LMU KLINIKUM DER UNIVERSITÄT MÜNCHEN

CAMPUS GROSSHADERN
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KLINIK UND POLIKLINIK FÜR FRAUENHEILKUNDE UND GEBURTSHILFE
DIREKTOR: PROF. DR. MED. SVEN MAHNER

Brustzentrum im Klinikum der Universität München

SABCS
SAN ANTONIO BREAST CANCER SYMPOSIUM
December 10-14, 2019
Henry B. Gonzalez Convention Center
San Antonio, Texas, USA

# SABCS 2019:
## Meine persönlichen Highlights


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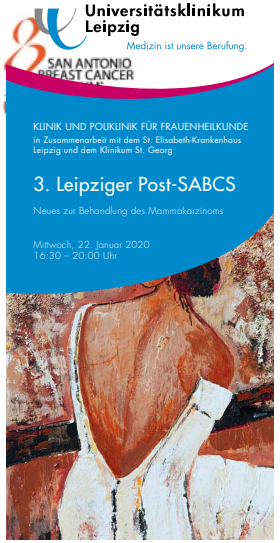
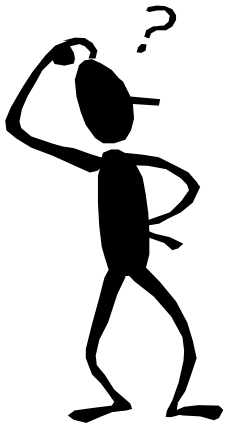
**Brustzentrum der Universität München**

Leitung:
Prof. Nadia Harbeck

# Was war wichtig für die Klinik morgen ?

SABCS
SAN ANTONIO BREAST CANCER SYMPOSIUM
December 10-14, 2019
Henry B. Gonzalez Convention Center
San Antonio, Texas, USA



## *Frühes* Mammakarzinom

- **Prognose verbessert sich mit moderner Therapie**
  - **HR+:** EBCTCG Metaanalyse
  - **HER2+:** APHINITY; ATEMPT
- **Immuntherapie: Viel Hoffnung, noch mehr Fragezeichen**
  **TNBC:** Keynote 522; NeoTRIPaPDL1

## *Fortgeschrittene* Erkrankung: Neue Hoffnung

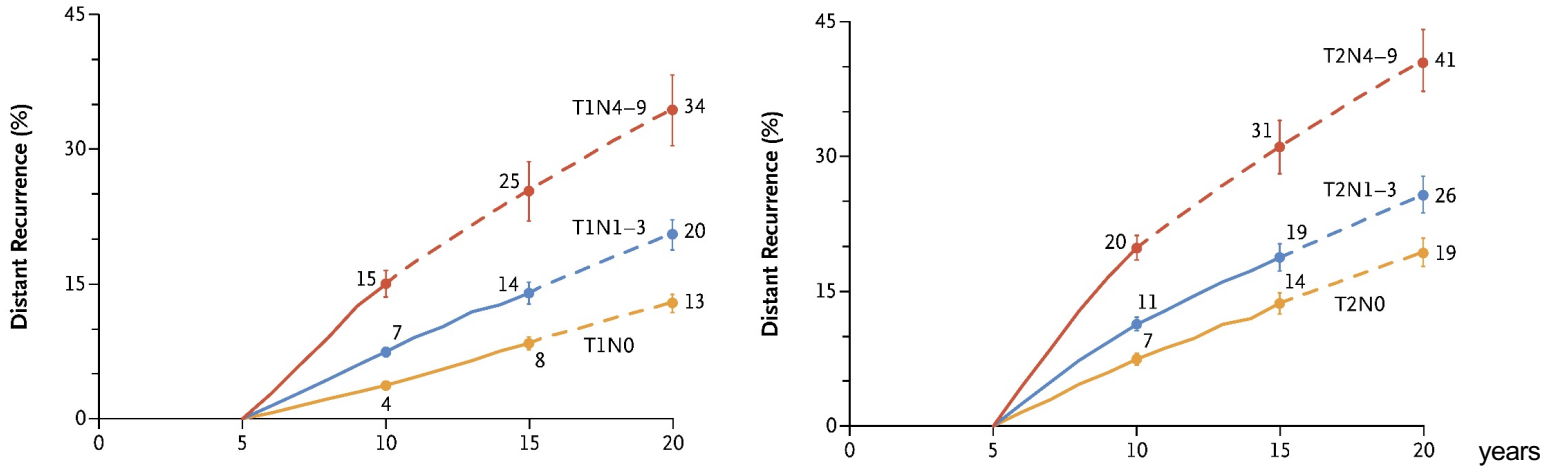
- **HER2+:** HERCLIMB; Destiny-Breast 01
- **HR+:** PEARL

## Ausblick 2020

EBCTCG *NEJM* 2017; 377: 1836

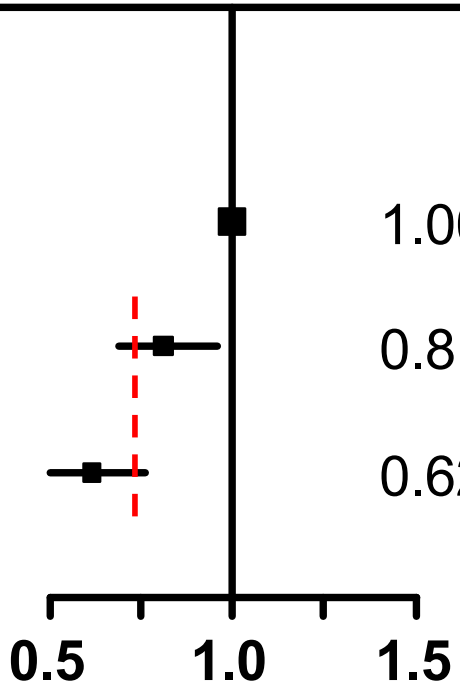
# Adjuvant endocrine therapy (ET) in ER+ disease

- In women given 5 years adjuvant ET, appreciable risks continue during years 5-20, even for T1N0
- After 5 years of ET for N0 disease, the risks of distant recurrence during years 5-20 were reported to be <u>T1N0: 13%</u> & T2N0: 19%



# EBCTCG analyses (n=86,000; 110 trials) - ER+ N0 disease: Distant recurrence during years 5-9,* by period of diagnosis

| Period of diagnosis | No. of women | No. of events | Fully adjusted RR (95% CI) |
|---|---|---|---|
| < 2000 | 19,924 | 898 | 1.00 (reference group) |
| 2000-04 | 11,691 | 220 | 0.81 (0.69-0.96) |
| ≥ 2005 | 9,646 | 131 | 0.62 (0.50-0.76) |




Heterogeneity NS
RR = 0.73
(0.63-0.85)

* Note: Women diagnosed since 2000 have limited follow-up beyond year 10

Pan et al, SABCS 2019

# Genexpressionstestung in der Regelversorgung

**Neu 2019**

## Pressemitteilung

Gemeinsamer Bundesausschuss

Gemeinsamer Bundesausschuss gemäß § 91 SGB V

Nr. 17 / 2019



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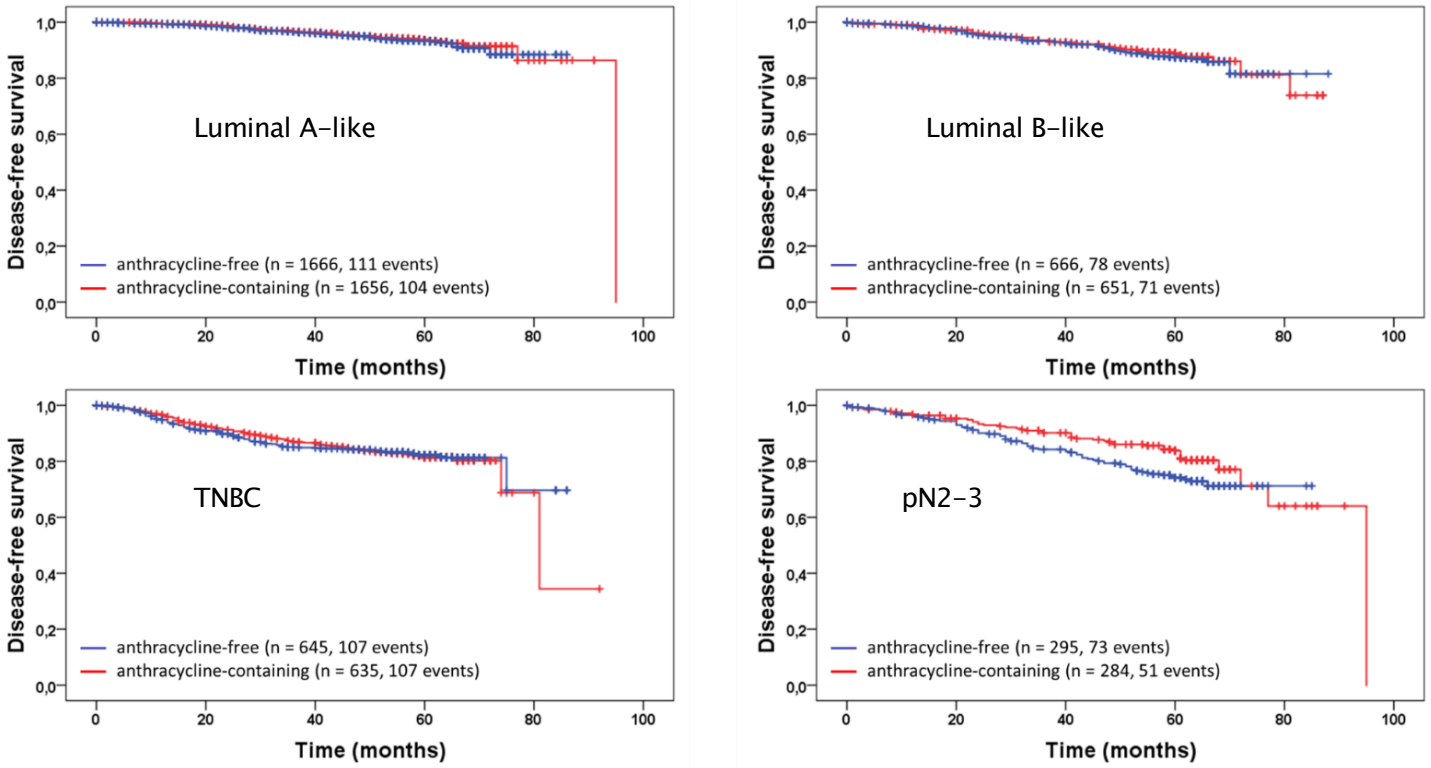
Methodenbewertung

### Unterstützung der Therapieentscheidung bei Brustkrebs im Frühstadium: Biomarker-Test künftig Kassenleistung

**Berlin, 20. Juni 2019** – Der Gemeinsame Bundesausschuss (G-BA) hat am Donnerstag in Berlin einen ersten Beschluss zum Einsatz von biomarkerbasierten Tests gefasst. Patientinnen mit Brustkrebs im frühen Stadium, bei denen das Rückfallrisiko nicht sicher bestimmt werden kann, können künftig einen Biomarker-Test als Leistung der gesetzlichen Krankenversicherung (GKV) in Anspruch nehmen. Die Ergebnisse sollen bei bestehender Unsicherheit hinsichtlich des zu erwartenden individuellen Nutzens einer Chemotherapie die gemeinsame Entscheidungsfindung von Patientinnen und Ärztinnen und Ärzten unterstützen. Für die ärztliche Aufklärung vor der Durchführung des Tests legt der G-BA die verpflichtende Verwendung einer Patientinneninformation fest, die auf den Internetseiten des G-BA als ausdruckbare Datei bereitgestellt wird.

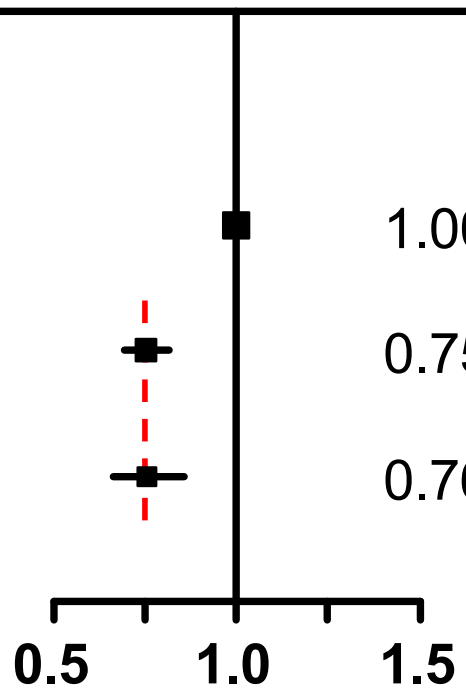
# Pooled analysis PlanB und SUCCESS C:
# DFS nach **6x TC vs. Anthrazyklin-Taxan Sequenz**
## (62 Monate medianes Follow-up; n=5923)




Janni et al, ASCO 2018

# EBCTCG analyses (n=86,000; 110 trials) - ER+ N+ disease: Distant recurrence during years 5-9,* by period of diagnosis

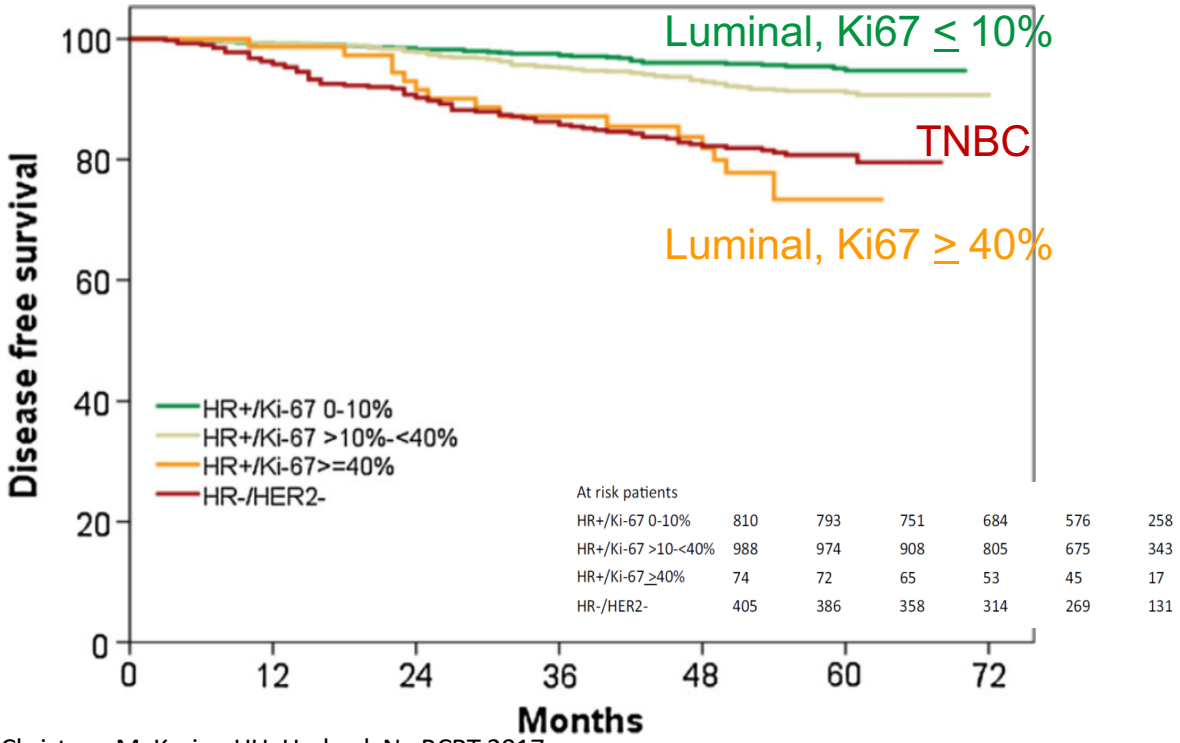
| Period of diagnosis | No. of women | No. of events | Fully adjusted RR (95% CI) |
|---|---|---|---|
| **< 2000** | 17,874 | 1,968 | 1.00 (reference group) |
| **2000-04** | 18,446 | 1,048 | 0.75 (0.69-0.82) |
| **≥ 2005** | 8,683 | 394 | 0.76 (0.67-0.86) |




