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Abstract Submission

Title: Cyclic Changes of Absorbed Dose as a Biomarker for Radiological Response in Neuroendocrine Tumours Treated with [177Lu]Lu-DOTATATE

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Abstract:

Current [^{177}Lu]Lu-DOTATATE treatment protocols for neuroendocrine tumours (NETs) apply fixed administered activities without individual optimisation. Given the late-responding nature of NETs, identifying biomarkers that predict treatment efficacy could enable adaptive therapeutic strategies.

Patients with positive [^{68}Ga]Ga-DOTATATE scans and confirmed NETs were enrolled in the OZMOSIS OZM-067 trial (NCT02743741) and were treated with 4 cycles of [^{177}Lu]Lu-DOTATATE, with SPECT-CT images acquired at 4, 24, and 72 hr post-injection after each cycle. The injected activity varied depending on kidney dose. Out of the 91 patients in the full dataset, 50 patients and 98 tumours were included in this ongoing analysis so

far. Absorbed dose to tumours (Gy) and administered activity (GBq) were recorded for all treatment cycles. Treatment response was defined as partial response (PR) assigned at best-response according to RECIST 1.1. The average total tumour dose and the average change in Gy/GBq per patient were also recorded.

A serial decline in Gy/GBq was observed across treatment cycles, with reductions of approximately 8%, 22%, and 32% in cycles 2, 3, and 4, respectively, relative to cycle 1. A greater reduction in Gy/GBq correlated with an increased likelihood of PR. Independently, a logistic dose-response relationship was also established. An average dose of 110 Gy was needed to achieve a 26% probability of PR, while higher than around 150 Gy average doses tended to a maximum PR probability of around 53%. Combining both metrics, 10 out of the 12 patients receiving an average absorbed dose of at least 100 Gy *and* exhibiting a ≥50% average decrease in Gy/GBq had PR.

Cyclic changes in absorbed dose could serve as a potential biomarker for treatment response in [^{177}Lu]Lu-DOTATATE therapy. Monitoring these changes, alongside total absorbed dose, could inform personalised treatment adaptations—enhancing therapeutic efficacy and guiding early treatment decisions.