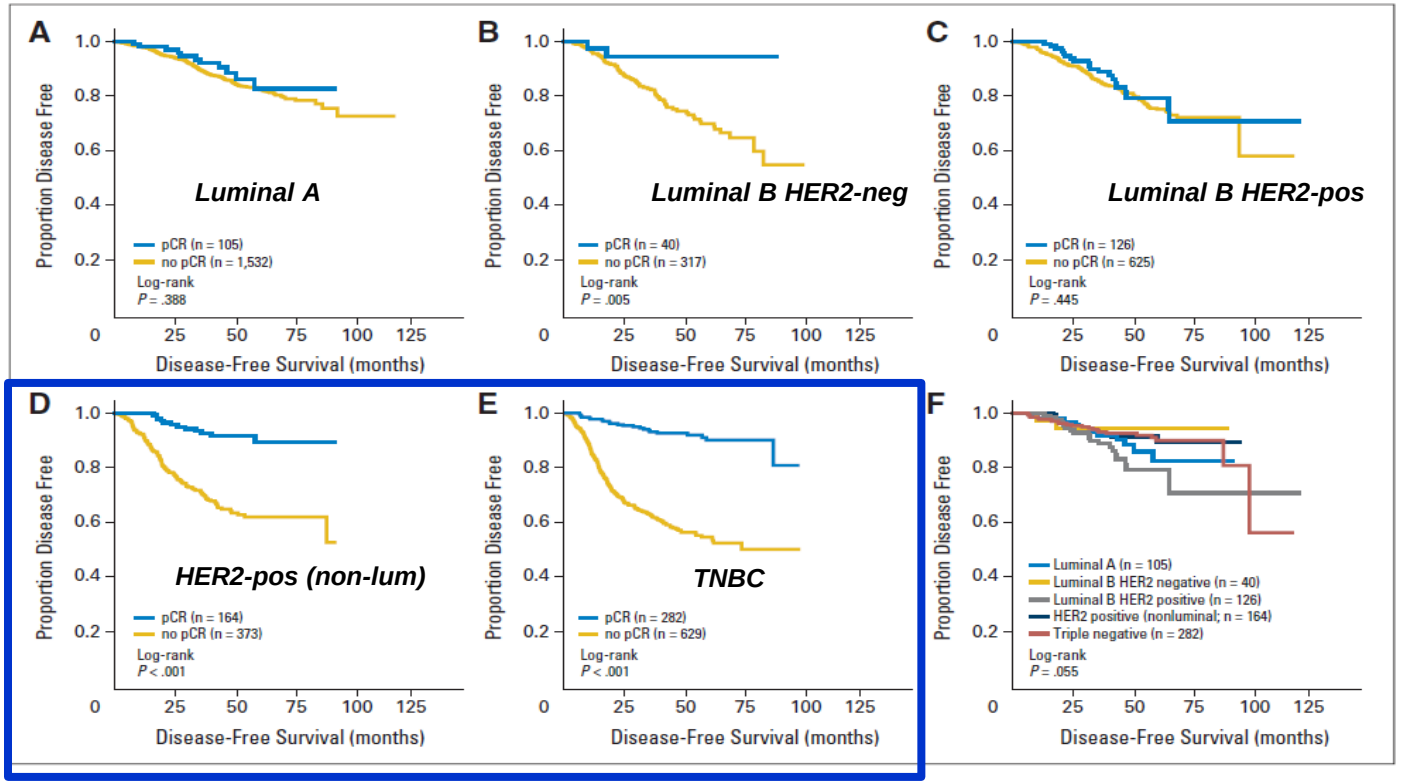
# Neoadjuvante Therapie – was bringt uns die Zukunft

