



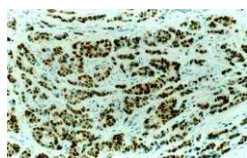
Carcinoma della mammella 2017

Unit of Investigative Clinical Oncology
Istituto di Candiolo (IRCCS)

Breast Cancer Targets and Subtypes

Major Biological Classes of Breast Cancer

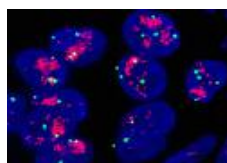
Potentially endocrine dependent



ER and/or PgR
Expression

- Endocrine therapies
 - Tamoxifen
 - Aromatase inhibitors
 - Fulvestrant
- ET + Biological Therapy
 - Everolimus
 - CDK 4/6 inhibitors

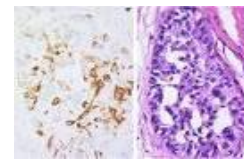
HER2-driven



HER2 amplification/
Overexpression

- Trastuzumab
- Pertuzumab
- T-DM1
- Lapatinib

Triple-negative

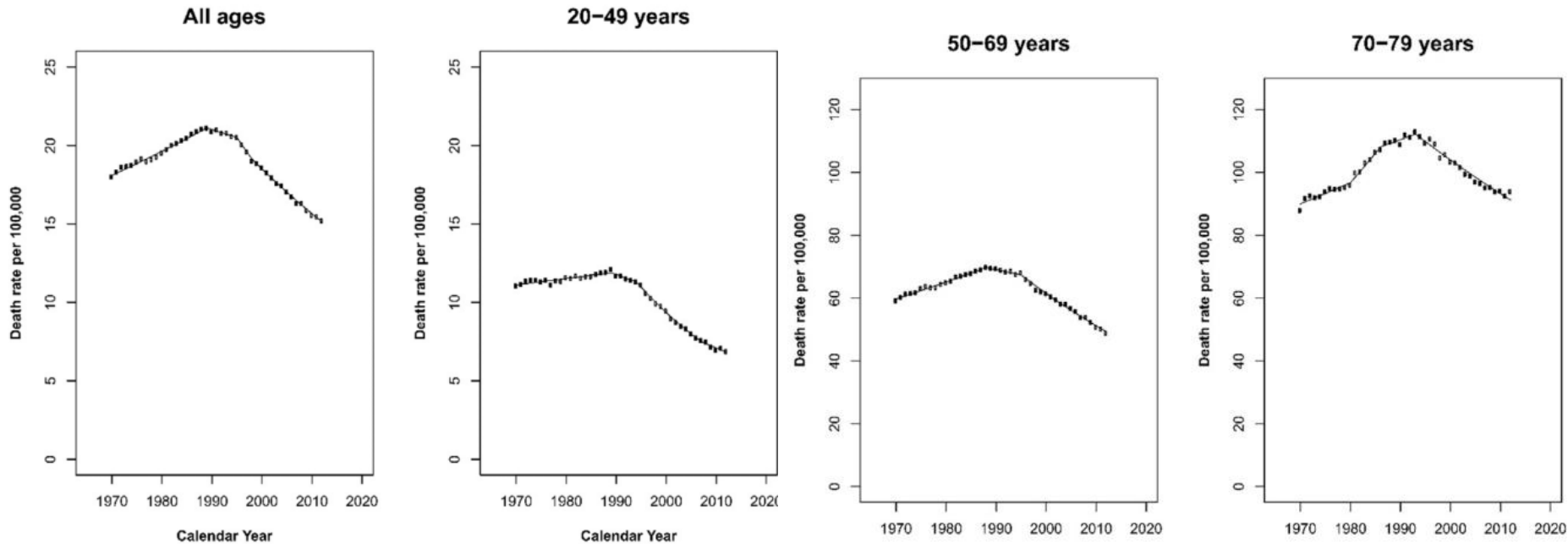


ER, PgR and HER2
Negative
Include BRCA1 mutated



Find a suitable
Target!

