innovaTV 207: NEW DOSING COHORT IN THE OPEN LABEL PHASE 2 STUDY OF TISOTUMAB VEDOTIN IN SOLID TUMORS

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TISSUE FACTOR TARGET

- In normal cells, tissue factor (TF) is involved in initiating blood coagulation and cellular release of pro-angiogenic and pro-inflammatory mediators.
- In tumors, high TF expression may be associated with enhanced metastatic potential, neo-angiogenesis, and cell survival.[1,2]
- TF is overexpressed across a broad range of tumor types including colorectal cancer, pancreatic adenocarcinoma, non-small cell lung cancer (NSCLC), and squamous cell carcinoma of the head and neck (SCCHN).[3,4]
- Expression of TF is associated with poor prognosis and patient outcomes.[3]

UNMET NEED IN NSCLC AND SCCHN PATIENTS

- The tumor types chosen for this study are known to express TF and have significant unmet need in the metastatic setting after failure of first line therapy. New therapies are needed to help these patients.
- Initial therapy for patients with metastatic NSCLC includes chemo-doublet and checkpoint inhibitors (CPIs) in combination or sequentially. For patients without a driver mutation, subsequent therapy comprises a single agent with objective response rate (ORR) of 7–9% and overall survival (OS) of ~6 months.[5,6]
- For patients with SCCHN that progress after first-line treatment, CPIs are recommended and have an ORR of 13–18% and OS of 7–8 months.[7,8]
  - After failure of first-line chemotherapy and CPI, responses to subsequent therapy are uncommon, and there is no evidence that survival is prolonged.[9]

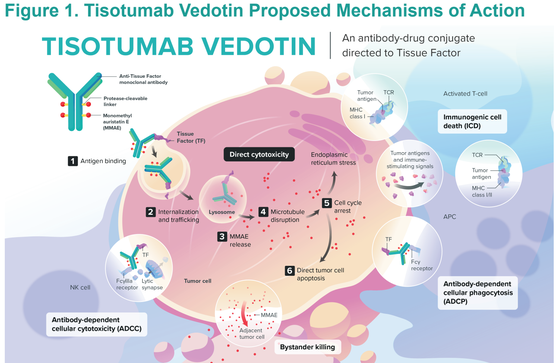
RATIONALE FOR ADDITION OF PART C TO THE STUDY

- Preliminary evidence from the GEN701 and GEN702 trials indicate that 1.2 mg/kg 3Q4W (3 times every 4 weeks) exposure profile may enhance efficacy compared to the 2.0 mg/kg Q3W dosing schedule.
- Populational pharmacokinetics (popPK) analysis suggests that dosing with 1.7 mg/kg 2Q4W (2 times every 4 weeks) will provide similar dose intensity to the 1.2 mg/kg 3Q4W schedule.
- 1.2 mg/kg 3Q4W dosing will be compared to 1.7 mg/kg 2Q4W in Part C to explore whether different exposure profiles at similar dose intensities can provide improved efficacy in patients with SCCHN and NSCLC.

TISOTUMAB VEDOTIN

- Tisotumab vedotin (TV) is an investigational antibody-drug conjugate (ADC) directed to tissue factor.
  - Human monoclonal immunoglobulin G1 (subtype κ) ADC
  - Conjugated to monomethyl auristatin E (MMAE)
  - Selectively binds to cells expressing TF
- Binding of TV to TF is followed by internalization of the TV-TF complex and release of MMAE via proteolytic cleavage.[10,11]
- MMAE binds to and disrupts the cellular microtubule network, leading to apoptotic cell death.[10,11]
- TV causes apoptosis in a manner consistent with immunogenic cell death.[12]

Figure 1. Tisotumab Vedotin Proposed Mechanisms of Action



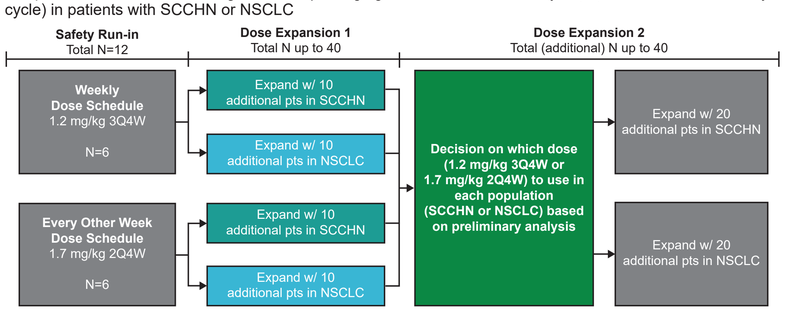
Tisotumab vedotin is an investigational agent, and its safety and efficacy have not been established.

