COM701 DEMONSTRATES ANTITUMOR ACTIVITY AS MONOTHERAPY AND IN COMBINATION WITH NIVOLUMAB IN PATIENTS WITH ADVANCED MALIGNANCIES

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DISCLOSURES

- Consulting/Advisor for Bristol Myers Squibb, Merck, Novartis, Replimune
- Research funding from Merck, Amgen

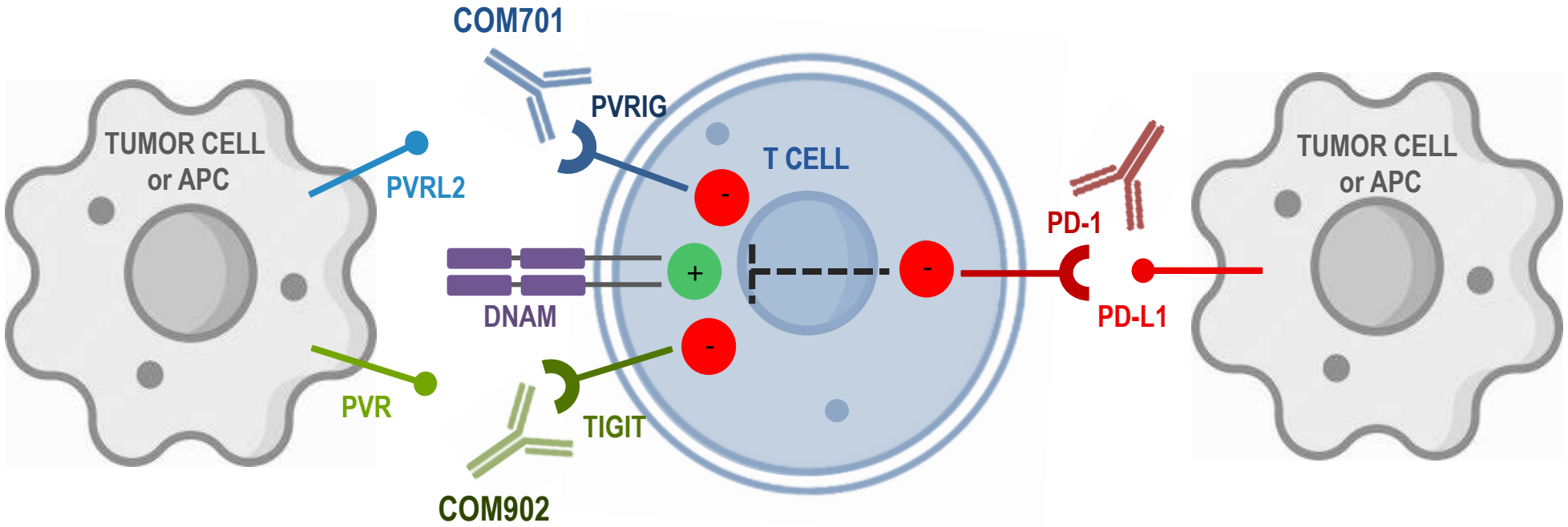
INTRODUCTION

- There is a high unmet medical need for the treatment of patients who are refractory to or relapse following treatment with checkpoint inhibitors
- Inhibition of poliovirus receptor related immunoglobulin domain containing (PVRIG) leads to enhanced activation of T and NK cells, and results in tumor growth inhibition in mouse tumor models[1]
- COM701 is a novel first-in-class humanized IgG4 monoclonal antibody that binds with high affinity PVRIG blocking its interaction with its ligand, PVRL2
- We have previously reported on the preliminary antitumor activity of COM701 monotherapy[2]
- We are now reporting the preliminary safety and antitumor activity of COM701 in combination with nivolumab (Arm B) and we provide data update in COM701 monotherapy dose cohorts (Arm A)

1. Spencer L, Ofer L et al, Discovery of COM701, a therapeutic antibody targeting the novel. immune checkpoint PVRIG, for the treatment of cancer. J Clin Oncol. 2017; (suppl; abstr 3074)
2. Dumbrava E, Fleming G, Hamilton E et al. Journal for ImmunoTherapy of Cancer 2019, 7(Suppl 1):P421. SITC Nov 2019.

PVRIG PATHWAY IN THE DNAM AXIS

Potential Molecular Interactions Between PVRIG/TIGIT and PD-1 Pathways Support Combination Approach to Overcome Immunotherapy Resistance



Biomarker and Biology - Driven Drug Combination Approach

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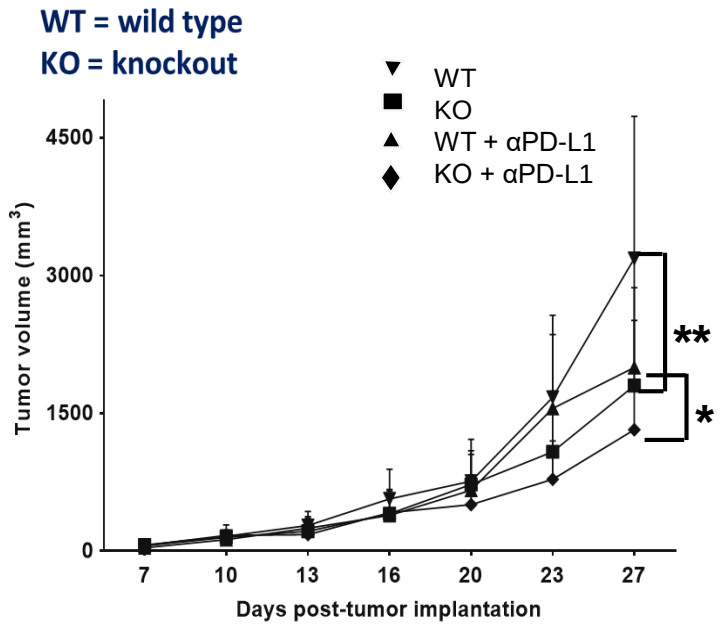
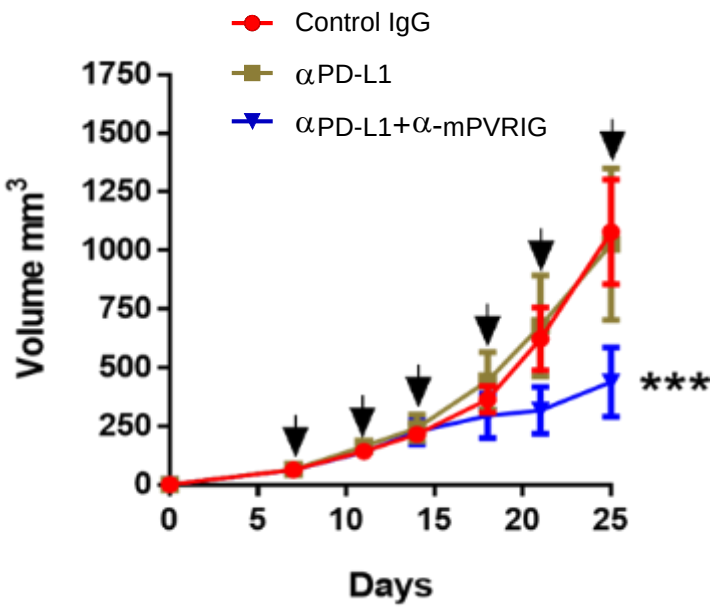
PVRIG KNOCKOUT OR INHIBITION REDUCES TUMOR GROWTH IN COMBINATION WITH PD-L1 OR TIGIT IN MOUSE MODELS

