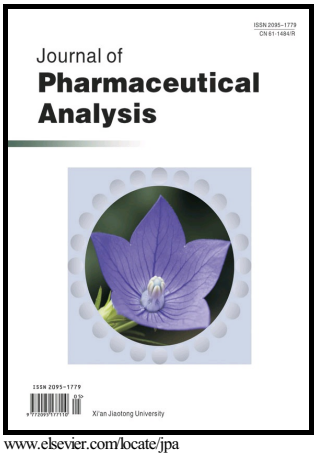
Author's Accepted Manuscript



A liquid chromatography with tandem mass spectrometry method for quantitating total and unbound ceritinib in patient plasma and brain tumor

Xun Bao, Jianmei Wu, Nader Sanai, Jing Li

PII: S2095-1779(17)30095-3
DOI: http://dx.doi.org/10.1016/j.jpha.2017.07.007
Reference: JPHA385

To appear in: *Journal of Pharmaceutical Analysis*

Received date: 5 June 2017
Revised date: 12 July 2017
Accepted date: 13 July 2017

Cite this article as: Xun Bao, Jianmei Wu, Nader Sanai and Jing Li, A liquic chromatography with tandem mass spectrometry method for quantitating tota and unbound ceritinib in patient plasma and brain tumor, *Journal o Pharmaceutical Analysis,* http://dx.doi.org/10.1016/j.jpha.2017.07.007

A liquid chromatography with tandem mass spectrometry method for quantitating total and unbound ceritinib in patient plasma and brain tumor

Xun Bao[1], Jianmei Wu[1], Nader Sanai[2], Jing Li[1*]

[1]Karmanos Cancer Institute, Wayne State University, Detroit, MI 48201
[2]Barrow Neurological Institute, St. Joseph's Hospital & Medical Center, Phoenix, AZ 85013

[*]Requests for reprints addressed to: Jing Li, Ph.D. Karmanos Cancer Institute, 4100 John R Street, HWCRC, Room 523, Detroit, MI 48201, USA. Tel.: 313 576 8258. lijin@karmanos.org

Abstract

A rapid, sensitive, and robust reversed-phase liquid chromatography with tandem mass spectrometry method was developed and validated for the determination of total and unbound ceritinib, a second-generation ALK inhibitor, in patient plasma and brain tumor tissue samples. Sample preparation involved simple protein precipitation with acetonitrile. Chromatographic separation was achieved on a Waters ACQUITY UPLC BEH C18 column using a 4-min gradient elution consisting of mobile phase A (0.1% formic acid in water) and mobile phase B (0.1% formic acid in acetonitrile), at a flow rate of 0.4 mL/min. Ceritinib and the internal standard ([$^{13}C_6$]ceritinib) were monitored using multiple reaction monitoring mode under positive electrospray ionization. The lower limit of quantitation (LLOQ) was 1 nM of ceritinib in plasma. The calibration curve was linear over ceritinib concentration range of 1 – 2000 nM in plasma. The intra- and inter-day precision and accuracy were within the generally accepted criteria for bioanalytical method (< 15%). The method was successfully applied to assess ceritinib brain tumor penetration, as assessed by the unbound drug brain-to-plasma concentration ratio, in patients with brain tumors.