MADRID 2023 ESMO congress

AdvanTIG-202: Phase 2 Randomized, Multicenter, Open-Label Study of Tislelizumab With or Without Ociperlimab in Patients With Previously Treated Recurrent or Metastatic Cervical Cancer

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Madrid, Spain; 22 October 2023

DECLARATION OF INTERESTS

Dr. Jung-Yun Lee

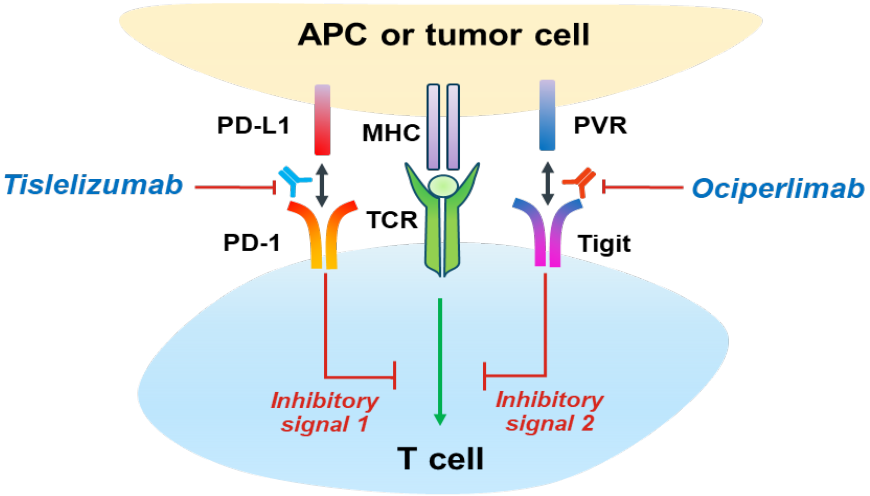
Advisory board positions: AstraZeneca (DP-02), GII (GI-101), OncoQuest (FLORA-5), Seagen (SGNTV-03), ImmunoGen (MIRASOL), Genmab (GEN1046-05), MSD (MK4830-002)

Lectures: AstraZeneca, Janssen, MSD, Roche, Takeda, ONO

Institutional financial interest: Advenchen, Ascendis Pharma, Alkermes, AstraZeneca, Beigene, BergenBio, BMS, Cellid, Clovis Oncology, Eisai, Genmab, GII, GSK, ImmunoGen, Janssen, Merck, Mersana, MSD, Novartis, Onconic Therapeutics, OncoQuest, ONO, Regeneron, Roche, Seagen, Sutro, Synthon, Takeda

Background

- CC is the 4th most common cancer and the 4th leading cause of cancer-related death in women worldwide[1]
- Despite advancements in the last 2 decades, pts with R/M CC continue to have poor prognoses and limited tx options[2]
  - Pembrolizumab was approved for late-line tx of advanced PD-L1(+) CC, defined as having a combined positive score of ≥1; however, the ORR was limited to 14.3%[3]
- Dual targeting of solid tumors with anti-TIGIT + anti-PD-1 mAbs has been shown to enhance antitumor activity in recent preclinical studies and clinical studies of other tumors[4-6]
  - Ociperlimab is a humanized Fc-intact IgG1 anti-TIGIT mAb
  - Tislelizumab is a humanized IgG4 anti-PD-1 mAb



AdvanTIG-202 (NCT04693234) is a randomized, multicenter, open-label phase 2 study that is investigating the efficacy and safety of tislelizumab ± ociperlimab in pts with previously treated R/M CC

