

PS3-08-24 : Association of Oncotype DX Recurrence Score with Germline Mutations in Cancer Susceptibility Genes Including BRCA1/2 in HR+/HER2- Early Breast Cancer



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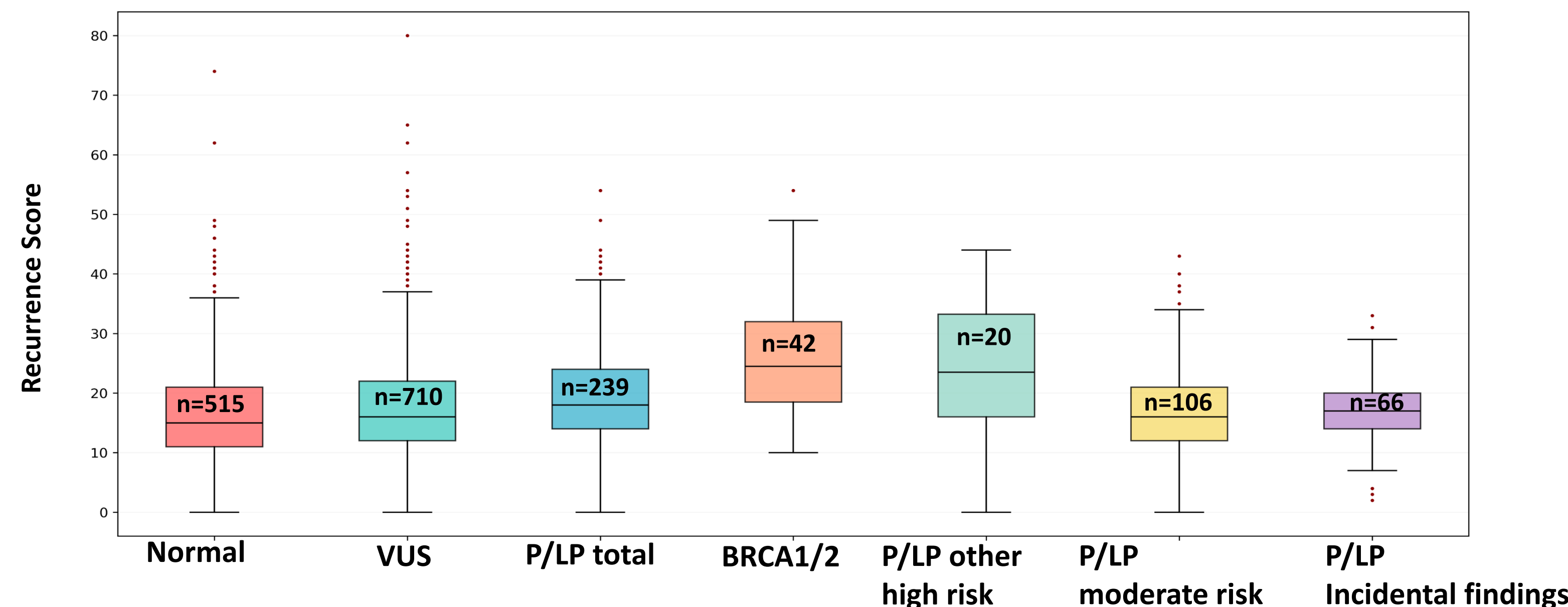
INTRODUCTION AND OBJECTIVES

In early-stage ER+/HER2- breast cancer, the Oncotype DX® Recurrence Score (RS) is a validated 21-gene assay guiding prognosis and chemotherapy benefit. Although germline pathogenic variants (PVs) may affect tumor biology and treatment response, their relationship with RS -beyond BRCA1/2- remains unclear. **This study examines the association between RS and germline PVs across a wider range of breast cancer susceptibility genes.**