## Jahrestreffen GBG
## Frankfurt 24.2.2021

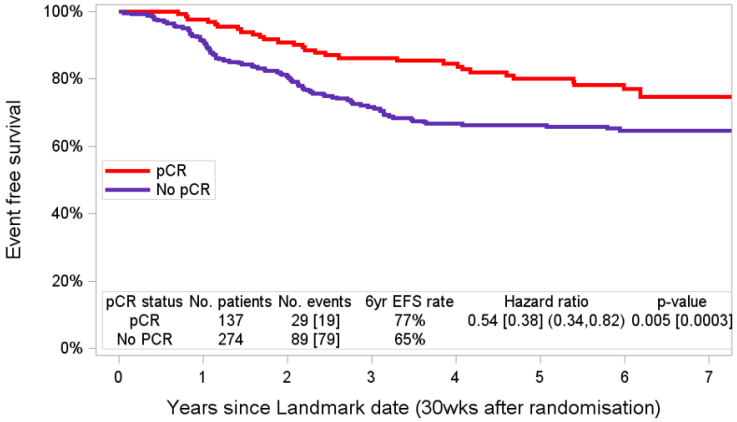
Jens Huober
Brustzentrum
Kantonsspital St Gallen

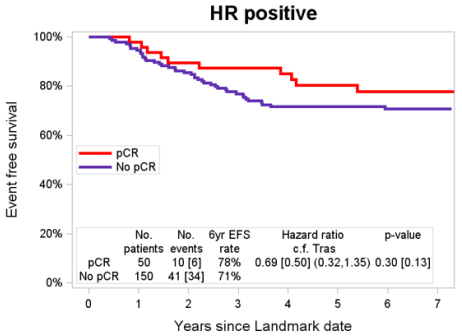
# Prognose in Abhängigkeit der pCR bei unterschiedlichen Subtypen (N=4193)

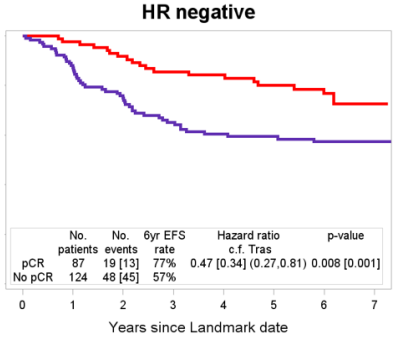



von Minckwitz G et al, J Clin Oncol 2012

# NeoALTTO Studie - Bessere Prognose bei pCR




Huober J et al. Eur J Cancer 2019

# Metaanalyse G3-G7 – Rezidive nach pCR

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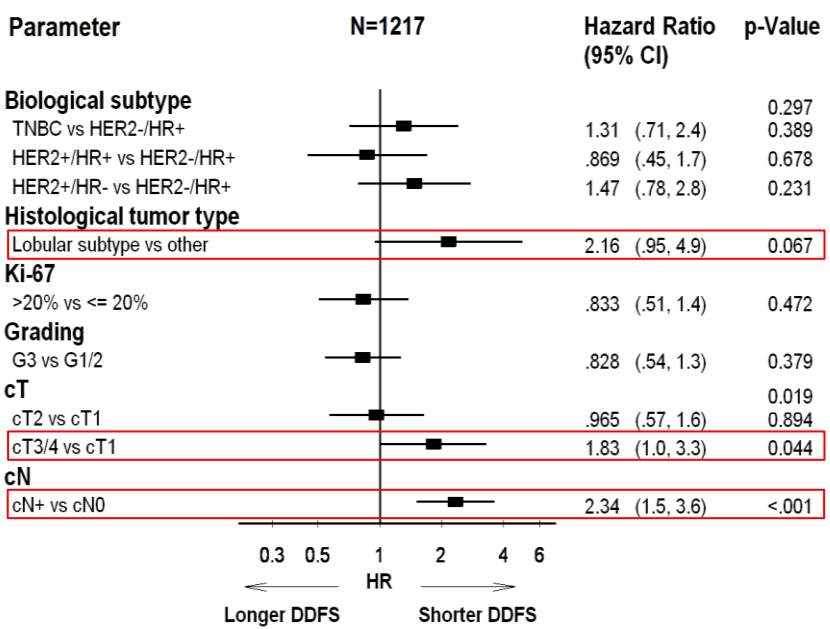
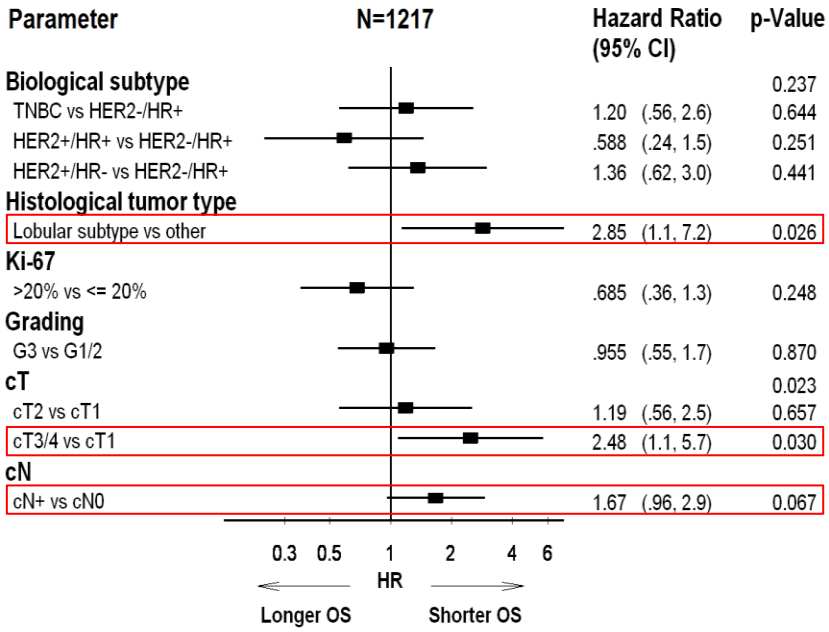
## DDFS




