22. ANNUAL SCIENTIFIC MEETING
06.03 – 07.03.2025
Frankfurt / Main

AGENDA

Einige kritische Gedanken zur „Deeskalitis“

15:20 – 16:50 Systemische Therapie des frühen Mammakarzinoms (II)

Vorsitz: Prof. Dr. Jens-Uwe Blohmer

Aktuelle Therapiestandards in der neoadjuvanten Behandlung 2025 Dr. Theresa Link (20 min)

Immunonkologie bei frühem Brustkrebs – Welches Target ist relevant
Prof. Dr. Andreas Schneeweiss (15 min)

Moderne kombinierte endokrine Therapie in der neoadjuvanten Behandlung von HRpos/HER2neg Brustkrebs (LOBSTER &PreCOOPERA) Prof. Dr. Vesna Bjelic-Radisic (10 min)

Moderne kombinierte endokrine Therapie in der neoadjuvanten Behandlung von HRpos/HER2pos Brustkrebs (GeparPiPPa) PD Dr. Mattea Reinisch (10 min)

Zukünftige Studien und Trends im neoadjuvanten Setting Prof. Dr. Michael Untch (10 min)

Kontroversen und Unsicherheiten (25 min)
Panel: Alle; Fallvorstellung: Prof. Dr. Christine Solbach

Prognosen sind schwierig,
vor allem, wenn sie die Zukunft betreffen
Karl Valentin

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Pathologic Complete Response After Neoadjuvant Chemotherapy Plus Trastuzumab Predicts Favorable Survival in Human Epidermal Growth Factor Receptor 2–Overexpressing Breast Cancer: Results From the TECHNO Trial of the AGO and GBG Study Groups

Michael Untch, Peter A. Fasching, Gottfried E. Konecny, Stephan Hasmüller, Annette Lebeau, Rolf Kreienberg, Oumar Camara, Volkmar Müller, Andreas du Bois, Thorsten Kühn, Elmar Stickeler, Nadia Harbeck, Cornelia Höss, Steffen Kahlert, Thomas Beck, Werner Fett, Keyur M. Mehta, Gunter von Minckwitz, and Sibylle Loibl

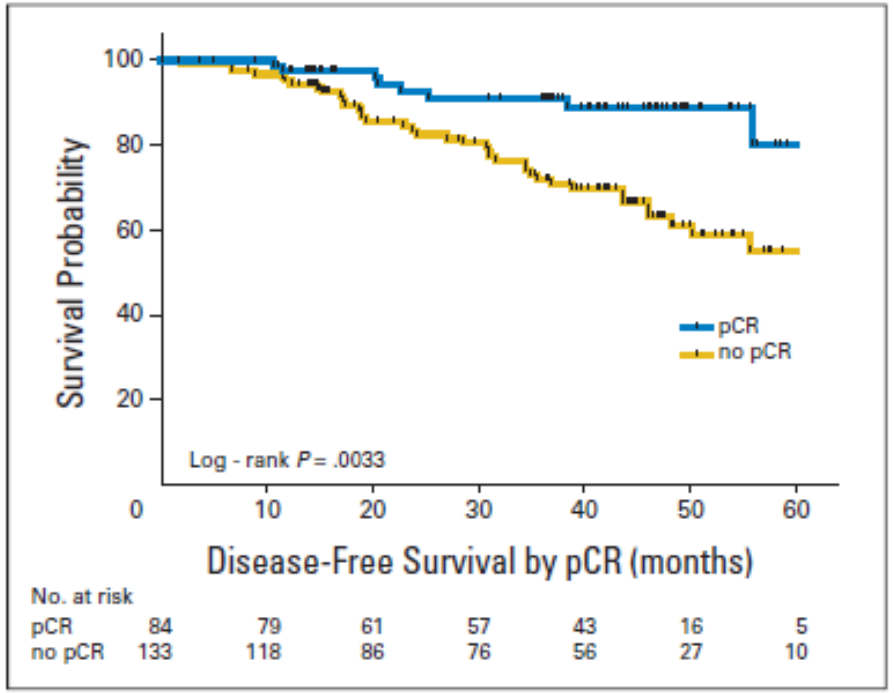


Fig 2. Disease-free survival in patients with pathologic complete response (pCR; blue) and without pCR (gold).

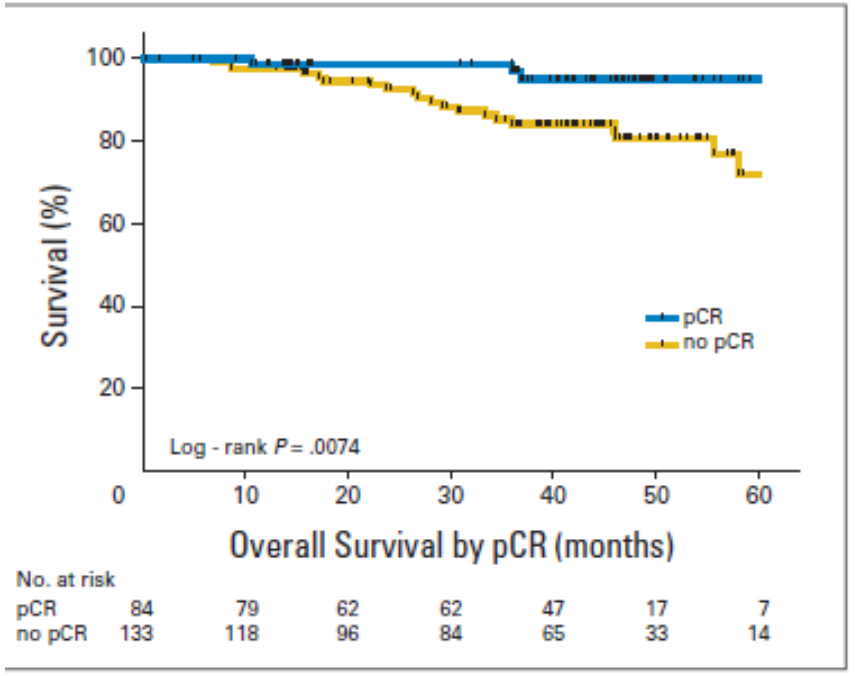
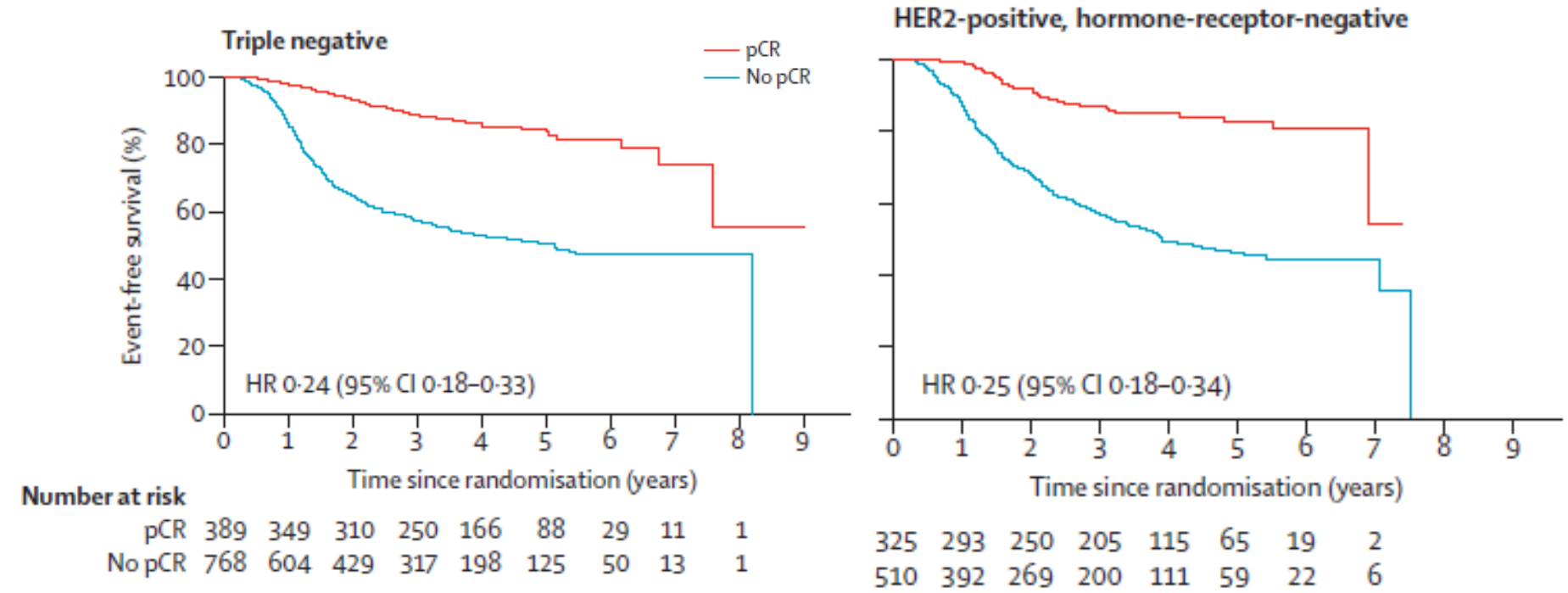


Fig 3. Overall survival in patients with pathologic complete response (pCR; blue) nd without pCR (gold).

Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis

Patricia Cortazar, Lijun Zhang, Michael Untch, Keyur Mehta, Joseph P Costantino, Norman Wolmark, Hervé Bonnefoi, David Cameron, Luca Gianni, Pinuccia Valagussa, Sandra M Swain, Tatiana Prowell, Sibylle Loibl, D Lawrence Wickerham, Jan Bogaerts, Jose Baselga, Charles Perou, Gideon Blumenthal, Jens Blohmer, Eleftherios P Mamounas, Jonas Bergh, Vladimir Semiglazov, Robert Justice, Holger Eidtmann, Soonmyung Paik, Martine Piccart, Rajeshwari Sridhara, Peter A Fasching, Leen Slaets, Shenghui Tang, Bernd Gerber, Charles E Geyer Jr, Richard Pazdur, Nina Ditsch, Priya Rastogi, Wolfgang Eiermann, Gunter von Minckwitz

www.thelancet.com **Published online February 14, 2014** **http://dx.doi.org/10.1016/S0140-6736(13)62422-8**

