Characterization of MammaPrint® UltraLow Risk tumors in more than 1400 patients from the real-world evidence FLEX study

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San Antonio Breast Cancer Symposium ® December 5-9, 2023

Presentation ID: PO1-02-11

Background

- MammaPrint is a 70-gene expression signature used to determine risk of distant recurrence for patients with all types of early-stage breast cancer.[1-3]
- Results from MINDACT, FOCUS, IKA, and STO-3 demonstrated that MammaPrint UltraLow Risk tumors are considered indolent in postmenopausal, node-negative patients.[4-7] These patients have excellent long-term survival outcomes with little to no endocrine treatment.[7]
- In MINDACT, premenopausal women with MammaPrint UltraLow Risk tumors had excellent 5-year Distant Metastasis Free Interval (97.1%).[4]
- These studies suggest that patients with an UltraLow Risk tumor are ideal candidates for treatment de-escalation, which has resulted in the inclusion of the UltraLow Risk result in NCCN guidelines.

Objective

To explore whether clinical factors alone may explain the indolent behavior of these tumors, we evaluated clinical characteristics of all patients with UltraLow Risk tumors from the real-world evidence FLEX study.

Methods

FLEX study

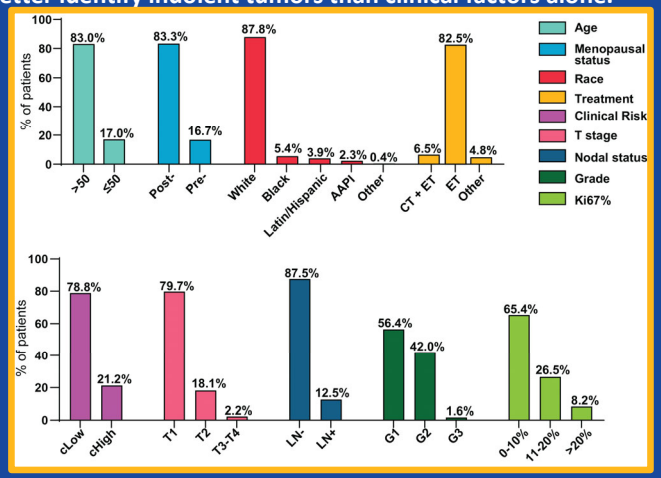
- FLEX (NCT03053193) is a prospective, observational registry study with 99 sites open in the United States, Canada, Greece, and Israel.
- Patients enrolled in FLEX have early-stage breast cancer and receive MammaPrint testing as standard of care (with or without BluePrint molecular subtyping), and consent to full transcriptome analysis and clinical data collection.
- Clinical data for this analysis was locked February 2023.
- Clinical risk was defined as low risk or high risk based on MINDACT Adjuvant Online criteria.[1-2]

Genomic testing

- MammaPrint is a gene expression signature of 70 genes that classifies tumors as having an UltraLow, Low, or High Risk of distant recurrence.

Conclusions

In this large real-world evidence study of patients with early-stage breast cancer, MammaPrint UltraLow Risk tumors can better identify indolent tumors than clinical factors alone.



Distribution of clinical characteristics among 1465 patients with UltraLow Risk tumors from FLEX. cLow = clinically low risk; cHigh = clinically high risk

- **At least 1 in 5 patients had high clinical risk but UltraLow genomic risk, and may be overtreated based on clinical characteristics alone.**
- **We report a substantial number of premenopausal patients with UltraLow Risk tumors, and these young women would be good candidates for treatment optimization.**

Results

- Among the 12,328 patients enrolled in FLEX, 1465 (11.9%) have UltraLow Risk tumors. All tumors with available BluePrint molecular subtyping were classified as Luminal A-Type.
- A majority of UltraLow Risk tumors were HR+HER2- (98.3%), few were HER2+ (n=19; 1.6%), and 1 patient had TNBC (0.1%) by IHC/FISH.
- Of patients with available clinical data, most patients self-reported as Caucasian (88%) and had clinically low risk breast cancer (79%).
- Notably 20% of patients with UltraLow Risk tumors exhibited overall clinical high risk features:
  - 17.0% were under 50 years of age
  - 16.7% were premenopausal
  - 20.1 % had tumors > 2 cm
  - 43.6% had grade 2-3 tumors
  - 34.6% had Ki67 tumor staining > 10%
- Among patients with treatment information (n=836):
  - 6.5% received a combination of chemotherapy with or without endocrine and HER2-targeted therapy
  - 82.5% received endocrine therapy
  - 4.8% received other treatment (endocrine with targeted therapy (CDK4/6), radiation alone, novel treatment regimen, or supporting agents)
  - 6.3% did not receive treatment.

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