innovaTV 207 Parts E and F: A Phase 2 Study of Tisotumab Vedotin in Patients with Head and Neck Squamous Cell Carcinoma (Trial in Progress)

Summary

- innovaTV 207 is an open-label, phase 2, multicenter study evaluating TV monotherapy or in combination for advanced solid tumors, including patients with r/m HNSCC
  - Two new HNSCC cohorts have been added to the study: Part E is evaluating 2L/3L TV monotherapy and Part F is evaluating 1L TV + pembrolizumab
- Enrollment for innovaTV 207 Parts E and F is currently open and enrolling in Europe, USA, and Brazil

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Background

- An estimated 932,000 patients were diagnosed with head and neck cancer in 2020, resulting in more than 467,000 deaths, and categorizing it as the seventh most common cancer worldwide[1]
  - SCC is the most common histology of head and neck cancers[2]
- Recently, the introduction of immunotherapy has improved outcomes in the frontline treatment of r/m HNSCC, though clinical outcomes can be further optimized[3]
- For patients with disease progression after prior immunotherapy and platinum-based chemotherapy, there remains a large unmet need for novel and effective therapies, with no global standard of care and available chemotherapy options demonstrating limited activity[3-5]
- Tisotumab vedotin (TV) is a TF-directed ADC composed of 1) a fully human monoclonal antibody specific for TF, 2) the microtubule-disrupting agent MMAE, and 3) a protease-cleavable linker that covalently links MMAE to the antibody
- Preclinical data suggest that vedotin-based ADCs, including TV, may induce cancer cell apoptosis in a manner consistent with immunogenic tumor cell death, providing a rationale for combining TV with immune checkpoint inhibitors[6]
- A recent study evaluating the combination of TV with other therapeutics, including immune checkpoint inhibitors, has shown promising data in cervical cancer[7]
- In patients with r/m HNSCC with disease progression after prior platinum therapy and immunotherapy, TV monotherapy has shown encouraging antitumor activity[8]
- Here, we present the newly added and enrolling cohorts to innovaTV 207 (NCT03485209) in patients with r/m HNSCC

Study Design

- innovaTV 207 is an open label, phase 2, multicenter study evaluating TV monotherapy or in combination with pembrolizumab ± carboplatin
- In the newly added Parts E and F, only patients with r/m HNSCC who are not eligible for surgery or radiation will be enrolled
- The decision to open Part G (not depicted) will be made after reviewing safety and efficacy data from Part F
  - In Part G, patients will receive carboplatin (Q2W), pembrolizumab (Q6W), and TV on Days 1, 15, and 29 of every 6-week cycle (1.7 mg/kg Q2W)

