PHASE 1 STUDY OF THE SAFETY, TOLERABILITY AND PRELIMINARY ANTI-TUMOR ACTIVITY OF COM701 MONOTHERAPY IN PATIENTS WITH ADVANCED SOLID TUMORS.

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BACKGROUND

- COM701 is a novel first-in-class immune checkpoint inhibitor (ICI) of poliovirus receptor related immunoglobulin domain (PVRIG) discovered by Compugen's computational discovery program[1]. It inhibits the binding of PVRIG with its ligand, PVRL2
- PVRIG is a member of the DNAM/TIGIT signaling axis regulating the activity of T/NK-cells
- In preclinical experiments we have demonstrated that PVRIG inhibition leads to activation of T cells in the tumor microenvironment generating an anti-tumor immune response and tumor growth inhibition[2]
- There is an urgent need to develop treatments for patients who are refractory or relapse after treatment with current ICIs
- We hypothesized that COM701 will be safe and tolerable and demonstrate preliminary antitumor activity as monotherapy in patients with advanced solid tumors

METHODS - STUDY SCHEMA

Phase 1a

Arm A

Monotherapy
Dose escalation
Hybrid study design - Single pt (first 4 dose levels) and 3+3 for subsequent dose levels

All comers (progressed on SOC)

Monotherapy
Cohort Expansion
(20 patients; progressed on SOC)

NSCLC, Ovarian, Breast, Endometrial

Arm B

Dual combination
(Escalating doses of COM701 with fixed dose of Nivolumab)

All comers

Phase 1b

Dual Combination
(COM701 + Nivolumab)
Expansion
(~20 patients/cohort)

NSCLC, Ovarian, Breast, Endometrial

Study objectives

- **Safety & Tolerability: Dose-limiting toxicities**
- **PK/PD**
- **Anti-tumor activity: COM701 monotherapy and in combination with Opdivo**

Imaging

- **CT/MRI scan Q6 weeks x6 cycles then Q12 weeks**
- **Investigator Assessed Response as per RECIST v1.1**

Identifier: NCT03667716

Red box – patient data presented in this poster

KEY ELIGIBILITY CRITERIA

INCLUSION

- Age ≥18 yrs
- Histologically or cytologically confirmed, locally advanced or metastatic solid malignancy and has exhausted all the available standard therapy or is not a candidate for the available standard therapy
- ECOG performance status 0-1
- Prior immune checkpoint inhibitor permissible
- Adequate hematological, hepatic & renal function

EXCLUSION

- Symptomatic interstitial lung disease or inflammatory pneumonitis
- Untreated or symptomatic central nervous system metastases
- History of immune-related events that led to immunotherapy treatment discontinuation

PATIENT CHARACTERISTICS – BASELINE CHARACTERISTICS

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	Dose of COM701 Monotherapy (mg/kg) IV Q3 weeks							Total
	0.01	0.03	0.1	0.3	1	3	10	
Age								
≤65yrs	0	1	1	1	3	1	3	10
>65yrs	1	0	0	0	0	2	0	3
ECOG Performance status 0	1	1	1	1	2	3	2	8
1					1		1	5
Gender Female				0	1	2	2	8
Male	1	1	1	1	2	1	1	5
Stage of disease on study enrollment	IV	IV	IV	IV	IV*	IV	IV	IV
Tumor type on study enrollment								
Colorectal cancer	-	-	1	-	2	1	2	6
Non small cell lung cancer	1	-	-	-	-	-	-	1
Pancreatic cancer	-	-	-	1	-	-	-	1
Ovarian cancer	-	-	-	-	-	1	-	1
Adenocystic cancer	-	1	-	-	-	-	-	1
Cancer of unknown primary	-	-	-	-	1	-	-	1
Gallbladder cancer	-	-	-	-	-	-	1	1
Pleural mesothelioma	-	-	-	-	-	1	-	1

*Includes a pt with carcinoma of unknown primary

PATIENT CHARACTERISTICS – TREATMENT DISPOSITION

	Dose of COM701 Monotherapy (mg/kg) IV Q3 weeks							Total
	0.01	0.03*	0.1*	0.3	1	3	10	
Number of patients enrolled and treated	1	1	1	1	3	3	3	13
Dose limiting toxicity	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Median number of cycles of COM701	2	18	5	1	2	7	8	5
Median number of prior therapies (regimen)	7 (5)	2 (2)	7 (3)	3 (1)	10 (3)	7 (5)	6 (2)	7 (3)
Reason for study treatment discontinuation								
Adverse event	-	-	-	-	-	-	-	0
Progressive disease as per RECIST v1.1	1	0	1	0	3	1	-	6
Investigator discretion/clinical progression/deterioration/death		-	-	1	-	2	2	5
Continuing on treatment	-	1	-	-	-	-	1	2

