Update Mammakarzinom - Onkotreff

Neue zugelassene Medikamente und Therapieabläufe

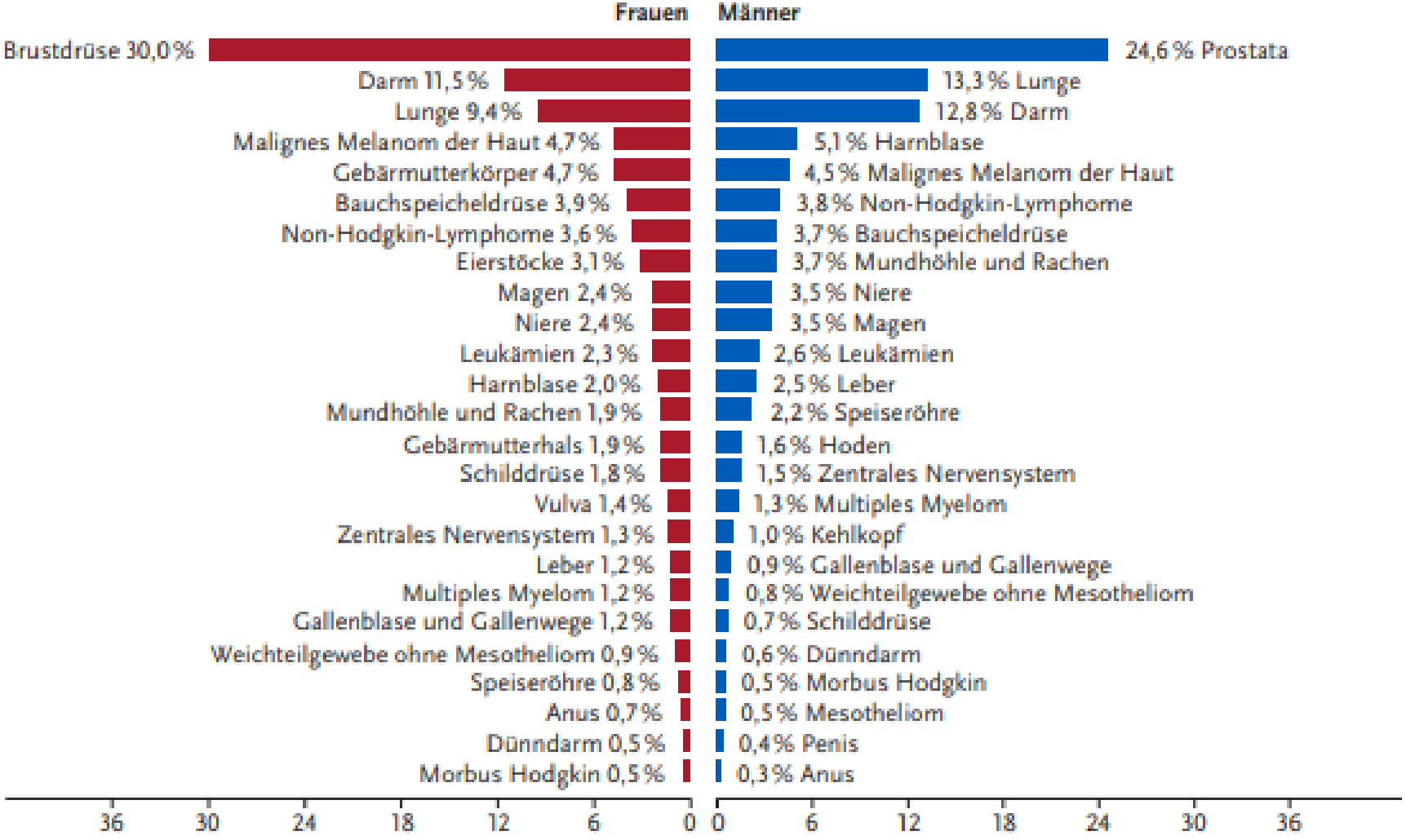
Alina Abramian, 07.09.2022

UNIVERSITÄT BONN

ukb universitäts klinikumbonn

Krebs*neu*erkrankungen[1] in Deutschland

Anteile der häufigsten Tumorlokalisationen (in %)



[1]Ohne nicht-melanotischen Hautkrebs
Krebs in Deutschland 2017/2018– www.krebsdaten.de

Brustchirurgie / Senologie (gyn. Onkologie)

Brustschwester

ggf. Plastisch Chirurgie

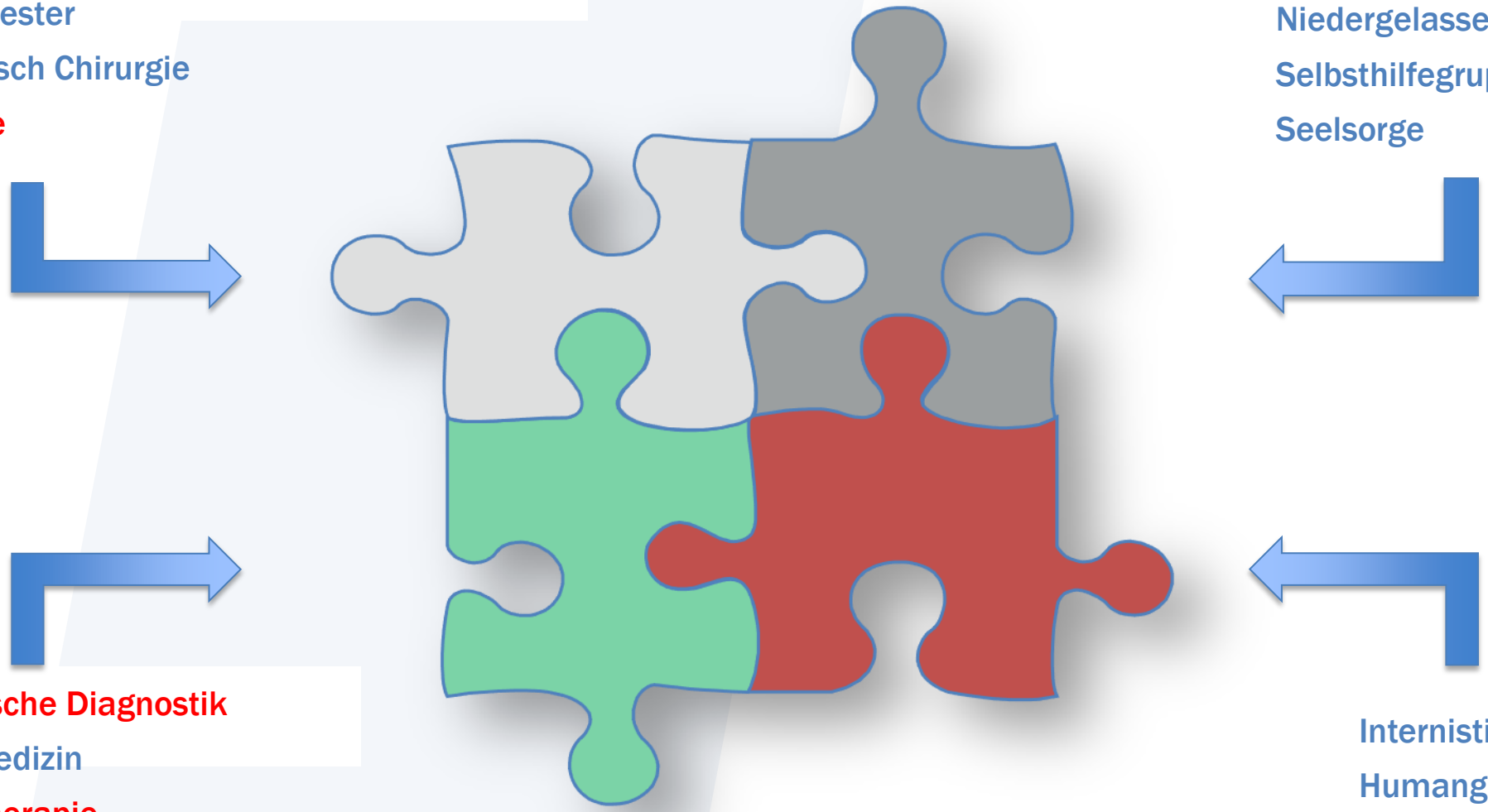
Pathologie

Psychoonkologie

Niedergelassene Kolleg*innen

Selbsthilfegruppen

Seelsorge



Radiologische Diagnostik

Nuklearmedizin

Strahlentherapie

ggf. Orthopädie / Neurochirurgie

Internistische Onkologie

Humangenetik

Palliativmedizin

Sanitätshaus / Reha

! Ein Brustzentrum lebt von der interdisziplinären Zusammenarbeit !

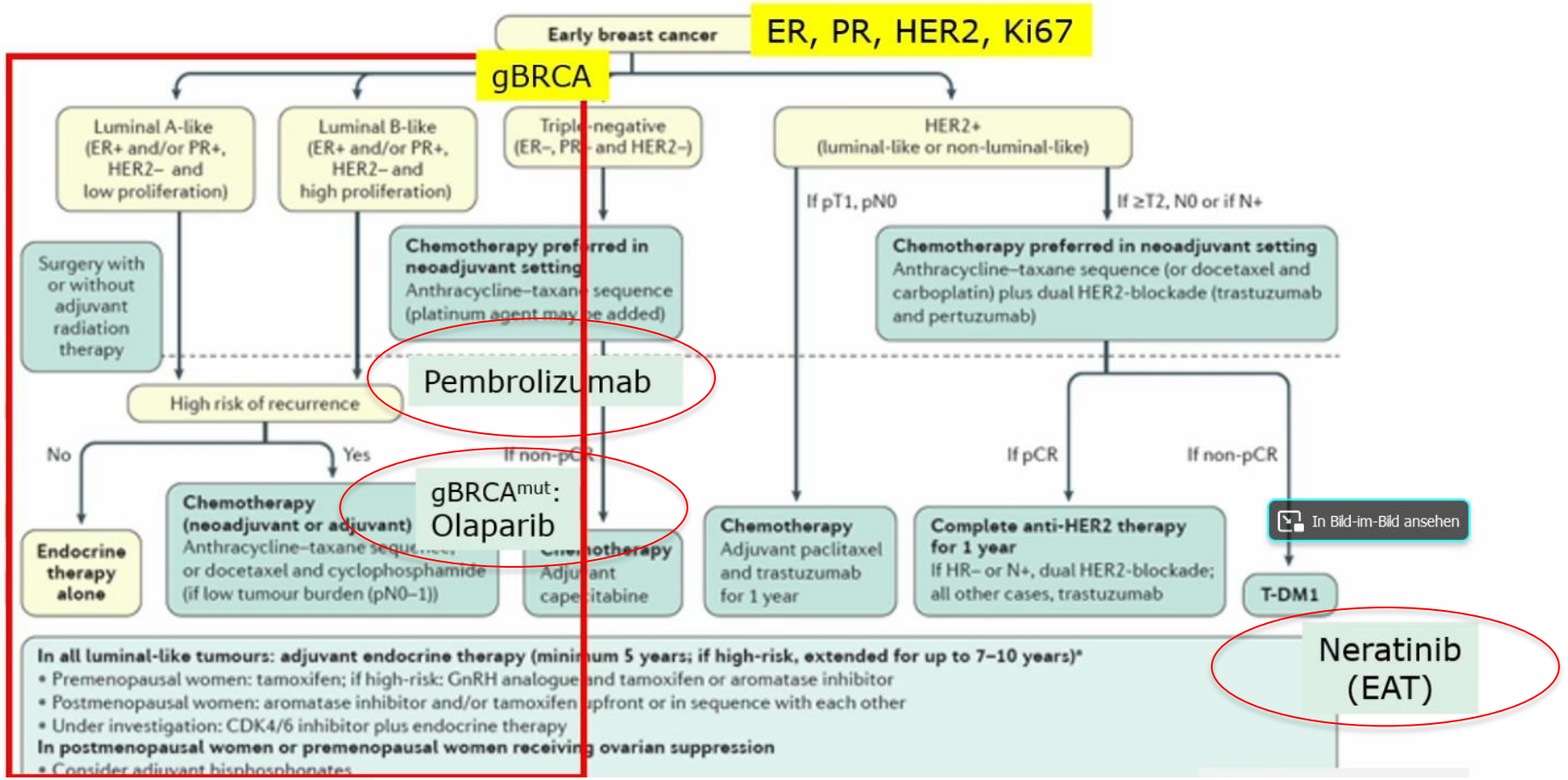
Therapiekonzepte und therapierelevante Biomarker[1]

Genexpressionstests
Endokrines Ansprechen
($Ki67_{post} \leq 10\%$)

Wer ist durch ET genug geschützt - wer braucht zusätzlich Chemotherapie?

