

*GIM, riunione annuale.
Le sfide della ricerca sul carcinoma mammario*

Sottogruppi Her2-positivi e triplo negativi
in stadio precoce.

LE NUOVE PROPOSTE

Trieste, 24-25 Settembre 2019

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U.O. Oncologia Medica 2
Ospedale Policlinico S.Martino, Genova





Early Her2+ e TN: le nuove proposte

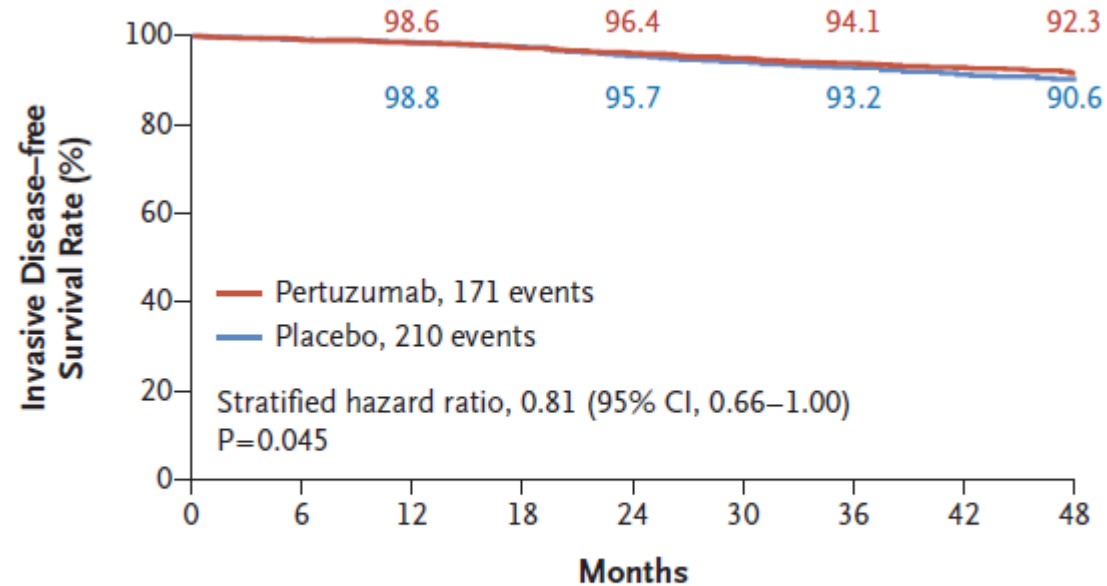
A retrospective analysis of secondary data use for the assessment of clinically meaningful PRognostic factOrs in a real-world cohort of women with HER2 Positive eaRLY breast cancer treated in the adjuvant setting.

The PROPERLY project

Dr. Lorenzo Gerratana

- Approximately 15-20% of all Breast Cancers are HER2-positive
- HER2 overexpression characterizes a more aggressive disease but is a positive predictive factor of response to target therapies
- A year of trastuzumab, starting with chemotherapy, is the standard adjuvant treatment for the HER2+ Early Breast Cancer
- Escalation and de-escalation strategies should be developed on the basis of the different risk of recurrence
- Pertuzumab plus trastuzumab significantly improved survival in metastatic disease and nearly doubled the rate pCR in the neoadjuvant setting

Intention-to-Treat Population



No. at Risk		0	6	12	18	24	30	36	42	48
Pertuzumab	2400	2309	2275	2236	2199	2153	2101	1687	879	
Placebo	2404	2335	2312	2274	2215	2168	2108	1674	866	

Dual HER2 blockade gave more nuanced results in the adjuvant setting but some interesting data were observed in high-risk patients

- Based on these results, it is gaining momentum the hypothesis that the adjuvant treatment of early HER2-positive breast cancer could be personalized and of variable intensity according to the risk of relapse (low, medium, high).