* Note: Women diagnosed since 2000 have limited follow-up beyond year 10

Pan et al, SABCS 2019

# PlanB:
## 5-Jahres DFS in molekularen Subgruppen

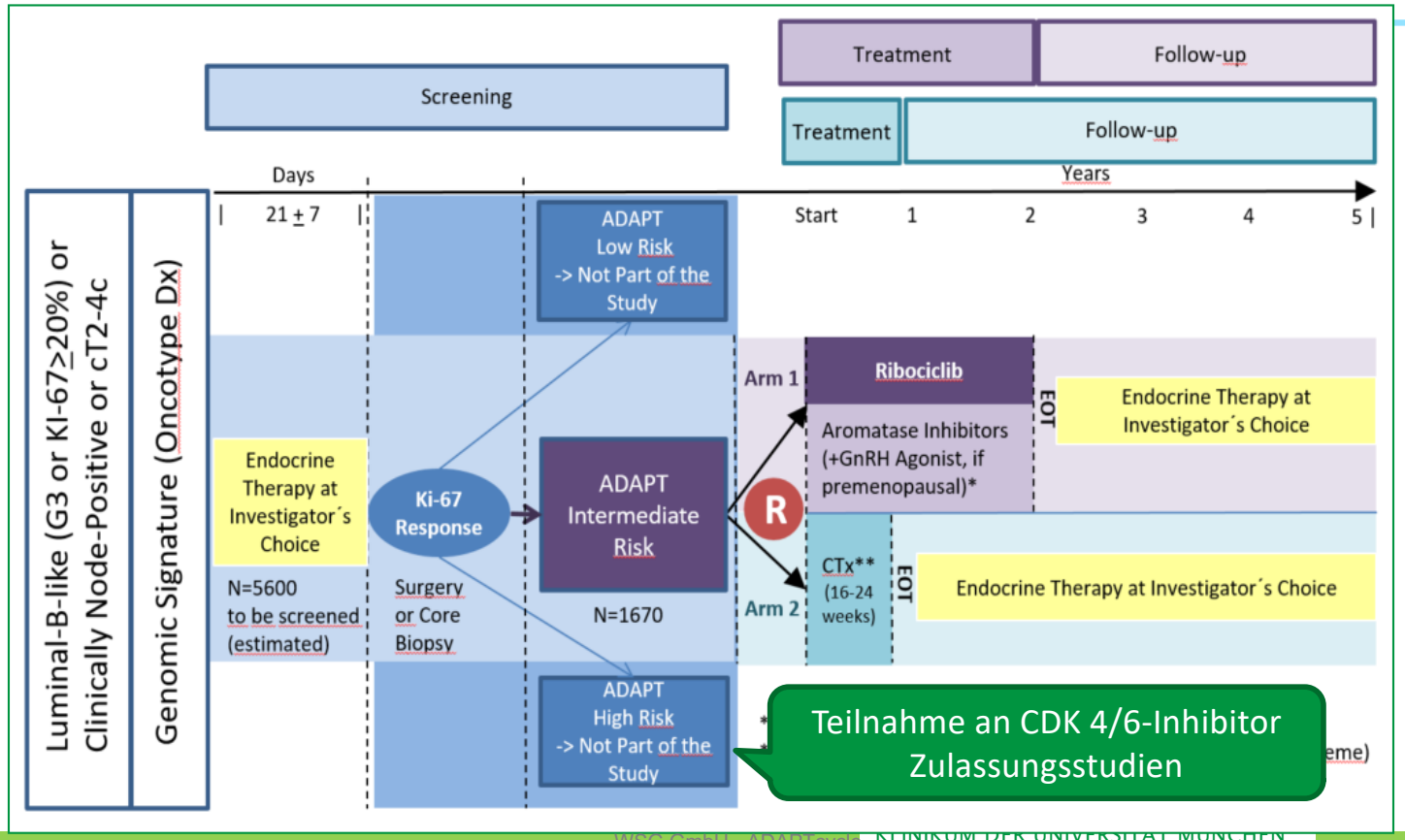



Gluz et al, ESMO 2017; Nitz U, Gluz O, Christgen M, Kreipe HH, Harbeck N; BCRT 2017

# Adjuvante Studien mit CDK 4/6i

| **PALLAS** NCT02513394 | **PENELOPE B** NCT01864746 | **MONARCH E** NCT03155997 | **NATALEE** NCT03701334 | **ADAPTcycle** EudraCT 2018-003749-40) |
|---|---|---|---|---|
| 5792 (M, W) | 1250 (W) | 4580 (M, W) | 4000 (M, W) | 1670 (W) – 5600 screened |
| Palbociclib$_{125}$ | Palbociclib$_{125}$ | Abemaciclib$_{125}$ | Ribociclib$_{400}$ | Ribociclib$_{600}$ |
| 2 years | 1 year (after non-pCR) | 2 years | 3 years | 2 years (vs.chemo) |
| iDFS | iDFS | iDFS | iDFS | DFS; 5y DDFS > 92% |
| completed | completed | completed | started 2019 | started 2019 |
| ABCSG, BIG GBG, NSABP, PrECOG | GBG, AGO-B, BIG, NSABP | Lilly | TRIO | WSG |

# ADAPTcycle




**N0*–1:** Low or Intermediate risk RS (≤ 25) *ohne* bzw. high risk RS (> 25) *mit* endokrinem Ansprechen

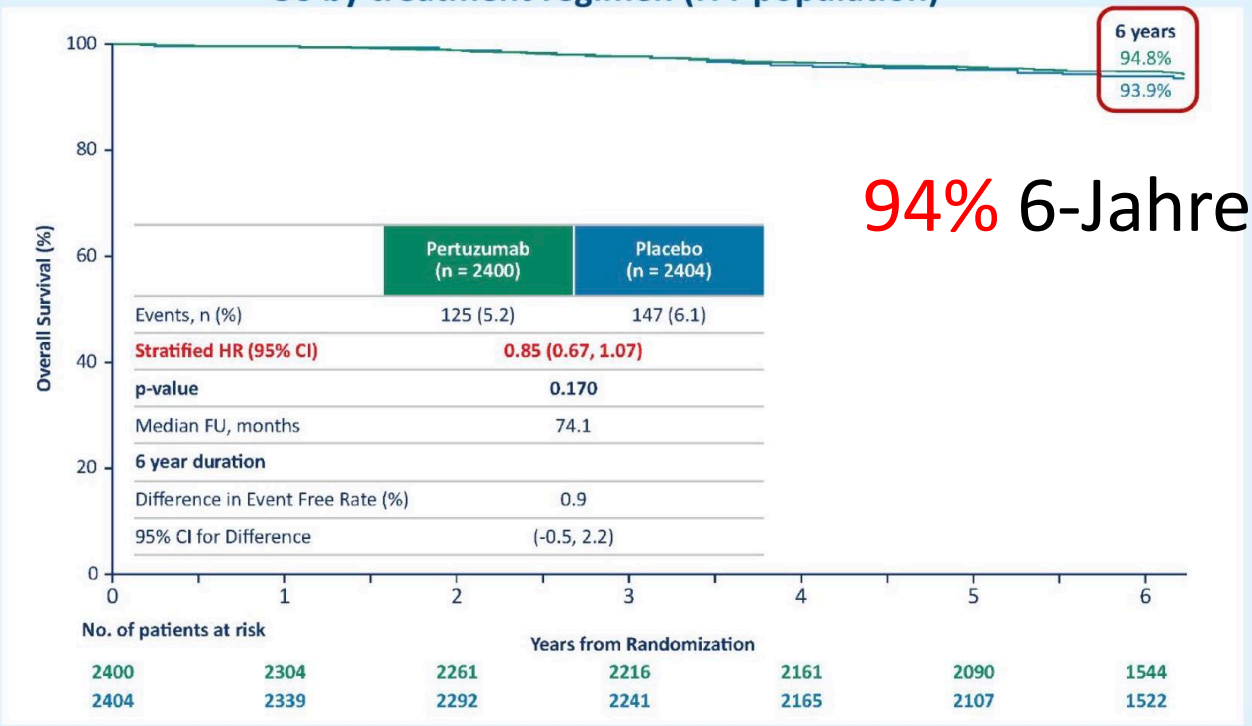
**N2–3:** RS ≤ 25 *mit* endokrinem Ansprechen

# APHINITY: Interim OS

SABCS SAN ANTONIO BREAST CANCER SYMPOSIUM December 10-14, 2019 Henry B. Gonzalez Convention Center San Antonio, Texas, USA

San Antonio Breast Cancer Symposium®, December 10-14, 2019

## APHINITY Interim Overall Survival Analysis 74.1 months median FU, OS by treatment regimen (ITT population)




| | Pertuzumab (n = 2400) | Placebo (n = 2404) |
|---|---|---|
| Events, n (%) | 125 (5.2) | 147 (6.1) |
| Stratified HR (95% CI) | 0.85 (0.67, 1.07) | |
| p-value | 0.170 | |
| Median FU, months | 74.1 | |
| 6 year duration | | |
| Difference in Event Free Rate (%) | 0.9 | |
| 95% CI for Difference | (-0.5, 2.2) | |

94% 6-Jahresüberleben

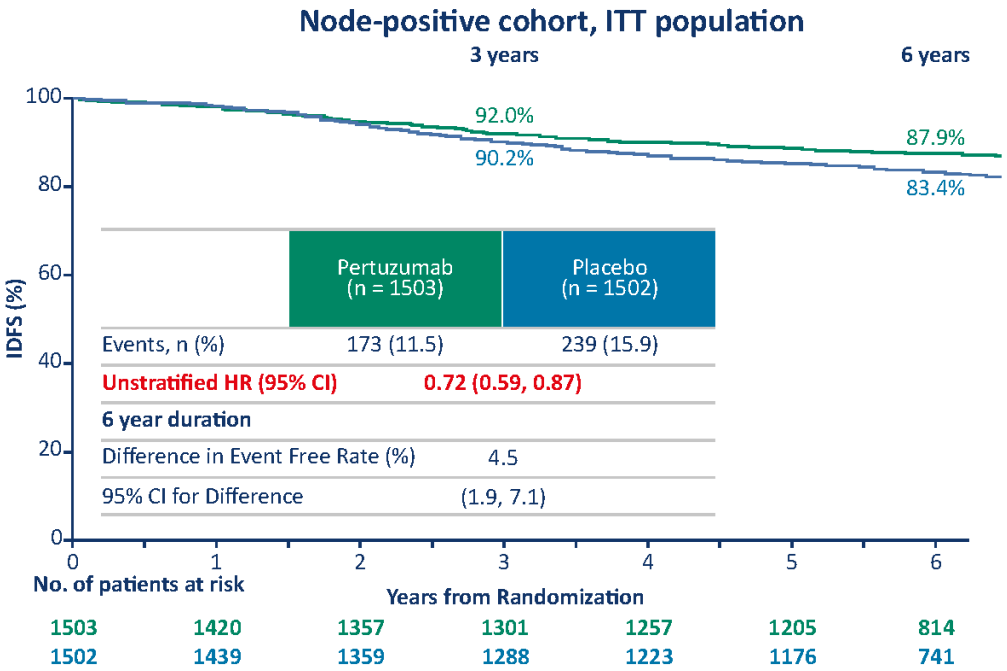
P-value of 0.0012 is required for statistical significance for OS. Survival data remain immature at this time.

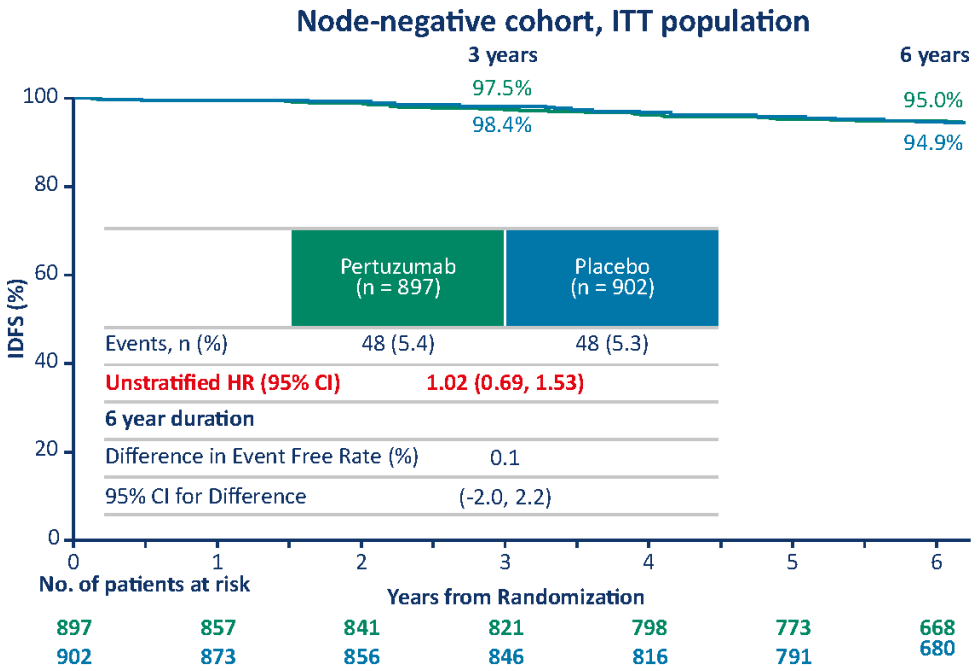


M. Piccart et al. SABCS 2019 #GS1-04

# APHINITY Updated descriptive analysis 74.1 months median FU
# Time to first IDFS event by treatment regimen and nodal status

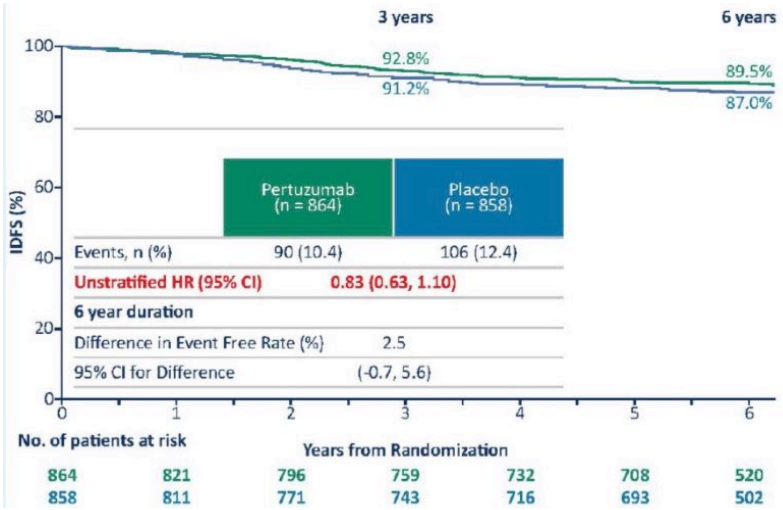
The node positive cohort continues to derive clear benefit from addition of pertuzumab.



