TREATMENT-FREE REMISSION (TFR) FOR NEWLY DIAGNOSED ACCELERATED-PHASE CHRONIC MYELOID LEUKEMIA (AP-CML)

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Introduction

AP-CML remains a difficult clinical challenge even with potent tyrosine kinase inhibitors (TKIs) and are hopefully a rare entity at diagnosis. Some AP-CML patients, however, achieve an optimal response and reach a sustained deep molecular response (DMR). To date, treatment-free remission (TFR) strategies are not recommended outside the first-line chronic-phase (CP) CML setting as mentioned in the ELN recommendations.

Aim

To assess the feasibility of TFR in patients with newly diagnosed AP-CML (per ELN 2013 criteria) who achieve a subsequent sustained DMR on TKI therapy.

Methods

Design: International, tricentric, retrospective cohort - Centre Léon Bérard (Lyon, France), Institut Bergonié (Bordeaux, France) & MD Anderson Cancer Center (Houston, USA)

Population: Adults with AP-CML confirmed at diagnosis (according to the ELN 2013 criteria)

TFR eligibility: sustained MR4.5 ≥ 2 years before TKI discontinuation.

Resumption trigger: Loss of major molecular response (MMR), i. e. *BCR::ABL1*^{IS} >0.1%.

Statistics: Kaplan-Meier estimates for MRFS/OS; univariate Cox regression; R v4.3.2

Conclusions

TFR appears feasible in carefully selected patients with newly diagnosed AP-CML who achieve a deep, sustained molecular response, with an MRFS of approx. 76.5% beyond 54 months and no excess mortality.

These preliminary results support individualized consideration of TFR in AP-CML, pending prospective validation.

RESULTS

Study population (n = 36)

36	50/50	47y
AP-CML patients attempted TFR	% AP-CE *vs* % AP-BASO	Median age (23-76)

Male sex, n (%)	20 (55.6%)
WBC, G/L, median (range)	41.1 (3.6–375)
Hemoglobin, g/dL, median	11.1 (7.9–15.1)
Platelets, G/L, median	423 (43–1066)
PB basophils, %, median	10 (1–38)
PB blasts, %, median	1 (0–26)
BM blasts, %, median	2.5 (0–19)
Clonal evolution, n/N (%)	18/35 (51.4%)
Atypical BCR::ABL1, n	3
1st TKI: IMA/DAS/NIL/PON	47/31/19/3%
Single TKI line, n (%)	26 (72.2%)
Mean MR4 before stop, mo	104.6 (±65.9)
Mean MR4.5 before stop, mo	85.3 (±69.7)

Median follow-up after TKI discontinuation: 61.3 months (range 1.87–211).

Individual and overall *BCR::ABL1*^{IS} kinetics

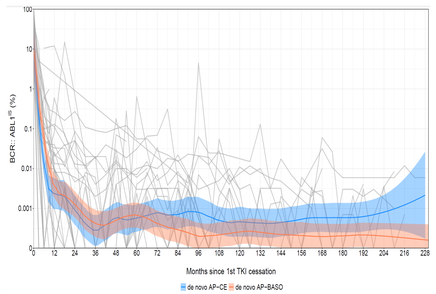

Figure 1. Individual BCR::ABL1^{IS} kinetics after TKI discontinuation (gray) with median/IQR band for de novo AP-CE (blue) vs AP-BASO (orange). Most patients showed a rapid decline to low/undetectable levels within 12–36 months, with intermittent low-level "blips" not triggering relapse.

Nine patients lost MMR, after a median of 4.34 months (range 1.48-48.99) post-discontinuation.

Molecular relapse-free survival

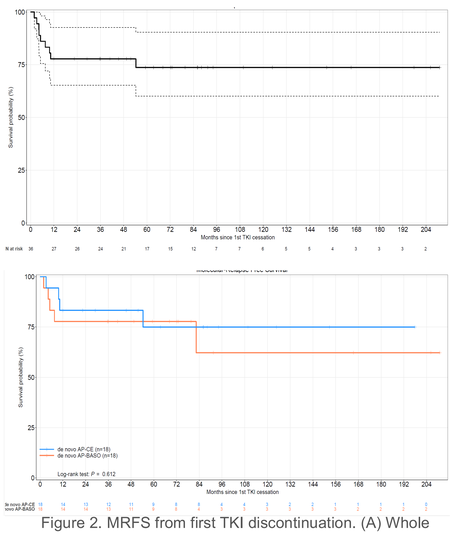

Figure 2. MRFS from first TKI discontinuation. (A) Whole cohort. (B) By AP subtype: AP-CE (blue, n=18) vs AP-BASO (orange, n=18); log-rank p=0.614.

97.2%	89.0%	80.6%	76.5%
3 mo	6 mo	≤54 mo	>54 mo

Overall survival

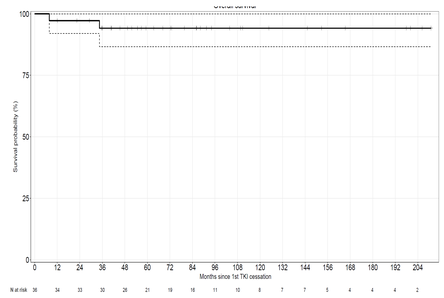

Figure 3. Two deaths occurred, both in DMR/MMR from competing causes (accidental trauma; terminal liver cirrhosis); one additional patient relapsed to chronic-phase disease in the context of end-stage kidney disease.

Predictors of relapse (Univariate Cox model)

Variable	HR [95% CI]	p
Age at diagnosis (/year)	1.09 [1.01–1.17]	0.028
BCR::ABL1^{IS}	1.03 [1.00–1.05]	0.048
MR4 duration (/month)	0.98 [0.96–0.99]	0.003
MR4.5 duration (/month)	0.97 [0.96–0.99]	0.003
AP-BASO vs AP-CE	**1.40 [0.38–5.25]**	**0.614**

No multivariable model performed (N=36; missing data for several covariates).

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