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POSTER ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Rationale for and Design of Papilio-1: A Phase 1/2, Multicenter, Open-Label Study to Evaluate the Feasibility, Safety, and Efficacy of Point-of-Care-Manufactured Anti-B-Cell Maturation Antigen Chimeric Antigen Receptor T Cells (GLPG5301) in Relapsed/Refractory Multiple Myeloma

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Background and Significance

Despite improvements in treatment, patients with multiple myeloma (MM) ultimately relapse or become refractory to available regimens. Triple-refractory (refractory to CD38 monoclonal antibodies [mAbs], 1 proteasome inhibitor [PI] and 1 immunomodulatory drug [IMiD]) or penta-refractory (refractory to CD38 mAbs, 2 PIs and 2 IMiDs) patients have a poor prognosis and are in urgent need of novel treatment options. Chimeric antigen receptor (CAR) T-cell therapies have been used to target B-cell maturation antigen (BCMA) and have shown good clinical activity in patients with relapsed/refractory MM (RRMM). Faster manufacturing procedures may improve clinical outcomes by lowering discontinuation rates and reducing the need for bridging therapy. GLPG5301, a BCMA-directed CAR T-cell therapy, is produced using a novel decentralized and automated point-of-care manufacturing model. This allows administration of a fresh product within 7 days of apheresis. The objective of Papilio-1 is to evaluate the feasibility, safety and efficacy of GLPG5301, manufactured at the point-of-care, in adult patients with RRMM.

Study Design and Methods

Papilio-1 (CTIS: 2022-500782-27-00) is a Phase 1/2, multicenter, open-label study of GLPG5301 in patients with RRMM after ≥2 prior lines of therapy. Key eligibility criteria are presented (**Table**). The study will be conducted in centers across Europe. The Phase 1 primary objective is to evaluate the safety of GLPG5301 and determine the recommended Phase 2 dose (RP2D). The Phase 1 primary endpoint is incidence of serious adverse events, including dose-limiting toxicities (DLTs), until 14 days post-infusion. The Phase 2 primary objective is to evaluate GLPG5301 efficacy. The Phase 2 primary endpoint is best objective response until 2 years post-infusion. Secondary endpoints include: type, frequency and severity of adverse events; duration of response; progression-free survival (PFS); overall survival (OS); minimal residual disease; soluble BCMA levels; time to response; time to progression; GLPG5301 levels in blood and bone marrow; serum levels of chemokines and cytokines; and number of successfully manufactured GLPG5301 products. Exploratory assessments include additional GLPG5301 pharmacokinetics (PK) and pharmacodynamics (PD).

Patients will undergo leukapheresis of mononuclear cells for point-of-care manufacturing of GLPG5301 after screening (**Figure**). Prior to infusion of GLPG5301, patients will receive fludarabine/cyclophosphamide lymphodepleting chemotherapy, followed by a resting period of at least 2 days. GLPG5301 will be administered as a fresh product, followed by in-hospital monitoring for 7 days. Safety, efficacy, PK and PD will be assessed until end of treatment (100 days post-infusion), and monthly until study completion (2 years). Patients will be enrolled in a long-term follow-up for up to 15 years.

In Phase 1, dose escalation will be based on the occurrence of DLTs occurring within 14 days of infusion, according to predefined criteria. Three dose levels (DLs) will be assessed (DL1, DL2 and DL3). Six patients will receive the lowest dose level (DL1) and be evaluated for DLTs and efficacy. The appropriate dose for the following cohort will be then determined by the Safety Review Committee. This will be repeated until RP2D is determined. Approximately 30 patients will be treated with the RP2D in Phase 2.

Safety and efficacy data will be analyzed using descriptive statistics. Response status will be summarized as best response (number, percentage, 95% confidence interval) and graphically displayed using swimmer plots by dose. Other binary endpoints will be described using a similar method. PFS and OS will be assessed using the Kaplan–Meier method and calculated from the median survival time.

Summary

In Papilio-1, the feasibility, safety and efficacy of GLPG5301, a point-of-care-manufactured BCMA-directed CAR T-cell therapy, will be evaluated in adult patients with RRMM.