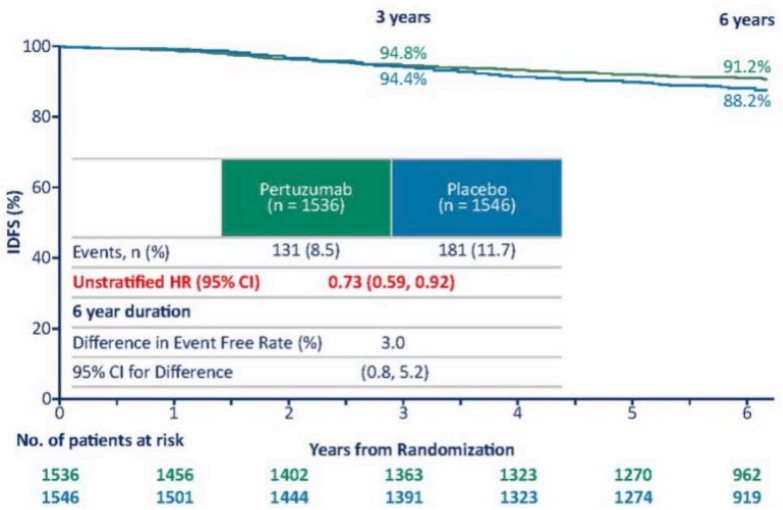
# APHINITY: updated iDFS – HR status

**HR positive cohort**
**ITT population**




**6y Δ: 2.5%**

**HR negative cohort**
**ITT population**

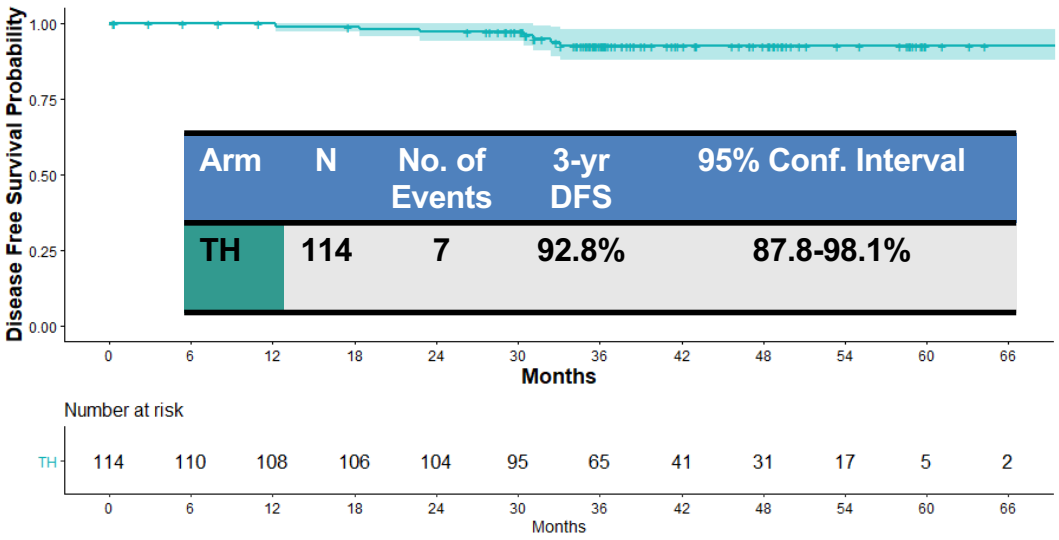



**6y Δ: 3.0%**

Piccart M et al. SABCS 2019 #GS1-04

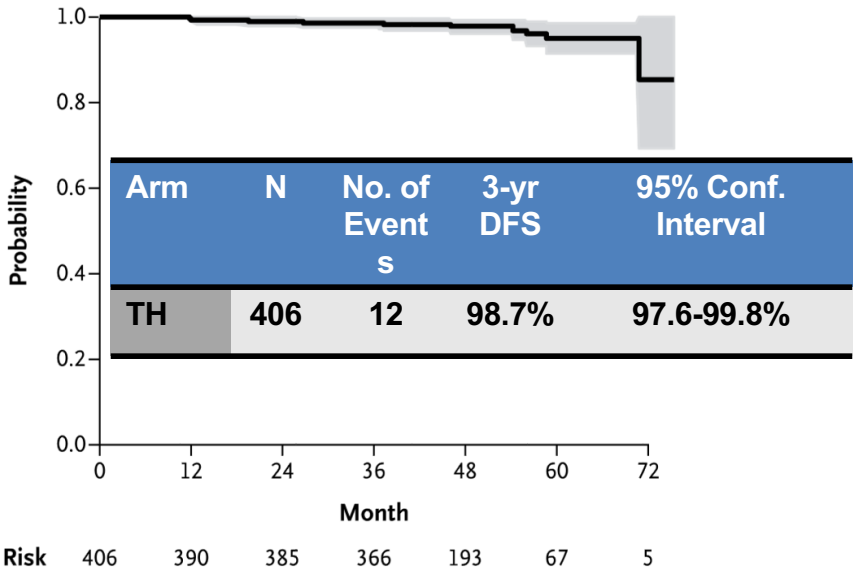
# Disease-Free Survival: TH

**TH (ATEMPT Trial): n=114**




| Arm | N | No. of Events | 3-yr DFS | 95% Conf. Interval |
|---|---|---|---|---|
| TH | 114 | 7 | 92.8% | 87.8-98.1% |

**TH (APT Trial): n=406**

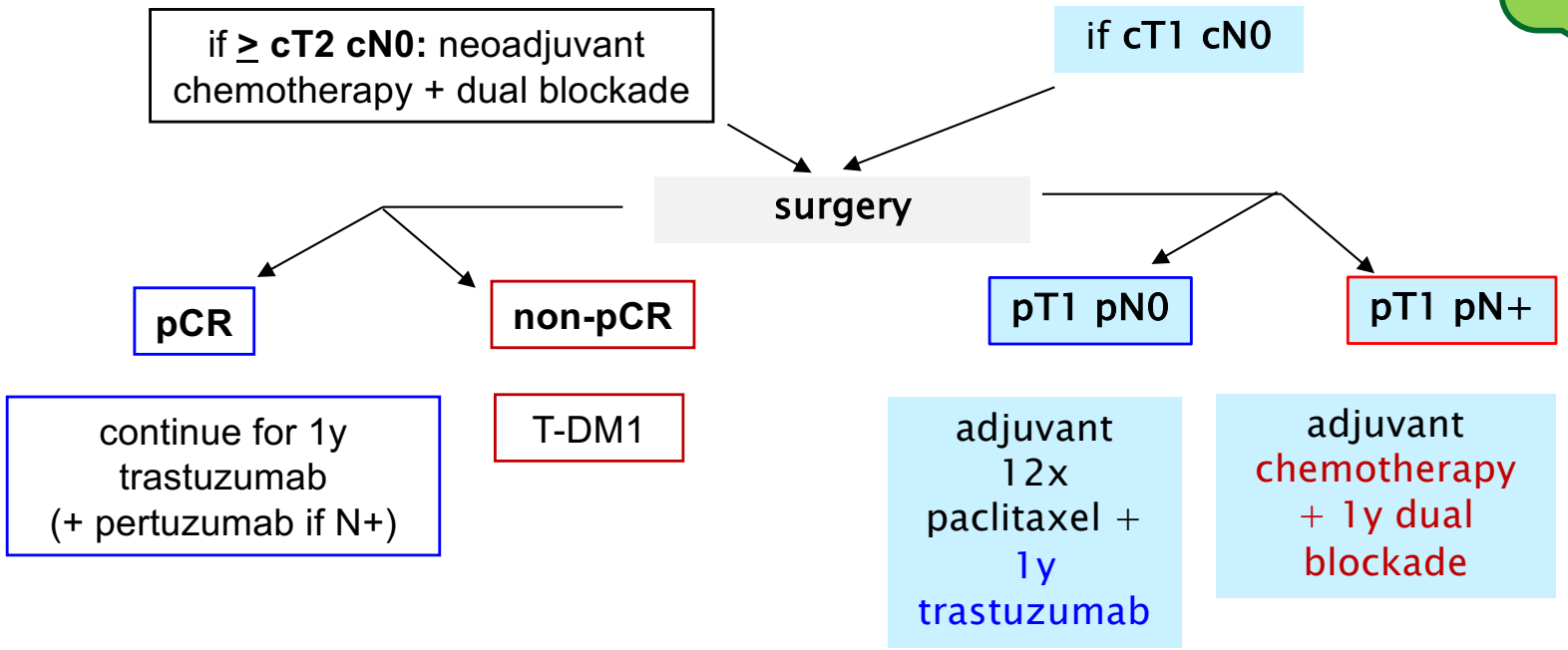



| Arm | N | No. of Events | 3-yr DFS | 95% Conf. Interval |
|---|---|---|---|---|
| TH | 406 | 12 | 98.7% | 97.6-99.8% |

Tolaney S et al, NEJM 2015

# HER2+ EBC: Therapiealgorithmus

Neu 2019




If indicated: **Radiotherapy**; Adjuvant **endocrine therapy if HR+***

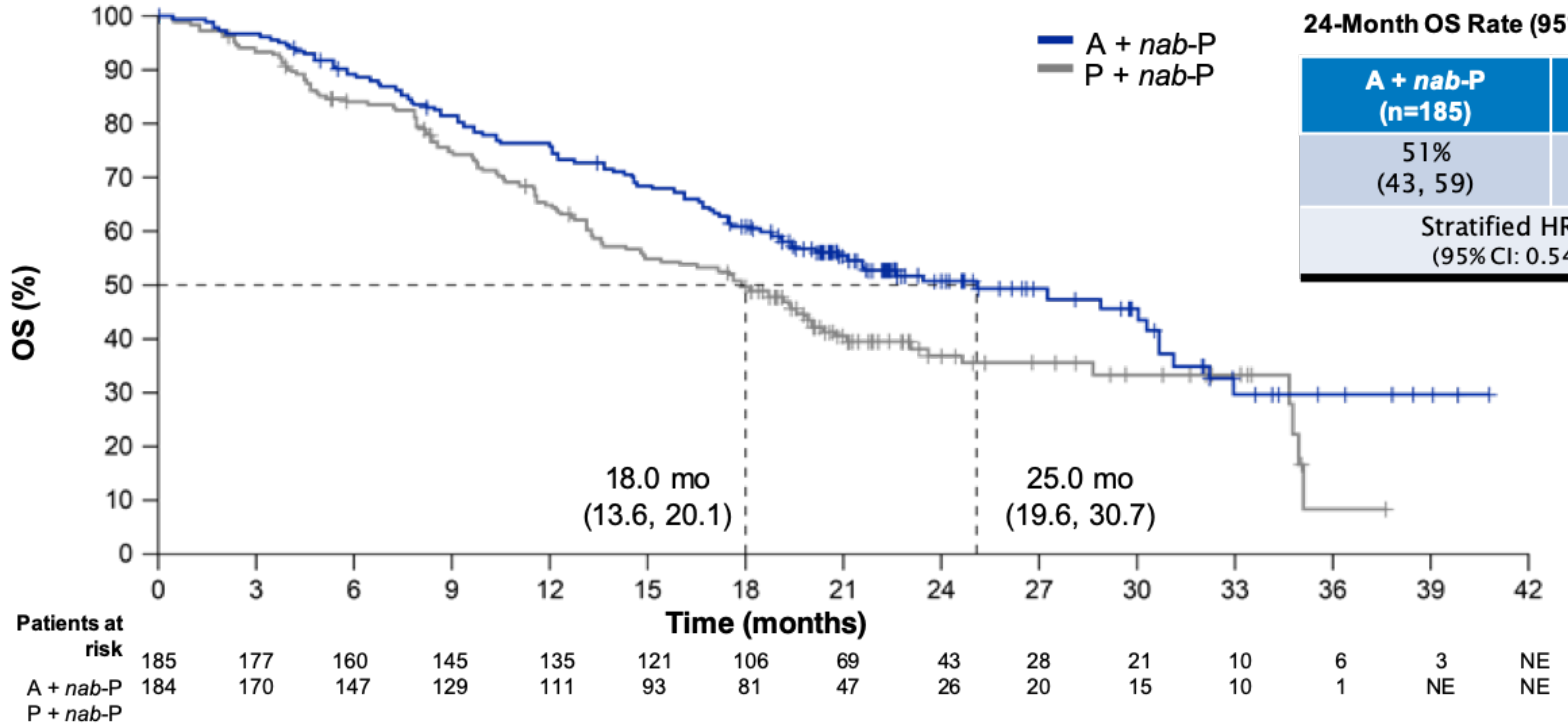
*DXA, offer adjuvant bisphosphonates (if postmenopausal / or with ovarian suppression)



Modifiziert nach Harbeck N, *Breast* 2019

# Immuntherapie jetzt auch bei Brustkrebs: IMPASSION 130 – Erstlinie TNBC (PD-L1$_{ic}$ +)

**Neu 2019**




**24-Month OS Rate (95% CI)**

| A + *nab*-P (n=185) | P + *nab*-P (n=184) |
|---|---|
| 51% (43, 59) | 37% (29, 45) |
| Stratified HR, 0.71[a] (95% CI: 0.54, 0.93) | |

[a]Not formally tested due to pre-specified hierarchical analysis plan.
Clinical cutoff date: January 2, 2019. Median PFS (95% CI) is indicated on the plot. Median FU (ITT): 18.0 months..