*Intrapt dose escalation

INCIDENCE OF TREATMENT EMERGENT ADVERSE EVENTS (≥2 PATIENTS)

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	COM701 Monotherapy (N=13)			
Treatment-emergent adverse events (TEAE, PT), n (%)	Grade 1–2	Grade 3	Grade 4	Grade 5
Fatigue	6 (46)	-	-	-
Nausea	4 (31)	-	-	-
Vomiting	3 (23)	1 (8)	-	-
Disease progression/malignant neoplasm progression	3 (23)	-	-	3 (23)
Anxiety	3 (23)	-	-	-
Abdominal distension	2 (15)	-	-	-
Abdominal pain	2 (15)	1 (8)	-	-
Constipation	2 (15)	-	-	-
Cough	2 (15)	-	-	-
Dyspnea	2 (15)	1 (8)	-	-
Pyrexia	2 (15)	-	-	-
Hypotension	2 (15)	-	-	-
Stomatitis, mucosal inflammation	2 (15)	-	-	-
Rash	2 (15)	-	-	-

INCIDENCE OF TREATMENT EMERGENT SERIOUS ADVERSE EVENTS

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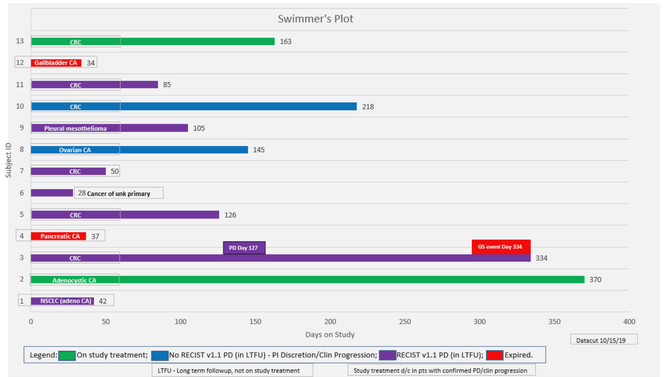
	COM701 Monotherapy (N=13)	Grade	Relationship to COM701	Relationship to Disease
	Any Grade N (%)			
Patients with any serious adverse event (by PT)	5 (38)	-	Not related (3/5 pts)	Related in 4/5 pts
Malignant Neoplasm Progression, disease progression	3 (23)	5	Not related	Related
Vomiting	1 (8)	3	Not related	Related
Abdominal Pain	1 (8)	3	Not related	Related
Pyrexia	1 (8)	1	Possibly related	Not related
Atrial fibrillation	1 (8)	3	Unlikely related	Related
Blood bilirubin increased	1 (8)	3	Not related	Related



PATIENTS WITH STABLE DISEASE - DOSE-RESPONSE RELATIONSHIP

SUBJECT ID	COM701 dose	Best on-study treatment response	Confirmed stable disease (Y/N)	Tumor type	Days on study treatment prior to PD or death
2	0.03 mg/kg	Stable disease	Y	Adenocystic cancer	N/A (ongoing on study treatment)
3	0.1 mg/kg	Stable disease	Y	CRC*†	PD –day 127, (Death on day 334)
4	0.3 mg/kg	Stable disease	N	Pancreatic cancer*†	37 (death)
5	1 mg/kg	Stable disease	Y	CRC*	126 (in LTFU)
8	3 mg/kg	Stable disease	N	Ovarian cancer (prior exposure to pembrolizumab)	145 (in LTFU)
9	3 mg/kg	Stable disease	N	Pleural mesothelioma (prior exposure to durvalumab)	105 (in LTFU)
10	3mg/kg	Stable disease	Y	CRC* (MS-S post data-cut date)	218 (in LTFU)
11	10 mg/kg	Stable disease	N	CRC*†	85 (in LTFU)
13	10 mg/kg	Stable disease	Y	CRC*†	N/A (ongoing on study treatment)

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BEST ON TREATMENT TIMEPOINT RESPONSE IN PTS WITH PRIOR TREATMENT REFRACTORY DISEASE