## OS




Huober J et al ESMO Breast 2019

# Five year survival rates for DFS, DDFS and OS

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| | DFS rate (95% CI) | DDFS rate (95% CI) | OS rate (95% CI) |
|---|---|---|---|
| **Overall** | **86.8% (85.2%, 88.3%)** | **90.6% (89.1%, 91.8%)** | **93.7% (92.4%, 94.7%)** |
| **Subgroups** | | | |
| cT1 | 87.3% (82.9%, 90.7%) | 90.4% (86.3%, 93.4%) | 95.1% (92.0%, 97.1%) |
| cT2 | 88.0% (85.9%, 89.8%) | 91.7% (89.9%, 93.2%) | 94.3% (92.7%, 95.5%) |
| **cT3/4** | **82.4% (77.9%, 86.0%)** | **86.8% (82.8%, 89.9%)** | **90.7% (87.1%, 93.3%)** |
| cN0 | 90.4% (88.4%, 92.2%) | 93.4% (91.6%, 94.9%) | 95.5% (93.9%, 96.7%) |
| cN+ | 82.7% (79.9%, 85.2%) | 87.3% (84.8%, 89.4%) | 91.6% (89.5%, 93.4%) |
| Lobular tumor type | 77.5% (65.3%, 85.8%) | 81.5% (69.5%, 89.1%) | 84.5% (73.0%, 91.4%) |
| Other tumor type | 87.2% (85.5%, 88.7%) | 90.9% (89.5%, 92.2%) | 94.1% (92.8%, 95.1%) |

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# Detection of ctDNA and CTCs after neoadjuvant chemotherapy is associated with disease recurrence in triple-negative breast cancer: preplanned analyses from trial BRE12-158

Milan Radovich[1], Guanglong Jiang[1], Bradley A. Hancock[1], Christopher Chitambar[2], Rita Nanda[3], Carla Falkson[4], Filipa C. Lynce[5], Christopher Gallagher[5], Claudine Isaacs[5], Marcelo Blaya[6], Elisavet Paplomata[7], Radhika Walling[8], Karen Daily[9], Reshma Mahtani[10], Michael A. Thompson[11], Robert Graham[12], Maureen E. Cooper[13], Dean C. Pavlick[13], Lee Albacker[13], Jeffrey Gregg[13,14], Jeffrey P. Solzak[1], Casey L. Bales[1], Erica Cantor[1], Fei Shen[1], Anna Maria V. Storniolo[1], Sunil Badve[1], Tarah J. Ballinger[1], Chun-Li Chang[15], Yuan Zhong[15], Cagri Savran[15], Kathy D. Miller[1], Bryan P. Schneider[1]

