



## Scientific Comment

# BCR-ABL1 level monitoring in chronic myeloid leukemia by real time polymerase chain reaction in Brazil – not so real<sup>☆</sup>



Katia Borgia Barbosa Pagnano\*

Universidade Estadual de Campinas (Unicamp), Campinas, SP, Brazil

Chronic myeloid leukemia (CML) has been successfully managed since tyrosine kinase inhibitors (TKI) became available. Quantitative monitoring of the percentage of the fusion transcript BCR-ABL1 (breakpoint cluster region – c-Abelson murine leukemia oncogene 1, non-receptor tyrosine kinase) by reverse transcription-quantitative real-time polymerase chain reaction (RQ-PCR) is currently the standard of care after starting TKIs, as recommended by the European Leukemia Net and Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular (ABHH) guidelines.<sup>1,2</sup>

The prognostic value of early molecular responses was demonstrated in several trials, in first and second-line scenarios. Patients with BCR-ABL levels >10% at three months have lower rates of overall and progression-free survival and increased risk of disease progression.<sup>3-6</sup>

The European Leukemia Net recommends RQ-PCR to determine the BCR-ABL1 transcript level on the international scale every three months until a major molecular response (MMR – BCR-ABL  $\leq$ 0.1%, or MR3.0) has been achieved, then every three to six months.<sup>2</sup> Patients with failure of current treatment should switch therapy to avoid disease progression to advanced phases.

More recently, the successful results of international discontinuation trials demonstrated that it is possible to discontinue TKI treatment in approximately 40–50% of patients that achieve stable deep molecular responses.<sup>7,8</sup> This kind of approach is not feasible without close monitoring of BCR-ABL levels by RQ-PCR.

The standardization of RQ-PCR is challenging and involves sample exchanges with reference laboratories, equipment, trained staff, reagents and calibrators, all of which have an impact on the cost of the test.<sup>9,10</sup> In Brazil, there are not many standardized laboratories able to perform BCR-ABL monitoring and to report the results according to the international scale.

In the current issue of the *Revista Brasileira de Hematologia e Hemoterapia*, in the article “Molecular response to imatinib mesylate of Brazilian patients with chronic myeloid leukemia”, Mion et al. describe the results of RQ-PCR monitoring in a large group of patients and demonstrate the importance of this test in managing CML patients.<sup>11</sup>

Unfortunately, RQ-PCR is not widely available for all CML patients in Brazil, where most are treated by the public national health system (SUS). The cost of TKIs is high and

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<sup>☆</sup> See paper by Vieira-Mion et al. on pages 210–5.

\* Corresponding author at: Centro de Hematologia e Hemoterapia, Universidade Estadual de Campinas (Unicamp), Rua Carlos Chagas 480, Cidade Universitária Zeferino Vaz, 13092-801 Campinas, SP, Brazil. Tel.: +55 19 35218740.

E-mail address: [kborgia@unicamp.br](mailto:kborgia@unicamp.br)

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paid for by the government. However, RQ-PCR is not reimbursed, and, as a consequence, who will pay the cost? An additional problem is the standardization of laboratories and the distance from many centers to a reference laboratory.

Adequate BCR-ABL monitoring may save costs in CML treatment by allowing changes in treatment before disease progression and allowing for some patients to safely stop treatment at the correct point in time. But so far, it is not a reality for most CML patients in Brazil.

### Conflicts of interest

The author declares no conflicts of interest

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