

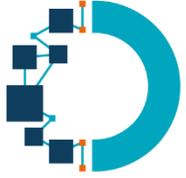


Mardi 21 novembre 2023

Palais de la Bourse - Bordeaux

Laura SALABERT – Institut Bergonié

Les « Actus » de l'ESMO – Soirée Post-ESMO Bordeaux 2023



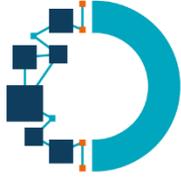
Liens d'intérêts

- Board : Seagen, Viatris, Lilly
- Hospitalité : Gilead, Pfizer



Cancer du sein métastatique

RH+ HER2 négatif

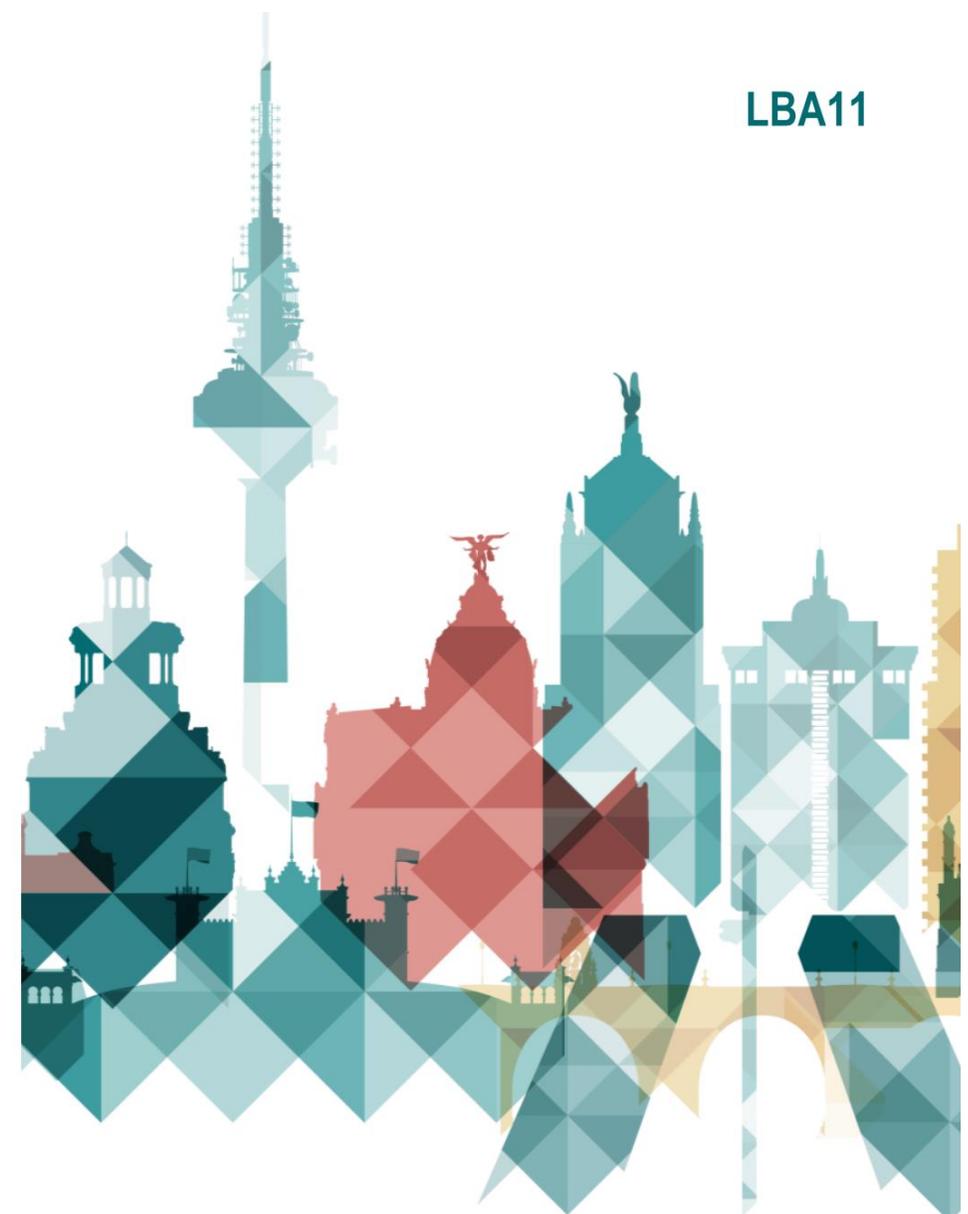


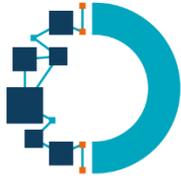
Datopotamab deruxtecan (Dato-DXd) vs chemotherapy in previously-treated inoperable or metastatic hormone receptor-positive, HER2-negative (HR+/HER2-) breast cancer: Primary results from the randomised Phase 3 TROPION-Breast01 trial

Aditya Bardia,¹ Komal Jhaveri,² Seock-Ah Im,³ Sonia Pernas,⁴ Michelino De Laurentiis,⁵ Shusen Wang,⁶ Noelia Martínez Jañez,⁷ Giuliano Borges,⁸ David W. Cescon,⁹ Masaya Hattori,¹⁰ Yen-Shen Lu,¹¹ Erika Hamilton,¹² Qingyuan Zhang,¹³ Junji Tsurutani,¹⁴ Kevin Kalinsky,¹⁵ Lu Xu,¹⁶ Neelima Denduluri,¹⁷ Hope S. Rugo,¹⁸ Binghe Xu,^{19*} Barbara Pistilli^{20*}

*Contributed equally

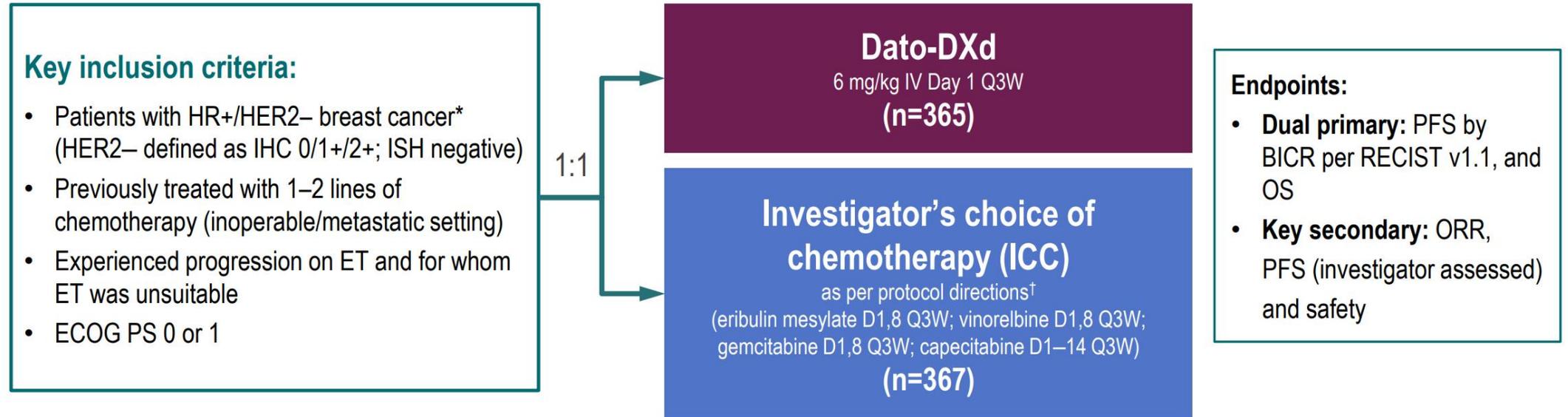