PVRIG KO MICE (MC38)



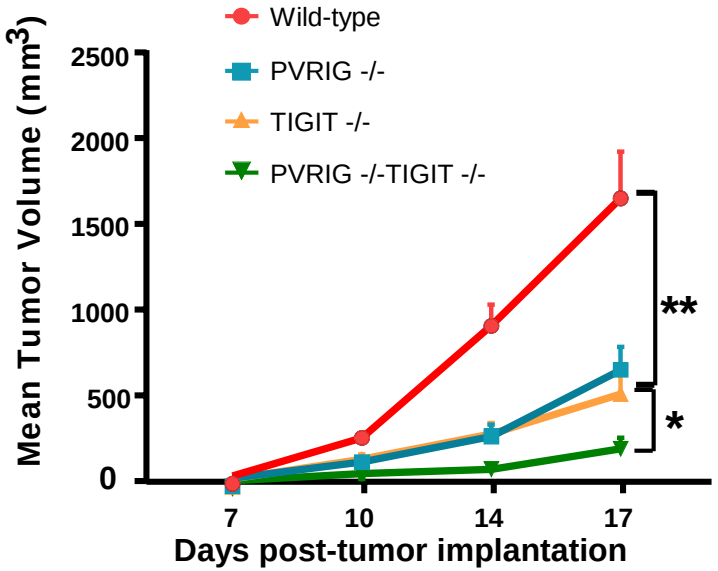
Reduced tumor growth in KO mice

anti-PVRIG + anti-PD-L1 (CT26)



Synergistic tumor growth inhibition with anti-PD-L1

PVRIG + TIGIT Double KO (B16)



Reduced tumor growth in PVRIG + TIGIT double KO mice

Ganguly and Pardoll, Johns Hopkins Univ. MC38 model

SITC, November 2016, Hunter, *et al.*, oral presentation
SITC, November 2019, Logronio, *et al.*, poster presentation

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STUDY DESIGN

PHASE 1 (Identifier: NCT03667716)

Arm A

Monotherapy Dose Escalation	Monotherapy Cohort Expansion (20 patients; progressed on SOC)
All-comers (progressed on SOC)	NSCLC, Ovarian, Breast, Endometrial, Colorectal

Arm B

Dual Combination
Escalating doses of COM701 with fixed dose of nivolumab (Up to 20 patients)

All-comers (progressed on SOC)

Study Objectives

- Safety & Tolerability
- PK/PD
- Clinical activity – COM701 monotherapy and in combination

Response Assessment

CT Imaging Q6 or Q8 wks as per schedule of study drugs

Responses per Investigator assessment – RECIST v1.1

PHASE 1/2 (in development)

Triple Combination Dose Escalation
Escalating doses of COM701 with fixed doses of nivolumab + BMS-986207

All-comers (progressed on SOC); expected initiation in 2H 2020

Triple Combination
Cohort Expansion

Ovarian, Endometrial, additional tumor types with high PVRL2 expression

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PATIENT BASELINE CHARACTERSTICS

Parameter	Arm A (COM701 monotherapy) N=16	Arm B (COM701 + nivolumab) N=12
Sex, F (n)	9	9
Age ≤ 65 yrs (n)	13	7
Median prior therapies (range)	6 (2, 15)	4 (2, 12)
ECOG (0, 1) 0	8	3
Cancer type at study entry (n)	CRC (6), PDAC (2), ovarian/PPSC (2), NSCLC (1), adenoid cystic carcinoma (1), melanoma (1), mesothelioma (1), CUP (1), gallbladder carcinoma (1)	Endometrial (3), CRC (2), NSCLC (2), neuroendocrine, lung (1), anal SCC (1), RCC (1), mesothelioma (1), cervical (1)

DLT evaluable set

DATA CUT DATE 31MAR2020

CRC – colorectal cancer; NSCLC – non-small cell lung cancer; PPSC – primary peritoneal serous carcinoma; PDAC – pancreatic ductal adenocarcinoma; CUP – carcinoma of unknown primary; SCC – squamous cell carcinoma; RCC – renal cell carcinoma

PATIENT DISPOSITION SUMMARY

Parameter	Arm A (COM701 monotherapy) N=16	Arm B (COM701 + nivolumab) N=12
Number of DLTs	0	0
Number of patients continuing on study treatment	2	6
Number of patients treated at IV Q4 wks schedule (dose) Number of patients continuing	3 (20 mg/kg) 2	3 (10 mg/kg + nivolumab 480 mg) 2
Reasons for study treatment discontinuation (n) • PD per RECIST v1.1 • Physician decision • Clinical progression/deterioration	 10 2 2	 5 0 1

