innovaTV 208: New Weekly Dosing Cohort in the Phase 2 Study of Tisotumab Vedotin in Platinum-Resistant Ovarian Cancer (Trial in Progress)

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DISEASE BACKGROUND

- In 2018, approximately 295,000 new cases of ovarian cancer and 185,000 ovarian cancer-related deaths occurred worldwide[1]
- Although the majority of patients initially respond to first-line treatment, the vast majority will relapse[2]
  - Disease recurrence within 6 months after completing platinum-based therapy is known as platinum-resistant ovarian cancer (PROC) and is associated with poor prognosis[2]
- Standard therapy for PROC is single-agent chemotherapy and bevacizumab, despite lack of evidence that the addition of bevacizumab prolongs OS[3]
- There is no standard of care for patients who relapse after first-line therapy for PROC and clinical benefit diminishes significantly with increasing lines of therapy[4]
- There is an urgent need for novel therapeutic strategies for the treatment of PROC, particularly for patients previously treated with bevacizumab

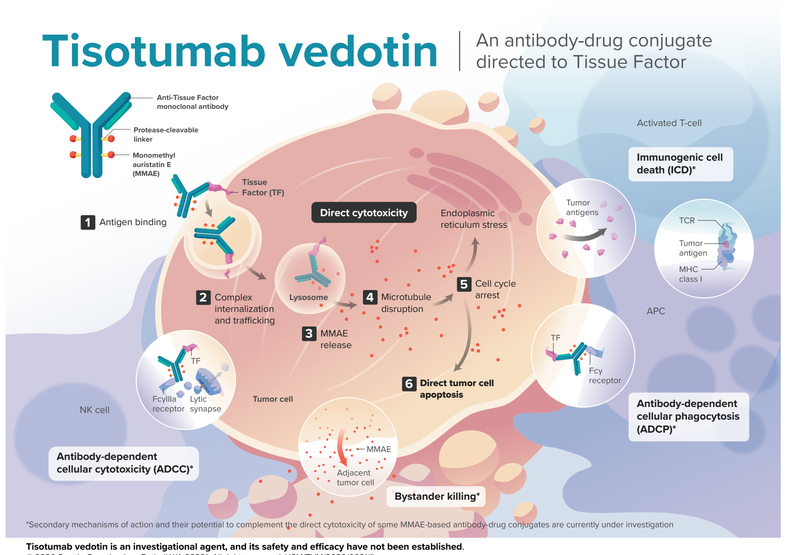
TISSUE FACTOR TARGET

- Tissue Factor (TF) is a transmembrane cell surface receptor that plays an essential role in the initiation of the coagulation pathway[5]
- TF is prevalent in several solid tumors, including cervical cancer. In these tumors where TF is present, levels are elevated relative to normal tissue[6-7].
- Expression of TF on tumor cells has been associated with negative OS or disease-free survival as described in several indications, including ovarian cancer[8]

TISOTUMAB VEDOTIN DESCRIPTION

- Tisotumab vedotin is an investigational antibody-drug conjugate composed of a TF-directed human monoclonal immunoglobulin G1 (IgG1κ) antibody covalently linked to the microtubule disrupting agent monomethyl auristatin E (MMAE) via a protease-cleavable linker.
- Tisotumab vedotin has multiple proposed mechanisms of action[9-11] (figure 1)

Figure 1: Tisotumab Vedotin Proposed Mechanisms of Action



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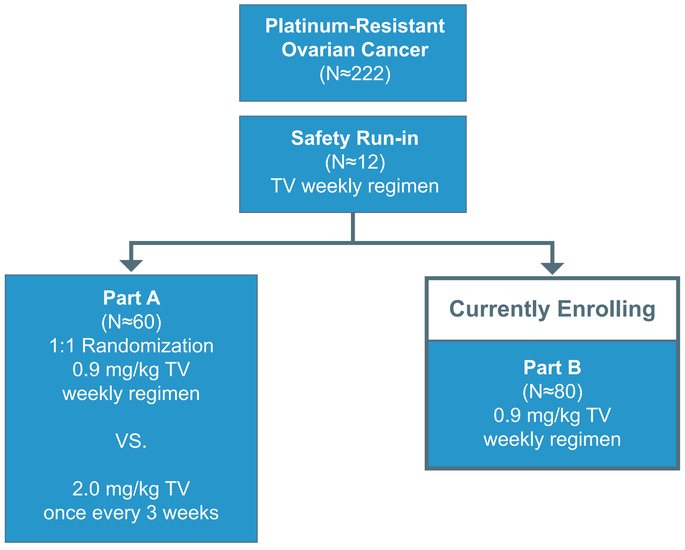
CLINICAL SAFETY AND EFFICACY OF TISOTUMAB VEDOTIN

