

Accelerated CLL

clinical significance and treatment outcomes

Project proposal

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Accelerated CLL - definition

- **Gine E. et al.** criteria based on **proliferation centers (PCs)** characteristics
- **at least 1 of 3** morphologic criteria should be met:
 - 1) expanded proliferation centers (broader than a 20x microscopic field)**
 - 2) increased mitotic activity (> 2.4 mitotic figures per PC)**
 - 3) high Ki-67 index (> 40% per PC)**

Giné E, et al. Expanded and highly active proliferation centers identify a histological subtype of chronic lymphocytic leukemia ("accelerated" chronic lymphocytic leukemia) with aggressive clinical behavior. *Haematologica*. 2010 Sep;95(9):1526-33

Accelerated CLL (A-CLL): unanswered questions

- **How common it is ?**
- **What is the clinical course?**
- **Should we treat it differently than typical CLL?**

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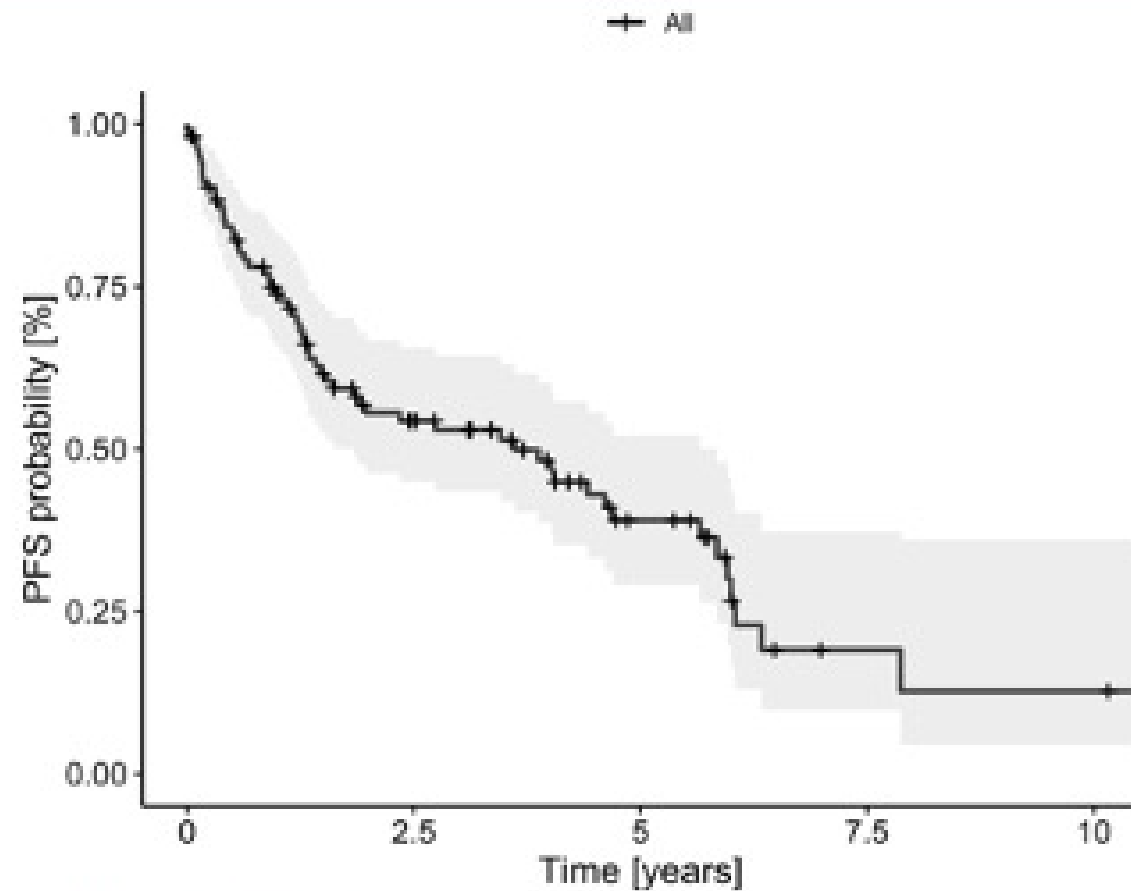
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- **106 patients with histologically confirmed A-CLL between 2013 -2023**
- median age 62, 64% males
- median ECOG - 2, median CIRS - 4
- **83 (78%) treatment-naive**, median no. of prior CLL therapies –1 (0-12)
- *TP53* pathway aberrations: del17p - **22.9% [19/83]**, *TP53*mut 29.6% [8/27]