Reduction in mortality



Cairolì et al, The Breast epub 2017 EU data

Achievement in operable breast cancer

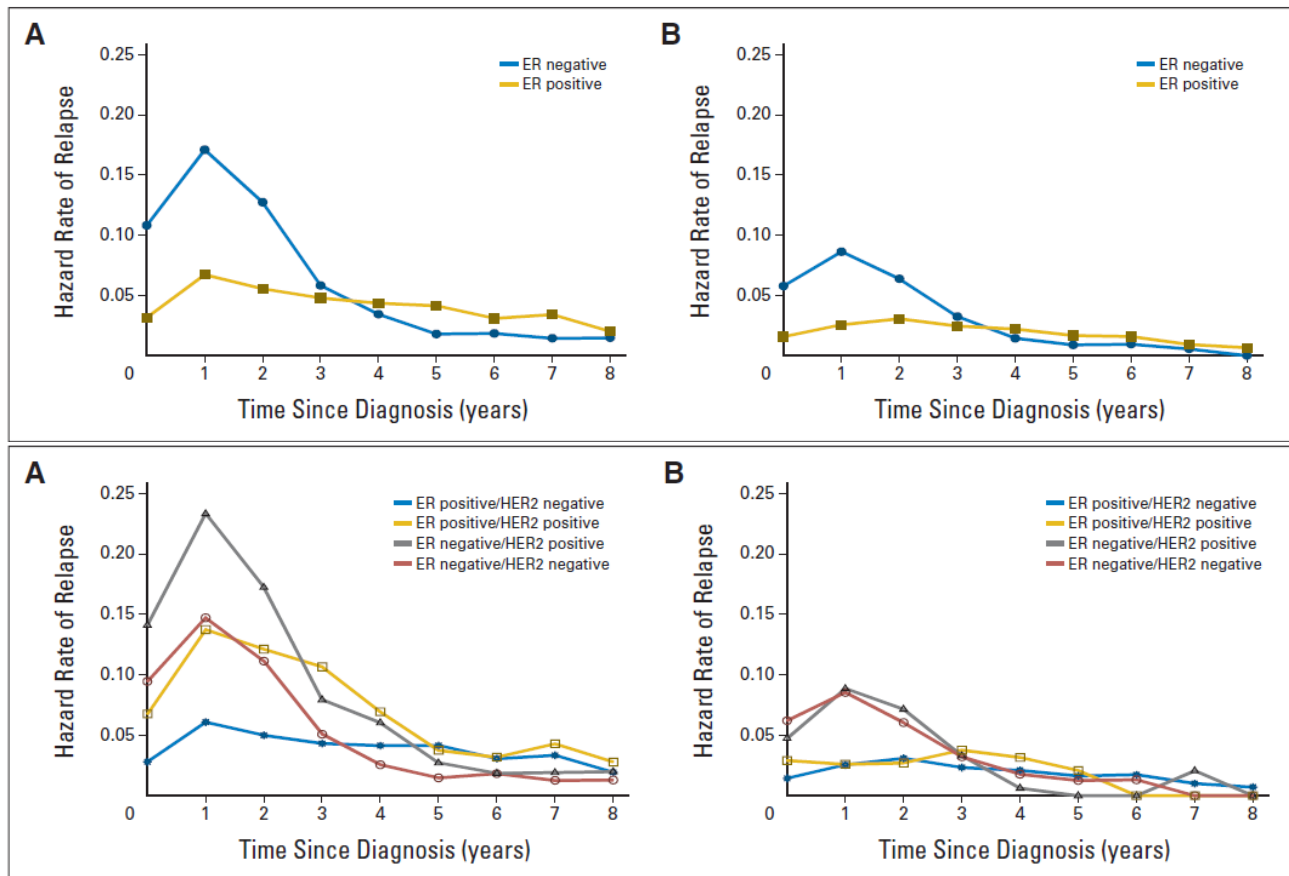


Fig 3. Hazard rate of relapse according to tumor subtype in (A) cohort 1 and (B) cohort 2. ER, estrogen receptor; HER2, human epidermal growth factor receptor 2.

