Research Area:

Hepatocellular Carcinoma, Metastatic Liver Tumors, and Advanced Solid Tumors

Talimogene Laherparepvec

Amgen Study ID Number: 20140318
NCT Number: 02509507

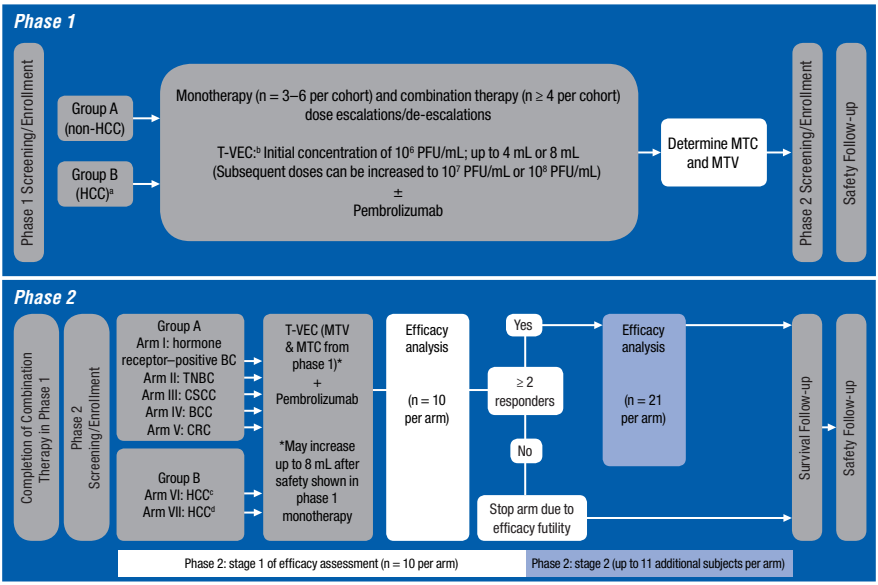
Phase 1b/2, Multicenter, Open-label, Basket Trial to Evaluate the Safety of Talimogene Laherparepvec (T-VEC) Injected into Liver Tumors Alone and in Combination with Systemic Pembrolizumab in Phase 1b and to Evaluate the Efficacy and Safety of T-VEC Injected into Advanced Solid Tumors in Combination with Systemic Pembrolizumab in Phase 2 (MASTERKEY-318)

Primary Endpoints:

- Phase 1: Incidence of DLTs
- Phase 2:
  - ORR per modified irRC-RECIST
  - Incidence of treatment-emergent and treatment-related AEs

Key Secondary Endpoints:

- Phase 1: ORR, BOR, DRR, DOR, response in injected and uninjected lesions, DCR, PFS, and OS
- Phase 2: BOR, DRR, DOR, response in injected and uninjected lesions, DCR, PFS, and OS
- Phase 1 and 2: Incidence of treatment-emergent and treatment-related AEs



[a]Cohort 1 of group B will be initiated only after safety has been established in cohort 1 of group A. [b]The first cycle of T-VEC will be 21 (+3) days and subsequent cycles will be 21 (±3) days. [c]Without viral hepatitis. [d]With well-controlled viral hepatitis.

AE: adverse event; BC: breast adenocarcinoma; BCC: basal cell carcinoma; BOR: best overall response; CRC: colorectal adenocarcinoma; CSCC: cutaneous squamous cell carcinoma; DCR: disease control rate; DLT: dose-limiting toxicity; DOR: duration of response; DRR: durable response rate; HCC: hepatocellular carcinoma; irRC-RECIST: immune-related response criteria–Response Evaluation Criteria in Solid Tumors; MTC: maximum tolerated concentration; MTV: maximum tolerated volume; ORR: objective response rate; OS: overall survival; PFS: progression-free survival; PFU: plaque-forming unit; TNBC: triple negative breast cancer

Products under investigational study have not been approved by any regulatory authority.