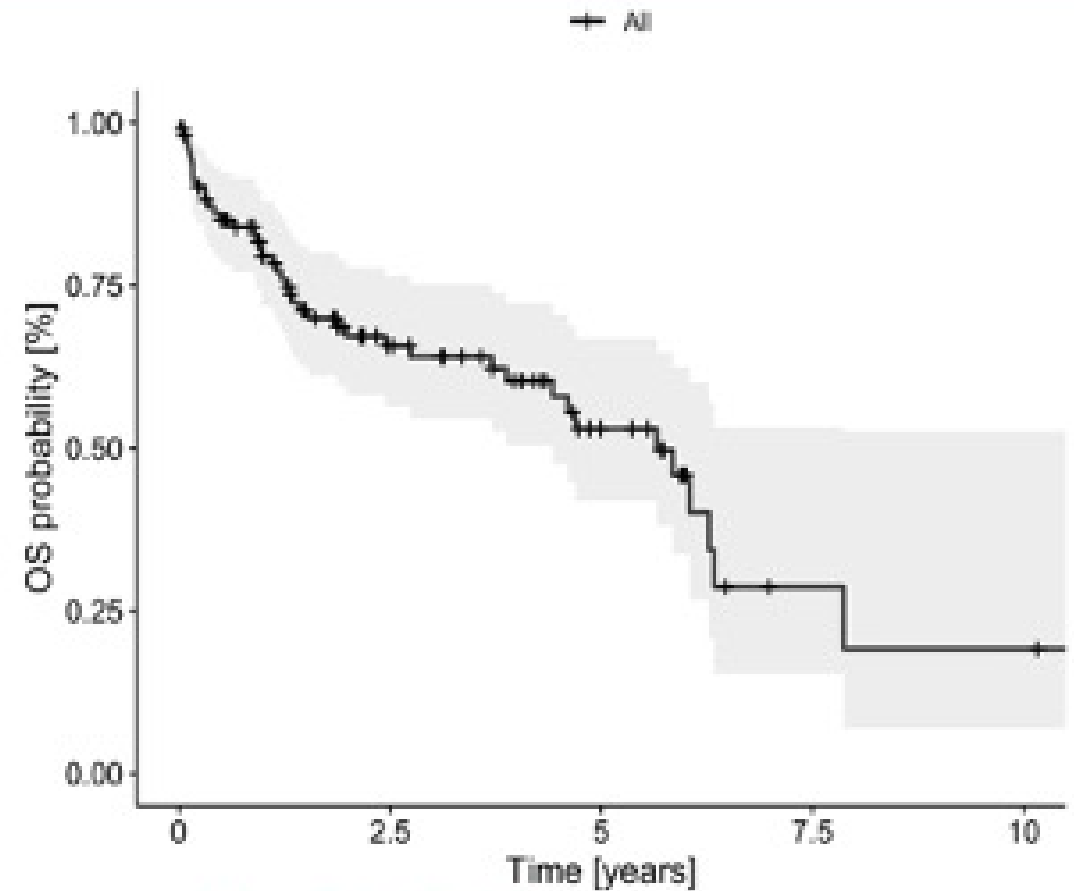
Treatment protocols used for A-CLL

Therapy of patients with A-CLL	No. of patients
A-CLL patients requiring therapy	97
First line of A-CLL therapy	
- Fludarabine-based	17
- R-CHOP-like	22
- Bendamustine-based	21
- Targeted therapy	23
Regimens used in any line of A-CLL treatment	
- Fludarabine-based	19
- R-CHOP-like	27
- Bendamustine-based	26
- Targeted therapy	49

A-CLL: PFS and OS



median PFS 3.61 years (95% CI: 1.84- 5.85)

