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AdvanTIG-202: A Phase 2 study investigating anti-TIGIT monoclonal antibody ociperlimab plus anti-PD-1 monoclonal antibody tislelizumab in patients with previously treated recurrent or metastatic cervical cancer

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Introduction

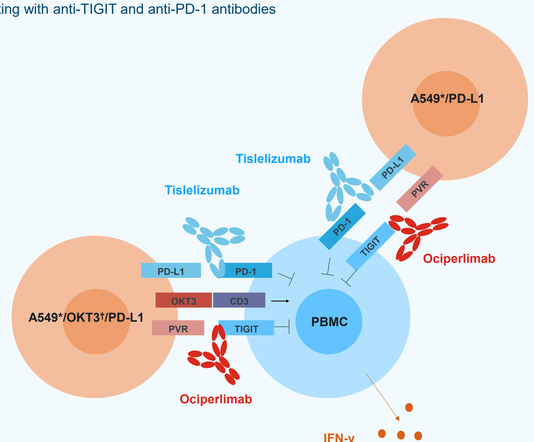
Unmet need in cervical cancer

- Cervical cancer is the fourth most common cancer in women with approximately 604,127 new diagnoses and 341,831 deaths worldwide in 2020[1]
- The first-line current standard of care for patients with recurrent or metastatic cervical cancer is a platinum-based chemotherapy, with the option of adding the antiangiogenic agent bevacizumab. However, the treatment options for second-line are limited[2]
- As the majority of cervical cancers have a viral etiology, which impairs the immune system, immunotherapy treatments such as a checkpoint inhibitors appear to be a viable approach[2]
- Second-line treatment with programmed cell death protein 1 (PD-1)/programmed death-ligand 1 (PD-L1) inhibitors has been shown to provide moderate efficacy with durable responses in patients with recurrent or metastatic cervical cancer[3–6]

Introduction to ociperlimab, tislelizumab, and the AdvanTIG-202 study

- T cell immunoglobulin and immunoreceptor tyrosine-based inhibitory motif (ITIM) domain (TIGIT) is a co-inhibitory, immune checkpoint receptor that is upregulated on T cells and natural killer cells in multiple solid tumors, which can inhibit anticancer immune responses[7,8]
- Ociperlimab (BGB-A1217) is a novel, humanized monoclonal antibody (mAb) that binds to TIGIT with high affinity and specificity, blocking the interaction with its ligands on tumor cells[9]
- Tislelizumab is an anti-PD-1 antibody engineered to minimize binding to FcγR on macrophages to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy[10,11]
- Dual targeting of tumors with anti-TIGIT and anti-PD-1 mAbs (**Figure 1**) produces synergistic immune cell activation and enhanced antitumor activity in preclinical and clinical studies[9,12]
- We report the design of the ongoing Phase 2 AdvanTIG-202 study, which is investigating the efficacy and safety of ociperlimab plus the anti-PD-1 mAb tislelizumab and tislelizumab monotherapy, in patients with previously treated recurrent or metastatic cervical cancer

Figure 1. Dual targeting with anti-TIGIT and anti-PD-1 antibodies



*Chen X, et al. Data presented at AACR 2021. *PVR positive A549 cells; †anti-CD3 antibody clone*
IFN, interferon; PBMC, human peripheral blood mononuclear cells; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PVR, poliovirus receptor; TIGIT, T cell immunoglobulin and immunoreceptor tyrosine-based inhibitory motif domain

Conclusions

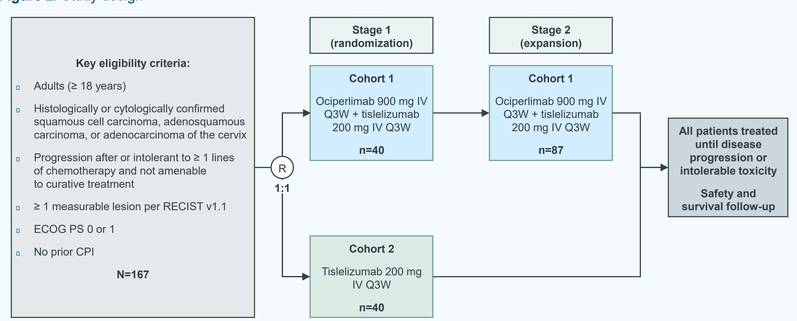
- AdvanTIG-202 is an ongoing **Phase 2 study** investigating the **efficacy and safety of tislelizumab with or without ociperlimab** in patients with **previously treated recurrent or metastatic cervical cancer**
- This study will provide insight into the effect of dual targeting with anti-TIGIT and anti-PD-1 antibodies (ociperlimab and tislelizumab) in cervical cancer