Mod. Schmid P et al. ASCO 2019, Oral Abstract Session – Breast Cancer – Metastatic, Abstract No. 1003

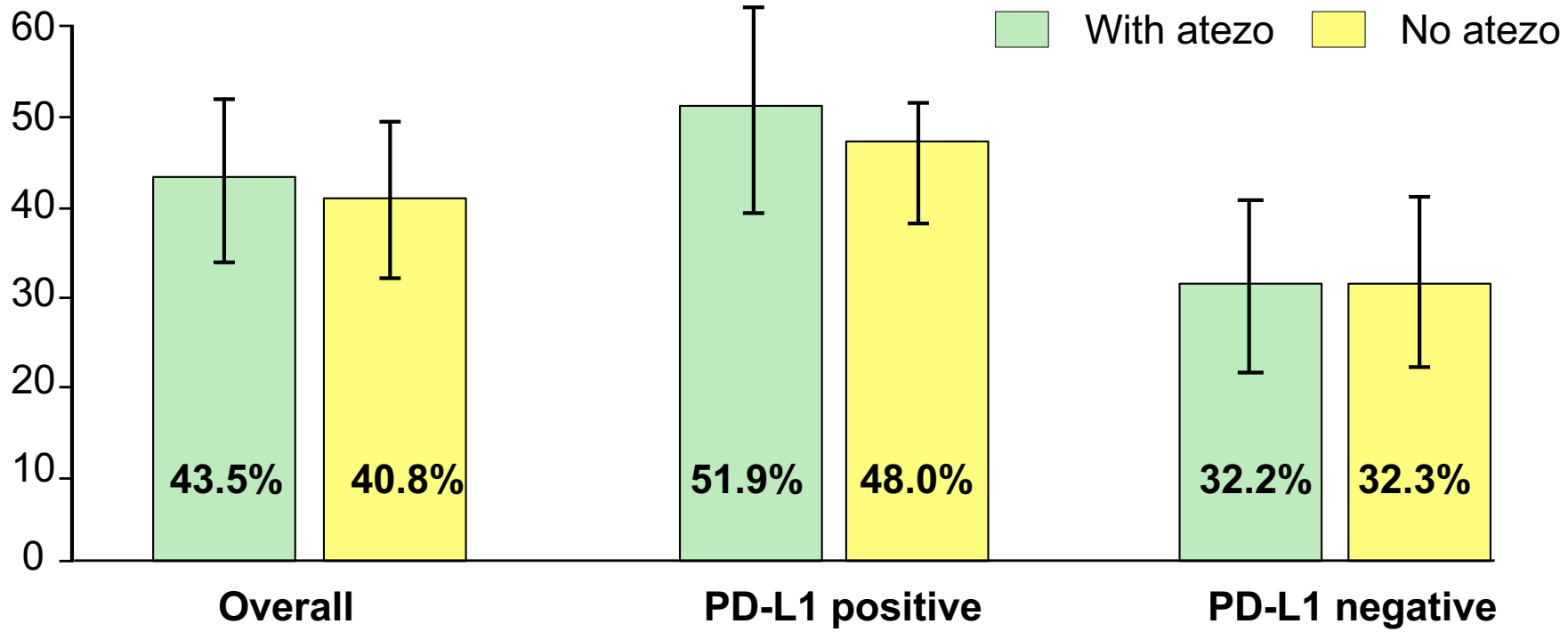
**Chemotherapie**
8x nab-P/Cb d1,8 q21
Postop: Anthra

# NeoTRIP: ITT analysis - pCR rate

| | ITT population | |
|---|---|---|
| | **With atezo** (138) | **No atezo** (142) |
| **% pCR rate** | **43.5** | **40.8** |
| 95% CI | 35.1-52.2 | 32.7-49.4 |
| **Difference: atezo vs no atezo (95% CI)** | **2.63** (14.0-8.8) | |
| ***Odds ratio (95% CI)** | **1.11 (0.69-1.79)** | |
| ***p-value** | **0.66** | |

*Cochran-Mantel-Haenszel test, controlling for PD-L1 expression and disease stage and quantified by OR and rate difference

# pCR rate and *PD-L1 expression*



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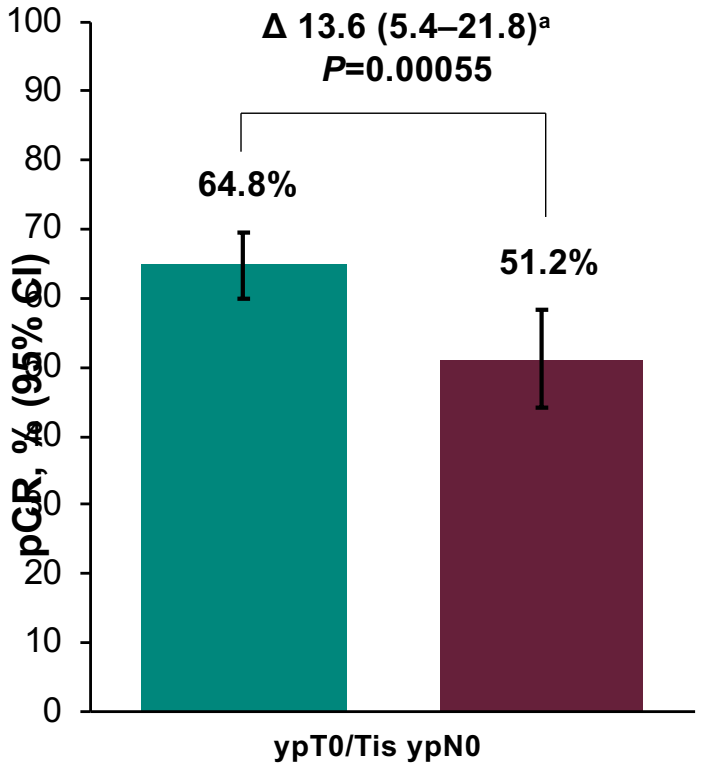
**Chemotherapie**
12x P-Cb q7 – 4x Anthra q21

# KEYNOTE 522: Definitive pCR Analysis




- Definitive pCR analysis to test primary hypothesis of pCR based on prespecified first 602 patients (pre-calculated P value boundary for significance of 0.003)
- Consistent benefit seen with pCR defined as ypT0 ypN0 and ypT0/Tis

**Placebo + Chemo**

**Pembro + Chemo**

[a]Estimated treatment difference based on Miettinen & Nurminen method stratified by randomization stratification factors. Data cutoff date: September 24, 2018.

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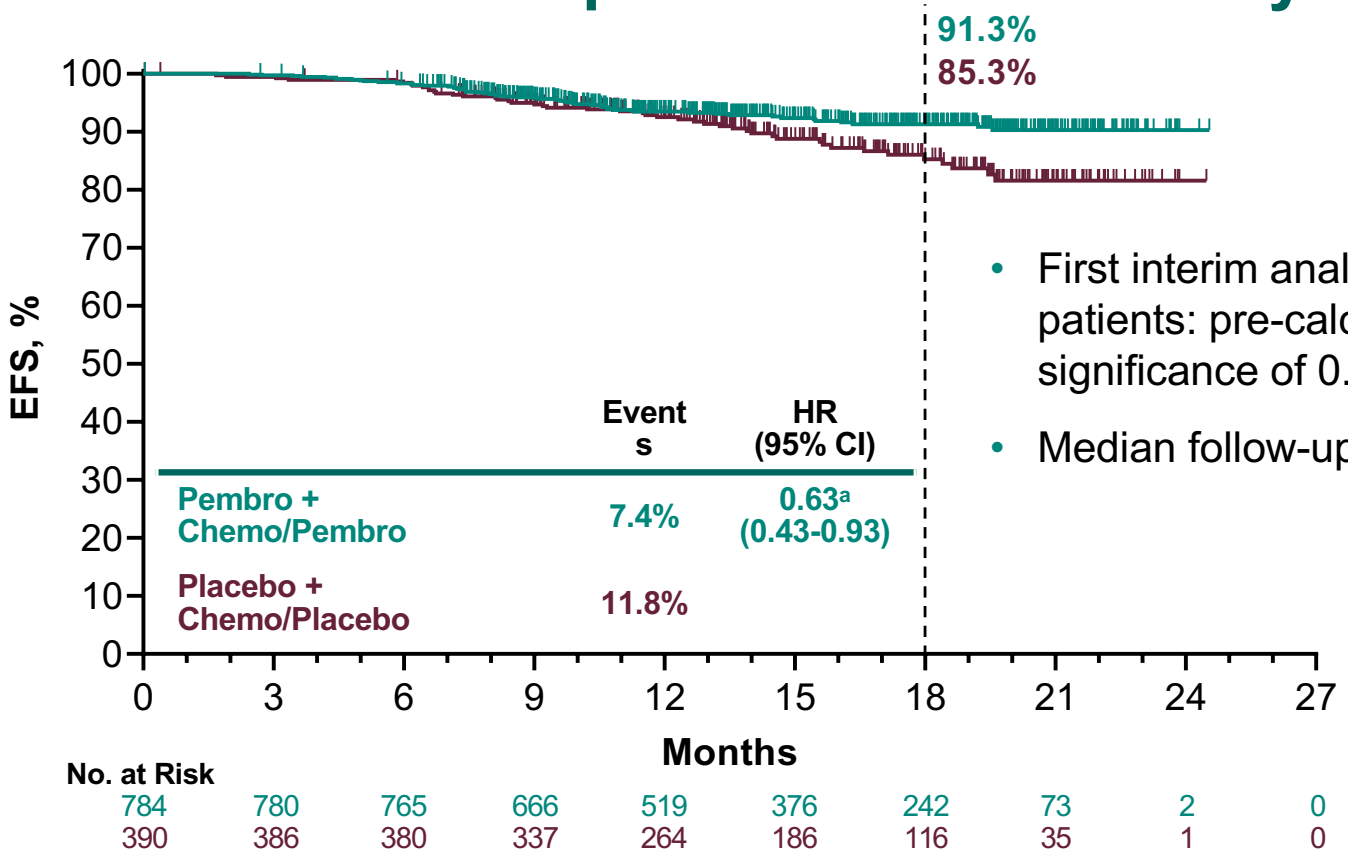
# KN 522: First Pre-planned Interim Analysis for EFS




- First interim analysis of EFS based on 1174 patients: pre-calculated P value boundary for significance of 0.000051 (HR <0.4)
- Median follow-up, 15.5 months

[a]Pre-specified P value boundary of 0.000051 not reached at this analysis (the first interim analysis of EFS). Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. Data cutoff April 24, 2019.

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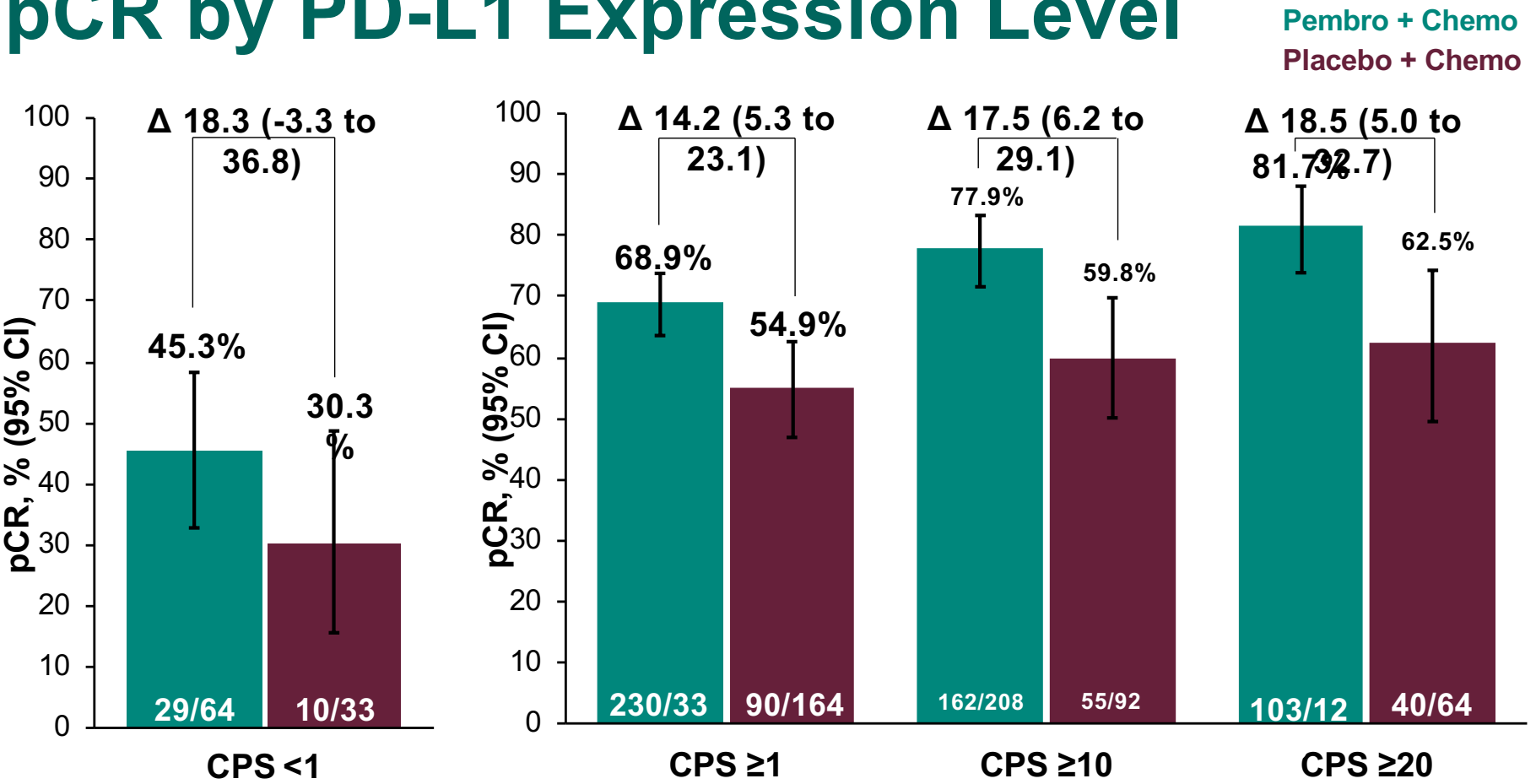
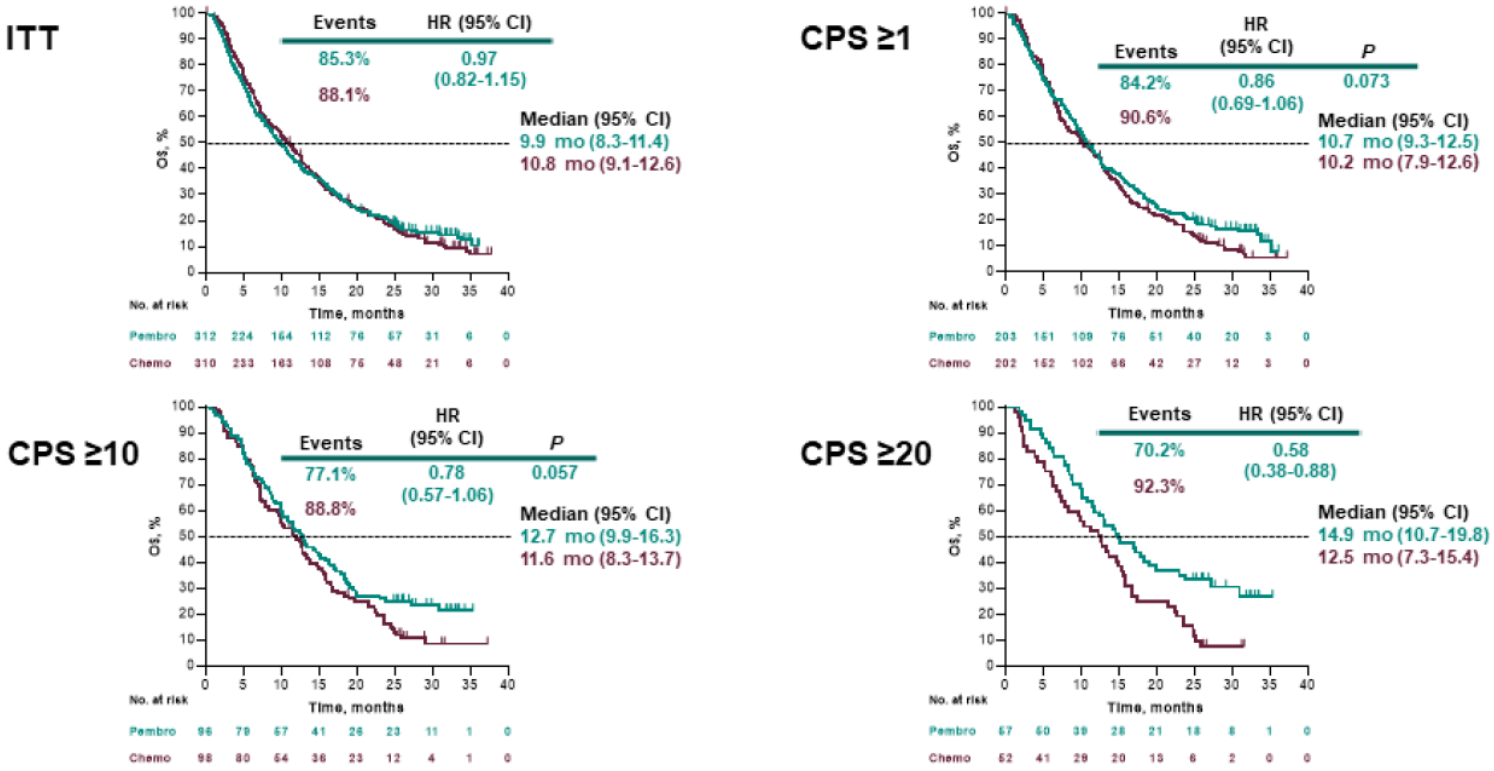
# pCR by PD-L1 Expression Level




Pre-specified analysis. PD-L1 assessed at a central laboratory using the PD-L1 IHC 22C3 pharmDx assay and measured using CPS; number of PD-L1–positive tumor cells, lymphocytes, and macrophages divided by total number of tumor cells x 100); PD-L1–positive = CPS ≥1. Estimated treatment difference based on Miettinen & Nurminen method stratified by nodal status (positive vs negative), tumor size (T1/T2 vs T3/T4) and choice of carboplatin (Q3W vs QW). Data cutoff date: September 24, 2018.

