Ac-225-DOTATOC – dose finding for alpha particle emitter based radionuclide therapy of neuroendocrine tumors

Abstract:
Objectives: There are no established dosimetry tools to predict toxicity of “targeted alpha-therapy” (TAT) yet. We conducted an dose escalation study to find the maximum tolerable dose (MTD) of single cycle and fractionation concepts for Ac-225-DOTATOC radionuclide therapy. Methods: According to Declaration of Helsinki’s “Unproven interventions in Clinical Practice” we performed 46 treatment cycles in 34 patients with progressive neuroendocrine tumors (NET). After each cycle acute toxicity was documented according to CTCAE criteria. First observations are also available for chronic kidney toxicity as the follow up for the first 17 patients has now reached 2 years. Results: The MTD of a single cycle Ac-225-DOTATOC was considered to be 40 MBq. Multiple fractions were tolerated with 25 MBq every 4 months or 18.5 MBq every 2 months. Cumulative activities of 75 MBq were found tolerable in regard to delayed toxicity. The radiologic treatment response that was observed in some patients is without clear preference of a particular fractionation concept until now. Conclusions: We present a well tolerable treatment protocol for TAT with Ac-225-DOTATOC in NET patients that also demonstrated promising treatment efficacy in various patients. Whether TAT provides general advantages in comparison to beta emitter based radionuclide therapy cannot be derived from the available data yet. Comparative trials are needed in the future.

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