[1]Indiana University Simon Comprehensive Cancer Center, Indianapolis, IN, [2]Medical College of Wisconsin, Milwaukee, WI, [3]University of Chicago, Chicago, IL, [4]University of Alabama at Birmingham, Birmingham, AL, [5]Georgetown University, Washington, DC, [6]Memorial Healthcare System, Hollywood, FL, [7]Winship Cancer Institute of Emory University, Atlanta, GA, [8]Community Regional Cancer Care, Indianapolis, IN, [9]University of Florida, Gainesville, FL, [10]University of Miami, Miami, FL, [11]Aurora Health Care, Milwaukee, WI, [12]Erlanger Health System, Chattanooga, TN, [13]Foundation Medicine, Inc., Cambridge, MA, [14]University of California at Davis, Davis, CA, [15]Purdue University, West Lafayette, IN

SABCS 2019 GS5-02

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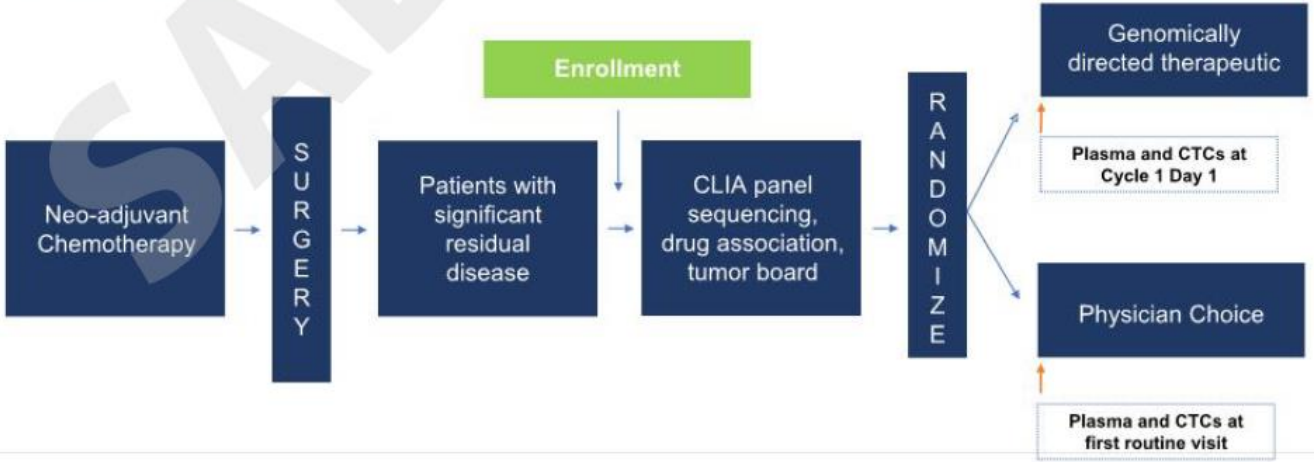
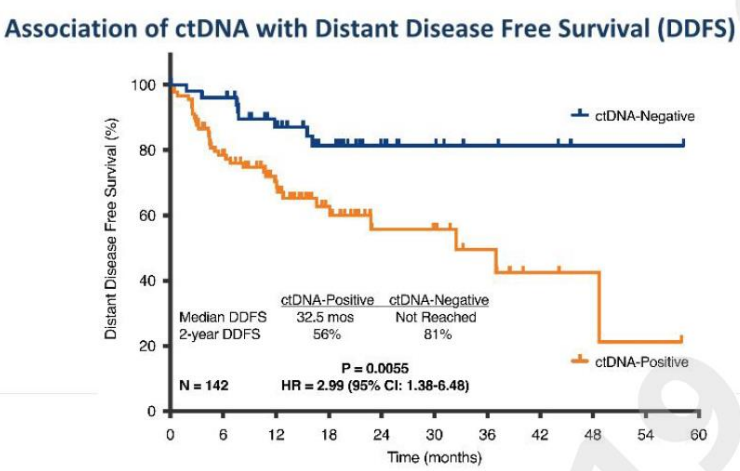
## **BRE12-158:** A phase II randomized control trial of genomically directed therapy after preoperative chemotherapy in patients with triple negative breast cancer