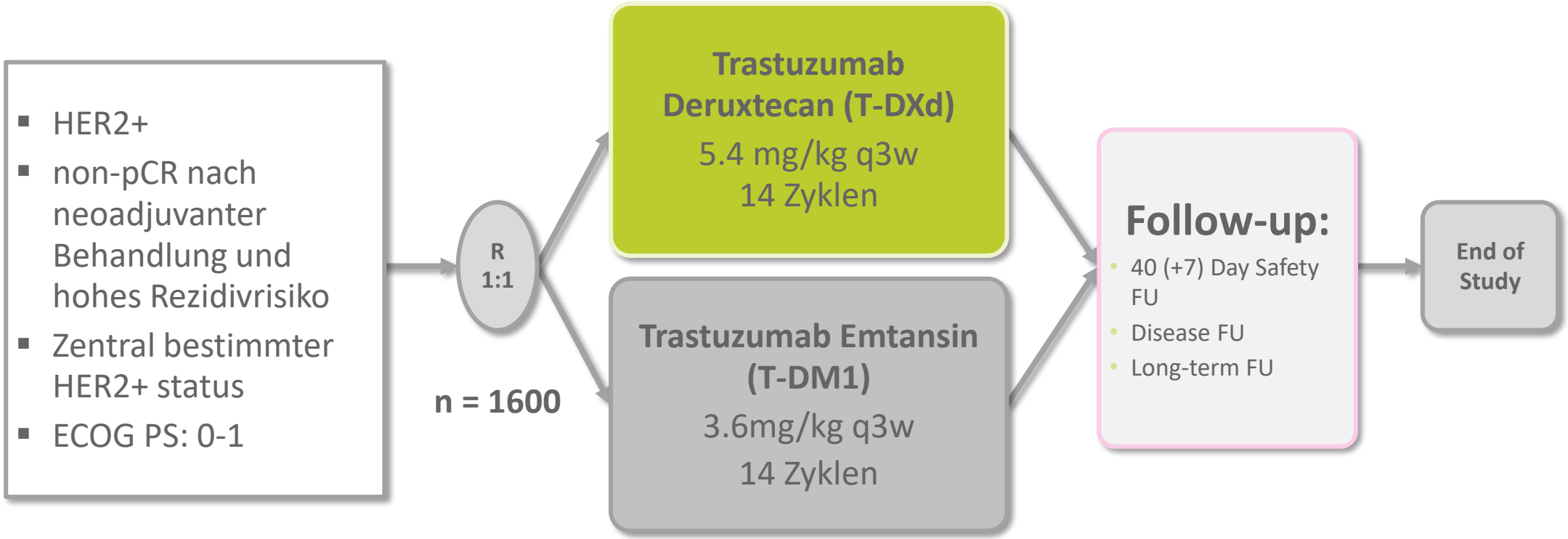


Survival with Trastuzumab Emtansine in Residual HER2-Positive Breast Cancer

Charles E. Geyer, Jr., M.D., Michael Untch, M.D., Ph.D.,
Chiun-Sheng Huang, M.D., Ph.D., M.P.H., Max S. Mano, M.D., Ph.D.,
Eleftherios P. Mamounas, M.D., M.P.H., Norman Wolmark, M.D.,
Priya Rastogi, M.D., Andreas Schneeweiss, M.D., Andres Redondo, M.D., Ph.D.,
Hans H. Fischer, M.D., Véronique D'Hondt, M.D., Ph.D., Alison K. Conlin, M.D.,
Valentina Guarneri, M.D., Ph.D., Irene L. Wapnir, M.D.,
Christian Jackisch, M.D., Ph.D., Claudia Arce-Salinas, M.D., Ph.D.,
Peter A. Fasching, M.D., Michael P. DiGiovanna, M.D., Ph.D., John P. Crown, M.D.,
Pia Wuelfing, M.D., Zhimin Shao, M.D., Elena Rota Caremoli, M.D.,
Hervé R. Bonnefoi, M.D., Bryan T. Hennessy, M.D., Ljiljana Stamatovic, M.D., Ph.D.,
Hugo Castro-Salguero, M.D., Adam M. Brufsky, M.D., Ph.D., Adam Knott, Ph.D.,
Asna Siddiqui, Ph.D., Chiara Lambertini, Ph.D., Thomas Boulet, M.S.,
Beatrice Nyawira, M.D., Eleonora Restuccia, M.D., and Sibylle Loibl, M.D., Ph.D.,
for the KATHERINE Study Group*

„Die **Langzeitstudie** von Fresenius Helios in Deutschland zur Wirksamkeit von **Antikörper-Wirkstoff Konjugaten** bei Brustkrebspatientinnen lieferte nun vielversprechende Ergebnisse, die jüngst im renommierten „New England Journal of Medicine" veröffentlicht wurden. Nach über acht Jahren sind neun von zehn Patientinnen, die an einer besonders aggressiven Form des Brustkrebses erkrankt sind, am Leben."

GBG 103- TruDy (DESTINY-Breast05)



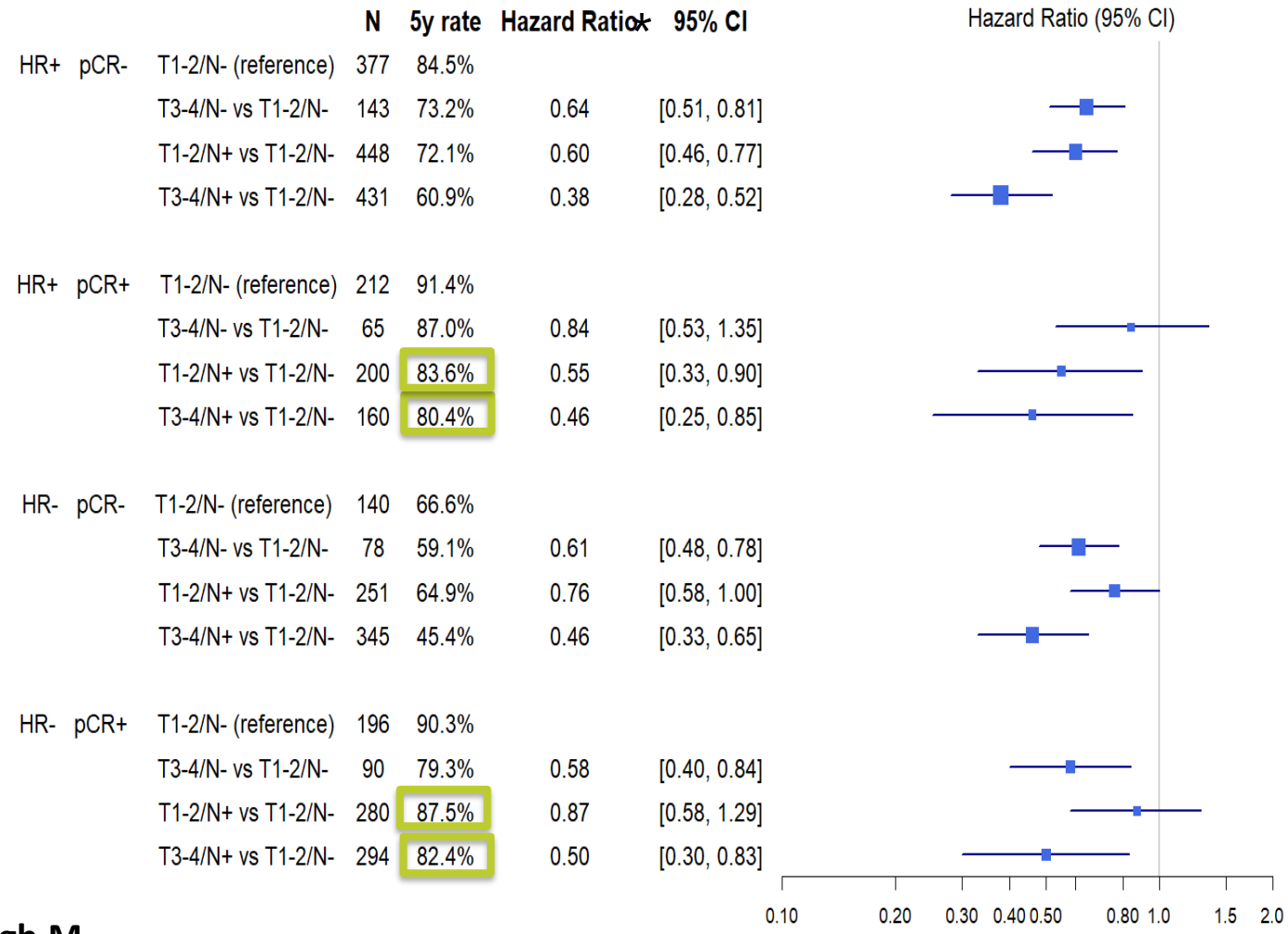
- **Randomisierung < 12 Wochen nach Brust-OP**
- **Adjuvante Radiotherapie und/oder endokrine Therapie per Protokoll und lokalen Richtlinien**

Strata:

- Operabel versus Inoperabel
- Nodalstatus nach NACT (positiv versus negativ)
- Hormonrezeptorstatus (positiv versus negativ)
- NACT (einfache Blockade versus doppelte Blockade)

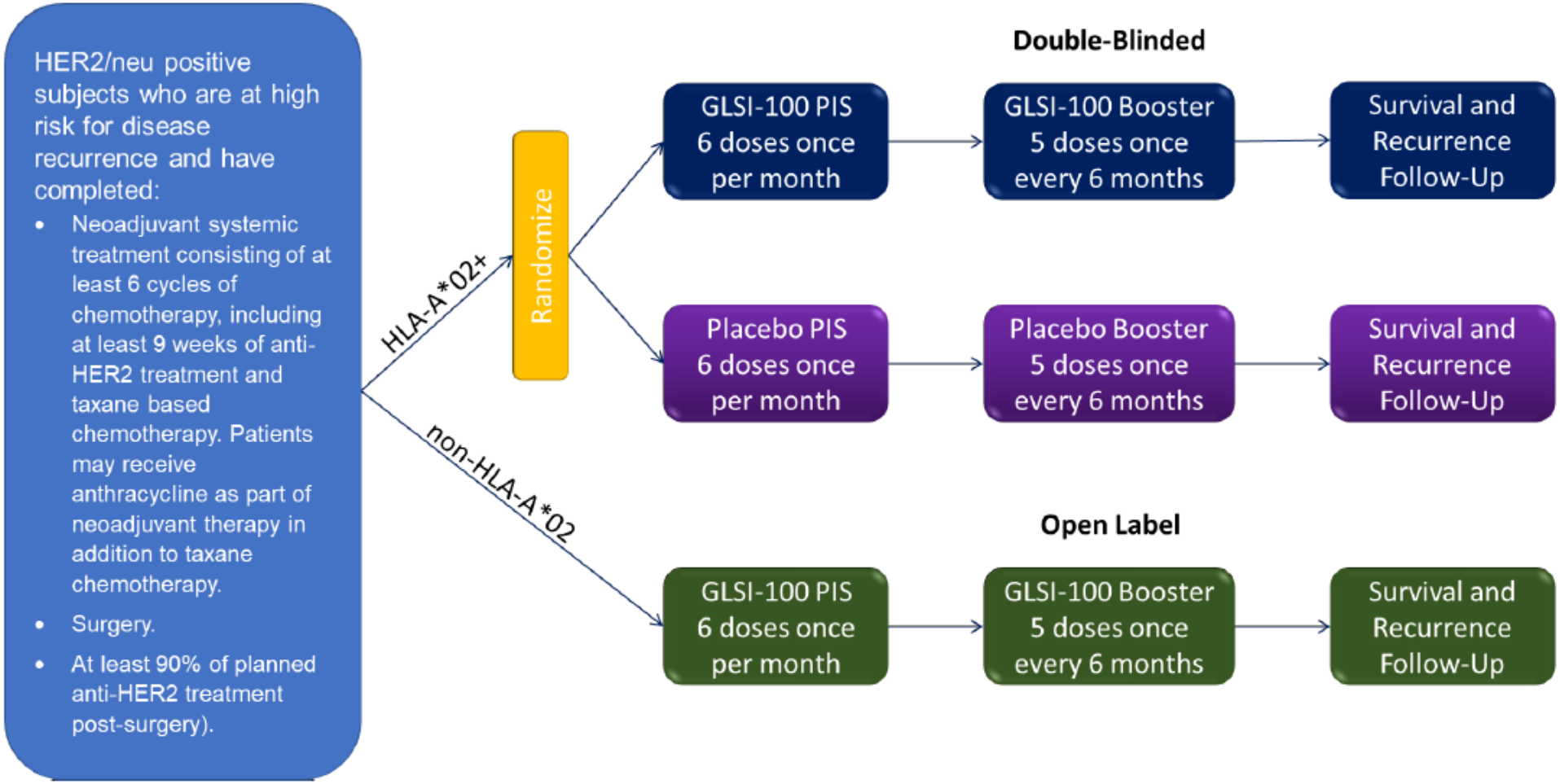
pCR and prognosis following neoadjuvant chemotherapy plus anti-HER2 therapy of HER2-positive early breast cancer (EBC)