Here we present the primary analysis based on a data cutoff of June 16th, 2022

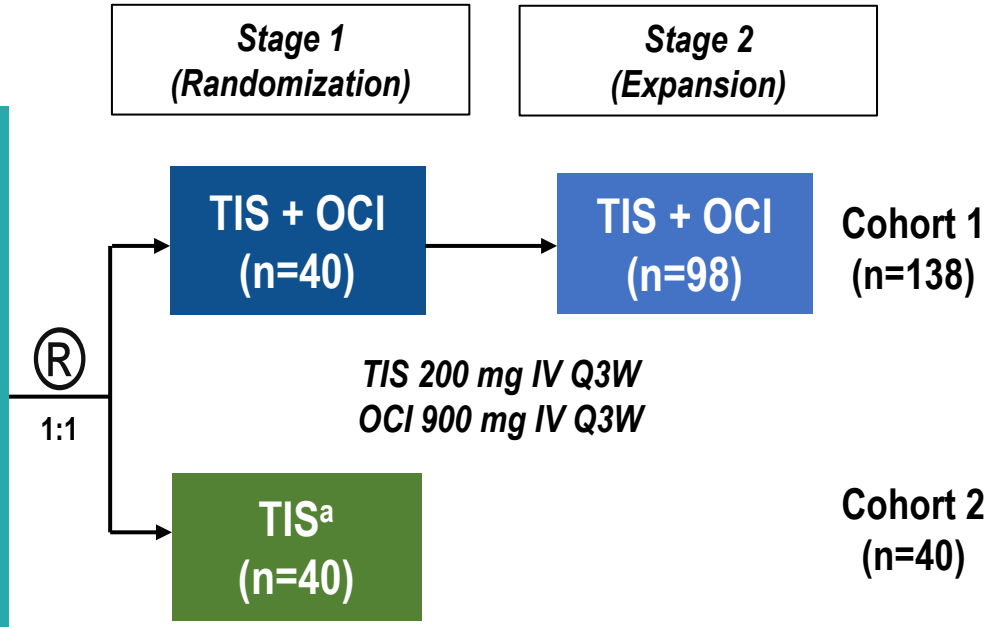
APC, antigen presenting cell; CC, cervical cancer; mAb, monoclonal antibody; ORR, objective response rate; PD-L1, programmed cell death (ligand) protein 1; pts, patients; PVR, poliovirus receptor; R/M, recurrent or metastatic; TIGIT, T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains; tx, treatment.

1. Sung H, et al. *CA Cancer J Clin*. 2021;71(3):209-249; 2. Gennigens C, Jerusalem G, Lapaille L, et al. *ESMO Open*. 2022;7(5):100579; 3. Chung HC, et al. *J Clin Oncol*. 2019;37(17):1470-1478; 4. Johnston RJ, et al. *Cancer Cell*. 2014;26(6):923-937; 5. Dixon KO, et al. *J Immunol*. 2018;200(8):3000-3007; 6. Shapira-Frommer R, et al. *Cancer Res*. 2022;82(suppl_12):CT508.

Study Design

Key eligibility criteria

- Histologically confirmed recurrent or metastatic CC
- Progression after or intolerant to ≥1 lines of chemotherapy
- Measurable disease per RECIST v1.1
- ECOG PS 0 or 1
- Prior IO excluded



Primary endpoint

- ORR determined by IRC using RECIST v1.1 in both PD-L1(+) and all-comer pts of Cohort 1

Secondary endpoints

- DoR, PFS, OS, safety & tolerability, HRQoL
- ORR determined by investigator

Exploratory endpoints

- Biomarkers, QoL

All pts will be treated until disease progression, unacceptable toxicity, or withdrawal of consent

The **safety analysis set (Cohort 1, n=138; Cohort 2 n=40)** included all pts who received ≥1 dose of any study drug for each cohort

This was the primary analysis set for baseline characteristics, efficacy, and safety analyses

- This presentation focuses on the primary analysis of Cohort 1 (TIS + OCI)
- The purpose of Cohort 2 was to investigate the efficacy and safety of TIS monotherapy, thus only some analyses will be briefly mentioned; given limited enrollment (n=40), Cohort 2 was not directly compared with Cohort 1 (n=138) due to the unbalanced number of patients

[a] PD-L1 expression was defined by the total % of the tumor area covered PD-L1-stained tumor cells and immune cells, using the Ventana PD-L1 (SP263) IHC assay and visually estimated via the Tumor Area Positivity (TAP) scoring algorithm. PD-L1(+) refers to pts whose tumors have a PD-L1 TAP score ≥5%.

