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

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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}, volume (cm^3), and SUV_{total} (SUV_{mean} x volume) 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 Profile 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

FIGURES AND TABLES

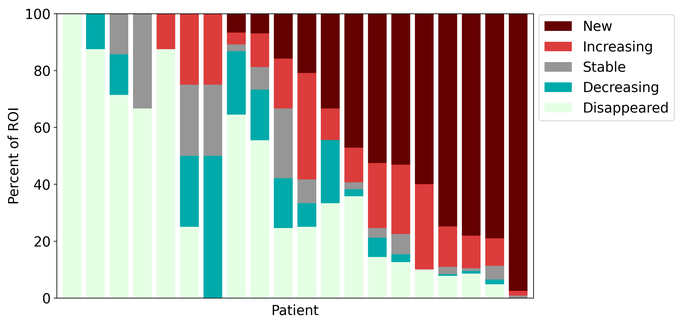

Figure 1: Heterogeneity plot depicting new, increasing, stable, decreasing, and disappeared lesion ROI as a percent of total ROI for each patient

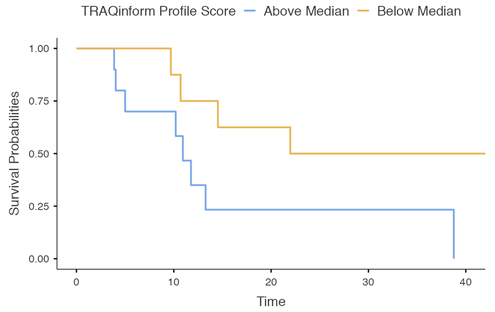

Figure 2. Kaplan-Meier curves showing associations between TRAQinform Profile scores and OS

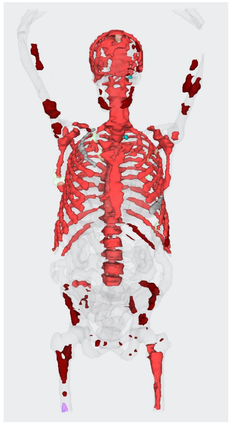

Figure 3A
Age: 78
Number of Cycles: 2
TRAQinform Profile Score: 1
Lesions: 58 new, 15 increasing, 3 stable, 3 decreasing, and 44 disappeared
OS from ePET: 5 mo

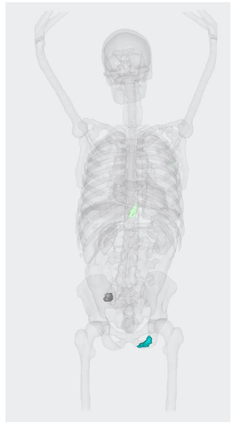

Figure 3B
Age: 71
Number of Cycles: 1
TRAQinform Profile Score: 0.007
Lesions: 0 new, 0 increasing, 1 stable, 1 decreasing, and 5 disappeared
Last Follow-Up from ePET: 40.4 mo

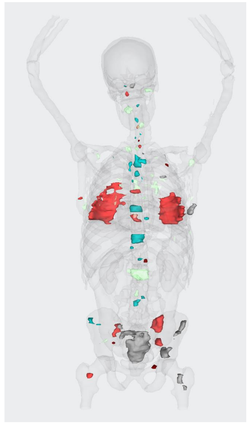

Figure 3C
Age: 60
Number of Cycles: 3
TRAQinform Profile Score: 0.22
Lesions: 7 new, 12 increasing, 8 stable, 18 decreasing, and 56 disappeared
OS from ePET: 9.7 mo

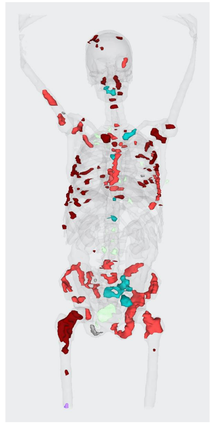

Figure 3D
Age: 67
Number of Cycles: 3
TRAQinform Profile Score: 0.30
Lesions: 62 new, 27 increasing, 4 stable, 8 decreasing, and 17 disappeared
OS from ePET: 3.9 mo

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}, volume, 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