Welche ET ist optimal ?

Wer benötigt mehr als Chemo- und endokrine Therapie (ET) ?



Modifiziert nach Harbeck et al, 2019

Neue zugelassene Medikamente

Neratinib

Olaparib

Abemaciclib

Pembrolizumab

Trastuzumab Deruxtecan

Endokrine Therapie

Östrogenentstehung im Körper und Ihre Hemmung

Verhinderung der Wirkung der Hormone direkt an der Zelle

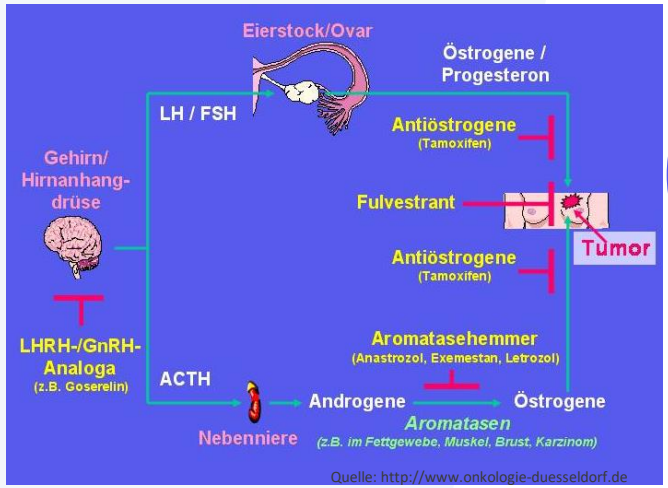
Aromatasehemmer
ANASTROZOL
EXEMESTAN
LETROZOL

Selektive Östrogenrezeptormodulator
TAMOXIFEN

Kompetitiver Östrogenrezeptorantagonist
FULVESTRANT

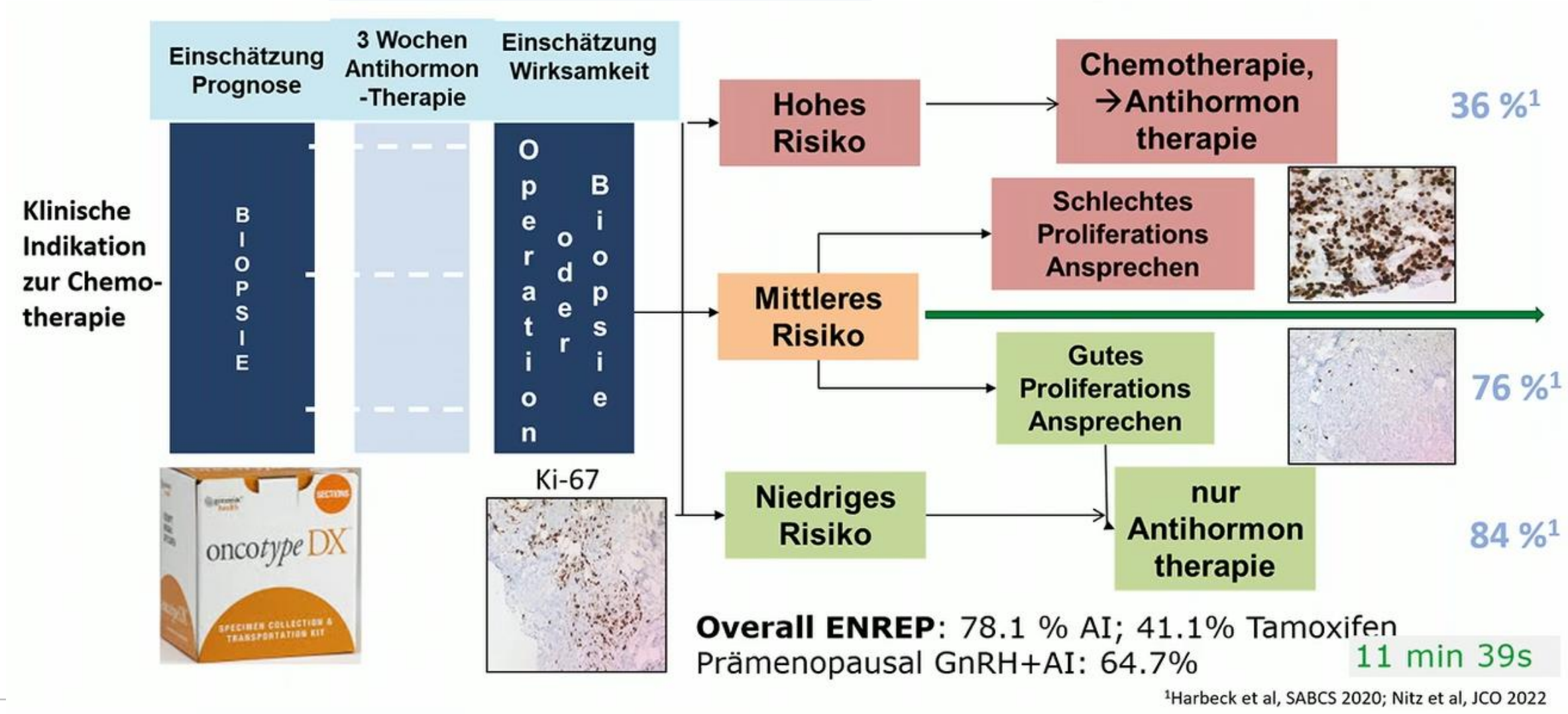
Operative Entfernung der Eierstöcke

LHRH-/GnRH -Analoga
GOSELERIN



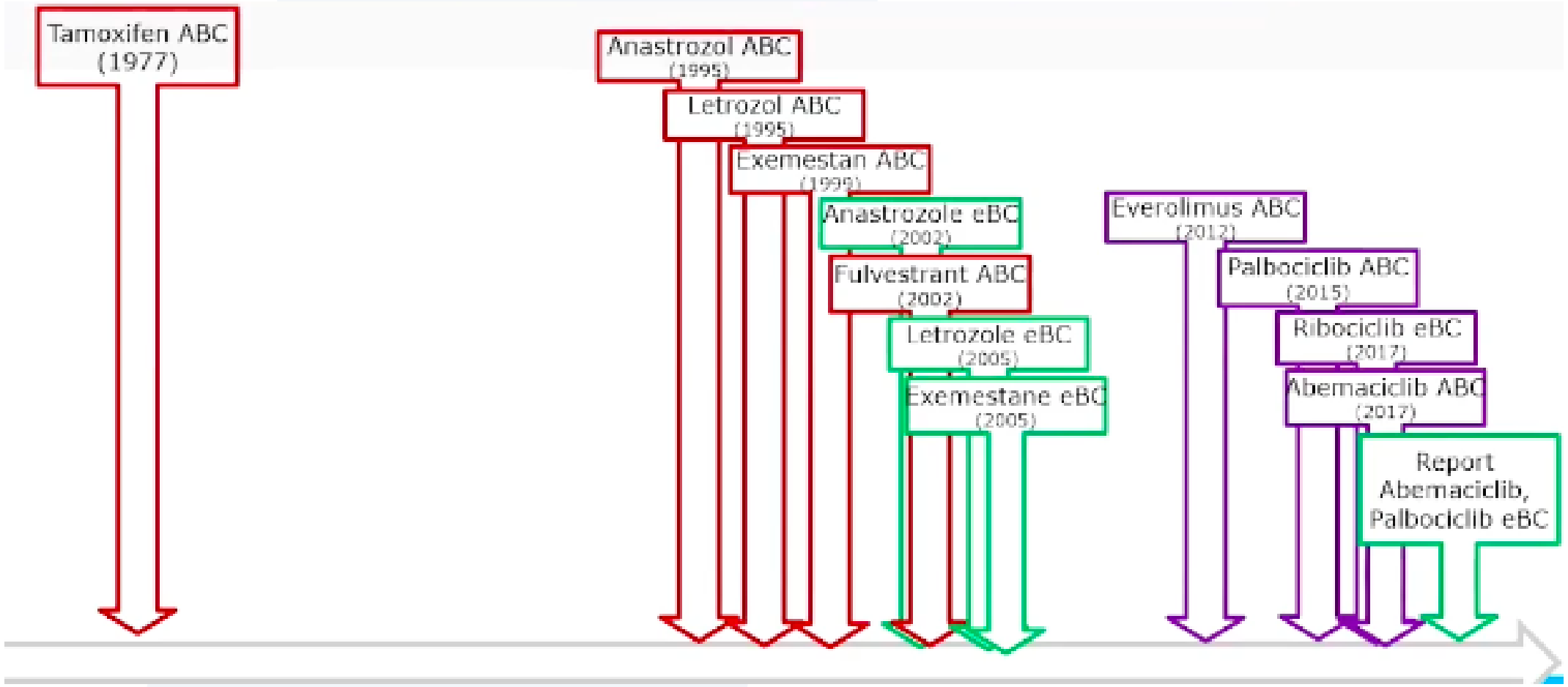
Verhinderung der Entstehung der Hormone durch Hemmung der Bildung oder der Eierstocksfunktion

Neoadjuvante endokrine Therapie



[1]Harbeck et al, SABCS 2020; Nitz et al, JCO 2022

Erweiterte endokrine Therapie in der Adjuvans



Modifiziert nach Fasching, 2021

Endokrine Therapie mit CDK4/6 Inhibitor

Wann?

- ≥ 4 positive Lymphknoten oder
- 1-3 paLN und mindestens eines der Kriterien:
  - ≥ 5 cm Tumorgröße oder G3

Funktioniert das Konzept auch in der adjuvanten Situation?

Adjuvant/postneoadjuvant treatment with CDK 4/6

	MonarchE	PALLAS	PENELOPE[B]
N	5,637	5,600	1,250
CDK4/6i	Abemaciclib	Palbociclib	Palbociclib
% of pts. with NACT	37%	n.r.	100%
Duration of CDK4/6i treatment	24 mths	24 mths	12 mths
Follow-up	27.1 mths	24 mths	43 mths
Discontinuation rate	28%	42%	20%
Discontinuation rate due to AE_{CDKi}	17 %	27 %	5 %
IDFS-HR (95%-CI)	**0.70 (0.59-0.82) p<0.0001**	0.96 (0.81-1.14) p=0.65	0.93 (0.74-1.16) p=0.525
2-yrs IDFS	**92.7% vs. 90.0%**	n.r.	88% vs. 78%
3-yrs IDFS	**88.8% vs. 83.4%**	88% vs. 89%	81% vs. 78%
4-yrs IDFS	n.r.	84.2% vs. 84.5%	73% vs. 72%

