The Efficacy and Safety of Sunitinib in Patients with Advanced Well-differentiated Pancreatic Neuroendocrine Tumors

Eric Raymond[1]; Matthew Kulke[2]; Shukui Qin[3]; Michael Schenker[4]; Antonio Cubillo[5]; Wenhui Lou[6]; Jiri Tomasek[7]; Espen Thiis-Evensen[8]; Jianming Xu[9]; Karoly Racz[10]; Adina Croitoru[11]; Mustafa Khasraw[12]; Eva Sedlackova[13]; Ivan Borbath[14]; Paul Ruff[15]; Paul Oberstein[16]; Tetsuhide Ito[17]; Kathrine Fernandez[18]; Brad Rosbrook[18]; Nicola Fazio[19]

[1]Paris Saint-Joseph Hospital Group; [2]Dana-Farber Cancer Institute; [3]PLA Cancer Center of Nanjing Bayi Hospital; [4]Centrul de Oncologie Sf. Nectarie, Oncologie Medicala; [5]Hospital Universitario Madrid Sanchinarro, Centro Integral Oncológico Clara Campal; [6]Zhongshan Hospital, Fudan University; [7]Masarykuv onkologicky ustav/Klinika komplexní onkologické péče; [8]Oslo University Hospital, Department of Gastroenterology; [9]No.307 Hospital, Academy of Military Medical Sciences; [10]Semmelweis University, Faculty of Medicine, 2nd Department of Internal Medicine; [11]Fundeni Clinical Institute, Department of Medical Oncology; [12]Andrew Love Cancer Center, Geelong Hospital; [13]Všeobecné Fakultní Nemocnice v Praze Onkologická Klinika;[14]Cliniques Universitaires Saint-Luc, King Albert II Institute Cancerology and Hematology; [15]University of the Witwatersrand, Faculty of Health Sciences; [16]Columbia University Medical Center, Division of Hematology/Oncology; [17]Kyushu University Hospital; [18]Pfizer Inc; [19]IEO, European Institute of Oncology, Unit of Gastrointestinal Medical Oncology and Neuroendocrine Tumors

Background: Sunitinib was approved by the FDA in 2011 for treatment of progressive, well-differentiated, advanced pancreatic neuroendocrine tumors (pNETs) on the basis of a pivotal phase III study (NCT00428597) that showed a significant increase in progression-free survival (PFS) over placebo following early study termination. Subsequently, the FDA requested a post-approval study to support these findings.

Methods: In this open-label, phase IV clinical trial (NCT01525550), patients with confirmed, progressive, well-differentiated, unresectable advanced or metastatic pNETs received continuous sunitinib 37.5 mg once daily. Eligibility criteria were similar to the phase III study. Primary endpoint was investigator-assessed PFS per RECIST 1.0. This study is still ongoing.

Presented at NANETS 2016

Results: Sixty one treatment-naïve and 45 previously-treated patients with progressive pNETs were treated with sunitinib: mean age, 54.6 years; males, 59.4%; white, 63.2%; ECOG performance status 0, 65.1% or 1, 34.0%; and prior somatostatin analog, 48.1% (treatment-naïve, 39.3%; previously-treated, 60.0%). At the data cutoff date, 82 (77%) patients discontinued treatment, mainly due to disease progression (46%). Median duration of treatment was ~11.9 months. Investigator-assessed median PFS (mPFS) was 13.2 months (95% CI, 10.9–16.7) in the overall population, with comparable mPFS in treatment-naïve and previously-treated patients (Table 1). mPFS per independent radiologic review was 11.1 months (95% CI, 7.4–16.6). Objective response rate (ORR) per RECIST was 24.5%. Median overall survival, although not yet mature, was 37.8 months. Treatment-emergent, all-causality adverse events (AEs) reported by ≥20% of all patients included neutropenia, diarrhea, leukopenia, fatigue, hand–foot syndrome, hypertension, abdominal pain, dysgeusia, and nausea. Most common grade 3/4 AEs were neutropenia (22%) and diarrhea (9%).

Conclusion: The mPFS of 13.2 months and ORR of 24.5% observed in this study support the outcomes of the pivotal phase III study of sunitinib in pNETs and confirm its activity in this setting. AEs were consistent with known safety profile of sunitinib.

Table 1: Efficacy outcomes per investigator assessment

	Overall population	Treatment-naïve patients	Previously-treated patients
Median PFS, months	13.2	13.2	13.0
95% CI	10.9-16.7	7.4-16.8	9.2-20.4
Median OS, months	37.8	NE	33.8
95% CI	33.0-NE	28.9-NE	20.3-NE
ORR, %	24.5	21.3	28.9
95% Exact CI	16.7-33.8	11.9-33.7	16.4-44.3

NE, not estimable