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The Predictive Quotient Index Comprising Gene Cluster Analysis and Grading is Specifically Predictive of PRRT Efficacy

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BACKGROUND: The efficacy of PRRT is based upon NET over expression of somatostatin receptor (SSR) to deliver targeted isotope therapy. SSR expression (Krenning scale) compared to Predictive Quotient Index (PQI) [circulating NET transcript analysis mathematically integrated with grade] indicates the latter is more accurate for predicting PRRT efficacy. We evaluated whether PQI was specifically predictive or was prognostic for PRRT compared to other therapeutic strategies.

METHODS: We evaluated 3 treatment cohorts. 177Lu-PRRT-treatment (n=130 [Rotterdam: Meldola; Bad Berka]; Comparator cohort: (n=106) non-PRRT treated GEPNETs and somatostatin analog (SSA)-therapy GEP-NETs (n=28).

Blood prospectively collected. Baseline evaluations: Grade (Ki67) and NETest (qRT-PCR - multianalyte algorithmic analyses). The PQI (NETest genes regulating metabolism and growth factor signaling) integrated with the Ki67 index. The PQI has two prediction outputs: “PRRT-responder” (R) vs “PRRT-non-responder” (NR). Disease control was by RECIST criteria [R (stable, partial and complete response) vs NR)] All samples were blinded. Statistics: Kaplan-Meier survival analysis.

RESULTS: PRRT cohort (n=130). Median follow-up: 9-16 months. Cohort Meldola: mPFS for patients identified as "PRRT-responders" was not reached versus predicted "non-responders" mPFS 17 months (Chi2=38, p<0.0001). Cohort Bad Berka: Not reached vs. 17 months (Chi2=27.4, p<0.0001). Cohort Rotterdam: Not reached vs. 9 months (Chi2=27, p<0.0001). The PQI accurately predicted response in 94-97% of PRRT-treated individuals.
SSA cohort (n=28). Median follow-up 11 months (9-15). No significant difference in mPFS was noted between "Responders" and "Non-responders". The PQI does not predict SSA response.

Comparator cohort (n=106). Median follow-up 19 months (1-36). No significant differences in median survival between those identified as "Responder" vs Non-Responder (both mPFS: 24 months). The PQI is neither predictive nor prognostic.

CONCLUSION: An integrated measurement (PQI) of "omic" NET gene analysis with grading in an individual tumor is a specific predictive marker for PRRT therapeutic efficacy in neuroendocrine tumors.