New paradigms in adjuvant endocrine therapy



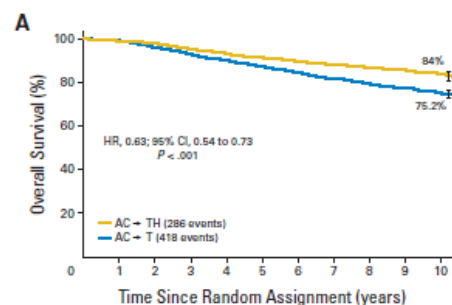
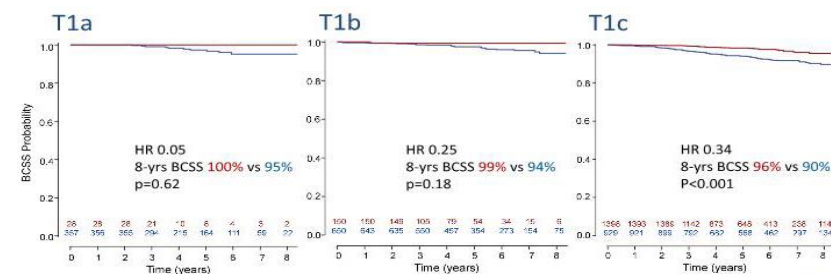
Adjuvant Chemotherapy and HER2 targeting

Trastuzumab + Chemotherapy + Pertuzumab

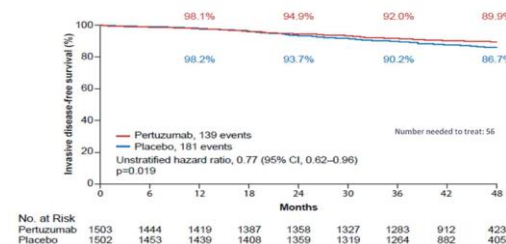
Trastuzumab + Chemotherapy

Depotentiate chemotherapy?

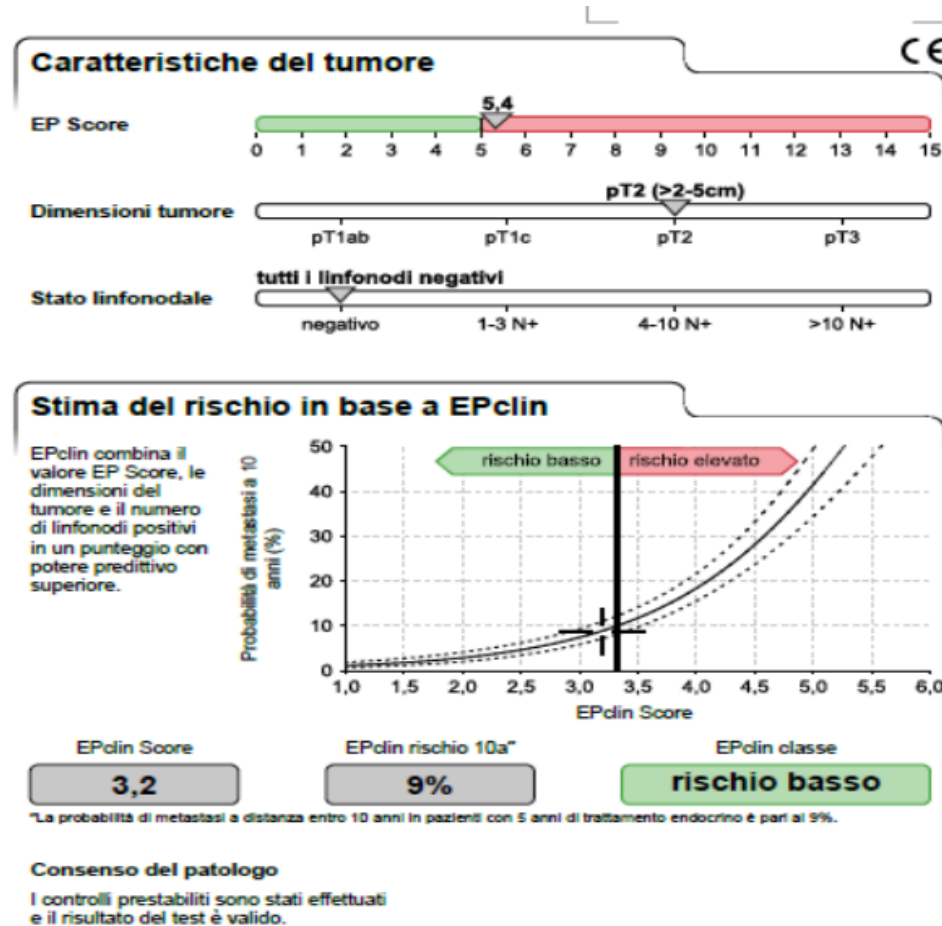
Stage I			Stage II		Stage III	
pT1a	pT1b	pT1c	N0	N+	Operable	Non Operable



