Digital PCR vs qPCR for BCR::ABL1 Monitoring and Treatment-Free Remission Prediction in Chronic Myeloid Leukemia: A Systematic Review and Meta-Analysis

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INTRODUCTION

Accurate molecular monitoring of BCR::ABL1 is critical for identifying CML patients eligible for treatment-free remission (TFR) after TKI discontinuation.

Conventional real-time qPCR has limited sensitivity at deep molecular response (DMR) levels, potentially misclassifying patients at the threshold most relevant to TFR decisions.

Digital PCR (dPCR) offers absolute quantification with superior analytical sensitivity, but its comparative clinical value over qPCR for TFR prediction remains to be systematically evaluated.

Keywords: *CML, digital PCR, BCR::ABL1, treatment-free remission, molecular recurrence*

AIM

To systematically review and meta-analyze studies comparing digital PCR (dPCR) with real-time qPCR for BCR::ABL1 monitoring in chronic-phase CML.

Specifically, in patients with deep molecular response (DMR) or undergoing TKI discontinuation, to determine whether dPCR adds value over qPCR for predicting molecular recurrence (MolR) and identifying patients eligible for treatment-free remission (TFR).

METHOD

Design: Systematic review and meta-analysis of studies comparing dPCR with qPCR for BCR::ABL1 monitoring in chronic-phase CML patients with DMR or undergoing TKI discontinuation.

Eligibility: Studies reporting ≥1 prespecified outcome — molecular recurrence (MolR), TFR rate, dPCR positivity in qPCR-undetectable patients, method agreement, or diagnostic accuracy.

Analysis: Hazard ratios (HRs) and proportions pooled using DerSimonian–Laird random-effects models. Heterogeneity assessed with Cochran's Q and I^2.

CONCLUSIONS

dPCR is significantly superior to qPCR for predicting molecular relapse and identifying TFR-eligible CML patients, with a consistent, clinically meaningful effect across diverse settings.

The standardized 0.0023% International Scale cutoff provides the most validated threshold for TKI discontinuation guidance.

These findings support incorporating dPCR as the preferred molecular monitoring tool for TFR-eligibility assessment in clinical practice and future discontinuation trials.

RESULTS

Eighteen studies (n=1,403 patients) were included.

- Patients with a dPCR result above the study-defined threshold (most commonly 0.0023%–0.003% International Scale) had a significantly higher hazard of molecular recurrence (MolR) than those below it (pooled HR 2.68, 95% CI 2.13–3.37; P<0.001; I^2=0%; k=7).
- Pooled TFR rates were 68.0% (95% CI 56.3–77.9%) in the dPCR-low group vs 34.9% (95% CI 26.0–45.0%) in the dPCR-high group — an absolute difference of 33.1 percentage points (NNT≈3).
- ~32.7% (95% CI 22.7–44.6%) of qPCR-undetectable patients harbored residual BCR::ABL1 detectable only by dPCR, and this occult disease carried independent prognostic significance.
- qPCR-based DMR classification showed no significant independent predictive value for MolR in studies directly comparing both methods.
- Analytical agreement between methods was high across the full molecular response range (R=0.86–0.99) but diverged substantially at MR4.0–MR5.0.
- GRADE certainty was moderate for the primary HR outcome.

2.68×

hazard of molecular recurrence, dPCR-high vs dPCR-low

68% vs 35%

TFR rate: dPCR-low vs dPCR-high group

32.7%

of qPCR-undetectable patients had residual disease detectable only by dPCR

Agreement between dPCR and qPCR was strong across the measurable response range (R=0.86–0.99) but diverged at deep molecular response levels (MR4.0–MR5.0), where dPCR's higher analytical sensitivity detected residual disease that qPCR missed.

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