Abstract TPS5601 – Poster 327b

# A Single-Arm, Phase 2, Multicenter, International Trial of Tisotumab Vedotin in Previously Treated, Recurrent, or Metastatic Cervical Cancer


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## BACKGROUND

### Current Treatment Paradigm in Patients With Recurrent/ Metastatic Cervical Cancer

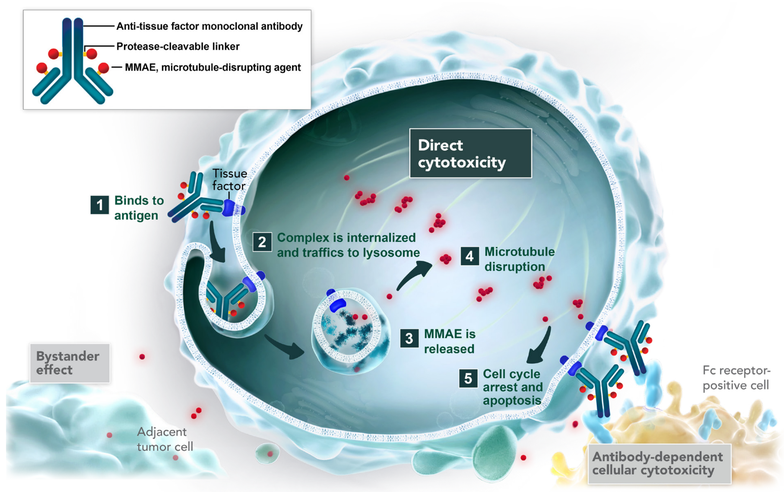
- Cervical cancer is underserved with the available treatment options[1]
  - Recurrent or metastatic cervical cancer has a poor prognosis, is generally considered incurable, and has a poor survival[2]
  - Beyond first-line treatment, there are no approved therapies[3]
  - Available treatment options have short overall survival (OS), and low and limited response rates[3]
    - A meta-analysis demonstrated a 10.7% objective response rate to second-line treatment[4]
- The poor prognosis and lack of effective options necessitate development of novel therapies for this patient population with high unmet needs[1]

### Tisotumab Vedotin

- Tisotumab vedotin (TV) is an antibody-drug conjugate (ADC) comprised of a fully human monoclonal antibody specific for tissue factor (TF) conjugated to the microtubule disrupting-agent monomethyl auristatin E (MMAE) via a protease cleavable linker[5,a]
- TF is aberrantly expressed in a broad range of solid tumors, including cervical cancer and is associated with poor prognosis[6,7]
- TV selectively targets TF to deliver a cytotoxic payload to tumor cells[5,8] **(Figure 1)**

[a]MMAE-based ADC technology was licensed from Seattle Genetics, Inc. in a license and collaboration agreement.

**Figure 1. Proposed mechanism of action of tisotumab vedotin.[5,8]**






- innovaTV 201 (GEN701) is an open-label, single-arm, multicenter, phase 1/2a dose-escalation and expansion trial, evaluating the safety and activity of TV at an every 3-week (q3w) schedule, in patients with previously treated locally advanced or metastatic solid tumors (NCT02001623)[9,10]
  - Phase 1 portion of the trial: the recommended phase 2 dose for TV was identified as 2.0 mg/kg[10]
  - Phase 2 portion of the trial: consists of 7 disease-specific expansion cohorts including cervical cancer. Preliminary results (data cutoff date July 24, 2017) have shown a favorable benefit-risk profile in patients with previously treated recurrent or metastatic cervical cancer, with a confirmed objective response rate (ORR) of 26% and manageable safety events[11,12,a] **(Table 1)**

[a]Disease-specific expansion cohorts include cervical, ovarian, prostate, bladder, esophageal, endometrial, and non-small cell lung cancer.

