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High lapatinib plasma levels in breast cancer patients: risk or benefit?

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ABSTRACT

Aims and background. Lapatinib is a tyrosine kinase inhibitor targeting epidermal growth factor receptors 1 (EGFR/HER1) and 2 (HER2) used in the treatment of patients with HER2-positive breast cancer. The aim of the present study was to determine lapatinib plasma levels in breast cancer patients treated with lapatinib plus capecitabine.

Patients and methods. We assessed lapatinib plasma levels in blood samples from 21 breast cancer patients treated with lapatinib plus capecitabine using the standard regimen in an expanded access program. Liquid chromatography tandem mass spectrometry was used for measuring lapatinib plasma concentrations. The validated method was applied for measurement of 55 plasma samples.

Results. The median lapatinib plasma level was 5.09 μg/mL, with large interindividual differences. Patients of lower weight tended to have higher lapatinib plasma levels (Spearman correlation coefficient R = -0.435, $P = 0.055$). One patient's lapatinib plasma levels were markedly higher than those of the others, with a median level of 11.25 μg/mL and repeatedly exceeding 7.80 μg/mL. The treatment was terminated after 8 months when hyperbilirubinemia occurred.

Conclusions. The lapatinib plasma levels reported here are twice as high as the clinically effective steady-state geometric mean maximum concentration. We conclude that increased lapatinib body levels occur when patients are in a nonfasting state at the time of drug intake and when lapatinib doses are not adjusted to low body weight or weight loss during treatment. In Europe, dose adjustments are not recommended in the case of hepatic function impairment. Thus, attention should be paid to changes in liver function test results in clinical practice, especially in patients of small stature and weight, given the risk of high plasma concentrations. Prospective lapatinib plasma level assessment in treated patients might be useful to confirm or refute the possible correlation of high lapatinib plasma levels with hepatic and/or other toxicities.

Key words: lapatinib plasma level, tyrosine kinase inhibitor, epidermal growth factor receptor 1 (EGFR/HER1), epidermal growth factor receptor 2 (HER2), hepatic toxicity.

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