Radiation absorbed dose in patients with metastatic castration-resistant prostate cancer treated with [¹⁶¹Tb]Tb-PSMA-I&T

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Background

[¹⁷⁷Lu]Lu-PSMA is a proven therapy for patients with metastatic castration-resistant prostate cancer (mCRPC). Terbium-161 has high linear energy transfer, emitting abundant Auger electrons in addition to beta particles. It has shown superior in-vitro and in-vivo results in comparison with Lutetium-177. Post-therapy imaging and dosimetry are feasible with low-energy gamma emission from Terbium-161. We aim to calculate radiation absorbed dose to normal organs in men with mCRPC who were treated with [¹⁶¹Tb]Tb-PSMA-I&T.

Methods

VIOLET (NCT05521412) is a single-center, single-arm, phase I/II trial recruiting 30 patients with progressive mCRPC. The phase I dose-escalation is designed with a 3+3 model to establish the safest dose of [¹⁶¹Tb]Tb-PSMA-I&T (dose levels: 4.4, 5.5 and 7.4 GBq). [¹⁶¹Tb]Tb-PSMA-I&T was compounded on-site using a kit formulation (Isotopia Molecular Imaging). In the dose escalation phase, a triple bed quantitative SPECT/CT from vertex to mid-thigh was acquired at three time-point intervals (2-6h, 18-24h, 72-120h) after the first cycle of [¹⁶¹Tb]Tb-PSMA-I&T. Acquisitions were obtained on low-energy, high resolution collimators, using a triple energy window peaked at 74keV with upper and lower scatter limits. Retention of [¹⁶¹Tb]Tb-PSMA-I&T was estimated from voxel-based time-activity curves based on a multi-phase exponential clearance model and convolved using a GATE-derived voxel dose kernel based on decay of Terbium-161 in ICRP soft tissue to yield three-dimensional absorbed dose maps. Radiation absorbed dose to the respective organs was calculated for the beta particles using the voxel S values.

Results

Twelve patients received their first cycle of [¹⁶¹Tb]Tb-PSMA-I&T in the dose escalation phase. The quality of the SPECT/CT images was visually similar to those acquired post-[¹⁷⁷Lu]Lu-PSMA in our center. The mean (standard deviation) total absorbed dose in the parotid glands, submandibular glands, kidneys, liver and spleen was 0.92 (\pm 0.43), 0.92 (\pm 0.41), 2.21 (\pm 0.73), 0.42 (\pm 0.15), and 0.38 (\pm 0.12) Gy, respectively. The mean absorbed dose per GBq for the same organs was 0.14 (\pm 0.05), 0.15 (\pm 0.06), 0.35 (\pm 0.10), 0.07 (\pm 0.03), 0.06 (\pm 0.03) Gy/GBq.

Conclusion

Beta radiation absorbed dose following [¹⁶¹Tb]Tb-PSMA-I&T are within a safe and expected range for normal organs. Additional radiation from Auger electrons is not accounted for in current models.

Funding Acknowledgements

This investigator-initiated clinical trial is funded by Challenge Award from the Prostate Cancer Foundation (PCF) through funds from CANICA AS (Oslo, Norway) and the Peter MacCallum Foundation. Isotopia is supplying [¹⁶¹Tb]Tb and PSMA-I&T kit as part of a commercialization agreement with the Peter MacCallum Cancer Centre.

Conflicts of Interest Disclosure Statement

JPB receives support from a Prostate Cancer Foundation (PCF) Young Investigator Award and PhD support through an Australian Government Research Training Program Scholarship. LK received PhD support through an Australian Government Research Training Program Scholarship. MSH is supported through an NHMRC Investigator Grant and has consulted or served in an advisory role for Janssen, MSD and Novartis, received travel funding from Novartis and Debiopharm Group, and received research funding from Bayer (institutional), Novartis (institutional), Isotopia Molecular Imaging (institutional) and Debiopharm Group (institutional). AAA has consulted or served in an advisory role for Astellas Pharma, Novartis, Janssen, Sanofi, AstraZeneca, Pfizer, Bristol-Myers Squibb, Tolmar, Telix Pharmaceuticals, Merck Sharpe & Dohme, Bayer, Ipsen, Merck Serono, Amgen, Noxopharma, Aculeus Therapeutics and Daiichi Sankyo, participated in a speakers' bureau for Astellas Pharma, Novartis, Amgen, Bayer, Janssen, Ipsen, Bristol-Myers Squibb and Merck Serono, received travel funding from Astellas Pharma, Sanofi, Merck Serono, Amgen, Janssen, Tolmar, Pfizer, Bayer and Hinova Pharmaceuticals, received honoraria from Janssen, Astellas Pharma, Novartis, Tolmar, Amgen, Pfizer, Bayer, Telix Pharmaceuticals, Bristol-Myers Squibb, Merck Serono, AstraZeneca, Sanofi, Ipsen, Merck Sharpe & Dohme, Noxopharm, Aculeus Therapeutics and Daiichi Sankyo, and received research funding Astellas Pharma (institutional), Merck Serono (institutional), Novartis (institutional), Pfizer (institutional), Bristol-Myers Squibb (institutional), Sanofi (institutional), AstraZeneca (institutional), GlaxoSmithKline (institutional), Aptevo Therapeutics (institutional), MedImmune (institutional), Bionomics (institutional), Synthorx (institutional), Astellas Pharma (institutional), Ipsen (institutional), Merck Serono (institutional), Lilly (institutional), Gilead Sciences (institutional), Exelixis (institutional), MSD (institutional) and Hinova Pharmaceuticals (institutional). SS is supported through an NHMRC Investigator Grant and has consulted or served in an advisory role for AstraZeneca, Bristol-Myers Squibb, Merck Sharp & Dohme, Novartis, Skyline Diagnostics and Abbvie, received honoraria from Bristol-Myers Squibb, Merck, AstraZeneca and Janssen, and received research funding from Amgen (institutional), AstraZeneca (institutional), Merck (institutional), Endocyte/Advanced Accelerator Applications (institutional), Genentech/Roche (institutional), Novartis (institutional), Pfizer (institutional) and Senhwa Biosciences (institutional).

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