Presentation of current protocols

Florent Malard, MD, PhD
Hématologie Clinique et Thérapie Cellulaire
Sorbonne University
Hôpital Saint-Antoine
Paris

Conflict of interest disclosure

- Honoraria: *Therakos/Mallinckrodt, Janssen, Sanofi, JAZZ pharmaceutical, Astellas, Biocodex, Novartis, Gilead, BMS*

ARES Study, a pivotal Phase 3 clinical trial investigating MaaT013 in aGvHD

ARES, a pivotal study to treat GI-aGvHD

- International study incl. **6 to 8 countries**– up to 50 reference centers
- **Pivotal single arm trial** of MaaT013 as 3rd line (steroid- & ruxolitinib-refractory patients)
- 29 months total duration
- Up to one year follow-up
- Est. **75 patients**
- **First patient treated in March 2022** in Spain

Countries with active sites (France, Spain, Germany)

Additional countries opening soon (Italy, Belgium, Austria)

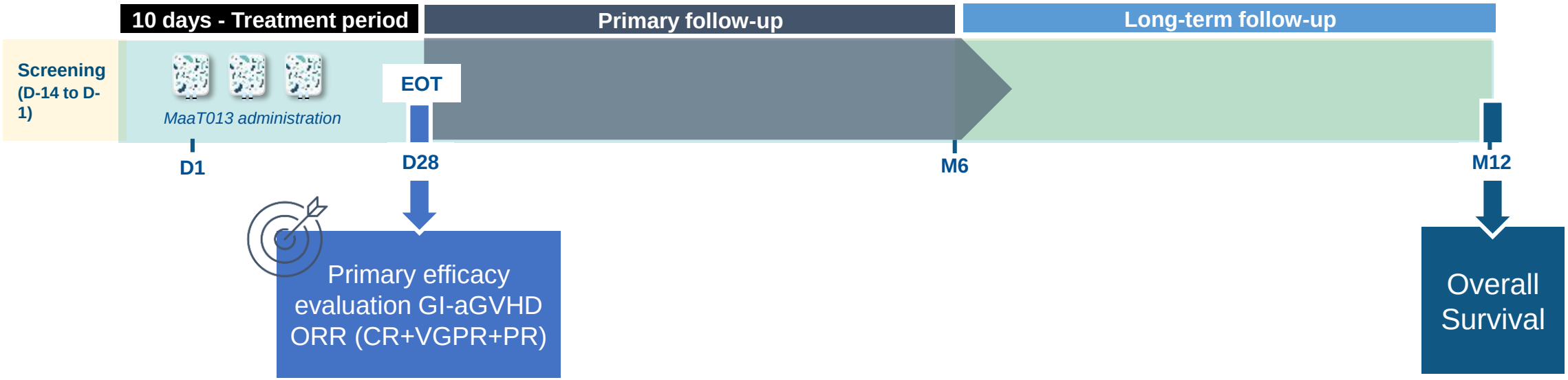
Sponsor MaaTPharma, ClinicalTrials.gov Identifier: NCT04769895

ARES, a pivotal Phase 3 trial to treat aGvHD in 3rd line

Patients with SR-GI-aGvHD

Inclusion criteria

- ✓ **Refractory or intolerant to ruxolitinib**
- ✓ Refractory to corticosteroids
- ✓ aGvHD with GI symptoms
- ✓ Allo-HSCT
- ✓ Age > 18

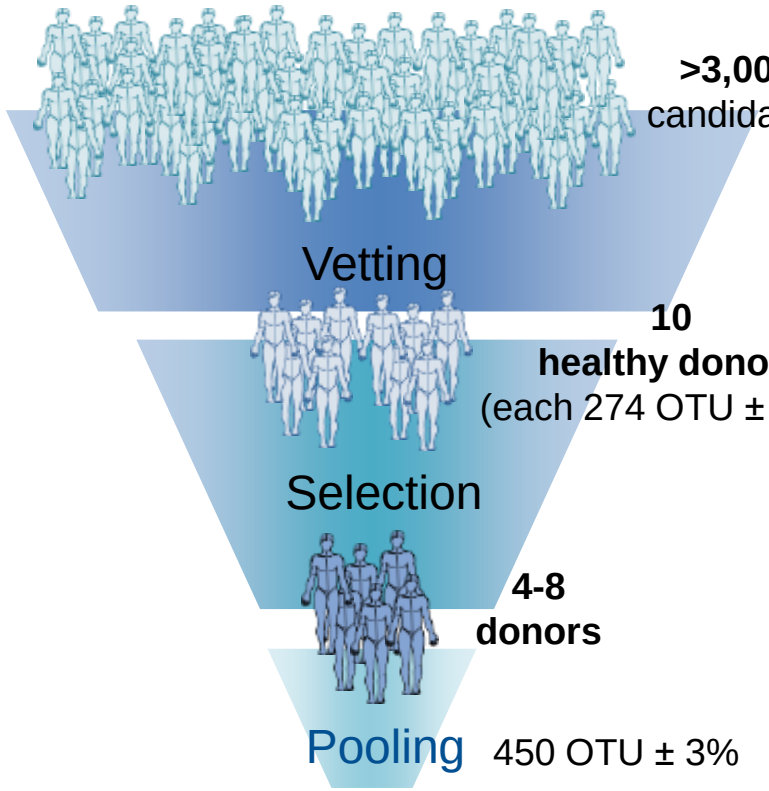


Abbreviations:

- D: Day, M: Month, EOT: End of treatment
- SR-GI-aGvHD: Steroid-refractory gastro-intestinal acute Graft-versus-Host Disease
- ORR: Overall Response Rate; CR: Complete Response; VGPR: Very Good Partial Response; PR: Partial Response