DLT evaluable set

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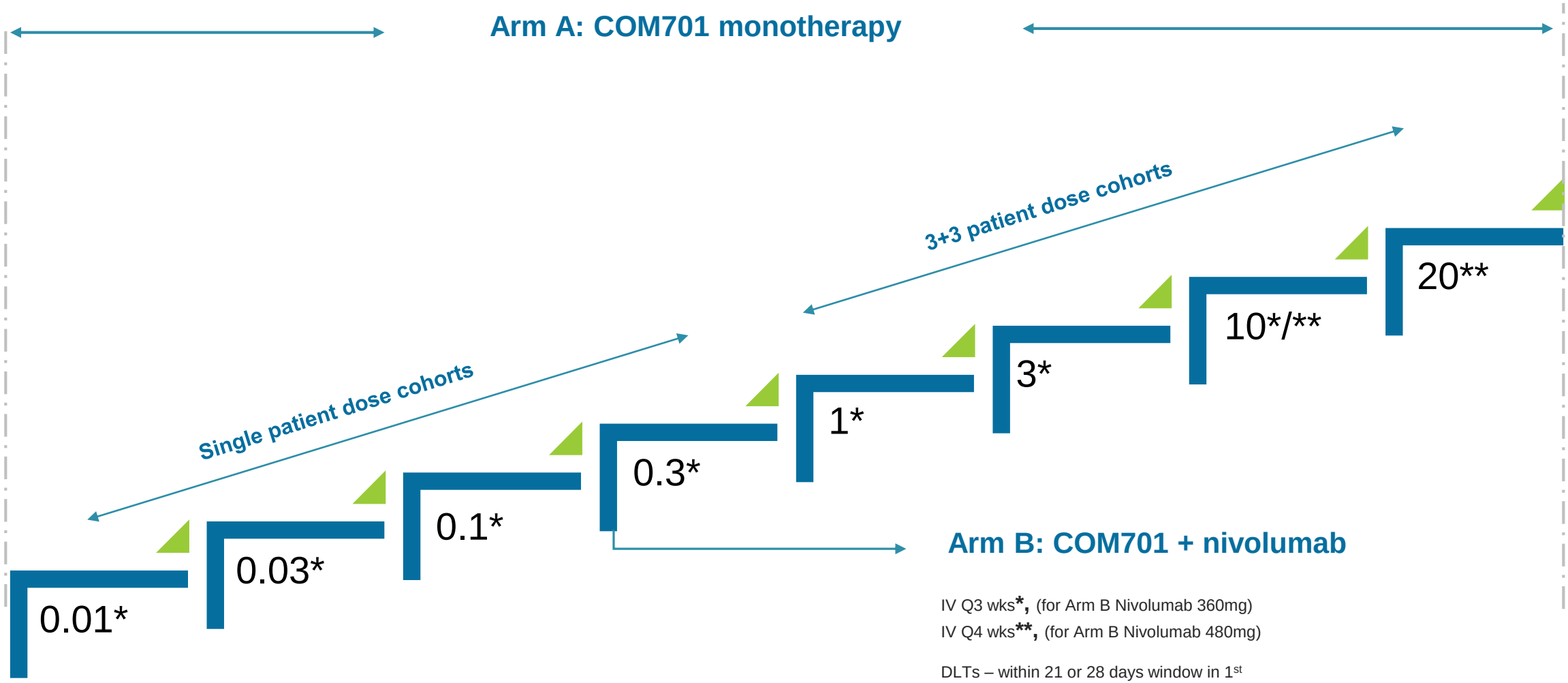
DOSE ESCALATION SCHEMA



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SUMMARY OF ADVERSE EVENTS – SAFETY ANALYSIS SET

Parameter	Arm A	Arm B
Dose escalation (All patients)	N= 18 n (%)	N=13 n (%)
Any TEAE (n, %) ≤G2 G3 G4 Grade 5 AE leading to study treatment discontinuation	17 (95) 10 (56) 6 (33) - 1* (6) 5 (28)	13 (100) 7 (54) 5 (38) - 1** (8) -
Any SAE (n, %) ≤G2 G3 G4 Grade 5 SAE leading to study treatment discontinuation	7 (39) 1 (6) 5 (27) - 1* (6) 5 (28)	5 (39) 1 (8) 3 (23) - 1** (8) -

Safety analysis set – all subjects who received ≥1 dose of any of the study drugs

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AEs/SAEs leading to study treatment discontinuation were deemed related to disease per investigator assessment.

*Cardiac arrest
**Progressive disease

SUMMARY OF SERIOUS ADVERSE EVENTS LEADING TO STUDY TREATMENT DISCONTINUATION

Subject ID (Arm)	Tumor type	Adverse event	Relatedness (per investigator assessment)
801 (A)	Pancreatic cancer	Cardiac arrest (G5)	Related to disease
4 (A)	Pancreatic cancer	Vomiting (G3)	Related to disease
13 (A)	CRC	Pulmonary embolism, worsening ascites (both G3)	Related to disease
10 (A)	CRC	Worsening Atrial fibrillation (G3)	Related to disease
12 (A)	Gallbladder CA	Progressive disease, Urinary retention (G1), Blood bilirubin increased (G2), Diarrhea (G3)	Related to disease

Safety analysis set – all subjects who received ≥1 dose of any of the study drugs

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INCIDENCE OF TREATMENT EMERGENT ADVERSE EVENTS (TEAE) IN ≥3 PATIENTS - MONOTHERAPY

Preferred Term	Grade 1/2 N (%)	Grade 3/4/5* N (%)	All Grades N (%)
Any TEAE	10 (56)	7 (39)	17 (95)
Fatigue	7 (39)	-	7 (39)
Nausea	5 (28)	-	5 (28)
Anxiety	4 (22)	-	4 (22)
Diarrhea	3 (17)	1 (5)	4 (22)
Dyspnea	3 (17)	1 (5)	4 (22)
Vomiting	3 (17)	1 (5)	4 (22)
Abdominal Pain	2 (11)	1 (5)	3 (16)
Pyrexia	3 (17)	-	3 (17)

Safety analysis set – all subjects who received ≥1 dose of any of the study drugs

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No Grade 4 events*. 1 G5 AE (cardiac arrest) was reported in Any TEAE.
Cardiac arrest unrelated to study drug, related to disease progression per investigator assessment.

