C8

Evaluation of progression-free survival by blinded independent central review in patients with progressive, well-differentiated pancreatic neuroendocrine tumors treated with sunitinib or placebo

Pascal Hammel[1], Daniel Castellano[2], Eric Van Cutsem[3], Patricia Niccoli[4], Sandrine Faivre[1], Shem Patyna[5], Deno Klademenos[6], Dongrui Ray Lu[5], Richard Chao[5], Eric Raymond[1]

[1]Service Inter-Hospitalier de Cancérologie et Service de Gastroenteropancréatologie, Hôpital Beaujon, Clichy 92118, France; [2]Servicio de Oncologia, Hospital 12 de Octubre, Madrid 28041, Spain; [3]University Hospital Gasthuisberg/Leuven, Leuven 3000, Belgium; [4]Assistance Publique, Hôpitaux de Marseille CHU Timone, Institut Paoli-Calmettes and RENATEN Network, Marseille 13385, France; [5]Pfizer Oncology, Development, La Jolla, CA 92037, USA; [6]Pfizer Oncology, Development, New York, NY 10017, USA

Background: Sunitinib is an oral, multitargeted receptor tyrosine kinase inhibitor with antitumor and antiangiogenic activity. In a phase III, double-blind, randomized trial of 171 patients with advanced, well-differentiated progressive pancreatic neuroendocrine tumors (NET) (86 sunitinib, 85 placebo), median investigator-assessed progression-free survival (PFS, the primary endpoint) was 11.4 months for sunitinib 37.5 mg continuous daily dosing vs 5.5 months for placebo (hazard ratio [HR] 0.418; 95% CI: 0.263, 0.662; P=0.0001). Treatment-related adverse events (AEs) differed between the two arms, potentially effectively unblinding investigators. The effect of potential bias on PFS was evaluated by a retrospective, blinded independent central review (BICR) of tumor scans in a large subset of patients with available imaging data.

Methods: Baseline and on-study MRI/CT scans and radiology data were evaluated independently according to a two-reader, two-time point lock, followed by a sequential locked read, batch mode paradigm, by independent, third party radiologists using Response Evaluation Criteria in Solid Tumors (RECIST) 1.0 criteria. Reading radiologists were blinded to investigator assessments and AEs; discrepancies were adjudicated by a similarly blinded and independent third radiologist.

Results: Retrospective BICR was conducted on the first 84 patients (49%) whose MRI/CT scans were available (41 sunitinib, 43 placebo). This subset was representative of the intent-to-treat population for demographics, baseline disease characteristics, prior treatment, on-study AEs, and investigator-assessed PFS. Median investigator-assessed PFS was 19.8 months for sunitinib vs 5.8 months for placebo (HR 0.449, 95% CI: 0.218, 0.924, P=0.0249). In the analysis of PFS by BICR of scans, the median PFS was 20.6 months for sunitinib vs 6.2 months for placebo (HR 0.289, 95% CI: 0.117, 0.716, P=0.0042).

Conclusions: This BICR of imaging data supported the investigator-assessed PFS benefit of sunitinib in the treatment of pancreatic NET, and argued against any bias favoring sunitinib. BICR on the remaining patients is ongoing.