AGO: Endokrine Therapie nach Menopausenstatus — 1a — A — ++

Endokrine Therapie + Abemaciclib (high risk gemäß MonarchE) — 1b — B — +

Sledge GW: JAM 0
Gnant M: JCO 20
Loibl S: JCO 2021;3

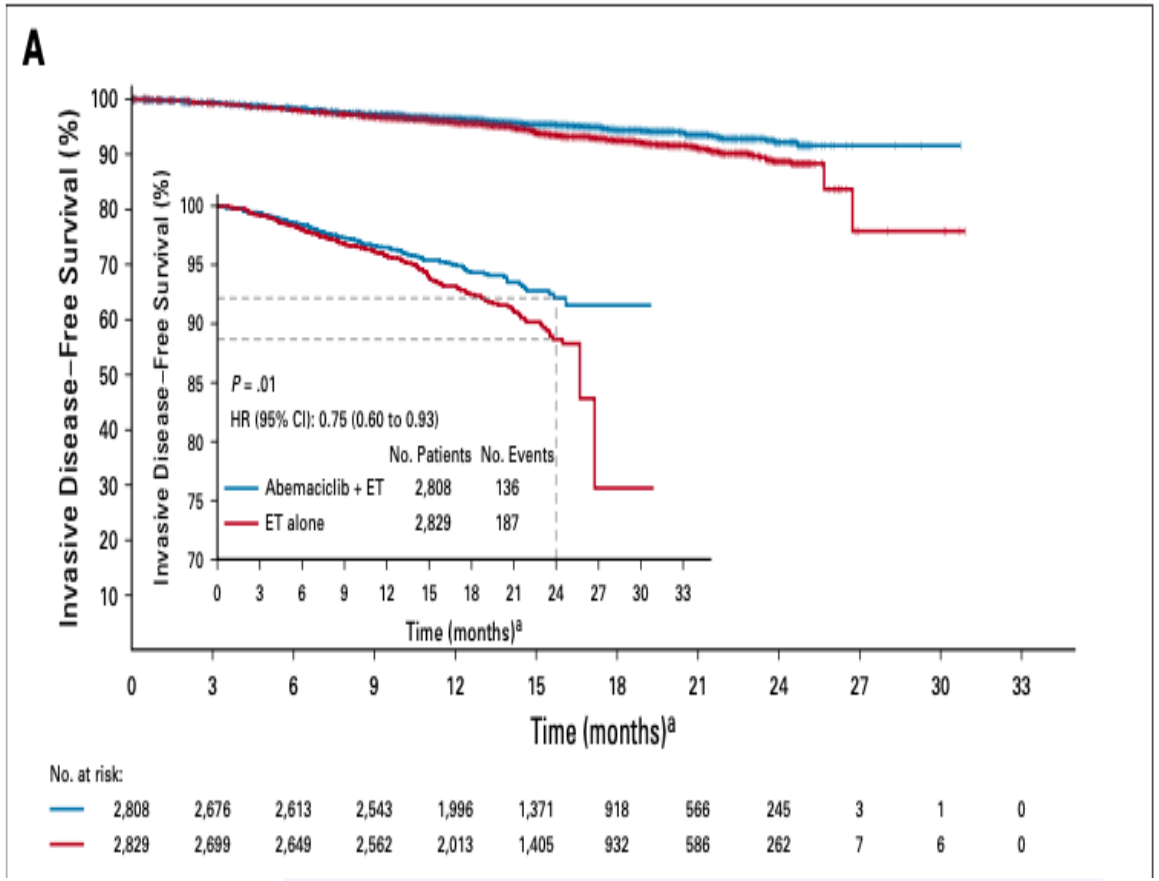
rapid communications

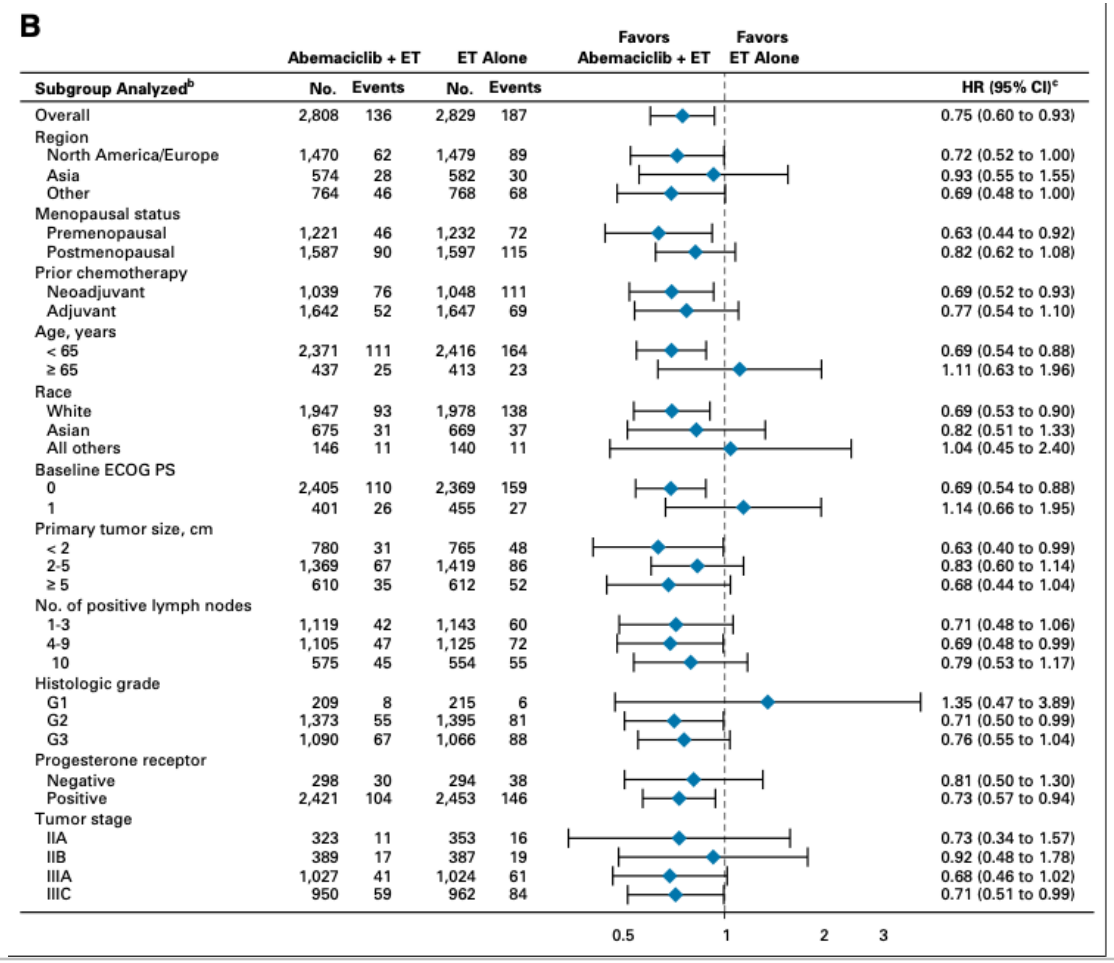
Abemaciclib Combined With Endocrine Therapy for the Adjuvant Treatment of HR+, HER2−, Node-Positive, High-Risk, Early Breast Cancer (monarchE)

Stephen R. D. Johnston, MD, PhD[1]; Nadia Harbeck, MD, PhD[2]; Roberto Hegg, MD, PhD[3]; Masakazu Toi, MD, PhD[4]; Miguel Martin, MD, PhD[5]; Zhi Min Shao, MD[6]; Qing Yuan Zhang, MD, PhD[7]; Jorge Luis Martinez Rodriguez, MD[8]; Mario Campone, MD, PhD[9]; Erika Hamilton, MD[10]; Joohyuk Sohn, MD, PhD[11]; Valentina Guarneri, MD, PhD[12]; Morihito Okada, MD, PhD[13]; Frances Boyle, MD, MBBS, PhD[14]; Patrick Neven, MD, PhD[15]; Javier Cortés, MD, PhD[16]; Jens Huober, MD[17]; Andrew Wardley, MD, MBChB[18]; Sara M. Tolaney, MD, MPH[19]; Irfan Cicin, MD[20]; Ian C. Smith, MD[21,22]; Martin Frenzel, PhD[22]; Desirée Headley, MSc[22]; Ran Wei, PhD[22]; Belen San Antonio, PhD[22]; Maarten Hulstijn, PhD[22]; Joanne Cox, MD[22]; Joyce O'Shaughnessy, MD[23]; and Priya Rastogi, MD[24]; on behalf of the monarchE Committee Members and Investigators

Johnston et al., J Clin Oncol 38:3987-3998

Mit Abemaciclib scheint das Konzept zu funktionieren





Johnston et al., J Clin Oncol 38:3987-3998

NW Abemaciclib

Appetitverlust,
Erbrechen
Übelkeit

Durchfälle

Leukopenie, Anämie,
Neutropenie

Alopezie

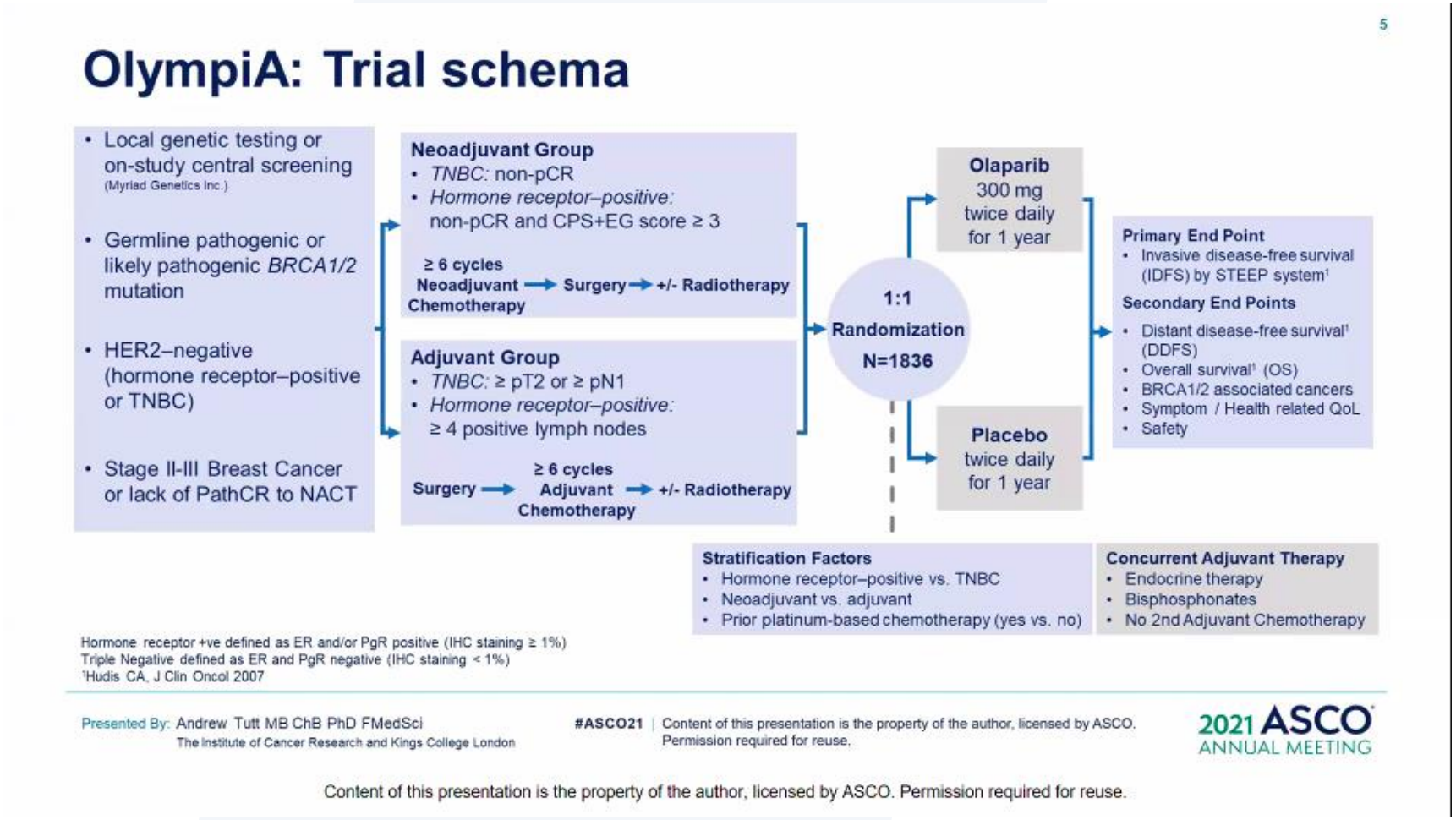
Fatigue

Olaparib- BRCA Patienten

LBA1 OlympiA: A phase III, multicenter, randomized, placebo-controlled trial of adjuvant olaparib after (neo)adjuvant chemotherapy in patients with germline BRCA1/2 mutations and high-risk HER2-negative early breast cancer.

Andrew Tutt *et al.*, London, UK.