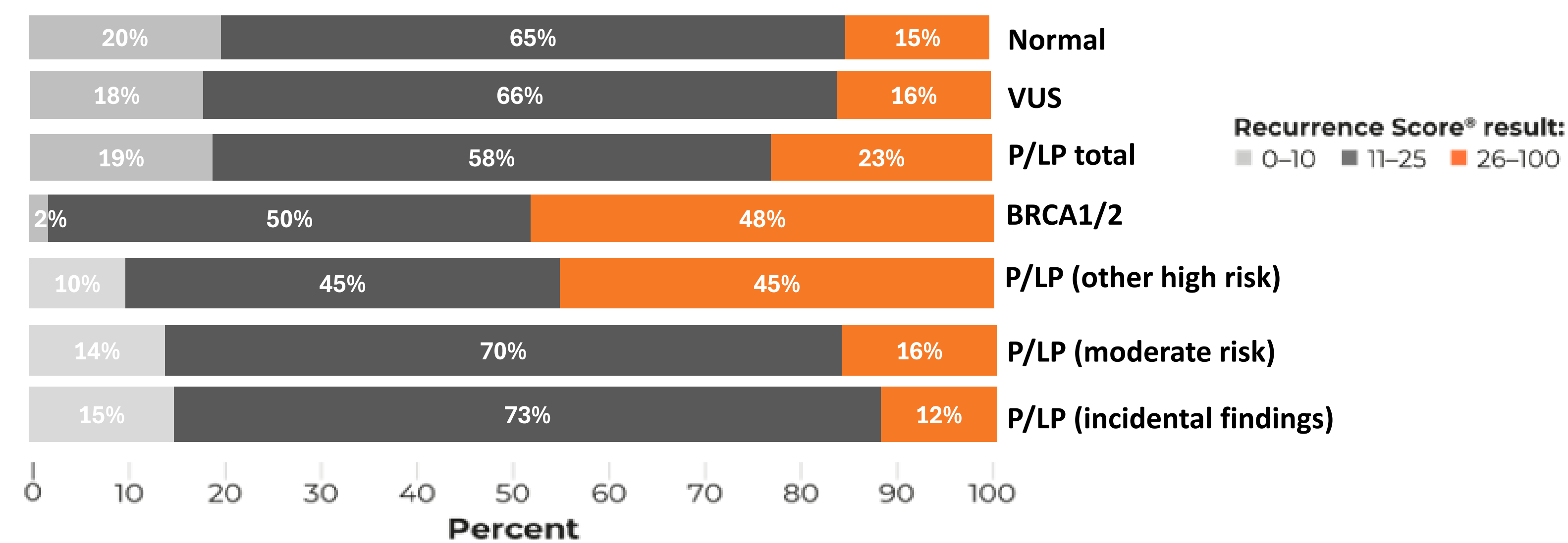
METHODS AND RESULTS

We retrospectively analyzed **1,465** Greek patients with early-stage ER+/HER2- breast cancer who underwent both **germline testing** with a 52-gene panel and **Oncotype DX®** testing between 2015 and 2025. Patients were categorized by Recurrence Score (RS) as low (0-10), intermediate (11-25), or high (>25), and germline results as pathogenic/likely pathogenic (P/LP), variants of uncertain significance (VUS), or negative. P/LP variants were further classified as BRCA1/2, other high-risk, moderate-risk, or incidental findings.

Graph 1. Continuous Recurrence Score Distribution (0-100) and Median Values by Cohort



Graph 2. Distribution of Patients by Recurrence Score Risk Group (Low, Intermediate, High)



DISCUSSION

The distribution of RS varied notably across genetic variant groups. **Patients with P/LP BRCA1/2 and other high-risk gene variants exhibited statistically significant higher median RS values (p<0.0001) and higher percentage of patients with RS>25 (p<0.0001) compared to all other subgroups (moderate risk variants, incidental findings, VUS and cases without detected variants).**

CONCLUSION

This retrospective analysis suggests that patients with germline mutations in high-risk susceptibility genes are more likely to have an unfavorable prognosis for distant recurrence and a greater likelihood of receiving chemotherapy, as indicated by their elevated RS values.

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1. Kalinsky et al., 21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer. N Engl J Med. 2021 Dec 16;385(25):2336-2347.