- **Data from 3,710 patients randomized in 11 neoadjuvant trials for HER2-positive EBC. Receiving anti-HER2 therapy with trastuzumab or trastuzumab plus either Pertuzumab or Lapatinib**
- **CHERLOB, GeparQuattro, GeparQuinto, GeparSixto, HANNAH, LAPATAX, NEOALTTO, NEOSPHERE, NOAH, NSABP B-41, and TRYPHAENA**
- **pCR, EFS, and OS, and follow-up ≥3 years: The pCR was defined as ypT0/Tis ypN0.**



Loibl S, Untch M, et al, SABCS 2019 AND van Mackelenbergh M et al. J Clin Oncol 2023

FLAMINGO-01 Studiendesign



PIS = Primary Immunization

DESTINY-Breast 11 Trial

Population

HER2+ EBC

HR+ or HR-

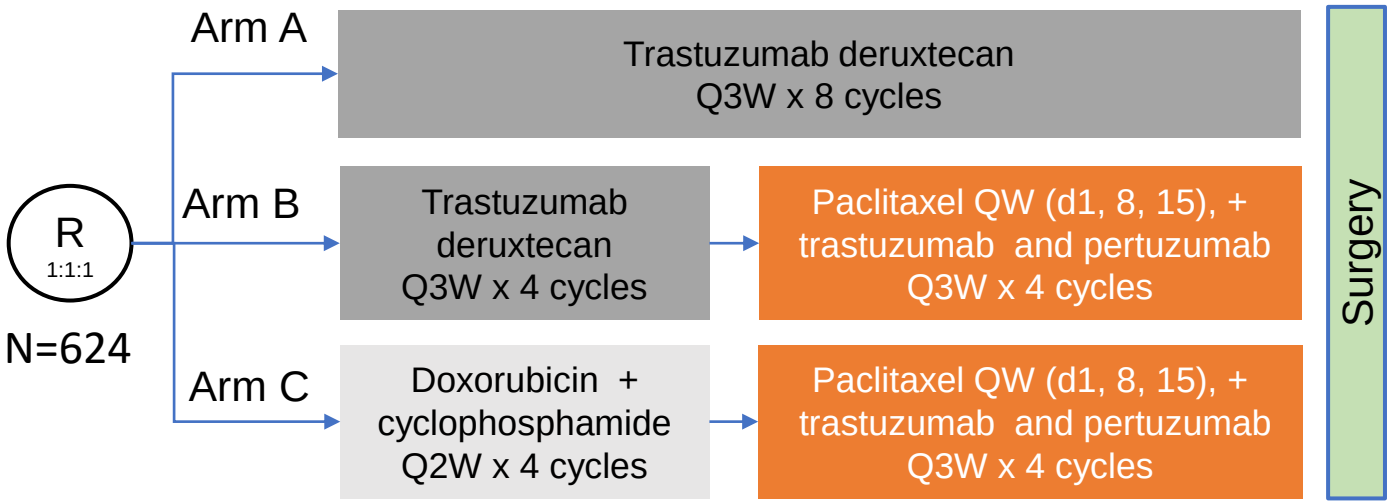
High-risk defined as one of the following:

- $T_xN_{1-3}M_0$
- $T_{3-4}N_xM_0$
- Inflammatory BC

Stratification factors:

- HR Status
  - HR+ vs HR-
- HER2 IHC
  - IHC3+ vs Other

Study Design



Endpoints

Primary Endpoint:

- pCR (ypT0/Tis ypN0)

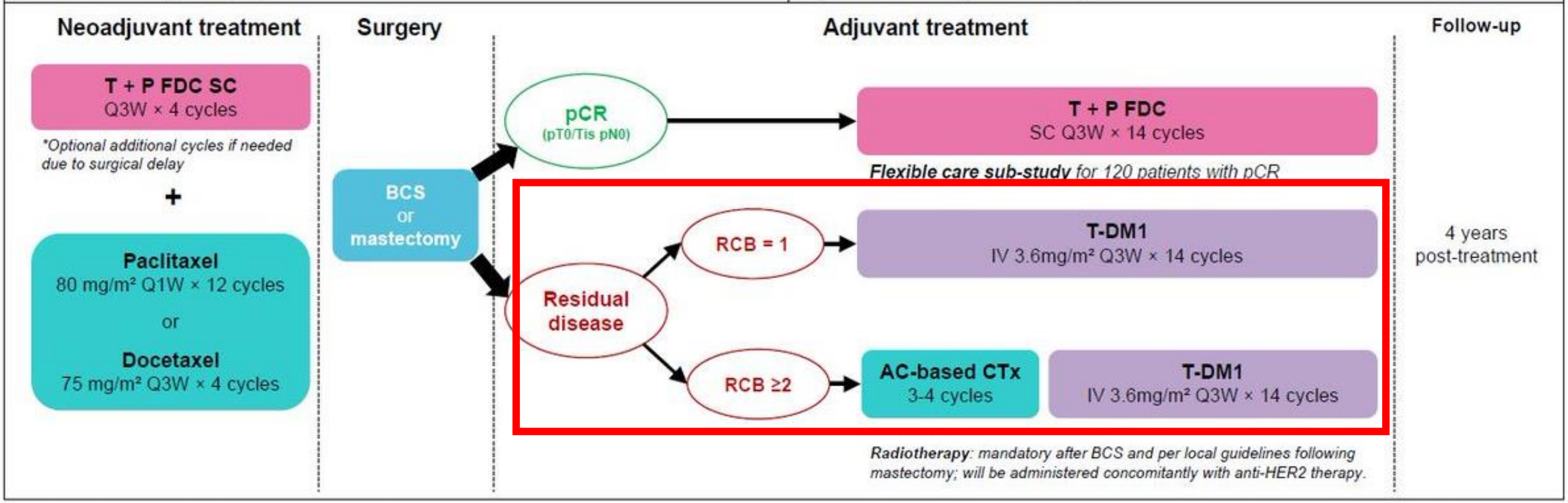
Secondary Endpoints:

- pCR (ypT0 ypN0)
- EFS
- IDFS
- OS
- HRQoL
- Safety
- PK and immunogenicity

DECRESCENDO TRIAL

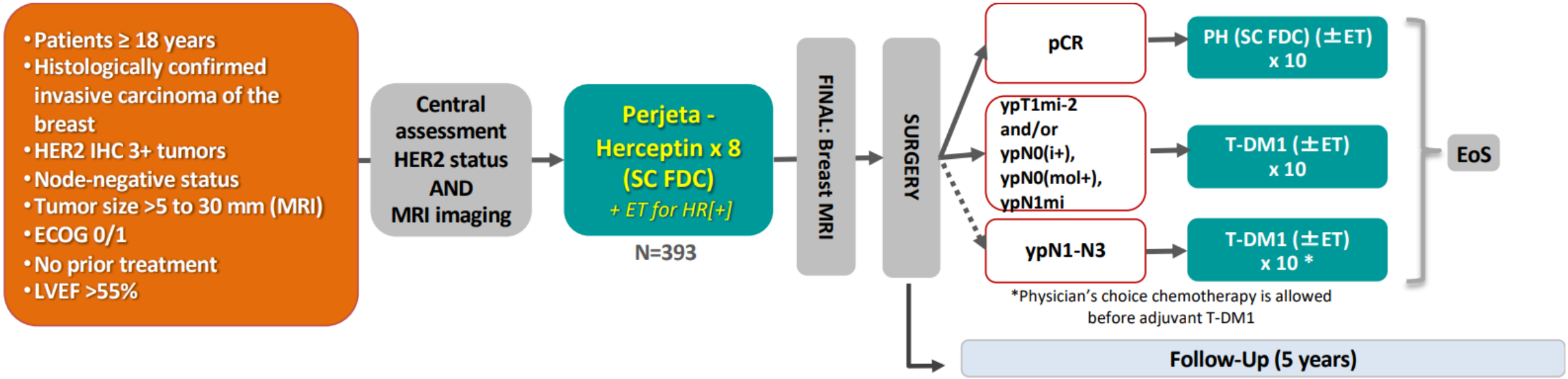
Patients (N=1065)
HER2-positive HR-negative invasive non-metastatic BC
Tumor size: ≥15mm and ≤50mm
Nodal status: negative (N0)

1° endpoint
3-year RFS in 500 patients with pCR, HER2-enriched intrinsic subtype
Key 2° endpoint (hierarchical testing)
3-year RFS in all patients with pCR