¹Mass General Cancer Center, Harvard Medical School, Boston, MA, USA; ²Memorial Sloan Kettering Cancer Center, New York, NY, USA, and Weill Cornell Medical College, New York, NY, USA; ³Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Seoul National University, Seoul, Republic of Korea; ⁴Institut Català d'Oncologia, IDIBELL, L'Hospitalet, Barcelona, Spain; ⁵Istituto Nazionale Tumori Napoli IRCCS "Fondazione Pascale", Napoli, Italy; ⁶Cancer Center of Sun Yet-sen University, Guangzhou, China; ⁷Ramón y Cajal University Hospital, Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS), Madrid, Spain; ⁸Catarina Pesquisa Clínica, Santa Catarina, Brazil; ⁹Princess Margaret Cancer Centre/UHN, Toronto, ON, Canada; ¹⁰Aichi Cancer Center, Nagoya, Japan; ¹¹National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan; ¹²Sarah Cannon Research Institute / Tennessee Oncology, Nashville, TN, USA; ¹³Harbin Medical University Cancer Hospital, Harbin, China; ¹⁴Showa University Hospital, Tokyo, Japan; ¹⁵Winship Cancer Institute at Emory University, Atlanta, GA, USA; ¹⁶AstraZeneca, New York, NY, USA; ¹⁷AstraZeneca, Arlington, VA, USA; ¹⁸University of California San Francisco Comprehensive Cancer Center, San Francisco, CA, USA; ¹⁹National Cancer Center / National Clinical Research Center for Cancer / Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; ²⁰Gustave Roussy Cancer Center, Villejuif, France