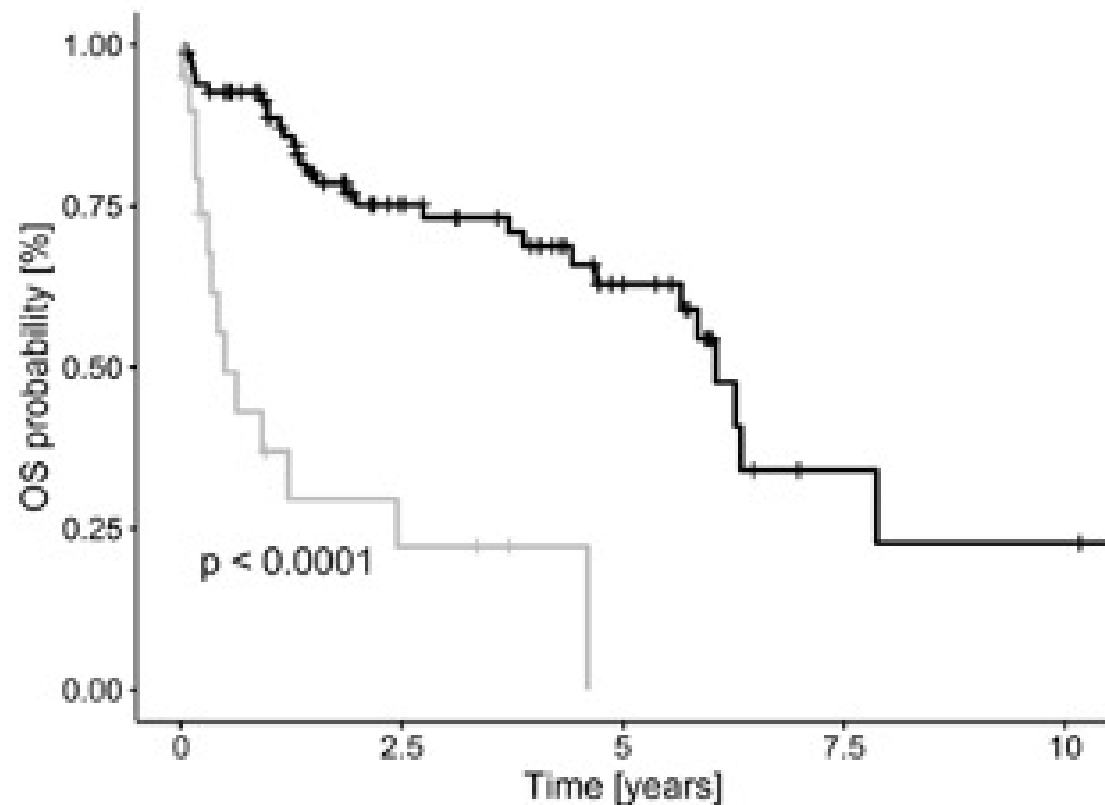


median OS 5.66 years (95% CI: 4.42-NA)