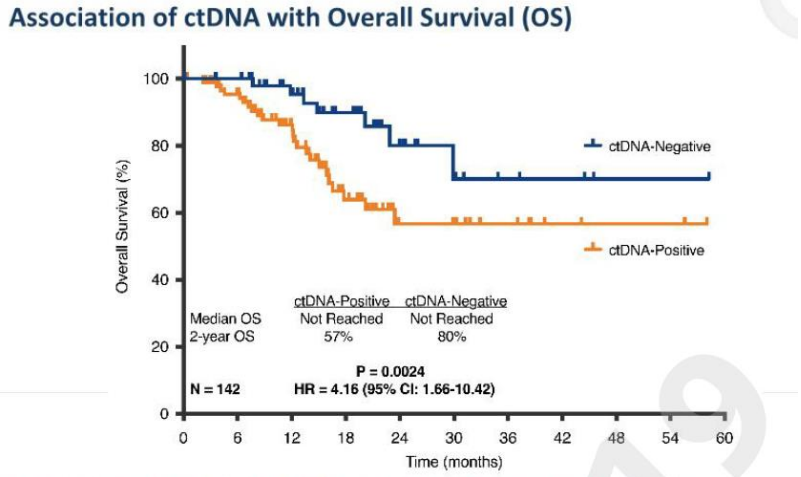



- Primary endpoint: 2-year DFS (N=196)

SABCS 2019 GS5-02

# Keine pCR nach neoadjuvanter Therapie
# Zusätzliche Prognoseabschätzung durch cDNA




Radovich M et al SABCS 2019

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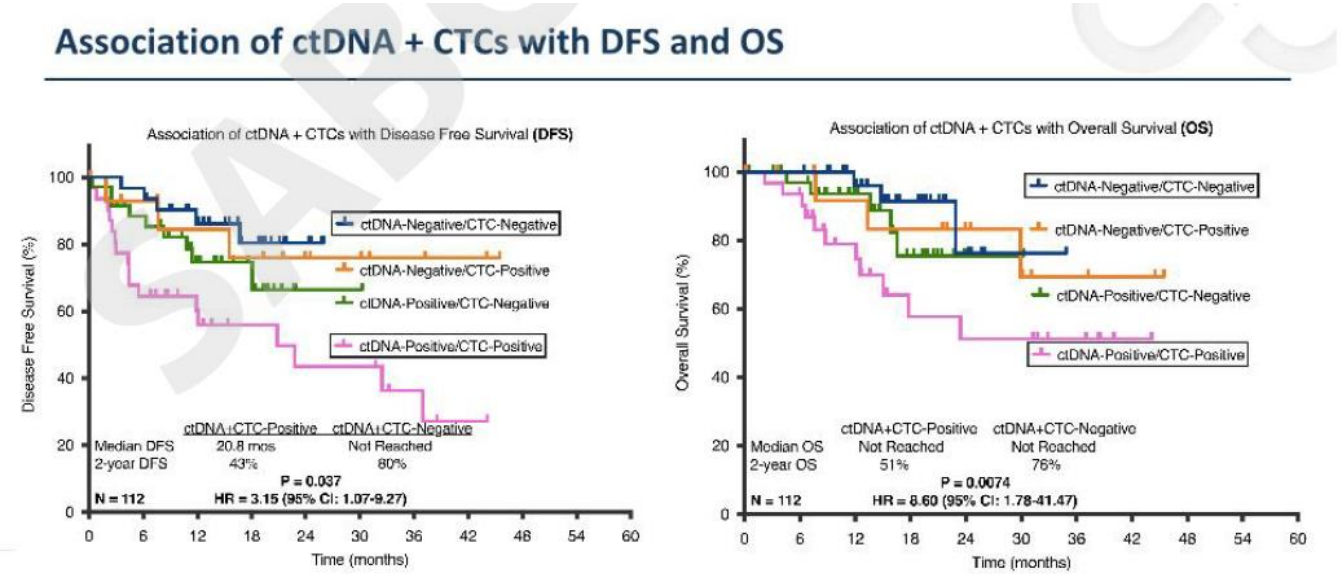


