UNIKLINIK KÖLN | Department I of Internal Medicine, University Hospital of Cologne

DEUTSCHE CLL STUDIENGRUPPE

Acalabrutinib Treatment Achieves Durable Responses and Quality of Life Improvements in Older (≥80y) and/or Frail Patients with CLL
Final Analysis of the CLL-Frail Trial

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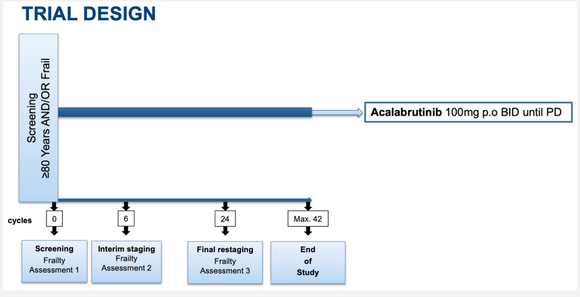
INTRODUCTION

- Older and/or frail patients with CLL are underrepresented in clinical trials — dedicated trial data are scarce
- The CLL-Frail trial is a prospective study specifically designed for this population
- Primary endpoint analysis (Simon et al., Blood, 2025): ORR of 81.1%, frailty improvement in 53.5% of patients
- However, AEs were common and ~1/3 of patients discontinued therapy prematurely
- This final analysis presents new efficacy & safety data after 3 years of median follow-up, plus the first comprehensive QoL report

PATIENTS AND METHODS

- Investigator-initiated, prospective, multicenter **Phase II** trial
- Eligibility: active CLL, age **≥80 years** and/or **frailty by FRAIL-scale** self-assessment; ≤1 prior line of therapy
- Treatment: **acalabrutinib monotherapy** until intolerance, progression, or death

TRIAL DESIGN



- QoL assessed via **EORTC-QLQ30** and **CLL17** questionnaires every 3 months until final restaging

RESULTS – PATIENTS AND TREATMENT

Patient characteristics, N (%)	
Median age	81 years
Frail (> 2)	25 (47.2)
ECOG >1	17 (32.1)
Median CIRS	9 (2-11)
Median creatinine clearance (ml/min)	58.8
Cr clearance <70	39 (73.6)
TP53mut/del17p	12 (23)
IgHV unmutated	32 (60)
Massive LAP or splenomegaly	26 (49.1)

Table 1: Patient characteristics. LAP: lymphadenopathy

Feasibility parameters, N (%)		
Median Follow-Up		34 Months
Median number of cycles		30 (1-42)
Patients on treatment		29 (56%)
Reasons for treatment discontiuation		23
	Adverse event (AE)	14
	Death (on treatment)	5
	Patients wish/withdrawal of consent	4
Dose intensity		Median 89.57
Dose modifications		45 (86.5)
Inpatient therapy for AE		9% of AEs with a median time of 9 days to resolution

Table 2: Feasibility parameters. AE: adverse event.

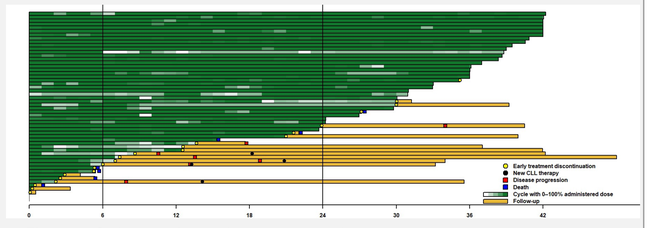


Figure 1: Swimmer plot study treatment and events.

- Baseline characteristics show **a representative cohort** of elderly and frail CLL patients.
- **High treatment adherence** and intensity
- However, most treatment discontinuations (60%) occur before month 18, primarily **due to adverse events**

RESULTS – PFS, OS AND PROM

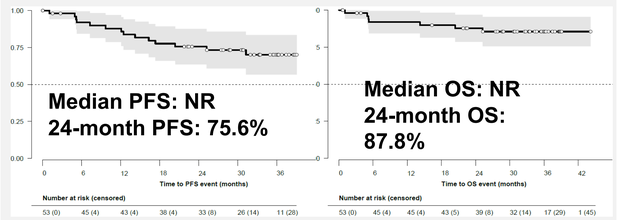


Figure 2: PFS and OS. Based on Intention-to-treat population (ITT).