TROPION-Breast01 Study Design¹

Randomised, phase 3, open-label, global study (NCT05104866)



Randomisation stratified by:

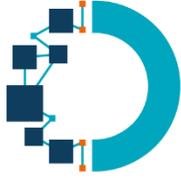
- **Lines of chemotherapy** in unresectable/metastatic setting (1 vs 2)
- **Geographic location** (US/Canada/Europe vs ROW)
- **Previous CDK4/6 inhibitor** (yes vs no)

- Treatment continued until PD, unacceptable tolerability, or other discontinuation criteria

Detailed description of the statistical methods published previously.¹ *Per American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines. †ICC was administered as follows: eribulin mesylate, 1.4 mg/m² IV on Days 1 and 8, Q3W; capecitabine, 1000 or 1250 mg/m² orally twice daily on Days 1 to 14, Q3W (dose per standard institutional practice); vinorelbine, 25 mg/m² IV on Days 1 and 8, Q3W; or gemcitabine, 1000 mg/m² IV on Days 1 and 8, Q3W. BICR, blinded independent central review; CDK4/6, cyclin-dependent kinase 4/6; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; IV, intravenous; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; ROW, rest of world.

1. Bardia A, et al. *Future Oncol* 2023; doi: 10.2217/fon-2023-0188.





Demographics and Baseline Characteristics

ICC:

- Eribulin mesylate: n=220
- Vinorelbine: n=38
- Capecitabine: n=76
- Gemcitabine: n=33