**Table 1. Preliminary Activity Profile of TV in the Cervical Cancer Expansion Cohort of InnovaTV 201 (GEN701) (n=34)[12]**

| | |
|---|---|
| Response rate, n (%)[a] (95% CI) | 11 (32) (17%-50%) |
| Confirmed response rate, n (%) | 9 (26) |
| PR, n (%) | 11 (32) |
| DCR (CR+PR+SD), n (%)[b] | 17 (50) |

CR, complete response; DCR, disease control rate; DoR, duration of response; PFS, progression-free survival; PR, partial response; SD, stable disease.

[a]Confirmed and unconfirmed responses. [b]Clinical benefit, after 12 weeks.

## OBJECTIVES AND ENDPOINTS

- To evaluate the activity, safety, and tolerability of TV monotherapy in patients with previously treated, recurrent or metastatic cervical cancer **(Table 2)**

**Table 2. Objectives and Endpoints**

| | Objective | Endpoint |
|---|---|---|
| **Primary** | • Determine the antitumor activity | • Confirmed ORR by IRC[a] |
| **Secondary** | • Evaluate tumor response durability | • DoR by IRC and investigator[b]<br>• ORR by investigator review<br>• TTR by IRC and investigator[c] |
| | • Evaluate clinical response | • PFS by IRC and investigator[d]<br>• OS[e] |
| | • Assess safety and tolerability | • AEs and safety laboratory parameters<br>• Pharmacokinetics<br>• Immunogenicity |
| **Exploratory** | • Assess biomarkers related to clinical response | • TF expression in pretreatment and postprogression tumor biopsies, circulating TF, proteomic analyses, and genetic/transcriptomic variations |
| | • Assess potential pharmacodynamics biomarkers | • Circulating TF and proteomic analyses |
| | • Assess health-related quality of life | • EORTC-QLQ-C30<br>• EORTC-QLQ-CX24 |

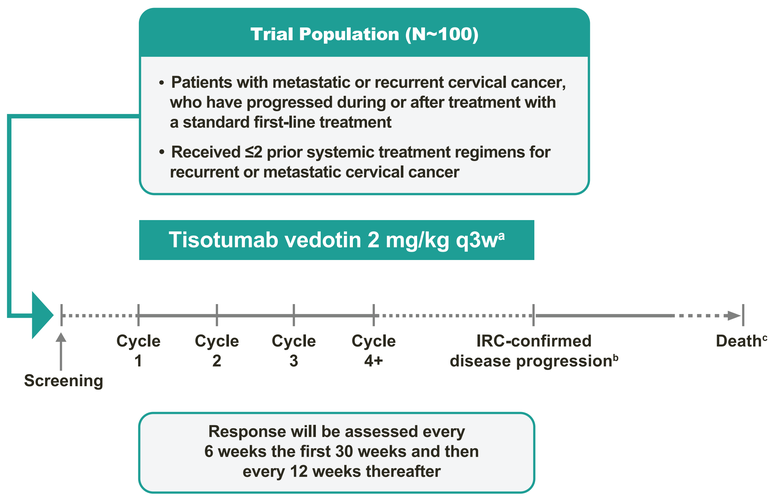
AE, adverse event; EORTC-QLQ-C30, European organization for research and treatment of cancer quality of life version 3.0 of the core questionnaire; EORTC-QLQ-CX24, European organization for research and treatment of cancer quality of life questionnaire, cervical cancer module; IRC, independent review committee; TTR, time to response.

[a]ORR is defined as a best overall response (PR or better) confirmed by a subsequent response ≥4 weeks later. [b]DoR applies only to a subset of patients whose best overall response is CR or PR. DoR is defined as the time from the first documented response to the date of first documented IRC-confirmed disease progression or death. [c]TTR is defined as the time from the date of the first trial dose to the first documented response of either CR or PR (subsequently confirmed by IRC). [d]PFS is defined as the time from the first trial dose to the first documented disease progression, or death due to any cause. [e]OS is defined as the time from the date of the first trial dose to the date of death due to any cause.