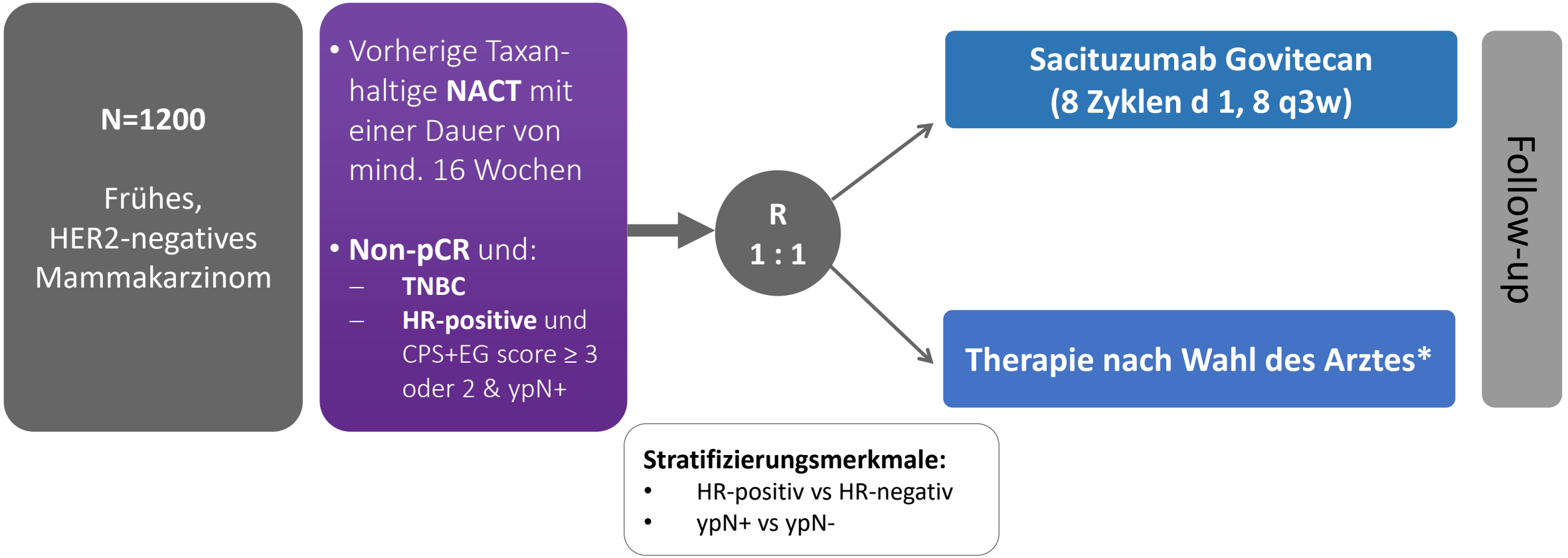


AC: anthracycline; **BC**: breast cancer; **BSC**: breast-conserving surgery; **CTx**: chemotherapy; **HER2:** human epidermal growth factor receptor-2; **HR**: hormone receptor; **IV**: administered by intravenous injection; **pCR**: pathological complete response; **Q1W**: every week; **Q3W**: every 3 weeks; **RCB**: residual cancer burden score; **RFS**: relapse-free survival; **SC**: administered by subcutaneous injection; **T-DM1**: trastuzumab emtansine; **T + P FDC**: trastuzumab + pertuzumab fixed-dose combination

PHERGAIN-2 TRIAL

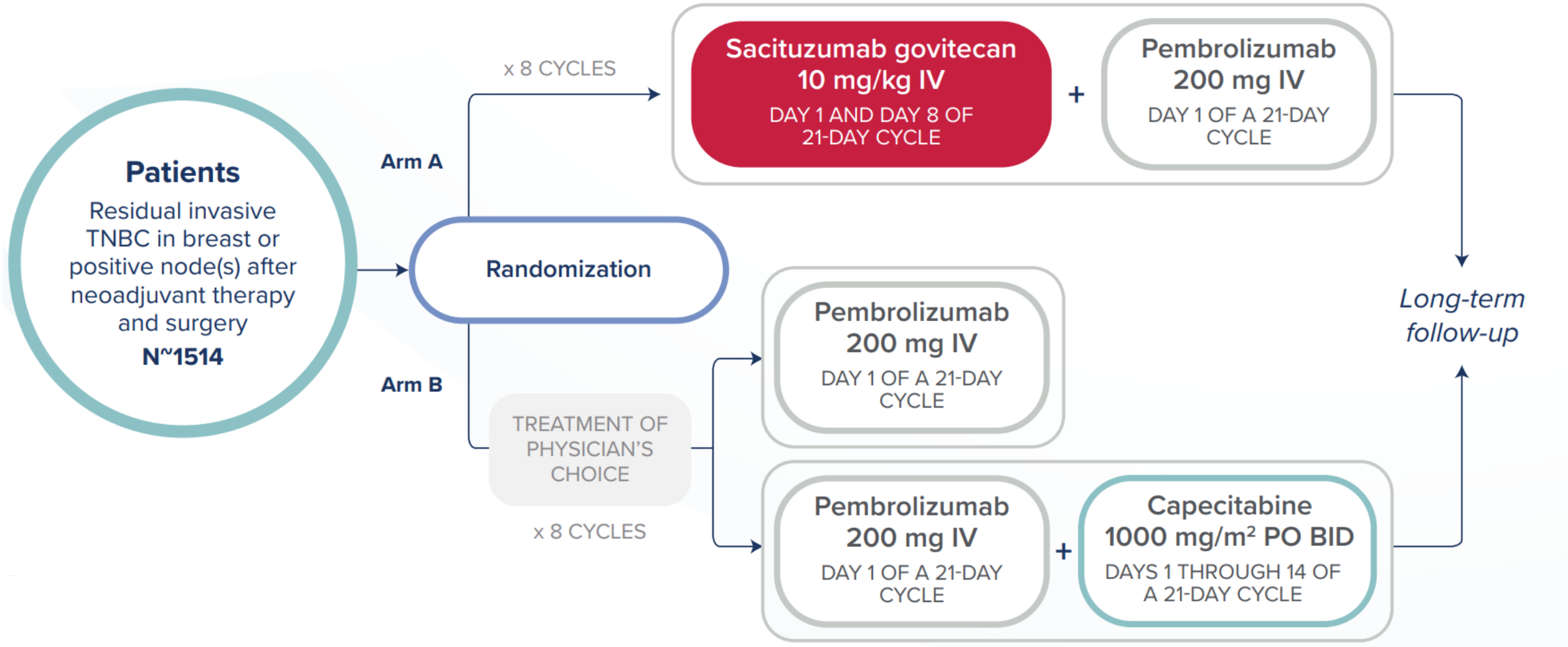


SASCIA: Studiendesign



***Capecitabine** (8 Zyklen) oder **platinhaltige Chemotherapie** (8 Zyklen) oder Beobachtung
Hintergrundtherapie: bei HR-positiven Patientinnen wir die endokrine Therapie nach lokalen Leitlinien durchgeführt
The start of endocrine therapy will be at the discretion of the investigator

Nachfolgestudie GBG 119 – Ascent-05



GILEAD
Creating Possible

Sacituzumab Tirumotecan (MK-2870) Plus Pembrolizumab Versus TPC in TNBC Who Did Not Achieve pCR

(MK2870-012 Studie). Phase: III. Rezeptorstatus: triple negativ

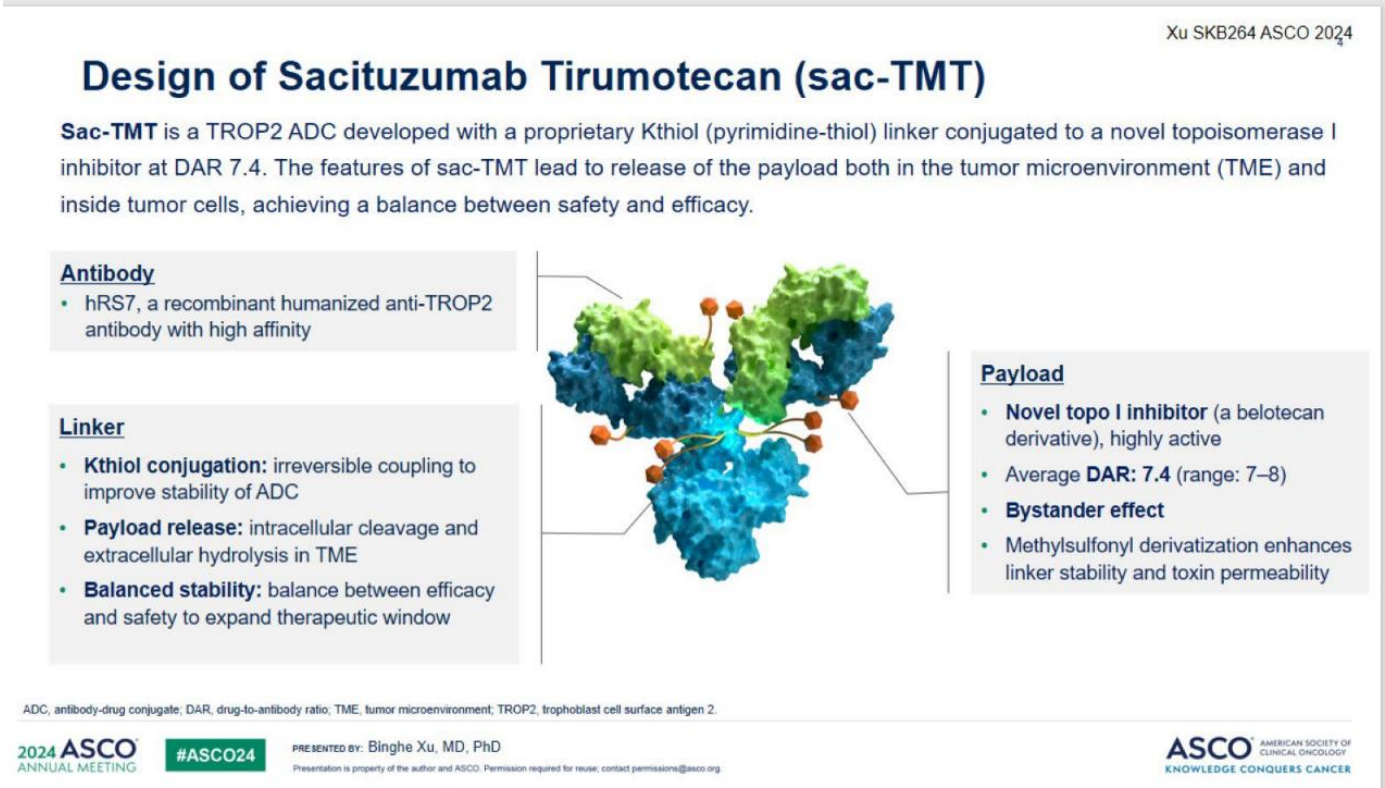
Stadium: eBC nach neoadjuvanter Therapie und Operation ohne pCR

Studiendesign: Experimenteller Arm Pembrolizumab + Sacituzumab Tirumotecan vs. Vergleichsarm Pembrolizumab oder Pembrolizumab + Capecitabine nach Wahl des behandelnden Arztes

Primärer Endpunkt: Invasive disease-free survival (iDFS)

Sekundäre Endpunkte: Gesamtüberleben (OS), Distant Disease-free Survival (dDFS), patient-reported outcome (PRO), Nebenwirkungen.

