C-40

Clinical Outcomes in Patients with Baseline Renal Dysfunction in the NETTER-1 Study: 177Lu-DOTATATE vs. High Dose Otreotide in Progressive Midgut Neuroendocrine Tumors

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BACKGROUND: Due to risk of nephrotoxicity, impaired renal function is considered to be a contraindication to therapy with 177Lu-DOTATATE. Among patients randomised in the NETTER-1 study, nephrotoxicity and treatment efficacy were evaluated in the two study arms (Lu vs. Oct) according to renal function categories at baseline (eCrClC-G ≥ 60 ml/min vs. stage 3 (mild eCrClC-G = 50 – 59.99 ml/min and moderate 30<eCrClC-G < 50 ml/min).

METHODS: Changes in renal function were assessed in both arms and analysed with the Fisher's exact test. The primary endpoint of the NETTER-1 study, progression-free survival (PFS), was evaluated in the two arms by baseline renal function stage (normal vs. stage 3). At the time of data analysis, median duration of follow up was 14 months.

RESULTS: Ninety-three Lu and 85 Oct patients had baseline eCrClC-G ≥ 60 ml/min, 11 Lu and 16 Oct had mild- and 13 Lu and 9 Oct had moderate-stage 3. The rates of deterioration of renal function over baseline in the two treatment arms for each of the three categories of baseline renal function, were similar (p=0.70695; 1.0000; 1.000, respectively).

Among patients with eCrClC-G ≥ 60 ml/min, Kaplan-Meier analysis showed a greater PFS (p < 0.0001; HR 0.180 [0.102 – 0.318]) in favour of Lu.
Among those with stage 3 at baseline, PFS was much greater in the Lu arm (p < 0.001; HR 0.251 [0.084 – 0.751].

CONCLUSION: The NETTER-1 study did not show any evidence of nephrotoxicity associated with 177Lu-DOTATATE treatment, even among patients with mild to moderate baseline impairment in renal function. Long-term analysis of renal function will be performed at time of overall survival analysis. Treatment with 177Lu-DOTATATE resulted in a markedly longer progression-free survival regardless of whether baseline renal function was normal or impaired.

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