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RESPONSE TO LETTER

Is Bodyweight-Based Dosing Truly Better Than Flat Dosing for Panitumumab? [Response to Letter]

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Dear editor

Thank you for the opportunity to respond to the letter by Dr. Hendrikx and colleagues.

We wish to thank Dr. Hendrikx and colleagues for their interest in our recent publication by Liao et al[1] and their comments about the optimal dosing regimen for panitumumab.

The body weight-based dosing, 6 mg/kg once every two-week (Q2W) regimen, for panitumumab as an optimal dosing regimen is fully supported by clinical study data and pharmacokinetic modeling and simulations.[2]

Based on our analysis of 352 patients from 3 studies, body weight impacted panitumumab exposure. Observed C_{max} and C_{min} increased with increasing body weight after administration of panitumumab 6 mg/kg. In addition, a population pharmacokinetic model of panitumumab developed based on 1200 patients and 14 clinical studies identified body weight as a significant covariate for the greatest contribution of interpatient variability.[3] Consistent with observed data, model-based simulation demonstrated that the weight-based dose (6 mg/kg) led to substantially lower variability in panitumumab exposure across the range of body weights than fixed dosing (480 mg), supporting that a body weight–based approach leads to lower variability in drug exposure across patients. Importantly, the scientific justification of 6 mg/kg Q2W regimen for panitumumab was accepted and approved by global regulatory agencies in the USA, European Union, Japan, and over 70 countries in total.

The body weight-based dosing of 6 mg/kg Q2W regimen for panitumumab was based on thorough pharmacokinetic analysis aimed to reduce interpatient variability in drug exposure with the goal to optimize dosing and improve patient efficacy and safety, as recommended by the FDA.[4] Fixed doses of panitumumab are not FDA approved and suboptimal dosing may impede efficacy and safety. It is now well understood that not all monoclonal antibody (mAb)-based therapies should be administered as flat dose regimen, nor should all be dosed based on body size as previously thought. Some mAb demonstrate clinically relevant impact of body size on exposure whereas others do not. The dosing rationale of mAb should therefore always be data-driven and based on the totality of the scientific evidence.

Disclosure

Michael Z. Liao, Johannes Kast, Sandeep Dutta and Vijay V. Upreti are employees of and stockholders in Amgen. Marloes Berkhout is an employee of Amgen B. V. and has restricted shares in Amgen. Hans Prenen has received honoraria and/or

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