Clinical Activity of Avapritinib in ≥4th Line (4L+) and PDGFR Exon 18 Gastrointestinal Stromal Tumors (GIST)

Michael Heinrich,1 Robin L. Jones,2 Margaret von Mehren,3 Sebastian Bauer,4 Yoon-Koo Kang,5 Patrick Schöffski,6 Ferry Eeskens,7 Olivier Mir,8 Philippe Cassidy,9 Cesar Sarrano,10 William D. Tap,11 Jonathan Trent,12 Piotr Rutkowski,13 Shreyas Kumar Patel,14 Sant P. Chawla,15 Eyal Meiri,16 Teresa Zhou,17 Khalid Mamlouk,18 Maria Roche,19 Suzanne George20

1Genentech, South San Francisco, CA, USA; 2Pfizer, Cambridge, MA, USA; 3Blueprint Medicines Corporation, Cambridge, MA, USA; 4Boehringer-Ingelheim Pharmaceuticals, Ridgefield, CT, USA; 5Pfizer Pharmaceutical Research, Groton, CT, USA; 6Velaz, Roche, Basle, Switzerland; 7University of Cincinnati College of Medicine, Cincinnati, OH, USA; 8Royal Marsden Hospital and Institute of Cancer Research, London, UK; 9Memorial Sloan Kettering Cancer Center, New York, NY, USA; 10Cleveland Clinic, Cleveland, OH, USA; 11University of Pennsylvania School of Medicine, Philadelphia, PA, USA; 12University of Maryland School of Medicine, Baltimore, MD, USA; 13Cancer Care Ontario, Sunnybrook Health Sciences Centre, Toronto, ON, Canada; 14University of Chicago, Chicago, IL, USA; 15University of Texas MD Anderson Cancer Center, Houston, TX, USA; 16KCI USA Inc., South San Francisco, CA, USA; 17Astellas Pharma US Inc., Deerfield, IL, USA; 18Memorial Sloan Kettering Cancer Center, New York, NY, USA; 19Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; 20Genentech, South San Francisco, CA, USA.

OBJECTIVE

To evaluate the anti-tumor activity of avapritinib (AG-120), the first-in-class PDGFRA inhibitor, to assess outcomes in ≥4th line (4L+) GIST patients whose disease progressed following at least 2 prior standard therapies and to characterize safety in ≥4L+ patients.

METHODS

A single-arm, open-label phase 2 study of patients with ≥4L+ GIST treated with avapritinib 300/400 mg PO daily. All 4L+ patients received ≥2 prior kinase inhibitors. Key eligibility: ≥4L+, PDGFRA Exon 18 non-D842V mutation. Key objectives: 1) assess anti-tumor activity in 4L+ patients; 2) assess safety in ≥4L+ patients.brook Medicines’ clinical database, and determined patient eligibility for enrollment. Antitumor activity in ≥4L+ patients treated with avapritinib at 300/400 mg PO daily was assessed using mRECIST 1.1. Patients who have had ≥1 post-baseline radiographic assessment. Response evaluable only if ≥90% of target lesions measured.

RESULTS

At the data cutoff (November 16, 2018), 213 patients had received ≥2 prior kinase inhibitors, 121 patients received ≥4L+ therapy and 46 patients were assigned to ≥4L+ therapy; median age 62 years (51-74) and 62% male. PDGFRA Exon 18 mutations were confirmed in 90% of ≥4L+ patients. 90.9% of ≥4L+ patients had a ≥90% measurable target lesion. Clinical Activity of Avapritinib in ≥4th Line (4L+) and PDGFR Exon 18 Gastrointestinal Stromal Tumors (GIST)