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CONFERENCE

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TITLE

Validation of a Method for the Determination of Lapatinib in Human Plasma by LC-MS/MS

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ABSTRACT

Novel Aspect: This assay allows accuracy and precision in sample analysis at low cost and ideal automation, while requiring minimal oversight.

Introduction

Lapatinib functions as an inhibitor to the EGFR and erbB-2 receptors. These specific receptors are part of the Type I receptor kinase family involved in cell proliferation. Because cells with inactive Type I receptors don't exhibit uncontrolled growth, it is believed that an inhibitor of erbB kinases could be useful in inhibiting uncontrolled cell growth via stasis or cell death. Presented here is the validation of an LC/MS/MS assay for lapatinib in human plasma.

Methods

Fifty µL plasma was spiked with 250 µL of ([13C, 2H7]-Lapatinib), and treated with 50 µL of 5% ammonium hydroxide. Cartridge conditioning and equilibration used methanol and water, respectively. Samples were eluted using 1 mL of methanol and evaporated at 40°C under a nitrogen stream. Samples were reconstituted with 400 µL of acetonitrile:water:formic acid/50:50:0.1 and analyzed using gradient elution on a reverse phase 100 x 2.1 mm HPLC column, followed by Turbo Ion Spray® MS/MS detection. Run time was six minutes. Positive $(M+H)^+$ ions for lapatinib were monitored in MRM mode. Drug-to-IS peak area ratios for the standards were used to create a linear calibration curve using $1/x^2$ weighted least-squares regression analysis.

Preliminary results

The LC/MS/MS assay was validated over a range of 1 to 1,000 ng/mL for lapatinib in human plasma using 50 µL of the human plasma. The precursor > product ion transition under multiple reaction monitoring (MRM) was: m/z 581.1$(M+H)^+ \rightarrow$ 365. Quality control samples at 4 concentrations were used to determine precision and accuracy. Intra-assay precision ranged from 2.2 to 5.5%, while inter-assay precision ranged from 3.8 to 4.9%. The intra-assay accuracy (defined as % error from nominal) ranged from 7.9 to –0.1% and the Inter-assay accuracy ranged from -4.8 to 0.6%. The analyte has been shown to be stable in plasma for 21 hours at room temperature and after 5 freeze/thaw cycles. The analyte is also stable in processed sample for 140 hours at 4°C. In addition, the selectivity, dilution reproducibility, matrix effect and recovery were also demonstrated. The assay was shown to be sensitive, selective, accurate, reproducible and reliable.