Sponsor: Merck Sharp & Dohme LLC



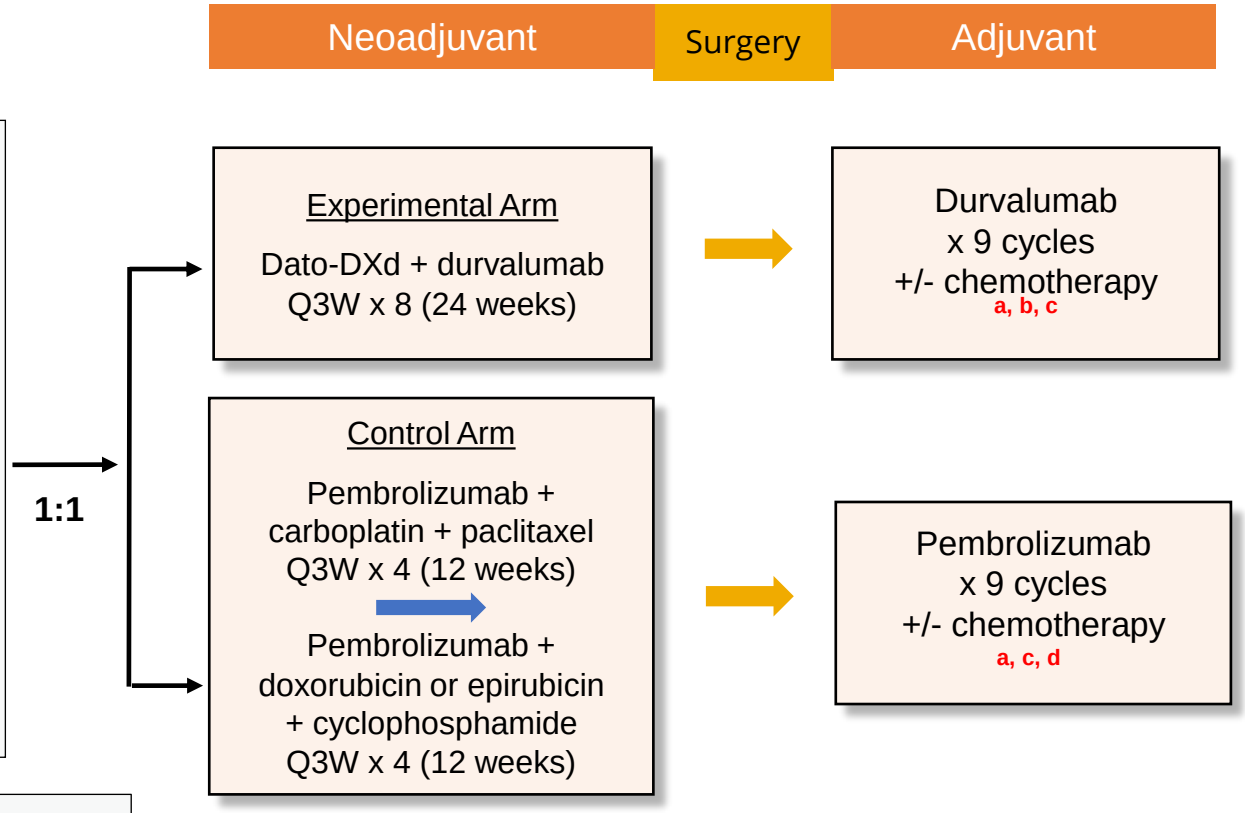
Tropion Breast 04: Dato-DXd + Durva in Neoadjuvant/Adjuvant TNBC

Key Eligibility Criteria

- Histologically confirmed Stage II or III unilateral or bilateral primary invasive breast cancer.
- TNBC (ER and PR < 1%) or hormone receptor-low breast cancer (ER and/or PR 1% to < 10%, neither hormone receptor may be ≥ 10%), and HER2-negative. [e, f]
- No evidence of distant disease.
- No prior surgery, radiation, or systemic anticancer therapy.
- ECOG PS 0 or 1.
- Adequate hematologic and organ function.

Stratification factors:

- Lymph node status (positive versus negative)
- Tumour stage (cT1 to cT2 versus cT3 to cT4
- Hormone receptor status (hormone receptor-negative [ER and PR < 1%] versus hormone receptor-low (ER and/or PR 1% to < 10%, neither hormone receptor may be ≥ 10%])
- Geographic region (US/Canada/Europe/Australia versus Rest of World).



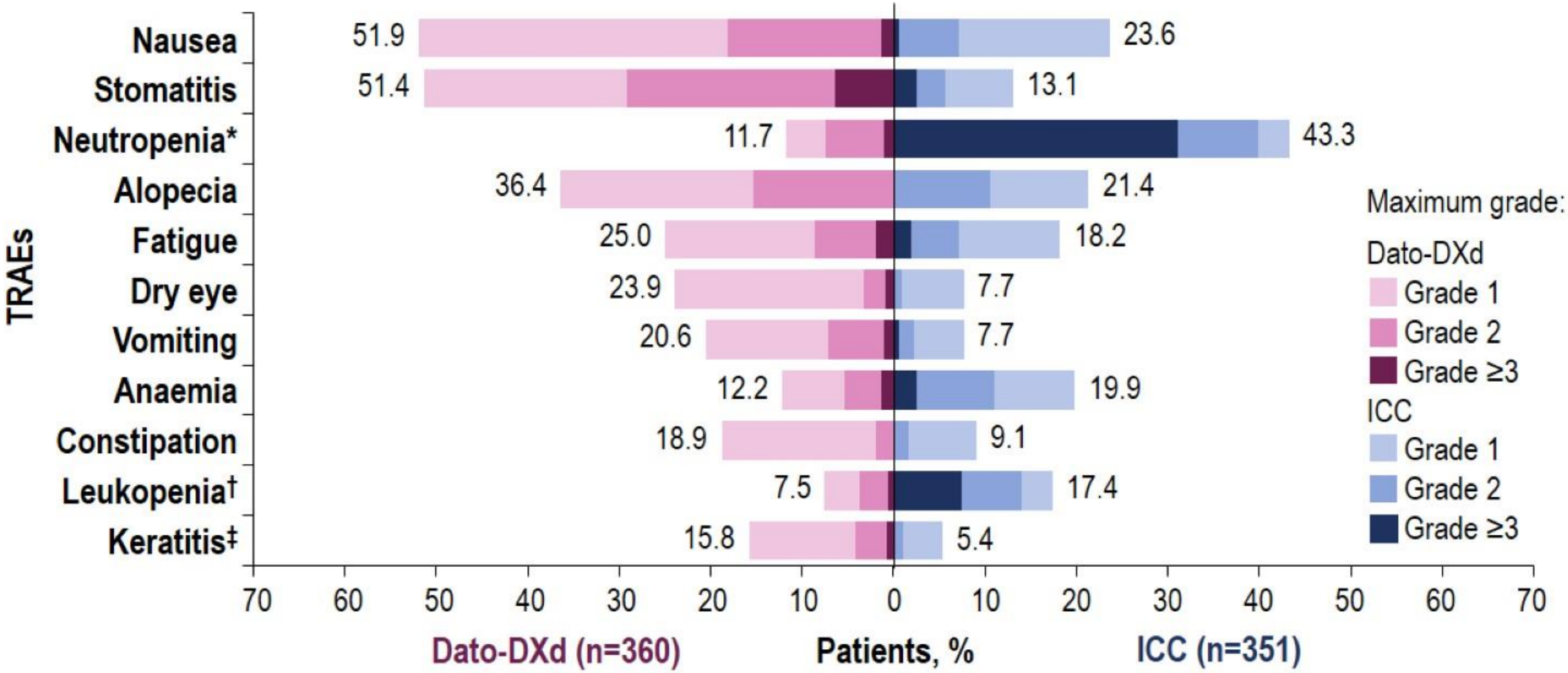
Dual primary endpoints:
pCR and EFS

Secondary endpoints:
OS, DDFS, safety and tolerability, PROs, PK, immunogenicity

Exploratory endpoints include but are not limited to:
TROP2, PD-L1 [e]

a. Endocrine therapy is permitted for participants with hormone receptor-low tumours. No adjuvant CDK4/6 inhibitor (eg, abemaciclib, ribociclib).
b. Adjuvant chemotherapy may be given in combination with durvalumab for participants with residual disease. Chemotherapy options at discretion of investigator, either: doxorubicin/epirubicin + cyclophosphamide, followed by paclitaxel + carboplatin; doxorubicin/epirubicin + cyclophosphamide followed by paclitaxel; carboplatin + paclitaxel; capecitabine.
c. Olaparib may be administered to participants who are g*BRCA*-positive with residual disease.
d. Adjuvant capecitabine may be given in combination with pembrolizumab for participants with residual disease, at the discretion of investigator.
e. Hormone receptor, HER2: local testing. *BRCA*: no mandatory testing, use local testing results. PD-L1 and TROP2: retrospective central small batch testing.
f. *BRCA* mutation is allowed.

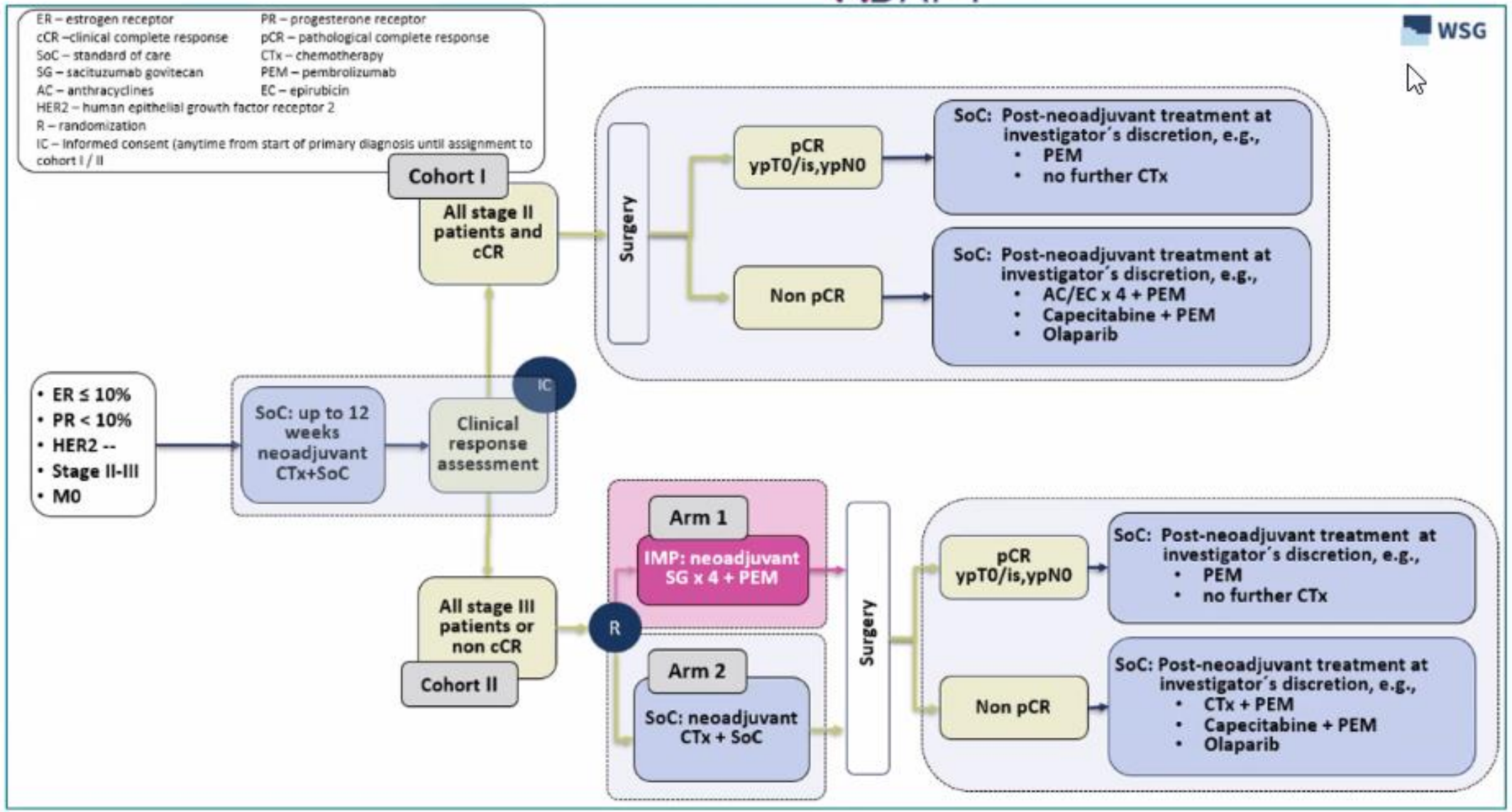
TRAEs Occurring in ≥15% of Patients



Data cutoff: 24 July 2024. Data are ordered according to frequency in either the Dato-DXd or ICC arms.