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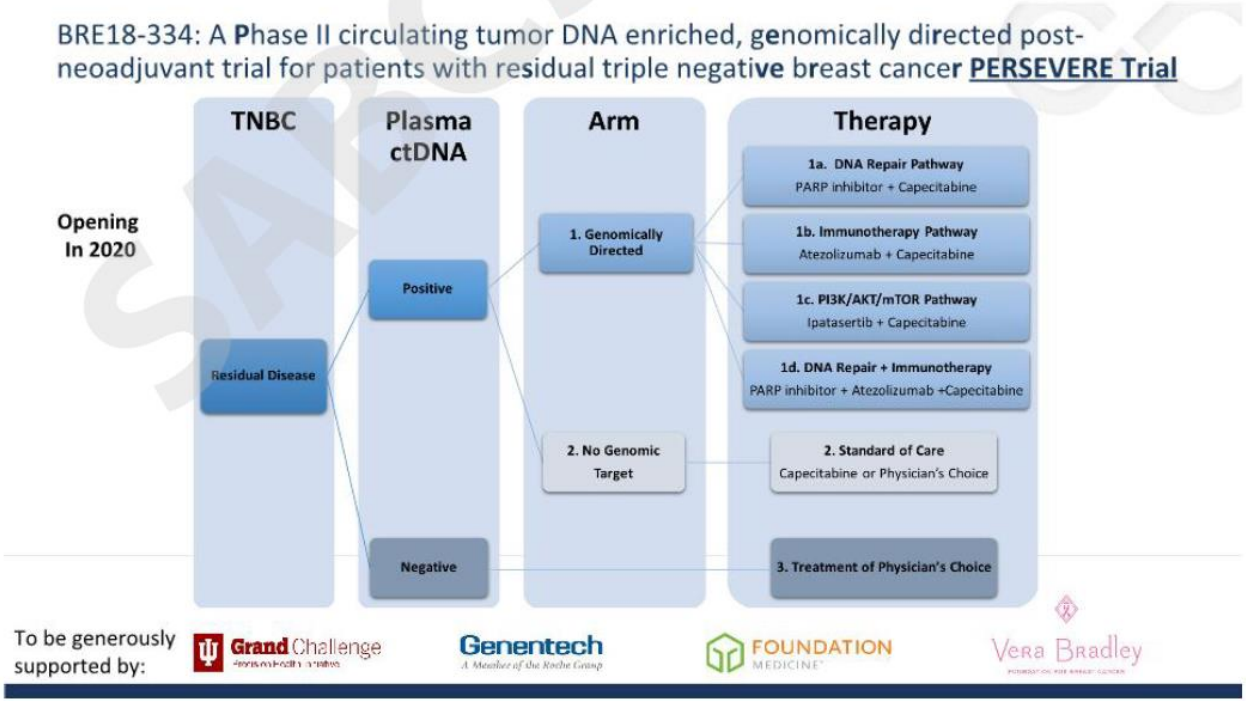
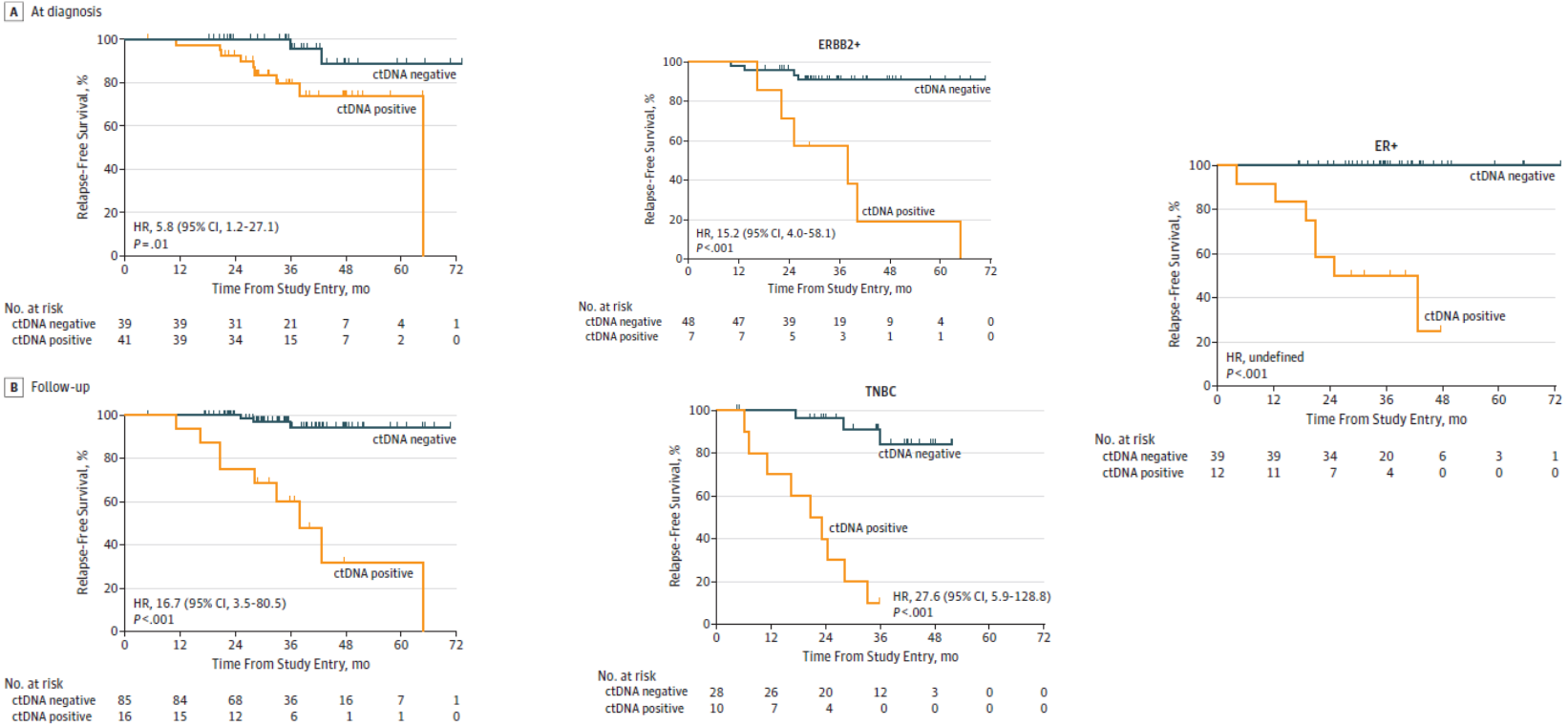