# KEYNOTE-119 (Pembrolizumab vs. Monochemotherapie): Gesamtüberleben ITT und nach PD-L1 Status



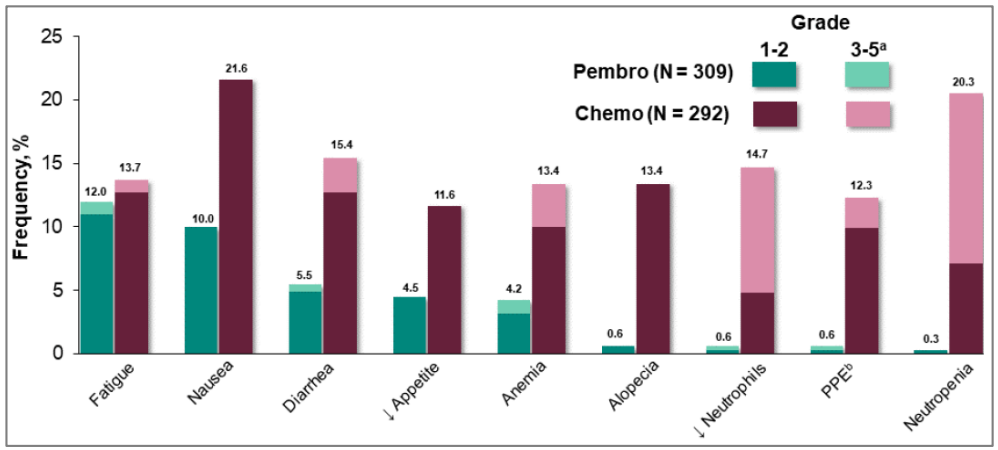

Cortes J. et al., ESMO 2019 (#LBA21)

Primäre Endpunkte OS: ITT, CPS ≥1 und CPS ≥10; OS für CPS ≥20 war explorativer Endpunkt

Data cut-off 11.April 2019

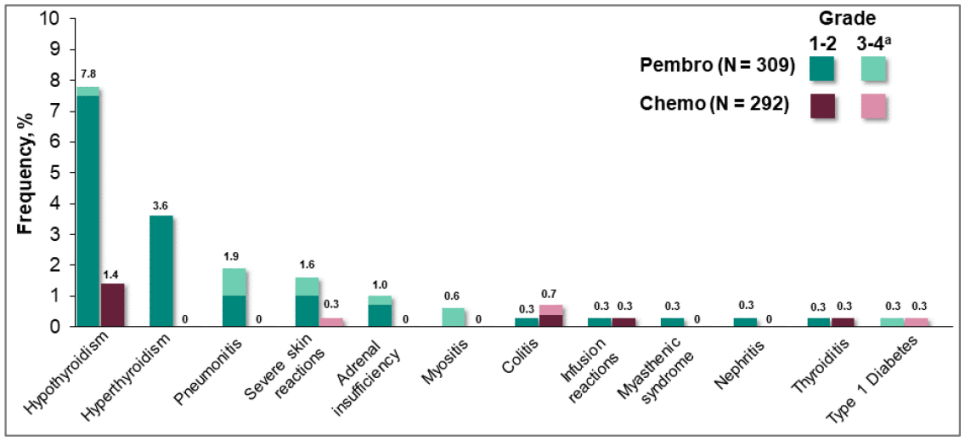
# KEYNOTE-119: Nebenwirkungen (Pembrolizumab vs. Monochemotherapie)

## Behandlungsbedingte Nebenwirkungen ≥10%




[a] Grad 5 Nebenwirkungen: Panzytopenie und Sepsis (n=1), Hämothorax (n=1): Chemotherapie; Kreislaufkollaps (n=1): Pembrolizumab
[b] Hand-Fuss-Syndrom
Data cut-off 11.April 2019

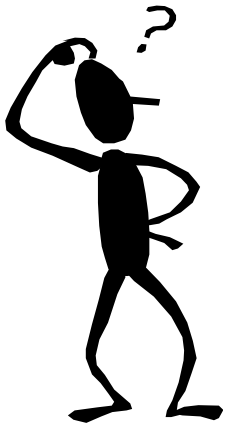
## Immunvermittelte Nebenwirkungen und Infusionsreaktionen




[a] Keine Grad 5 Nebenwirkungen; Data cut-off 11.April 2019

Cortes J. et al., ESMO 2019 (#LBA21)

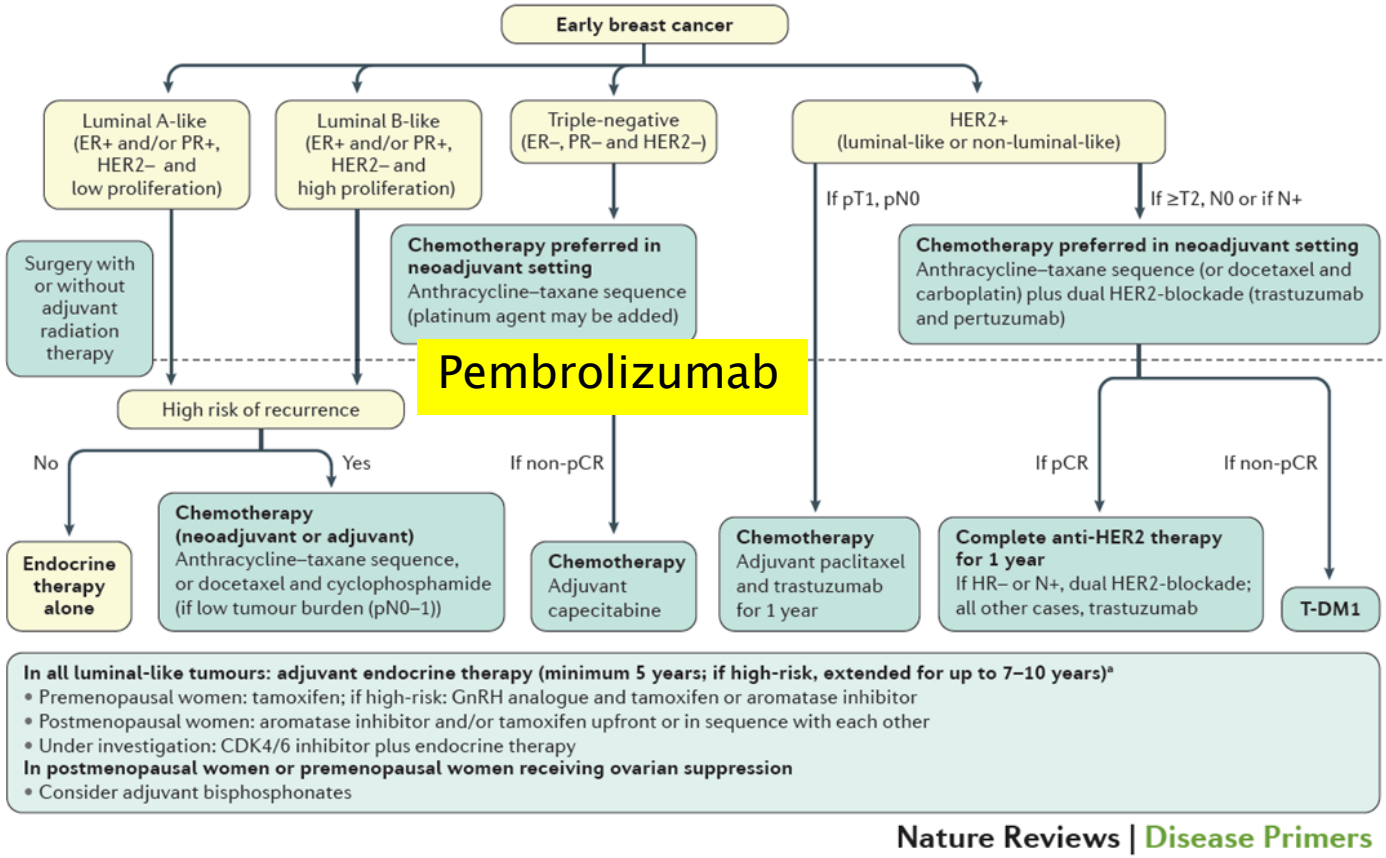
# Immuntherapie jetzt auch bei Brustkrebs – viele offene klinische Fragen und noch (viel zu) wenig Antworten



- Optimale IO Medikamente
- Optimale Biomarker
- Optimales Anwendungsgebiet
- Optimales Therapieregime
- Optimale Kombinationspartner
- Optimale Dauer
- …

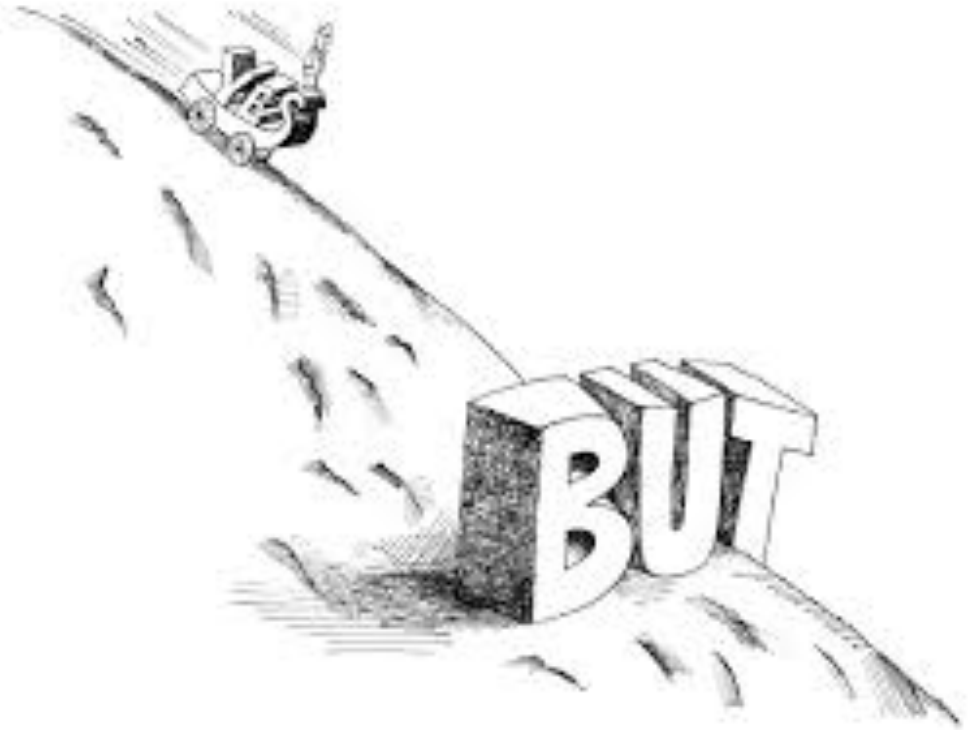
**“Before I came here, I was confused about this subject. Having listened to your lecture, I am still confused –– but on a higher level.” Enrico Fermi**

# *Early* breast cancer: Treatment strategies




Harbeck et al, 2019

# *Advanced or Metastatic* Breast Cancer: Will we do something different on Monday morning?



# *Metastasiertes* HER2+ Mammakarzinom: Klinische Herausforderungen bei immer besserer (neo-) adjuvanter Therapie

San Antonio Breast Cancer Symposium®, December 10-14, 2019

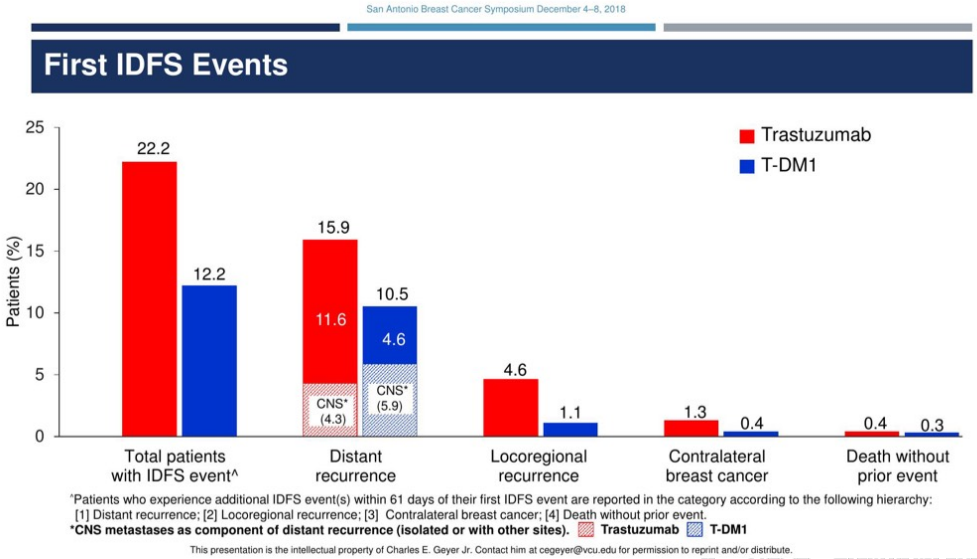
**APHINITY Updated descriptive analysis 74.1 months median FU, Site of First Occurrence of an IDFS event**

| | Pertuzumab n=2400 | Placebo n=2404 |
|---|---|---|
| Total patients with IDFS event: n (%) | 221 (9.2%) | 287 (11.9%) |
| Category of IDFS event: n (%) | | |
| • Distant recurrence | 141 (5.9%) | 184 (7.7%) |
| • CNS metastases | 49 (2.0%) | 49 (2.0%) |
| • Locoregional BC recurrence | 28 (1.2%) | 49 (2.0%) |
| • Contralateral invasive BC recurrence | 13 (0.5%) | 15 (0.6%) |
| • Death without prior event | 39 (1.6%) | 39 (1.6%) |

