Differential early response to neoadjuvant endocrine therapy (NET) in lobular versus non-lobular breast cancer on the Endocrine Optimization Pilot (EOP) of the I-SPY2 Trial

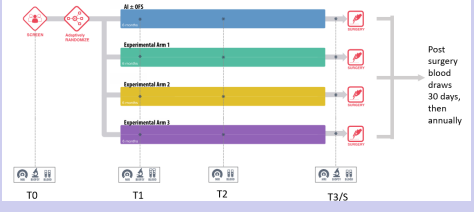
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BACKGROUND

- Invasive lobular carcinoma (ILC) has unique estrogen receptor (ER) signaling, response to systemic therapy, and imaging features.
- We evaluated differences in 3-week Ki67 and features on magnetic resonance imaging (MRI) after novel endocrine based neoadjuvant therapy in **lobular versus non-lobular cases** on the I-SPY2 EOP Trial.

STUDY DESIGN

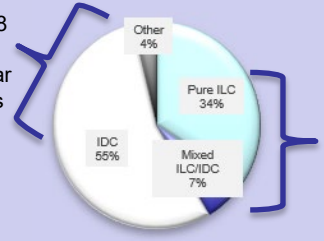


- EOP is a prospective, randomized, multicenter, neoadjuvant platform trial for patients with MammaPrint Low Risk or Mammaprint H1 ER+HER2 negative stage II-III breast cancer
- At 3 weeks from treatment start (T1) patients undergo repeat core biopsy for **Ki67**, and **MRI for functional tumor volume (FTV), a biomarker of treatment response**
- Treatment arms:
  - novel oral SERDS with or without CDK4/6 inhibitors, aromatase inhibitors, and SERMs with or without ovarian function suppression in pre-menopausal patients

Patients with lobular histology had similar early reduction in Ki67 after NET but higher residual pre-operative functional tumor volume on MRI than those with non-lobular histology

RESULTS

n=148 non-lobular cases



n=105 lobular cases

- Study cohort n= 253
- Mean age 53.3 years
- 63.8% grade 2 tumors
- 86.5% MammaPrint Low risk tumors

	Baseline (T0)			3 weeks (T1)		
	Lobular (n=105)	Non-lobular (n=148)	P-value	Lobular (n=105)	Non-lobular (n=148)	P-value
Mammaprint Low	92.4%	83.4%	**0.035**			
Ki67 (mean, %, SD)	11.2% (12.8)	16.4% (14.4)	**0.0038**	3.4% (5.1)	5.4% (8.7)	**0.0415**
Ki67 <10% (proportion)	60.4%	39.3%	**0.001**	88.6%	79.7%	0.08
	Baseline (T0)			24 weeks (T3, pre-surgical)		
MRI FTV (mean cc^3, SD)	21 (20.8)	16.3 (27.2)	0.134	5.7 (7.1)	3.8 (5.4)	**0.034**

CONCLUSIONS

- Lobular cases had lower baseline Ki67, and similar rates of decrease in Ki67 after 3 weeks of NET than non-lobular cases.
- Despite this, mean FTV after completion of 6 months of NET was higher in lobular tumors. These findings may reflect differences in early versus late indicators of response to NET, or differential response patterns by histology.
- Ongoing work includes central assessment of Ki67 from surgical specimens and evaluation of surgical outcomes including breast conservation rates by histologic subtype.

ACKNOWLEDGEMENTS

This research was supported by the NCI of the National Institutes of Health (NIH) P01CA210961. The authors wish to acknowledge the generous support of the 501(c)3 study sponsors, Quantum Leap Healthcare Collaborative and express appreciation for the ongoing support for the I-SPY program from the Safeway Foundation, the William K. Bowes, Jr. Foundation, Give Breast Cancer the Boot, and the Breast Cancer Research Foundation. Sincere thanks to our patient advocates and patients who volunteered to participate in the I-SPY trials.