Radovich M et al SABCS 2019

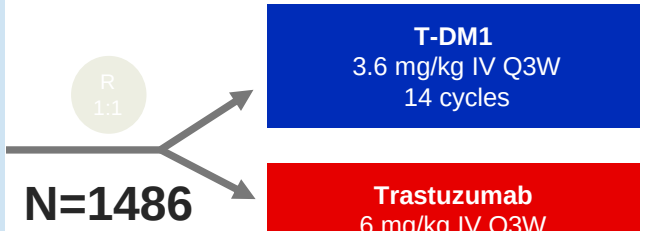
# ctDNA zur Prognoseabschätzung nach neoadjuvanter Chemotherapie




Garcia-Murillas JAMA Oncol 2019

# Katherine Studie - postneoadjuvant

- cT1-4/N0-3/M0 at presentation (cT1a-b/N0 excluded)
- Centrally confirmed HER2-positive breast cancer
- Neoadjuvant therapy must have consisted of
  - **Minimum of 6 cycles of chemotherapy**
    - Minimum of 9 weeks of taxane
    - Anthracyclines and alkylating agents allowed
    - All chemotherapy prior to surgery
  - **Minimum of 9 weeks of trastuzumab**
    - Second HER2-targeted agent allowed
- **Residual invasive tumor in breast or axillary nodes**
- Randomization within 12 weeks of surgery




Radiation and endocrine therapy per protocol and local guidelines

Charakteristika:
- HR pos
  72%
- Vortherapie Trastuzumab / Pertuzumab
  18%
- ypT1a, ypT1b or ypT1mic and ypN0)
  21%

# Katherine Studie - Ergebnisse

| | T-DM1 | Trastuzumab | Δ | HR | P-Wert |
|---|---|---|---|---|---|
| **3 J-IDFS (%)** | **88.3** | **77** | **11** | 0.5 | *P*<0.0001 |
| **3 J-DDFS (%)** | **89.7** | **83** | **7** | 0.6 | |
| 3 J-OS (%) | 94.3 | 92.5 | 1.8 | 0.7 | *P*=0.0848 |

