Exploring the Generalizability of the Prognostic Value of Machine Learning Models Trained on Mid-Treatment PSMA PET/CT to End-of-Treatment PSMA PET/CT in mCRPC Patients Treated with $^{177}$Lu-PSMA Radioligand Therapy Using the TRAQinform Profile: A Retrospective, Single-Center Analysis

Vishnu Murthy¹, Ojaswita Lokre², Timothy Perk², Pan Thin³, Kathleen Nguyen⁴, Lucia Chen⁵, Andrei Gafita⁶, Johannes Czerinin⁷, Jeremie Calais⁸

¹Ahmanson Translational Theranostics Division, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA
²AIQ Solutions, Madison, WI, USA, ³Department of Medicine Statistics Core, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

OBJECTIVE

• To explore the prognostic value of the TRAQinform Profile trained on mid-treatment prostate-specific membrane antigen (PSMA) PET/CT (PSMA-PET) patients when applied to end-of-treatment PSMA-PET (ePET) in patients with metastatic castration-resistant prostate cancer (mCRPC) treated with $^{177}$Lu-PSMA Radioligand Therapy (PSMA-RLT)

METHODS

I) Patients

• mCRPC patients who underwent PSMA-RLT with available baseline PSMA-PET (bPET) and ePET within 6 mo of the last PSMA-RLT cycle were included in this retrospective analysis

• Overall survival (OS) from ePET was collected

II) Analysis of PSMA PET Images

• TRAQinform IQ technology (AIQ Solutions-Madison, WI) was used to conduct lesion region of interest (ROI)-based analyses at bPET and ePET, and changes in SUV$_{max}$, SUV$_{mean}$, and SUV$_{total}$ across all lesion ROI from bPET to ePET were extracted

• ROI were matched across time points and categorized into new, increasing, stable, decreasing, and disappeared based on changes in SUV$_{total}$ (Figure 1)

III) Statistical Analysis

• This study applied TRAQinform Profile (a random forest model), trained on 185 external PSMA-PET, to generate TRAQinform scores for early identification of optimal vs. suboptimal responders to PSMA-RLT

• Associations between TRAQinform Profile scores and OS were evaluated by Kaplan-Meier analysis

• Associations between % new, % increasing, % stable, % decreasing, and % disappeared lesion and OS were evaluated using univariate Cox regression models

RESULTS

Patients

• Twenty mCRPC patients were included

• Twelve of 20 patients (60%) had died at the last follow-up, the median follow-up time from ePET for survivors was 31.2 mo (IQR, 6.8–40.7 mo), and the median survival time from ePET was 13.3 mo (IQR, 10.2–NR)

Image Analysis

• The median number of lesion ROI identified on bPET and ePET were 13.5 (IQR: 5.8–59.5) and 33 (IQR: 2.8–86.3) respectively

• The median % changes in SUV$_{max}$, SUV$_{mean}$, and SUV$_{total}$ from bPET to ePET were -33.9%, -20.7%, 4.3%, and -13.9% respectively

Statistical Analysis

• An increase in percent new and percent new or increasing lesions was associated with a higher risk of death (HR = 1.03; p = 0.004, HR = 1.03; p = 0.01 respectively), while an increase in percent disappeared or decreasing lesions was associated with a lower risk of death (HR = 0.97; p = 0.024)

• The median TRAQinform Profile score was 0.27, and patients with a TRAQinform Profile score above the median had shorter OS compared with patients with a TRAQinform Profile score below the median (median OS, 10.9 mo [95% CI, 5.0–NR] vs. median OS, 22.0 mo [95% CI, 14.5–NR]; P = 0.049) (Figure 2). Figure 3 shows sample cases from our cohort.

CONCLUSION

• In this retrospective study of 20 mCRPC patients treated with PSMA-RLT, the TRAQinform Profile score was prognostic for OS

• Percent new, percent new or increasing, and percent disappeared or decreasing lesions were significantly associated with OS

• Validation in larger, prospective multicentric clinical trials is warranted