Research Area:

Advanced Non–Central Nervous System Tumors

Talimogene Laherparepvec

Amgen Study ID Number: 20110261
NCT Number: 02756845
EudraCT Number: 2015-003645-25

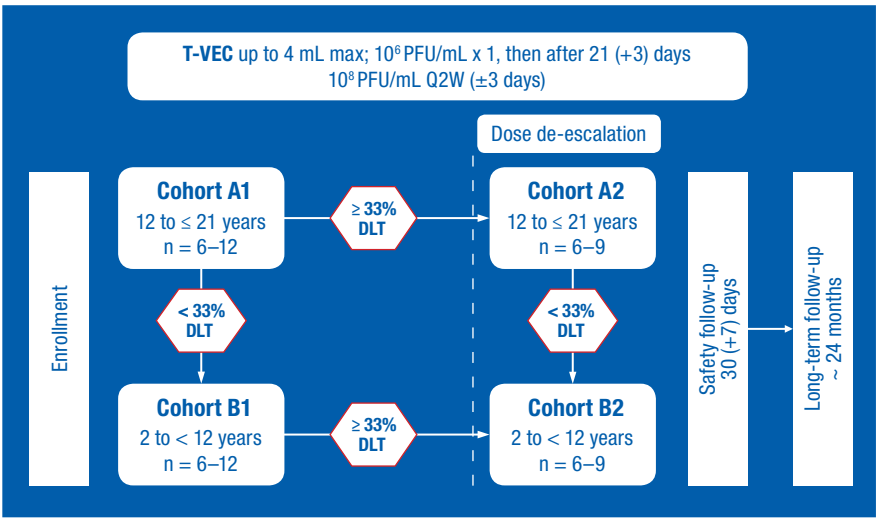
A Phase 1, Multicenter, Open-label, Dose De-escalation Study to Evaluate the Safety and Efficacy of Talimogene Laherparepvec in Pediatric Subjects With Advanced Non–Central Nervous System (CNS) Tumors That Are Amenable to Direct Injection

Primary Endpoint:

- Incidence of dose-limiting toxicities (DLTs)

Key Secondary Endpoints:

- Efficacy: overall response rate, duration of response, time to response, time to progression, progression-free survival using modified Immune-Related Response Criteria Simulating Response Evaluation Criteria In Solid Tumors (irRC-RECIST), and overall survival
- Safety: subject incidence of adverse events and significant laboratory abnormalities



DLT: dose-limiting toxicity; PFU: plaque-forming unit; Q2W: once every 2 weeks; T-VEC: talimogene laherparepvec
DLT evaluation period is 35 days. If dose de-escalation is needed and if permissible based on the incidence of DLTs, a minimum of nine additional subjects may be enrolled and treated at a lower dose level of T-VEC (4 mL max; 10^6 PFU/mL x 1, then after 21 (+3) days, 10^6 PFU/mL Q2W (±3 days)).

Products under investigational study have not been approved by the FDA for the use under investigation in this trial.

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Talimogene Laherparepvec

Key Summary Points:

This phase 1, multicenter, open-label study is designed to determine the safety and tolerability of talimogene laherparepvec in pediatric subjects with advanced non-CNS tumors that are amenable to direct injection in the clinical setting.

Approximately 18 treated pediatric subjects will be enrolled into two cohorts stratified by age (permissible based on the incidence of DLTs; n = 6–12/cohort). Initially, three subjects aged 12 to ≤ 21 years will be enrolled and treated at 100% of the recommended adult dose regimen of talimogene laherparepvec (cohort A1). Once cohort A1 is determined safe by the dose level review team, the younger cohort B1 (2 to < 12 years) will be opened for enrollment.

Key Schedule of Assessments:

- Radiographic scans and clinical tumor assessments at week 8, week 16, and then every 12 weeks

Key Inclusion Criteria:

- Subjects aged 2 to ≤ 21 years with histologically or cytologically confirmed non-CNS solid tumors that recurred after standard/frontline therapy, or for which there is no standard/frontline therapy available
- Measurable or nonmeasurable disease eligible for intralesional injection only into injectable cutaneous, subcutaneous, and nodal tumors with or without ultrasound guidance (Note: visceral lesions, and bone lesions without soft-tissue component are not eligible for injection)
- Performance status:
  - Karnofsky score ≥ 70% for subjects aged 12 to ≤ 21 years
  - Lansky play scale ≥ 70% for subjects aged 2 to < 12 years
- Life expectancy > 4 months from the date of enrollment
- Adequate hematological, renal, coagulative, and hepatic function

Key Exclusion Criteria:

- Diagnosis of leukemia, non-Hodgkin's lymphoma, Hodgkin's disease, or other hematologic malignancy
- CNS tumor or clinically active brain metastases
- Primary ocular or mucosal melanoma
- Radiotherapy to the bone marrow within 6 weeks prior to enrollment
- History or evidence of xeroderma pigmentosum
- History of other malignancy within the past 5 years (except if treated with curative intent, no presence of active disease, last chemotherapy > 5 years before enrollment, and at low risk of recurrence)
- Prior treatment with talimogene laherparepvec or any other oncolytic virus, or a tumor vaccine; received chemotherapy, radiotherapy, or biological cancer therapy within 14 days prior to enrollment
- History or evidence of active autoimmune disease requiring systemic treatment with steroids or immunosuppressive agents, or evidence of clinically significant immunosuppression
- Active herpetic skin lesions or prior complications of herpetic infection; requiring intermittent or chronic treatment with an antiherpetic drug (eg, acyclovir), other than intermittent topical use

Additional Information:

- www.amgentrials.com Protocol Number: 20110261
- www.clinicaltrials.gov Identifier: NCT02756845
- eudract.ema.europa.eu EudraCT Number: 2015-003645-25

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