CT180

Safety and efficacy of vibostolimab plus pembrolizumab and coformulation of vibostolimab with pembrolizumab in ovarian cancer naive to PD-1/PD-L1 inhibitors in KEYVIBE-001

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Background

- Vibostolimab is a humanized monoclonal antibody that inhibits the interaction between the immune checkpoint receptor T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains (TIGIT) and its ligands
  - TIGIT is an immunomodulatory receptor expressed primarily on activated CD4+ and CD8+ T cells and natural killer cells[1]
- Pembrolizumab, a monoclonal antibody that inhibits PD-1, has shown modest efficacy when used as monotherapy in advanced ovarian cancer, with an objective response rate (ORR) of 7% in patients with PD-L1–positive (combined positive score [CPS] ≥ 1) tumors at the final analysis of the KEYNOTE-100 study[2]
- TIGIT is highly co-expressed with PD-1 on both CD4+ and CD8+ tumor-infiltrating lymphocytes
- Combination therapy with vibostolimab and pembrolizumab has shown promising antitumor activity in PD-1/PD-L1 inhibitor–naive non–small cell lung cancer[3]
- A vibostolimab/pembrolizumab coformulation has been developed as a 30-minute intravenous infusion, presenting a convenient combination therapy option for patients with advanced solid tumors

Objective

- To evaluate the safety and efficacy of vibostolimab and pembrolizumab given sequentially (vibostolimab + pembrolizumab) or as a coformulation (vibostolimab/pembrolizumab) in patients with advanced epithelial ovarian cancer (EOC) naive to PD-1/PD-L1 inhibitors

Methods

Study design and patients

- This is a cohort of the ongoing, multicenter, multicohort, phase 1 KEYVIBE-001 trial (NCT02964013) that enrolled patients with advanced EOC naive to PD-1/PD-L1 inhibitors
- Patients were nonrandomly assigned to receive vibostolimab 200 mg intravenously (IV) and pembrolizumab 200 mg IV every 3 weeks given sequentially or as a coformulation for up to 35 cycles
  - Patients who were administered vibostolimab plus pembrolizumab sequentially must have received a platinum-containing first-line therapy followed by a platinum-free interval of <6 months or received ≥2 prior lines of therapy including a platinum-containing first-line treatment
  - Patients who were administered the vibostolimab/pembrolizumab coformulation must have received a platinum-containing first-line therapy followed by a platinum-free interval of <6 months; patients who received subsequent lines of therapy were permitted provided their disease progressed within 6 months of completion of a platinum-containing regimen
  - Treatment was discontinued if patients experienced unacceptable toxicity, progressive disease (PD), or withdrew from the study

Assessments and statistical analyses

- Primary end points were safety and tolerability
- Secondary end points included ORR as assessed by investigator review per RECIST v1.1 and pharmacokinetic (PK) profiles of vibostolimab + pembrolizumab and vibostolimab/pembrolizumab
- Exploratory end points included duration of response (DOR) and progression-free survival (PFS) as assessed by investigator review per RECIST v1.1
- Safety was analyzed in all patients who received ≥1 dose of study treatment
- Efficacy was analyzed in all patients with measurable disease at baseline who received ≥1 dose of study treatment
- PK profile was analyzed in patients who had at least 1 postdose observed concentration to ensure that the data generated would exhibit effects of the treatment
- Database cutoff date was October 6, 2021

Results

- Median follow-up (time from first dose to date of death or database cutoff) was 18 months (range, 11–42) in the sequentially administered vibostolimab + pembrolizumab arm and 13 months (range, 7-14) in the vibostolimab/pembrolizumab coformulation arm

Table 1. Baseline characteristics in patients with PD-1/PD-L1 inhibitor–naive EOC

Characteristic	Vibostolimab + pembrolizumab, sequentially administered n = 21	Vibostolimab/pembrolizumab coformulation n = 40
Age, median (range), years	58 (36-73)	59 (32-76)
ECOG PS, n (%)		
0	13 (62)	19 (48)
1	8 (38)	21 (53)
PD-L1 status, n (%)		
CPS ≥1[a]	6 (29)	15 (38)
CPS <1	11 (52)	20 (50)
Unknown	4 (19)	5 (13)
BRCA1 and/or *BRCA2* mutation status		
Positive	0 (0)	9 (23)
Negative	0 (0)	20 (50)
Unknown	21 (100)	11 (28)
Prior lines of therapy, n (%)[b]		
Adjuvant/neoadjuvant	4 (19)	0 (0)
1	2 (10)	2 (5)
2	5 (24)	10 (25)
≥3	10 (48)	28 (70)
Prior platinum therapy category, n (%)[c]		
Platinum refractory	1 (5)	6 (15)
Platinum resistant[d]	12 (57)	33 (83)
Platinum sensitive	8 (38)	0 (0)

ECOG PS, Eastern Cooperative Oncology Group performance status.
[a]When CPS [calculated as the number of PD-L1–staining cells (tumor cells, macrophages, and lymphocytes) divided by the total number of viable tumor cells, multiplied by 100] was scoring a tumor proportion score of 1% or a combined positive score of 1 was used to define PD-L1 positivity.
[b]Prior treatment line: cited 66% of patients who received 1 line of treatment and over 70% who received ≥ 2 lines of therapy.
[c]Prior platinum therapy was not required for 1 patient in the coformulation arm.
[d]Platinum-resistant disease was defined as disease relapse ≤ the 6 months after completion of platinum-based chemotherapy.

