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An LC–MS/MS method for quantification of AC0010, a novel mutant-selective epidermal growth factor receptor (EGFR) inhibitor, and its metabolites in human plasma and the application to a pharmacokinetic study

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Highlights

- We developed a method for determining a third generation EGFR-TKI AC0010 and six of its metabolites.
- We validated the method and applied it to a pharmacokinetic study.
- We obtained the PK parameters of AC0010 and its metabolites in patients with NSCLC.

Abstract

AC0010 is an irreversible, mutant-selective EGFR inhibitor that effectively inhibits EGFR active and T790M resistance mutations in non-small cell lung cancer (NSCLC). A sensitive ultra-performance liquid chromatography - tandem mass spectrometry (UPLC–MS/MS) method was developed and fully validated for determining AC0010 and its metabolites in human plasma. The samples were purified by solid-phase extraction (SPE) columns and separated on a BEH C₁₈ column. Electrospray ionization (ESI) in positive ion mode and multiple reaction monitoring (MRM) were used to monitor the ion transitions of AC0010 (m/z 488→257) and its metabolites M1 (m/z 474→403), M2 (m/z 504→487), M4 (m/z 434→377), M7 (m/z 490→405), MII-1 (m/z

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