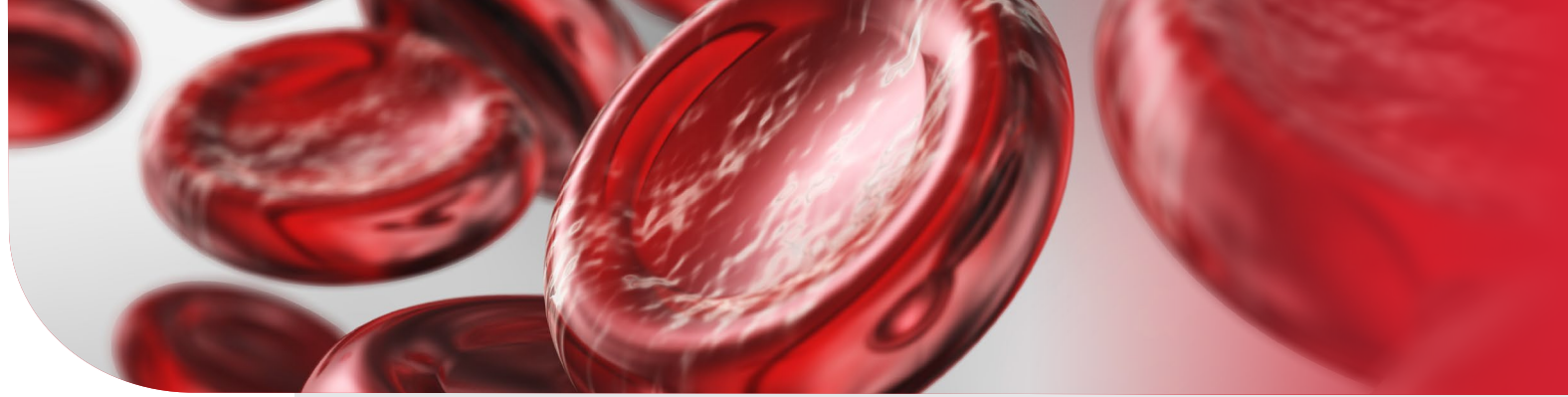




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# **MaaT013 for Ruxolitinib-Refractory Acute Graft-versus-Host Disease with Gastrointestinal Involvement: Results from the ARES Phase III Trial**