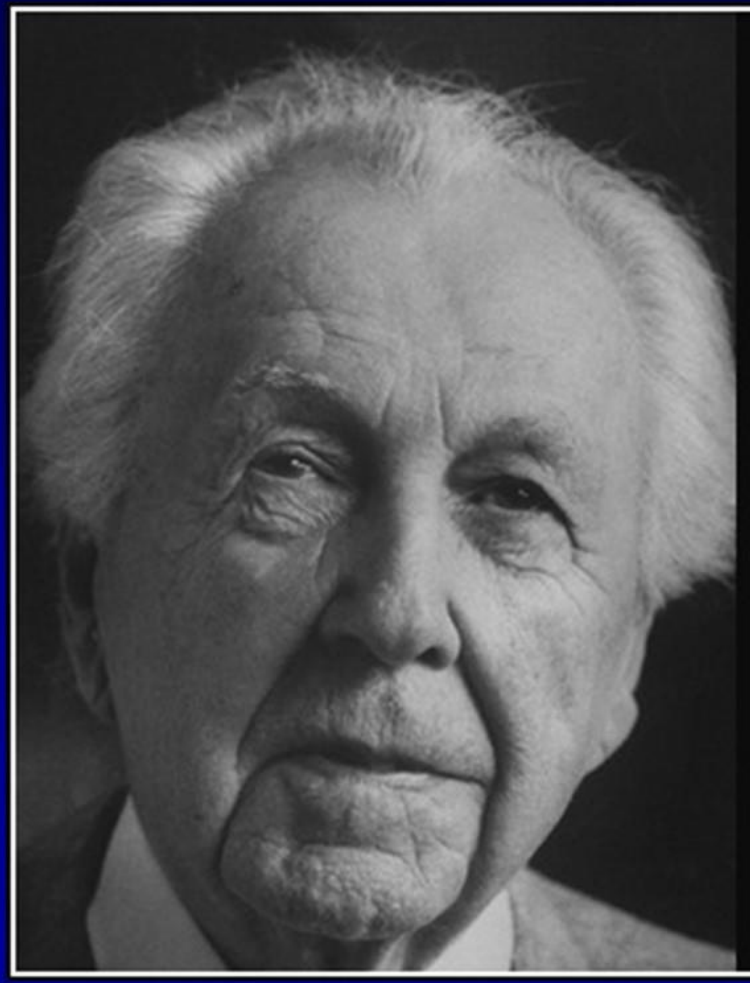
*Grouped term comprising neutropenia and neutrophil count decreased. †Grouped term comprising white blood cell count decreased and leukopenia. ‡Grouped term comprising keratitis, punctate keratitis, ulcerative keratitis.

Study Design



Zusammenfassung

1. **Her 2 pos→ Neoadjuvant A +T plus T/ P bei >T2 oder N + Standard**
2. **Bei non pCR→TDM 1 Standard.**
3. **TDM1 oder TDXD bei non pCR abwarten (DB 05, TRUDY Studie)**
4. **Deeskalation zu „neoadjuvant T+P“ um pCR zu erreichen ohne weitere Therapie ist herausfordend**
5. **Bei pCR nach PST, wird deeskaliert : weniger Chirurgie, weniger Bestrahlung**
6. **TNBC: Durva plus DATO DXD versus Chemo plus Pembro (TROPION Breast 04 Studie)**
7. **TNBC: SG bei non pCR (SASCIA Studie)**
8. **TNBC: bei non pCR, SG plus Pembro (ASCENT 05 Studie)**
9. **TNBC: bei non pCR, SAC-TMT plus Pembro (MK2870-012 Studie)**
10. **Was können wir für pCR Patientinnen mit hohem Risiko noch tun ?**
11. **Primum nihil nocere ist gut, Heilung ist besser!!**



Less is more only when more is too much.

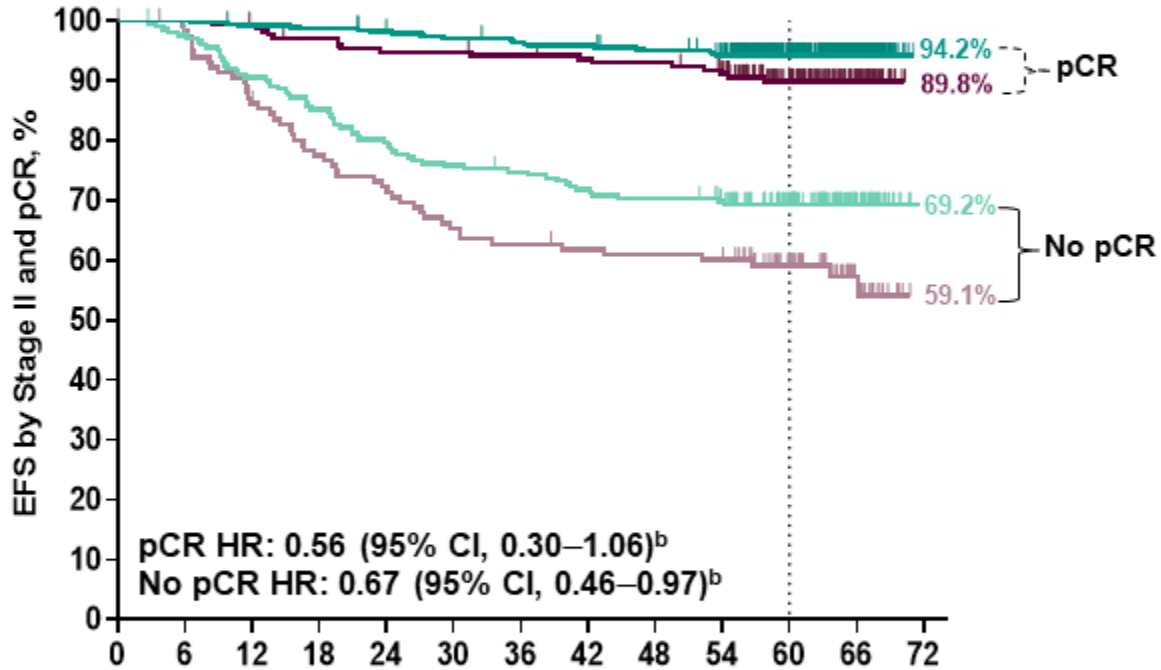
— Frank Lloyd Wright —

Christine Mau, Holger Schultz,
Katja Jugel, Heike Klocke, Katharina Kappo


Willst du an deine
Lieben denken,
musst du heut' ein
Märzchen
schenken. Es
ringt Glück und
Wohlergehn' und
sagt: "Man kann
den Frühling
schon deutlich
sehn'!"

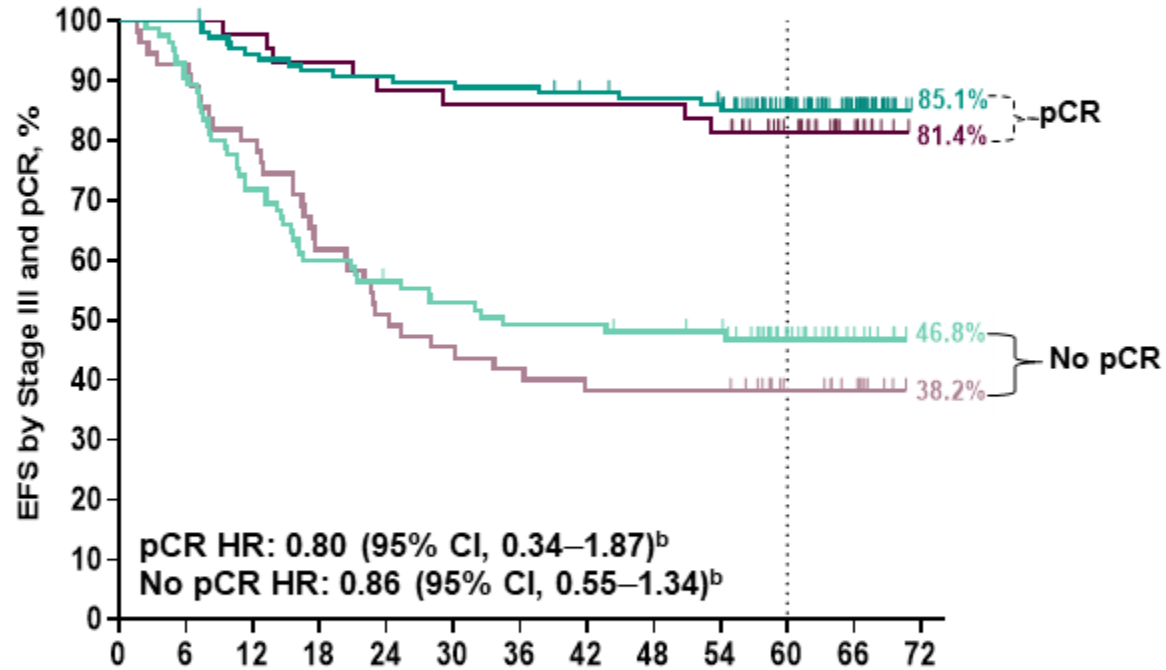
EFS at IA6 by Baseline Disease Stage in Patients With and Without pCR

Stage II by pCR Status[a]



No. at risk													
Pembro + Chemo/Pembro pCR	386	386	382	380	375	371	367	365	360	351	236	90	0
Pbo + Chemo/Pbo pCR	173	173	171	166	162	162	160	158	157	150	106	42	0
Pembro + Chemo/Pembro no pCR	204	197	183	172	161	153	150	144	141	135	95	35	0
Pbo + Chemo/Pbo no pCR	118	114	100	89	83	75	72	70	69	68	47	18	0

Stage III by pCR Status[a]



No. at risk													
Pembro + Chemo/Pembro pCR	109	109	102	99	98	97	96	93	91	88	59	30	0
Pbo + Chemo/Pbo pCR	43	43	42	40	38	37	37	37	37	35	24	11	0
Pembro + Chemo/Pembro no pCR	85	77	61	51	47	44	41	41	39	38	21	7	0
Pbo + Chemo/Pbo no pCR	55	51	44	34	28	25	23	21	21	21	12	8	0

[a]Post-hoc exploratory analyses, non-randomized comparison. [b]Hazard ratio (95% CI) analyzed based on the unstratified Cox model.
Data cutoff date of March 23, 2023.

