Overview of patients with invasive lobular breast carcinoma included in the post-mortem tissue donation program, UPTIDER

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LAY ABSTRACT

Of all patients with breast cancer (BC), 15% get diagnosed with invasive lobular BC (ILC). During disease progression, distant tumors will lose or gain certain characteristics in comparison to the primary tumor, as well as between distant tumors. This is driven by alterations at a DNA level, the local tissue environment and treatment. This is referred to as tumor heterogeneity. This heterogeneity is responsible for therapeutic resistance and disease progression. To study and tackle this, there is a scientific and clinical need to better characterize heterogeneity in metastatic BC. One way to achieve this is through post-mortem tissue donation programs, a procedure in which many tumor samples are collected after death for the purpose of translational research. Here, we present the findings of patients with metastatic ILC from included in our post-mortem tissue donation program, UPTIDER (NCT04531696).

INTRODUCTION & OBJECTIVE

Invasive lobular carcinoma (ILC)
- Up to 15% of invasive breast cancer diagnoses
- Distinct clinicopathological features in comparison to no-special type breast cancer:
  - Older age at diagnosis
  - Higher stage at diagnosis
  - More lymph node positivity
  - Diffuse metastatic pattern with i.e. more often bone and brain metastases[1,2,3]

Objectives:
- Histopathological characterisation of metastatic ILC

RESULTS

At diagnosis
- Median age 52 years (range 37 – 80 years)
- Average distant recurrence free survival 163 months (range 55 – 358 months)
- Average time between metastatic spread and death 44.8 months (range: 15 – 83 months)

Survival data
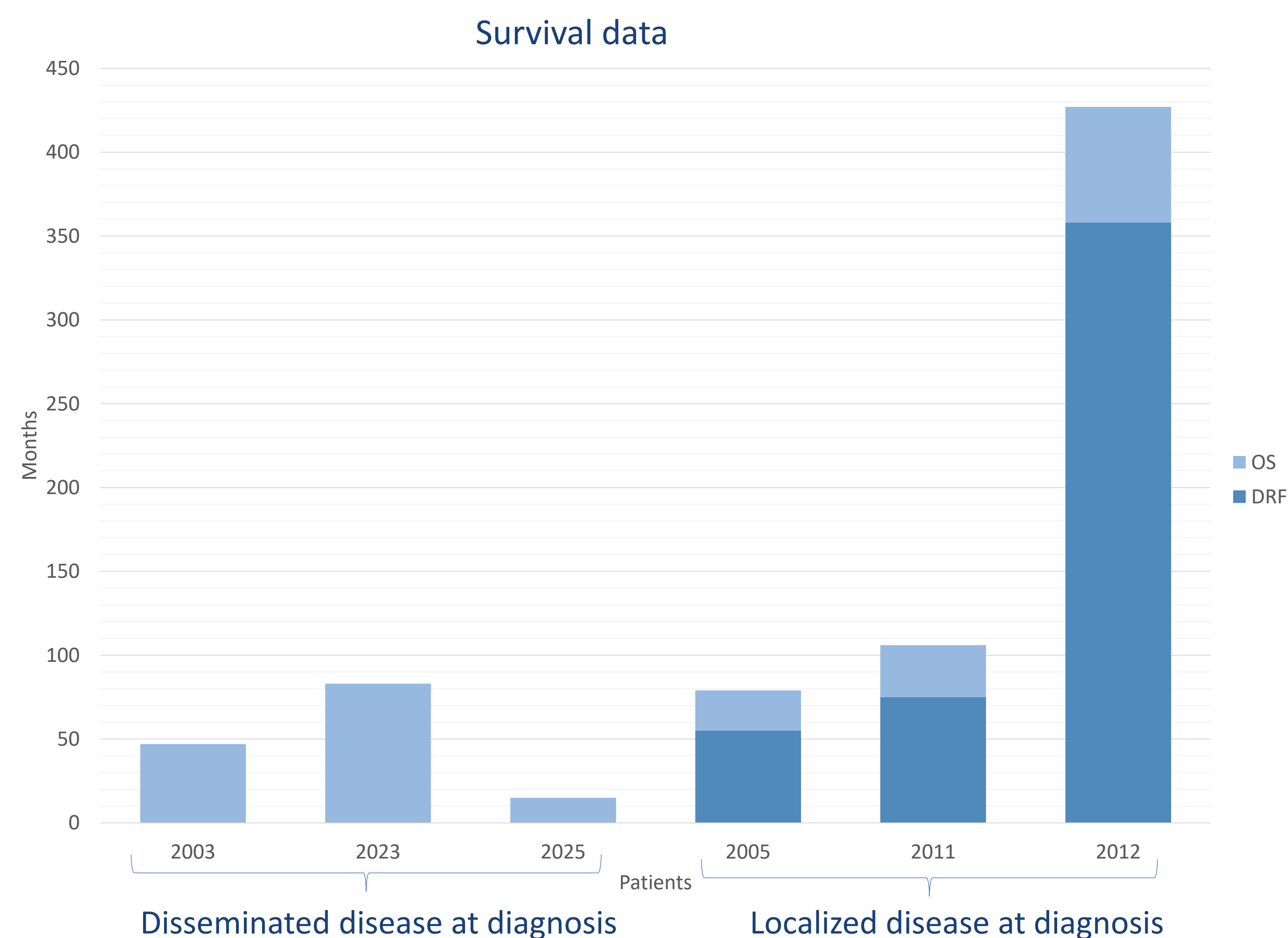
Disseminated disease at diagnosis — Localized disease at diagnosis