Hierarchy applied if a patient experiences additional IDFS event(s) within 61 days of their 1st IDFS event

35% ZNS bei Fernmetastasen nach T-P

56 % ZNS bei Fernmetastasen nach T-DM1



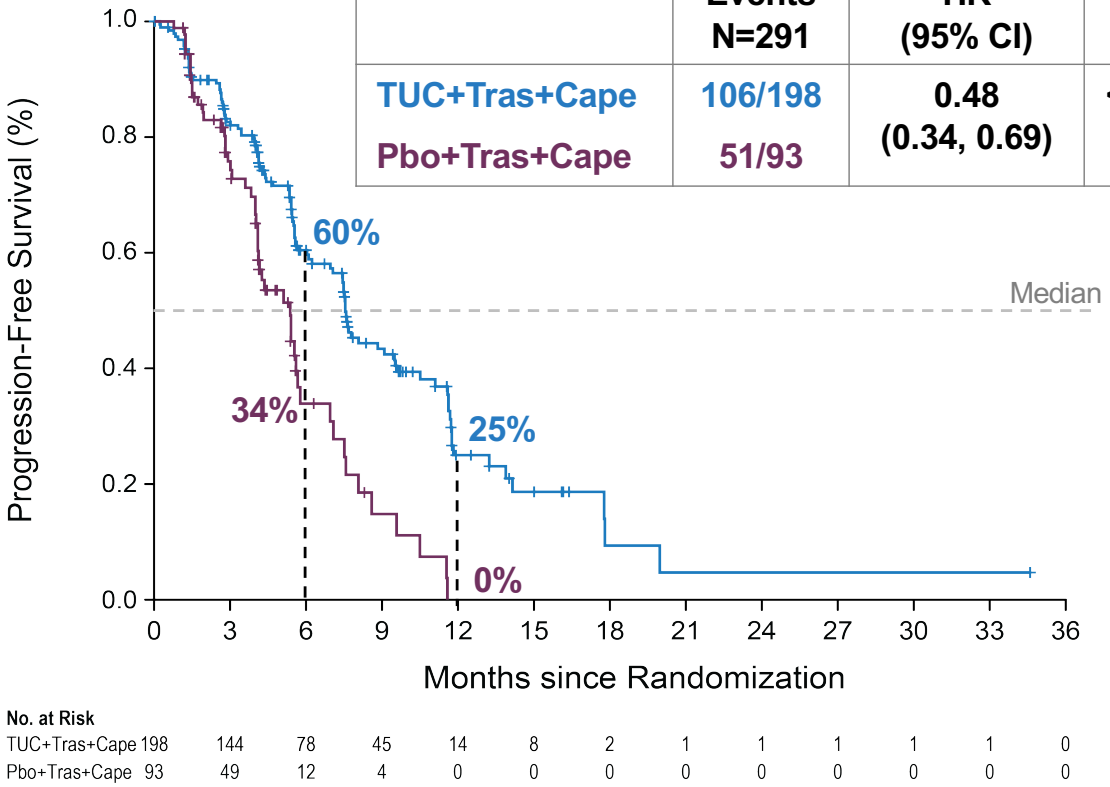
# HER2CLIMB: Key Baseline Demographics and Disease Characteristics

| Characteristic, n (%) | | Total Population, N=612<br>TUC+Tras+Cape<br>n=410 | <br>Pbo+Tras+Cape<br>n=202 |
|---|---|---|---|
| Female | | 407 (99) | 200 (99) |
| Age (years), median (range) | | 55.0 (22, 80) | 54.0 (25, 82) |
| ECOG performance status | 0 | 204 (50) | 94 (47) |
| | 1 | 206 (50) | 108 (54) |
| Stage IV at initial diagnosis | | 143 (35) | 77 (39) |
| Hormone receptor status | ER and/or PR-positive | 243 (60) | 127 (63) |
| | ER and PR-negative | 161 (40) | 75 (37) |
| Prior lines of therapy, median (range) | Overall | 4.0 (2, 14) | 4.0 (2,17) |
| | Metastatic setting | 3.0 (1, 14) | 3.0 (1, 13) |
| Presence/history of brain metastases | | 198 (48) | 93 (46) |
| Treated, stable | | 118 (59.6) | 55 (59.1) |
| Untreated | | 44 (22.2) | 22 (23.7) |
| Treated, progressing | | 36 (18.2) | 16 (17.2) |

Baseline characteristics were balanced between endpoint populations and treatment arms

# Progression-Free Survival for Patients with Brain Metastases

| | Events N=291 | HR (95% CI) | P Value |
|---|---|---|---|
| TUC+Tras+Cape | 106/198 | 0.48 (0.34, 0.69) | <0.00001 |
| Pbo+Tras+Cape | 51/93 | | |



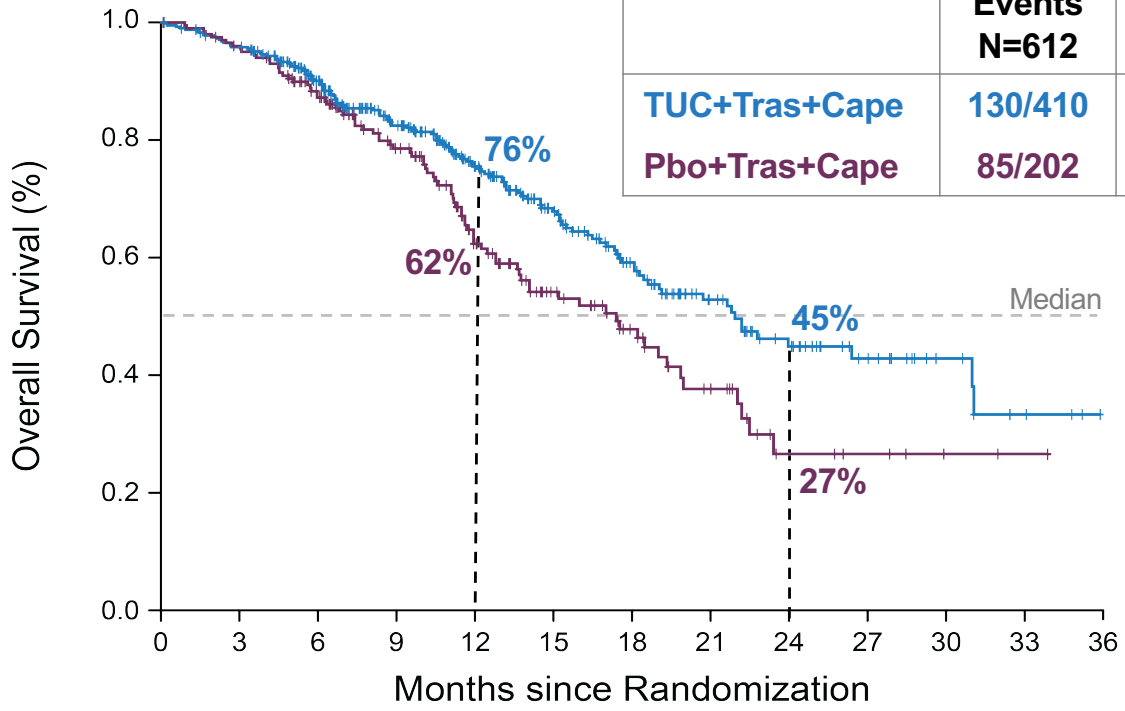

**Risk of progression or death in patients with brain metastases was reduced by 52% in the total population**

| One-year PFS (95% CI): | |
|---|---|
| TUC+Tras+Cape 25% (17, 34) | Pbo+Tras+Cape 0% |
| **Median PFS (95% CI):** | |
| 7.6 months (6.2, 9.5) | 5.4 months (4.1, 5.7) |

Prespecified efficacy boundary for $PFS_{BrainMets}$ (P=0.0080) was met at the first interim analysis.
Data cut off: Sep 4, 2019

# Overall Survival in the Total Study Population

| | Events N=612 | HR (95% CI) | P Value |
|---|---|---|---|
| TUC+Tras+Cape | 130/410 | 0.66 (0.50, 0.88) | 0.00480 |
| Pbo+Tras+Cape | 85/202 | | |




No. at Risk

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| TUC+Tras+Cape | 410 | 388 | 322 | 245 | 178 | 123 | 80 | 51 | 34 | 20 | 10 | 4 | 0 |
| Pbo+Tras+Cape | 202 | 191 | 160 | 119 | 77 | 48 | 32 | 19 | 7 | 5 | 2 | 1 | 0 |

**Risk of death was reduced by 34% in the total population**

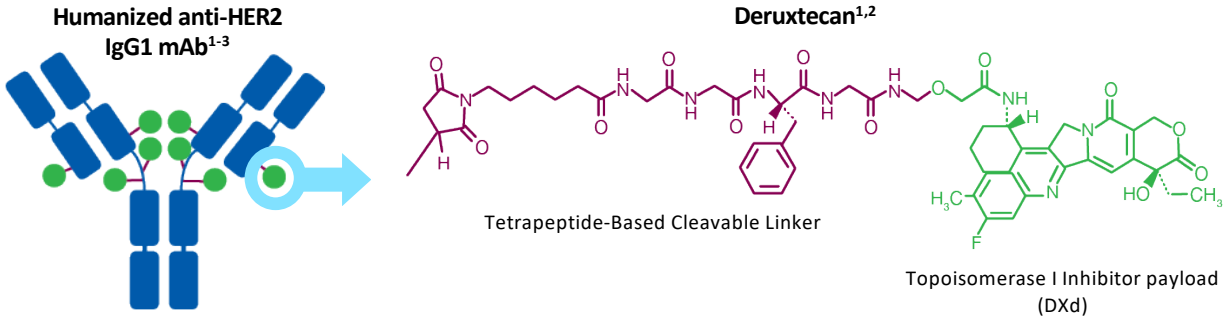
| Two-year OS (95% CI): | |
|---|---|
| TUC+Tras+Cape | Pbo+Tras+Cape |
| 45% (37, 53) | 27% (16, 39) |
| **Median OS (95% CI):** | |
| 21.9 months (18.3, 31.0) | 17.4 months (13.6, 19.9) |

Prespecified efficacy boundary for OS (P=0.0074) was met at the first interim analysis.
Data cut off: Sep 4, 2019

# Trastuzumab Deruxtecan (DS-8201) is a Novel ADC Designed to Deliver an Optimal Antitumor Effect

## Trastuzumab deruxtecan is an ADC composed of 3 components:

- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload, an exatecan derivative
- A tetrapeptide-based cleavable linker




- Payload MOA: topoisomerase I inhibitor
- High potency of payload
- High drug to antibody ratio ≈ 8
- Payload with short systemic half-life
- Stable linker-payload
- Tumor-selective cleavable linker
- Membrane-permeable payload

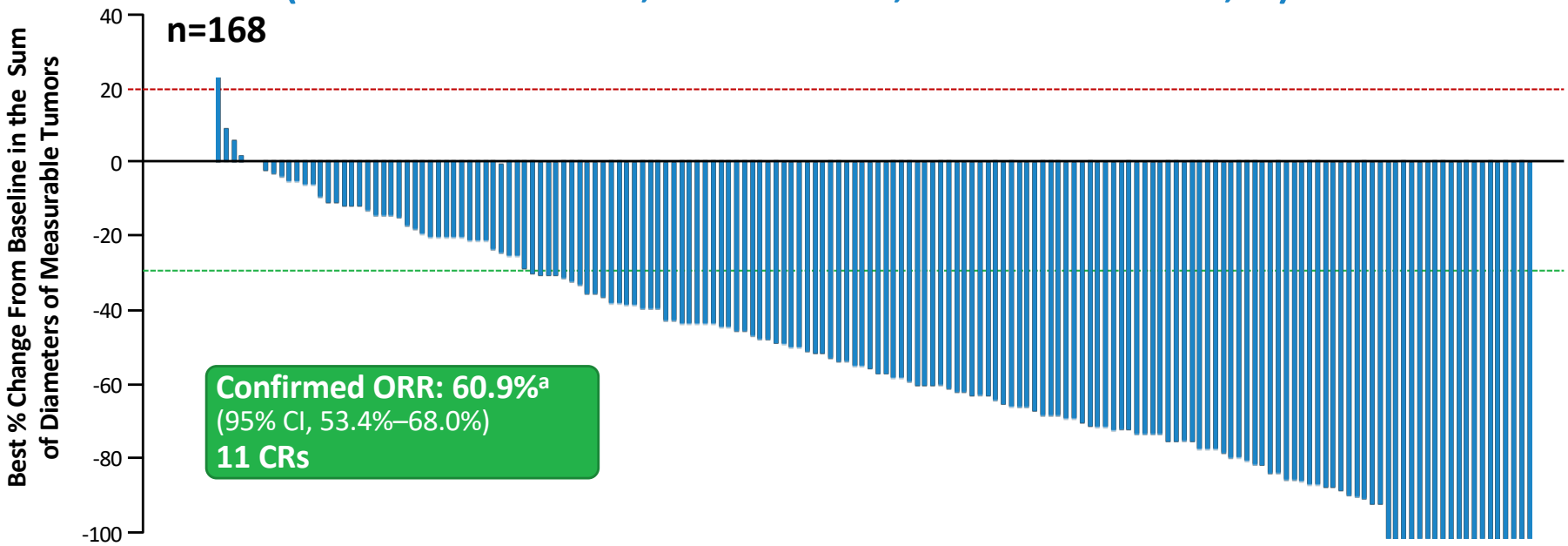
The clinical relevance of these features is under investigation.

ADC, antibody-drug conjugate; MOA, mechanism of action.

1. Nakada T, et al. Chem Pharm Bull (Tokyo). 2019;67(3):173-185. 2. Ogitani Y, et al. Clin Cancer Res. 2016;22(20):5097-5108. 3. Trail PA, et al. Pharmacol Ther. 2018;181:126-142. 4. Ogitani Y, et al. Cancer Sci. 2016;107(7):1039-1046.

# Best Change in Tumor Size

## Median prior lines of cancer therapy: 6 (range 2-27)
## (100% Trastuzumab; 100% T-DM1; 66% Pertuzumab; …)




By independent central review.
The line at 20% indicates progressive disease; the line at −30% indicates partial response.
[a] Includes all patients who received T-DXd 5.4 mg/kg (intent-to-treat analysis; N=184).

# Adverse Events of Special Interest: Interstitial Lung Disease

| | Patients who received T-DXd 5.4 mg/kg (N=184) | | | | | |
|---|---|---|---|---|---|---|
| **Preferred Term, n (%)** | **Grade 1** | **Grade 2** | **Grade 3** | **Grade 4** | **Grade 5** | **Any Grade/ Total** |
| **Interstitial lung disease** | 5 (2.7) | 15 (8.2) | 1 (0.5) | 0 | 4 (2.2) | **25 (13.6)** |

Drug related; ILD was determined by the Independent ILD Adjudication Committee based on 44 preferred terms.