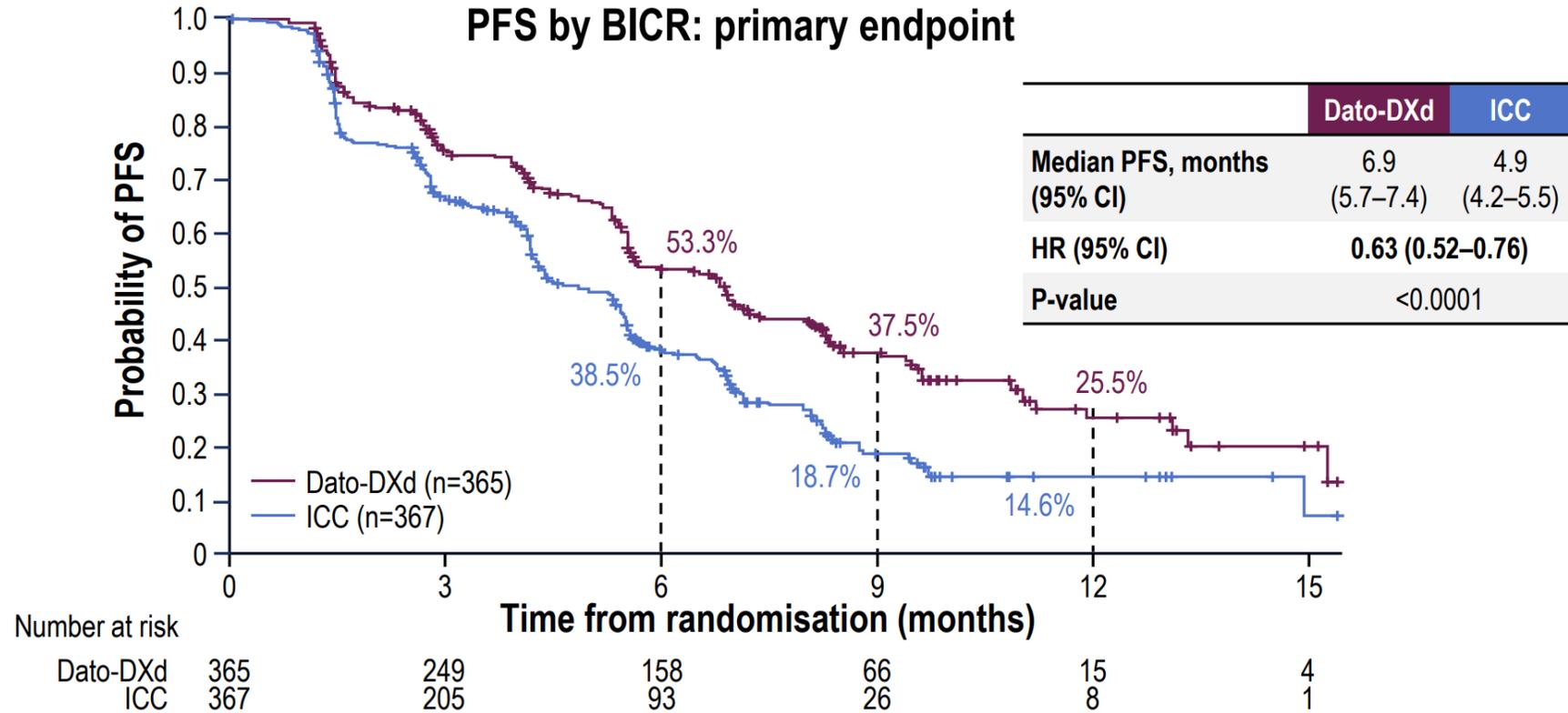
	Dato-DXd (n=365)	ICC (n=367)
Age, median (range), years	56 (29–86)	54 (28–86)
Female, n (%)	360 (99)	363 (99)
Race, n (%) Black or African American / Asian / White / Other*	4 (1) / 146 (40) / 180 (49) / 35 (10)	7 (2) / 152 (41) / 170 (46) / 38 (10)
Ethnicity, n (%) Hispanic or Latino / Not Hispanic or Latino [†]	40 (11) / 322 (88)	43 (12) / 318 (87)
Prior lines of chemotherapy,[‡] n (%) 1 / 2	229 (63) / 135 (37)	225 (61) / 141 (38)
Prior CDK4/6 inhibitor, n (%) Yes / No	299 (82) / 66 (18)	286 (78) / 81 (22)
Prior taxane and/or anthracycline, n (%)	Taxane and/or Anthracycline	330 (90)
	Neither	35 (10)
		339 (92)
		28 (8)

*Including not reported. [†]Ethnicity missing: 3 patients in Dato-DXd group; 6 patients in ICC group.

[‡]In the inoperable/metastatic setting; one patient in the Dato-DXd group had 3 prior lines of chemotherapy; one patient in the ICC group had 4 prior lines.



Progression-Free Survival

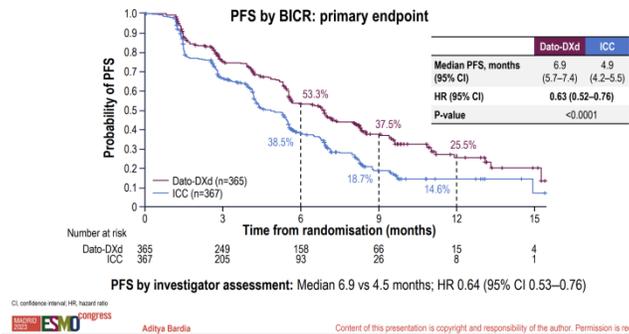


PFS by investigator assessment: Median 6.9 vs 4.5 months; HR 0.64 (95% CI 0.53–0.76)

