

# ELN 2025 treatment recommendations

## What is new??

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### Disclosures























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## CHRONIC MYELOID LEUKEMIA

# 2025 European LeukemiaNet recommendations for the management of chronic myeloid leukemia

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Long document (pros and cons) - Good tables  
Not always consensus

# Outline of this talk

- Diagnosis
- Accelerated phase (AP). Hot or not?
- Treatment goals: OS or TFR?
- Milestones and classification of response
- Dosing
- Pregnancy

# Diagnosis

- **Karyotype:** Additional chromosomal aberrations (ACA) at debut in 7%
- **ACA** patients often respond well. ACA remains a *warning*
- **NGS myeloid panel:** Not ready for the clinic. ASXL1 may be bad
- **ELTS-score:** % blasts in PB, Splenic margin distance the costal arch, trc, age
- **NGS** is preferred method for BCR::ABL mutation detection

# Should AP be resuscitated??

## Reintroduce AP (traditionalists)

- ✓ Different prognosis in CP, AP and BP
- ✓ Comparison with old AP studies.

## Not reintroduce AP (pragmatics)

- ✓ Molecularly two relatively distinct conditions
- ✓ All pats receive 2GTKI anyway. evaluation is all about response
- ✓ Easy to teach and understand

No consensus achieved. ELN or WHO 2022 may be used

# Aim of treatment

Survival with good QoL and minimal side effects

Treatment free remission

# Treatment in 1L: Similar OS for all drugs!

**IM:** tangible side effects like edemas, GI, cramps. eGFR

**NIL:** Cardiovascular events (glucose, blood pressure, lipids)

**DAS:** serositis

**BOS:** GI tox, serositis, transaminases

**ASC:** ASC4first shows good 2-year response and toxicity. Approved in 1L in ELN Panel: Too early to conclude about ASC

Which are the reasons for treatment switch?

Tolerance 35-40%      resistance 5-10%

# Treatment milestones: No major change

**Table 4.** Response milestones for 1st, 2nd and 3rd line TKI expressed as BCR::ABL1<sup>15</sup>.

	<b>Favorable</b> Low risk of developing resistance: treatment switch unnecessary	<b>Warning</b> Possible risk of developing resistance: treatment switch may become necessary	<b>Unfavorable</b> High risk of developing resistance: treatment switch preferred
Baseline	NA	High-risk ACA, high-risk ELTS score	NA
3 months	≤10%	>10%	>10% if confirmed within 1–3 months
6 months	≤1%	>1–10%	>10%—established resistance
12 months	≤0.1%	>0.1–1%	>1% (1–10%—see text for other considerations)
At any time	≤0.1%	>0.1–1% loss of ≤0.1% (MMR)	Loss of a previous response, resistant <i>BCR::ABL1</i> mutations, high-risk ACA

MR1 (1-10%) at M12 may be observed further without switch  
 Important for older and comorbid patients.  
 Pats failing ELN milestones still benefit from continued TKI treatment

Consensus reached

# 2L

Choice based on comorbidity and expected tox profile  
If resistance to 2GTKI, use PON or ASC  
If intolerant to 2GTKI remember IM

# Is TFR important for our patients??

Younger patients improve in cognitive, social and psychological function  
Patients >70 report poorer physical function and more pain

Efficace et al Leukemia 2024 PMID: 38987274 DOI: 10.1038/s41375-024-02341-4  
EuroSKI QoL paper (imatinib-treated)

Most important in younger patients

# TFR prerequisites and implementation

Motivated patient

**Minimum** 5 years treatment and 2 yrs MR4 or better

**Strongly considered** if >5 yrs treatment and MR4 for 3 yrs or MR4.5 for 2 yrs

No rush. Trend is to wait longer

BCR::ABL PCR sampling interval	
Time	ELN2025
M1-M6	6-8 weeks
M7-M12	2 months
Y2-3	3-6 months
Later	Cont'd monitoring
Threshold for restart	Loss of MR3

# How to stop treatment?

Abrupt stop like in EURO-SKI?  
Gradual dose reductions (DESTINY/HALF)?