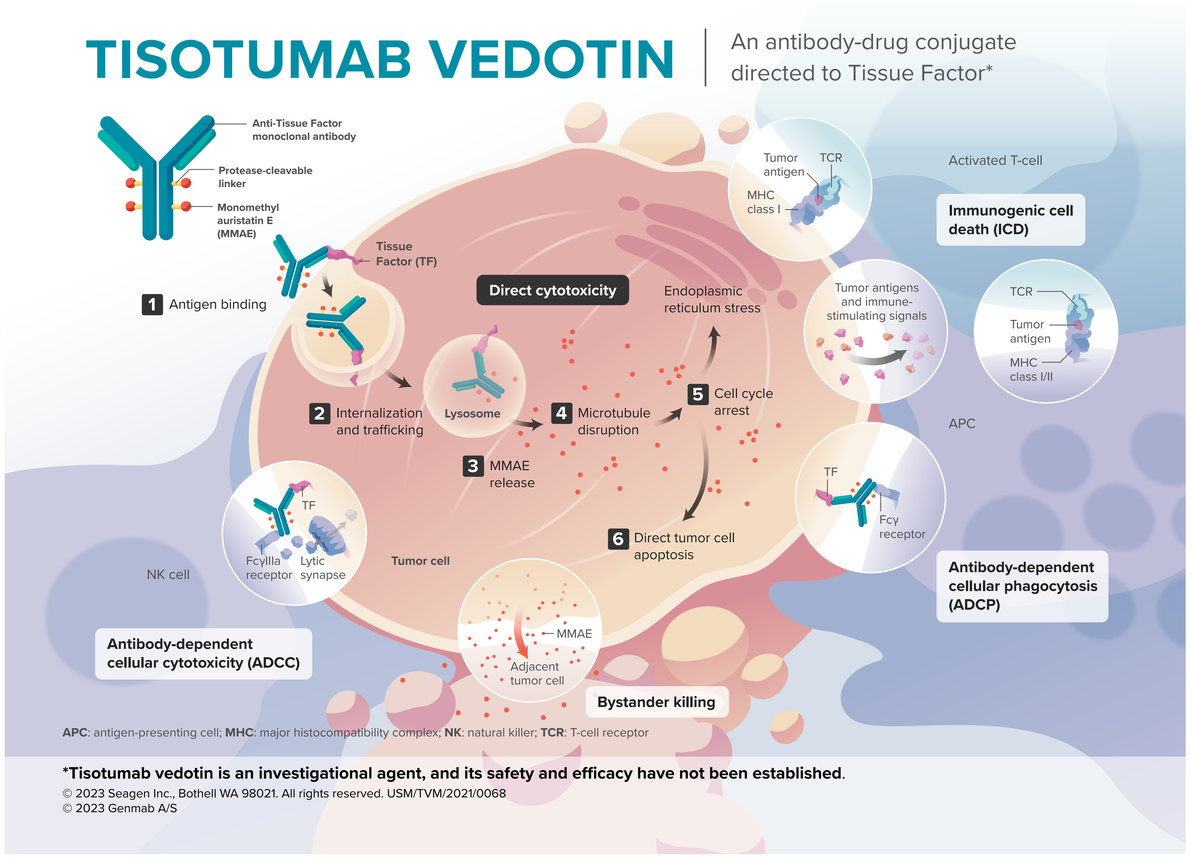
innovaTV 207 Part E

Patient population	Treatment	Endpoints
• r/m HNSCC • No more than 2 prior systemic lines of therapy • Prior platinum-based regimen and a PD-(L)1 inhibitor	**Tisotumab vedotin** 1.7 mg/kg Days 1 and 15 of a 28-day cycle (Q2W) (n≈100)	**Primary endpoint:** Confirmed ORR by BICR, RECIST v1.1 **Key secondary endpoints:** • Safety • Tolerability • DCR • PFS • DOR • ORR • OS

innovaTV 207 Part F

Patient population	Safety run-in		Dose expansion	Endpoints
• r/m HNSCC • No previous systemic therapy for r/m HNSCC; multimodal treatment given in the curative setting must have been completed >6 months prior without disease progression during this time • CPS ≥1 by tumor PD-L1 testing	**Tisotumab vedotin** 1.7 mg/kg Days 1 and 15 of a 28-day cycle (Q2W) + **Pembrolizumab** 400 mg Q6W (n=6)	+n=4 SMC	**Tisotumab vedotin** 1.7 mg/kg Days 1 and 15 of a 28-day cycle (Q2W) + **Pembrolizumab** 400 mg Q6W (n=20)	**Primary endpoint:** Confirmed ORR by investigator, RECIST v1.1 **Key secondary endpoints:** • Safety • Tolerability • DCR • PFS • DOR • ORR • OS

Proposed Mechanism of Action



Assessments

- Response assessments every 6 weeks after screening/baseline during the first 30 weeks, and every 12 weeks thereafter
- Eye examinations by investigator occured at baseline and at each treatment cycle, Day 1 (±1 day). Steroid and lubricating eye drops administered per the ocular mitigation plan. Patients referred to an ophthalmologist should an ocular AE occur
- Antitumor activity determined by ORR as defined by RECIST v1.1
- OS, PFS, DOR, and TTR estimated by using the Kaplan-Meier method
- Safety assessments summarized descriptively, including TEAEs, treatment-related TEAEs, SAEs, and deaths
- Blood samples for PK and ATA analyses collected at protocol-defined time points for PK and immunogenicity assessments
- Safety summarized using the safety analysis set, which will include all patients who received any amount of study drug

Eligibility

Key Inclusion Criteria

Part E (n≈100)

- r/m HNSCC
- Disease progression on or after the most recent systemic therapy with no more than 2 lines of therapy in the r/m setting
- One of the following prior regimens inclusive of platinum-based chemotherapy and a PD-(L)1 inhibitor as detailed below:
  1. A platinum-based regimen in combination with a PD-(L)1 inhibitor in the 1L r/m setting; no more than 1 prior line of therapy in the r/m setting
  2. A platinum-based regimen in the 1L setting followed by a PD-(L)1 inhibitor (monotherapy or combination) in the 2L setting; no more than 2 prior lines of therapy in r/m setting
  3. A PD-(L)1 inhibitor in the 1L setting followed by a platinum therapy in the 2L setting; no more than 2 prior lines of therapy in the r/m setting
  4. Treatment with platinum therapy given as part of a multimodal therapy in the curative setting and experiencing recurrence/progression <6 months after the last dose followed by treatment with a PD-(L)1 inhibitor (monotherapy or combination); no other lines of therapy prior to receiving study drug
- Baseline measurable disease per RECIST v1.1
- ECOG PS 0-1

Part F

- r/m HNSCC
- No previous systemic therapy for r/m disease; multimodal treatment given in the curative setting must have been completed >6 months prior without disease progression during this time
- CPS ≥1 by local PD-L1 testing
- Baseline measurable disease per RECIST v1.1
- ECOG PS 0-1

Key Exclusion Criteria

Both Parts

- Primary site of disease is nasopharynx or salivary gland
- Active bleeding conditions
- Active ocular surface disease, including any prior episode of cicatricial conjunctivitis or Steven Johnson syndrome
- Grade ≥2 peripheral neuropathy
- Inflammatory lung disease
- Active brain metastasis

Part F

- Prior therapy with an anti-PD-(L)1 or anti-PD-L2 agent or an agent directed to another stimulatory or coinhibitory T-cell receptor

Abbreviations

ADC, antibody-drug conjugate; ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; APC, antigen-presenting cell; ATA, anti-therapeutic antibody; BICR, blinded independent central review; CPS, Combined Positive Score; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Score; HNSCC, head and neck squamous cell carcinoma; ICD, immunogenic cell death; MHC, major histocompatibility complex; MMAE, monomethyl auristatin E; NK, natural killer; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PK, pharmacokinetics; Q2W, once every 2 weeks; Q6W, once every 6 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1; r/m, recurrent or metastatic; SAE, serious adverse event; SCC, squamous cell carcinoma; SMC, Safety Monitoring Committee; TCR, T-cell receptor; TEAE, treatment-emergent adverse event; TF, tissue factor; TTR, time-to-response; TV, tisotumab vedotin

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