Poster

[P25-9] P25-9: Oncologic drugs (1)

Chair: Ryuji Ikeda, Japan

Mon. Sep 25, 2017 12:30 PM - 1:30 PM Annex Hall (1F)

(Mon. Sep 25, 2017 12:30 PM - 1:30 PM Annex Hall)

[P25-9-8] LC-MS/MS analysis of 5-fluorouracil in plasma for clinical research

Stephen Balloch[1], Gareth Hammond[2] (1.Waters Corporation, 2.Waters Corporation)

Keywords: 5-Fluorouracil, Plasma, LC-MS/MS, Mass spectrometry

Background

5-Fluorouracil (5-FU) is an anti-cancer agent used predominantly in the study of several solid tumor cancers, including colorectal, pancreatic, breast, esophageal and head and neck tumors in clinical research. There is a high degree of inter-individual variability for 5-FU metabolism. An accurate, analytically sensitive and specific method may play a role in researching the pharmacokinetic and pharmacodynamic effects of 5-FU administration.

Methods

Matrix-matched calibrators (20–2000 ng/mL) and quality control samples (40, 350, 750 and 1500 ng/mL) were prepared using in-house stocks of 5-FU and pooled plasma. All samples (50L) were spiked with 5-FU-$^{13}C^{15}N_2$ internal standard prior to liquid-liquid extraction using ethyl acetate. Analytical separation of the extracted sample was achieved within 3 minutes using a HSS PFP UPLC column (2.1x100mm, 1.8m) on the Waters ACQUITY UPLC® I-Class and a water/acetonitrile gradient. 5-FU was quantified using a Waters XEVO® TQD mass spectrometer operating in electrospray ionization in negative mode and multiple reaction monitoring detection mode.

Results

Analytical sensitivity was calculated to be 7.5 ng/mL (n=10 extractions, over five occasions, 20% CV). Linearity was demonstrated over the concentration range 14–2600 ng/mL and system carryover was negligible in samples 10000 ng/mL. Precision studies (n=5, over five occasions) demonstrated repeatability and total precision 9.0%. The mean recovery for 5-FU pooled plasma samples (n=3, 40 and 1500 ng/mL) was between 85–115 % in the presence of high concentrations of endogenous and exogenous compounds. Qualitative ion suppression experiments, using post-column infusion, showed that 5-FU elutes in a region of minimal ion suppression using these conditions. Six individual plasma extracts were used in testing and compared to a solvent blank. Negligible matrix effects were observed at low (40 ng/mL) and high (1500 ng/mL) concentrations as indicated by respective mean internal standard adjusted matrix factors in the range 0.90–1.10.

Conclusions

The clinical research method developed for the quantification of plasma 5-Fluorouracil demonstrated good linearity, analytical sensitivity and precision with negligible matrix effects.

For Research Use Only, Not for use in diagnostic procedures.