A Multicentre, Randomized, Double-Blinded, Phase 2b Study Evaluating The Efficacy And Safety Of MaaT033, an Oral, Pooled Microbiome Ecosystem Therapy In Patients Undergoing Allogenic Hematopoietic Cell Transplantation to Improve Overall Survival: the PHOEBUS trial

Abstract# 858

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INTRODUCTION

Allogenic hematopoietic cell transplantation (alloHCT) is a well-established therapy for various life-threatening hematologic malignancies. The use of alloHCT is constantly increasing, with nearly 20 000 transplantations reported to the EBMT per year. However, this treatment is limited by high morbidity and mortality, mainly related to relapse, infection, graft-versus-host disease (GvHD), and conditioning-related toxicity. Several pioneering studies have shown that the diversity of the gut microbiota of patients not only correlates with the occurrence of medical complications after alloHCT, including GvHD (*Jenq et al. 2012, Stein-Thoeringer et al. 2019)* and bloodstream infections *(Taur et al. 2012),* but also with relapse of the underlying disease *(Peled et al. 2017).* Gut microbiota diversity restoration with fecal microbiotherapy could be an effective treatment to improve patients' clinical outcomes including overall survival (OS) after alloHCT, through the prevention and resolution of gut microbiota dysbiosis.

MaaT033 is a freeze-dried, full-ecosystem, high-diversity, fecal microbiota medicinal product, formulated as delayed-release capsules and derived from pooled allogenic human fecal material.

The PHOEBUS trial is a phase 2b study to evaluate the efficacy of MaaT033 in improving survival of 387 adult alloHCT patients (Clinicaltrials.gov identifier: NCT05762211).

METHODS

01

Characteristics

Pooled microbiota: high-richness, high-diversity, full ecosystem, Microbiome Ecosystem Therapy™ containing Butycore®. Capsule with ileo-caecal delivery

02

Treatment schedule

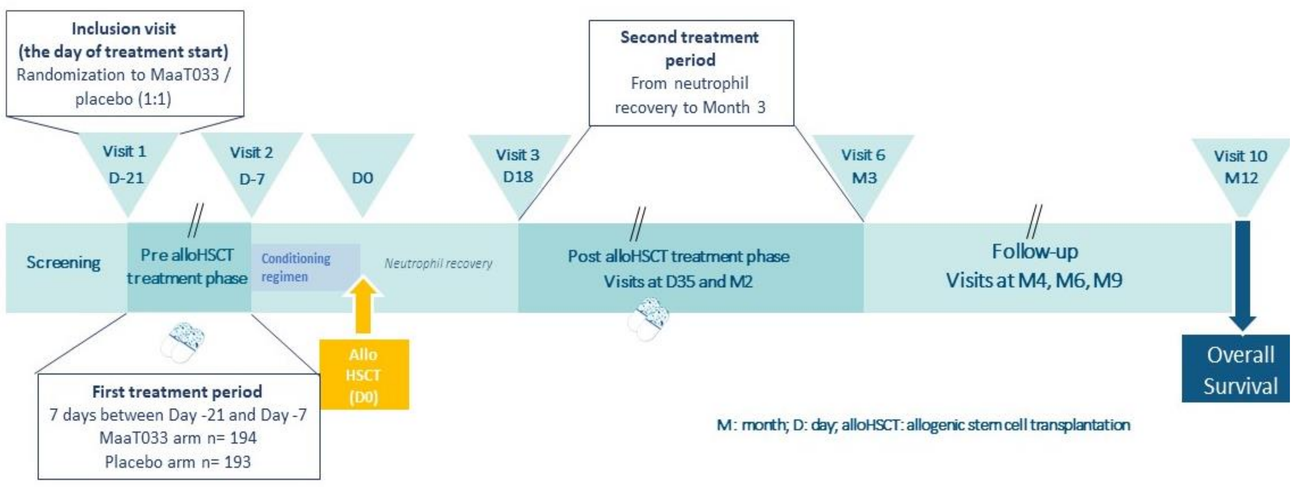
MaaT033 or placebo (3 capsules/day) for 1 week, between Day-21 (D-21) and D-7 before alloHCT (Day 0, D0).

MaaT033 or placebo (3 capsules/day) will be resume at neutrophil recovery (around D+18) and pursued up to 90 days after alloHCT.

No administration of MaaT033 or placebo planned during the neutropenic phase after alloHCT.

STUDY DESIGN

Study flowchart



Objectives

- **Primary**: Overall survival at 12 months after randomization
- **Secondary**: Evaluation of:
  - Safety
  - GvHD-free survival at 12 months after alloHCT
  - Incidence of grade 2-4 and grade 3-4 aGvHD within 6 months after alloHCT
  - Cumulative incidence of cGvHD
  - Cumulative incidence of non-relapse mortality, of infectious-related mortality and GvHD-related mortality within the first 12 months after alloHCT
  - Relapse-free survival (RFS) and GvHD- Relapse-free survival (GRFS) at 12 months
  - Proportion of patients with severe infections within 12 months after alloHCT
  - Quality of life (QoL)

Stratification

- **Donor-host crossmatch:** HLA-identical (geno-identical and pheno-identical 10/10) versus HLA-mismatch (8/10, 9/10 and haplo-identical)
- **Disease risk index** (low-intermediate versus high-very high).

Main inclusion criteria

- Patients aged ≥ 50 years old
- Presence of a hematologic malignancy for which an alloHCT is indicated with a reduced toxicity or reduced intensity conditioning regimen
- Patients with polynuclear neutrophils >0,5 x G/L
- Patients having received wide spectrum antibiotics within the last 90 days prior to inclusion
- Use of wide spectrum antibiotics is defined as use of at least 3 days of antibiotics within the last 90 days prior start of alloHCT conditioning.
- Refer to the current study protocol re the list of wide spectrum antibiotics.
- Karnofsky index ≥ 70%
- Availability of a sibling donor, an unrelated stem-cell donor or a familial haploidentical donor

Main exclusion criteria

- Patients planned to receive:
  - a non myeloablative conditioning regimen (2 Gray Total Body Irradiation +/- purine analog, fludarabine & cyclophosphamide or equivalent)
  - a conventional myeloablative conditioning regimen (e.g. high dose cyclophosphamide and high dose TBI (≥10Gy); high dose busulfan (12.8 mg/kg IV) + high dose cyclophosphamide)
- Patients receiving a manipulated graft (in-vitro T-cell depletion)
- Patients planned to receive: a conditioning regimen with alemtuzumab (CAMPATH®), alloHCT with cord blood cells, alloHCT from unrelated donor with ≥ 3/10 HLA-mismatches, vedolizumab or abatacept for GvHD prophylaxis
- Patients receiving a large spectrum antibiotic at time of randomization for a serious infection or active uncontrolled infection
- Contra-indication to allo-HCT (creatinine clearance <30 mL/min, bilirubin or amino-transferases abnormalities, cardiac ejection fraction less than 40%, pulmonary impairment with <50% lung carbon monoxide diffusing capacity (DLCO))
- Documented confirmed or suspected intestinal ischemia, toxic megacolon, bowel obstruction or gastrointestinal perforation, history of gastro-intestinal surgery in the past 3 months + any documented history of chronic digestive disease
- Patients with EBV-IgG negative serology
- Pregnancy and breastfeeding (urine or serum pregnancy test within 72 hours prior to randomization).

STUDY STATUS

First patient dosed in November 2023

Recruitment: est. **387** patients

Active countries

NEXT

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