- PARP-Inhibitoren zielen auf Malignome mit homologen Rekombinationsreparaturdefekten durch ihren Wirkmechanismus synthetische Letalität ab
- Olaparib ist bislang für metastasierten Her2-negativen Brustkrebs mit BRCA1/2-Keimbahnmutation zugelassen
- Trotz adäquater Systemtherapie können die Rezidivraten bei dieser Population hoch sein
- → erfordert neue Behandlungsoptionen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OlympiA: Trial schema
• Local genetic testing or on-study central screening (Myriad Genetics Inc.)
• Germline pathogenic or likely pathogenic BRCA1/2 mutation
• HER2–negative (hormone receptor–positive or TNBC)
• Stage II-III Breast Cancer or lack of PathCR to NACT
Neoadjuvant Group
• TNBC: non-pCR
• Hormone receptor–positive: non-pCR and CPS+EG score ≥ 3
≥ 6 cycles Neoadjuvant Chemotherapy → Surgery → +/- Radiotherapy
Adjuvant Group
• TNBC: ≥ pT2 or ≥ pN1
• Hormone receptor–positive: ≥ 4 positive lymph nodes
Surgery → ≥ 6 cycles Adjuvant Chemotherapy → +/- Radiotherapy
1:1 Randomization N=1836
Olaparib 300 mg twice daily for 1 year
Placebo twice daily for 1 year
Primary End Point
• Invasive disease-free survival (IDFS) by STEEP system†
Secondary End Points
• Distant disease-free survival† (DDFS)
• Overall survival† (OS)
• BRCA1/2 associated cancers
• Symptom / Health related QoL
• Safety
Stratification Factors
• Hormone receptor–positive vs. TNBC
• Neoadjuvant vs. adjuvant
• Prior platinum-based chemotherapy (yes vs. no)
Concurrent Adjuvant Therapy
• Endocrine therapy
• Bisphosphonates
• No 2nd Adjuvant Chemotherapy
Hormone receptor +ve defined as ER and/or PgR positive (IHC staining ≥ 1%)
Triple Negative defined as ER and PgR negative (IHC staining < 1%)
†Hudis CA, J Clin Oncol 2007
Presented By: Andrew Tutt MB ChB PhD FMedSci
The Institute of Cancer Research and Kings College London
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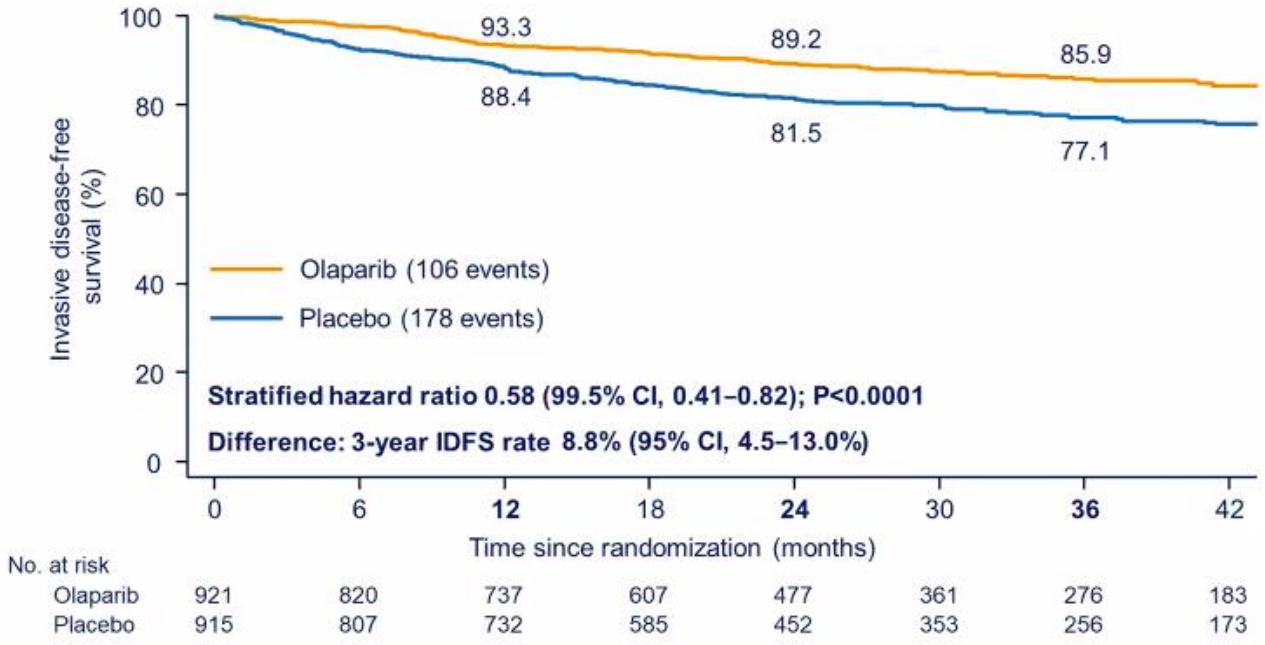
OlympiA: Invasive disease-free survival (ITT)



No. at risk								
Olaparib	921	820	737	607	477	361	276	183
Placebo	915	807	732	585	452	353	256	173

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Welche Patientinnen profitieren?

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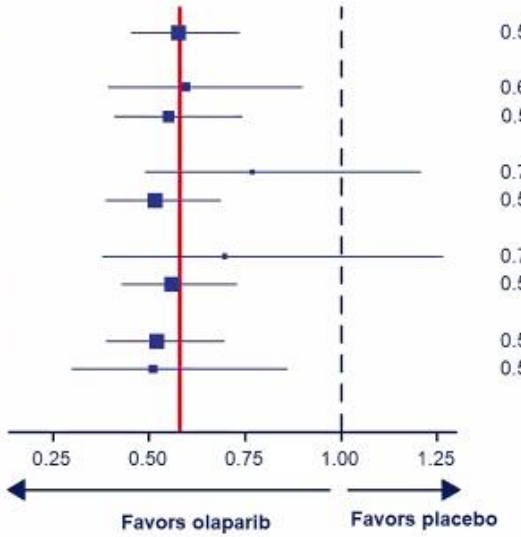
OlympiA: Subgroup analysis invasive disease-free survival

Subgroup	Olaparib	Placebo	Stratified hazard ratio for invasive-disease-free survival	P value for heterogeneity
	No. of patients with an invasive-disease event/total no.			
All patients	106 / 921	178 / 915	0.581 (0.455–0.737)	NA
Prior chemo				0.763
Adjuvant	36 / 461	61 / 455	0.601 (0.394–0.901)	
Neoadjuvant	70 / 460	117 / 460	0.555 (0.411–0.745)	
Prior platinum				0.144
Yes	34 / 247	43 / 239	0.773 (0.490–1.209)	
No	72 / 674	135 / 676	0.520 (0.389–0.689)	
HR status				0.509
HR+/HER2-	19 / 168	25 / 157	0.701 (0.381–1.268)	
TNBC	87 / 751	153 / 758	0.563 (0.431–0.730)	
BRCA				0.998
BRCA1	70 / 558	126 / 558	0.524 (0.389–0.699)	
BRCA2	22 / 230	38 / 209	0.515 (0.300–0.862)	
BRCA1/2 both	0 / 1	0 / 3	NC	



No statistical evidence of heterogeneity between any subgroup and the ITT IDFS treatment effect

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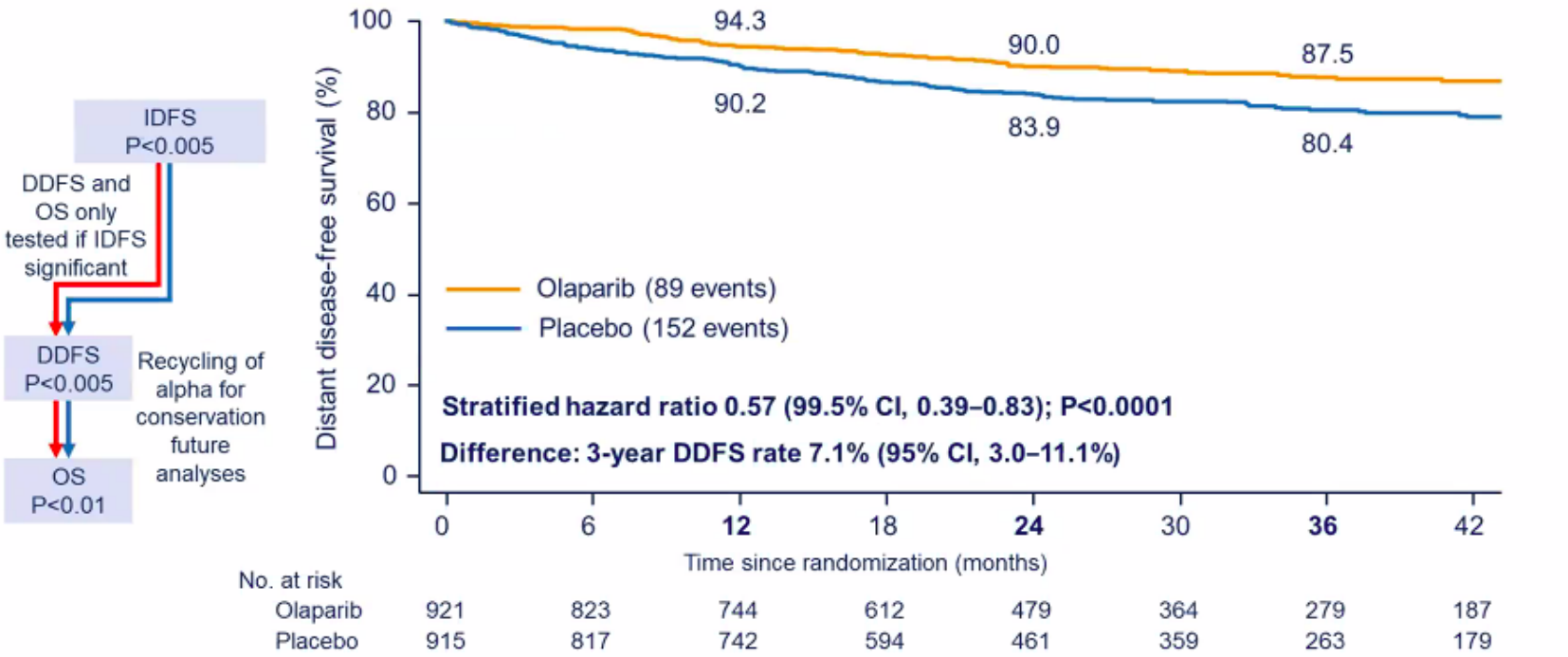
OlympiA: Distant disease-free survival



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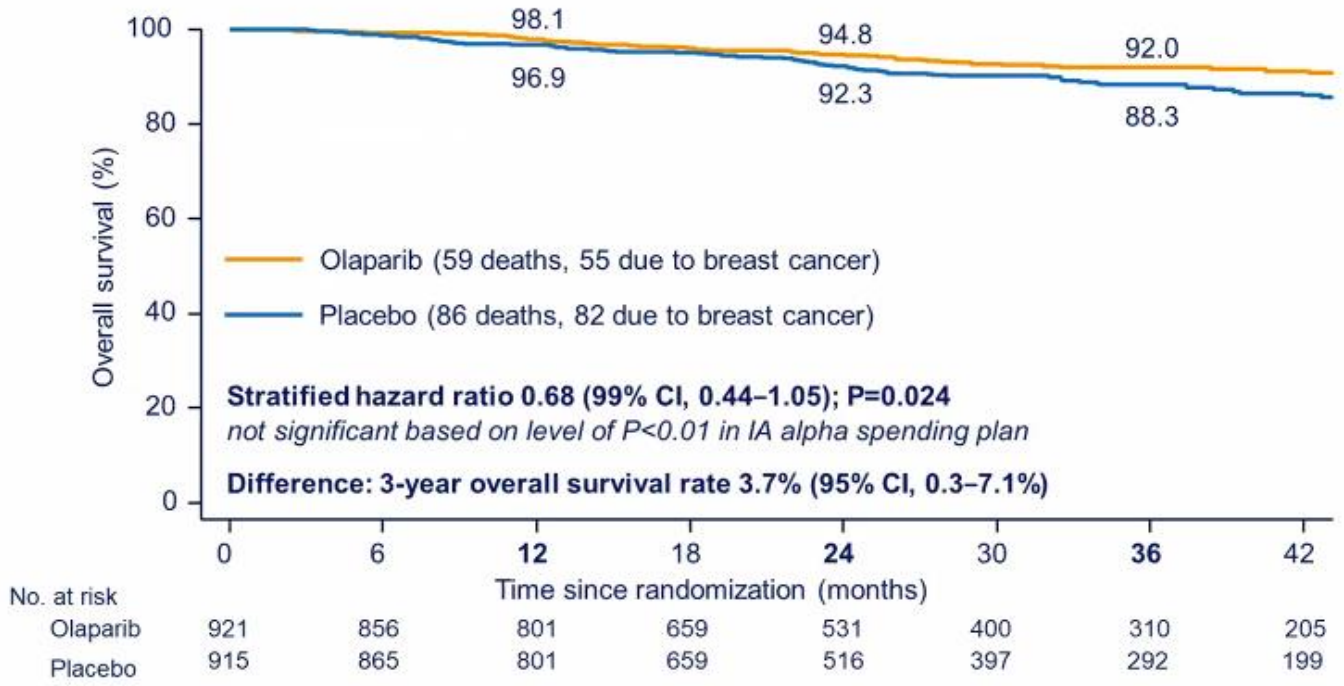
OlympiA: Overall survival