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Pr Florent Malard

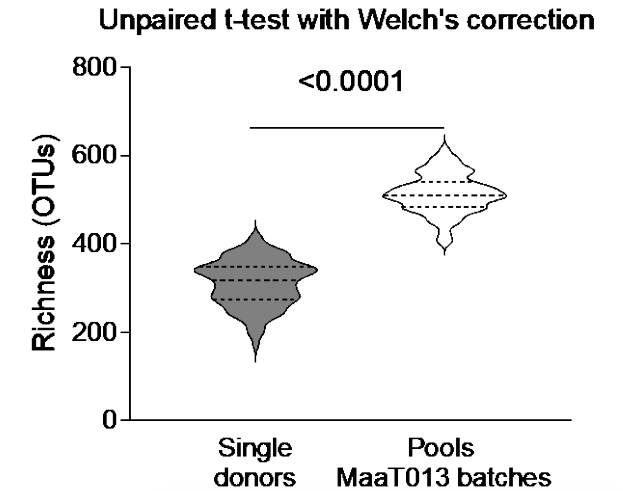
Sorbonne University, AP-HP, INSERM

Paris, France

Publication Number: 817

# MaaT013, an immunosuppressant sparing agent to restore the microbiome and treat aGvHD

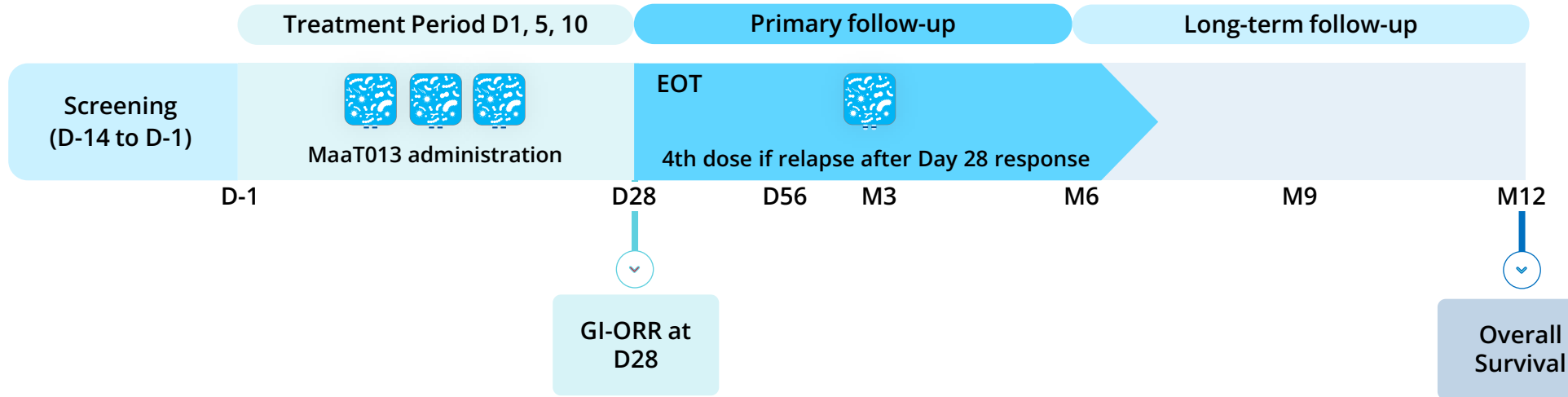
<b>Administration</b>	<ul style="list-style-type: none"><li>✓ Rectal suspension (150 mL enema)</li><li>✓ 3 doses within 10 days</li></ul>
<b>Characteristics: Pooled allogeneic fecal microbiota</b>	<ul style="list-style-type: none"><li>✓ A high-richness, high-diversity, full ecosystem, containing Butycore™ and not less than <math>1.35 \times 10^{11}</math> viable bacteria.</li><li>✓ 36 months stability at <math>-80^{\circ}\text{C}</math></li></ul>
<b>Available clinical data</b>	<ul style="list-style-type: none"><li>✓ <i>HERACLES</i> (Phase 2) Trial, n=24</li><li>✓ <i>ARES</i> (Phase 3) Trial, n= 66</li><li>✓ Ongoing Early Access Program (Europe – US (&gt; 240 patients treated as of November 2025))</li></ul>
<b>Efficacy Evaluation</b>	<ul style="list-style-type: none"><li>✓ GI- and all-organ response rate (ORR) at Day 28</li><li>✓ Complete response, Very Good Partial Response, Partial Response</li></ul>



# ARES: a Pivotal Phase 3 Trial Exploring MaaT013 in Third-Line aGvHD Following Corticosteroids and Ruxolitinib Failure



**66** Subjects Treated  
(Full Analysis Set) →



## Key Inclusion Criteria

- Age > 18
- aGvHD with GI symptoms (MAGIC criteria)
- Refractory to corticosteroids
- Refractory or intolerant to ruxolitinib

## Key Exclusion Criteria

- CMV colitis
- Lines of aGvHD treatment other than CS and ruxolitinib
- Overlap chronic GvHD
- Hyperacute GvHD
- Active uncontrolled infection

**Primary Analysis: after all subjects completed Day 28 or discontinued earlier. Cut-off date: 11 Nov 2024**

### Primary endpoint

GI-aGvHD Overall Response Rate (GI-ORR) at Day 28  
Assessed by an Independent Review committee (IRC)

### Main Secondary endpoints

- GI-ORR at D56 and M3 (IRC and investigator)
- All-organ ORR at D28, D56, M3 (IRC and investigator)
- Duration of Response (IRC and investigator)
- Overall Survival

