

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



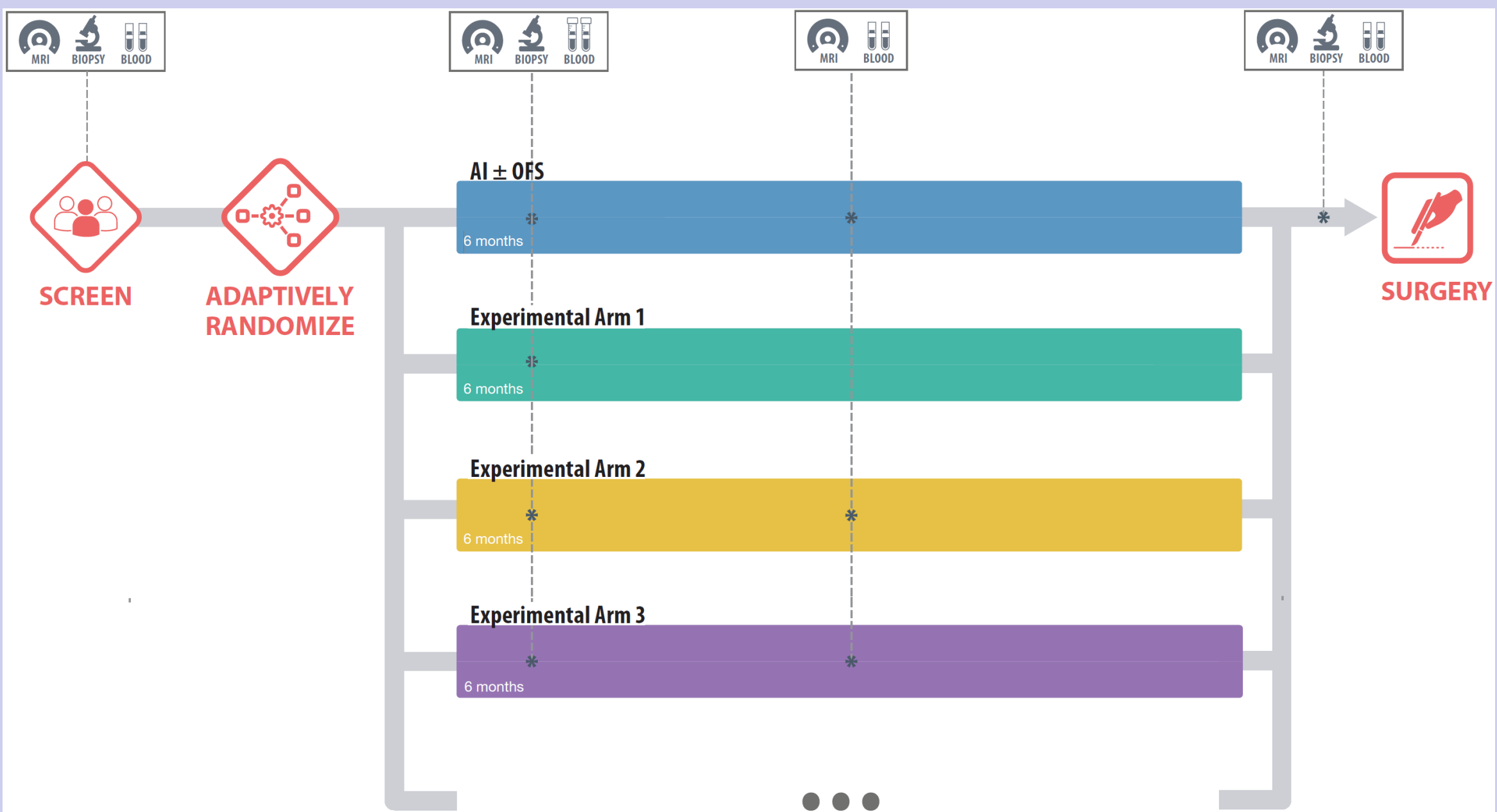
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BACKGROUND

- 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.