DoR, duration of response; HRQoL, Health-Related Quality of Life; IO, immunotherapy; IRC, Independent Review Committee; IV, intravenous; OCI, ociperlimab; ORR, objective response rate; OS, overall survival; PD-L1, programmed death ligand 1; pts, patients; PFS, progression-free survival; Q3W, every 3 weeks; QoL, Quality of Life; RECIST, Response Evaluation Criteria in Solid Tumors; TIS, tislelizumab.

Baseline characteristics were representative of the target population

Demographics and Baseline Characteristics of Cohort 1 (TIS + OCI)[a]	
	Cohort 1 (n=138)
Age, median (range), y	53 (30-77)
Race, n (%)	
Asian	117 (84.8)
White	21 (15.2)
ECOG performance status, n (%)	
0	53 (38.4)
1	85 (61.6)
PD-L1 expression, n (%)	
PD-L1(+) [TAP score ≥5%]	84 (60.9)
PD-L1(-) [TAP score <5%]	53 (38.4)
Histology, n (%)	
Squamous cell carcinoma	107 (77.5)
Adenocarcinoma	27 (19.6)
Adenosquamous carcinoma	4 (2.9)
FIGO stage at initial diagnosis, n (%)	
IA	3 (2.2)
IB	23 (16.7)
IIA	15 (10.9)
IIB	23 (16.7)
IIIA	2 (1.4)
IIIB	25 (18.1)
IIIC	21 (15.2)
IVA	3 (2.2)
IVB	19 (13.8)
Target lesions sum of diameters by IRC, n	132
Median (range), mm	45.5 (10, 276)
Distant metastatic disease at study entry, n (%)	80 (58.0)
No. of previous lines of therapy, n (%)	
1	80 (58.0)
2	43 (31.2)
≥3	15 (10.9)
Previous anti-angiogenesis agent, n (%)	69 (50.0)
Previous radiotherapy, n (%)	126 (91.3)
Previous cancer-related surgery, n (%)	80 (58.0)

[a] Safety analysis set.

ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; OCI, ociperlimab; PD-L1, programmed death ligand 1; pts, patients; TIS, tislelizumab; TAP, Tumor Area Positive.

All-comer pts in Cohort 1 (TIS + OCI) and the PD-L1(+) subgroup showed significant improvement in ORR vs historical control ORR of 15% with anti-PD-1 therapy (ie, pembrolizumab)[1,a]

- Cohort 1 had an ORR of 22.5% with 13 CRs, and the PD-L1(+) subgroup had an ORR of 26.2% with 10 CRs[b]

	Cohort 1[b] (n=138)	PD-L1(+)[b] (n=84)
ORR, % (95% CI)	22.5 (15.8-30.3)	26.2 (17.2-36.9)
1-sided *P* value[c]	0.0127	0.0054
Best overall response, n (%)		
CR	13 (9.4)	10 (11.9)
PR	18 (13.0)	12 (14.3)
SD	56 (40.6)	34 (40.5)
PD	39 (28.3)	20 (23.8)
ND	12 (8.7)	8 (9.5)
DCR, % (95% CI)[d]	63.0 (54.4-71.1)	66.7 (55.5-76.6)
mPFS, mo (95% CI)	3.5 (2.6, 4.9)	4.2 (2.7-6.9)
mOS, mo (95% CI)	9.0 (8.1-10.4)	10.4 (8.1-NE)

- In Cohort 2 (TIS; n=40), the ORR was 32.5% with 5 CRs and 8 PRs, suggesting the benefit of TIS monotherapy in pts with previously treated R/M CC; however, the small sample size limits interpretability

