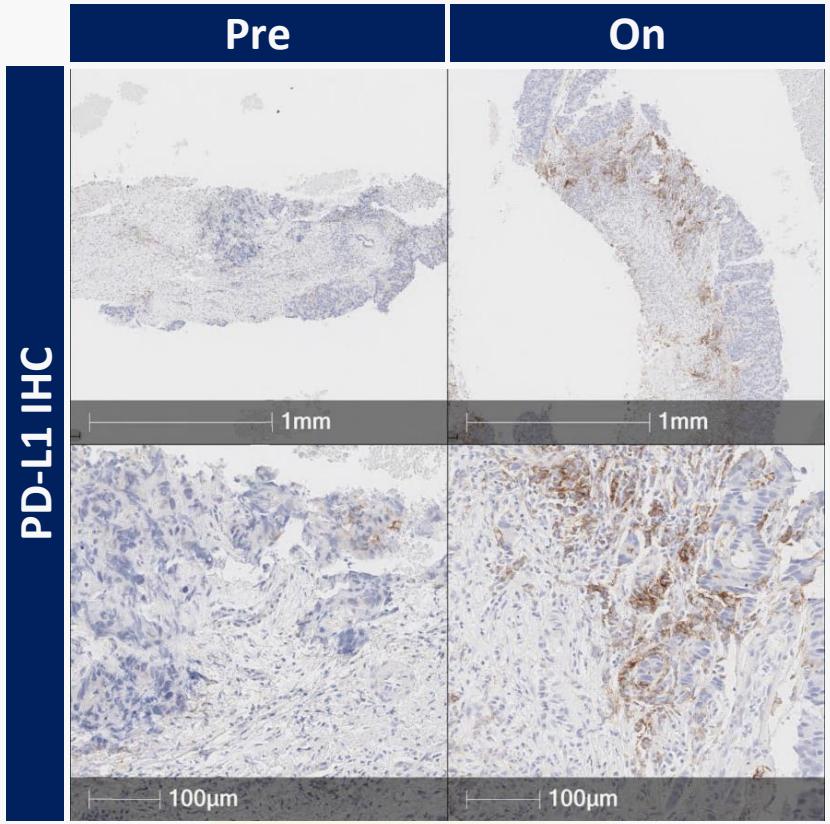
2nd post Screening Target Lesion 2 [11 mm; RECIST v1.1] - 11/03/21

RECIST v1.1: Partial response with 32% reduction in target lesions

COM701 + Nivolumab Combination Induces TME Immune Modulation in Patients with MSS-CRC