Effekt auch bei: Pertuzumab Vortherapie
Residualtumor < 1cm und ypN0

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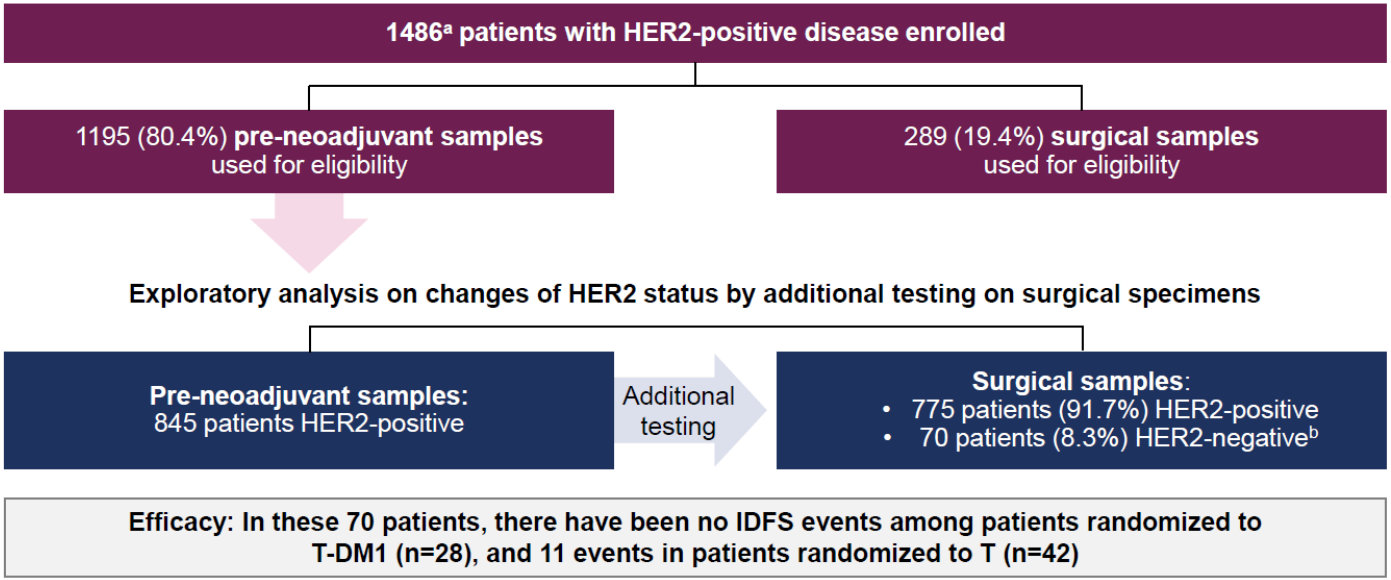
# PATIENTS WITH HER2-NEGATIVE DISEASE AT SURGERY




*Access slides at: https://bit.ly/3dYtolk*

ESMO BREAST CANCER 2020
VIRTUAL MEETING

[a]Two patients (both in T arm) are not included in this analysis: One did not have centrally confirmed HER2-positive disease and one was inadvertently randomized twice.
[b]53 HER2-negative and 17 HER2-unknown by IHC 0-1+/ISH unknown.

Loibl et al ESMO Breast 2020

# Zusammenfassung

- Ein Teil der Pat mit einer pCR haben ein erhöhtes Rezidivrisiko

- Neue molekulare Marker (ctDNA) prä aber v.a. posttherapeutisch
  - zeigen ein erhöhtes Rezidivrisiko an
  - Identifizieren Pat ohne pCR und trotzdem guter Prognose

- Bestimmung neuer molekularer Marker bieten Möglichkeit einer zielgerichteten postneoadjuvanten Therapie

- Bisher noch keine Evidenz für die Wirksamkeit einer postneoadjuvanten molekular gerichteten Therapie

- HER2 Untersuchung des postneoadjuvanten Residualtumors war nicht wegweisend
  **Bitte nicht auf eine effektive Therapie verzichten!!!!!**

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