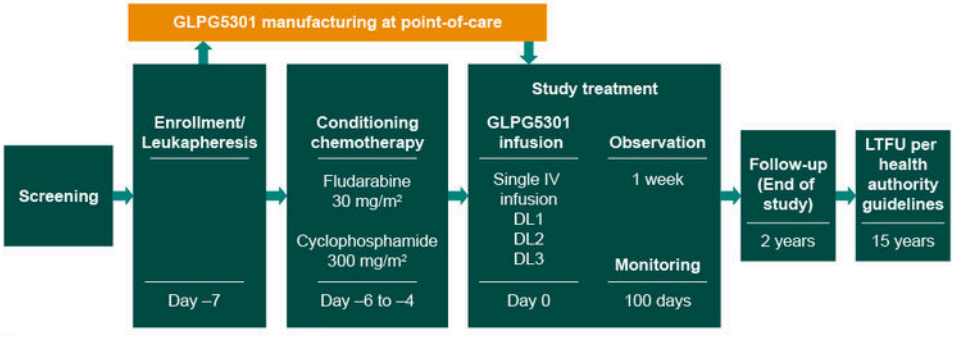
Disclosures van de Donk: *Servier:* Membership on an entity's Board of Directors or advisory committees; *Celletics:* Research Funding; *Takeda:* Membership on an entity's Board of Directors or advisory committees; *Amgen:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Celgene:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Roche:* Membership on an entity's Board of Directors or advisory committees; *Bristol Myers Squibb:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Bayer:* Membership on an entity's Board of Directors or advisory committees; *Janssen Pharmaceuticals:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Adaptive Biotechnologies:* Membership on an entity's Board of Directors or advisory committees; *Novartis:* Membership on an entity's Board of Directors or advisory committees, Research Funding. **Caers:** *Janssen-Cilag:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Amgen:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Johnson & Johnson:* Consultancy, Research Funding; *Sanofi:* Membership on an entity's Board of Directors or advisory committees. **Liefaard:** *Cellpoint BV, a Galapagos company:* Current Employment. **Jacques:** *Cellpoint BV, a Galapagos company:* Consultancy. **van Muyden:** *Cellpoint BV, a Galapagos company:* Current Employment, Current equity holder in publicly-traded company.

Table. Inclusion and exclusion criteria

Inclusion criteria
Age ≥18 years
MM diagnosis (IMWG criteria)
Relapsed or refractory[a] disease after ≥2 prior lines of therapy, including anti-CD28 mAbs, an IMiD and a PI
Measurable disease at screening
ECOG performance status 0–2[b]
Adequate bone marrow function
Adequate renal, hepatic, cardiac and pulmonary function
Exclusion criteria
AL amyloidosis, Waldenström's macroglobulinemia, POEMS syndrome
History of another primary malignancy
Toxicity from previous anticancer therapy that has not resolved to Grade ≤2[c] or patient's baseline level
Uncontrolled infection at screening
Infection with HIV-1/2, hepatitis B or C virus[d]
Clinically significant cardiac disease within 12 months of screening
Other medical contraindications: • Known active or prior history of CNS involvement or clinical signs of meningeal involvement of MM • Primary immunodeficiency • Stroke or seizure within 6 months of screening • History of autoimmune disease resulting in end organ injury or requiring systemic immunosuppression/systemic disease-modifying agents ≤2 years prior to screening • Contraindications to leukapheresis or inadequate venous access • Known allergy or hypersensitivity to tocilizumab
Any prior BCMA-directed therapy, or any permitted prior treatment if not discontinued within the appropriate period prior to leukapheresis

[a]Refractory defined as documented evidence of progressive disease by IMWG criteria on or within 60 days of the last regimen; [b]Patients with ECOG 2 must have serum albumin ≥3.4 g/dL; [c]According to CTCAE v5.0; [d]A history of hepatitis B or C is permitted if the viral load is undetectable per quantitative polymerase chain reaction and/or nucleic acid testing.AL, amyloid light-chain; BCMA, B-cell maturation antigen; CNS, central nervous system; CTCAE, Common Terminology Criteria for Adverse Events; ECOG, Eastern Cooperative Oncology Group; G-CSF, granulocyte colony-stimulating factor; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; mAbs, monoclonal antibodies; MM, multiple myeloma; PI, proteasome inhibitor; POEMS, Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal plasma cell disorder, Skin changes.

Figure. Papilio-1 study design



DL, dose level; IV, intravenous; LTFU, long-term follow-up.

Figure 1

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