Refining prognosis of Endometrioid Ovarian Carcinoma subtypes using hormone receptors expression

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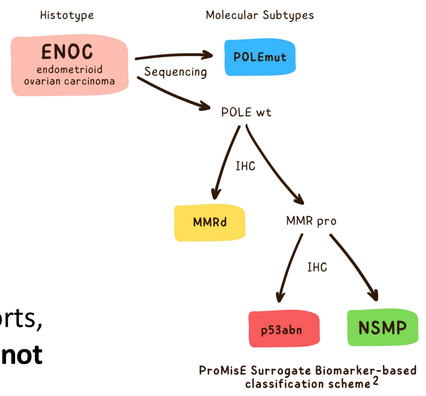
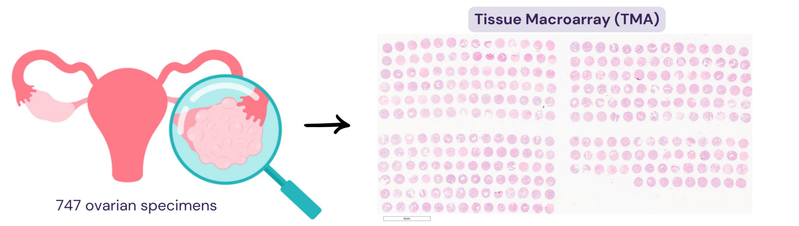
Background

- **Endometrioid Ovarian Carcinoma** (**ENOC**) is the **least studied** histotype of ovarian carcinoma.
- It often affects **pre-menopausal** women and is associated with **endometriosis**.
- **Most** ENOC patients (70%) fall into a molecularly **heterogeneous** subtype called **no specific molecular profile** (**NSMP**).[1]
- Past ENOC studies are based on **small** cohorts, confounded by histotype **inaccuracies**, and **did not** account for **molecular subtype** context.



Methods

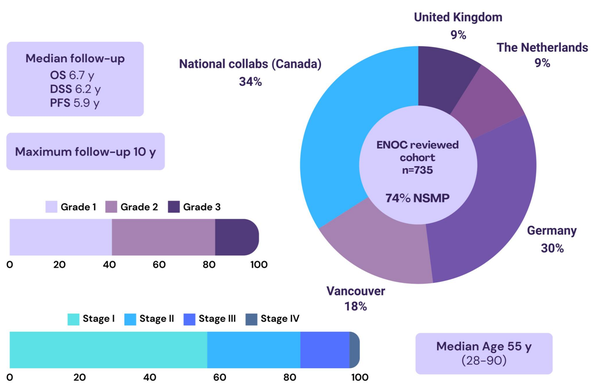


Immunohistochemistry (IHC) Surveying
Adress ENOC missclassification WT1
Subtypes Biomarkers MLH1, MSH2, MSH6, PMS2, p53
Additional Biomarkers ER, PR, CTNNB1

Mutation Screening
Scroll and **Macrodissect** tissues
DNA Extraction
Sequencing POLE exons 9, 13, 14

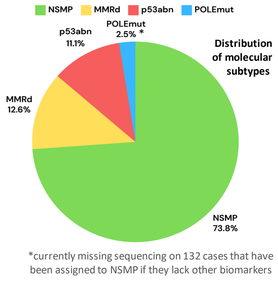
Prognostic evaluation
ER, PR, CTNNB1
OS Overall Survival
DSS Disease-specific Survival
PFS Progression-free Survival
Within **ENOC** and **NSMP**