No. at risk								
Olaparib	921	856	801	659	531	400	310	205
Placebo	915	865	801	659	516	397	292	199

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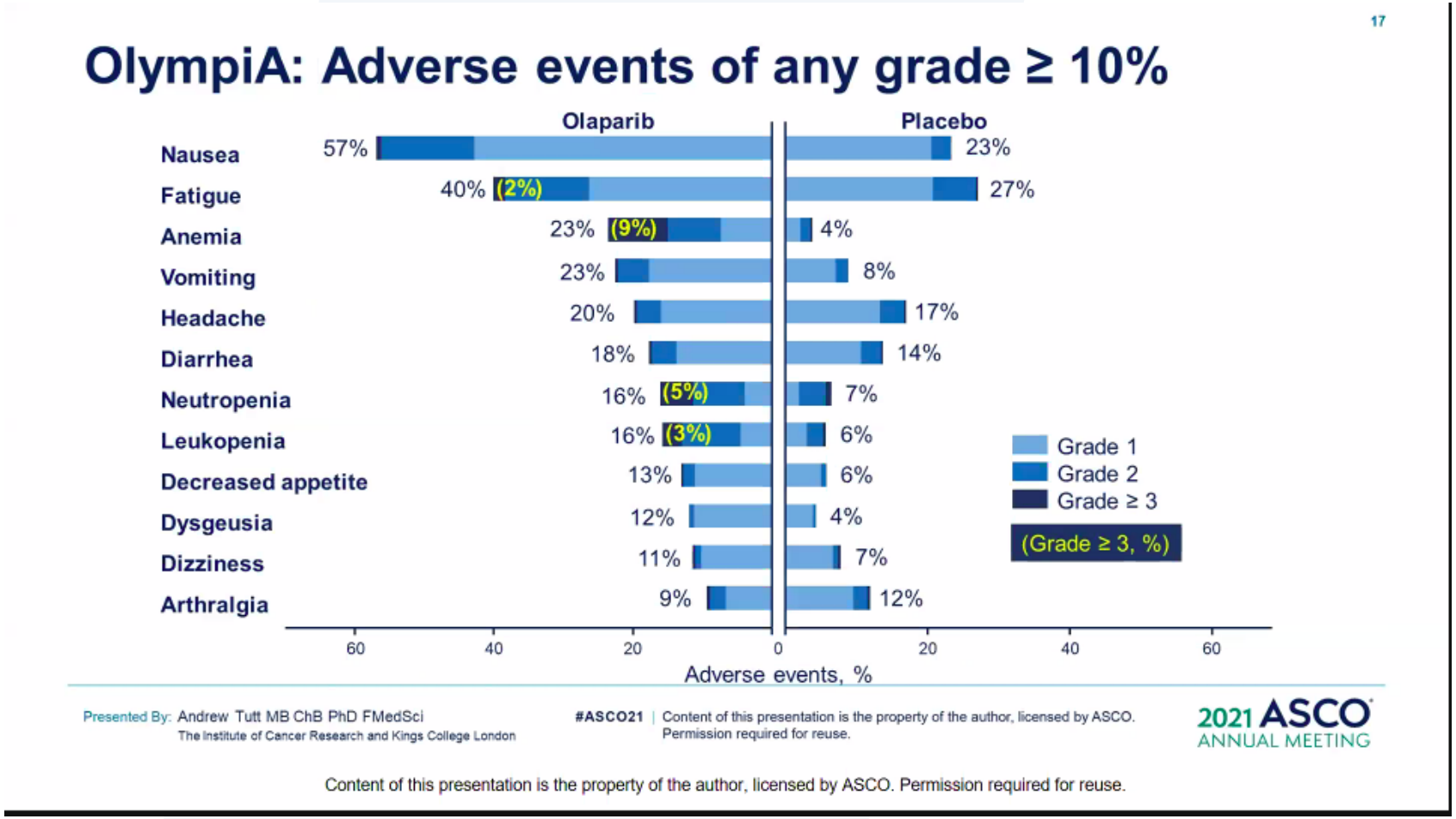
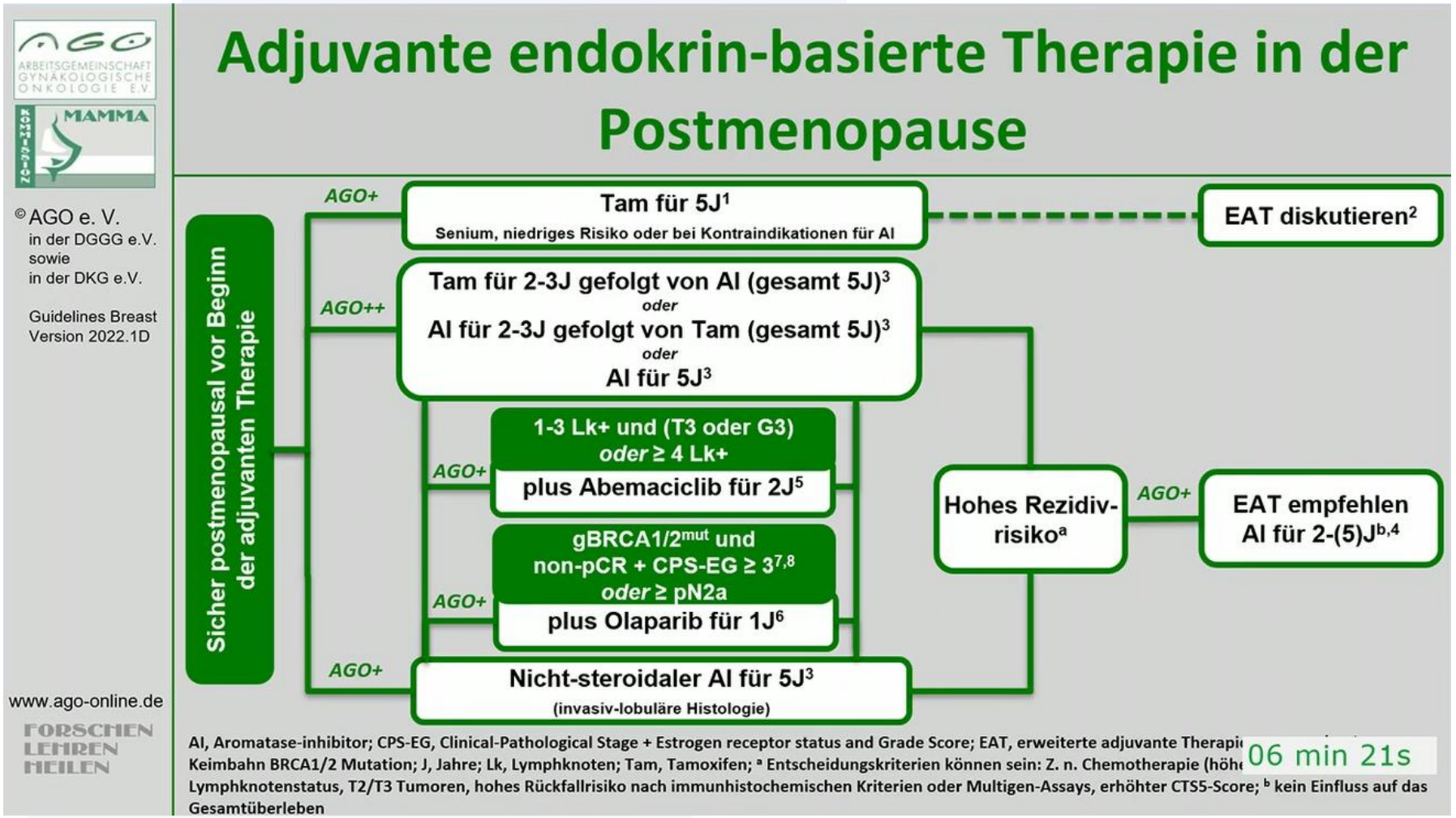
The Institute of Cancer Research and Kings College London

2021 ASCO ANNUAL MEETING

Mit welchen NW muss man rechnen?




Adjuvante endokrin-basierte Therapie in der Postmenopause
AGO ARBEITSGEMEINSCHAFT GYNÄKOLOGISCHE ONKOLOGIE E.V.
MAMMA
© AGO e. V.
in der DGGG e.V.
sowie
in der DKG e.V.
Guidelines Breast
Version 2022.1D
www.ago-online.de
FORSCHEN
LEHREN
HEILEN
Sicher postmenopausal vor Beginn der adjuvanten Therapie
AGO+
Tam für 5J[1]
Senium, niedriges Risiko oder bei Kontraindikationen für AI
EAT diskutieren[2]
AGO++
Tam für 2-3J gefolgt von AI (gesamt 5J)[3]
oder
AI für 2-3J gefolgt von Tam (gesamt 5J)[3]
oder
AI für 5J[3]
AGO+
1-3 Lk+ und (T3 oder G3)
oder ≥ 4 Lk+
plus Abemaciclib für 2J[5]
AGO+
gBRCA1/2mut und
non-pCR + CPS-EG ≥ 3[7,8]
oder ≥ pN2a
plus Olaparib für 1J[6]
AGO+
Nicht-steroidaler AI für 5J[3]
(invasiv-lobuläre Histologie)
Hohes Rezidiv-risiko[a]
AGO+
EAT empfehlen
AI für 2-(5)J[b,4]
AI, Aromatase-inhibitor; CPS-EG, Clinical-Pathological Stage + Estrogen receptor status and Grade Score; EAT, erweiterte adjuvante Therapi
Keimbahn BRCA1/2 Mutation; J, Jahre; Lk, Lymphknoten; Tam, Tamoxifen; [a] Entscheidungskriterien können sein: Z. n. Chemotherapie (höh
Lymphknotenstatus, T2/T3 Tumoren, hohes Rückfallrisiko nach immunhistochemischen Kriterien oder Multigen-Assays, erhöhter CTS5-Score; [b] kein Einfluss auf das Gesamtüberleben
06 min 21s