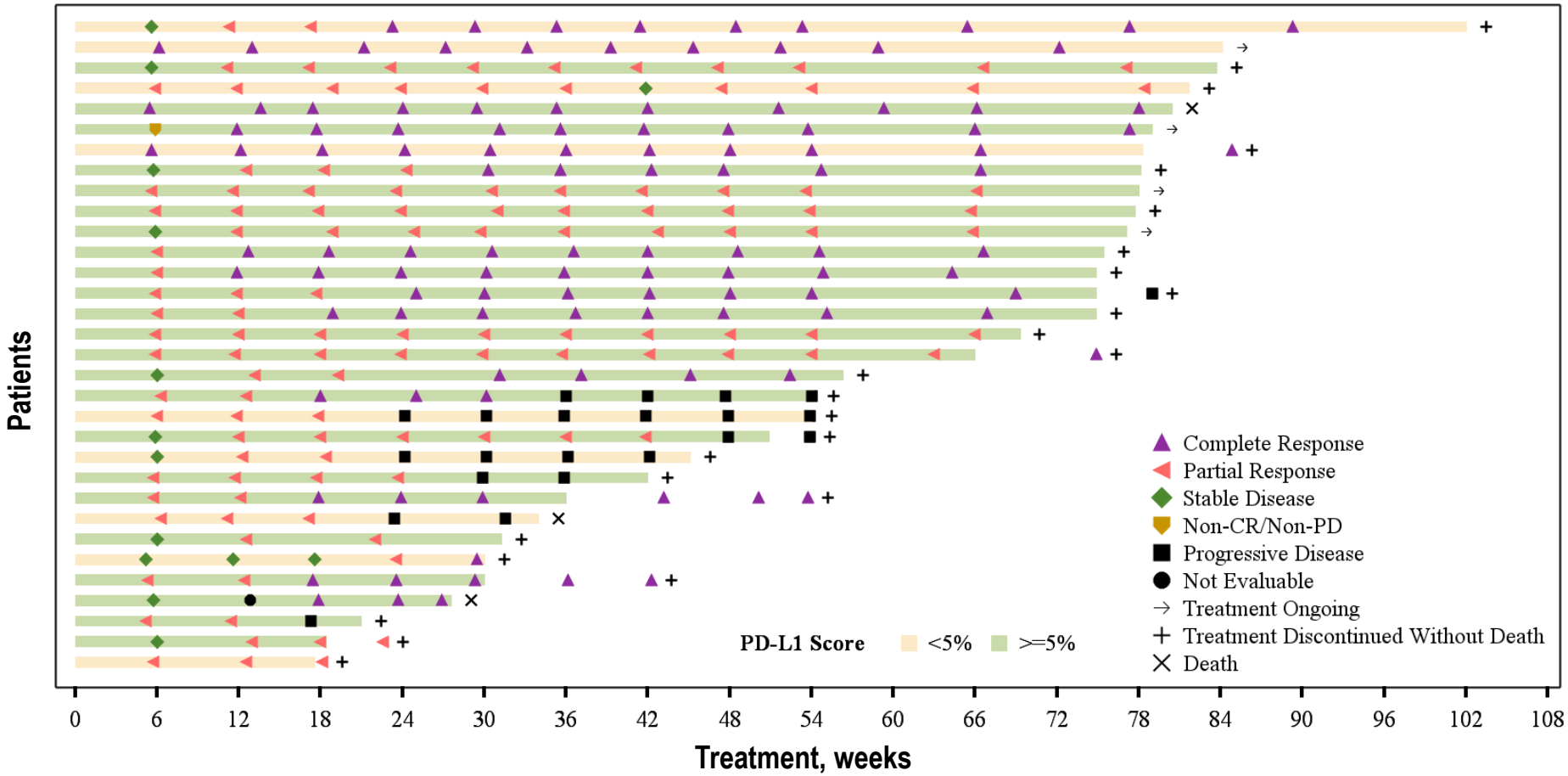
[a] In the pembrolizumab study, pts with PD-L1(+) R/M CC (n=77) achieved 2 CRs and 9 PRs, with an ORR of 14.3%; there were no responders in PD-L1(-) arm.[1]. [b] All the efficacy in the table (except OS) are IRC-assessed results, based on the DCO of June 16th, 2022, with the median study follow up of 7.4 mos. [c] The *P* value was calculated using the binomial exact test at the 1-sided significance level of 0.025. The 2 tests were performed in a sequential way. [d] DCR was defined as the proportion of patients who achieved CR, PR, or SD.

CR, complete response; DCO, data cutoff; DCR, disease control rate; IRC, independent review committee; ND, not determined; NE, not estimable; OCI, ociperlimab; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-L1, programmed death ligand 1; PFS, progression-free survival; PR, partial response; pts, patients; SD, stable disease; TIS, tislelizumab.