Post-mortem samples
- Total number of 175 samples with a median of 26 lesions per patient (range: 22 – 47 lesions)
- Samples retrieved from a median of 8 different sites (range 4 – 16 sites)
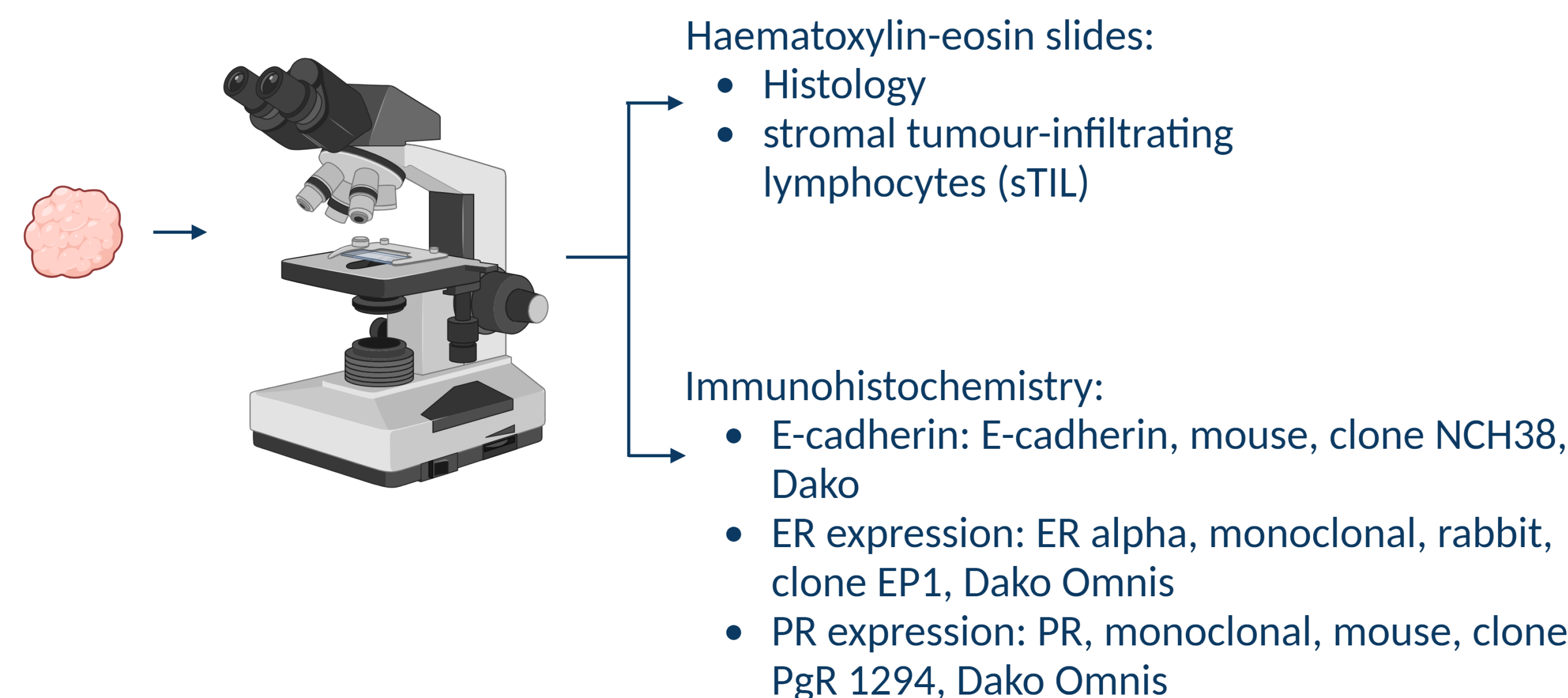
Markers	Results
sTIL	ILC in a metastastic setting shows a low level of sTIL with a mean level of 1,67% (range: 0 – 13.33%)