Primary objective

- To analyze the prognostic impact of clinical-pathological features in a multicenter real-world cohort of HER2+ Breast Cancer patients treated with trastuzumab in the adjuvant setting (OS and DFS)

Secondary objectives

- To evaluate the impact of lymphocyte ratios (LMR and NLR) on OS and DFS
- To define a decisional nomogram through the definition of a composite risk score based on the combination of the identified prognostic factors



Inclusion Criteria

- Female patients ≥ 18 years
- Patients with early Breast Cancer diagnosis from 2004 to 2018
- Histologically proven diagnosis of HER2 positive Breast Cancer
- Patients treated with conservative or radical surgery
- Having received a trastuzumab-based adjuvant treatment

Exclusion Criteria

- Diagnosis of any secondary malignancy within the previous 3 years, except for adequately treated basal cell or squamous cell skin cancer, or carcinoma in situ of the cervix
- Evidence of stage IV disease at diagnosis
- Having received a primary/neoadjuvant therapy

For each enrolled patient we chose to collect the following data:

- Clinical characteristics patient-related: age and menopausal state;
- Pathological features disease-related: Tumour Grade, HR status, HER2 status (IHC and/or –ISH assessment), Proliferation Rate (expressed as Ki67 protein expression)
- Types of surgery (conservative vs radical)
- Tumour Stage at diagnosis (according to TNM System)
- Adjuvant therapeutic history
- Recurrences (specifically, time and site – loco-regional or distant- of first recurrence after the adjuvant treatment) and survival



Early Her2+ e TN: le nuove proposte

The prognostic role of tumor-associated macrophages in early Breast cancer patients