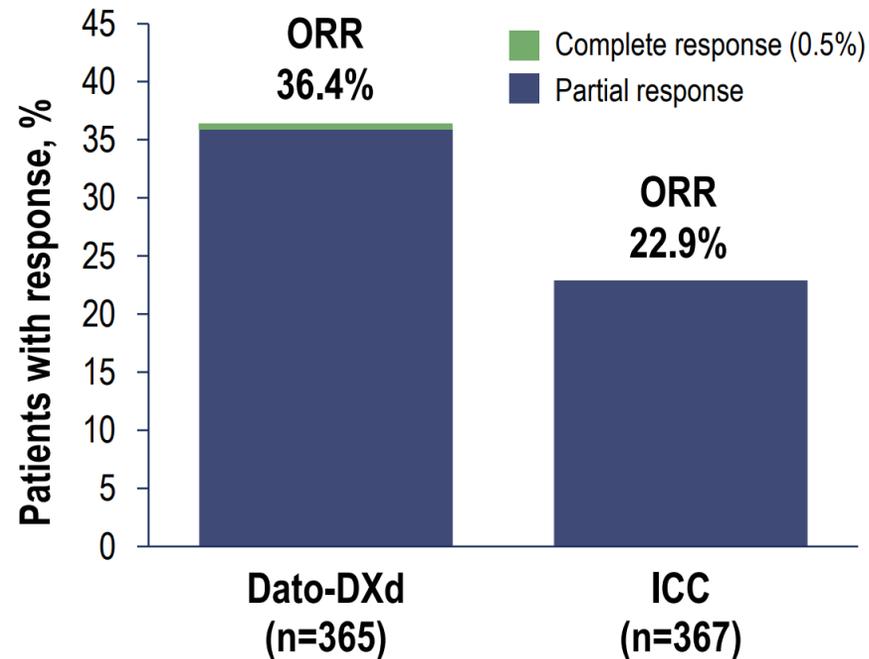
CI, confidence interval; HR, hazard ratio