*CMV: cytomegalovirus, CS: corticosteroids; D: Day; M: Month;*

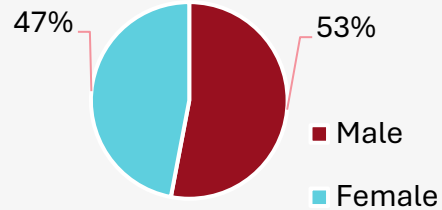


# ARES subjects: Baseline Characteristics

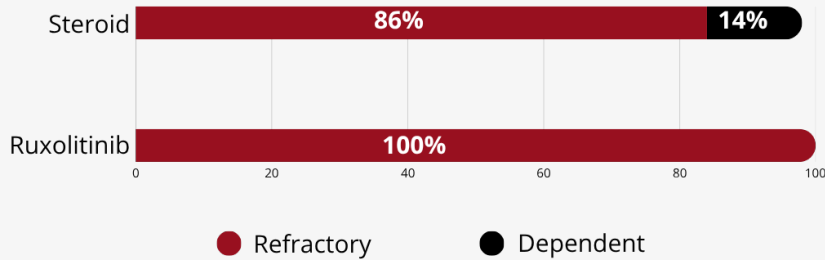
All patients treated with MaaT013 (n=66) - Full Analysis Set

## Patients profile

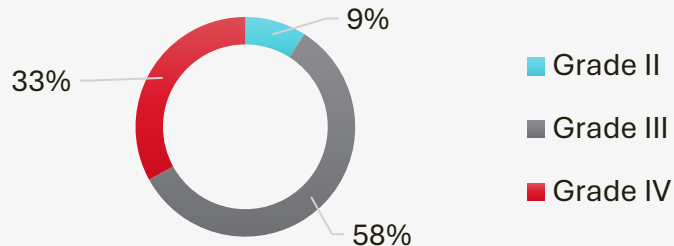
 Median age, years  
(range): 55,5 (24; 76)



## Steroid & Ruxolitinib status, n (%)



## aGvHD grading (MAGIC\*) n (%) - Assessed by IRC



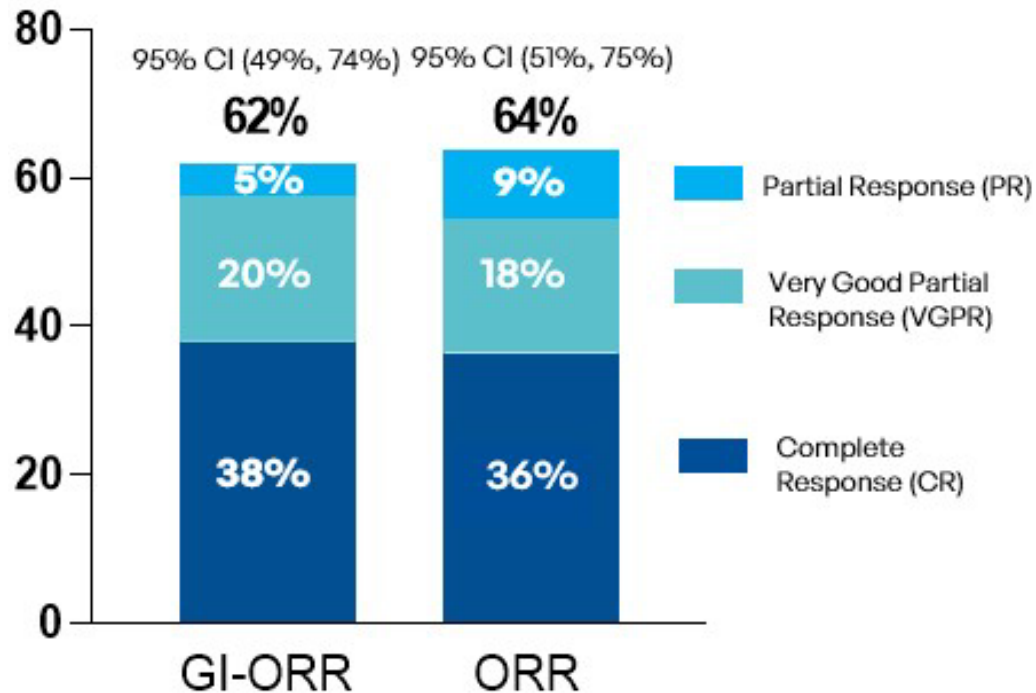
Type of aGvHD	N (%)	Organ involvement	N (%)
Classical	58 (88)	GI only	51 (77)
Late onset	3 (4)	GI + skin	11 (17)
Post-DLI	4 (6)	GI + liver	2 (3)
Other	1 (2)	GI + liver + skin	2 (3)