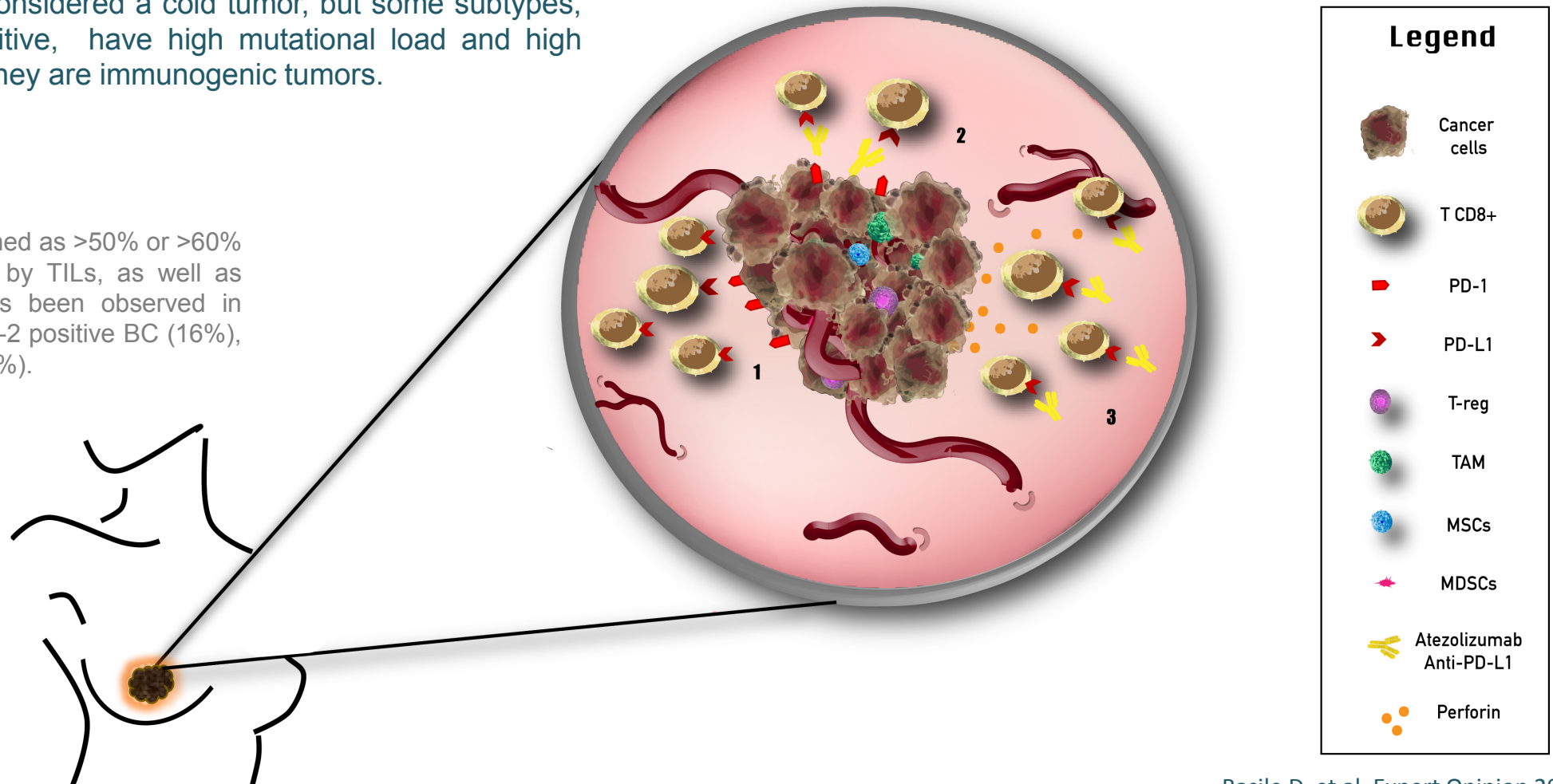
The AMBeR study

Dr. ssa Debora Basile

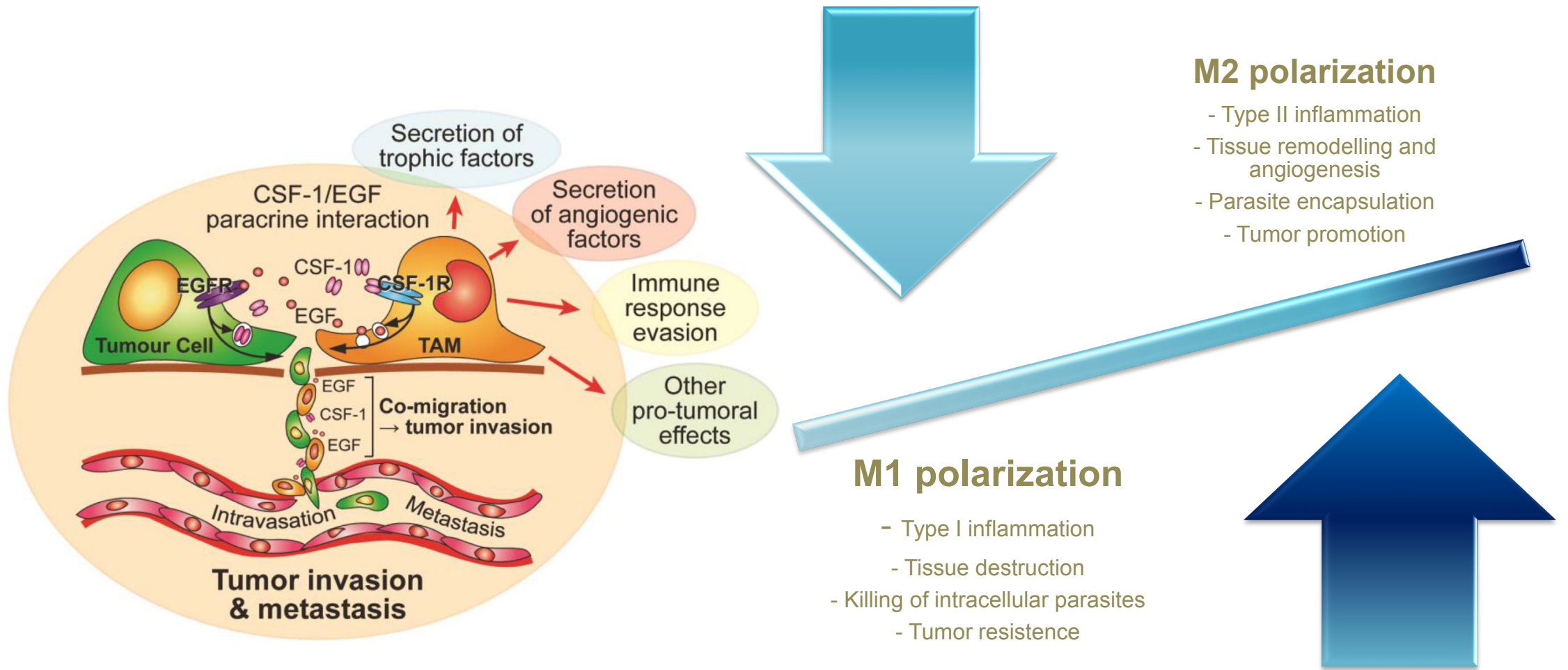
Immune system and breast cancer

Usually BC has been considered a cold tumor, but some subtypes, TNBC and HER-2 positive, have high mutational load and high immune infiltrate, thus they are immunogenic tumors.

High TILs presence, defined as >50% or >60% of tumor area occupied by TILs, as well as high mutational rate has been observed in TNBC (20%) and in HER-2 positive BC (16%), less in ER-positive BC (6%).



A functional link between immune-suppression and cancer



The prognostic role of tumor-Associated Macrophages in early BrEast cancer patients

To analyze the within-patient modification of the M1/M2 ratio between baseline biopsy and tissue sample collected, during in a multicenter real-world cohort of BC patients treated with neoadjuvant treatment.



Primary endpoint:

- Effect size

Association of tumor infiltrating macrophages, M1/M2 ratio with prognosis in neoadjuvant BC patients



Secondary endpoints:

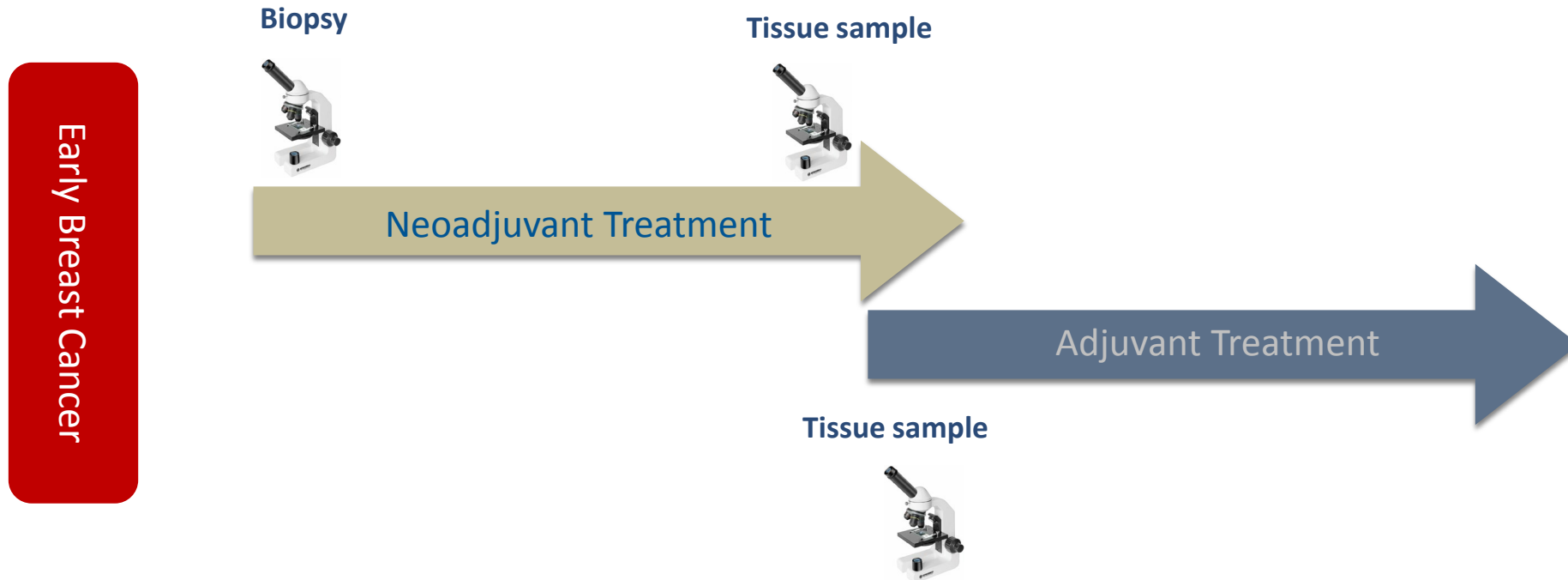
- DFS
- OS

Association of tumor infiltrating macrophages, M1/M2 ratio with prognosis in adjuvant BC patients

Association between TILs with macrophages and PD-L1

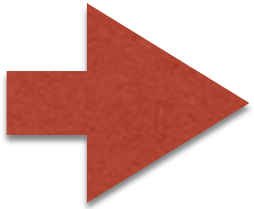
Correlation between immune TME and circulating biomarkers, such as MLR and LDH

The prognostic role of tumor-Associated Macrophages in early BrEast cancerR patients



Twelve months for the recruitment of the cohorts (from 01.01.2010 to 30.06.2018)

The prognostic role of tumor-Associated Macrophages in early BrEast cancer patients



- Voluntary, written, dated and signed Informed Consent
- Enrollment with the assignment of a digits ID code
- Collection of anagrafic data, demographic data, medical history, follow-up through RedCap Cloud
- Send tissue samples to IRCCS Aviano

Fill out our participation form



Prof. Fabio Puglisi

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Early Her2+ e TN: le nuove proposte

The compassionate Use Program T-DM1 for Her2-positive breast cancer patients with residual of disease after neoadjuvant treatment

Prof. Lucia Del Mastro
Dr. Francesca Poggio

INCLUSION CRITERIA

- **Adult patient \geq 18 years of age, HER2-positive breast cancer**
- **Histologically confirmed invasive breast carcinoma with clinical stage at presentation: T1–4, N0–3, M0 (Note: Patients with T1a/bN0 tumors will not be eligible)**
- **Completion of preoperative systemic chemotherapy and HER2-directed treatment including trastuzumab and a taxane-based therapy**
- **Pathological evidence of residual invasive carcinoma in the breast or axillary lymph nodes following completion of preoperative therapy**
- **An interval of no more than 12 weeks between the date of surgery and the date of initiation of T-DM1**
- Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1
- Adequate cardiopulmonary, hematologic, renal and liver function
- Screening Left ventricular ejection fraction (LVEF) \geq 50%
- No Stage IV (metastatic) breast cancer
- No evidence of clinically evident gross residual or recurrent disease following preoperative therapy and surgery
- No progressive disease during preoperative systemic therapy
- No current NCI CTCAE (Version 4.0) Grade \geq 2 peripheral neuropathy
- No prior treatment with trastuzumab emtansine
- No known active liver disease, e.g. due to HBV, HCV, autoimmune hepatic disorders, or sclerosing cholangitis
- Current severe, uncontrolled systemic disease (e.g., clinically significant cardiovascular, pulmonary, or metabolic disease; wound healing disorders; ulcers)

Fill out the participation form

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ESMO BREAST CANCER

Annual Congress

The Role of Dose-Dense Adjuvant Chemotherapy in HER2-positive Early Breast Cancer Patients before and after the Introduction of Trastuzumab: Exploratory Analysis of the GIM2 Trial