INCIDENCE OF TEAEs IN ≥3 PATIENTS – COMBINATION THERAPY

Preferred Term	Grade 1/2 N (%)	Grade 3/4/5* N (%)	All Grades N (%)
Any TEAE	7 (54)	6 (46)	13 (100)
Fatigue	5 (39)	-	5 (39)
Anemia	3 (23)	1 (7)	4 (31)
Constipation	3 (23)	-	3 (23)
Nausea	2 (15)	1 (8)	3 (23)
Oedema peripheral	3 (23)	-	3 (23)

Safety analysis set – all subjects who received ≥1 dose of any of the study drugs

DATA CUT 31MAR2020

No Grade 4 events*. 1 G5 SAE (cardiac arrest) was reported in Any TEAE.
Cardiac arrest unrelated to study drug, related to disease progression per investigator assessment.

INCIDENCE OF SERIOUS TEAEs IN ALL PATIENTS - MONOTHERAPY (N = 18)

Preferred Term	Grade 1/2 N (%)	Grade 3/4/5[#] N (%)	All Grades N (%)
Any serious TEAE	1 (6)	6 (33)	7 (39)
Ascites*	-	1 (11)	1 (11)
Abdominal pain*	-	1 (6)	1 (6)
Atrial fibrillation*	-	1 (6)	1 (6)
Blood bilirubin increased*	1 (6)	-	1 (6)
Cardiac arrest*	-	1 (6)	1 (6)
Pulmonary embolism*+	-	1 (6)	1 (6)
Pyrexia*	1 (6)	-	1 (6)
Sepsis*	-	1 (6)	1 (6)
Vomiting*	-	1 (6)	1 (6)

Safety analysis set – all subjects who received ≥1 dose of any of the study drugs

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*Deemed related to disease per investigator assessment
+Deemed possibly related to COM701 per investigator assessment

[#]1 G5 event of cardiac arrest – deemed related to disease per investigator assessment; No G4 events

INCIDENCE OF SERIOUS TEAEs IN ALL PATIENTS - COMBINATION (N = 13)

Preferred Term	Grade 1/2 N (%)	Grade 3/4/5* N (%)	All Grades N (%)
Any serious TEAE	1 (8)	4 (31)	5 (39)
Pulmonary embolism*	-	2	2 (15)
Hypokalaemia*	-	1 (8)	1 (8)
Malignant neoplasm progression*	-	1 (8)	1 (8)
Pyrexia*	1 (8)	-	1 (8)

Safety analysis set – all subjects who received ≥1 dose of any of the study drugs

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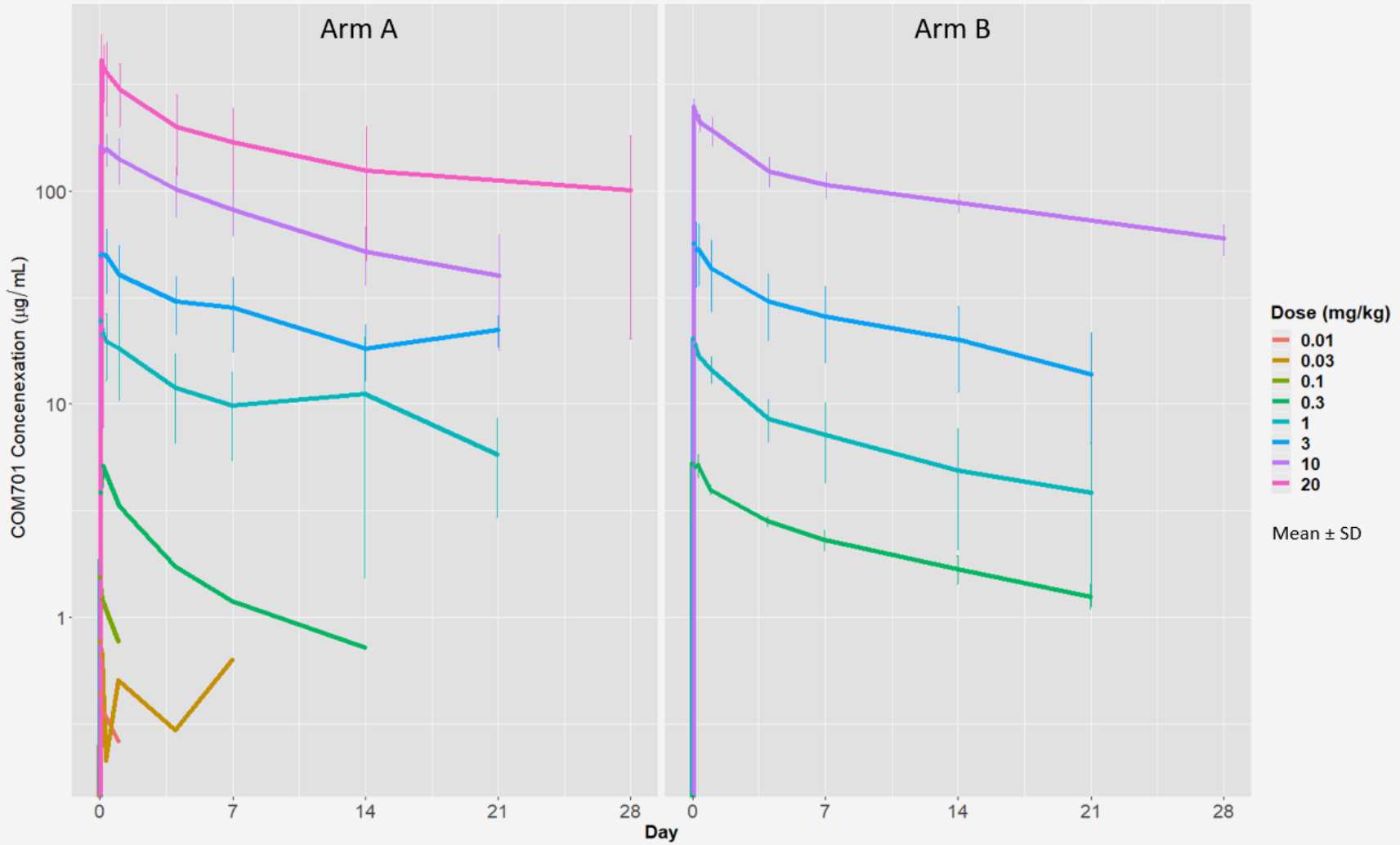
*Deemed related to disease per investigator assessment