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Key Summary Points:

This phase 1b/2, multicenter, open-label, basket trial is designed to evaluate the safety of T-VEC injected into liver tumors alone and in combination with systemic pembrolizumab in subjects with non-HCC liver metastases or HCC (with/without viral hepatitis) in phase 1 and to evaluate the efficacy and safety of intratumoral T-VEC in combination with systemic pembrolizumab to treat subjects with advanced solid tumors in phase 2.

The phase 1, dose-escalation portion will evaluate the safety of intrahepatic injection of T-VEC into liver tumors alone and in combination with pembrolizumab for the non-HCC and HCC cohorts separately.

Phase 2 has a two-stage design that will evaluate the efficacy and safety of T-VEC in combination with systemic pembrolizumab separately by tumor type.

Key Schedule of Assessments:

- Clinical tumor assessment, radiographic imaging (including PET, CT, or MRI) at week 10 and then every 9 weeks
- Hematology, coagulation, and chemistry panel laboratory tests weekly for the first 8 weeks of treatment and then prior to each T-VEC administration until end of study treatment

BC: breast adenocarcinoma; BCC: basal cell carcinoma; CNS: central nervous system; CRC: colorectal adenocarcinoma; CSCC: cutaneous squamous cell carcinoma; CT; computed tomography; ECOG: Eastern Cooperative Oncology Group; GEC: gastroesophageal carcinoma; HBV: hepatitis B virus; HCC: hepatocellular carcinoma; HCV: hepatitis C virus; IV: intravenous; MRI: magnetic resonance imaging; NSCLC: non-small cell lung cancer; PET: positron emission tomography; RCC: clear cell renal cell carcinoma; TNBC: triple negative breast cancer

Key Inclusion Criteria:

- Adults with histologically or cytologically confirmed NSCLC, melanoma, BC, CRC, GEC, or RCC with liver metastasis; or HCC (phase 1) or advanced hormone receptor–positive BC, TNBC, CSCC, CRC, or BCC with/without liver metastases; or HCC (phase 2)
- Child-Pugh score of A and ECOG performance status of 0 or 1
- Non-HCC subjects must have had progression on or following ≥ 1 prior standard of care systemic anticancer therapy for locally advanced or metastatic disease
- For phase 1 (cohort 6b) and phase 2 (arm VII): subjects must have a diagnosis of well-controlled HBV/HCV infection
- Measurable and injectable liver lesion(s)
- Life expectancy approximately ≥ 5 months
- Lymph node lesions should be located such that potential swelling after injection will not lead to morbidity, obstruction, or bleeding
- Adequate hematological, renal, coagulation, and hepatic function

Key Exclusion Criteria:

- Candidate for
  - Any surgery or locoregional therapy for their respective cancer with curative intent
  - Planned systemic anticancer therapy
- More than one-third of the liver estimated to be involved with the tumor
- Liver tumor-directed therapy, hepatic surgery/major surgery, antibody-based therapy, or immunotherapy < 28 days prior to enrollment; chemotherapy < 21 days prior to enrollment; and targeted small-molecule therapy or hormonal therapy < 14 days prior to enrollment
- Non-HCC with active acute or chronic HBV/HCV infection
- For phase 1, group B (cohorts 1-5, 6a) and phase 2 (arms I-VI): HCC with HBV/HCV and detectable viral load
- Phase 1: any tumor type with history of CNS metastases or carcinomatous meningitis
- Phase 2: history or evidence of active CNS metastases, except subjects with previously treated cerebral metastases may be enrolled.* Carcinomatous meningitis is excluded regardless of clinical stability
- History of symptomatic autoimmune disease or immunosuppression
- Prior therapy with T-VEC or any other oncolytic viruses
- For subjects planned to receive intrahepatic injections: macroscopic intravascular invasion into major vessels, active herpetic skin lesions or prior complications of herpes simplex virus 1 infection, and intermittent or chronic systemic (IV or oral) antiherpetic drug treatment

*Provided that all lesions have been adequately treated with stereotactic radiation therapy, craniotomy, or gamma knife therapy, with no evidence of progression, and have not required steroids, for ≥ 1 month prior to enrollment.

Additional Information:

- www.amgentrials.com Protocol Number—20140318
- www.clinicaltrials.gov Identifier—NCT02509507

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