# Pregnancy



## CHRONIC MYELOID LEUKEMIA

# How I manage chronic myeloid leukemia during pregnancy

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# In brief:

Organogenesis from W5-W16: **No TKI!!**  
IFN-alpha may be used safely through pregnancy  
**NIL and IM may be used** from W17-40 (not DAS or BOS)

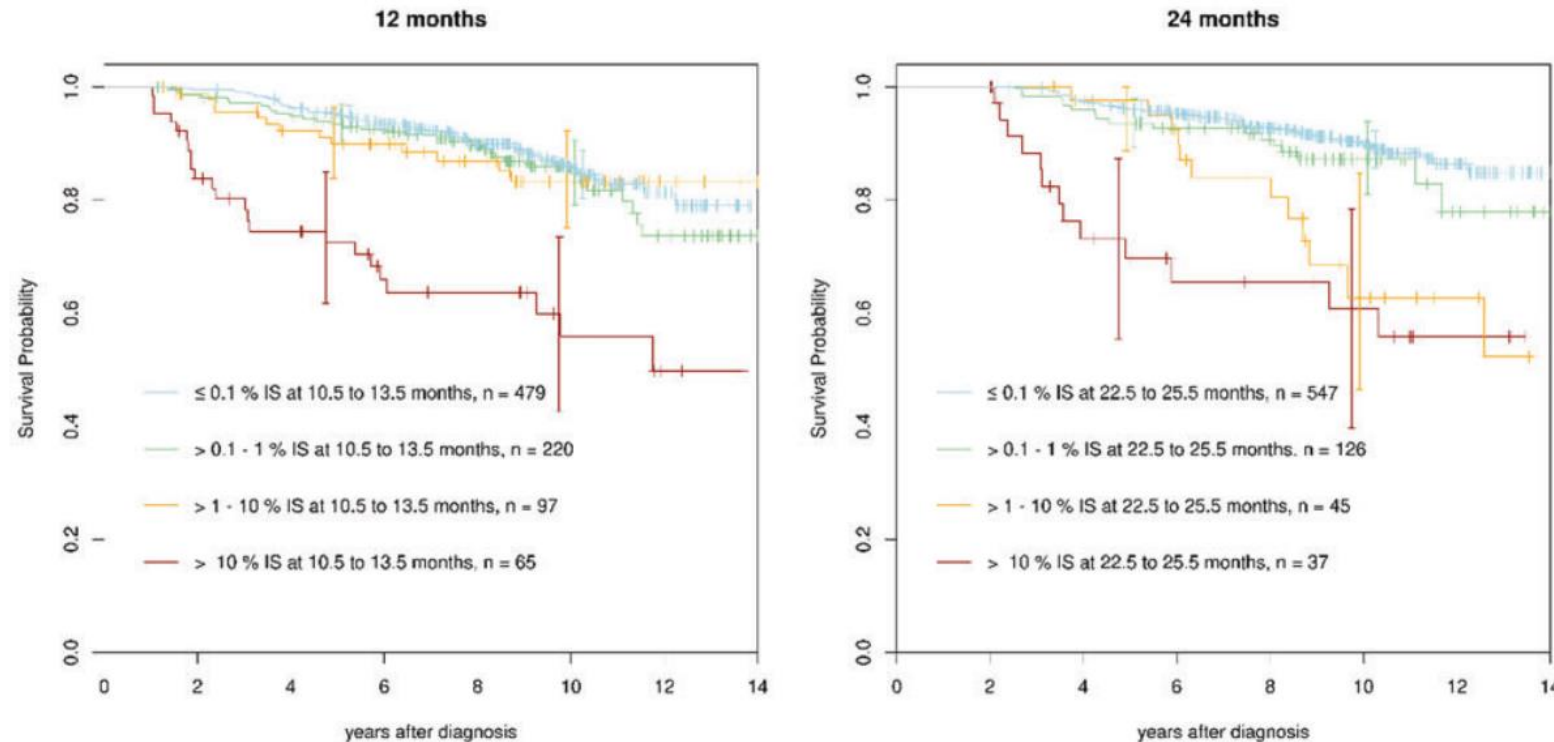
Pregnancy is safe if properly monitored and treated  
Pregnancy planning is very desirable

# Conclusions

The field of CML is maturing  
We are still learning for patient benefit

# Which response levels are adequate?

## Are the ELN milestones biologically pertinent?



*Lauseker, Leukemia (2023) 37:2231 – 2236*

«Failure» definition of >10% at M12 and 1% at M24 appears more precise for bad outcome  
Pats failing ELN milestones may benefit from continued TKI treatment

Alternatives (SCT, PON) and comorbidities have risks