Neratinib

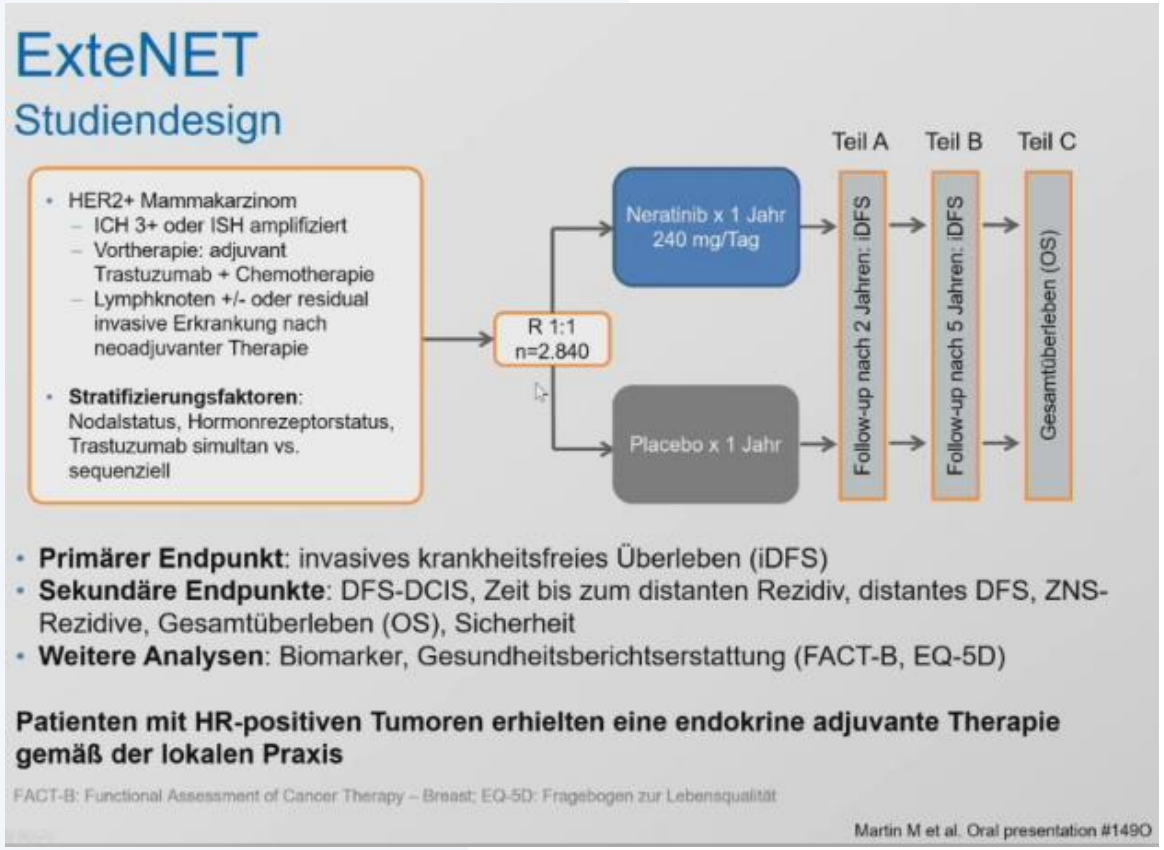
Postneoadjuvante Therapie HER2-positiv

	Oxford LoE	Oxford GR	Oxford AGO
pCR			
▪ Low risk: Trastuzumab (bis 12 Mon. komplett)	2a	C	++
▪ High risk (cN+): Trastuzumab + Pertuzumab (bis 12 Mon. komplett)	2b	C	+
▪ Neratinib nach 1 Jahr* Trastuzumab (HR-positiv)*	2b	B	-
non-pCR			
▪ T-DM1	1b	B	+
▪ Trastuzumab + Pertuzumab (bis 12 Mon. komplett)	2b	C	+/-
▪ Zusätzlich nach 1 Jahr (erweiterte adj. Therapie)			
▪ Neratinib nach Trastuzumab (HR-positiv)*	2b	B	+
▪ Neratinib nach anderer anti-HER2-Therapie (HR-positiv)*	5	D	+/-

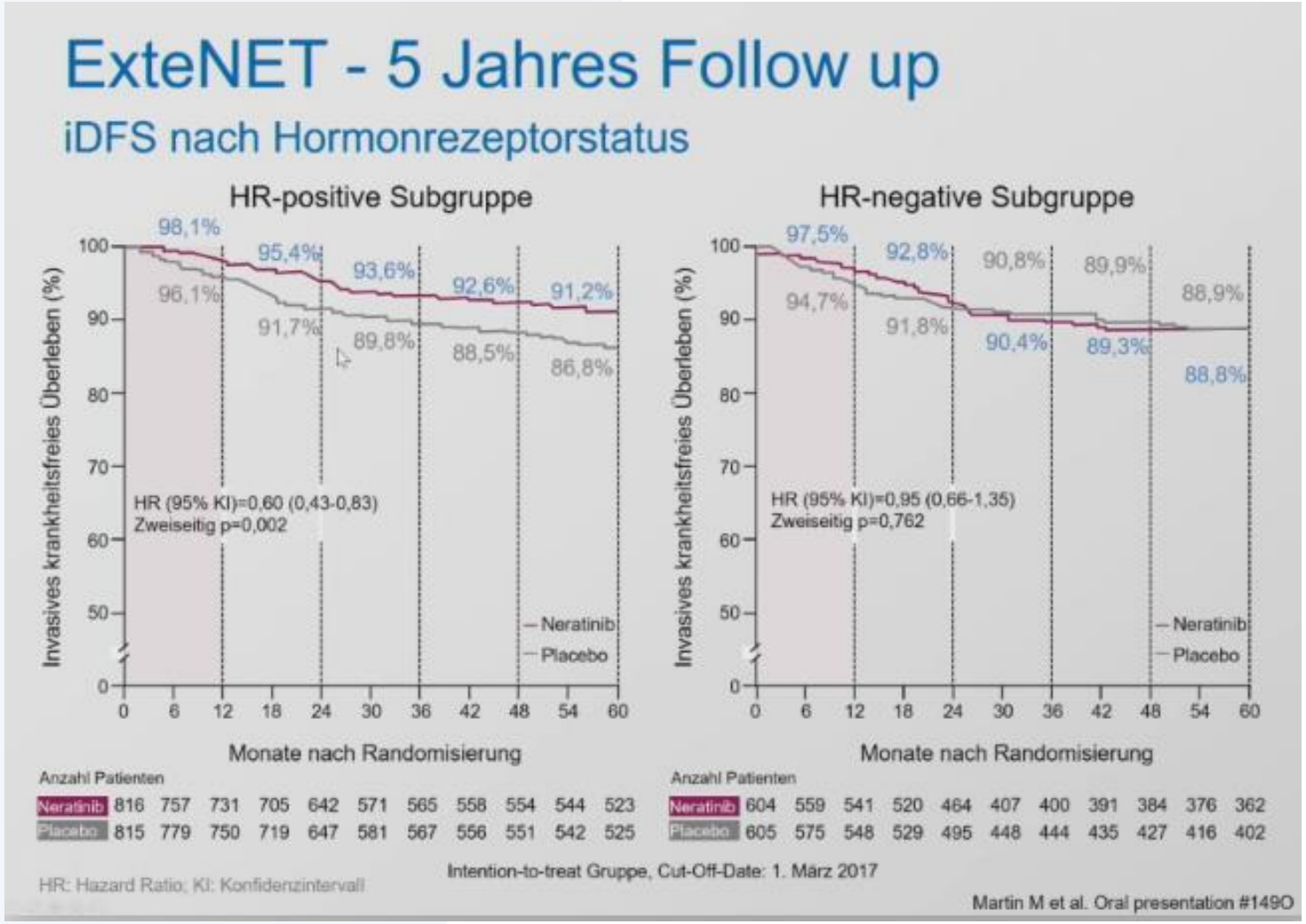
* kombiniert mit Standard endokriner Therapie

Neratinib after trastuzumab-based adjuvant therapy in HER2-positive breast cancer (ExteNET): 5-year analysis of a randomised, double-blind, placebo-controlled, phase 3 trial

*Miguel Martin, Frankie A Holmes, Bent Ejlertsen, Suzette Delaloge, Beverly Moy, Hiroji Iwata, Gunter von Minckwitz, Stephen K L Chia, Janine Mansi, Carlos H Barrios, Michael Gnant, Zorica Tomašević, Neelima Denduluri, Robert Šeparović, Erhan Gokmen, Anna Bashford, Manuel Ruiz Borrego, Sung-Bae Kim, Erik Hugger Jakobsen, Audrone Ciceniene, Kenichi Inoue, Friedrich Overkamp, Joan B Heijns, Anne C Armstrong, John S Link, Anil Abraham Joy, Richard Bryce, Alvin Wong, Susan Moran, Bin Yao, Feng Xu, Alan Auerbach, Marc Buyse, Arlene Chan, for the ExteNET Study Group**



Daten aus Martin et al. 2021 SABCS, Oral presentation # 1490



Daten aus Martin et al. 2021 SABCS, Oral presentation # 1490

Nebenwirkungen Neratinib

Durchfall

Fatigue

Muskelkrämpfe

Hautausschläge

Schwindel, Dehydratation

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trastuzumab Deruxtecan versus Trastuzumab Emtansine for Breast Cancer

J. Cortés, S.-B. Kim, W.-P. Chung, S.-A. Im, Y.H. Park, R. Hegg, M.H. Kim, L.-M. Tseng, V. Petry, C.-F. Chung, H. Iwata, E. Hamilton, G. Curigliano, B. Xu, C.-S. Huang, J.H. Kim, J.W.Y. Chiu, J.L. Pedrini, C. Lee, Y. Liu, J. Cathcart, E. Bako, S. Verma, and S.A. Hurvitz, for the DESTINY-Breast03 Trial Investigators*

DESTINY-Breast03: Study Design

An open-label, multicenter, phase 3 study (NCT03529110)

Patients
- Unresectable or metastatic HER2 positive[a] breast cancer
- Previously treated with trastuzumab and taxane in advanced/metastatic setting[b]
- Could have clinically stable, treated brain metastases

Stratification factors
- Hormone receptor status
- Prior treatment with pertuzumab
- History of visceral disease

R 1:1

- **T-DXd** 5.4 mg/kg Q3W (n = 261)
- **T-DM1** 3.6 mg/kg Q3W (n = 263)

Primary endpoint
- PFS (BICR)

Key secondary endpoint
- OS

Secondary endpoints
- ORR (BICR and investigator)
- DOR (BICR)
- PFS (investigator)
- Safety

Interim analysis for PFS (data cutoff: May 21, 2021)
- Efficacy boundary for superiority: $P < 0.000204$ (based on 245 events)
- IDMC recommendation to unblind study (July 30, 2021)

Key secondary endpoint, OS: boundary for efficacy: $P < 0.000265$ (based on 86 events)

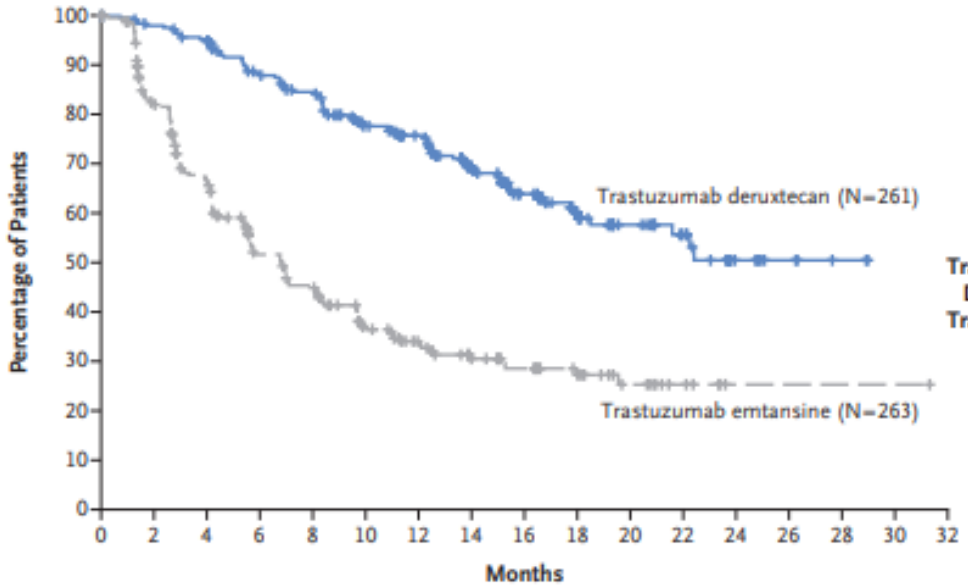
[a]HER2 IHC3+ or IHC2+/ISH+ based on central confirmation. [b]Progression during or <6 months after completing adjuvant therapy involving trastuzumab and taxane.
Cortés J et al. Presented at: ESMO Virtual Congress 2021; September 17-21, 2021. Presentation 2525.