159TiP

TROPION-Breast04: A phase 3 study of neoadjuvant datopotamab deruxtecan (Dato-DXd) + durvalumab followed by adjuvant durvalumab vs standard of care in treatment-naïve early-stage triple negative and HR-low/HER2– breast cancer

Sibylle Loibl,[1] Sara M. Tolaney,[2] Peter Schmid,[3] Barbara Pistilli,[4] Rebecca A. Dent,[5] Jamil Asslelah,[6] Qiang Liu,[7] Jane Lowe Meisel,[8] Naoki Niikura,[9] Yeon Hee Park,[10] Gustavo Werustky,[11] Giampaolo Bianchini,[12] Jay C. Andersen,[13] Robert Kozarski,[14] Nana Rokutanda,[15] Heather L. McArthur[16]

[1]Department of Medicine and Research, German Breast Group, Neu-Isenburg, Germany; [2]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, USA; [3]Barts Cancer Institute, Queen Mary University of London, London, UK; [4]Department of Medical Oncology, Gustave Roussy Cancer Center, Villejuif, France; [5]Department of Medical Oncology, National Cancer Center Singapore, Singapore; [6]Gerald Bronfman Department of Oncology, McGill University Health Centre, Cedars Cancer Centre, Montreal, QC, Canada; [7]Breast Tumor Center, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China; [8]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [9]Department of Breast Oncology, Tokai University School of Medicine, Kanagawa, Japan; [10]Samsung Medical Center, Sungkyunkwan University School of Medicine / Samsung Advanced Institute for Health Sciences & Technology, Sungkyunkwan University, Seoul, Republic of Korea; [11]Breast Cancer Program, Hospital Moinhos de Vento, Porto Alegre, Brazil; [12]Department of Medical Oncology, IRCCS Ospedale San Raffaele, Milan, Italy; [13]Medical Oncology, Compass Oncology/Sarah Cannon Research Institute, Portland, OR, USA; [14]Biostatistics, AstraZeneca, Cambridge, UK; [15]Oncology R&D, AstraZeneca, Gaithersburg, MD, USA; [16]Department of Medicine, Breast Cancer Program, Harold C. Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas, TX, USA

Plain language summary

Why are we performing this research?

- Triple-negative breast cancer (TNBC) is a type of breast cancer where cells do not have the HER2, oestrogen, or progesterone receptors. Therapies that target these receptors do not work in TNBC, making it difficult to treat. Currently, the standard of care for nearly TNBC is neoadjuvant chemotherapy plus pembrolizumab (a drug that blocks the activity of a protein called PD-1), followed by surgical removal of the tumour, then additional pembrolizumab. However, there remains a need for new therapies that improve response to treatment and long-term survival and reduce side effects associated with chemotherapy.
- Datopotamab deruxtecan (Dato-DXd) is a drug that consists of two parts: datopotamab (an antibody) and DXd (an anticancer drug), which are connected via a linker. Datopotamab binds to a protein called trophoblast cell surface antigen 2 (TROP2), which is found on TNBC tumours. Once bound, Dato-DXd is taken inside the tumour cell where the linker breaks, releasing DXd to kill the tumour.
- Durvalumab is a drug that blocks the activity of a protein called PD-L1, making tumours more susceptible to being killed by immune cells.
- Promising antitumour activity has been seen in patients with TNBC treated with Dato-DXd alone (in the phase 1 TROPION-PanTumor01 study[1]) or in combination with durvalumab (in the phase 1b/2 BEGONIA study[2]).
- This study, called TROPION-Breast04, was designed to compare Dato-DXd plus durvalumab followed by surgery and durvalumab alone, with the standard-of-care chemotherapy plus pembrolizumab in patients with previously untreated early-stage TNBC or HR-low/HER2–breast cancer (where cells do not have HER2 receptors, but can have low levels of oestrogen or progesterone receptors). The study will assess how well Dato-DXd plus durvalumab works and describe the side effects.

How are we performing this research?

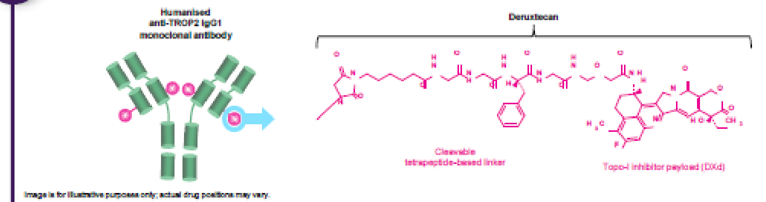
- We aim to recruit approximately 1728 patients who have:
  - TNBC or HR-low/HER2– breast cancer that has not spread from the original site
  - Not received any prior treatment.
- Eligible patients will randomly be assigned to a treatment group in equal numbers:
  - Dato-DXd plus durvalumab, followed by surgery, then further durvalumab-based therapy
  - Chemotherapy plus pembrolizumab, followed by surgery, then further pembrolizumab-based therapy.
- Patients will continue to receive treatment until they complete the planned course of therapy, unless side effects become unacceptable, or they choose to leave the study.

1. Bardia A, et al. Poster P6-10-03. Presented at SABCS 2022; 2. Schmid P, et al. Mini Oral 379MO. Presented at ESMO 2023.

Background

- The current SoC for patients with treatment-naïve stage II–III TNBC is neoadjuvant anthracycline/taxane/platinum-based chemotherapy plus pembrolizumab followed by surgery and adjuvant pembrolizumab monotherapy.[1–3]
  - However, among patients who received chemotherapy plus pembrolizumab in the KEYNOTE-522 trial (NCT03036488), 28% discontinued therapy due to treatment-related adverse events, and 37% had residual disease at the time of surgery, which was associated with poor outcomes.[3] Consequently, there remains an unmet need to develop a treatment approach that improves pCR rates and long-term survival while reducing chemotherapy-associated toxicity in patients with early-stage TNBC.
- There is considerable evidence to show that HR-low/HER2– breast cancer is biologically similar to TNBC, supporting the inclusion of these patients into clinical trials of TNBC.[4]
- Dato-DXd is an ADC consisting of a humanised anti-TROP2 IgG1 mAb covalently linked to a potent Topo-I inhibitor payload via a plasma stable, tumour-selective, tetrapeptide-based cleavable linker (**Figure 1**).
  - In the phase 1 TROPION-PanTumor01 study (NCT03401385), Dato-DXd monotherapy demonstrated a manageable safety profile and encouraging preliminary efficacy in patients with metastatic TNBC, with a confirmed ORR of 32% in all patients and 44% in Topo-I inhibitor-naïve patients with measurable disease at baseline.[5]
  - In the phase 3 TROPION-Breast01 study (NCT05104866), Dato-DXd monotherapy demonstrated statistically significant and clinically meaningful improvement in PFS with Dato-DXd compared with chemotherapy (hazard ratio 0.63 [95% CI: 0.52–0.76]; p<0.0001) in patients with previously-treated inoperable or metastatic HR-positive/HER2– breast cancer.[6]
- Durvalumab is a selective, high-affinity human IgG1 mAb that inhibits interaction of PD-L1 with PD-1 and CD80 by binding to PD-L1.[7]
  - In the phase 1b/2 BEGONIA study (NCT03742102), Dato-DXd plus durvalumab demonstrated durable responses in unresectable locally advanced/metastatic TNBC (ORR 79%; median DoR 15.5 months; median PFS 13.8 months).[8]
- The ongoing phase 3 TROPION-Breast03 trial (NCT05629585) is evaluating Dato-DXd with or without durvalumab versus SoC as adjuvant treatment in patients with stage I–III TNBC with residual invasive disease at the time of surgery after neoadjuvant treatment.
- The TROPION-Breast04 trial aims to determine if improved efficacy and safety can be achieved with neoadjuvant Dato-DXd plus durvalumab followed by adjuvant durvalumab, compared with the chemotherapy plus pembrolizumab SoC regimen in patients with previously untreated early-stage TNBC or HR-low/HER2–breast cancer.

Figure 1. Structure of Dato-DXd[9]



Optimised drug to antibody ratio ≈4
Stable linker-payload
Tumour-selective cleavable linker
Bystander antitumour effect

Image is for illustrative purposes only; actual drug positions may vary.

TROPION-Breast04 (NCT06112379): phase 3, randomised, open-label, multicentre, global study

Patients with histologically confirmed stage II or III unilateral or bilateral primary invasive TNBC or HR-low/HER2– breast cancer*
No evidence of distant disease
No prior surgery, radiation, or systemic anticancer therapy
ECOG PS 0 or 1

N≈1728 randomised 1:1

Stratified by:
- Lymph node status (pos. vs neg.)
- Tumour stage (cT1–cT2 vs cT3–cT4)
- HR status (HR-negative [ER and PR <1%] vs HR-low [ER and/or PR 1% to <10%; neither may be ≥10%])
- Geographic region (US/Canada/Europe/Australia vs other geographic regions)

Neoadjuvant	Surgery	Adjuvant[†]
Dato-DXd[a] + durvalumab[b] for 8 cycles	→	Durvalumab[c] for 9 cycles ± olaparib[‡,d] chemotherapy[§]
Pembrolizumab[e] + carboplatin[f] + paclitaxel[g] for 4 cycles then pembrolizumab[e] + cyclophosphamide[h] + doxorubicin[i]/epirubicin[j] for 4 cycles	→	Pembrolizumab[e] for 9 cycles ± olaparib[‡,d] capecitabine[k] for 8 cycles[¶]

*TNBC defined as: ER and PR <1% on IHC; negative for HER2 with 0 or 1+ intensity on IHC, or 2+ intensity on IHC and no evidence of amplification on ISH. HR-low/HER2– breast cancer defined as: ER 1% to <10% and/or PR 1% to <10% (neither hormone receptor may be ≥10%); negative for HER2 with 0 or 1+ intensity on IHC, or 2+ intensity on IHC and no evidence of amplification on ISH. †Adjuvant therapy regimen will be based on pCR rates with neoadjuvant treatment. ‡Olaparib may be given for a total period of one year in patients with gBRCA-positive tumours and residual disease; treatment may overlap with the 9 adjuvant cycles of durvalumab/pembrolizumab but may not be given concurrently with chemotherapy. §Chemotherapy may be given in combination with durvalumab only if patients have residual disease. Chemotherapy may be one of four regimens: 1) Either doxorubicin[] or epirubicin[] + cyclophosphamide[] for 4 cycles followed by paclitaxel[] and carboplatin[] for 4 cycles; 2) Either doxorubicin[] or epirubicin[] + cyclophosphamide[] for 4 cycles followed by paclitaxel[] for 4 cycles; 3) Carboplatin[] + paclitaxel[] for 4 cycles; 4) Capecitabine[] for 8 cycles. ¶Capecitabine may be given in combination with pembrolizumab only if patients have residual disease. [a]6 mg/kg IV Q3W; [b]1120 mg IV Q3W; [c]300 mg PO BID for 1 year; [d]200 mg IV Q3W; [e]AUC 5 mg/mL/min IV Q3W; OR AUC 1.5 mg/mL/min IV QW (based on investigator preference); [f]80 mg/m² IV QW; [g]600 mg/m² IV Q3W; [h]60 mg/m² IV Q3W; [i]90 mg/m² IV Q3W; [j]1000 or 1250 mg/m² (based on standard institutional practice) PO BID on Days 1 to 14, Q3W.