1. Chung HC, et al. *J Clin Oncol.* 2019;37(17):1470-1478

Swimlane Plot of Tx Duration With Overall Response by IRC for Responders in Cohort 1[a]

- At the primary analysis (DCO June 16, 2022), the median DoR[b] was not reached for both Cohort 1 and PD-L1(+) pts
- At the updated analysis[c] (DCO June 1, 2023), the median DoR was 17.3 (95% CI, 16.9-NE) months for Cohort 1 and 16.9 (95% CI, 16.9-NE) months for PD-L1(+) pts; at 12 months, the event-free rate was 74.3% (95% CI, 53.5-86.8) and 80.0% (95% CI, 55.1-92.0), respectively, indicating a durable response



[a] Safety analysis set. [b] DoR was defined as the time from the 1st confirmed objective response to disease progression documented after treatment initiation or death, whichever occurred first. [c] There were 32 responders by IRC as of the DCO June 1, 2023.
CR, complete response; IRC, independent review committee; NE, not evaluable; PD, progressive disease; PD-L1, programmed death ligand 1.

The safety profile remained manageable with the addition of OCI to TIS

	Cohort 1 (TIS + OCI)[a] (n=138)	
	Any Grade	≥Grade 3
Pts with any TRAE, n (%)	93 (67.4)	18 (13.0)
Hypothyroidism	23 (16.7)	0
Pyrexia	16 (11.6)	0
Rash	14 (10.1)	2 (1.4)
AST increased	12 (8.7)	1 (0.7)
Pruritus	10 (7.2)	0
Anemia	9 (6.5)	3 (2.2)
Chills	9 (6.5)	0
Nausea	9 (6.5)	0
WBC count decreased	9 (6.5)	0
ALT increased	8 (5.8)	1 (0.7)
Pts with any imAE, n (%)	30 (21.7)	9 (6.5)

	Cohort 2 (TIS)[a] (n=40)	
	Any Grade	≥Grade 3
Pts with any TRAE, n (%)	24 (60.0)	2 (5.0)
Hypothyroidism	8 (20.0)	0
Pyrexia	4 (10.0)	1 (2.5)
Rash	1 (2.5)	0
AST increased	4 (10.0)	0
Pruritus	4 (10.0)	0
Anemia	3 (7.5)	0
Chills	1 (2.5)	0
Nausea	1 (2.5)	0
WBC count decreased	3 (7.5)	1 (2.5)
ALT increased	4 (10.0)	0
Pts with any imAE, n (%)	9 (22.5)	0

- In both cohorts, HRQoL, as measured by 3 validated PRO questionnaires[b], was maintained or improved compared with the baseline

[a] Safety analysis set. [b] Scores for EORTC QLQ C30 (functional scales/symptom scales/single items and the GHS/QoL scale), EORTC QLQ-CX24 (index and symptom scales/items), and EQ-5D-5L (a descriptive module and a Visual Analogue scale) were calculated and summarized for each assessment timepoint.

ALT, Alanine aminotransferase; AST, aspartate aminotransferase; HRQoL, Health-Related Quality of Life; imAE, immune-mediated adverse event; OCI, ociperlimab; PRO, patient related outcomes; pts, patients; TIS, tislelizumab; TRAE, treatment-related adverse event; WBC, white blood cell.

Conclusions

- Notably, the **AdvanTIG-202** study is the 1st study to explore the combination therapy of an anti-PD-1 mAb and anti-TIGIT mAb in pts with R/M CC, regardless of PD-L1 expression
- TIS + OCI demonstrated promising antitumor activity and durable responses for both the overall population and PD-L1(+) subgroup when compared with historical data
- This combination treatment was well tolerated among this pt population

CC, cervical cancer; mAb, monoclonal antibody; OCI, ociperlimab; PD-L1, programmed cell death (ligand) protein 1; pts, patients; R/M, recurrent or metastatic; TIGIT, T-cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domains; TIS, tislelizumab.

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Acknowledgements

The authors wish to thank all BGB-A317-A1217-202 study investigators, research staff, and patients.

This study was sponsored by BeiGene, Ltd. Medical writing support, under the direction of the authors, was provided by Nancy Tang, PharmD, of Medical Expressions (Chicago), an Inizio company, and was funded by BeiGene, Ltd.

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