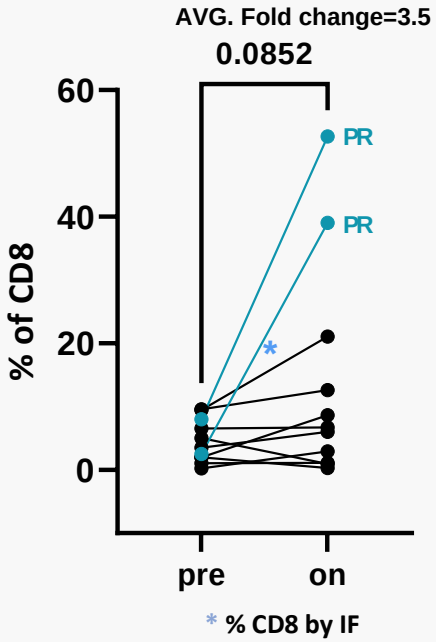
PD-L1 expression



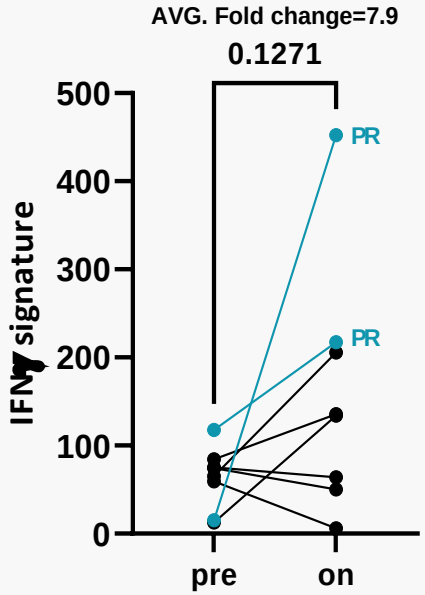


PR = patient with partial response per RECIST

CD8 IHC



IFNγ signature

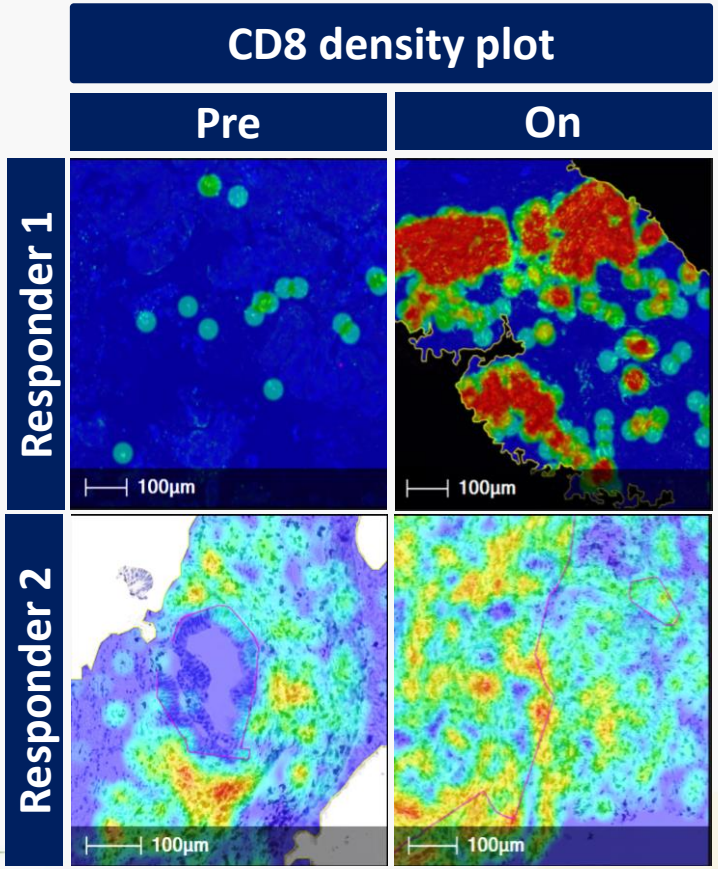


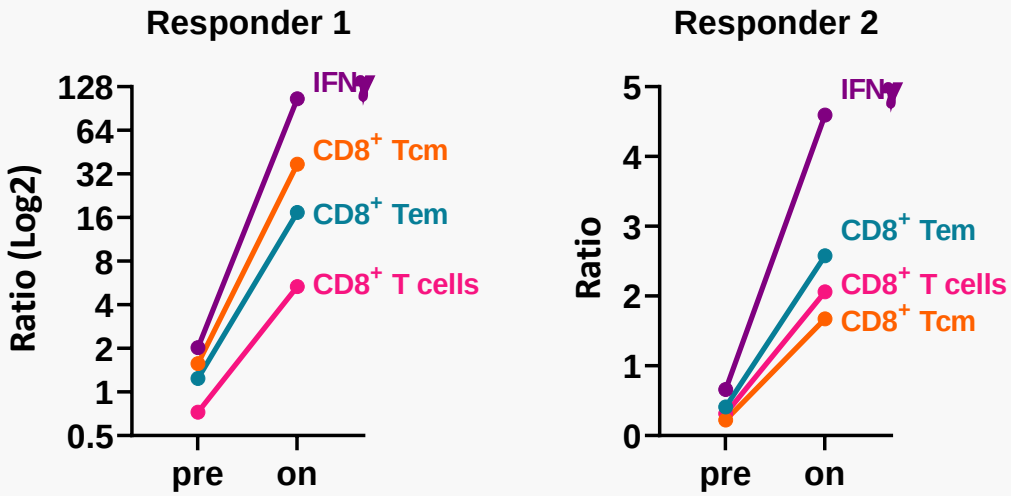
PR = patient with partial response per RECIST

- 9/13 patients showed an increase in CPS PD-L1
- 7/11 patients showed an increase in % CD8
- 5/8 patients showed an increase in IFNγ signature

Extensive TME Modulation in MSS-CRC Patients Partially Responding to COM701+ Nivolumab

Increased CD8 infiltration and IFNγ signature





- Responder 1 had immune desert TME pretreatment with an extensive T cell infiltration following treatment
- Responder 2 had an excluded TME pretreatment, becoming inflamed following treatment

Conclusion

- Combination of COM701 + nivolumab is well tolerated with a favorable safety profile
- Cumulative ORR 2/22 [9%] COM701+nivolumab; in heavily pretreated subject population [median 3 prior lines]
  - The ORR [9%] is higher than ORR [1-2%] reported for SOC- regorafenib or TAS-102
- Exploratory analysis demonstrated encouraging preliminary antitumor activity in the patients with liver metastases – ORR 2/17 [12%], disease control rate 5/17 [29%]
  - Historically patients with liver metastases appear to be not responsive to ICI
- Translational data demonstrated potent TME immune activation, most notable in responders and consistent with COM701 MOA. Such modulation is not typical of CPIs treatment in “cold” indications.
- Previous preclinical and clinical translational data have shown most potent immune activation with PVRIG&PD-1&TIGIT triple blockade, suggesting that adding TIGIT blocker could increase response rate
- Phase 1 study evaluating COM701 + COM902 [TIGIT inhibitor] and a PD-1 inhibitor is planned
- COM701 therapeutic activity in “cold” indications will be further demonstrated at ESMO/IO by data from dual (PVRIG&PD-1) and triple (PVRIG&PD-1&TIGIT) combination blockade in PROC patients

Watch out for PVRIG oral presentation tomorrow

Session Date: Friday, November 11, 2022, 5:20pm ET

Title: PVRIG, a novel T cell checkpoint, is preferentially expressed in TLS on stem-like memory T cells, potentially inhibiting their expansion

Presenter: Eran Ophir, SVP Research and Drug Discovery, Compugen

Abstract Number: 504

Session Title: Next Generation Checkpoint Blockade: Mechanisms of Action

Acknowledgment

- We thank the patients for participating in this clinical trial and their families
- The investigators and their staff at the clinical trial sites
- Study Sponsor – Compugen Ltd in collaboration with Bristol-Myers Squibb