MaaT013 Full Ecosystem Therapeutics

cGMP Process



>3,000 candidates

10 healthy donors (each 274 OTU ± 15%)

4-8 donors

450 OTU ± 3%

MaaT013

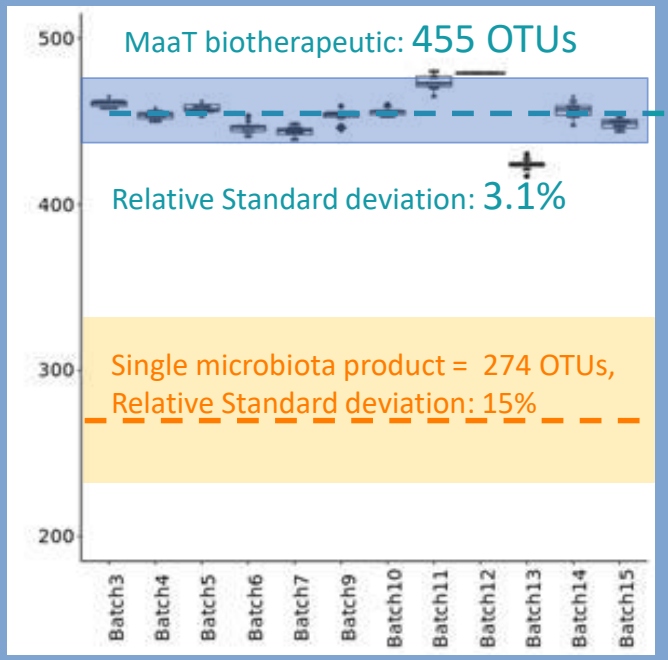
- ✓ Strict screening tests based on European consensus recommendations, ANSM guidelines and discussions with national regulatory agencies
- ✓ Sars-cov2 detection

- ✓ Full Ecosystem biotherapeutics
- ✓ Standardized, off-the shelf
- ✓ High, consistent richness and diversity
- ✓ Preserved Butycore (patented cryoprotectant)
- ✓ Manufactured under cGMP conditions

MaaT013

- ✓ Enema for direct colonic delivery
- ✓ 80% restoration
- ✓ 1 bag > 10^{11} CFU
- ✓ 24 months stability at -80°C

Microbial richness



Cammarota et al., 2016; Dubuisson et al., 2018; Sebastian D. Burz et al. 2019
Drug Product characteristics presented during EMBO|EMBL

ARES objectives

Primary: Evaluation of treatment response

MaaT13 efficacy evaluation assessed by the **ORR**
(CR, VGPR and PR) of GI-aGVHD response at Day 28

Secondary - SAFETY

Overall Safety Assessment
- AEs
- SAEs
- Laboratory abnormalities

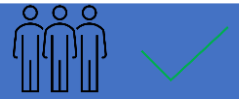
Secondary - EFFICACY

- ORR for GI and all organs up to M3
- Duration of response
- Overall survival, Progression-free survival
- Incidence of chronic GvHD
- Quality of life

Secondary - EXPLORATORY

- MaaT013 activity on immune markers
- Resource utilization evaluation

Inclusion / exclusion criteria



- Age ≥ 18 years old
- Allo-HSCT with any type of donor, stem cell source, GVHD prophylaxis or conditioning regimen.
- Acute GvHD episode with GI involvement per MAGIC guidelines (= grades II to IV), with or without involvement of other organs (Harris, Young, et al. 2016).
- Patients resistant to steroids AND either resistant to OR with intolerance to ruxolitinib
- Signature of informed and written consent

- Known hypersensivity to vancomycin or to any of the excipients listed in SmPC
- CMV colitis
- Other systemic drugs than CS and Ruxolitinib for GVHD treatment
- Grade IV hyper-acute GVHD (MD Anderson's criteria)
- Overlap chronic GVHD (NIH Consensus Criteria)
- Relapsed/persistent malignancy requiring rapid immune suppression withdrawal
- Liver stage 4 and/or skin stage 4 aGvHD
- Active uncontrolled infection according to the attending physician
- Severe organ dysfunction unrelated to underlying GvHD
- Current or past veno-occlusive disease or other uncontrolled complication unless otherwise agreed in writing by the sponsor
- Absolute neutrophil count <500/µL
- Absolute platelet count < 10 000/µL,
- Patient with negative IgG EBV serology
- Current or past evidence of toxic megacolon, bowel obstruction or gastrointestinal perforation
- Any condition that would, in the investigator's judgment, interfere with full participation in the study
- Known allergy or intolerance to trehalose or maltodextrin
- Vulnerable patients
- Pregnancy; lactation; absence of contraceptive method
- Other ongoing interventional protocol that might interfere with the current study primary endpoint

Secondary objectives

1 Safety

- Safety and tolerability : Incidence of AEs, treatment-emergent AEs (TEAEs), Serious Adverse Events (SAEs), deaths, and laboratory abnormalities related to MaaT013, NCI-CTCAE v5.0., and results from physical examination from D1 to M6.
- Evaluation of safety from Month 6 to M12: Incidence of SAEs and key events

2 Efficacy

- Evaluation of ORR for GI at D56 and M3
- Evaluation of ORR for all organs at D28, D56 and M3
- Evaluation of the best ORR (for GI and all organs) achieved between D0 and D28
- Duration of response assessment
- Overall survival (OS) assessment
- Progression-free survival (PFS) assessment
- Time to progression assessment
- Steroid-free survival assessment
- Evaluation of the frequency of patients that tapered off CS
- Measurement of the incidence of chronic GvHD
- Evaluation of changes in patient reported outcomes (PROs)

3 Exploratory

- MaaT013 activity on immune markers evaluation
- Resource utilization evaluation