Study endpoints

1°
- pCR rate by central assessment
- EFS by investigator assessment

2°
- Overall survival
- Distant disease-free survival
- Pharmacokinetics and immunogenicity
- Safety and tolerability
- PROs in terms of:
  - Breast and arm symptoms, physical function, fatigue, GHS/QoL

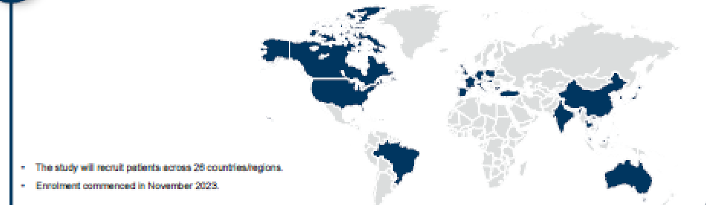
Key inclusion criteria

- Adults (aged ≥18 years) with histologically confirmed stage II or III unilateral or bilateral primary invasive TNBC or HR-low/HER2– breast cancer per AJCC 8th edition,[10] as assessed by the investigator.
  - TNBC defined as: ER and PR <1% on IHC; negative for HER2 with 0 or 1+ intensity on IHC, or 2+ intensity on IHC and no evidence of amplification on ISH.
  - HR-low/HER2– breast cancer defined as: ER 1% to <10% and/or PR 1% to <10% (neither hormone receptor may be ≥10%); negative for HER2 with 0 or 1+ intensity on IHC, or 2+ intensity on IHC and no evidence of amplification on ISH.
- ECOG PS of 0 or 1.
- Provision of an acceptable tumour sample prior to randomisation.
- Adequate bone marrow reserve and organ function within 7 days before randomisation.

Key exclusion criteria

- Evidence of severe/uncontrolled systemic diseases including active infection requiring intravenous treatment, serious chronic gastrointestinal conditions associated with diarrhoea, active bleeding diseases, significant cardiac or psychological illness, chronic or previously complicated diverticulitis, or history of allogenic organ transplant.
- History of another primary malignancy except for malignancy treated with curative intent with no known active disease within 3 years before randomisation and of low potential risk for recurrence. Exceptions include adequately resected non-melanoma skin cancer and curatively treated in situ disease.
- Active or prior documented autoimmune or inflammatory disease (with certain exceptions).
- Evidence of distant disease.
- Clinically significant corneal disease.
- Active or uncontrolled hepatitis B or C infection, uncontrolled HIV infection, or active tuberculosis.
- Suspected, current, or previous non-infectious ILD/pneumonitis that require(d) steroids.
- Any prior or concurrent surgery, radiotherapy or systemic anticancer therapy for TNBC or HR-low/HER2– breast cancer including chemotherapy, radiation therapy, endocrine therapy, immune-mediated therapy (e.g., anti-CTLA-4 and anti-PD-(L)1 antibodies, excluding therapeutic anticancer vaccines), retinoid therapy, or targeted therapy.
- Prior exposure to the following treatment:
  - Chloroquine/hydroxychloroquine with ≤14 days washout before randomisation
  - Immunosuppressive medication <14 days before first dose of study intervention
  - Live, attenuated vaccine <30 days before first dose of study intervention.

Study status



- The study will recruit patients across 26 countries/regions.
- Enrolment commenced in November 2023.

Planned/active recruitment

Poster

Mobile-friendly Poster

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Abbreviations

ADC, antibody-drug conjugate; AJCC, American Joint Committee on Cancer; AUC, area under the curve; BID, twice daily; CI, confidence interval; CTLA-4, cytotoxic T-lymphocyte-associated protein 4; Dato-DXd, datopotamab deruxtecan; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; ER, oestrogen receptor; GHS, global health status; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IgG, immunoglobulin G; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH, in situ hybridisation; IV, intravenous; mAb, monoclonal antibody; ORR, objective response rate; pCR, pathologic complete response; PD-(L)1, programmed cell death (ligand)-1; PFS, progression-free survival; PO, orally; PR, progesterone receptor; PRO, patient-reported outcome; QoL, quality of life; QxW, every x weeks; SoC, standard of care; TNBC, triple-negative breast cancer; Topo-I, topoisomerase I; TROP2, trophoblast cell surface protein 2.

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Disclosures

Sibylle Loibl has participated in advisory board/advisory role for AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, Celgene, DSI, Eirgenix, Gilead, GSK, Lilly, Merck, Novartis, Olema, Pfizer, Pierre Fabre, Relay Therapeutics, Roche, Sanofi, SeaGen; has been an invited speaker for AstraZeneca, DSI, Gilead, MedScape, Novartis, Pfizer, Roche, SeaGen, Stemline-Menarini, WMScope; employment as CEO for GBG Forschungs; has received research grants/funding from AbbVie, AstraZeneca, Celgene, Daiichi-Sankyo, Greenwich, Immunomedics, Molecular Therapeutics, Novartis, Pfizer, Roche; has served as Principal Investigator for PI Agility; is a member of AGO, DKG, ASCO and ESMO; and has other financial relationships with AstraZeneca, Daiichi-Sankyo, Immunomedics, Novartis, Pfizer, Roche, SeaGen; and involvement with patients.
For co-author disclosures, please refer to abstract.

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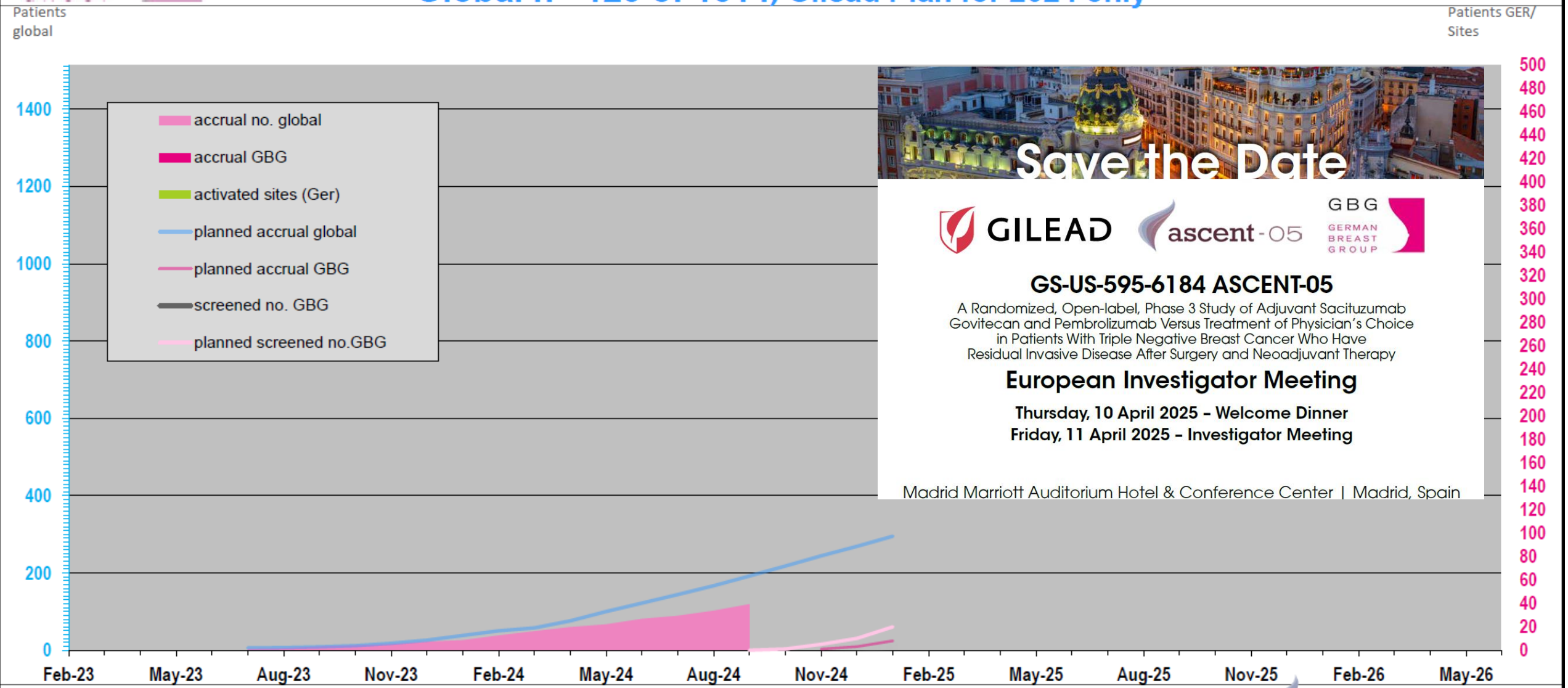
Ascent-05- Recruitment on 02.09.2024

Global n =123 of 1514, Gilead Plan for 2024 only



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GILEAD ascent-05 GBG GERMAN BREAST GROUP

GS-US-595-6184 ASCENT-05

A Randomized, Open-label, Phase 3 Study of Adjuvant Sacituzumab Govitecan and Pembrolizumab Versus Treatment of Physician's Choice in Patients With Triple Negative Breast Cancer Who Have Residual Invasive Disease After Surgery and Neoadjuvant Therapy

European Investigator Meeting

Thursday, 10 April 2025 – Welcome Dinner
Friday, 11 April 2025 – Investigator Meeting

Madrid Marriott Auditorium Hotel & Conference Center | Madrid, Spain

Tropion Breast 04 - Studie:

Einschluss-Kriterien:

Histologically confirmed Stage II or III unilateral or bilateral primary invasive breast cancer.

TNBC (ER and PR < 1%) or hormone receptor-low breast cancer (ER and/or PR 1% to < 10%, neither hormone receptor may be ≥ 10%), and HER2-negative.

No evidence of distant disease.

No prior surgery, radiation, or systemic anticancer therapy.

ECOG PS 0 or 1.

Adequate hematologic and organ function

Intervention:

A Phase III Randomised Study to Evaluate Dato-DXd and Durvalumab for Neoadjuvant/Adjuvant Treatment of Triple-Negative or Hormone Receptor-low/HER2-negative Breast Cancer