No Serious TEAEs deemed related to COM701 per investigator assessment

COM701 PK PROFILE FOLLOWING IV INFUSION AT CYCLE 1 DAY 1 - ARMS A and B



SUMMARY OF INVESTIGATOR-ASSESSED RESPONSE (per RECIST v1.1 DLT-EVALUABLE POPULATION)

	Arm A (N = 16) N (%)	Arm B (N = 12) N (%)
ORR (CR+PR)	1 (6)	1 (8)
Disease control rate (CR+PR+SD)	11 (69)	9 (75)
Durable SD (SD ≥ 6 months)	2 (13)	4 (33)
Best response CR PR SD PD NA	 0 1 (6) 10 (63) 4 (25) 1 (6)	 0 1 (8) 8 (67) 2 (17) 1 (8)

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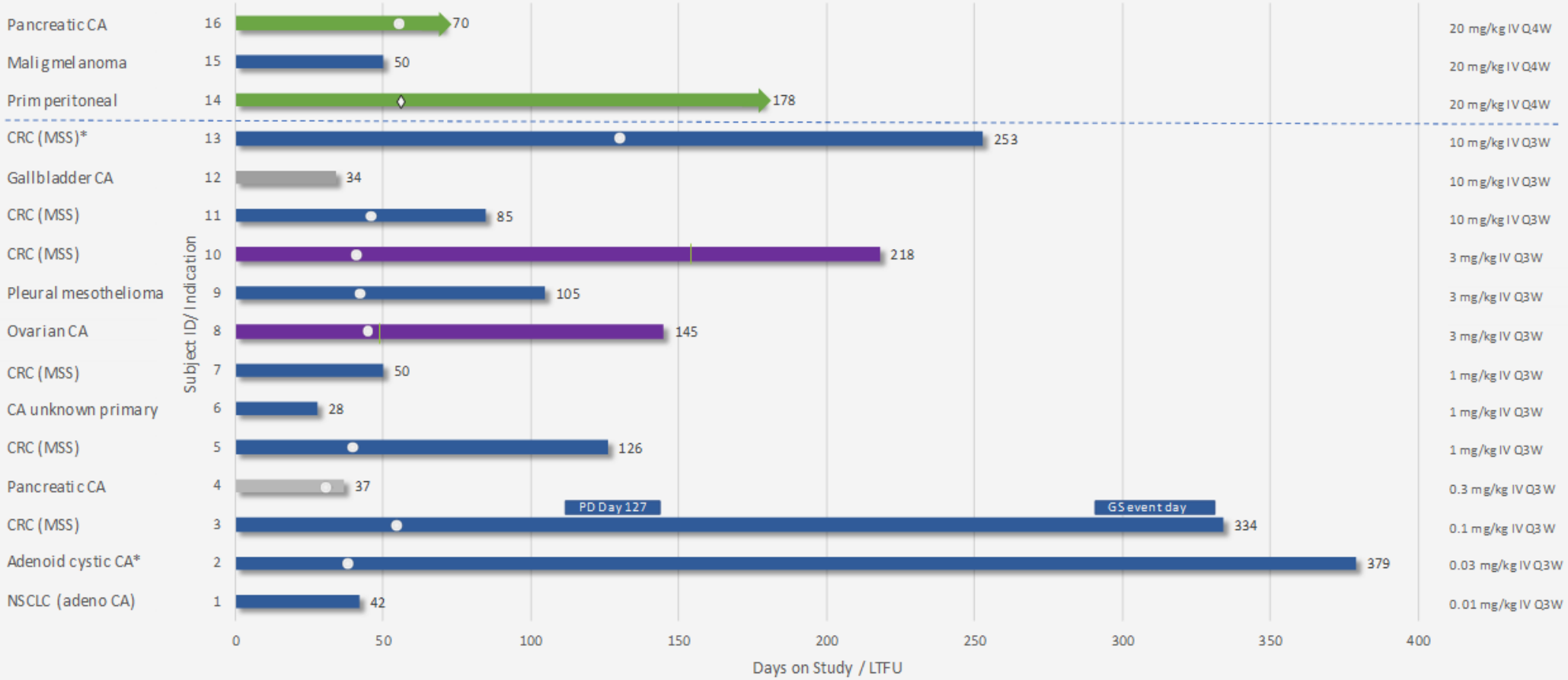
SWIMMER PLOT – ARM A