APHINITY: Node-positive Subgroup



Gene Expression Profiling Allows Better Selection of Candidates to Chemotherapy in ER+/HER2- patients



ER+/HER2- metastatic breast cancer: current standards

Study	Treatment	ORR	CBR	Median DFS (m)	Median OS (m)
	Letrozole+Placebo	34.7%	70.3%	14.5	N.A.
	Letrozole+Plac	27.5%	72.8%	14.7	33
	Let. or Ana. + Placebo	34.5%	71.5%	14.7	N.A
FALCON	Anastrozole + Placebo	44.9%	74.1%	13.8	N.R.
	Fulvestrant + Placebo	46.1%	78.3%	16.6	N.R.
SWOG S0226	Anastrozole	22%	70%	13.5	41.3
	Anastrozole + Fulvestrant	27%	73%	15	47.7**

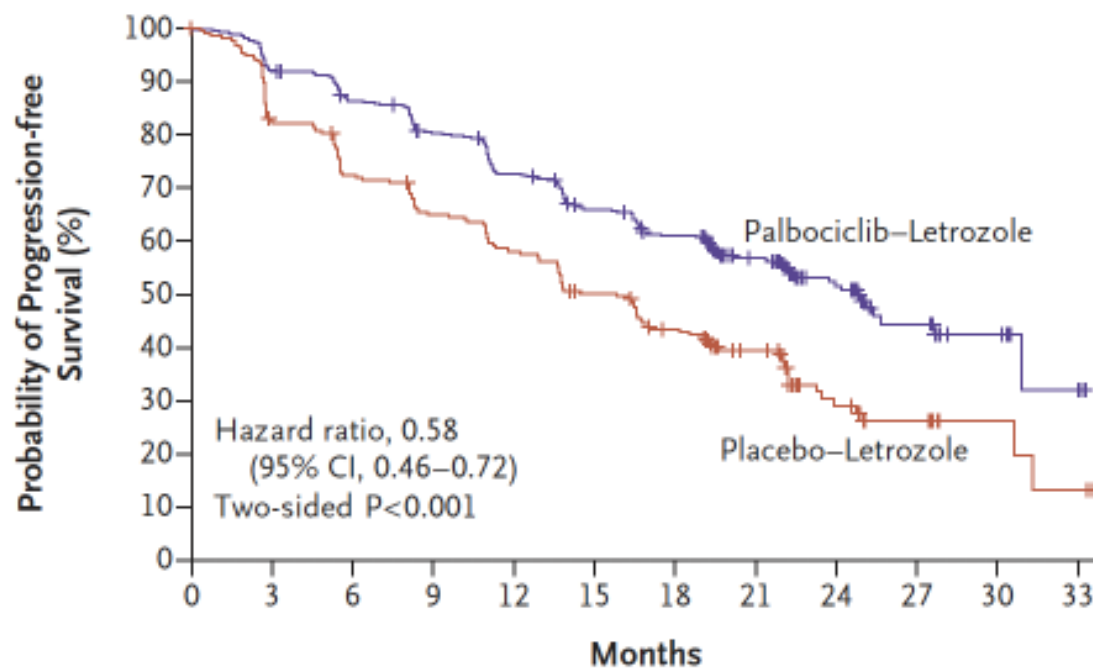
*Difference is not statistically significant