A-CLL: prognostic factors

ECOG

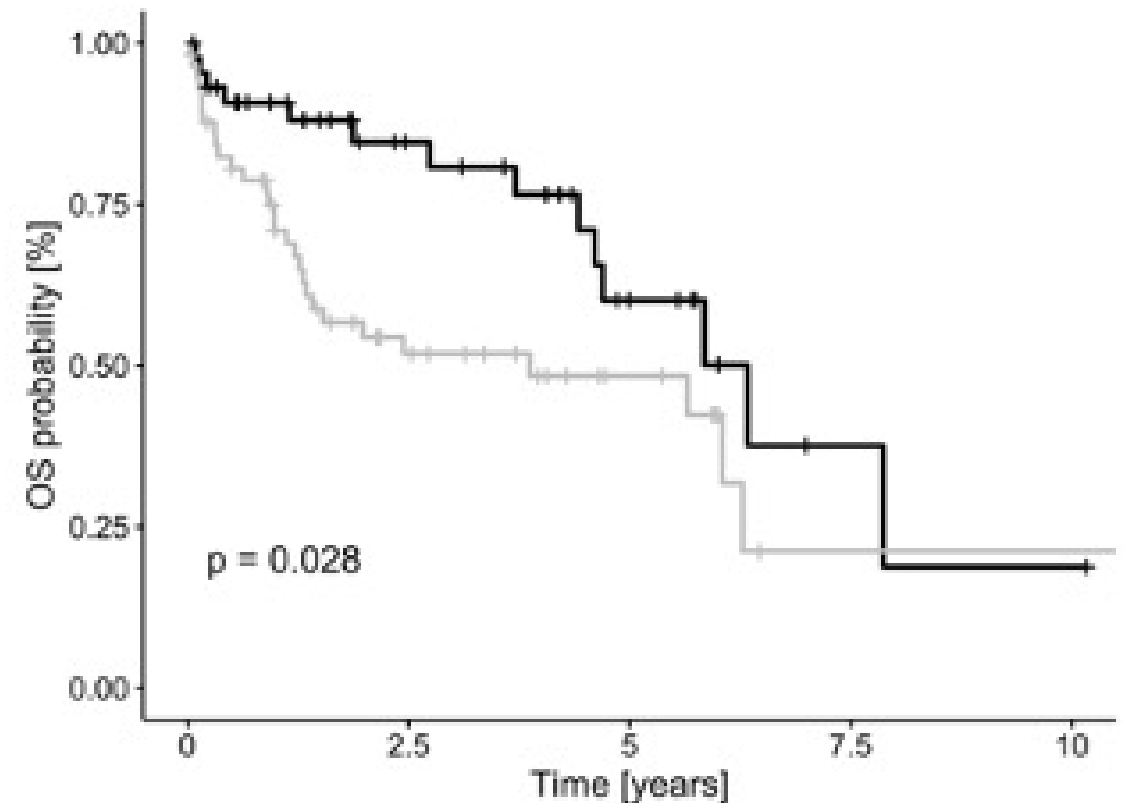
—+ ECOG <2 —+ ECOG ≥2



HR 5.74, 95%CI 2.87-11.46 $p < 0.0001$

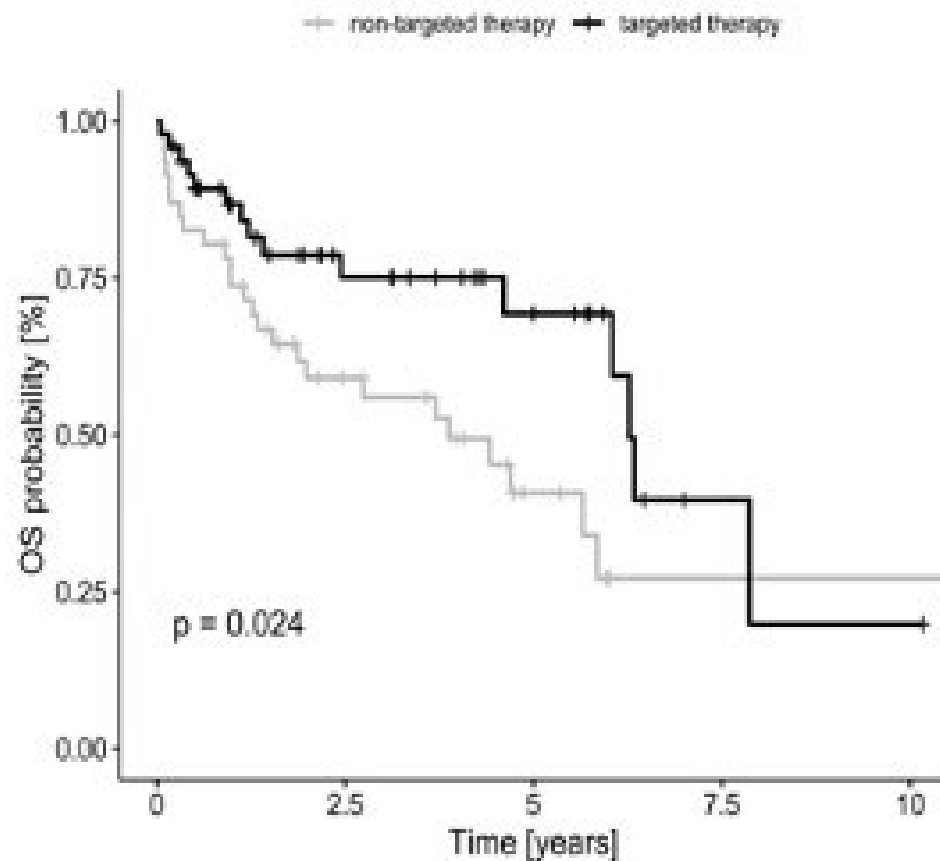
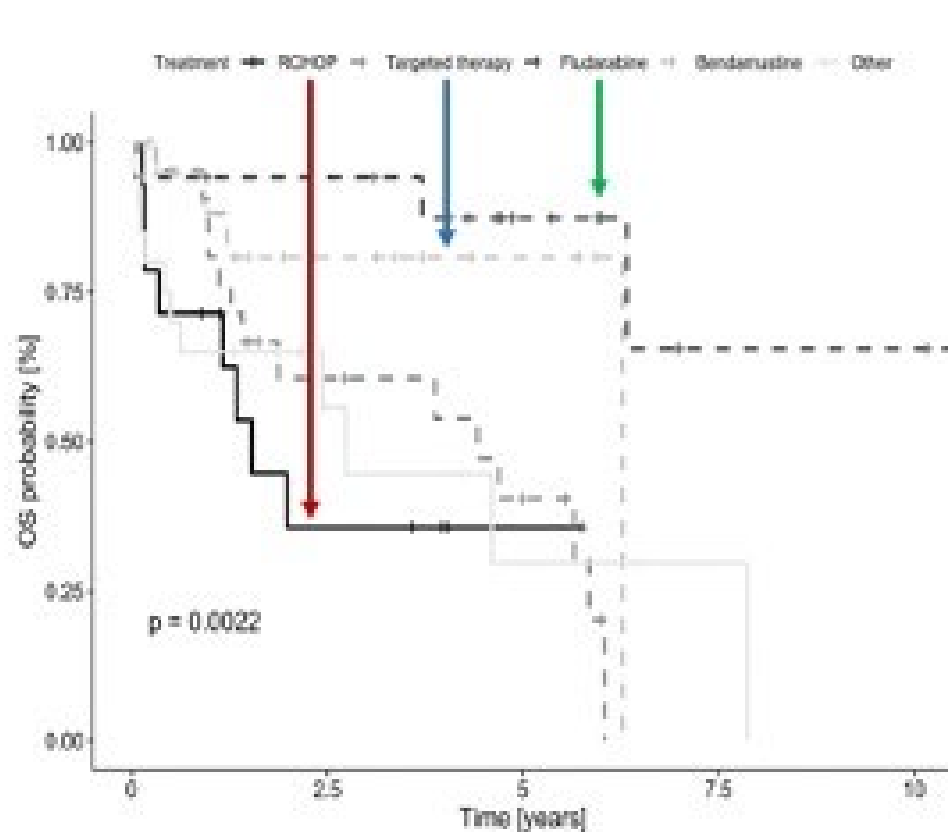
General symptoms

