Pharmacokinetically-guided dosing to improve the efficacy of brigatinib in non-small cell lung cancer patients

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Abstract

Brigatinib was recently approved for the treatment of anaplastic lymphoma kinase-positive non-small cell lung cancer and is dosed according to a one-dose-fits-all paradigm. We aimed to identify a pharmacokinetically-guided precision dosing strategy to improve treatment response with brigatinib through simulations using a previously published pharmacokinetic-pharmacodynamic model. Dosing strategies explored were the approved 180mg QD, the highest tolerable dose tested in clinical trials: 240mg QD, and two precision dosing strategies targeting the median trough concentrations following 180mg QD, and 240mg QD. We investigated the impact of alternative dosing regimens on progression-free survival (PFS), overall survival (OS), and the probability of developing a grade [?]2 rash or grade [?]2 amylase increase. Median PFS and OS increased by 1.6 and 7.8 months, respectively between the currently approved dosing strategy and precision dosing to the median trough concentration of the 240mg dosing strategy, with only a minor increase in the probability of developing toxicity.

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