PEGylated IL-10
Pegilodecakin, LY3500518, AM0010
Target

FOLFOX‡ AM0010 † + FOLF OX‡

The safety and efficacy of the agents under investigation have not been established. There is no guarantee that the agents will receive regulatory approval and become commercially available for the uses being investigated.

PEGylated interleukin-10 (IL-10) is a noncovalent homodimeric alpha-helical cytokine with structural similarities to interferon gamma (IFNγ). PEGylated IL-10 promotes the expansion and activation of cytotoxic intratumoral CD8+ T cells, despite its known physiological anti-inflammatory properties. PEGylated IL-10 has demonstrated single-agent antitumor activity in preclinical tumor models, inducing CD8+ T-cell mediated tumor rejection of large, high-grade tumors in mice. Mice cured by PEG-murine IL-10 have a long-lasting immunity to the rejected tumor. PEGylated IL-10 combines preclinically and clinically with chemotherapy and immune checkpoint inhibitors, including anti-PD-1.

Molecule

Pegilodecakin (LY3500518, AM0010) is a PEGylated form of recombinant human IL-10 (rHuIL-10). rHuIL-10 is a noncovalent homodimeric cytokine with an approximate monomeric MW of 18–19 kD and a dimeric MW of approximately 38 kD. AM0010 is derived from a human cDNA clone, recombinantly produced in E. coli and PEGylated at its N-terminus. Pegilodecakin is PEGylated at the N-terminal amino acid of one or both of the rHuIL-10 monomers with a 5 kD polyethylene glycol (PEG), resulting in an approximate 50%/50% mixture of mono- and di-PEGylated rHuIL-10. Pegilodecakin has been shown in vitro to increase the cytotoxic activity of CD8+ T cells.

Clinical Development

Pegilodecakin is being investigated in clinical trials in patients with pancreatic cancer or non-small cell lung cancer, and in a phase I clinical trial in early development.


* This clinical trial is being conducted globally.
† AM0010 5 µg/kg is administered SQ on days 1-5 and 8-12.
‡ FOLFOX (leucovorin 400 mg/m² and oxaliplatin 85 mg/m² followed by bolus 5-FU 400 mg/m² and 46-hour infusion of 5-FU 2400 mg/m²) is administered intravenously on day 1 of a 14-day cycle until disease progression.

Sequoia: A Randomized Study of AM0010 in Combination With FOLFIRI Compared to FOLFIRI Alone as Second-line Tx in Pts With Meta Pancreatic Cancer That Has Progressed During or Following a First-line Gemcitabine-containing Regimen

Key Inclusion Criteria

- Metastatic pancreatic adenocarcinoma
- Measurable disease as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1
- Tumor progression during or following a gemcitabine-containing regimen (as evidenced by PET or CT scan) or documented disease progression on a gemcitabine-containing regimen
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 (ECOG ≥2 is a reason for exclusion)
- Prior chemotherapy at least 2 weeks prior to randomization and recovered from toxicity to grade 1 or baseline

Key Exclusion Criteria

- Diagnosis of pancreatic islet neoplasm, acinar cell carcinoma, nonadenocarcinoma (ie, lymphoma, sarcoma), adenocarcinoma originating from the biliary tree, or cystadenocarcinoma
- Prior treatment with Coumadin and not willing to change to low molecular weight heparin or oral Factor II or Xa inhibitor with half-life <24 hours
- Prior treatment with AM0010 or fluoropyrimidine/platinum-containing regimen
- Intolerant to a gemcitabine-containing regimen
- Known history of HIV infection or activated/reactivated hepatitis A, B, or C
- Prior radioactive therapy or investigational therapy for the treatment of advanced metastatic disease
- Radiated/irradiated area or gangrenous or any other chronic osteomyelitis or ulcerated islet cell carcinoma
- Peripheral neuropathy or known history of dihydroxypropyryline dehydrogenase deficiency
- Clinically significant bleeding within 2 weeks prior to randomization
- Drug use or breastfeeding
- Prior history of severe interstitial lung disease or any other interstitial lung disease not resolving with therapy
- Major surgery within 28 days prior to randomization or anticipated surgery during the study period
- Prior history of receiving immune modulators including, but not limited to, anti-CTLA4, anti-PD-1, and anti-PD-L1
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Primary endpoint: Objective response rate

Cypress 1: A Randomized Phase 2 Trial of AM0010 in Combination With Pembrolizumab vs Pembrolizumab Alone as First-line (1L) Therapy in Patients With Stage IV/Metastatic Non-small Cell Lung Cancer and Tumors With High Expression of PD-L1 (>50%)*

Key Inclusion Criteria
- Metastatic or recurrent stage IV non-small cell lung cancer
- Tumor proportion score (TPS) ≥50%
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Measurable disease by CT or MRI scan as defined by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1
- Prior radiotherapy or radiosurgery completed at least 2 weeks prior to randomization
- No prior therapy for advanced disease. Previous neoadjuvant or adjuvant therapy is allowed for patients who successfully underwent complete radical surgery and ONLY if the last treatment was administered more than 6 months prior to the start of the trial treatment

Key Exclusion Criteria
- Active central nervous system metastases or carcinomatous meningitis
- Serious or uncontrolled medical disorder
- Active HIV or hepatitis infection
- ≥ Grade 1 toxicities as defined by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.03 attributed to prior anticancer therapy (other than alopecia and fatigue) prior to randomization
- History of severe hypersensitivity reactions to monoclonal antibodies
- Pregnant or breastfeeding
- Prior use of an investigational agent within 28 days of first administration of trial treatment
- Prior use of antitumor vaccines or other immunostimulatory antitumor agents
- Prior use of anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, and/or anti-CTLA4 antibodies
- Nonsquamous non-small cell lung cancer with known EGFR mutation or ALK rearrangement

* This clinical trial is being conducted in the United States.
† AM0010 is dosed per body weight and administered SQ QD.
‡ Pembrolizumab 200 mg is administered intravenously over 30 min on day 1 of a 21-day cycle.

The safety and efficacy of the agents under investigation have not been established. There is no guarantee that the agents will receive regulatory approval and become commercially available for the uses being investigated.

Please visit www.clinicaltrials.gov for more information on this clinical trial [NCT03382899].
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Active Trials Currently Not Enrolling

[NCT02009449] Early Development
IVY: A Phase 1 Study of Pegilodecakin (LY3500518) in Patients With Advanced Solid Tumors

[NCT03382912] Lung Cancer
Cypress 2: A Study of Pegilodecakin (LY3500518) With Nivolumab Compared to Nivolumab Alone Second-line Tx in Participants With Metastatic Non-small Cell Lung Cancer

Pipeline information is current through October 23, 2019.