Cohort's characteristics

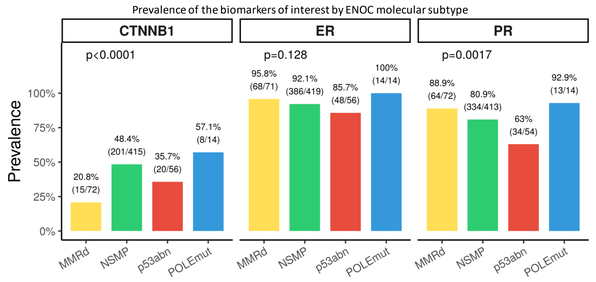


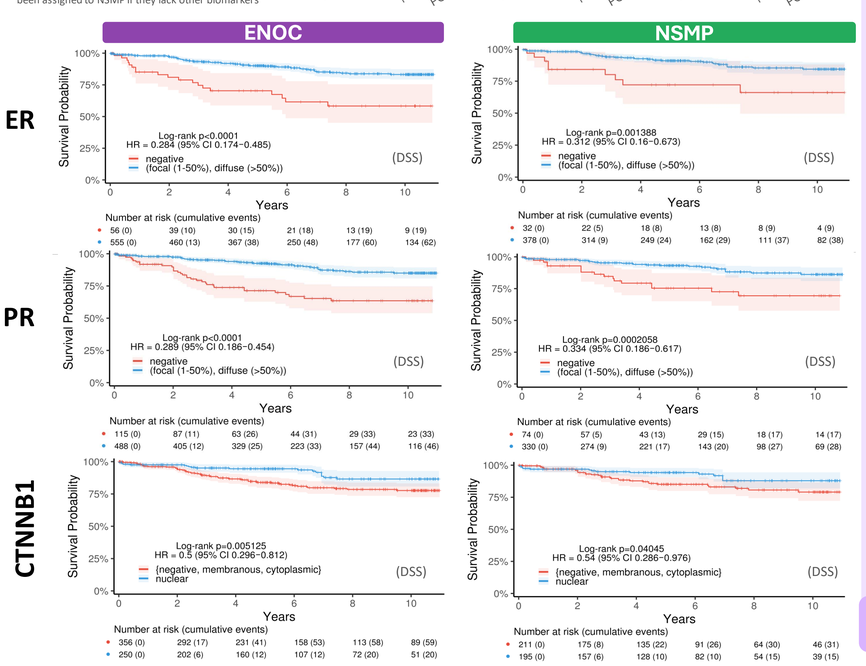
Aim Investigate the **prognostic** value of **estrogen** receptor (**ER**), **progesterone** receptor (**PR**), and **β-catenin** (**CTNNB1**) among all **ENOC** and within **NSMP** subtype.

Results

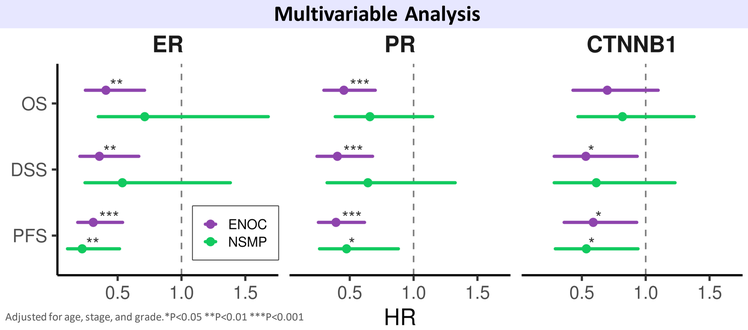


*currently missing sequencing on 132 cases that have been assigned to NSMP if they lack other biomarkers





