C39

177-Lu-Dotatate Significantly Improves Progression-Free Survival in Patients with Midgut Neuroendocrine Tumors: Results of the Phase III NETTER-1 Trial

Jonathan Strosberg[1]; Edward Wolin[2]; Beth Chasen[3]; Matthew Kulke[4]; David Bushnell[5]; Martyn Caplin[6]; Richard P. Baum[7]; Erik Mittra[8]; Timothy Hobday[9]; Andrew Hendifar[10]; Kjell Oberg[11]; Maribel Lopera Sierra[12]; Dik Kwekkeboom[13]; Philippe Ruszniewski[14]; Eric Krenning[13]

[1]Moffitt Cancer Center, Tampa, FL 33612, USA
[2]Markey Cancer Center, University of Kentucky, Lexington, KY 40536-0093, USA
[3]University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA
[4]Dana-Farber Cancer Institute, Boston, MA 02215, USA
[5]University of Iowa, Iowa City, IA 52242, USA
[6]Royal Free Hospital, London, United Kingdom
[7]Zentralklinik, Bad Berka, Germany
[8]Stanford University Medical Center, Stanford, CA 94305, USA
[9]Mayo Clinic College of Medicine, Rochester, MN 55905, USA
[10]Cedars Sinai Medical Center, Los Angeles, CA 90048, USA
[11]University Hospital, Uppsala University, Uppsala, Sweden
[12]Advanced Accelerator Applications, New York, NY 10118, USA
[13]Erasmus Medical Center, Rotterdam, Netherlands
[14]Hopital Beaujon, Clichy, France

Background: Currently, there are limited therapeutic options for patients with advanced midgut neuroendocrine tumors (20-45% of NETs) progressing on first-line somatostatin analog therapy. Since 2000, thousands of patients have been treated with ^{177}Lu-DOTA^{0}-Tyr^{3}-Octreotate (Lutathera®) peptide receptor radionuclide therapy (PRRT) with promising results.

Methods: NETTER-1 is the first Phase III multicentric, stratified, open, randomized, controlled trial evaluating Lutathera® in patients with inoperable, progressive, somatostatin receptor positive midgut NETs. 230 patients with Grade 1-2 metastatic midgut NETs were randomized to receive Lutathera 7.4 GBq every 8 weeks (x4 administrations) with renal protection (amino acid solution infusion) versus Octreotide LAR 60 mg every 4-weeks. The primary endpoint was PFS per RECIST 1.1 criteria, with objective tumor assessment performed by an independent reading center every 12 weeks until tumor progression. Secondary objectives included objective response rate, overall survival, TTP, safety, tolerability and health-related quality of life. An independent Data Safety Monitoring Board regularly assessed the safety outcome.

Results: Enrolment was completed in February 2015, with a target of 230 patients randomized (1:1) in 35 European and 15 sites in the United States. At the time of the statistical analysis, the median PFS was not reached for Lutathera and was 8.4 months with 60 mg Octreotide LAR [95% CI: 5.8-11.0 months], $p<0.0001$, with a hazard ratio of 0.21 [95% CI: 0.13-0.34]. The number of centrally confirmed disease progressions or deaths was 23 in the Lutathera group and 67 in the Octreotide LAR 60 mg group. The safety profile observed in the study was consistent with the safety information generated in the Phase I-II clinical trial.

Conclusions: The Phase III NETTER-1 trial provides evidence for a clinically meaningful and statistically significant increase in PFS in patients with advanced midgut neuroendocrine tumors treated with Lutathera.