## TRIAL DESIGN

- innovaTV 204 (NCT03438396) is an open-label, single-arm, international, multicenter, phase 2 trial **(Figure 2)**

**Figure 2. Trial design.**




[a]TV is administered on day 1 of each cycle, each of which is 3 weeks. [b]Treatment and response assessment to continue until IRC-verified disease progression, start of a new anticancer therapy, trial withdrawal, or death, whichever occurs first. [c]Survival follow-up will be performed every 60 (±7) days, starting from the day of last dose of TV.

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- Patients with recurrent or metastatic cervical cancer who have progressed during or after treatment with a standard first-line treatment and who have not received more than 2 prior systemic treatment regimens for recurrent or metastatic disease will be included in this trial **(Table 3)**

**Table 3. Key Patient Eligibility Criteria**

| Inclusion Criteria | Exclusion Criteria |
|---|---|
| • Extra-pelvic metastatic or recurrent cervical cancer including squamous cell, adenocarcinoma or adenosquamous histology | • Received >2 prior systemic treatment regimens for recurrent or metastatic cervical cancer |
| • Metastatic or recurrent cervical cancer who have progressed during or after treatment with paclitaxel + cisplatin or carboplatin OR paclitaxel + topotecan in combination with bevacizumab (if eligible for bevacizumab treatment) | • Known past or current coagulation defects leading to an increased risk of bleeding, or ongoing major bleeding |
| • Measurable disease according to RECIST v1.1 as assessed by IRC | • Clinically significant cardiac disease |
| • Acceptable organ function | • Active ocular surface disease |
| • ECOG score of 0 or 1 | • Known past or current malignancy other than the inclusion diagnosis[a] |
| • Age ≥18 years | • Peripheral neuropathy grade ≥2 |
| | • Received prior treatment with MMAE-derived drugs; radiotherapy within 21 days prior to the first trial dose; small molecules, chemotherapy, immunotherapy, monoclonal antibodies, or any experimental agent within 28 days prior to the first trial dose |

ECOG, Eastern Cooperative Oncology Group; RECIST, Response Evaluation Criteria in Solid Tumors.

[a]Except for noninvasive basal cell or squamous cell skin carcinoma; noninvasive, superficial bladder cancer; any curable cancer with a CR of >5 years duration.

## KEY ASSESSMENTS

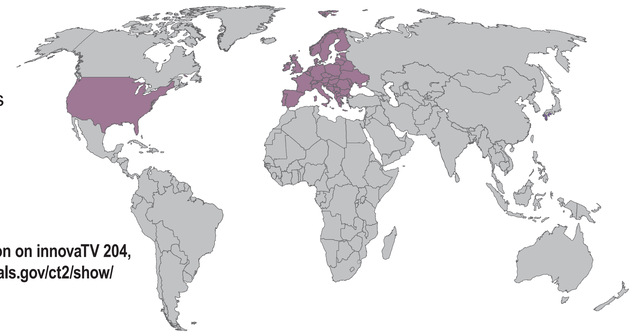
- Screening: computer tomography (CT) and/or magnetic resonance imaging (MRI) scans of the abdomen and pelvis, IRC-confirmed measurable disease according to RECIST v1.1, ocular assessment, central and local laboratory assessments, electrocardiogram (ECG), tumor biopsy (may be either fresh or archival)
- Response will be assessed using RECIST v1.1
- AEs will be monitored and graded using Common Terminology Criteria for Adverse Events (CTCAE) v5.0

## STATISTICAL ANALYSES

- For the ORR analyses, a 2-sided 95% exact CI will be calculated using the Clopper-Pearson method
- PFS and OS will be analyzed using the Kaplan-Meier method, and 95% CI of the median will be presented

## TRIAL SITES

Approximately 100 patients will be enrolled in sites across the United States and the European Union.



**For further information on innovaTV 204, visit https://clinicaltrials.gov/ct2/show/NCT03438396.**

## REFERENCES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