Biodistribution and Dosimetry of the CCK2R Ligand [68Ga]Ga-DOTA-CCK-66: First Clinical Results

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Meeting ReportOncology, Basic and Translational - Early Phase (Phase 0 or I) human studies

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Abstract

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Introduction: Medullary thyroid carcinoma (MTC) is a rare neuroendocrine tumor that arises from the parafollicular cells of the thyroid gland and accounts for approximately 5% of all thyroid carcinomas. Since patients with MTC currently can only be cured by complete resection of the primary tumor and any locoregional or distant metastases, accurate imaging techniques are required for staging the disease. Recently, the cholecystokinin-2 receptor (CCK2R) has been shown to be a suitable target for positron emission tomography/computed tomography (PET/CT) imaging of MTC. [^{68}Ga]Ga-DOTA-CCK-66 is a new PET tracer for visualizing CCK2R expression in vivo. In a retrospective analysis of clinical data, the biodistribution and dosimetry of this promising ligand were evaluated.

Methods: Six patients with MTC were injected intravenously with 142 to 193 MBq [^{68}Ga]Ga-DOTA-CCK-66 (mean ± SD, 169 ± 19 MBq). Images were acquired 10, 60, 120 and 240 min after injection. The time-activity curves of the whole body and individual organs as well as selected metastases were determined from the images using ROI and VOI techniques, for the red bone marrow using an estimate from L2-L4. The mean organ dose (±SD) and effective dose were calculated with Olinda/EXM 1.0, assuming bladder emptying was assumed after 1 h and from then on every 3.5 h. Mean values across all patients were calculated and normalized.

Results: Physiological activity was only seen in the stomach. Individual patients showed intensive tracer uptake in metastases. Rapid clearance of the tracer from the blood and rapid excretion of the tracer via the kidneys into the urinary bladder were observed. The tracer showed stable binding in the tumor lesions. The injected standard activity of 150 MBq [^{68}Ga]Ga-DOTA-CCK-66 resulted in a whole-body effective dose of 4.5 ± 0.9 mSv/150 MBq (24 - 41 µSv/MBq). The highest dose was absorbed by the urinary bladder with 269 ± 103 µGy/MBq (98 - 416 µGy/MBq). Other organ doses were 98 ± 77 µGy/MBq (46 - 249 µGy/MBq) for the stomach wall, 39 ± 20 µGy/MBq (26 - 77 µGy/MBq) for the kidneys and 9.6 ± 1.4 µGy/MBq (8.1 - 11 µGy/MBq) for the red bone marrow. No patient suffered adverse drug reactions.

Conclusions: The radiopharmaceutical [^{68}Ga]Ga-DOTA-CCK-66 is safe to use and shows no adverse drug reactions. The agent has a low radiation exposure to patients comparable to other 68Ga- and 18F-based tracers. Further studies are warranted to investigate the potential diagnostic superiority over already established imaging modalities, and to evaluate the therapeutic option using 90Y- or 177Lu-labeled DOTA-CCK-66, which represents an advantage over the currently used gold standard, [^{18}F]F-DOPA, as this tracer does not offer a therapeutic option.