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Dried blood spot sampling of nilotinib in CML patients: a comparison with venous blood sampling

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Introduction

Dried blood spot (DBS) sampling of capillary blood obtained by finger prick is a convenient and simple sampling method with low costs and patient comfort.
DBS sampling of venous blood has shown to be a feasible method of tyrosine kinase inhibitor blood testing in CML patients [Kralj 2012]. However, DBS sampling of nilotinib has not been evaluated in daily clinical practice.

Objective To evaluate nilotinib concentrations in DBS compared to venous blood samples in patients with CML.

Methods

A prospective cross-sectional validation study was designed (figure 1). DBS and venous blood samples were collected simultaneously according to the EP09A2 guideline. The primary outcome was the slope of the Deming fit, comparing the nilotinib concentration in DBS adjusted for hematocrit with the plasma concentration (Deming regression). The secondary outcome was the bias between the two methods at medical decision levels (weighted Deming regression). The data were statistically analyzed using Analyse-it.

Results

Forty duplicate DBS and venous samples were collected from 20 patients (65% male, mean age 56 ± 14 years). Mean hematocrit was 0.41 ± 0.05 L/L. The nilotinib concentrations in DBS adjusted for hematocrit ranged from 233 to 2759 mcg/L (CV 7.3%) and the plasma concentration ranged from 376 to 2663 mcg/L (CV 3.9%). Using general Deming regression, the slope was 0.94 (Figure 2). The mean bias between the two methods was -136.3 mcg/L (Figure 3). The bias and 95% CI between the methods at two medical decision levels were computed (Table 1).

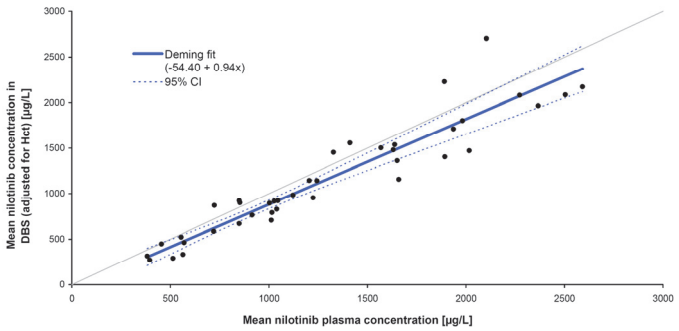

Figure 2 Scatter plot with Deming fit (n=40) with a slope of 0.94 (SE 0.07; 95% CI 0.97 to 1.09) and an intercept of -54.4 (SE 72.7; 95% CI -201.5 to 92.8)

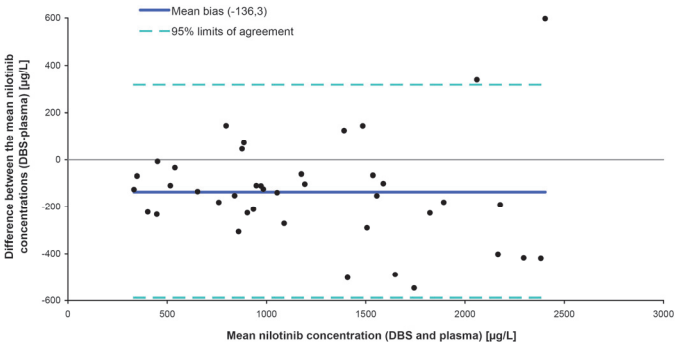

Figure 3 Bland-Altman difference plot. Mean bias was 136.3 mcg/L (SE 34.8; 95% CI -206.7 to -65,9). 95% limits of agreement were -558.8 and316.0 mcg/L

Table 1 The estimated bias between the methods at medical decision levels

Decision level $Nilotinib_{plasma}$ [µg/L]	Bias	95% CI	SE
829	-106.9	-156.4 to -57.3	24.5
1569	-153.7	-259.4 to -48.0	52.2

Conclusion

DBS sampling of capillary blood obtained by a finger prick is a valid sampling method to assess nilotinib plasma concentration in CML patients

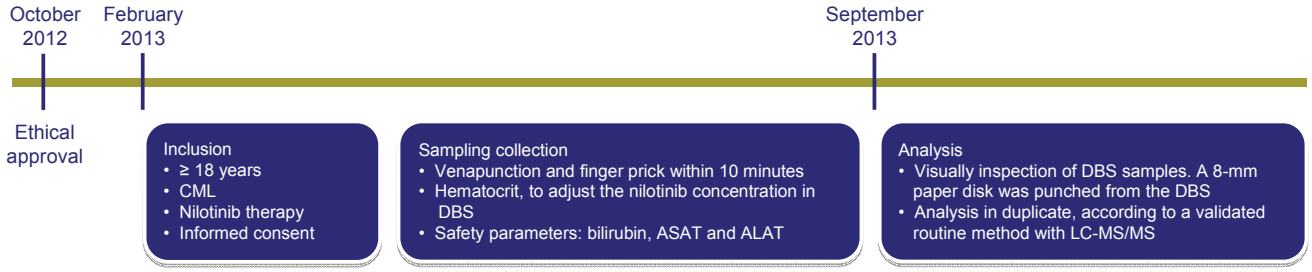

Figure 1 Study design