MaaT013 exposure and retention time	ARES
At least 1 dose	100%
At least 2 doses	92%
At least 3 doses	80%
4 doses	12%
Median number of doses	3
Mean retention time	151.6 min
Median retention time	124 min

# ARES: The Study met its Primary Endpoint

Day 28 GI-ORR (Primary Endpoint) assessed by IRC was significantly higher than the historical control ORR of 22% ( $p < 0.0001$ )

## D28 Response Rate (%)

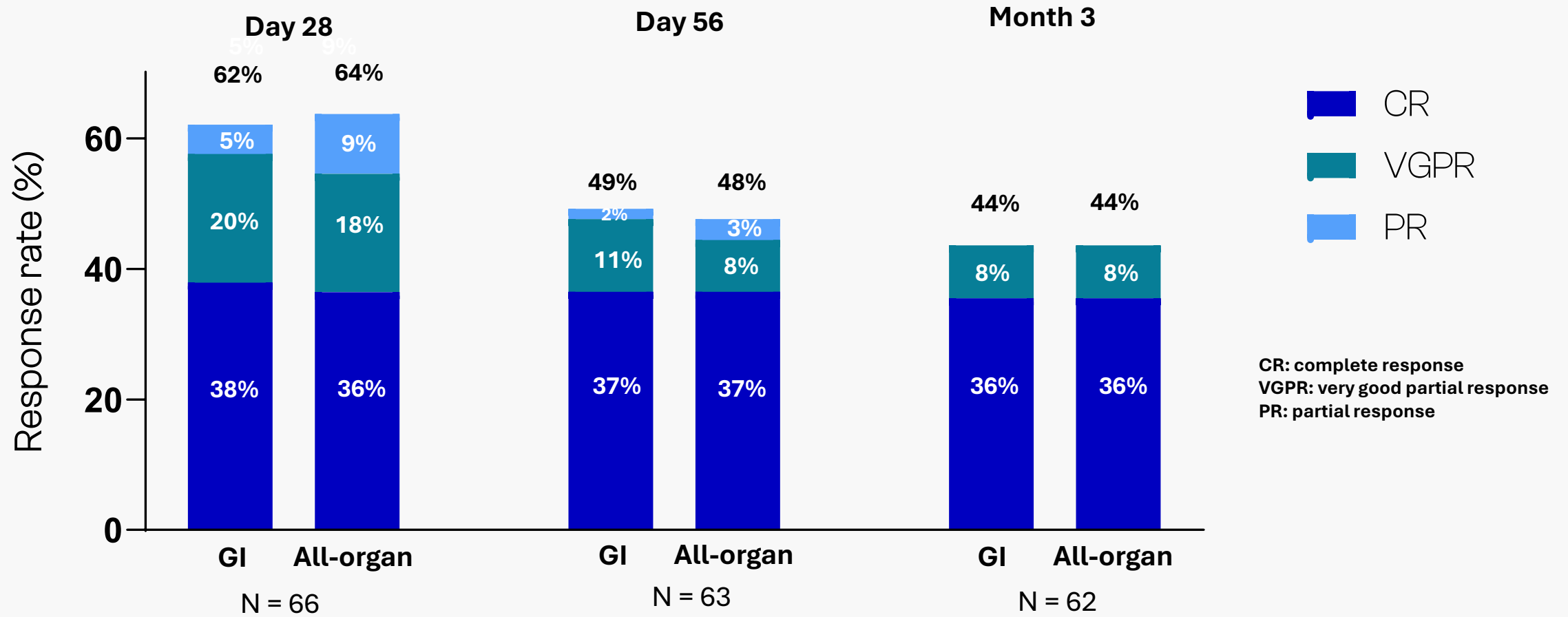


## Primary Analysis

- 62% GI-ORR with high CR and VGPR rates
- 64% ORR indicating a global systemic response and with high CR and VGPR rates
- Average Duration of Response (DOR):
  - 6.4 months for GI-DOR [95% CI = 4.8;8.0]
  - 6.4 months for all-organ DOR [95% CI = 4.8;8.0]

IRC & Investigator assessments highly concordant (96.4% for D28 GI-ORR; 94.5% for D28 all-organ ORR)

# Durable Response at D56 and M3, assessed by IRC (FAS)



# ARES: Survival probability at the Data Cut-Off (11 Nov 2024)

Survival Probability for all subjects and according to Day 28 GI-Response

- Median Follow-up: 140.5 days
- Median OS not reached

Survival probability	All subjects	D28 GI- Responders	D28 GI- non Responders
Month 6	59%	75%	28%
Month 12	54%	<b>67%</b>	<b>28%</b>

*Landmark analysis from D28*

*D28: Day 28; GI: GastroIntestinal; OS: Overall survival; R: Day 28 GI-Responder; NR: Day 28 Non-responder*

MaaT013 demonstrates response-driven prolonged survival with **54% probability of survival at 1 year**



# ARES: Safety Results

- 886 AEs in 65 (98%) subjects were reported
  - 1 patient with no AE (withdrew his consent after Dose 1)
- 157 serious TEAEs reported in 50 (76%) subjects