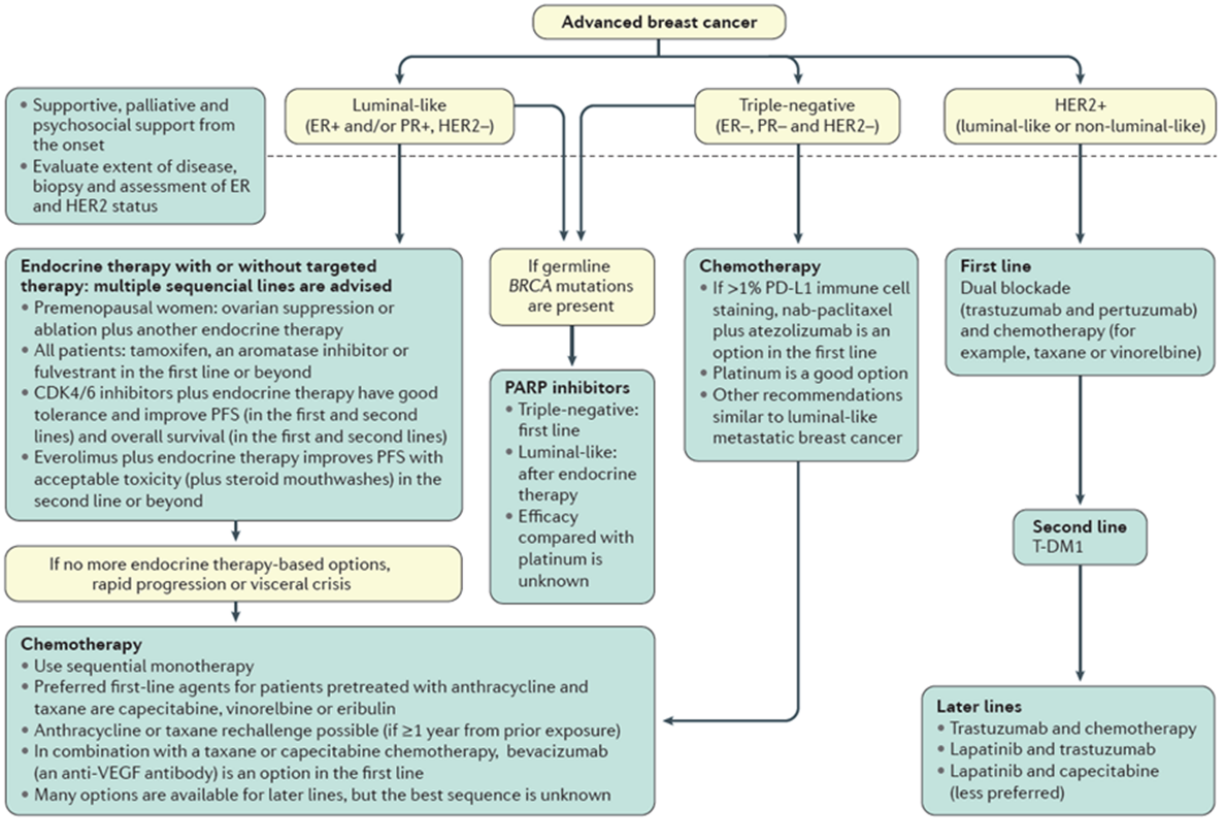
Among the 25 total events:

- **Median time to investigator-reported onset was 193 days (range, 42-535 days)**
- 13 of 20 patients with grade ≥2 ILD received corticosteroids
- 7 patients recovered, 2 were recovering, 12 were either outcome unknown or not followed until resolution, and 4 died
- Of the 4 fatal cases, onset was from 63-148 days, 3 received steroids as part of treatment, and death occurred 9-60 days after ILD diagnosis

**Recommendations: Monitor for symptoms. Hold T-DXd and start steroids as soon as ILD is suspected**

ILD, interstitial lung disease.

# *Metastatic* breast cancer: Treatment strategies




DS-8201 Tucatinib

Harbeck et al, 2019

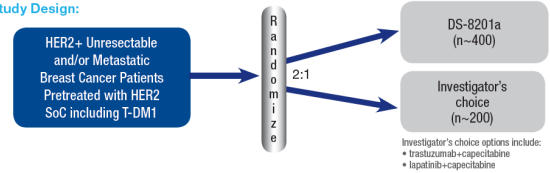
# DS-8201a (Trastuzumab Deruxtecan) → DESTINY Breast Phase 3 Programm

## DESTINY-Breast02

**DS-8201a in Human Epidermal Growth Factor Receptor 2 (HER2)-Positive Breast Cancer**

A Phase 3, Multicenter, Randomized, Open-Label, Active-Controlled Trial of DS 8201a, an Anti-HER2-Antibody Drug Conjugate (ADC), Versus Treatment of Investigator's Choice for HER2-Positive, Unresectable and/or Metastatic Breast Cancer Patients Pretreated with Prior Standard of Care (SoC) HER2 Therapies, Including Ado-Trastuzumab Emtansine (T-DM1)

**Study Design:**




**Primary Endpoint:** Progression Free Survival (PFS)

**Secondary Endpoints:**

- Overall Survival (OS)
- Objective Response Rate (ORR)
- Duration of Response (DoR)
- Pharmacokinetics (PK)
- Safety
- Clinical Benefit Rate (CBR)

**ClinicalTrials.gov Identifier:** NCT03523585

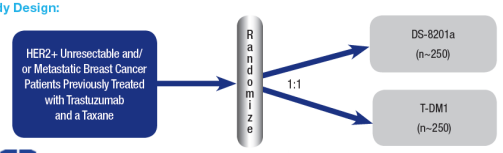
HER2 positiv

## DESTINY-Breast03

**DS-8201a in Human Epidermal Growth Factor Receptor 2 (HER2)-Positive Breast Cancer**

A Phase 3, Multicenter, Randomized, Open-label, Active Controlled Study of DS-8201a, an Anti-HER2-Antibody Drug Conjugate, Versus Ado-Trastuzumab Emtansine (T-DM1) for HER2-Positive, Unresectable and/or Metastatic Breast Cancer Patients Previously Treated with Trastuzumab and a Taxane

**Study Design:**




**Primary Endpoint:** Progression Free Survival (PFS)

**Secondary Endpoints:**

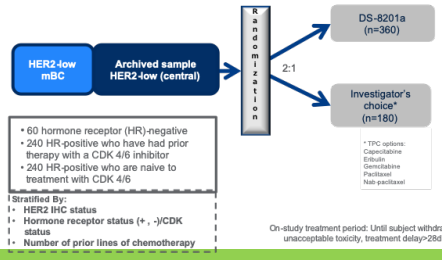
- Overall Survival (OS)
- Objective Response Rate (ORR)
- Duration of Response (DoR)
- Pharmacokinetics (PK)
- Safety
- Clinical Benefit Rate (CBR)

**ClinicalTrials.gov Identifier:** NCT03529110

## DESTINY-Breast 04

A Phase 3, multicenter, randomized, open-label, active-controlled trial of DS-8201a, an anti-HER2-antibody drug conjugate (ADC), versus treatment of physician's choice for HER2-low, unresectable and/or metastatic breast cancer subjects

HER2 low




**Primary Outcome Measures:**

- (PFS) based on Blinded Independent Central Review (BICR)]

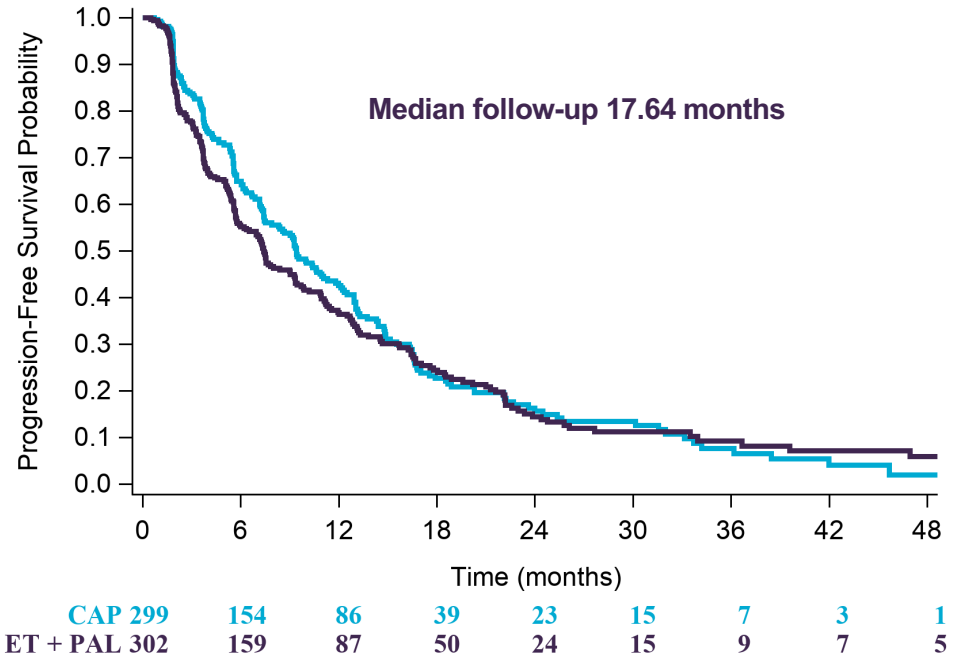
**Secondary Outcome Measures:**

- PFS based on Investigator Assessment
- Overall Survival (OS)
- Objective Response Rate (ORR)
- Duration of Response (DoR)

**ClinicalTrials.gov Identifier:** NCT03734029

Andre et al, SABCS 2018; Verma et al, SABCS 2018

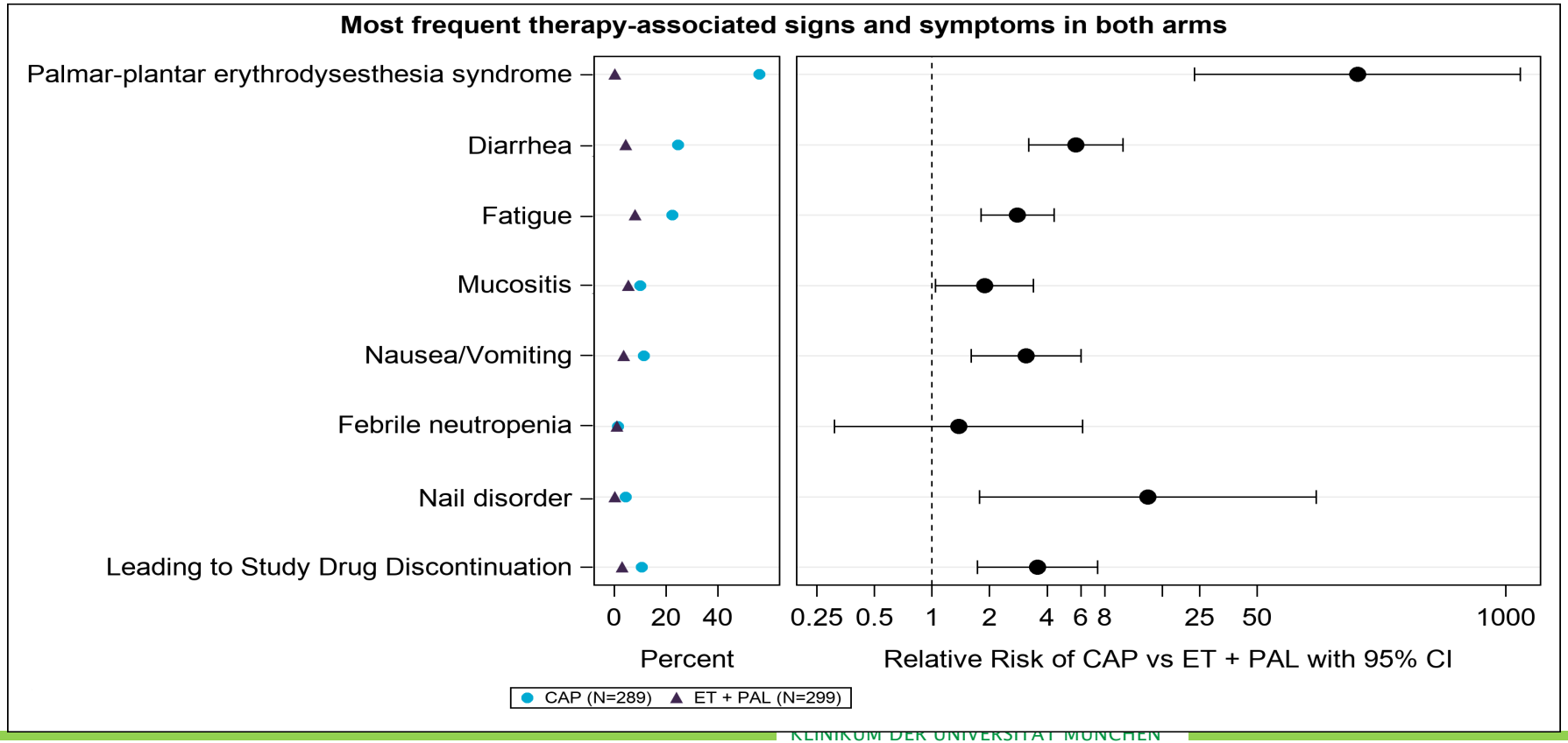
# PEARL: Secondary Objective: PFS Cohort 1 + Cohort 2 (N=601)



