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Quantitation of ^{14}C -GDC-0032 (^{14}C -taselisib) in human plasma by UPLC-accelerator mass spectrometry for the determination of absolute bioavailability of GDC-0032 in humans

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GDC-0032 (taselisib) is a potent, selective small-molecule inhibitor of Class I phosphoinositide 3-kinase (PI3K). It is being developed by Genentech for the treatment of various malignancies and is currently in multiple clinical trials. An Accelerator Mass Spectrometry (AMS) method for the determination of ^{14}C -GDC-0032 concentrations in human plasma was developed and qualified for the first time according to the Guidance for Industry: Bioanalytical Method Validation issued by the Food and Drug Administration (FDA). The absolute bioavailability of GDC-0032 was determined following oral administration of 3-mg GDC-0032 and IV administration of 3- $\mu\text{g}/200$ nCi ^{14}C -GDC-0032 in male healthy volunteers in a clinical trial. UPLC-AMS method provided high selectivity and high sensitivity due to its nature of measuring the absolute ^{14}C label. The method was qualified over the calibration curve range 0.168 to 100.8 pg/mL (0.025 to 15.0dpm/mL) using linear regression and $1/y^2$ weighting. Within-run relative standard deviation (%RSD) ranged from 1.87 to 8.59%, while the between-run %RSD varied from 3.21 to 7.29% for QCs using a standard curve model. The accuracy ranged from 98.60% to 109.93% of nominal for within-run and 100.96% to 106.95% of nominal for between-run at all concentrations. Extraction recovery factor of ^{14}C -GDC-0032 was 0.9050. Stability of ^{14}C -GDC-0032 was established in human plasma for 51 days at -70°C and established in reconstituted sample extracts for 20 hours at -70°C . The absolute bioavailability of GDC-0032 capsules was 57.4% (34.6% - 80.3%).

Biography

Xiao Ding has completed her PhD in Analytical Chemistry in 1997 and Postdoctoral studies in 1999 from Department of Chemistry in University of Arizona. She has been working in the bioanalytical field to support drug discovery and development for more than 15 years. Currently she is a Senior Scientist in the department of Metabolism and Pharmacokinetics in Genentech (Roche), a pharmaceutical company. She has published more than 25 papers in reputed journals and presented more than 40 posters at major conferences.

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