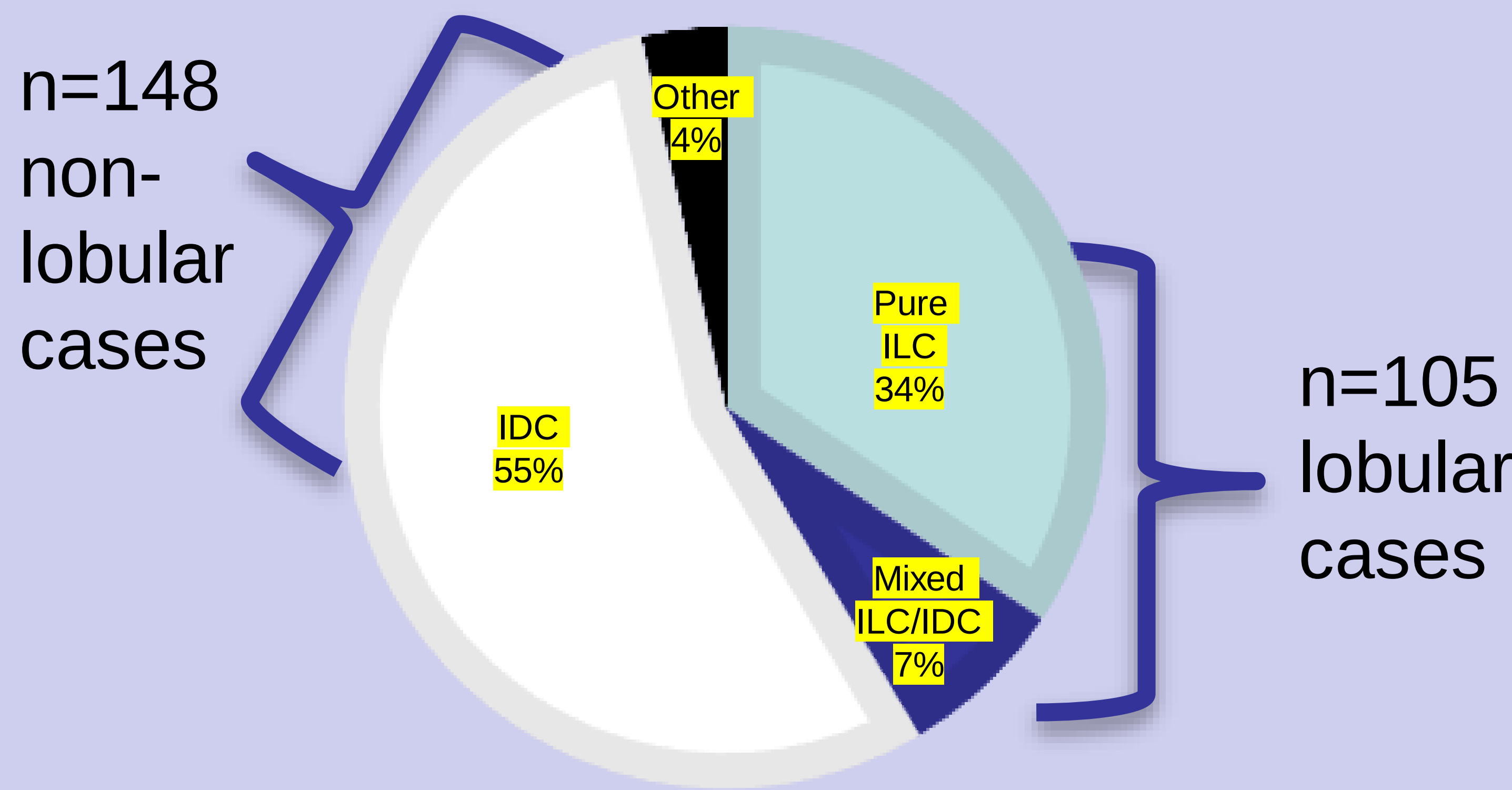
STUDY DESIGN



- EOP is a prospective, randomized, multicenter, neoadjuvant platform trial for patients with MammaPrint Low Risk or Mammprint 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



- 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 cc³, 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.

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