CLINICAL SAFETY AND EFFICACY OF TV

- Safety profile of TV in the pivotal innovaTV 204 trial (at the 2.0 mg/kg Q3W schedule) was manageable[13]
- Safety profile consistent with known safety profile of other MMAE-based ADCs with the exception of ocular toxicity
- Frequency and severity of ocular events were reduced with ocular mitigation measures[14]
- Clinically meaningful and durable results in the Phase 2 innovaTV 204 trial
  - Confirmed ORR per Independant Review Committee (IRC) of 24% (95% CI)
  - Median DOR per IRC of 8.3 months (95% CI)
- Antitumor activity has been seen in multiple tumor types across both innovaTV 201 and innovaTV 204 studies

innovaTV 207 STUDY DESIGN: PART C

A novel, 2Q4W dosing schedule (1.7 mg/kg TV administered on Days 1 and 15 of a 28-day cycle) will be compared with the 3Q4W dosing schedule (1.2 mg/kg TV administered on Days 1, 8, and 15 of a of a 28-day cycle) in patients with SCCHN or NSCLC



- Up to 92 patients will be enrolled
- Initial safety run-in with 6 patients with SCCHN or NSCLC per dosing schedule (N=12)
- Dose expansion phase with enrollment of 20 SCCHN (10 3Q4W + 10 2Q4W) and 20 NSCLC (10 3Q4W + 10 2Q4W) patients (N=40)
- Possibility of 20 more patients enrolled per indication at 1 given dosing schedule to evaluate preliminary antitumor activity (N=40)

ELIGIBILITY: KEY INCLUSION CRITERIA

NSCLC	SCCHN
Relapsed, locally-advanced or metastatic disease that has failed prior lines of systemic treatment	
Measurable disease progression per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 as assessed by investigator	
Prior therapy with a platinum-based regimen and a CPI, if eligible	
Eastern Cooperative Oncology Group (ECOG) Performance Status score of 0 or 1	
• Prior therapy with tyrosine kinase inhibitor (TKI), if eligible. • Not more than 3 systemic regimens for TKI-eligible patients in the metastatic setting • Not more than 2 systemic regimens in the metastatic setting	• Prior therapy with anti-epithelial growth factor receptor (anti-EGFR) therapy, if eligible • Not more than 3 systemic regimens in the recurrent/metastatic setting.

ELIGIBILITY: KEY EXCLUSION CRITERIA

- Coagulation defects with increased risk of bleeding; active bleeding conditions
- Ocular surface disease at the time of enrollment (Note: cataract is not considered active ocular surface disease)
- Pulmonary disease requiring chronic medical therapy, unrelated to underlying cancer
- Uncontrolled tumor-related pain
- Peripheral neuropathy ≥ Grade 2
- History of another malignancy within 3 years of the first dose of study drug, or any evidence of residual disease from a previously diagnosed malignancy
- Known active CNS lesions or brain metastasis
- Patients who are breastfeeding, pregnant, or planning to become pregnant from the time of informed consent until 6 months after the final study dose is administered
- Chronic treatment with acetylsalicylic acid (ASA) in combination with other anticoagulant therapy

OBJECTIVES

Primary Objective

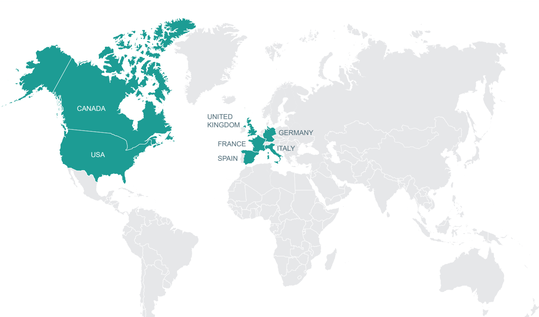
- Evaluate antitumor activity of TV as measured by investigator-determined confirmed ORR per RECIST v1.1

Secondary Objectives

- Evaluate safety and tolerability
- Evaluate preliminary antitumor activity as measured by confirmed and unconfirmed ORR
- Evaluate stability and control of disease; disease control rate (DCR)
- Evaluate duration of response (DOR)
- Evaluate time to response (TTR)
- Assess progression-free survival (PFS)
- Assess OS
- Assess pharmacokinetics (PK) and immunogenicity

STUDY SITES

- 36 sites across 7 countries: US, Canada, Italy, France, UK, Germany, and Spain
- Part C added: Feb 2021



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