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

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Introduction

While the recent optimization of Graft-versus-Host Disease (GvHD) prophylaxis protocols has decreased the incidence of severe GvHD, **GvHD remains a major source of mortality following allogenic hematopoietic cell transplantation (allo-HCT) with an important unmet medical need, especially after failure to respond to corticosteroids and ruxolitinib.**

Fecal microbiotherapies are reported to be **safe** in immunocompromised patients and have shown **promising results** in refractory-GI-GVHD.

MaaT013 is a pooled allogenic fecal Microbiome Ecosystem Therapy administered as enema, aiming at improving microbial diversity, richness and functionality and leading to GI symptoms resolution.

Here we report clinical outcomes from a **111-patient cohort with refractory gastrointestinal acute GvHD** treated with **MaaT013** within an early access program (EAP) in Europe.

Methods

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

02 Treatment protocol — 3 doses within 2 weeks (150 mL enema bag for direct colonic delivery)

03 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

As of Oct 3rd, 2023, **149** patients have been treated within the EAP

EAP ongoing in Europe

Main inclusion criteria

- Steroid refractory / dependent
- Acute GVHD with gut involvement, grade II to IV
- Any line of treatment
- MaaT013 used as a monotherapy and/or combination therapy
- ≥ 12 hours discontinuation of systemic antibiotics surrounding MaaT013 administration
- Patient not eligible to ARES trial - NCT04769895

Patient's characteristics (n=111)

Gender, n (%)	Male	60 (54%)
	Female	51 (46%)
Age at first MaaT013 administration (years)	Median [range]	57 [15;74]
Time between aGvHD diagnosis and first MaaT013 dose, days	Median [range]	49 [10;1328]
Number of previous lines of treatment, n	Median [range]	**3 [1;6]**
Steroid status	**Steroid refractory-aGvHD**	**94 (85%)**
	Steroid dependent-aGvHD	17 (15%)
Type of aGvHD	Classical	70 (63%)
	Late onset	12 (11%)
	Hyper-acute	13 (12%)
	Overlap syndrome	16 (14%)
GvHD grading (MAGIC), n (%)	I	0
	II	10 (9%)
	III	**54 (49%)**
	IV	**47 (42%)**
GvHD organ involvement at EAP inclusion	GI only	67 (60%)
	GI + skin	27 (24%)
	GI + liver	6 (5%)
	GI + skin + liver	4 (4%)
	Missing data for skin and liver	7 (6%)
Stage skin GvHD	Stage 0	77 (69%)
	Stage 1	17 (15%)
	Stage 2	8 (7%)
	Stage 3	**6 (5%)**
	Stage 4	**0 (0%)**
	Missing data	**3 (3%)**
Stage liver GvHD	**Stage 0**	**94 (85%)**
	Stage 1	**6 (5%)**
	Stage 2	**3 (3%)**
	Stage 3	**1 (1%)**
	Stage 4	**0 (0%)**
	Missing data	**7 (6%)**
Stage gut GvHD	**Stage 0**	**0 (0%)**
	Stage 1	**12 (11%)**
	Stage 2	**22 (20%)**
	Stage 3	**30 (27%)**
	Stage 4	**47 (42%)**

Global EAP Population (n=111)

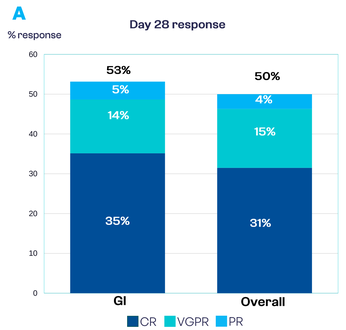
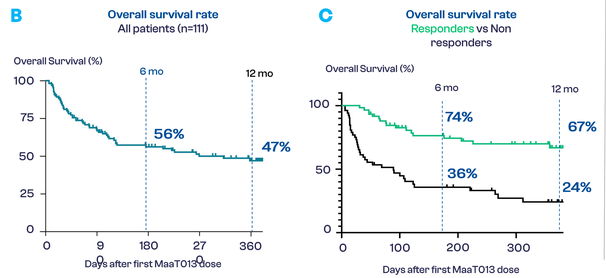


Fig. 1 : Patients' response and outcomes after MaaT013 treatment (n=111)
A. Gastrointestinal overall response rate at day 28 (D28) and Overall Response rate at Day 28
B. Overall survival in all patients
C. Overall survival according to MaaT013 response (responders being patients who achieved at least a PR at day 28)

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



> Clinical response to MaaT013 translates to an increased overall survival

Focus on steroid (1L) and ruxolitinib-refractory (2L) patients (n=38)

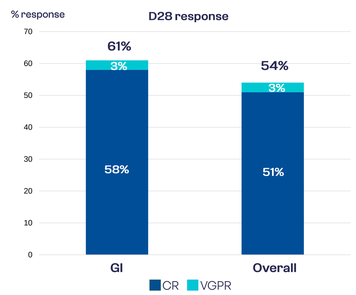
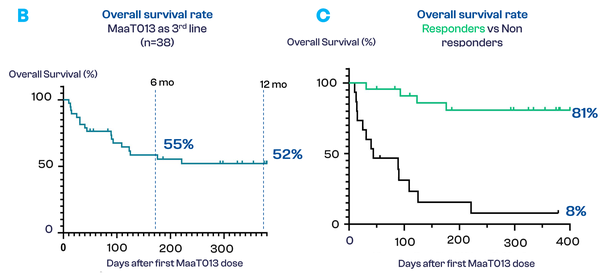


Fig. 2 : Patients' response and outcomes treated with MaaT013 treatment as 3rd line(n=38)
A. Gastrointestinal overall response rate and Overall Response rate at day 28
B. Overall survival in all 38 patients
C. Overall survival according to MaaT013 response (responders being patients who achieved at least a PR at day 28)

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



> GI-response strongly correlates with survival, especially in this subgroup of patients

Good tolerability and safety profile in aGVHD population

- 16% of EAP patients presented adverse events possibly related to MaaT013: GI symptoms in 3 patients (abdominal pain, anorectal disorder, rectal haemorrhage), infectious complications in 15 patients (5 sepsis, 7 bacteremia, 1 *C.difficile* colitis, 1 *E. coli* osteoarthritis, 1 detection of G. silvicola in stools)
- No pathogen transmission reported. For 2 patients, non-pathogenic commensal bacteria isolated following infectious events were detected in the administered MaaT013. Causality could not be formally excluded in these cases.
- No death was attributed to MaaT013 administration with 55 patients alive at last follow-up.

Conclusion

- Treatment of 111 SR-GI-aGVHD patients with **MaaT013 is safe** and translates into a **high response rate in refractory aGvHD patients** : **D28 GI-ORR 53%**
- The **benefit on GI-response positively and significantly impacted OS in responder patients** : 74% OS at M6 and 67% at M12 in responders respectively, when compared to non-responder patients (36% at M6 and 24% at M12) and compared to previous reports (Castilla-Llorente, 2014; Jagasia, 2020; Abedin, 2021). MaaT013 used as 3rdline treatment after corticosteroids and ruxolitinib failure is even more promising with 61% GI-ORR at D28 and 52% OS at 1Y (81% in responders vs 8% in non-responders)
- MaaT013 is currently being evaluated in a European **Phase 3 clinical trial** in 75 patients with steroid- and ruxolitinib-refractory aGvHD patients (NCT04769895)

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