- The phase 1/2 innovaTV 201 study (NCT02001623) evaluated tisotumab vedotin in patients with previously treated, locally advanced, or metastatic solid tumors, including ovarian cancer[12]
  - In the heavily pretreated ovarian cancer cohort (n=36), tisotumab vedotin suggested a manageable safety profile and encouraging antitumor activity, with confirmed ORR of 13.9% at a dose of 2.0 mg/kg once every 3 weeks[12]
- In the innovaTV 208 study, preliminary data from the safety run-in demonstrated a manageable safety profile of 0.9 mg/kg tisotumab vedotin delivered on Days 1, 8, and 15 of a 28-day cycle (weekly regimen).

innovaTV 208 STUDY DESIGN

- innovaTV 208 (NCT03657043; EudraCT 2019-001219-22) is a phase 2, open-label, multicenter trial of tisotumab vedotin trial with a safety run-in followed by a multipart dose expansion in patients with platinum-resistant ovarian cancer (figure 2).
- The safety run-in evaluated the safety of 0.9 mg/kg and 1.2 mg/kg tisotumab vedotin delivered on Days 1, 8, and 15 of a 28-day cycle (weekly regimen).
  - 0.9 mg/kg tisotumab vedotin was selected as the recommended weekly dose for Parts A and B.
- Part A will randomize 60 patients in a 1:1 ratio to receive tisotumab vedotin weekly or once every three weeks. One treatment arm may be expanded to enroll up to an additional 70 patients.
- Part B is an expansion phase enrolling about 80 patients to further assess the safety and efficacy of 0.9 mg/kg tisotumab vedotin administered following the weekly regimen.

Figure 2: innovaTV 208 Study Design



ENROLLMENT

- innovaTV 208 study is currently recruiting in Europe and the United States and will enroll up to approximately 222 patients
- For more information about the innovaTV 208 study, please visit https://clinicaltrials.gov/ct2/show/NCT03657043

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ELIGIBILITY

Key Inclusion Criteria

- Histologic documentation of epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer
- Measurable disease at baseline by RECIST v1.1
- ECOG performance status of 0 or 1
- Aged ≥18 years
- Able to provide fresh or archival tissue for biomarker analysis

Parts A and B only

- Received 1 but no more than 3 prior anticancer regimens overall, including at least 1 line of therapy containing bevacizumab or a bevacizumab biosimilar

Key Exclusion Criteria

- Primary platinum-refractory disease, defined as disease progression within 3 months of completion of first-line platinum-based therapy
- Active ocular surface disease at baseline, prior episode of cicatricial conjunctivitis, or Stevens-Johnson syndrome
- Grade ≥2 peripheral neuropathy

ECOG, Eastern Cooperative Oncology Group; PROC, platinum-resistant ovarian cancer; RECIST v1.1, Response Evaluation

OBJECTIVES

Primary Objective

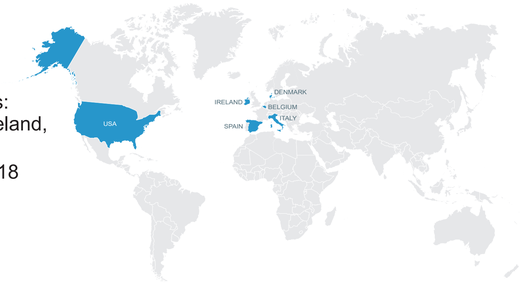
- Safety run-in phase: Evaluate the safety and tolerability of the dose-dense regimen of tisotumab vedotin by measuring the incidence of dose-limiting toxicities or other unacceptable toxicities
- Parts A and B: Evaluate the antitumor activity of tisotumab vedotin by investigator-assessed confirmed ORR according to RECIST v1.1

Secondary Objectives

- Antitumor activity as determined by the cancer antigen 125 (CA-125) response rate according to Gynecologic Cancer InterGroup criteria, time to and duration of response, disease control rate, PFS, and OS
- Safety as determined by the frequency, duration, and severity of adverse events

STUDY SITES

- 34 sites across 6 countries: US, Belgium, Denmark, Ireland, Italy, and Spain
- Study Start: December 2018



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