I-SPY2 Endocrine Optimization Pilot (EOP): Neoadjuvant Lasofoxifene in Molecularly Selected Patients with hormone receptor positive (HR+)/HER2 negative (HER2-) Stage 2/3 Breast Cancer

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Introduction

- EOP is an I-SPY2 sub-study designed to test the tolerability and impact of novel endocrine-based strategies in stage 2/3 breast cancer (BC) patients (pts) predicted to have lower benefit from chemotherapy.
- Lasofoxifene, a selective estrogen receptor modulator (SERM) has shown activity in HR+ /HER2- metastatic BC.
- Only feasibility, advance events, 3-week Ki67 and MRI data are presented here.

Methods

- Pts with HR+/HER2-, MammaPrint (MP) low risk, Stage 2/3 BC were enrolled, along with those with MP High1 tumor, clinically node-negative tumors.
- Pts received lasofoxifene 5mg daily for six 28-day cycles, continuing until the day before surgery.
- Premenopausal pts received ovarian function suppression (OFS) starting cycle 2.
- Baseline (BL) and 3-wk on-treatment biopsies were performed, with Breast MRIs at BL (T0), 3 weeks (T1), 12 weeks (T2), and 6 months (T3).
- The primary endpoint was feasibility (≥75% of patients completing ≥75% study therapy).

Results

- From 3/2023 to 5/2024, 20 pts were enrolled.
- 16 pts(80%) completed ≥ 75% of therapy.
- Median age 50.5 years, with 50% premenopausal, and 5% male. 75% pts had cT2 tumors. Median ER expression was > 95%. 60% of pts were cN-. 80% pts had MP low risk tumors and 85% of tumors were Sensitivity to Endocrine Therapy (SET) index high.
- Ki67 expression was suppressed (Table 1).
- The median BL and 3-week MRI FTV was 8.4 ccs and 6.2 ccs, respectively with a median percent change of -13.3 %.
- Adverse events were all grade 1-2. Most common AEs include hot flushes (65%), constipation (40%), fatigue (40%), and nausea (25%).

Table 1.Ki67 expression at baseline, and 3-week time point

	All Patients (n=20)[1]	Premenopausal (n=10)	Postmenopausal (n=9)
Median Ki67 expression			
BL (range)	10.0% (1.0-40.0%)	12.5% (1.0-40.0%)	10.0% (3.0-33.0%)
3-week	4.0% (1.0-18.0%)	3.0% (1.0-15.0%)	6.0% (1.0-18.0%)
Number of pts with Ki67 expression <10% at 3-week[2]	14	7	6
Number of pts with Ki67 expression <2.7% at 3-week	6	4	2

1. One male pt; 2. One male pt had Ki67<10% at 3-week time point

Conclusion

- The primary end point is met. At data analysis, 80% pts completed ≥ 75% of therapy.
- Neoadjuvant lasofoxifene therapy is well tolerated and demonstrates activity in suppressing 3-week Ki67 in both pre and postmenopausal pts with HR+/HER2- early-stage BC.
- Early Ki67 suppression in premenopausal pts was seen in the absence of OFS.
- Full results including pre-operative MRI, surgical pathology results will be presented at a future meeting.