**Difference is statistically significant

Abbreviations: N.A, not available; N.R. not reached

How the PFS curves looks like

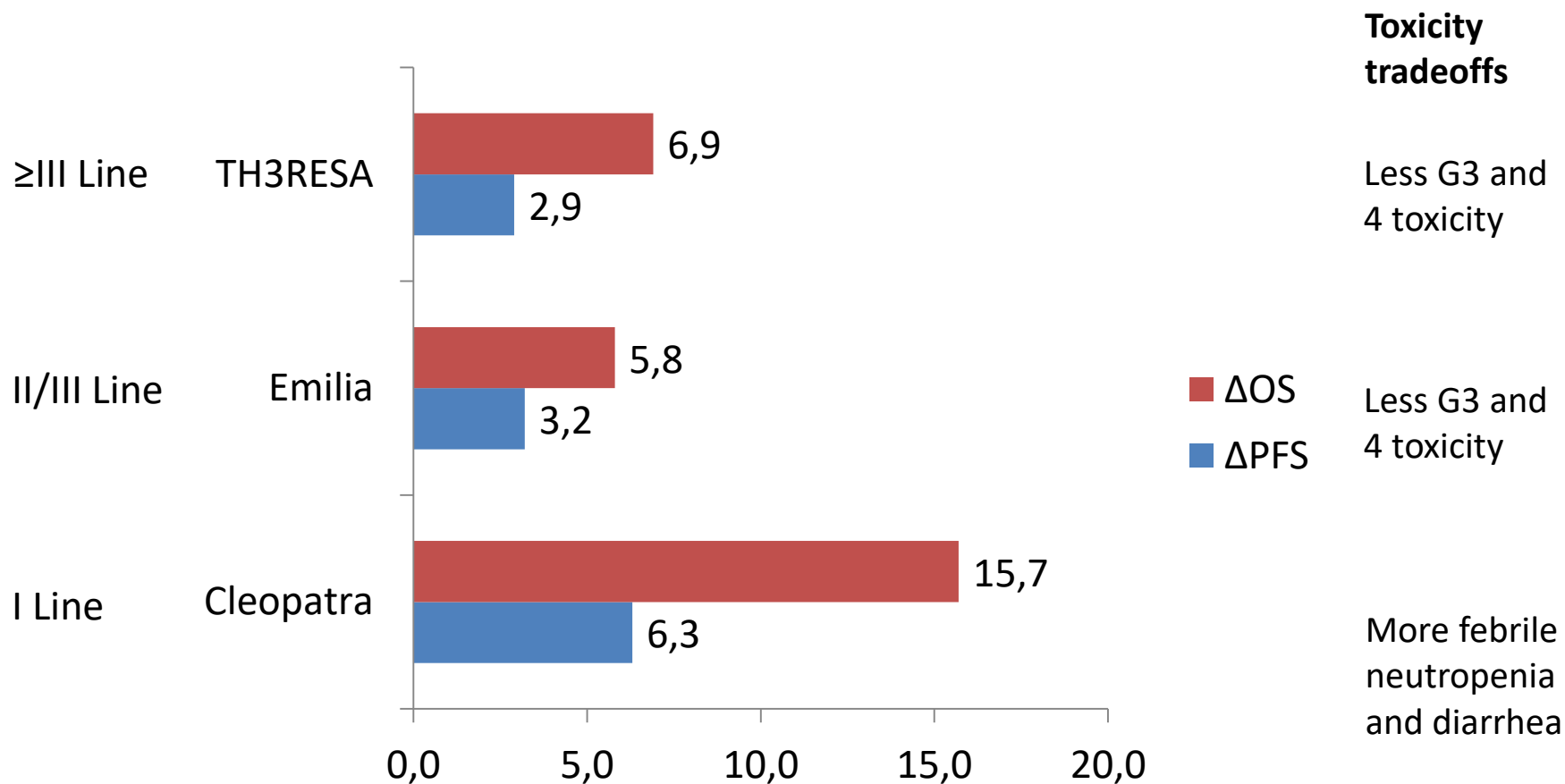
A Investigator Assessment



No. at Risk

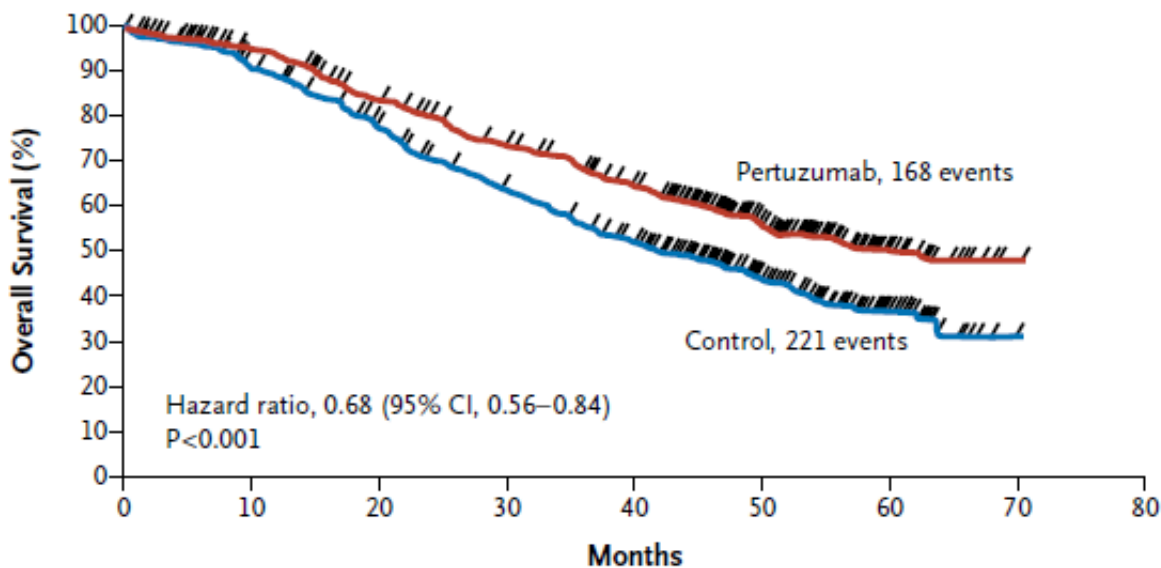
Palbociclib-Letrozole	444	395	360	328	295	263	238	154	69	29	10	2
Placebo-Letrozole	222	171	148	131	116	98	81	54	22	12	4	2

Metastatic HER2-positive disease



Overall Survival in the Cleopatra Study

A Overall Survival

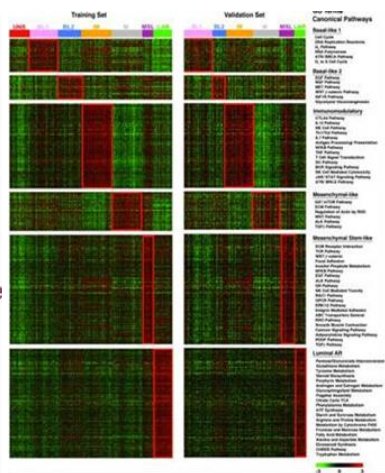


No. at Risk

Pertuzumab	402	371	318	268	226	104	28	1	0
Control	406	350	289	230	179	91	23	0	0

The Enigma of Triple-Negative Breast Cancer

BL1 Basal-like 1
BL2 Basal-like 2
IM Immunomodulatory
M Mesenchymal
MSL Mesenchymal Stem-like
LAR Luminal/AR



Type	MARKER	Study	Drug
PARPi	BRCA1/2 mut.	BRAVO	Niraparib
	BRCA1/2 mut.	EMBRACA	BMN 673
	BRCA1/2 mut.	OLYMPIAD	Olaparib
Checkpoint Inhib.	PD-L1+	Keynote-012	Pembrolizumab
	PD-L1-/+	KEYNOTE-086	Pembrolizumab
	PD-L1-/+	KEYNOTE-119	Pembrolizumab
	PD-L1-/+	IMpassion130	Atezolizumab
	PD-L1 -/+	NEOTRIP	Atezolizumab
	PD-L1 -/+	NCT02489448	MEDI4736
Antiandrogens	AR +/-	NCT00468715	Bicalutamide
	AR +/-	NCT01889238	Enzalutamide
	AR +	NCT01990209	Oteronel
	Apocrine	NCT01842321	Abiraterone

Take-home message

- ❑ Targeted therapy, where feasible, is associated with improved survival in early and metastatic disease
- ❑ On average, women with early or metastatic breast cancer will be on treatment for longer periods of time and will experience more chronic, rather than acute, side effects.