Treatment-free remission in chronic myeloid leukemia with rare *ABL1* gene fusions

D. REA[1], A. CHARBONNIER[1], G. ETIENNE[1], L. ROY1, L. LEGROS[1], G. ROTH-GUEPIN[1], C, ORVAIN[1], A. BOUVIER[1], E. CAYSSIALS[1], V. COITEUX[1], P. ROUSSELOT[1], F-X. MAHON[1], P. FLANDRIN-GRESTA[1], S. DULUCQ[1], D. LEBON[1], S. HAYETTE[1], J-M. CAYUELA[1], F-E. NICOLINI[1], H. JOHNSON-ANSAH[1,3]

1. France Intergroupe Leucémie Myéloide Chronique, France
2. 2. Hôpital Saint-Louis, Paris, France
3. 3. CHU de Caen, Caen, France

Introduction

Treatment-free remission (TFR) is achievable in 50-70% of CML patients (pts) with major *BCR::ABL1* transcripts and sustained deep molecular responses (DMR) (1,2). In contrast, outcome of TKI discontinuation in pts with rare *BCR::ABL1* rearrangements located outside the major *BCR* region or within exon 3 of *ABL1* has been poorly explored.

Aim

The aim of our observational real-life national study **was to assess TFR likelihood and safety of TKI discontinuation in adult pts with CML carrying rare *BCR::ABL1* transcripts** who discontinued targeted therapy for any reason while being in sustained DMR.

Objectives

The primary objective of our study was to estimate the probability of TFR at 12 months.

The secondary objectives were to assess the safety of TKI discontinuation and long-term TFR at 60 months.

Methods

Inclusion criteria were as follows: (1) adult pts with chronic (CP)-phase CML, (2) precise characterization of rare *BCR::ABL1* transcripts allowing quantification by individualized RT-qPCR or ddPCR, (3) first attempt of TKI discontinuation, (4) at least 2 years in DMR with undetectable MRD of at least 4-log in sensitivity, (5) no prior CML resistance, progression or allogeneic transplantation.

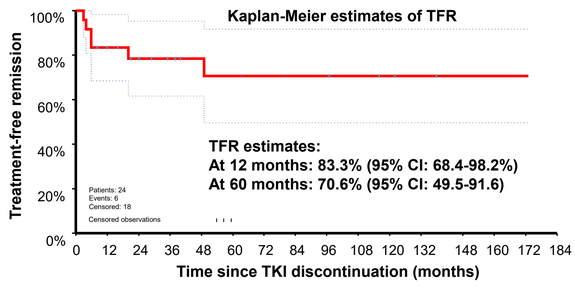
Molecular monitoring after TKI discontinuation followed the same agenda as that for pts with major transcripts: monthly for the 1st 6 months, every 2 months until month 12, every 3 months until month 24, then every 3 to 6 months. Molecular relapse was defined as an increase of MRD above 0.1% and triggered TKI resumption.

Results – 1: patients

24 pts including 75% males were included. Median age at TKI discontinuation was 63 years (range: 29-86). **ELTS score** was low in 66.7%, int. in 25%, high in 0% and unknown in 8.3% of pts. **Type of rare transcripts** were e13/e14a3 in 37.5%, e19a2 in 37.5%, e6/e8a2 in 25% of pts. **Median duration of TKI** was 62 months (range: 31-218). **Median duration of DMR with undetectable MRD** was 52 months (14-169). Last TKI before discontinuation was imatinib (37.5%) or a 2nd generation drug (62.5%). **Main reason for TKI discontinuation** was achieving TFR in 53.8%, toxicity in 25%, pt decision in 4.2% and unspecified in 12.5%.

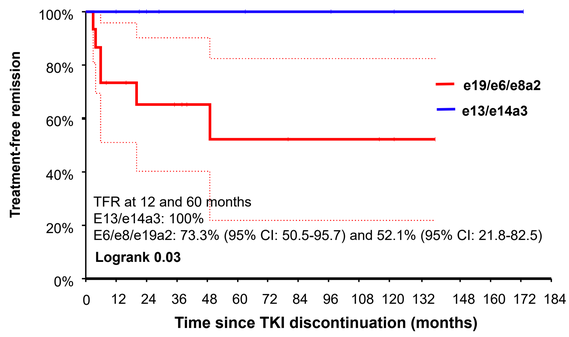
Results -2: TFR probabilities

Six pts relapsed including 4 within 6 months. Early relapses were sudden: 4 CHR loss including 1 acceleration. All were rescued.
TFR at 12 months: 83.3% (95%CI: 68.4-98.2)
TFR at 60 months: 70.6% (95% CI: 49.5-91.6)



Results -3: TFR prognostic factors

Association between type of transcripts and TFR



TFR rates in pts with e19a2 *versus* e6/e8a2
12-month probability (KM):
66.7% (95% CI: 35.9-97.4) *vs* 83.3% (95% CI: 53.5-100)
60-month probability (KM):
25.8% (95% CI: 0-64.2) *vs* 83.3% (95% CI: 53.5-100)
p=0.139

Discussion

TKI discontinuation in the view of TFR is feasible in pts with rare transcripts providing long DMR duration of at least 2 years. ddPCR may help better selecting pts based on reliable DMR measurement in the near future.

Early relapses seem abrupt and more aggressive than those usually seen in pts with major transcripts: higher risk of loss of CHR and progression during the 1st 6 months. Responses are restored upon prompt TKI resumption but caution is needed.

Pts with fusion variants involving a3 have higher TFR rates than those with exon a2 sequences. There is a trend towards higher relapse risk in pts with e19a2 as compared to pts with e6/e8a2.

References

1.Apperley J, et al, *Leukemia 2025.*
2.Shah NP, et al. *JNNCN 2024.*

Accepted for publication in Leukemia Research. Corresponding author: johnsonansah-a@chu-caen.fr

SOHO2025