A prospective, international, observational, real-world evidence database, and collaborative platform for Investigator-Initiated Studies in Early-Stage Breast Cancer tested with MammaPrint and BluePrint– the FLEX Study

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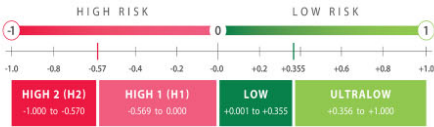
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SAN ANTONIO BREAST CANCER SYMPOSIUM

BACKGROUND

- Clinical trials provide improvements in the discovery, treatment, and quality of life for various diseases and disorders including breast cancer.
- The MammaPrint 70-gene signature along with BluePrint 80-gene molecular subtype signature are tools to provide such improvements in treatment planning.
- Historically, patient trial populations have not been racially diverse. Given recent publications supporting the ability of MammaPrint and BluePrint to identify genomic differences in outcomes of black women with breast cancer, the ongoing multi-center FLEX trial (NCT03053193) has proven to be an unparalleled source for improvement in breast cancer care.
- With a target of 30,000 enrolled patients, the collaborative research network within FLEX will use MammaPrint, BluePrint, full transcriptome, and clinical data to explore clinical and genomic differences in (sub)populations of interest to promote and advance precision medicine for patients with early-stage breast cancer

MAMMAPRINT INDEX

HIGH RISK — LOW RISK

-1 ___ 0 ___ 1

-1.0 -0.8 -0.57 -0.4 -0.2   0 +0.2 +0.355 +0.6 +0.8 +1.0

HIGH 2 (H2)	HIGH 1 (H1)	LOW	ULTRALOW
-1.000 to -0.570	-0.569 to 0.000	+0.001 to +0.355	+0.356 to +1.000

BLUEPRINT SUBTYPES

BASAL-TYPE	HER2-TYPE	LUMINAL-TYPE
HighRisk Basal-type (ER-)	Low Risk HER2-type	Low Risk Luminal-type A
High Risk Basal-type (ER+)	High Risk HER2-type	UltraLow Risk Luminal-type A
		High Risk 1 Luminal-type B
		High Risk 2 Luminal-type B

WHOLE GENOME EXPRESSION

> 800 CLINICAL DATA POINTS

99 FLEX SITES ACROSS 5 COUNTRIES *11 NCI INSTITUTES

40 ABSTRACTS & PRESENTATIONS

42 ACTIVE SUBSTUDIES

> 400 ACTIVE RESEARCHERS

METHODS

- FLEX is the first of its kind to link clinical data with full transcriptome data in breast cancer.
- It is a prospective, observational trial that enrolls patients who are ≥ 18 years old with histologically proven stage I-III breast cancer with up to 3 positive lymph nodes.
- Eligibility for study enrollment include standard of care MammaPrint testing with or without BluePrint and consent to clinically annotated full transcriptome data collection.
- The study's infrastructure facilitates the generation of hypotheses for targeted sub-studies that are important for breast cancer management.
- The FLEX network fosters collaboration with 99 active sites, including US, Canada, Greece, and Israel.
- All proposed substudies are reviewed and approved by both internal and external research and scientific review committees.
- Since launching in April 2017, 14,981 patients have been enrolled including those who have been historically underrepresented in trials (Black n =1032; Latin n= 373; AAPI n =276)
- 43 investigator initiated sub-studies have been approved and are in progress on a varied number of approaches like MammaPrint/ Blueprint clinical utilities, racial disparities, neoadjuvant treatment planning in ER+, and or HER2+ breast cancer with 31 abstracts accepted in national and international congresses.
- Five ongoing sub-studies within FLEX address differences in underlying biology and treatment response/management among Black, Latina, and Asian American patients with early-stage breast cancer. These studies provide a broader understanding of how differential gene expression patterns, identified with MammaPrint and BluePrint, are unique to racial/ethnic groups and can impact treatment outcomes.
- Overall, the FLEX study strives to use MammaPrint, BluePrint, and newly developed immune signatures, like ImPrint, along with full transcriptome data to improve precision medicine in early-stage breast cancer

For More Information

References:
1. https://clinicaltrials.gov/ct2/show/NCT03053193?term=flex&cond=breast&draw=2&rank=2

For more information about the FLEX Study please reach out to us at FLEX@Agendia.com
FLEX Study NCT03053193

ETHNIC DISPARITIES
- >10,000 patients
- 5 active studies
- 8 presentations
- Active investigators working group

ER+ BASAL TUMORS
- >1,000 patients
- 5 active studies
- 5 presentations
- Initiating investigators working group

HER2-LOW TUMORS
- >3,000 patients
- 1 new study
- Active investigators working group

LOBULAR TUMORS
- >800 patients
- 2 active studies
- Presentations
- Active investigators working group

INVESTIGATOR INITIATED SUBSTUDIES

FLEX serves as a vehicle to convey impactful research to the public at an accelerated rate. All physicians participating in FLEX may submit concept proposals for new research IIS. All proposals are reviewed through a committee of fellow FLEX physicians to confirm scientific need and impact in the breast cancer field. Once approved, analysis will be performed using data from the FLEX database to address their specific research aims.

INVESTIGATOR INITIATED STUDY EXAMPLES:

New Molecular Signatures
- ImPrint immune signature in 10,000 early-stage breast cancer patients from the real-world FLEX database. SABCS 2022 #PD9-08
- Investigation of a genomic signature for transcription factor MAF gene amplification and lack of bisphosphonate benefit in early breast cancer. ASCO 2022

Neoadjuvant Therapy & Surgery
- Identification of transcriptional changes with MammaPrint and BluePrint in early-stage breast cancer after neoadjuvant chemotherapy. ASCO 2022
- Impact of neoadjuvant endocrine therapy on tumor transcriptome in patients with early-stage breast cancer from the FLEX trial. SABCS 2022 #P5-09-02
- Molecular profiles & treatment recommendations for invasive lobular carcinoma in a real-world prospective breast cancer registry. ASCO 2020
- High Risk breast cancer genes at 8q22-24 and their role in over 5000 patients evaluated with MammaPrint risk of recurrence assay. ASCO 2020

Optimizing Therapy Strategies
- Differential gene expression and clinical utility of MammaPrint and BluePrint in male breast cancer patients. SABCS 2020
- BluePrint reclassification of HER2+ by IHC tumors. ASCO 2020

Breast Cancer Subtypes
- Distribution of breast cancer molecular subtypes within receptor classifications: Lessons from the I-SPY2 Trial and FLEX Registry. ASCO 2022
- Defining transcriptomic profiles of early-stage mucinous breast cancers: A FLEX sub study. ASCO 2022
- Defining transcriptomic profiles of breast cancer with early lymph node metastases: a FLEX database sub-study. SABCS 2021
- Using BluePrint to elucidate the molecular heterogeneity of triple negative breast cancers. SABCS 2021

Cancer Disparities: Biological, Genetic, Socioeconomic
- Whole transcriptomic analysis of HR+ breast cancer in Black women classified as basal-type by BluePrint. ASCO 2022
- MammaPrint and BluePrint identify genomic differences in HR+ HER2-breast cancers from young Black and White women. SABCS 2021
- Disparities within Luminal breast cancer: clinical and molecular features of African American and non-Hispanic White patients. ASCO 2021
- Molecular profiles and clinical-pathological features of Asian early-stage breast cancer patients. SABCS 2020

EMEA Sites