

# Influence of Anthropometric Characteristics in Patients With Her2-Positive Breast Cancer on Initial Plasma Concentrations of Trastuzumab

Annals of Pharmacotherapy  
2017, Vol. 51(11) 976–980  
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DOI: 10.1177/1060028017715727  
journals.sagepub.com/home/aop  


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## Abstract

**Background:** Plasma concentrations of trastuzumab  $<20$   $\mu\text{g/mL}$  in patients with gastric cancer are associated with reduced progression-free and overall survival. In breast cancer treatment, this relationship has not yet been studied, but a suboptimal pharmacodynamic exposure to trastuzumab could be a reason for therapeutic failure of treatment of HER2-positive breast cancer. **Objective:** The objective of the present study was to determine the proportion of nonmetastatic HER2-positive breast cancers that do not reach a minimum plasma concentration ( $C_{\min}$ ) of 20  $\mu\text{g/mL}$  after first drug administration, established as therapeutically effective in clinical trials. The secondary objective was to identify the physiological and anthropometric characteristics that determine interindividual pharmacokinetic variability. **Methods:** Serum concentrations of trastuzumab were assessed by ELISA on day 1 of the second cycle before administration of the second dose ( $C_{\min}$ ). **Results:** Of 19 patients included, 9 (47.4%) had a mean  $C_{\min}$  of 19.0  $\mu\text{g/mL}$  ( $\pm 12.1$ ) after the first administration. Body mass index (BMI) and weight was the main variable that determined the achievement of therapeutic levels after the first administration. Thus, the proportion of patients reaching the target concentration was 89% when BMI was  $\leq 30$   $\text{kg/m}^2$  but only 11% when BMI was  $>30$   $\text{kg/m}^2$  ( $P < 0.01$ ). **Conclusions:** The standard dose of 600 mg subcutaneous trastuzumab did not ensure adequate pharmacodynamic exposure from the first administration in 52% of patients, with weight and BMI being related to the plasma levels obtained.

## Keywords

trastuzumab, pharmacokinetics, breast cancer

## Introduction

HER2 receptor overexpression occurs in 15% to 20% of breast tumors.<sup>1-3</sup> The phenomenon of overexpression was first described by Slamon and colleagues in 1987, who also identified it as a negative prognostic factor for more frequent relapses and worse survival rates.<sup>2,3</sup> These findings established the HER2 receptor as a potential therapeutic target for the treatment of breast cancer, and years later, trastuzumab (Herceptin), a humanized monoclonal antibody,<sup>4</sup> showed how blockade of this receptor improved both progression-free and overall survival in these patients.<sup>5-7</sup>

During the preclinical development of the drug, it was established that the minimum concentration ( $C_{\min}$ ) at which trastuzumab achieved maximum inhibition of tumor growth was 20  $\mu\text{g/mL}$ .<sup>1</sup> Thus, reaching a  $C_{\min}$  of at least 20  $\mu\text{g/mL}$  from first administration of the drug has been one of the

main objectives in the galenic development of both the intravenous<sup>6</sup> and subcutaneous (SC) formulations.<sup>8</sup> Clinical trials demonstrated that such a pharmacokinetic target was achieved when trastuzumab was administered at a dose regimen adjusted to the patient's body weight of 6 mg/kg

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