E-cadherin

Patient	2003	2005	2011	2012	2023	2025	
Preserved	0%	0%	0%	0%	0%	0%	All samples show absent and/or aberrant E-cadherin staining pattern
Aberrant	58,33%	0%	0%	0%	0%	28,57%	
Absent	41,67%	100%	100%	100%	100%	71,43%	

ER

Patient	2003	2005	2011	2012	2023	2025	
Positive	96%	100%	70,83%	94,44%	100%	60%	Positive ER status in on average 86,33% of 90 samples (range: 71 - 100%) of patients with primary ER positive breast cancer
Negative	4,35%	0%	29,17%	5,56%	0%	40%	

PR

Patient	2003	2005	2011	2012	2023	2025	
Positive	0%	0%	0%	63,16%	100%	50%	PR status maintained in on average 42,63% of samples (range 0 – 100%) of 5 patients with primary PR positive breast cancer PR status was maintained in all metastatic samples from the one patient with primary PR negative breast cancer
Negative	100%	100%	100%	36,84%	0%	50%	

PATIENTS & METHODS

1. Selection of patients diagnosed with primary, pure ILC included in post-mortem tissue donation program, UPTIDER

UPTIDER ID	HR status	Age at diagnosis	DRFS (months)	OS (months)	Autopsy
2003	ER+/PR+	80 years	0	47	Yes
2005	ER+/PR-	53 years	55	79	Yes
2011	ER+/PR+	51 years	75	106	Yes
2012	ER+/PR+	37 years	358	427	Yes
2023	ER+/PR+	70 years	0	83	Yes
2025	ER+/PR+	44 years	0	15	Yes
2031	ER+/PR+	83 years	0	/	No
2039	ER-/PR-	83 years	0	20	Yes

☐ = included in this study so far

2. Centralized pathological review of primary and post-mortem samples

Haematoxylin-eosin slides:
- Histology
- stromal tumour-infiltrating lymphocytes (sTIL)

Immunohistochemistry:
- E-cadherin: E-cadherin, mouse, clone NCH38, Dako
- ER expression: ER alpha, monoclonal, rabbit, clone EP1, Dako Omnis
- PR expression: PR, monoclonal, mouse, clone PgR 1294, Dako Omnis

DRFS = distant reccurence free survival
OS = overall survival
HR status = hormone receptor status
ER = estrogen receptor
PR = progesteron receptor

CONCLUSIONS

- Post-mortem metastatic samples of primary ILC show very low sTIL levels and most lesions retain estrogen receptor status.
- In accordance with literature, E-cadherin staining pattern is absent and/or aberrant.
- Additionally, we will:
  - Join forces with University of Pittsburg Rapid Autopsy Program to better characterize ILC in a metastatic setting using various omics techniques.
  - Compare metastatic samples found at autopsy to lesions detected on pre- or post-mortem imaging

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