Pooled Fecal Allogenic Microbiotherapy for Refractory Gastrointestinal Acute Graft-Versus-Host Disease: Results from Early Access Program in Europe

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Introduction

Acute graft-*versus*-host disease (aGvHD) is a major source of mortality following allogeneic hematopoietic cell transplantation (allo-HCT). Fecal microbiotherapy has shown promising results in several pilot studies in patients with refractory gastrointestinal (GI)-aGvHD. Here we report long-term clinical outcomes of 154 patients diagnosed with refractory GI-GvHD treated with the pooled allogeneic microbiotherapy MaaT013 within an Early Access Program (EAP) in Europe.

Patients & Methods

154 patients treated

incl. two pediatric patients (aged 12 and 15 years) with steroid-refractory or -dependent GI-aGvHD

5 European countries

Patient's characteristics (n=154)

Gender, n (%)	Male	84 (55%)
	Female	70 (45%)
Age at first MaaT013 administration (years)	Median [range]	57 [12;74]
Time between aGvHD diagnosis and first MaaT013 dose, days	Median [range]	60 [11;1337]
Number of previous lines of treatment, n	Median [range]	**3 [1;6]**
Steroid status	**Steroid refractory (SR)-aGvHD**	**128 (83%)**
	Steroid dependent (SD)aGvHD	26 (17%)
Type of aGvHD	Classical	93 (60%)
	Late onset	16 (10%)
	Hyper-acute	20 (13%)
	Overlap syndrome	25 (16%)
GvHD grading (MAGIC), n (%)	I	0
	II	20 (13%)
	III	**73 (47%)**
	IV	**61 (40%)**
GvHD organ involvement at EAP inclusion	GI only	94 (61%)
	GI + skin	38 (25%)
	GI + liver	9 (5%)
	GI + skin + liver	7 (5%)
	Missing data for skin and liver	6 (4%)
Stage skin GvHD	Stage 0	105 (68%)
	Stage 1	25 (16%)
	Stage 2	11 (7%)
	Stage 3	9 (6%)
	Stage 4	0 (0%)
	Missing data	4 (3%)
Stage liver GvHD	Stage 0	132 (86%)
	Stage 1	9 (6%)
	Stage 2	5 (3%)
	Stage 3	1 (0.6%)
	Stage 4	1 (0.6%)
	Missing data	6 (4%)
Stage gut GvHD	Stage 0	0 (0%)
	Stage 1	20 (13%)
	Stage 2	34 (22%)
	Stage 3	39 (25%)
	Stage 4	61 (40%)

Methods

1 Characteristics — Pooled microbiota: high-richness, high-diversity, full ecosystem, (10^{11} CFU/bag) containing Butycore®

2 Treatment protocol — A total of **3 MaaT013 administrations** were planned every 7 +/- 2 days (median dose administered 3, range 1-3).

3 Administration — 30 g of feces in 150 mL/ dose from **4 to 8 healthy donors** administered by enema

4 Efficacy evaluation (GI response at Day 28) — Proportion of patient achieving a GI complete response (CR), Very Good Partial Response (VGPR), or Partial Response (PR) compared to Day 0

Global EAP Population (n=154)

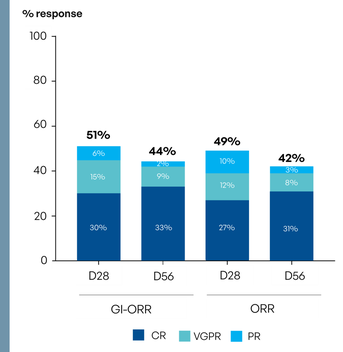
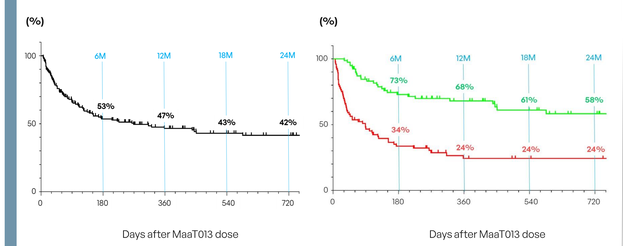


Fig. 1 : Patients' response and outcomes after MaaT013 treatment (n=154)

A. Gastrointestinal Overall Response Rate at day 28 (D28) and day 56 (D56) and Overall Response Rate at D28 and D56
B. Overall Survival in all patients
C. Overall Survival according to MaaT013 response (responders being patients who achieved at least a PR at day 28)

CR: complete response; VGPR: very good partial response; PR: partial response



3L patients (n=58)

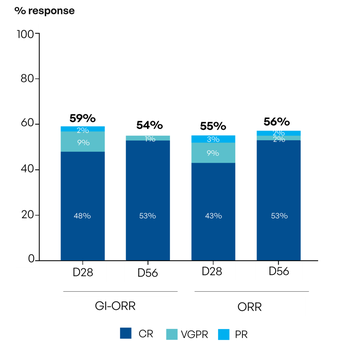
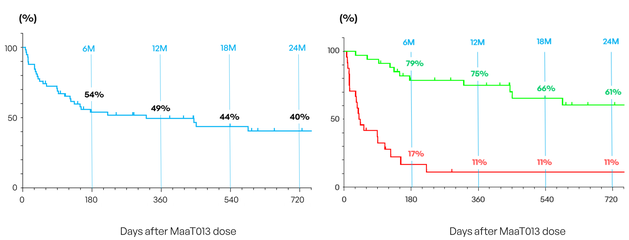


Fig. 2 : Patients' response and outcomes treated with MaaT013 treatment as 3rd line (n=58)

A. Gastrointestinal Overall Response Rate and Overall Response rate at D28 and D56
B. Overall Survival in all 58 patients
C. Overall Survival according to MaaT013 response (responders being patients who achieved at least a PR at D28)

CR: complete response; VGPR: very good partial response; PR: partial response



> **MaaT013 exhibits a high and durable response rate, translating into increased overall survival**

Good tolerability and safety profile in aGVHD population

- 37 serious pharmacovigilance cases reported in 34 patients, including 24 cases reported in 23 patients possibly related to MaaT013: GI symptoms in 3 patients (anorectal disorder, rectal haemorrhage), infectious complications (6 sepsis, 13 bacteremia, 1 *C.difficile* colitis)
- No pathogen transmission reported. No death was attributed to MaaT013 administration.
- 83 deaths reported: 34 due to GvHD, 30 due to severe infection (incl 5 COVID-19), 11 due to relapse of underlying malignancy, 2 due to hemorrhage, 2 due to neurological complications, 2 due to cardiac arrest, 1 due to acute respiratory distress and 1 due to natural death.

Conclusion

Poster #4902

- Overall, EAP clinical data showed that MaaT013 was **a safe and effective treatment of refractory GI-aGvHD** especially in patients having previously received ruxolitinib.
- **Response to MaaT013 correlates with increased OS**, suggesting a **strong favorable benefit-risk profile** for MaaT013.
- MaaT013 is currently being evaluated in a **European pivotal Phase 3 clinical trial in 66 patients** with steroid- and ruxolitinib-refractory aGvHD (NCT04769895), with **recruitment completed in October 2024** and **topline results expected in January 2025.**