Triple blockade of DNAM-1axis with COM701 (anti-PVRIG) + COM902 (anti-TIGIT) + pembrolizumab shows preliminary antitumor activity in patients with platinum resistant ovarian cancer, interim results of a phase I trial.

Type: Abstract

Topic: Therapeutic development

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Background

Treatment [tx] options for platinum resistant ovarian cancer [PROC] are limited. Responses in this patient [pt] group with immune check point inhibitors [ICI], including combination with anti-TIGIT antibodies, is <10% and ≈10% with chemotherapy[1,2,3]. COM701, a IgG4, potential 1st in-class ICI antibody blocks PVRIG, leading to activation of T-cells. COM902 is an IgG4 ICI blocker of TIGIT. A 20% objective response rate (ORR) following combination COM701 + BMS-986207 (anti-TIGIT) + nivolumab in PROC was previously reported[3]. We present an additional cohort of PROC pts treated with COM701, COM902 and pembrolizumab demonstrating encouraging antitumor activity, and safety, consistent with the prior report[4].

Methods

CPG-02-101 is ongoing. The PROC cohort enrolled 25 pts by April 2024. 25 safety-evaluable pts received COM701 15 mg/kg + COM902 3 mg/kg + pembrolizumab 200 mg Q3W. Primary objectives [obj]: safety/tolerability; secondary obj: antitumor activity. Key inclusion criteria: Age ≥ 18 yrs, up to 3 prior lines of tx for histologically confirmed PROC. Key exclusion criteria: prior receipt of any ICI. Investigator assessed responses per RECIST v1.1, AE severity per CTCAE v5.0.

Results

As of 16 May 2024, ORR was assessed in 23 efficacy evaluable pts median [med] age, 63yr, mean time on treatment 10.6 weeks [2-22 weeks, 10 pt ongoing, fig 3]. Best ORR 4/23 [17.4%] pts [1 CR, 3 PRs, table 2] and 6 pts with SD, resulting in a disease control rate [CR+PR+SD] of 10/23 [43.5 %, table 2]. ADC treatment was given to 6 of the pts prior to enrollment on to the study. One PR pt had prior treatment with mirvetuximab soravtansine-gynx. Strong peripheral IFN-γ induction was observed following treatment in 14 out of 14 pts tested. Majority of AEs were of ≤2 grade in severity. No grade 4/5 events were reported. One grade 3 event of serious immune related encephalopathy was reported in one pt, which was resolving following treatment with steroids [tables 3,4].

Conclusions

The combination of COM701 + COM902 + pembrolizumab demonstrates encouraging signal of antitumor activity with immune activation in pts with heavily pre-treated PROC. The study further supports the clinical utility of blocking PVRIG and TIGIT both of the DNAM -1 pathway + anti-PD1 in PROC. The trial is ongoing and updated data will be presented at the conference. Data extract 05/16/2024.

Table 1: Subject Disposition

Variable *Reason [n (%)]* [1]	*COM902+COM701+Pembro Safety Evaluable Population (N=25)*	*COM902+COM701+Pembro Efficacy Evaluable Population (N=23)*
Ongoing in study treatment	10 (40%)	10 (43%)
Discontinued study treatment	15 (60%)	13 (57%)
Adverse Event	1 (7%)	-
Progression per RECIST 1.1	12 (80%)	11 (85%)
Progressive Disease due to Clinical Evaluation	2 (13%)	2 (15%)
Ongoing in study	21 (84%)	19 (83%)
Discontinued study	4 (16%)	4 (17%)
Death	3 (75%)	3 (75%)
Other	1 (25%)	1 (25%)

[1] Denominator for each reason is the number of patients who discontinued study (treatment) in the respective dose group.

Table2: Summary of Overall Response Rate (ORR) and Disease Control Rate (DCR)

	Characteristics	*COM902+COM701+Pembro (N=23)*
ORR (CR+PR)[1]		4 (17%)
DCR (CR+PR+SD)[2]		10 (43%)
Best Overall Response (BOR)		
	CR	1 (4%)
	PR	3 (13%)
	SD	6 (26%)
	PD	12 (52%)
	Missing[3]	1 (4%)

CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease;
ORR, objective response rate; DCR, disease control rate.

[1]Unconfirmed assessments included - 1 PR.

[2]Unconfirmed assessments included - 1 PR, 2 SD.

[3]First post screening tumor assessment not yet performed by time of data cutoff

Table 3 - Overall Summary of TEAEs ovarian cancer, triplet dose expansion

Adverse Event Category [n (%)]	COM902+COM701 +Pembrolizumab (N=25)
Any TEAE	25 (100%)
Any Grade 3 or Greater TEAEs	7 (28%)
Any Serious TEAE	4 (16%)
Any Serious Related TEAEs*	1 (4%)
Any TEAEs Leading to Treatment Discontinuation	2 (8%)
Any Infusion-Related TEAEs	3 (12%)
Any Immune-Related TEAEs	*11 (44%)*
Any TEAE leading to Death	*0 (0%)*

TEAE – Treatment emergent adverse event

Table 4 - TEAEs by Preferred Term and Severity reported in at least 15% of the participants, Ovarian Cancer, *t*riplet *d*ose *e*xpansion.