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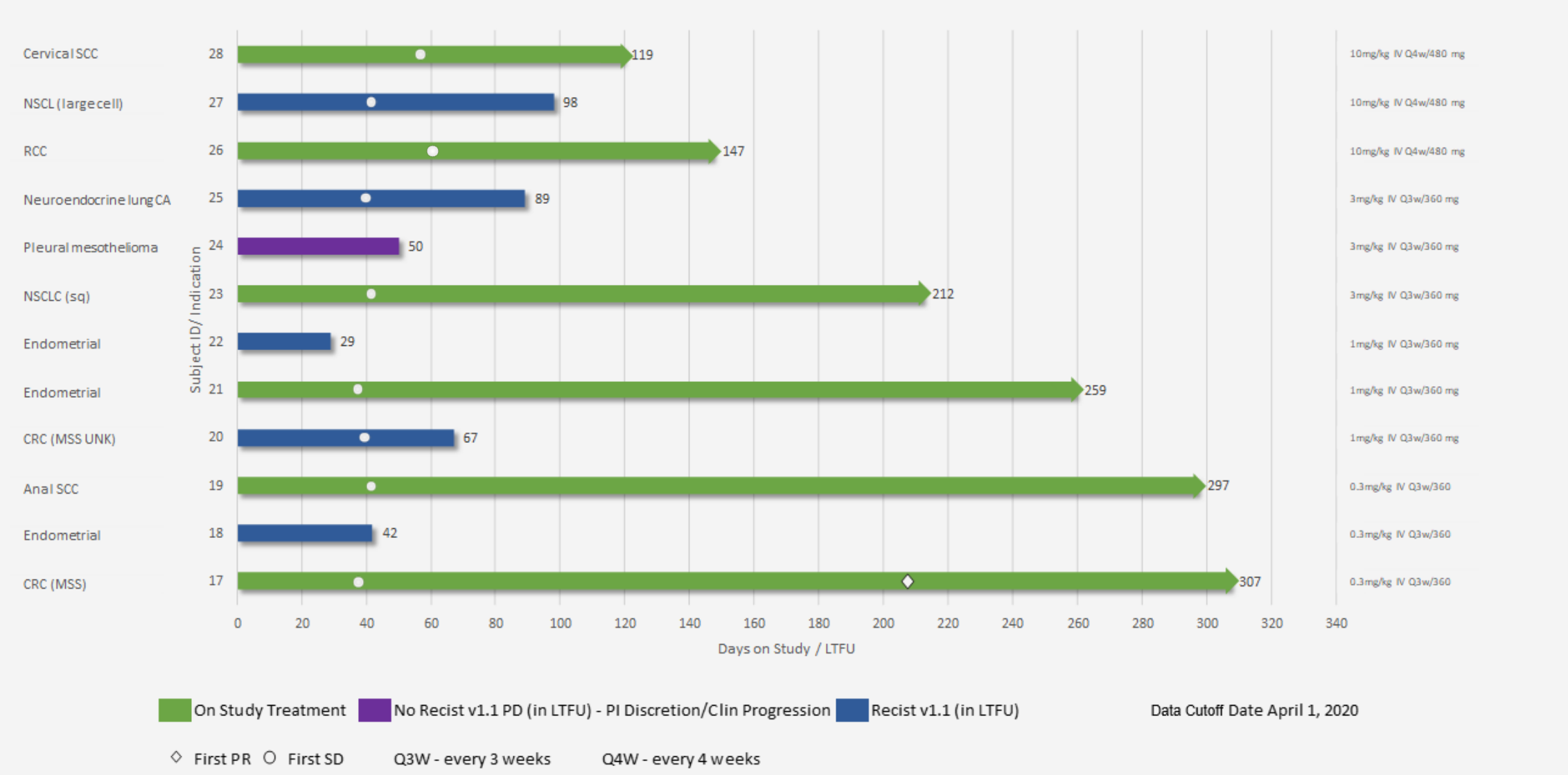
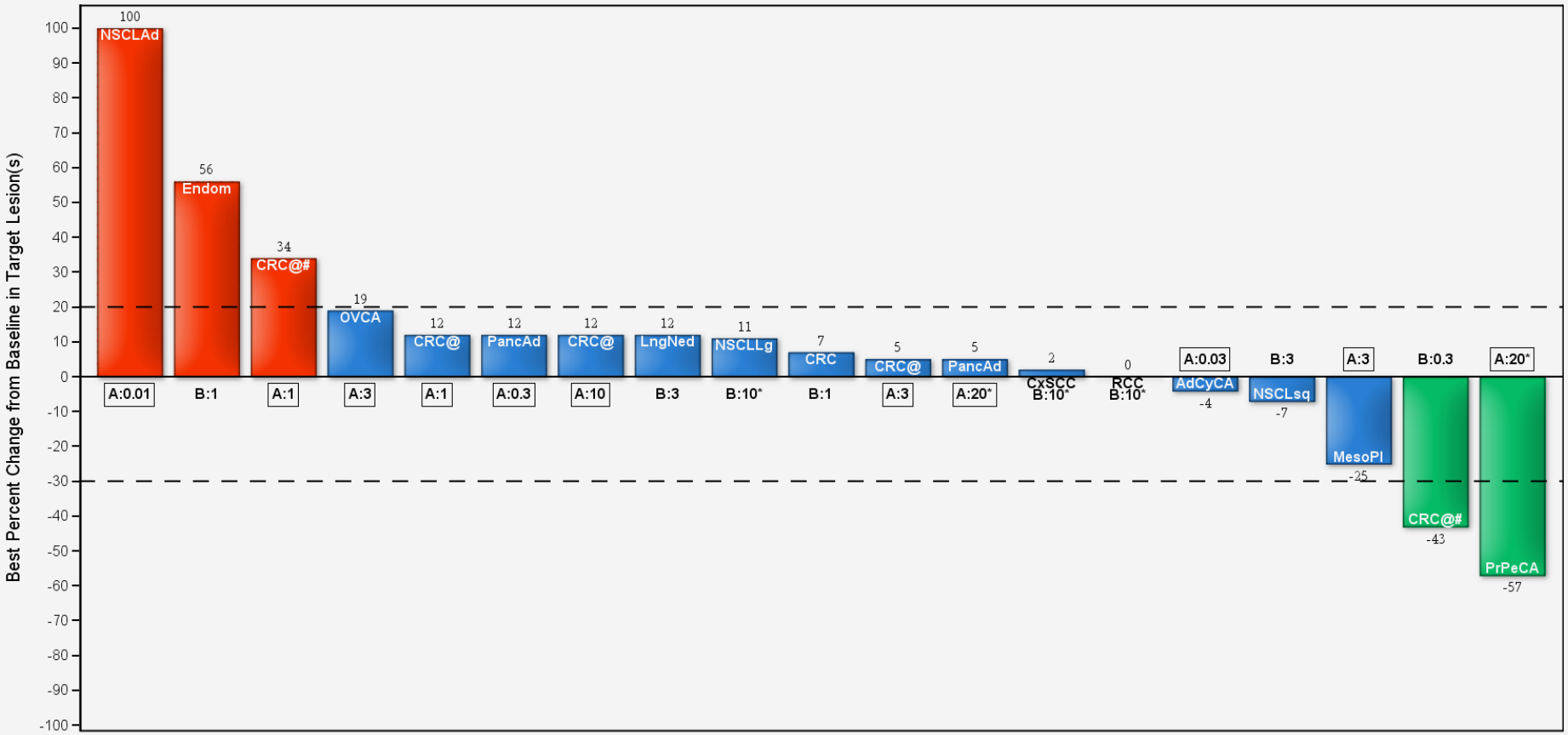
SWIMMER PLOT – ARM B