—+ no —+ yes



HR 2.02, 95%CI 1.07-3.85, $p = 0.028$

Outcomes of different A-CLL therapy



Fludarabine-based and targeted therapy associated with better OS than R-CHOP-like therapy

ERIC study objectives

Primary objective

- to obtain real world evidence regarding the survival outcomes of patients with A-CLL treated with different modern regimens

Secondary objectives

- to determine the **role of PET-CT assessment** in differential diagnosis of A-CLL with RT
- to determine A-CLL disease characteristic and **risk factors of progression to A-CLL**

ERIC study end points

Primary end point

- to determine the **event free survival (time to next therapy or death)** of patients with A-CLL for each type of treatment

Secondary endpoints

- to assess the **response** for each type of treatment according to 2018 iwCLL criteria
- to compare the **overall survival** of A-CLL patients treated with different treatment regimen
- to assess **range of maximal SUV** of lymph nodes, spleen, liver and/or other tissue infiltrations in A-CLL patients subjected to PET-CT testing at diagnosis

Design: A central reevaluation of A-CLL cases

- **4 experienced pathomorphologists** specializing in SLL, CLL and RT
- **only centrally confirmed A-CLL patients will be included to the analysis**
- histopathological images of the slides may be uploaded to a **digital ftp server**
- slides may also be **sent to the preselected center for digitalization**
- **Paraffin-embedded tissue blocks will not be necessary** at that stage

Design: retrospective clinical data collection

CLL pts diagnosed **between 2000 and 2024 (around 500 cases)**

- **demographic** characteristics (age, gender)
- CLL-related features (**date of diagnosis, stage, and disease burden**)
- **biomarkers** (i.e. *IGHV* status; FISH for 11q, 13q 17p, and 12; *TP53* mut)
- **treatment**-related features
- last **follow up status** (alive/dead)

Accelerated CLL ERIC Survey – 29.11.2024

1. Do you follow/treat patients with CLL?
2. Do you diagnose accelerated CLL based on lymph node histopathological assessment based on the criteria proposed by Giné et al. (Haematologica. 2010;95:1526-1533)?
3. How many patients in your center have been diagnosed with accelerated CLL in the last 10 years?
 - 0-10
 - 11-25
 - More than 25
4. Do you have tissue material in paraffin-embedded blocks from accelerated CLL patients and are willing to transfer this material for central verification and assessment?

49 centers responded