  - **Most common serious TEAEs:**
    - Escherichia sepsis (7 [11%] subjects)
    - General physical health deterioration (5 [8%] subjects)
    - Septic shock (5 [8%] subjects)
- 34 Treatment-related TEAEs in 19 (29%) subjects
  - 7 events in 6 subjects (9%) being serious
  - Majority of related AEs occurred within 14 days after last dose
- 26 fatal AEs
  - 1 considered treatment-related by the investigator (septic shock)



System Organ Class	N = 66
Preferred Term [n (%)]	
Any MaaT013 Treatment-Related Treatment-Emergent Adverse Events	19 (29)
Infections and infestations	11 (17)
Bacteraemia	3 (4)
Candida infection	2 (3)
Escherichia sepsis	2 (3)
Septic shock	2 (3)
Abscess limb	1 (2)
Bacterial sepsis	1 (2)
Bacteroides bacteraemia	1 (2)
Enterococcal bacteraemia	1 (2)
Escherichia bacteraemia	1 (2)
Pneumonia	1 (2)
Gastrointestinal disorders	9 (14)
Constipation	5 (8)
Abdominal pain	3 (4)
Abdominal distension	2 (3)
Proctalgia	1 (2)
Vomiting	1 (2)
General disorders and administration site conditions	2 (3)
Pyrexia	2 (3)
Blood and lymphatic system disorders	1 (2)
Anaemia	1 (2)

TEAE: Treatment-Emergent Adverse Event; AE: Adverse Event; SAS: Safety Analysis Set

**Overall safety & tolerability of MaaT013 treatment reviewed continuously by a DSMB**

# Overall benefit-risk assessment

- ✓ Acute GvHD in 3<sup>rd</sup> line is of high unmet medical need
- ✓ Deep and durable response rates, translating into prolonged survival in a population known for dismal clinical outcomes
- ✓ Overall good tolerability of MaaT013 treatment in severe aGvHD patient population

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