WATERFALL PLOT



DLT-Evaluable Population with Evaluable and Measureable Target Lesions (N = 19): PD SD PR @ CRC-MSS # KRAS mutant

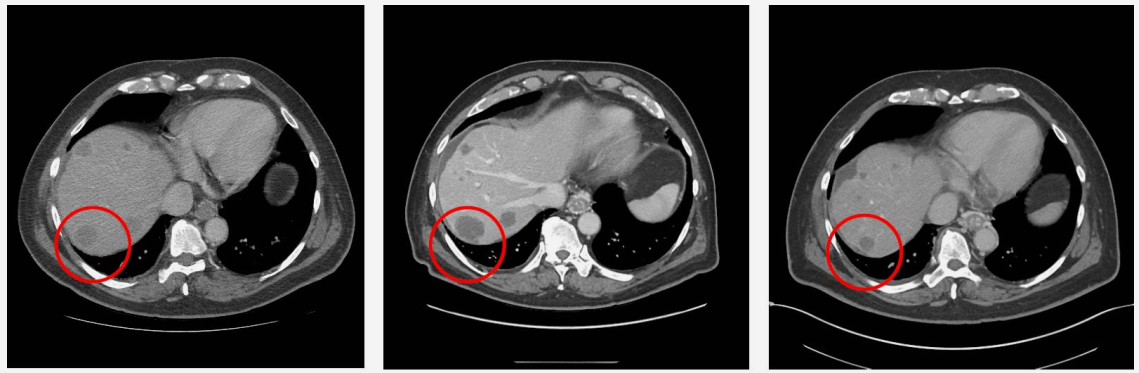
Treatment regimen (ARM:COM701 dose (mg/kg)) is displayed along the x-axis. A = monotherapy, B = combination therapy (Nivolumab 360 mg for COM701 doses < 10 mg/kg, Nivolumab 480 mg for higher COM701 doses), * = Q4W.

DATA CUT 01APR2020

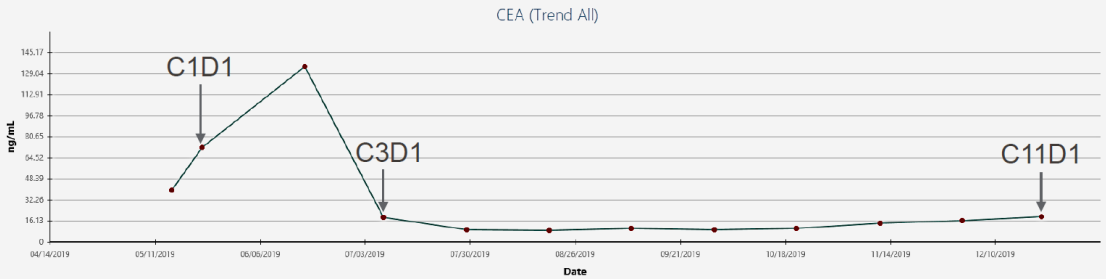
COM701 + NIVOLUMAB – CONFIRMED PR IN A PATIENT WITH MSS COLORECTAL CANCER (ONGOING STUDY TREATMENT 44 WKS)

66 year old male with metastatic CRC (MS Stable), with KRAS mutation
4 prior lines of chemotherapy; Best response of PD to anticancer therapy prior to study enrollment
Study Treatment: COM701 0.3 mg/kg + nivolumab 360 mg; both IV Q3 wks

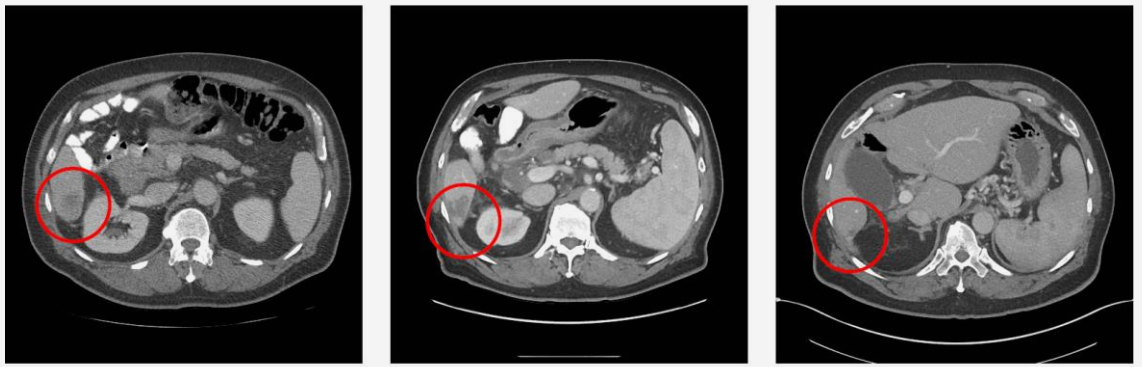
Target lesion 1



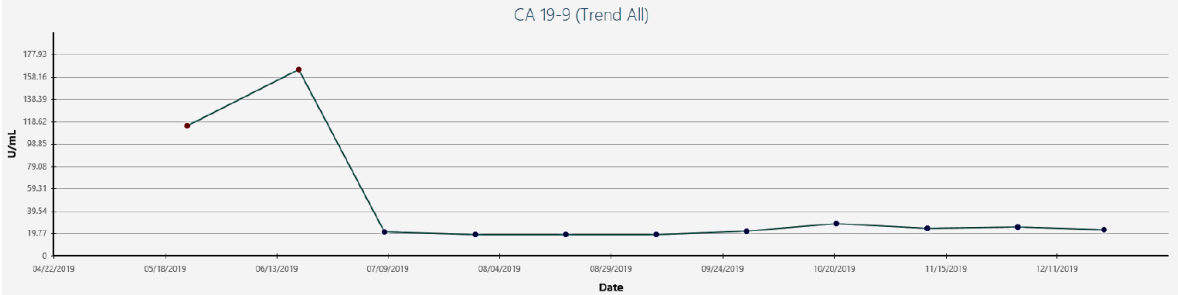
Baseline* (05/02/2019) | C3D1 (07/08/2019) | C11D1 PR (12/22/2019)



