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Safety and Response of an Evans Blue-Modified Radiolabeled Somatostatin Analogue 177Lu-DOTA-EB-TATE with Increased Effective Dose in the Treatment of Metastatic Neuroendocrine Tumors: A Pilot Prospective Study

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BACKGROUND: The aim of this study was to evaluate the safety and efficacy of 177Lu-DOTA-EB-TATE, a novel radiolabeled somatostatin analogue modified by Evans Blue to increase tumor retention in patients with progressive metastatic neuroendocrine tumors (NETs).

METHODS: Thirty-three patients with metastatic NETs were prospectively enrolled into four groups: Group A (n=6, 43±12y) administered approximately 3.7 GBq (100 mCi) 177Lu-DOTATATE as controls; Group B (n=7, 55±7y) administered approximately 1.11 GBq (30 mCi) 177Lu-DOTA-EB-TATE; Group C (n=6,55±10y) administered approximately 1.85 GBq (50 mCi) 177Lu-DOTA-EB-TATE; Group D (n=14, 50±10y) administered approximately 3.7 GBq (100 mCi) 177Lu-DOTA-EB-TATE. Treatment-related adverse events were graded according to the CTCAE v.5.0. 68Ga-DOTATATE PET/CT were performed at baseline and 2–3 months after treatment for response evaluation.

RESULTS: Administration was well tolerated as outlined in Table 1. No CTC 3 or 4 hematotoxicity, nephrotoxicity or hepatotoxicity was observed during or after treatment in group A-C. In group D, CTC-3 hematotoxicity was recorded in 2 patients with multicourse chemotherapy previously. After one-cycle treatment, the SUVmax decreased in group C (Δ%=-17.4±29.3%) and group D (Δ%=-15.1±39.1%), but greatly increased in Group B (Δ%=30.0±68.0%) and mildly increased in group A (Δ%=5.4±45.9%). According to EORTC criteria, 16.7% (1/6), 0% (0/7), 50% (3/6) and 50% (7/14) were evaluated as partial response in group A, B, C and D, respectively. When selecting lesions with comparable baseline SUVmax ranging from 15 to 40, SUVmax decreased in group B (Δ%=-7.3±24.5%), group C (Δ%=-34.9±12.4%) and group D (Δ%=-17.9±19.7%), but mildly increased in group A(Δ%=8.4±48.8%)(P=0.009). Suvmax significantly decreased in EBTATE group (group B plus C and D) (Δ%=-19.0±21.5%) than TATE group (P=0.045).

CONCLUSION: 177Lu-DOTA-EB-TATE is well tolerated and is more effective than 177Lu-DOTA-TATE. Both 1.85GBq (50mCi) and 3.7 GBq (100mCi) doses appear to be more effective than 1.11 GBq (30 mCi) dose. Further investigation with more cycles of 177Lu-DOTA-EB-TATE treatment and longer follow-up is warranted.

Table 1. Safety evaluation after one cycle of 177Lu-DOTA-EB-TATE according to CTCAE v.5.0

Group	Hematotocixity	Hepatotocixity	Nephrotocixity
30 mCi EBTATE group(n=7, 30.0±3.0mCi)	6 CTC-0, 1 CTC-1		7 CTC-0 7 CTC-0
50 mCi EBTATE group(n=6, 49.1±5.4mCi)	5 CTC-0, 1 CTC-1		6 CTC-0 6 CTC-0
100 mCi EBTATE group(n=14, 102.9±15.9mCi)	11 CTC-0, 1 CTC-1, 2 CTC-3	14 CTC-0	14 CTC-0