Title: High throughput routine determination of 17 tyrosine kinase inhibitors by LC-MS/MS

Authors: Camille Merienne, Marine Rousset, Dominique Ducint, Nadège Castaing, Karine Titier, Mathieu Molimard, Stéphane Bouchet

PII: S0731-7085(17)31473-5
DOI: https://doi.org/10.1016/j.jpba.2017.11.060
Reference: PBA 11634

To appear in: *Journal of Pharmaceutical and Biomedical Analysis*

Received date: 8-6-2017
Revised date: 22-11-2017
Accepted date: 26-11-2017

Please cite this article as: Camille Merienne, Marine Rousset, Dominique Ducint, Nadège Castaing, Karine Titier, Mathieu Molimard, Stéphane Bouchet, High throughput routine determination of 17 tyrosine kinase inhibitors by LC-MS/MS, Journal of Pharmaceutical and Biomedical Analysis https://doi.org/10.1016/j.jpba.2017.11.060

High throughput routine determination of 17 tyrosine kinase inhibitors by LC-MS/MS

Camille Merienne[1,2], Marine Rousset[1,2], Dominique Ducint[1], Nadège Castaing[1], Karine Titier[1,2], Mathieu Molimard[1,2], Stéphane Bouchet*[1,2].

[1]CHU de Bordeaux, Bordeaux, F-33000, France

[2]Univ. Bordeaux, Inserm, Bordeaux Population Health Research Center, team PHARMACOEPIDEMIOLOGY, UMR 1219, F-33000 Bordeaux, France

*Corresponding Author: Stephane Bouchet

Stephane BOUCHET
Laboratoire de Pharmacologie Clinique et Toxicologie
2e étage Tripode
1 place Amélie Raba Léon,
CHU Pellegrin
33076 BORDEAUX
France
Phone. + 33 5 56 79 59 91
Fax. + 33 5 56 79 57 95
E-mail. stephane.bouchet@chu-bordeaux.fr

Highlight:

- The aim of this assay is to develop a tool to quantify tyrosine kinase inhibitors.
- The tool must be fast with high throughput.
- Solid phase extraction, high-pressure liquid chromatography, and mass spectrometry were used.
- Assay validation procedure was performed according to international recommendations (EMA, FDA).
- Targeted plasma concentrations of TKI are proposed according to literature.

Abstract

Several studies have shown that therapeutic drug monitoring of tyrosine kinase inhibitors (TKI) can improve their benefit in cancer. An analytical tool has been developed in order to quantify 17 tyrosine kinase inhibitors and 2 metabolites in human plasma (afatinib, axitinib, bosutinib, crizotinib, dabrafenib, dasatinib, erlotinib, gefitinib, imatinib, lapatinib, nilotinib, ponatinib, regorafenib, regorafenib M2, regorafenib M5, ruxolitinib, sorafenib, sunitinib, vandetanib). Drugs were arranged in four groups, according to their plasma concentration range: 0.1-200 ng/ml, 1-200 ng/ml, 4-800 ng/ml and 25-5000 ng/ml. Solid phase extraction was used and separation was performed with HPLC using a gradient system on a solid core particle C18 column (5x2.1 mm, 1.6 µm). Ions were detected with a triple quadrupole mass spectrometry system. This assay allows rapid determination of 19 TKI in less than 5 min per run. This high throughput routine method will be useful to adjust doses of oral anticancer drugs in order to improve treatments efficacy.