Progression-Free Survival

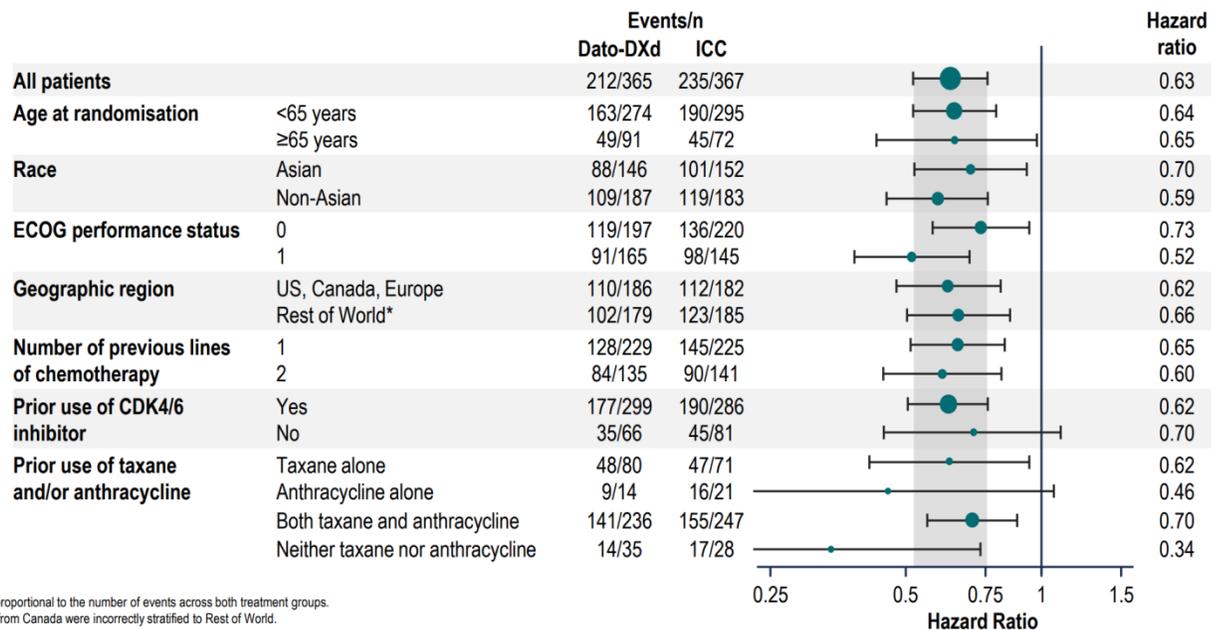


Response Rate



*Information fraction: 39%.
ORR, confirmed objective response rate by BICR

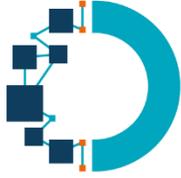
PFS by BICR Across Subgroups



Size of circle is proportional to the number of events across both treatment groups.
*Three patients from Canada were incorrectly stratified to Rest of World.

Données de SG non matures

Overall Safety Summary



TRAEs, n (%)	Dato-DXd (n=360)	ICC (n=351)
All grades	337 (94)	303 (86)
Grade ≥3	75 (21)	157 (45)
Associated with dose reduction	75 (21)	106 (30)
Associated with dose interruption	43 (12)	86 (25)
Associated with discontinuation	9 (3)	9 (3)
Associated with death	0	1 (0.3)
Serious TRAEs	21 (6)	32 (9)
Grade ≥3	17 (5)	31 (8)

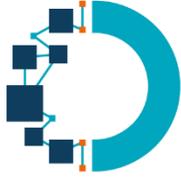
TRAEs, treatment-related adverse events.

System Organ Class Preferred term, n (%)	Dato-DXd (n=360)		ICC (n=351)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Blood and lymphatic system				
Anaemia	40 (11)	4 (1)	69 (20)	7 (2)
Neutropenia*	39 (11)	4 (1)	149 (42)	108 (31)
Eye				
Dry eye	78 (22)	2 (1)	27 (8)	0
Gastrointestinal				
Nausea	184 (51)	5 (1)	83 (24)	2 (1)
Stomatitis	180 (50)	23 (6)	46 (13)	9 (3)
Vomiting	71 (20)	4 (1)	27 (8)	2 (1)
Constipation	65 (18)	0	32 (9)	0
General				
Fatigue	85 (24)	6 (2)	64 (18)	7 (2)
Skin and subcutaneous				
Alopecia	131 (36)	0	72 (21)	0



Cancer du sein métastatique

HER2 Low



Trastuzumab Deruxtecan (T-DXd) Versus Treatment of Physician's Choice (TPC) in Patients With HER2-Low Unresectable and/or Metastatic Breast Cancer: Updated Survival Results of the Randomized, Phase 3 DESTINY-Breast04 Study

Presentation 3760

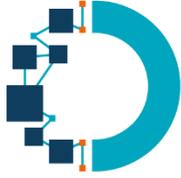
Shanu Modi,¹ William Jacot, Hiroji Iwata, Yeon Hee Park, Maria Jesus Vidal Losada, Wei Li, Junji Tsurutani, Khalil Zaman, Naoto Ueno, Aleix Prat, Konstantinos Papazisis, Hope S. Rugo, Nadia Harbeck, Seock-Ah Im, Michelino De Laurentis, Cecilia Orbegoso Aguilar, Lotus Yung, Fu-Chih Cheng, Yingkai Cheng, David Cameron

