

# Key Results from the CHRONOS Multicentre Retrospective Cohort Study Describing Patient Outcomes in Third-Line Acute Gastrointestinal GvHD

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## Introduction

Treatment options for acute graft-versus-host disease (aGvHD) refractory to corticosteroids and ruxolitinib are poorly characterized, none being approved for this indication. CHRONOS study aimed to describe response rates, duration of response, and survival following third-line (3L) systemic therapy **excluding microbiotherapy** in this high-risk setting.

## Patients & Methods

**A Multicentre, Non-Interventional, Retrospective Cohort Study**



<sup>1</sup>Harris et al, 2016

**Main exclusion criteria:** hyperacute GvHD, overlap chronic GvHD, relapsed malignancy, cytomegalovirus colitis, uncontrolled cardiac disease or significant respiratory disease.

**Primary Endpoints at D28** (closest assessment date):

- All-organ overall response rate (ORR),
- GI-specific ORR (GI-ORR) after 3L treatment initiation, based on MAGIC criteria for aGvHD assessment.

**Data** were collected via electronic case report forms with rigorous data curation ensuring highest standards of data quality and completeness.

**Secondary Endpoints:**

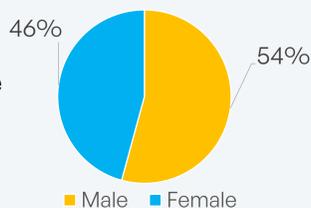
- D56 response (closest assessment date),
- Duration of response (DOR),
- Real-world progression-free survival (rwPFS) of the underlying malignancy,
- Overall survival (OS),
- Incidence of events of special interest (Grade $\geq$ 2 infectious events, grade 3-4 neutropenia and thrombocytopenia) up to 12 months.

## Results

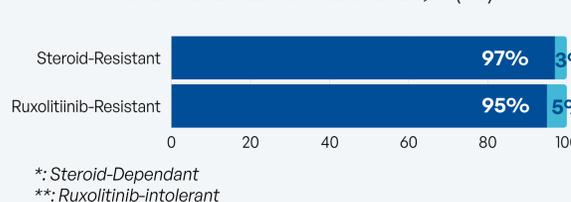
### Patients profile

Median age, years (range): **59** (InterQuartile Range (IQR), 49-64)

**Grade III/IV** (93%, n=55) aGvHD



Steroid & Ruxolitinib status, n (%)



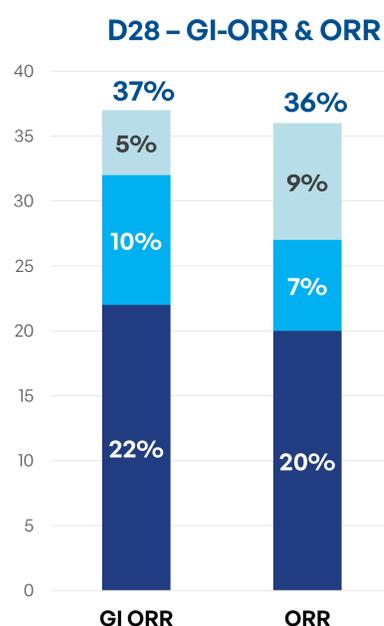
**13** 3L different therapies used (excluding microbiotherapy)

**Top 3 administered**

- Extracorporeal photopheresis (n = 17)
- Etanercept (n = 14)
- Vedolizumab (n = 10)

Overall Median Time from initial aGvHD diagnosis: **32 days** (IQR: 20-53 days)

Figure 1



### Rapid Loss of D28-Response

- 29%** (95% CI: 11%-49%) lost their all-organ response within the next **30 days**
  - 52%** (95% CI: 29%-72%) within **90 days**
- Same results were observed for the GI-aGvHD-responders

### Response rates declined by Day 56

- all-organ ORR:** 20% (12/59; 95% CI: 11%-33%)
- GI-ORR:** 22% (13/59; 95% CI: 12%-35%)

Figure 2

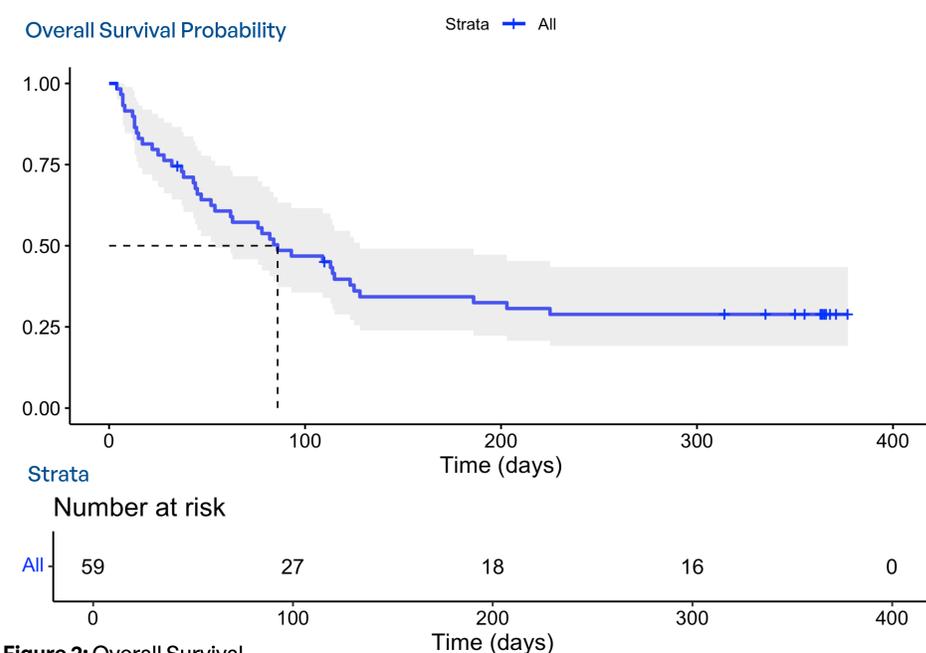


Figure 2: Overall Survival

Figure 1: ORR and GI-ORR at Day 28, showing ORR of 36% and GI-ORR of 37%, with detailed CR, VGPR, and PR rates indicated

- Median rwPFS** and **OS** were **86 days** (95% CI: 54-128).
- Median OS** was **186 days** in responders (95% CI: 115 days-not reached) vs **45 days** in non-responders (95% CI: 28-86 days).

- Up to M3**, Grade $\geq$ 2 infectious events occurred in 58% of patients, grade 3 to 4 thrombocytopenia and neutropenia in 64% and 32% respectively.
- Up to M12**, 41 patients died, mostly from aGvHD (n=25) and infectious complications (n=9).

## Conclusion

These findings illustrate the absence of standardization and the limited benefit of available third-line interventions, emphasizing the need for novel treatments. Survival outcomes were poor, particularly among non-responders, and infectious events were frequent. By establishing clear benchmarks, this study will facilitate the evaluation of novel therapeutic approaches.