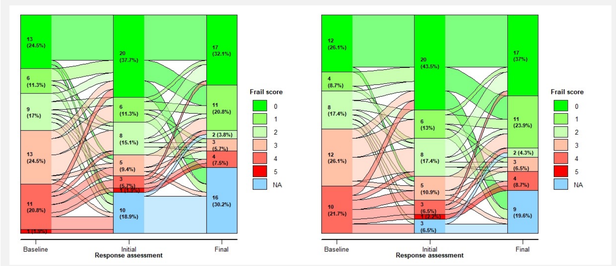


Figure 3: Sankey Plot of FRAIL scale score assessment for the ITT (left) and pts with at least 3 cycles of acalabrutinib (right). ≥3 is considered frail.

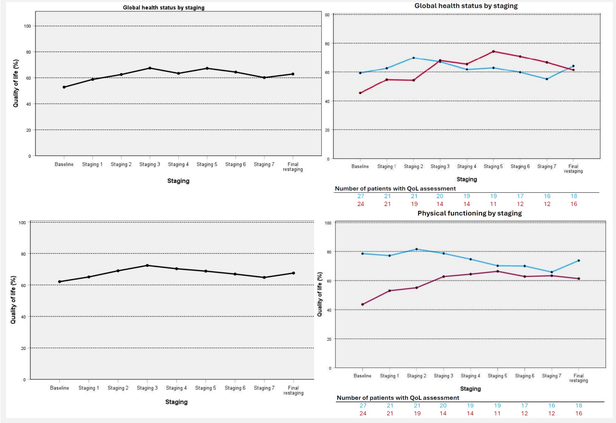


Figure 4: Patient reported Quality of Life. Red: Frail, Blue: Non-Frail

- **Frailty improved durably**: 47.8% frail at screening → 20.9% at interim → 18.9% at final restaging
- QoL improved across multiple EORTC domains, with **frail patients** showing **larger gains**
- Partial attenuation of QoL gains observed at month 24

RESULTS – SAFETY

Adverse Events (Patient level)		
Safety Population, N (%)	**52**	
	All grades	**Grade ≥3**
AEs	52 (100)	37 (71.2)
COVID-19	20 (38.5)	6 (11.5)
Hematoma	19 (36.5)	0
Diarrhea	12 (23.1)	1 (1.9)
Constipation	10 (19.2)	0
Fatigue	12 (23.1)	0
Dyspnea/Dyspnea exertional	12 (23.1)	0
Edema peripheral	11 (21.2)	0
Anemia	9 (17.3)	6 (11.5)
Headache	9 (17.3)	0
Pneumonia	8 (15.4)	6 (11.5)
Nasopharyngitis	8 (15.4)	0
Basal cell carcinoma	8 (15.4)	1 (1.9)
Palpitations	5 (9.6)	0
Cardiac failure	4 (7.7)	3 (5.8)
Atrial fibrillation	4 (7.7)	3 (5.8)
Hypertension	4 (7.7)	0

Table 3: Adverse events (patient level). Depicted are events occurring in ≥10% patients and cardiac events in ≥5%

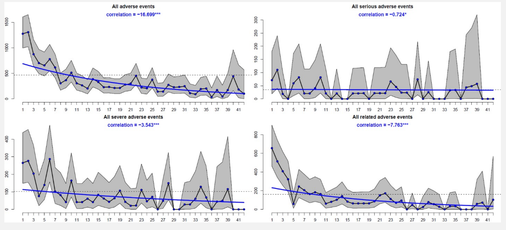


Figure 4: Adverse events trajectory per 1,000 patient months. Blue line shows correlation of event incidence with time.

CONCLUSIONS

- Acalabrutinib treatment in old and/or frail patients with CLL results in **durable responses** and sustained **improvements in frailty and quality of life**.
- These findings underscore the **potential of targeted therapies** to provide meaningful clinical benefit **across age and frailty groups**.

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