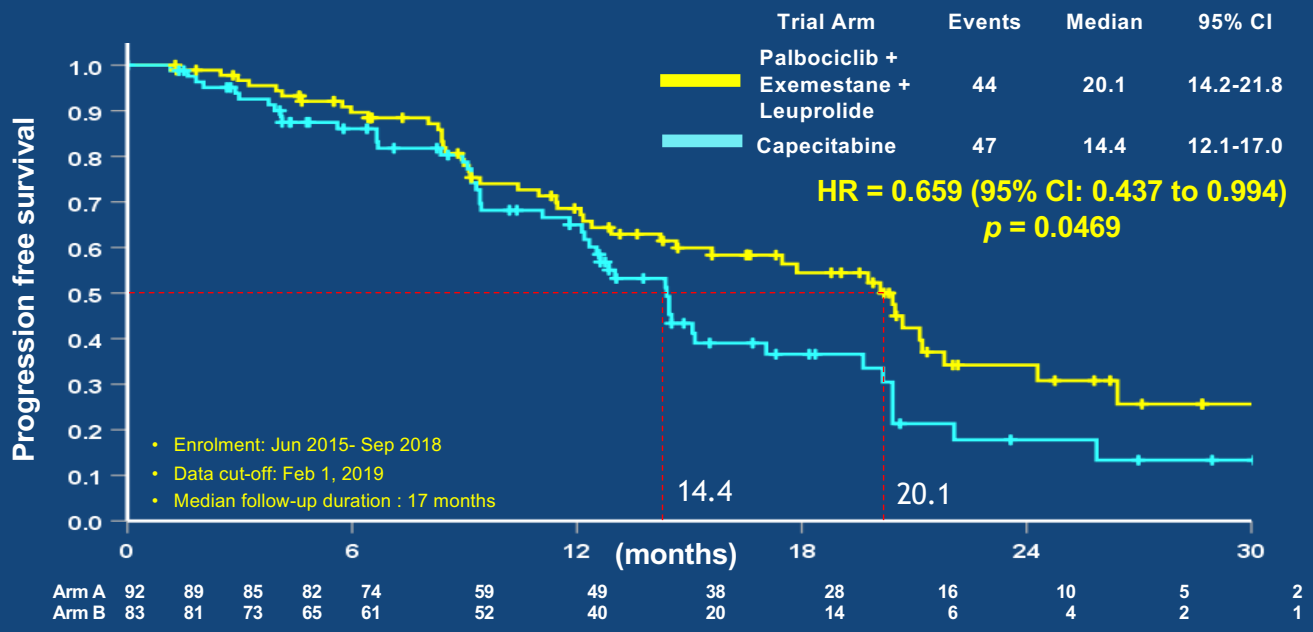

| | ET + PAL N=302 | CAP N=299 |
|---|---|---|
| Events, n (%) | 236 (78.1) | 203 (67.9) |
| Censored, n (%) | 66 (21.9) | 96 (32.1) |
| Median PFS, months (95% CI) | 7.4 (5.9, 9.3) | 9.4 (7.5, 11.3) |
| Adjusted Hazard Ratio (95% CI) | 1.09 (0.90, 1.31) | |
| Adjusted p-value (Cox) | 0.380 | |

The adjusted hazard ratio was obtained using a stratified Cox proportional hazard model with treatment arm and the stratification factors as covariates

# PEARL: Safety (Grade ≥ 2 per patient)



# Young-PEARL :
# Investigator-assessed Progression free survival

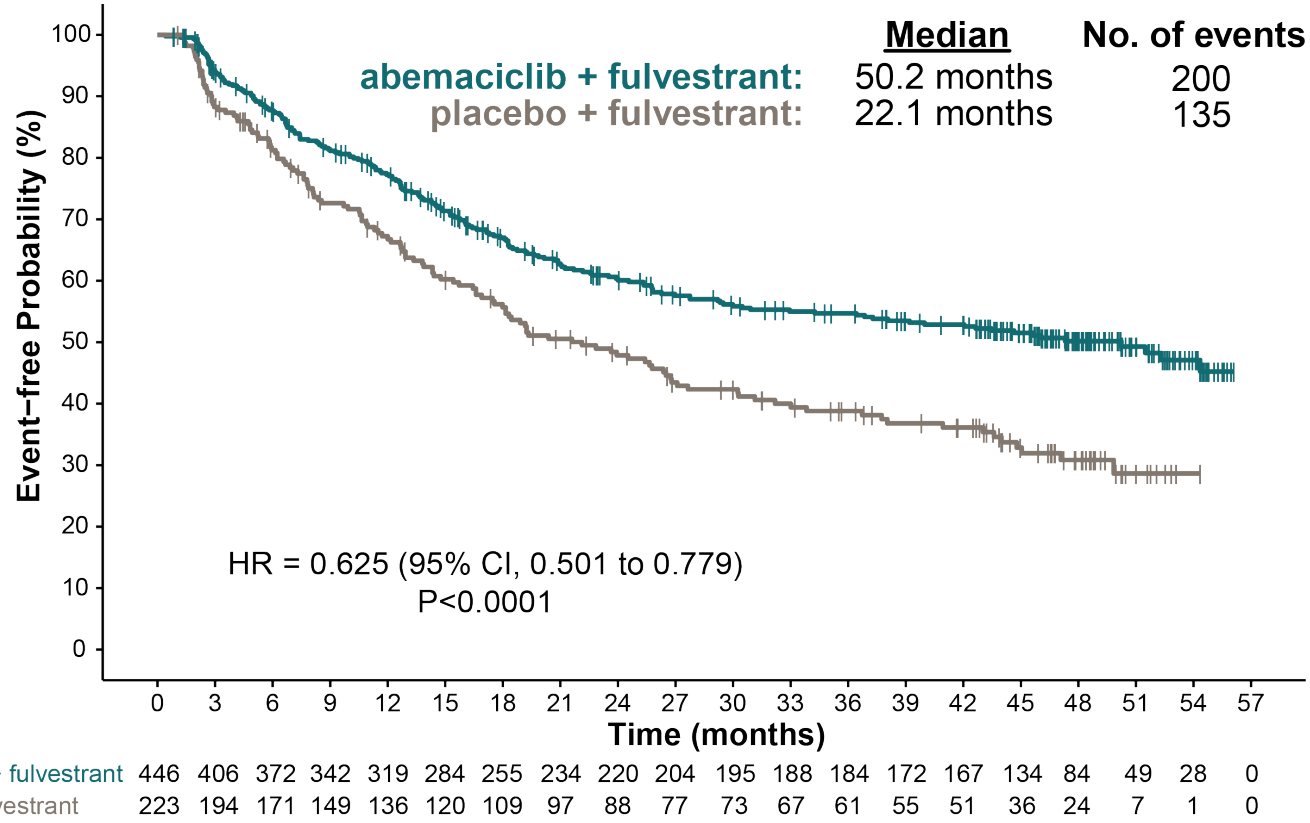


# **HR+ HER2- MBC:** Phase III Studien nach Progression unter ET

| Phase III trial | PALOMA 3 (n=521) | MONALEESA 3 (n=345) | MONARCH 2 (n=669) | BOLERO 2 (n=724) |
|---|---|---|---|---|
| CDK 4/6i | Palbociclib | Ribociclib | Abemaciclib | Everolimus |
| Endocrine agent | Fulvestrant | Fulvestrant | Fulvestrant | Exemestane |
| PFS (months) | 11.2 vs. 4.6 | 14.6 vs. 9.1 | 16.4 vs. 9.3 | 10.6 vs. 4.1 |
| **HR (PFS)** | **0.50** | **0.57** | **0.553** | **0.43** |
| **HR (OS)** | **0.81**(0.64–1.03) Endocrine sensitive: HR=0.72 (0.55–0.94); median Δ 10 months | **0.72** (0.57-0.92) p=0.0046 Δ alive at 42 months 11.9% (median OS n.r.) | **0.76** (0.61-0.95) p=0.014 median Δ 9.4 months | **0.89** (0.73-1.10) median Δ 4.4 months |
| Most frequent G3/4 side effects | neutropenia, leukopenia, anaemia | neutropenia, leukopenia, anaemia | diarrhoea, neutropenia, leukopenia, anaemia, nausea, fatigue | stomatitis, anaemia, dyspnea, hyperglycemia, fatigue, pneumonitis |

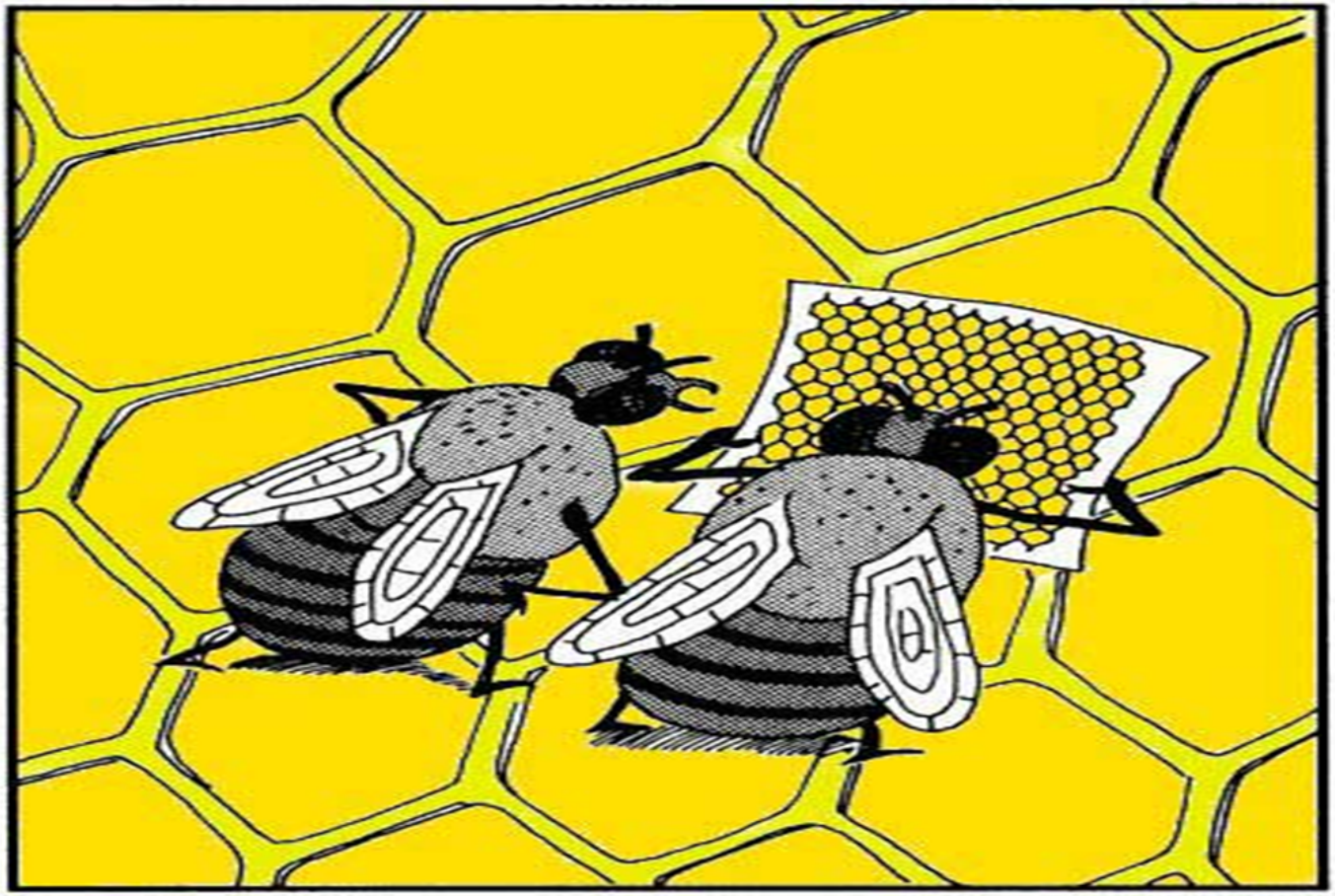
Turner et al. SABCS 2016; Christofanilli et al. 2016; Turner et al, NEJM 2018; Slamon et al, ASCO 2018 and ESMO 2019; Sledge et al. 2017 and ESMO 2019; Baselga et al. 2012; Piccart et al, 2014

# MONARCH 2:
## Exploratory Analysis - Time to Chemotherapy[a]




[a]Time to chemotherapy was analyzed from randomization to initiation of first post discontinuation chemotherapy (censoring patients who died prior to initiation of chemotherapy)

Sledge et al, ESMO 2019


So, Where are we exactly?

# Mammakarzinom-Therapie nach SABCS 2019


- ✓ Luminales Mammakarzinom (**HR+ HER2-**):
  - ✓ EBC: Prognoseverbesserung; *high-risk* luminal nach wie vor problematisch: CDK 4/6i vielversprechend – Studien als aktuelle Chance
  - ✓ MBC: CDK 4/6i haben Therapierealität verändert; Chemotherapie nur bei viszeraler Krise oder nach ausgeschöpfter endokriner Sequenz –

✓ **HER2+**: Prognoseverbesserung durch neo-adjuvante Therapie mit dualer Blockade und ggf. T-DM1; Änderung Metastasierungsmuster

✓MBC: Vielversprechend: Tucatinib und DS8201 (FDA Zulassung seit 12/19); Zugang in klinischen Studien (HER2CLIMB 02; DESTINY Programm)

✓ **TNBC**: Immuntherapie: Standard MBC Erstlinie; Zulassung EBC erwartet. Bei vielen offenen Fragen und ggf. permanenter Toxizität nur evidenzbasierter Einsatz sinnvoll

# Mammakarzinom 2019: Was haben wir erreicht ?

nature REVIEWS CLINICAL ONCOLOGY YEAR IN REVIEW

BREAST CANCER IN 2018

Truly personalized therapy — an end to the era of one size fits all

Nadia Harbeck and Rachel Wuerstlein

https://doi.org/10.1038/s41571-018-0165-1

- Vermeidung von Übertherapie HR+ HER2- (GBA Beschluss GEA)
- Eskalation nach non-pCR HER2+ (Zulassung T-DM1)
- Erste Immuntherapie: TN-MBC (Zulassungserweiterung Atezolizumab)
- Zielgerichtet statt Chemo bei gBRCA Mutation (Zulassung PARPi)
- Erste tumor-unabhängige Zulassung in EU bei NTRK Genfusion (Larotrectinib: Vitrakvi®)
- …

# Mammakarzinom 2020: Wie geht es weiter ?

nature REVIEWS CLINICAL ONCOLOGY YEAR IN REVIEW

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https://doi.org/10.1038/s41571-018-0165-1

- Weitere Daten zur **Immuntherapie**: Atezolizumab neoadjuvant (IMP031); Pembrolizumab Erstlinie MBC (KN355); …
- PIK3CA Mutation (HR+): zielgerichtete Therapie MBC (Alpelisib)
- Zulassungen (Einreichung) erwartet: Pembrolizumab (TNBC neoadjuvant); Tucatinib (MBC HER2+); DS8201(MBC HER2+ für EMA)
- …

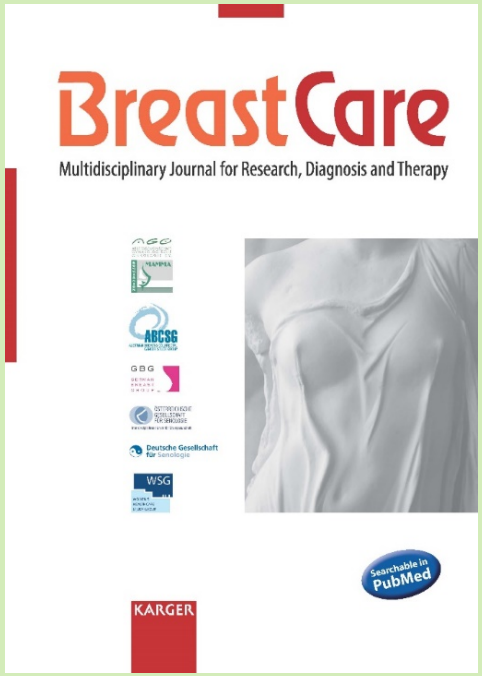

**Vorstellung der aktualisierten Empfehlungen zur Diagnostik und Therapie des frühen und fortgeschrittenen Mammakarzinoms 2020 durch die Mitglieder der AGO Kommission Mamma**

**InterContinental Hotel Frankfurt**
**Wilhelm-Leuschner-Strasse 43, 60329 Frankfurt am Main**

Für die Veranstaltung werden Fortbildungspunkte beantragt.
Weitere Informationen und Anmeldung auf www.GBG.de

www.ago-online.org

# Evidenzbasierte, patientenorientierte Brustkrebstherapie

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