On behalf of the DESTINY-Breast04 investigators

¹Memorial Sloan Kettering Cancer Center, New York, NY, USA

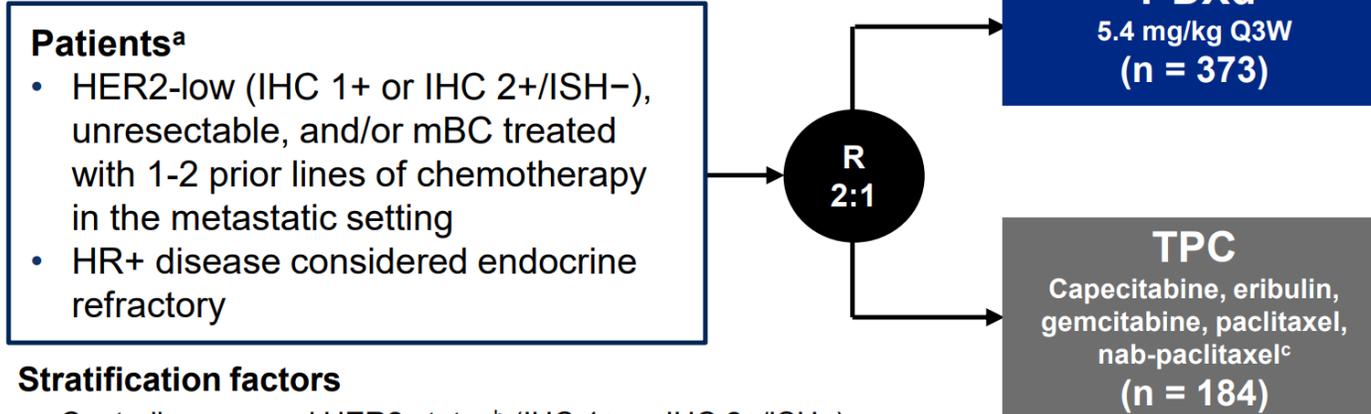
Madrid, Spain, October 20-24, 2023





DESTINY-Breast04 Study Design:

An open-label, multicenter study (NCT03734029)¹⁻³



Stratification factors

- Centrally assessed HER2 status^b (IHC 1+ vs IHC 2+/ISH-)
- 1 vs 2 prior lines of chemotherapy
- HR+ (with vs without prior treatment with CDK4/6i) vs HR-

Primary endpoint

- PFS by BICR (HR+)

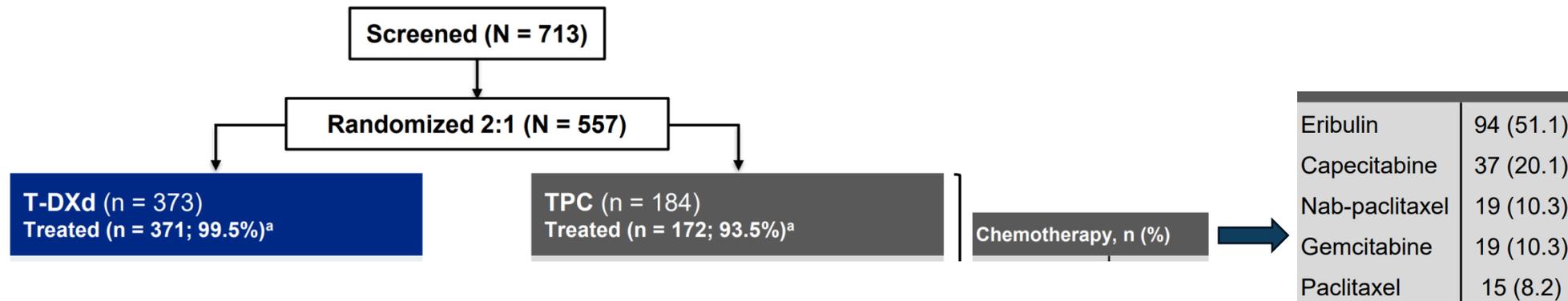
Key secondary endpoints^d

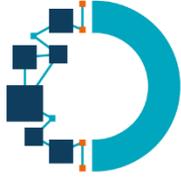
- PFS by BICR (all patients)
- **OS (HR+ and all patients)**

Secondary endpoints^d

- **PFS by investigator**
- ORR by BICR and investigator
- DOR by BICR
- **Safety**
- Patient-reported outcomes (HR+)^e