Multivariable Analysis

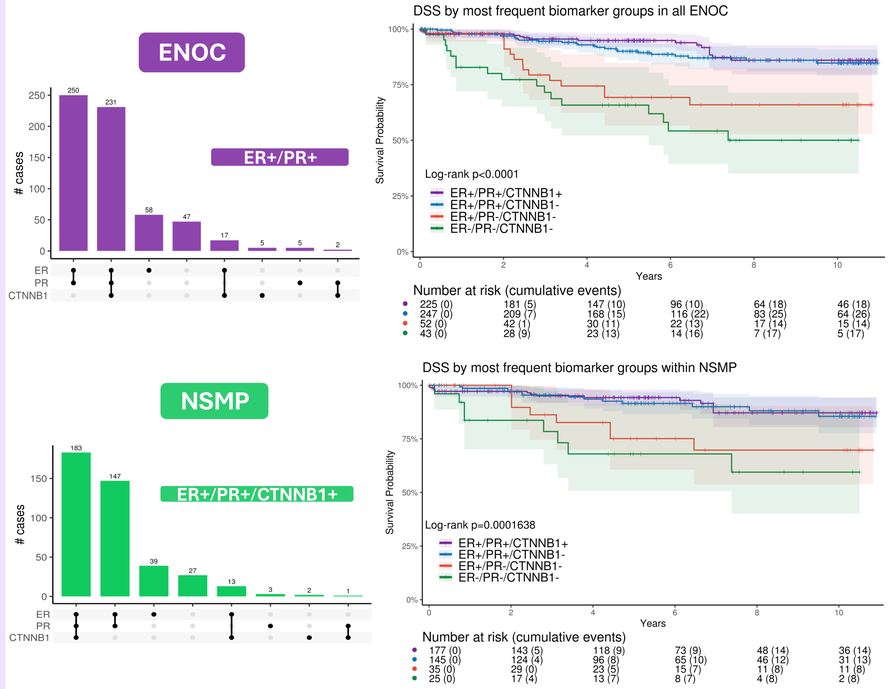


Adjusted for age, stage, and grade. *P<0.05 **P<0.01 ***P<0.001

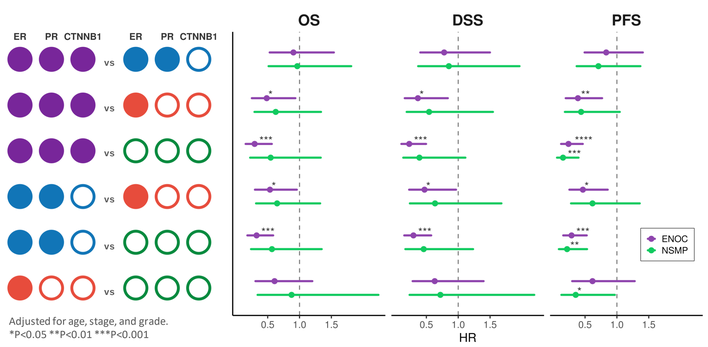
Main findings

- **ER+** and **PR+** were associated with **improved survival** outcomes for both **ENOC** (P<0.001) and **NSMP** subtype (P≤0.01) in **univariate analysis**.
- **CTNNB1+** was associated with **improved survival** in **ENOC** (P≤0.005) and **NSMP** (P<0.05) although with a **smaller effect** in univariate analysis.
- **Multivariable analysis** including age, stage, and grade confirmed the **prognostic association** of **ER+** (P<0.005), **PR+** (P<0.001), and **CTNNB1+** (P<0.05) in **ENOC**, while in **NSMP** they remained significant for **PFS** only (P≤0.03).
- The most **frequent biomarker combination** was **duo-positive ER+/PR+** in the full **ENOC** cohort while in **NSMP** it was **triple-positive** (**ER+/PR+/CTNNB1+**).
- When comparing among the **most common combinations**, the **duo-positive ER+/PR+** displayed the **most favorable outcome** in both **ENOC** and **NSMP** (P<0.001), **regardless** of **CTNNB1**.

Most frequent biomarker combinations



Multivariable Analysis



Adjusted for age, stage, and grade.
*P<0.05 **P<0.01 ***P<0.001

Conclusions

The **clear separation** of **prognosis** in this large cohort supports **further risk stratification**, especially within **NSMP.**

Hormone receptor targeting may be better than traditional platinum-based chemotherapies in **ER+/PR+ NSMP**

More work to identify targetable features in **hormone receptor-negative NSMP**

References
[1] Krämer et al. 2020
[2] Talhouk et al. 2017

Acknowledgments

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