Subject ID	Tumor type	Best response to last prior therapy before study enrollment	Best timepoint response on COM701 study treatment	Confirmed SD (Y/N)
1	NSCLC	PD	PD	N
3	CRC	PD	SD	Y
4	Pancreatic CA	PD	SD	N
6	Carcinoma of unknown primary	PD	PD	N
8	OVCA	PD	SD	N
11	CRC	PD	SD	N
12	Gallbladder CA	PD	Did not reach 1st imaging timepoint assessment	N
13	CRC	PD	SD	Y

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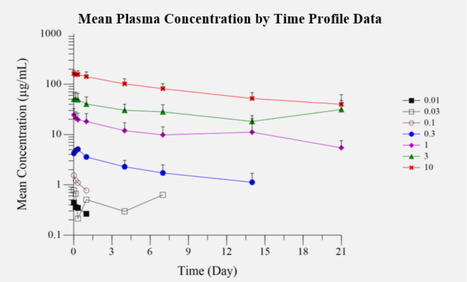
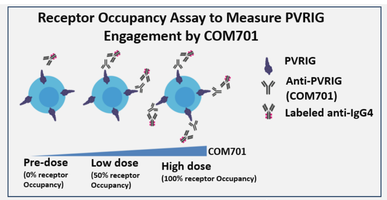
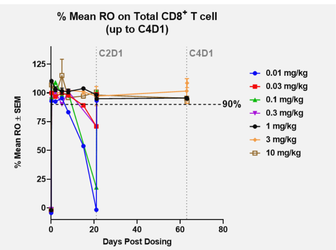
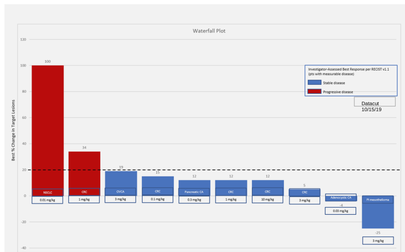






- >90% RO at ≥1 mg/kg observed for total CD3+ T cell and CD8+ T_{EMRA}



RESULTS

- No dose-limiting toxicities reported in the COM701 dose ranges evaluated (0.01 – 10 mg/kg)
- No treatment discontinuation due to adverse events were reported
- Majority of the TEAE were G1-2
- Frequent TEAE were fatigue (46%), nausea (31%) and anxiety (23%) – all G1-2; disease progression G5 (23%)
- Possible immune-related adverse events were rash (G1) and laboratory finding of elevated TSH (G1)
- Serious adverse events were reported in 5/13 pts
- In 3 pts, SAE were due to disease progression

- All pts had stage IV disease at study entry & 8/13 (62%) had best response of PD to last prior therapy (ie treatment-refractory disease) before enrollment on this study
- Best timepoint response of SD in 5/8 pts (63%) with prior treatment-refractory disease, 1/5 pt with confirmed SD
- Best timepoint response of SD/disease control rate reported in 9/13 pts (69%)
- Colorectal cancer was the most common tumor type enrolled with 6/13 pts, all 6 pts had microsatellite stable status (MSS-CRC)
- Disease control rate (SD) in 5/6 pts (83%) with CRC
- Confirmed SD (week 12) in 4/6 pts (67%) with CRC
  - Historical data 11% DCR & best timepoint response of SD at week 12 with pembrolizumab in pts with MSS-CRC [3]
- All 3 enrolled pts with CRC-kras mutation had a best timepoint response of SD; 2/3 with confirmed SD

- COM701 exposure dose proportional with repeat dosing
- Peripheral COM701 receptor occupancy ≥1 mg/kg IV Q3 weeks

CONCLUSIONS

- COM701 – 1st in-class ICI of PVRIG with a well tolerated safety profile with no DLTs and signal of antitumor activity
- Potential for combination with ICI and standard of care therapies
- Disease control rate (SD) - 9/13 pts (69%)
- Signal of antitumor activity in pts with MSS-CRC and pts with CRC with KRAS mutation
- Confirmed SD in 4/6 pts (67%) - MSS-CRC
- Confirmed SD in 2/3 pts with CRC-kras mutation
- Signal of antitumor activity in pts with: prior treatment-refractory disease, previously treated with ICI
- Trend in dose-response relationship
- COM701 exposure permits IV Q3 dosing
- Peripheral receptor occupancy at ≥90% with ≥1 mg/kg COM701 IV Q3 weeks
- 2 patients continue on study treatment
- Study enrollment is ongoing in Arms A (COM701 monotherapy) and B (COM701 in combination with nivolumab) - poster P422 at this scientific conference

ACKNOWLEDGMENT

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