VALIDATED BIOANALYTICAL METHOD

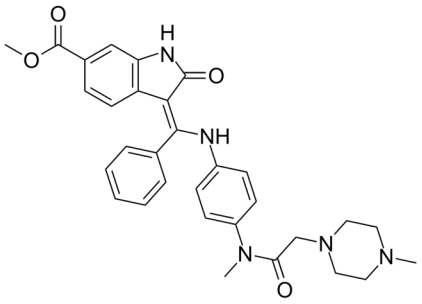
Bioanalytics, Metabolomics and Pharmacokinetics Shared Resource (BMPK)

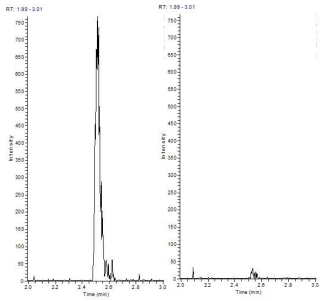
Nintedanib in EDTA Human Plasma

(Sensitivity: 0.500 ng/mL)

BMPK has validated a highly sensitive liquid chromatographic tandem mass spectral assay (LC-MS/MS) for the analysis of nintedanib. Nintedanib (BIBF 1120) is a potent small molecule tyrosine kinase inhibitor (PDGFR α/ß, FGFR 1-3, VEGFR 1-3), which is approved in the US for idiopathic pulmonary fibrosis and in combination therapy for non-small-cell lung cancer. This drug is also being investigated for several cancer indications including ovarian and colorectal cancer as well as renal cell and hepatocellular carcinoma. The validated method was applied to two Roswell Park clinical trials for treatment of metastatic colorectal cancer and carcinoid (neuroendocrine) tumors.

Specifications and Validation Performance	
Matrix (Anticoagulant):	Human Plasma (Disodium EDTA)
Required Volume:	100 µL
Preparation Procedure:	Solid Phase Extraction
HPLC Column:	C18
Mobile Phase:	Acetonitrile/Methanol with Formic Acid
Flow Rate:	300 µL/min
Detection Type:	Tandem Mass Spectral (MS/MS)
Calibration Range:	0.500 - 250 ng/mL
Calibrator Accuracy:	100% (97.5 - 103%; n=5)
Calibrator Precision:	1.98% CV (0.934 - 2.93%; n=5)
QC Concentrations:	2.00, 20.0, 185 ng/mL
QC Accuracy:	106% (101 - 109%; n=18)
QC Precision:	4.88% CV (4.30 - 5.50%; n=18)





Human Pharmacokinetic Parameters[1]	
Recommended Dose	200 mg bid (oral capsule)
Maximum Tolerated Dose (MTD)	250 mg bid (Caucasian), 200 mg bid (Japanese)
Bioavailability	5%
Active Metabolites	None
Plasma Protein Binding	97.8%
Maximum Plasma Concentration (C_{max}) at MTD	53.25 ng/mL (250 mg bid)
Time to Maximum Plasma Concentration (T_{max})	2 - 4 hours
Terminal Half-Life ($t_{1/2}$)	7 - 19 hours

[1]Boehringer Ingelheim Investigator's Brochure (Doc No: c01632700-18).

BMPK offers a wide range of bioanalytical and PK/PD modeling services to assist investigators in their basic research, preclinical, and clinical study objectives. For information on services and pricing, contact Joshua Prey, MS, Research Project Administrator at (716) 845-3313 or Joshua.Prey@RoswellPark.org.

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