Target lesion 2



Baseline* (05/02/2019) | C3D1 (07/08/2019) | C11D1 PR (12/22/2019)



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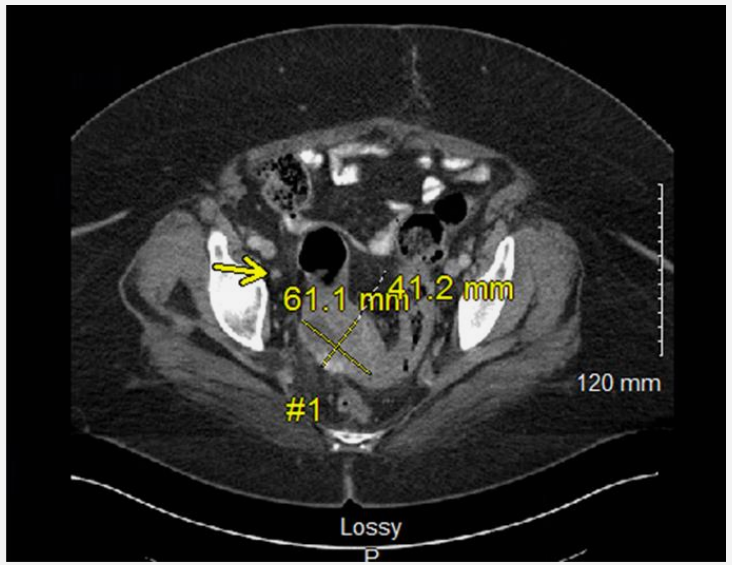
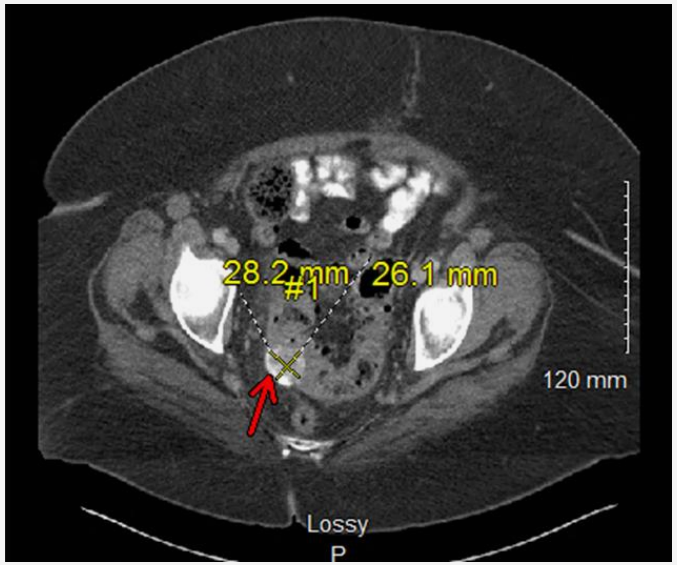
COM701 MONOTHERAPY – CONFIRMED PR IN A PATIENT WITH MSS PLATINUM RESISTANT PRIMARY PERITONEAL CANCER ONGOING STUDY TREATMENT 25 WKS

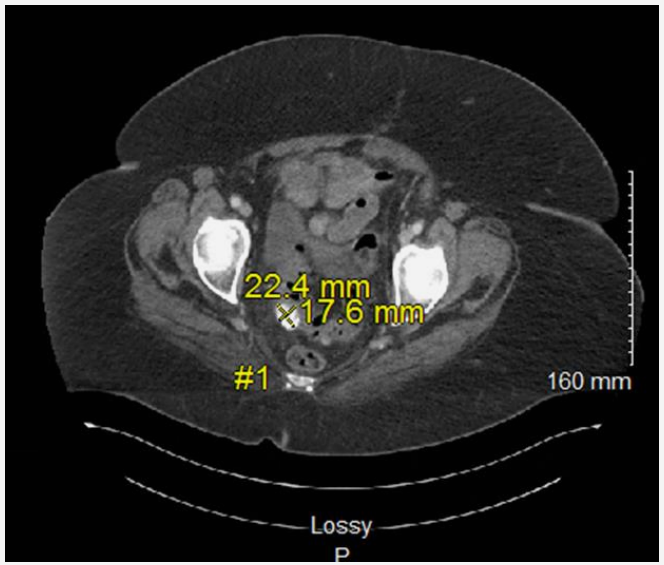
63 year old female with microsatellite stable platinum resistant primary peritoneal cancer.
PDL1 negative, MRE11 mutation; 3 prior lines of chemotherapy
Study Treatment: COM701 20 mg/kg IV Q 4 wks



Baseline: 9/11/19



C2D28: 12/2/19 (PR)



C6D28: 3/23/20 (PR)

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CONCLUSION

- COM701 well tolerated and with a manageable safety profile as monotherapy and in combination with nivolumab
  - No increase in toxicity in combination with nivolumab
  - No subjects discontinued study treatment due to toxicity of any study drug
- Single-agent MTD COM701 20 mg/kg IV Q4 wks; combination dose escalation continues
- Confirmed partial responses in 2 pts
  - COM701 monotherapy 20 mg/kg IV Q4 wks - primary peritoneal cancer (ongoing on study treatment 25 wks)
  - COM701 (COM701 0.3 mg/kg IV Q3 wks) + Nivolumab (480 mg IV Q3 wks) - MSS-CRC (ongoing on study treatment 44 wks)
- Disease control rate (COM701 monotherapy 11/16 [69%]; COM701+nivolumab 9/12 [75%]) in diverse tumor types
  - Durable stable disease (SD ≥ 6 months) in 6/28 pts [Arm A: 2 pts, Arm B: 4 pts]
    - Arm A: Adenoid cystic CA, CRC-MSS
    - Arm B: Anal SCC, CRC-MSS, Endometrial, NSCLC (squamous)
- Preliminary COM701 PK profile supports IV Q4 wks dosing
- COM701 monotherapy dose expansion at RDFE planned (NSCLC, OVCA, Breast, Endometrial, MSS-CRC)

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