AE preferred Term / n [%] *(N=25)*	Grade 1	*Grade 2*	*Grade 3*	*Grade 4/5*	*All Grades*
Any TEAE	7 (28)	11 (44)	7 (28)	-	25 (100)
Fatigue	4 (16)	3 (12)	1 (4)	-	8 (32)
Diarrhoea	6 (24)	1 (4)	-	-	7 (28)
Nausea	3 (12)	3 (12)	-	-	6 (24)
Abdominal pain	1 (4)	3 (12)	-	-	4 (16)
Vomiting	4 (16)	-	-	-	4 (16)

Figure 1: Waterfall plot

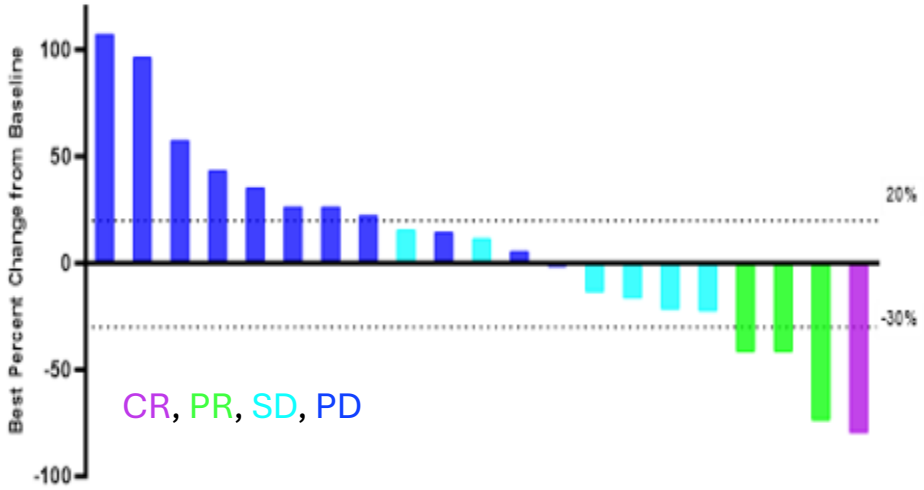


Figure 2: CA125 changes

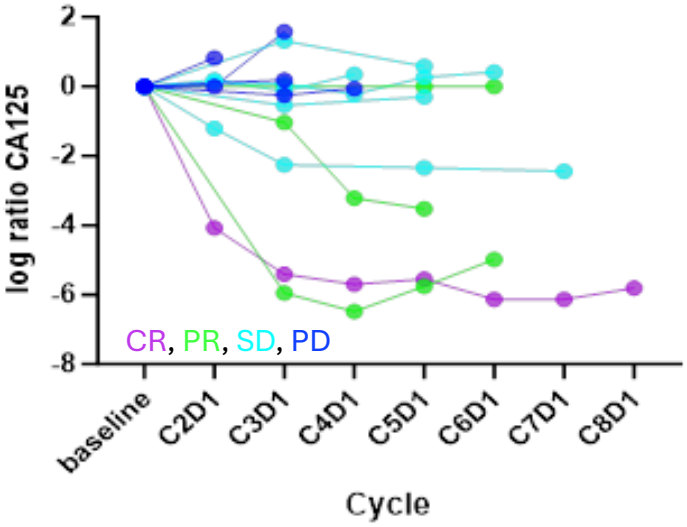
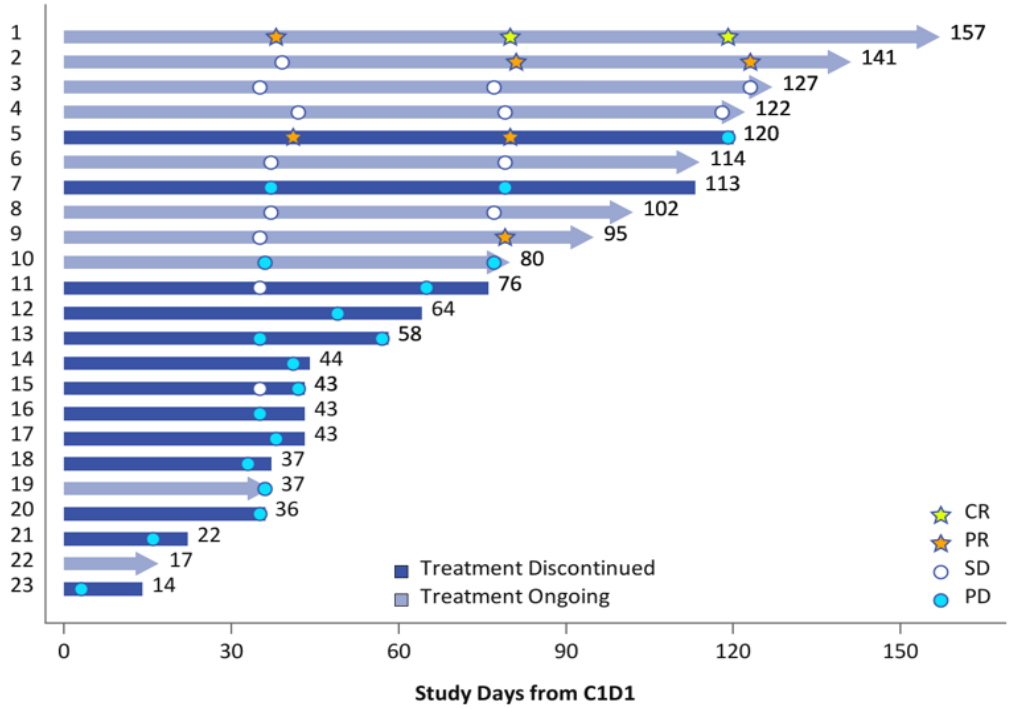


Figure 3: Swimmer's plot



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The CPG-02-101 trial is being conducted in accordance with the ethical principles stipulated in the Declaration of Helsinki. Clinical trial identification NCT04354246.