Matteo Lambertini, Marco Bruzzone, Francesca Poggio, Benedetta Conte, Evandro de Azambuja, Giancarlo Bisagni, Michele De Laurentiis, Sabino De Placido, Francesco Cognetti, Lucia Del Mastro

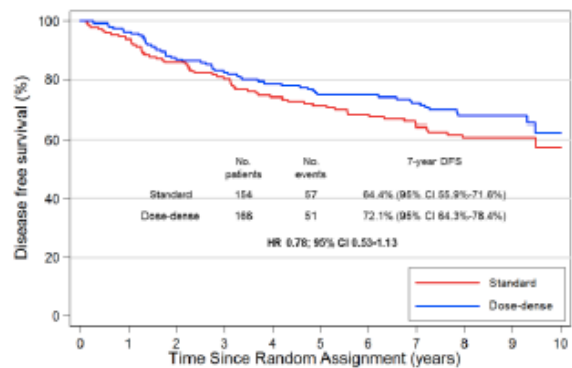
On behalf of the GIM2 investigators



RESULTS: DISEASE-FREE SURVIVAL

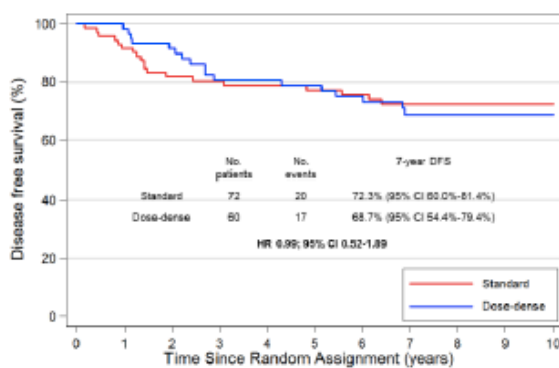
Median follow-up = 8.1 years (IQR, 7.0 - 9.3 years)

HER2-positive NO Trastuzumab



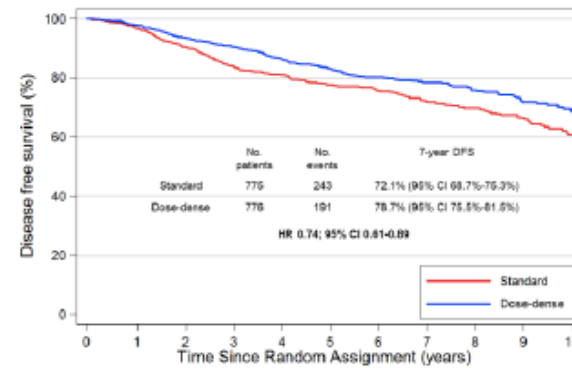
Number at risk	0	1	2	3	4	5	6	7	8	9	10
Standard	154	138	125	115	105	100	91	80	60	30	13
Dose-dense	166	156	139	130	123	115	108	99	65	35	11

HER2-positive Trastuzumab



Number at risk	0	1	2	3	4	5	6	7	8	9	10
Standard	72	66	55	52	51	49	48	35	22	13	9
Dose-dense	80	59	52	44	44	43	41	29	21	13	5

HER2-negative/unknown



Number at risk	0	1	2	3	4	5	6	7	8	9	10
Standard	775	725	662	606	578	548	520	430	300	170	80
Dose-dense	776	742	692	659	622	590	558	488	344	189	82

STUDY CONCLUSIONS

- Dose-dense chemotherapy was associated with a significant improvement in both disease-free survival and overall survival in high-risk early breast cancer patients with HER2-negative/unknown disease
- No significant interaction was observed between HER2 status, trastuzumab therapy and the effect of dose-dense chemotherapy
- In the subgroup of patients with HER2-positive early breast cancer treated with adjuvant trastuzumab, the benefit of dose-dense chemotherapy appeared to be smaller