Cortes et al, NEJ 2022

Characteristic	Trastuzumab Deruxtecan (N=261)	Trastuzumab Emtansine (N=263)
Hormone-receptor status — no. (%)		
Positive	131 (50.2)	134 (51.0)
Negative	130 (49.8)	129 (49.0)
Stable brain metastases — no. (%)¶	62 (23.8)	52 (19.8)
Visceral disease — no. (%)	184 (70.5)	185 (70.3)
Previous treatment for metastatic breast cancer — no. (%)	240 (92.0)	234 (89.0)
Lines of previous therapy in the context of metastatic disease		
Median number of lines (range)	1 (0–16)	2 (0–14)
Number of lines — no. (%)		
0	2 (0.8)	3 (1.1)
1	130 (49.8)	123 (46.8)
2	56 (21.5)	65 (24.7)
3	35 (13.4)	35 (13.3)
4	15 (5.7)	19 (7.2)
≥5	23 (8.8)	18 (6.8)
Previous cancer therapy — no. (%)**		
Trastuzumab	260 (99.6)	262 (99.6)
Pertuzumab	162 (62.1)	158 (60.1)

Cortes et al, NEJ 2022

A Progression-free Survival



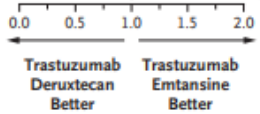
No. at Risk																
Trastuzumab deruxtecan	261	250	240	214	200	168	150	112	79	53	36	25	10	5	2	
Trastuzumab emtansine	263	200	155	108	93	65	51	37	29	21	12	6	1	1	1	1	0

	Median Progression-free Survival (95% CI)	12-Mo Progression-free Survival (95% CI)
	mo	%
Trastuzumab Deruxtecan	NR (18.5–NE)	75.8 (69.8–80.7)
Trastuzumab Emtansine	6.8 (5.6–8.2)	34.1 (27.7–40.5)

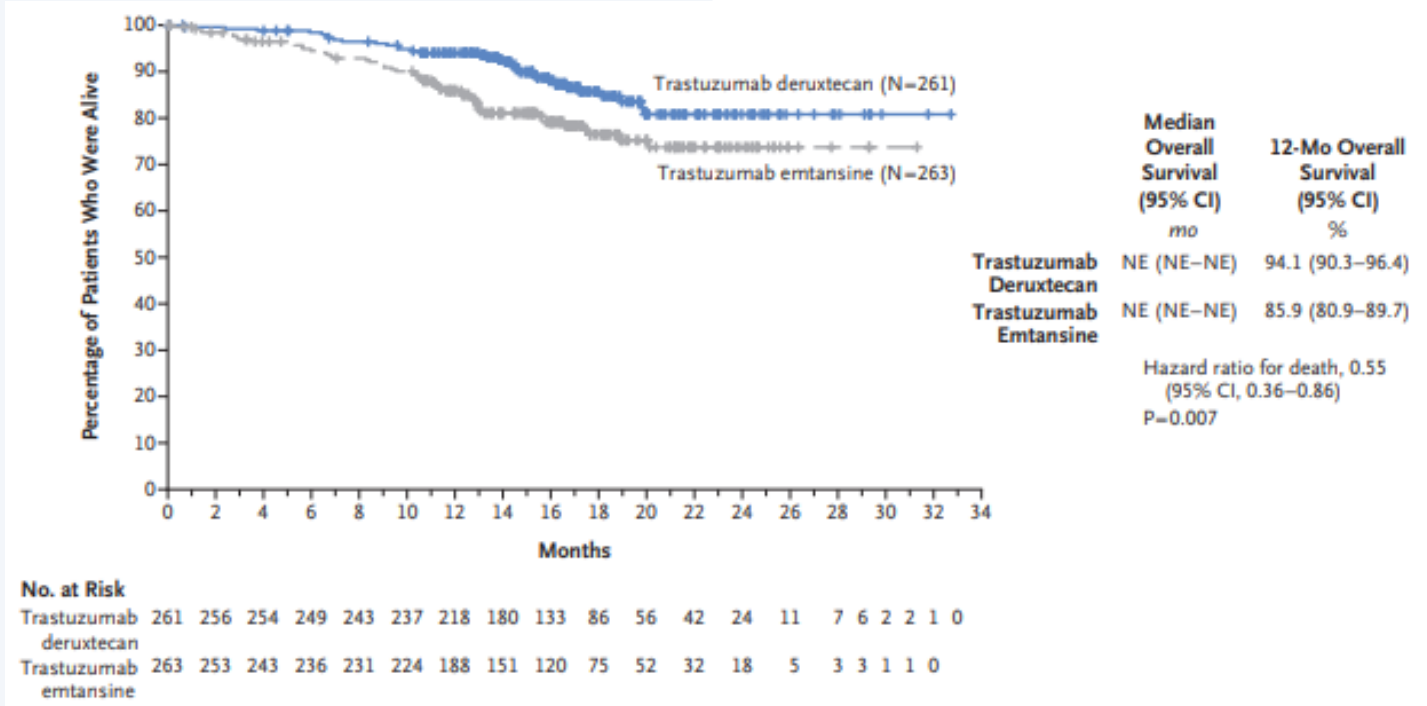
Hazard ratio for disease progression or death, 0.28 (95% CI, 0.22–0.37)
P<0.001

B Progression-free Survival in Prespecified Subgroups

Subgroup	No. of Patients	No. of Events/No. of Patients		Median Progression-free Survival (95% CI) *mo*		Hazard Ratio for Disease Progression or Death (95% CI)
		Trastuzumab deruxtecan	Trastuzumab emtansine	Trastuzumab deruxtecan	Trastuzumab emtansine	
All patients		87/261	158/263	NE (18.5–NE)	6.8 (5.6–8.2)	0.28 (0.22–0.37)
Hormone-receptor status						
Positive	272	46/133	84/139	22.4 (17.7–NE)	6.9 (4.2–9.8)	0.32 (0.22–0.46)
Negative	248	41/126	73/122	NE (18.0–NE)	6.8 (5.4–8.3)	0.30 (0.20–0.44)
Previous pertuzumab treatment						
Yes	320	57/162	98/158	NE (18.5–NE)	6.8 (5.4–8.3)	0.30 (0.22–0.43)
No	204	30/99	60/105	NE (16.5–NE)	7.0 (4.2–9.7)	0.30 (0.19–0.47)
Visceral disease						
Yes	384	72/195	123/189	22.2 (16.5–NE)	5.7 (4.2–7.0)	0.28 (0.21–0.38)
No	140	15/66	35/74	NE (NE–NE)	11.3 (6.8–NE)	0.32 (0.17–0.58)
Lines of previous therapy						
0 or 1	258	46/132	75/126	22.4 (17.9–NE)	8.0 (5.7–9.7)	0.33 (0.23–0.48)
≥2	266	41/129	83/137	NE (16.8–NE)	5.6 (4.2–7.1)	0.28 (0.19–0.41)
Stable brain metastases						
Yes	114	31/62	31/52	15.0 (12.6–22.2)	5.7 (2.9–7.1)	0.38 (0.23–0.64)
No	410	56/199	127/211	NE (22.4–NE)	7.0 (5.5–9.7)	0.27 (0.19–0.37)



Cortes et al, NEJ 2022



	Median Overall Survival (95% CI)	12-Mo Overall Survival (95% CI)
	mo	%
Trastuzumab Deruxtecan	NE (NE–NE)	94.1 (90.3–96.4)
Trastuzumab Emtansine	NE (NE–NE)	85.9 (80.9–89.7)

Hazard ratio for death, 0.55 (95% CI, 0.36–0.86)
P=0.007

Figure 2. First Interim Analysis of Overall Survival.

Shown are Kaplan–Meier estimates of overall survival at 12 months in the intention-to-treat population, stratified according to hormone-receptor status, previous treatment with pertuzumab, and history of visceral disease. At the time of the data cutoff date of May 21, 2021, a total of 86 deaths had occurred; this analysis was performed on the basis of a progression-free survival benefit with trastuzumab deruxtecan. The median overall survival was not reached in either treatment group (hazard ratio, 0.55; 95% CI, 0.36 to 0.86; P=0.007). The percentage of patients who were alive at 12 months was 94.1% (95% CI, 90.3 to 96.4) with trastuzumab deruxtecan and 85.9% (95% CI, 80.9 to 89.7) with trastuzumab emtansine. The tick marks indicate censored data.

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Nebenwirkungen??

Table 2. Most Common Drug-Related Adverse Events and Adjudicated Drug-Related Interstitial Lung Disease or Pneumonitis.

Event	Trastuzumab Deruxtecan (N=257)		Trastuzumab Emtansine (N=261)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	number of patients (percent)			
Most common drug-related adverse events				
Blood and lymphatic system disorders				
Neutropenia*	110 (42.8)	49 (19.1)	29 (11.1)	8 (3.1)
Anemia†	78 (30.4)	15 (5.8)	37 (14.2)	11 (4.2)
Leukopenia‡	77 (30.0)	17 (6.6)	20 (7.7)	1 (0.4)
Thrombocytopenia§	64 (24.9)	18 (7.0)	135 (51.7)	65 (24.9)
Gastrointestinal disorders				
Nausea	187 (72.8)	17 (6.6)	72 (27.6)	1 (0.4)
Vomiting	113 (44.0)	4 (1.6)	15 (5.7)	1 (0.4)
Diarrhea	61 (23.7)	1 (0.4)	10 (3.8)	1 (0.4)
Constipation	58 (22.6)	0	25 (9.6)	0
General disorders				
Fatigue¶	115 (44.7)	13 (5.1)	77 (29.5)	2 (0.8)
Investigations				
Aspartate aminotransferase increased	60 (23.3)	2 (0.8)	97 (37.2)	13 (5.0)
Alanine aminotransferase increased	50 (19.5)	4 (1.6)	71 (27.2)	12 (4.6)
Metabolism and nutrition disorders				
Decreased appetite	67 (26.1)	3 (1.2)	33 (12.6)	0
Skin and subcutaneous tissue disorders				
Alopecia‖	93 (36.2)	1 (0.4)	6 (2.3)	0
Adjudicated drug-related interstitial lung disease or pneumonitis**	27 (10.5)	2 (0.8)	5 (1.9)	0

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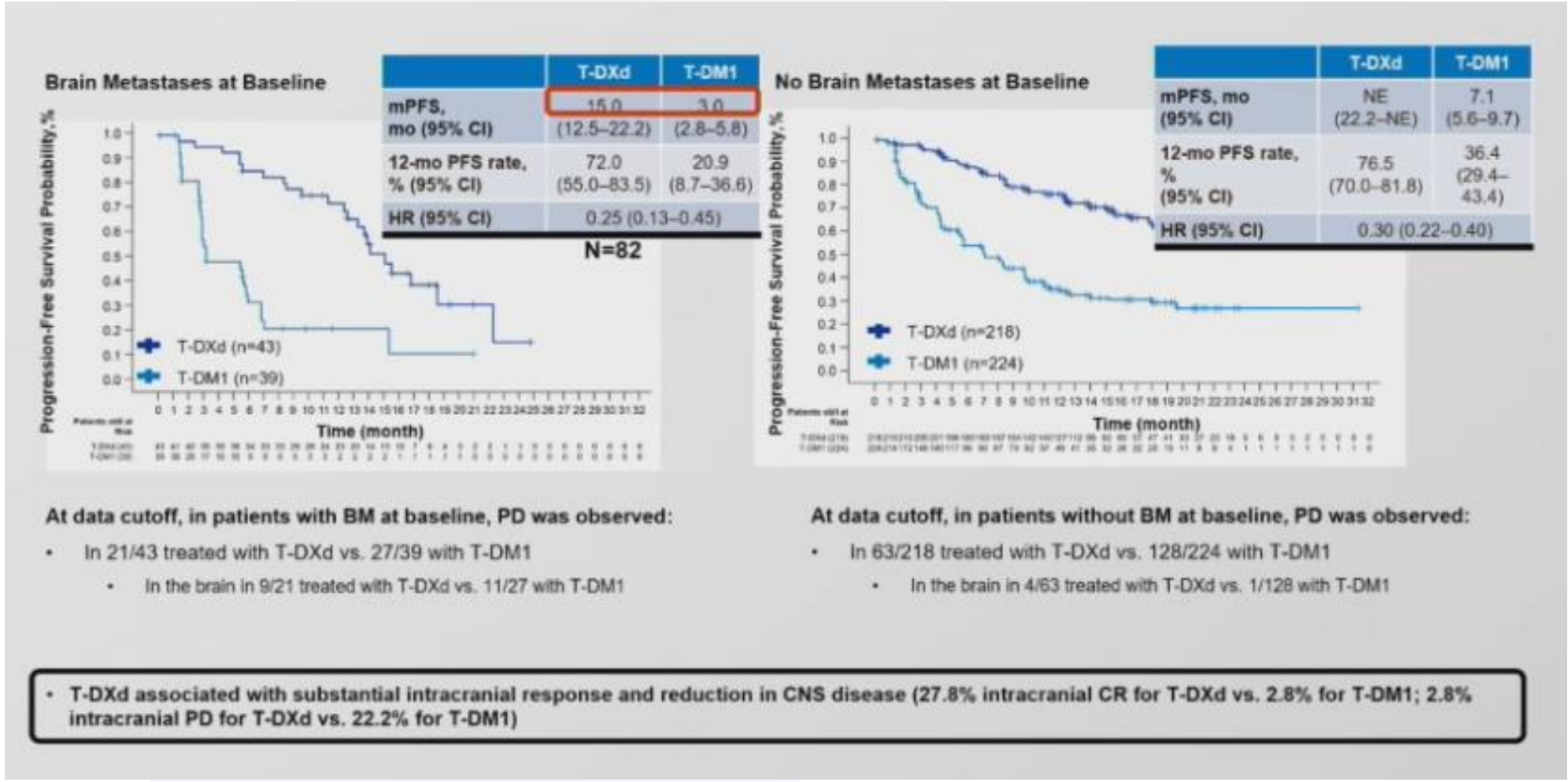
Hirnmetastasen