Methods

Study design and treatment

- AdvanTIG-202 is a Phase 2, multicenter, randomized, open-label study (NCT04693234)
- Approximately 167 patients with cervical squamous cell carcinoma, adenosquamous carcinoma or adenocarcinoma of the cervix, recruited from 100 centers, whose disease progressed on or after ≥ 1 prior line of chemotherapy for recurrent/metastatic disease will be included in this 2-stage study (**Figure 2**)
- Study enrollment has begun, and recruitment is ongoing
- **Stage 1 (randomization):**
  - Approximately 80 patients will be randomized (1:1) to either ociperlimab 900 mg intravenously (IV) in combination with tislelizumab 200 mg IV every 3 weeks (Q3W) (Cohort 1), or tislelizumab monotherapy 200 mg IV Q3W (Cohort 2), until disease progression, unacceptable toxicity, or withdrawal of consent
- **Stage 2 (expansion):**
  - Cohort 1 will be expanded by approximately 87 additional patients whose tumors are evaluable for PD-L1 expression
- In Stage 1, PD-L1 expression will be retrospectively tested centrally
- In Stage 2, PD-L1 expression will be prospectively tested centrally, and only patients whose tumors are evaluable for PD-L1 expression will be enrolled

Figure 2. Study design



CPI, checkpoint inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; Q3W, every 3 weeks; R, randomization; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1

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Study population

- Eligibility criteria included:
  - Aged ≥ 18 years
  - Histologically or cytologically confirmed squamous cell carcinoma, adenosquamous carcinoma, or adenocarcinoma of the cervix
  - Progression on or after one or more lines of chemotherapy for recurrent or metastatic disease and not amenable to curative treatment
  - Eastern Cooperative Oncology Group performance status (ECOG PS) ≤ 1
  - ≥ 1 measurable lesion, as per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1)
  - Life expectancy of at least 12 weeks
  - Patients must submit qualified archival tumor tissue with an associated pathology report or agree to a tumor biopsy for determination of PD-L1 expression and other biomarker analyses
  - For Stage 2, patients with evaluable PD-L1 expression are eligible
  - No prior treatment with anti-PD-1/L1 antibodies or any other checkpoint inhibitors (CPI) and other anti-TIGIT therapies

Endpoints and assessments

- The primary endpoint is overall response rate (ORR) (RECIST v1.1) assessed by independent review committee (IRC) in Cohort 1. Secondary endpoints and exploratory endpoints are listed in **Table 1**
- Tumor imaging will be performed ≤ 28 days before the first dose of study drugs. During the study, tumor imaging will be performed every 6 weeks for the first 54 weeks, then every 12 weeks after that
- Safety will be assessed through monitoring of the incidence and severity of adverse events (graded according to National Cancer Institute Common Terminology Criteria for Adverse Events v5.0), laboratory results, vital signs, ECOG PS, and other examinations
- Safety analyses will be performed using the safety analysis set (all randomized patients receiving ≥ 1 dose of study drug)
- Health-related quality of life (HRQoL) is an assessment of a patient's health state using the scores of European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30) and the EORTC Quality of Life Questionnaire-Cervical Cancer Module (QLQ-CX24) scales

Table 1. Endpoints of the study

AdvanTIG-202 endpoints		
Primary endpoints	•ORR (IRC-assessed per RECIST v1.1) for Cohort 1: •In patients with PD-L1 TAP score ≥ 5%* •Regardless of PD-L1 expression	
Secondary endpoints	•ORR (investigator-assessed) for Cohort 1 •IRC-assessed and investigator-assessed: •ORR for Cohort 2 •DoR for Cohorts 1 and 2 •DCR for Cohorts 1 and 2 •PFS for Cohorts 1 and 2 •TTR for Cohorts 1 and 2 •CBR for Cohorts 1 and 2	For Cohorts 1 and 2: •OS •Safety •HRQoL† •PK •Immunogenicity
Exploratory endpoints	•Biomarkers •QoL‡	

**PD-L1 expression is determined by PD-L1 score assessed by tumor area positive score (TAP) (previously referred to visually-estimated Combined Positive Score [vCPS] in the protocol), which is defined as the total percentage of the tumor area covered by tumor cells with any membrane staining above background and tumor-associated immune cells with any staining above background using Ventana PD-L1 (SP263) assay; †Measured using the EORTC QLQ-C30 and EORTC QLQ-CX24; ‡Measured using the EQ-5D-5L. CBR, clinical benefit rate; DCR, disease control rate; DoR, duration of response; EQ-5D-5L, European Quality of Life 5 Dimensional 5-Level; HRQoL, health related quality of life; IRC, independent review committee; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PK, pharmacokinetics; QoL, quality of life; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TAP, tumor area positive; TTR, time to response*

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