Prostate SBRT – Using 18F PSMA-1007 PET and Multiparametric MRI to escalate the dose to Dominant Intraprostatic Lesions (DILs) – ARGOS CLIMBER trial

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Abstract

Purpose: Most recurrences after primary prostate cancer radiation therapy originate from dominant intraprostatic lesions (DILs). Prostate multiparametric Magnetic Resonance Imaging (mpMRI) to target DILs during radiation planning has been shown to improve clinical outcomes for patients in the FLAME trial. 18-Fluorine Prostate Specific Membrane Antigen-1007 (18F PSMA-1007) Positron Emission Tomography (PET) can also target DILs and offers the further opportunities for targeted dose escalation.

Materials and Methods: ARGOS-CLIMBER is a prospective phase I/II trial enrolling 50 patients with unfavourable intermediate or high-risk disease across two Ontario centres. A hybrid PET/MR scanner was used to acquire co-registered 18F PSMA-1007 PET and mpMRI images prior to stereotactic body radiation therapy (SBRT). The images were rigidly fused with the computed tomography (CT) simulation scans. All patients received intra-prostatic fiducial markers. All DILs were delineated on mpMRI and PET images: on mpMRI, DILs were delineated in areas with low T2 signal and restricted diffusion, and included all lesions with a score of 4 or 5 on the Prostate Image Reporting And Data System (PIRADS v2.1); on 18F PSMA-1007 PET, DILs were delineated automatically by using a Standardized Uptake Value (SUV) threshold of 20–40% of the maximum SUV in the prostate, then this volume was manually edited to the anatomy of the DIL on mpMRI or CT. Final DIL volumes were the union of PET and mpMRI volumes. Planning targets were as follows: whole prostate 35Gy/5; seminal vesicles and elective nodal regions 25Gy/5; imaging involved nodes 35Gy/5; DILs up to 50Gy/5, while respecting organ at risk constraints. Patients were treated every other day with cone beam CT guidance and 6–18 months of adjuvant androgen deprivation. The primary outcome is chronic (6 month) toxicity. Secondary outcomes include acute (6 week) toxicity, quality of life metrics and cancer control outcomes including biopsy clearance at 2 years. PET, mpMRI and biologic biomarkers at 6 months and 2 years post treatment are exploratory endpoints.

Results: Between May 2022 and January 2023, 20 patients have been enrolled, with 18 patients having completed treatment. There were 29 and 34 DILs detected on mpMRI and 18F PSMA-1007 PET, respectively, with a median (range) of 2 (0 – 4) MR DILs and 1 (0 – 4) PET DILs per patient. The median (IQR) size of the MR and PET DILs was 14 mm (9 – 20 mm) and 11 mm (9 – 31 mm). The median (IQR) maximum dose delivered to the combined DIL was 46.9 Gy (45.5 – 48.0 Gy), and the median (IQR) D99% to this volume was 42.4 Gy (40.8 – 45.5 Gy). No patients experienced grade 3+ acute toxicity thus far.

Conclusions: Dose escalation to multi-modality imaging defined DILs on ARGOS/CLIMBER has been feasible with acceptable acute toxicity. Accrual completion is expected by Q2 2023, with the 6-month primary endpoint of GI/GU toxicity available by Q4 2023.

Prostate Stereotactic Body Radiation Therapy (SBRT) – Using 18F Prostate Specific Membrane Antigen-1007 (18F PSA-MA-1007) Positron Emission Tomography (PET) and Multiparametric Magnetic Resonance Imaging (mpMRI) to escalate the dose to Dominant Intraprostatic Lesions (DILs) – ARGOS CLIMBER trial.

Background

Stereotactic radiation has been shown to favorably impact patients in the 1-5 year survival in advanced prostate cancer and mpMRI with mpMRI/CT are standard of care for patients with local recurrence who have not been declared free of disease.

Methods

ARGOS CLIMBER is a prospective, phase III clinical trial of mpMRI/CT-MRI fusion imaging guided SBRT to escalate the dose to target DILs.

Pretreatment with a 18F PSA-MA-1007 LRC 3 or 5 scans were delineated on the basis of PET/CT and MRI. The target was delineated using a threshold of 5% above normal uptake. The volume of tissue was calculated using the liver as a template.

The following criteria were prescribed: (i) PET-CT was in the isocentric frame; (ii) the target matched the clinical target volume; (iii) the target was delineated through the entire target volume; (iv) the target was delineated on 3D imaging; (v) the target was delineated on the target volume.

Results

A total of 10 patients have been enrolled and treated. All were enrolled at a single site. The median follow-up was 12 months. The median age of patients was 65 years. The median Gleason score was 6 and the PSA was 10 ng/mL. The median dose was 100 Gy.

Conclusions

Stereotactic SBRT based on 18F PSA-MA-1007 PET/CT and mpMRI may provide a novel treatment option for patients with local recurrence who have been declared free of disease and who have not been adopted an alternative cancer treatment due to the potential for long-term survival and disease-free survival after the evaluation.