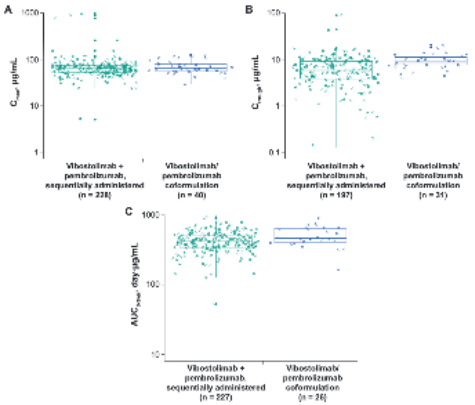
Table 2. Treatment-related adverse event summary in patients with PD-1/PD-L1 inhibitor–naive EOC

Event, n (%)	Vibostolimab + pembrolizumab, sequentially administered n = 21	Vibostolimab/pembrolizumab coformulation n = 40
Any	17 (81)	31 (78)
Grade 3-5	4 (19)	4 (10)
Serious[a]	1 (5)	3 (8)
Led to discontinuation[a]	0 (0)	1 (3)
Led to death	0 (0)	0 (0)
Any-grade with incidence ≥15% in any arm		
Diarrhea	5 (24)	6 (15)
Increased AST	5 (24)	3 (8)
Rash	5 (24)	7 (18)
Chills	4 (19)	6 (15)
Fatigue	4 (19)	10 (25)
Pruritus	4 (19)	10 (25)
Nausea	1 (5)	10 (25)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; TRAE, treatment-related adverse event.
[a]Serious TRAEs were anemia (n = 1) with sequentially administered vibostolimab + pembrolizumab and anemia, diarrhea, and infusion-related reaction (n = 1 each) with vibostolimab/pembrolizumab coformulation.
[b]Treatment was discontinued because of increased AST and ALT (n = 1) with vibostolimab/pembrolizumab coformulation.

- PK exposure was similar between the sequentially administered vibostolimab + pembrolizumab and the vibostolimab/pembrolizumab coformulation arms

Figure 1. Comparison between sequential administration and coformulation on the (A) observed peak vibostolimab concentrations at end of infusion (C_{max}) during cycle 1, (B) C_{trough} at the end of the dosing interval during cycle 1, and (C) AUC exposure during cycle 1



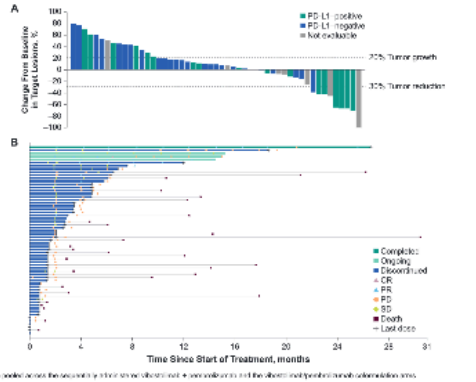
AUC_{tau}, area under the curve from 0 to 2 weeks; C_{max}, peak concentration; C_{trough}, trough concentration.
Data shown for all patients enrolled in KEYVIBE-001 in the observed PK data.

Table 3. Response summary based on investigator assessment per RECIST v1.1 in patients with PD-1/PD-L1 inhibitor–naive EOC

	By treatment arm		By PD-L1 status[a]		
	Vibostolimab + pembrolizumab, sequentially administered n = 21	Vibostolimab/ pembrolizumab coformulation n = 40	CPS ≥1 n = 21	CPS <1 n = 31	Total N = 61
Confirmed ORR, n (%)	2 (10)	3 (8)	5 (24)	0 (0)	5 (8)
CR, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
PR, n (%)	2 (10)	3 (8)	5 (24)	0 (0)	5 (8)
SD, n (%)	6 (29)	8 (20)	2 (10)	6 (28)	14 (23)
PD, n (%)	10 (48)	20 (50)	10 (48)	18 (58)	30 (49)
Not available,[b] n (%)	3 (14)	9 (23)	4 (19)	5 (16)	12 (20)
Median DOR[c,d] (range), months	11 (4-19)	NR (6-12+)	19 (4-19)	–	19 (4-19)
Median PFS[c] (95% CI), months	2 (2-4)	2 (2-2)	2 (2-8)	2 (2-2)	2 (2-2)

CR, complete response; NR, not reached; PR, partial response; SD, stable disease.
[a]PD-L1 status was missing for 9 patients; data pooled across the sequentially administered vibostolimab + pembrolizumab and the vibostolimab/pembrolizumab coformulation arms.
[b]Patients with no postbaseline assessment are available for response evaluation or patients who ineligible/died prior to assessment of response per RECIST v1.1.
[c]From product-limit (Kaplan–Meier) estimate.
[d]Individuals PD at the last disease assessment.

Figure 2. (A) Best change from baseline in target lesions and (B) time on treatment and response based on investigator assessment per RECIST v1.1 in patients with PD-1/PD-L1 inhibitor–naive EOC



Data cutoff date was October 6, 2021. [a]Patients who received ≥1 dose of vibostolimab + pembrolizumab and the vibostolimab/pembrolizumab coformulation arms.

Conclusions

- Safety and PK were comparable between the vibostolimab + pembrolizumab combination and the coformulation in patients with advanced EOC who were previously treated with platinum and were naive to PD-1/PD-L1 inhibitors
- Antitumor activity was equivalent between the combination and the coformulation
- Response in PD-L1–positive tumors was promising compared with historic pembrolizumab monotherapy, which suggests the need for further investigations of vibostolimab in combination with pembrolizumab, especially as the coformulation, in PD-L1–positive EOC

References

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