At data cutoff, in patients with BM at baseline, PD was observed:

- In 21/43 treated with T-DXd vs. 27/39 with T-DM1
  - In the brain in 9/21 treated with T-DXd vs. 11/27 with T-DM1

At data cutoff, in patients without BM at baseline, PD was observed:

- In 63/218 treated with T-DXd vs. 128/224 with T-DM1
  - In the brain in 4/63 treated with T-DXd vs. 1/128 with T-DM1

- **T-DXd associated with substantial intracranial response and reduction in CNS disease (27.8% intracranial CR for T-DXd vs. 2.8% for T-DM1; 2.8% intracranial PD for T-DXd vs. 22.2% for T-DM1)**

Daten aus : O'Sullivan C et al SABCS 2021, General Session 3, Abstract No, GS3-04; Hurvitz et al. 2021 SABCS, Abstract No. 957

Pembrolizumab in der Neodjuvans beim TNBC

Immuntherapie beim triple negativen Mammakarzinom

Wann?

pN1 und ≥ cT2

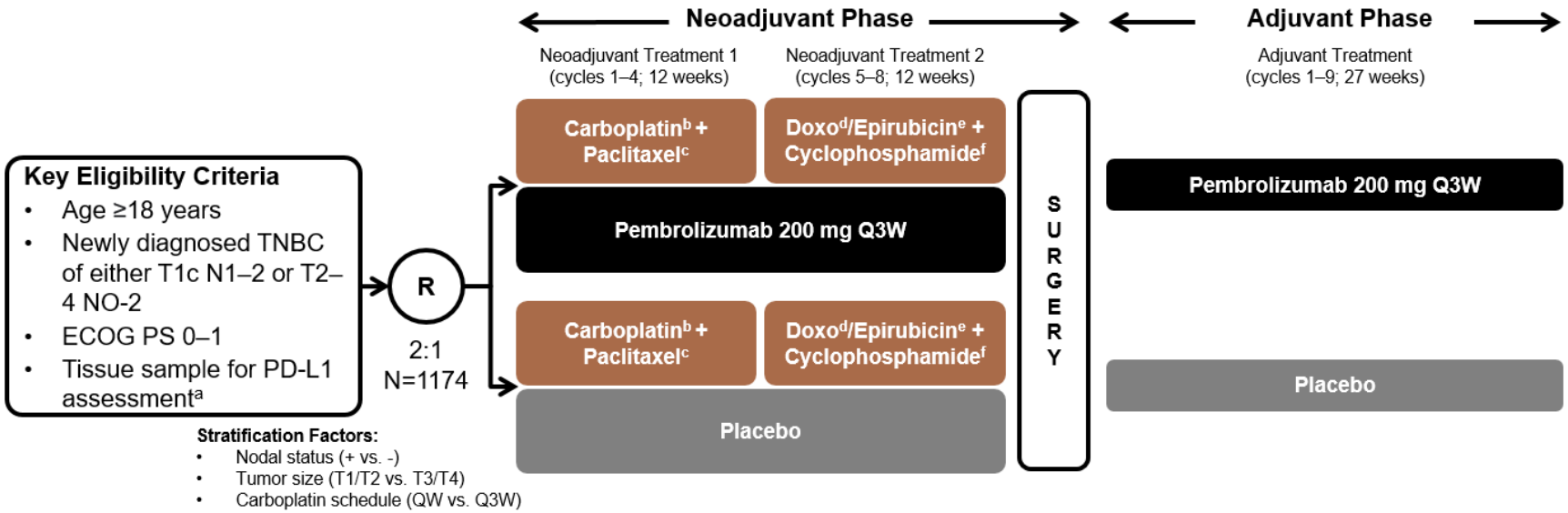
Pembrolizumab in der Neodjuvans beim TNBC

ICPi plus Neoadjuvant Chemotherapy for Triple Negative Breast Cancer Patients

	GeparNuevo	IMpassion031	Keynote 522	neoTRIP
Phase	II	III	III	II
N	174	333	602 (pCR) 1174 (EFS)	280
Prim. endpoint	pCR	pCR	pCR + EFS	EFS
CPi	Durvalumab (24-26 weeks)	Atezolizumab (1 y)	Pembrolizumab (1 y)	Atezolizumab (24 weeks)
Chemo	$NabPac_{125}$ q1w x12 → EC q2w x4	$NabPac_{125}$q1w x12 → EC q2w x4	Pac q1w x12 + carbo q3w AUC 5 or q1w AUC 1,5 → AC/EC q3w x4	$NabPac_{125}$ + carbo AUC 2 q1w d1 and d8
Inclusion criteria	cT1b-cT4a-d	cT2-cT4, cN0-cN3	cT1cN1-2 or cT2 N0-2	cT1cN1; cT2cN1; cT3cN0
PD-L1 positive	87%	46%	83%	56%
pCR ITT	53.4% vs. 44.2% Δ 10.8% (n.s.)	57.6% vs. 41.2% Δ 16.5% (p < 0.01)	64.8% vs. 51.2% Δ 13.6% (p < 0.00055)	43.5% vs. 40.8% Δ 2.6% (n.s.)
pCR PD-L1 positive	58% vs. 50%	69% vs. 49%	69% vs. 55%	52% 48%
pCR PD-L1 negative	44% vs. 18%	48% vs. 34%	45% vs. 30%	32% vs. 32%
Follow up/EFS/iDFS (months)/HR EFS/iDFS	43.7 months iDFS: 0.48 (p = 0.0389)	20 months EFS: 0.76 (n.s.)	39.1 months EFS: 15.7 vs. 23.8 m 0.63 (p = 0.00031)	---
EFS/iDFS adjusted to pCR/non-pCR	pCR 95.5% vs. 86.1% npCR 76.3% vs. 69.7%	---	pCR 94.4% vs. 92.5% npCR 67.4% vs. 56.8%	---

Pembrolizumab in der Neodjuvans beim TNBC

KEYNOTE-522 – Study Design (NCT03036488)



- **Neoadjuvant phase:** starts from the first neoadjuvant treatment and ends after definitive surgery (post treatment included)
- **Adjuvant phase:** starts from the first adjuvant treatment and includes radiation therapy as indicated (post treatment included)

[a]Must consist of at least 2 separate tumor cores from the primary tumor; [b]Carboplatin dose was AUC 5 Q3W or AUC 1.5 QW; [c]Paclitaxel dose was 80 mg/m² QW; [d]Doxorubicin dose was 60 mg/m² Q3W; [e]Epirubicin dose was 90 mg/m² Q3W; [f]Cyclophosphamide dose was 600 mg/m² Q3W.

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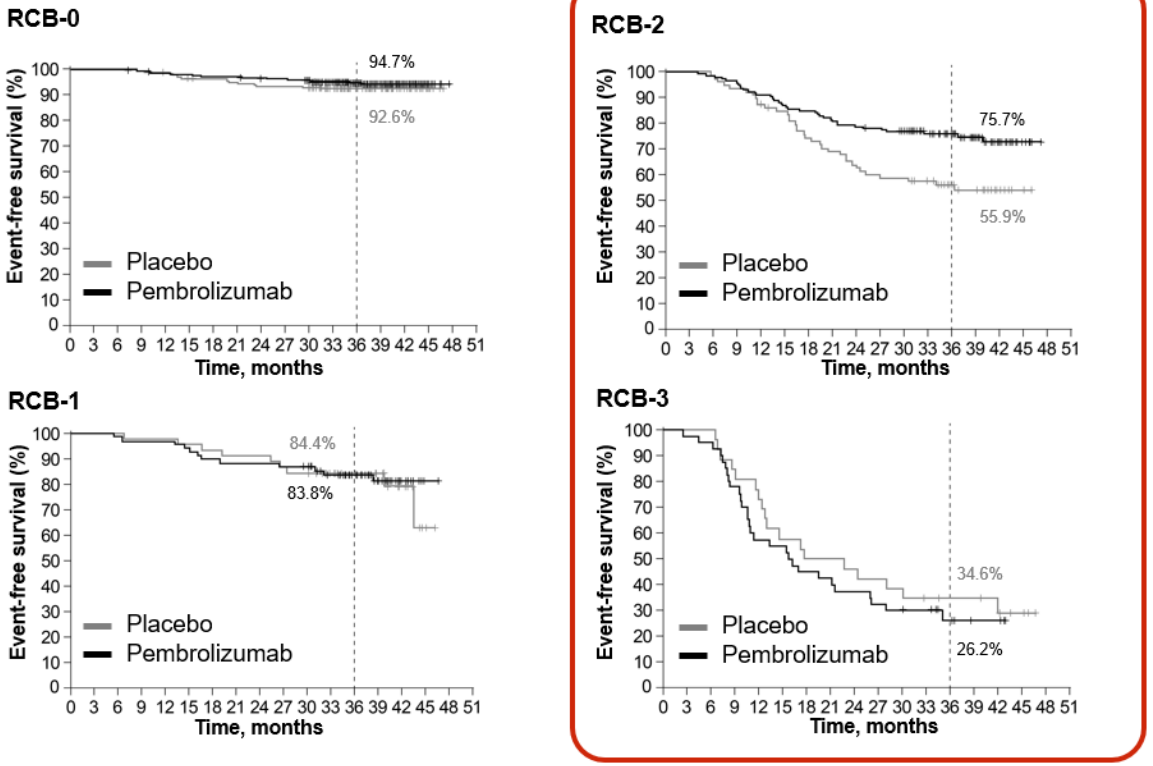
Mod. Pusztai L et al. 2022 ASCO Annual Meeting, Oral Abstract Session – Breast Cancer–Local/Regional/Adjuvant, Abstract No. 503

Pembrolizumab in der Neodjuvans beim TNBC

EFS by RCB Score



- The addition of Pembro lowered RCB scores
- Low RCB associated with improve EFS
- RCB 2–3 associated with poor survival

9

Mod. Stringer-Reasor E. 2022 ASCO Annual Meeting, Oral Abstract Session – Breast–Local/Regional/Adjuvant

Where does NeoPACT fit with other ICI Neoadjuvant Trials?

	GeparNuevo	KN-522	Impass-031	NeoTRIP	iSPY
N	174	1174	333	280	69/181
Target	PD-L1	PD-1	PD-L1	PD-L1	PD-1
Stage	35% stage 1	2/3	2/3	Incl N3	2/3
Anthracycline	Yes	Yes	Yes	No	Yes
Platinum	No	Yes	No	Yes	No
pCR (ITT)	**58%**	**65%**	**58%**	**44%**	**60%**
△pCR	9%	14%	17%	3%	22–66%
EFS (HR)	0.48 (0.24–0.97)	0.63 (0.43–0.93) (p=0.00031)	0.76 (0.4–1.44) (ns)	TBD	N/A
EFS	**3-yr DFS 85.6%**	**3-yr DFS 84.5%**	**TBD**	**TBD**	**N/A**

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Mod. Dent RA. 2022 ASCO Annual Meeting, Poster Discussion Session – Breast Cancer–Local/Regional/Adjuvant