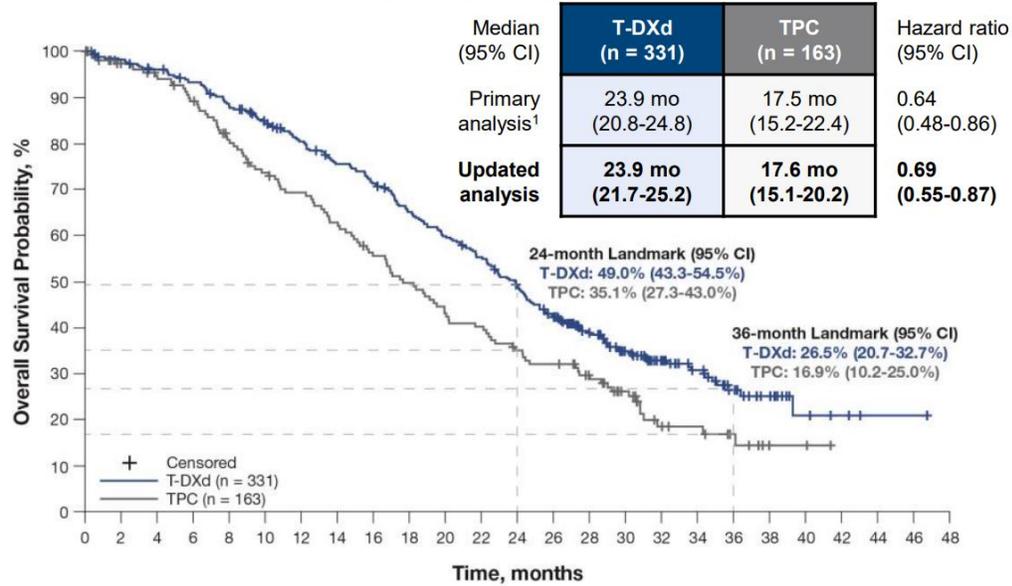
At the updated data cutoff (March 1, 2023), median follow-up was 32.0 months (95% CI, 31.0-32.8 months)





Overall Survival

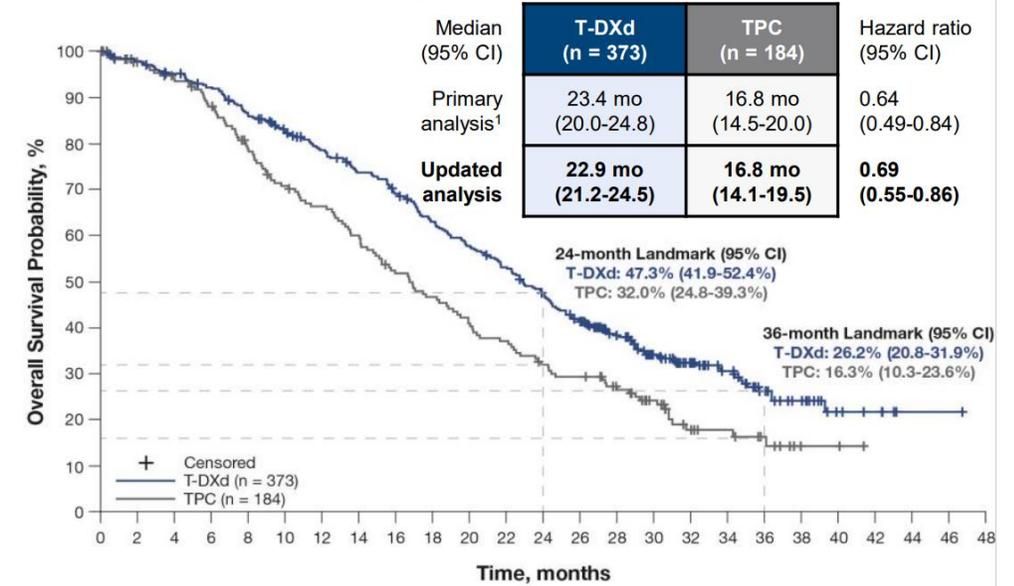
HR+ Cohort



Patients still at risk:

T-DXd (n = 331) 331 325 323 317 313 307 302 292 284 279 267 258 250 243 233 230 220 212 199 189 183 176 168 155 147 135 124 109 94 81 72 66 54 46 42 34 23 17 14 7 5 4 3 2 1 1 1 0
TPC (n = 163) 163 150 144 142 138 134 129 123 114 108 103 97 96 92 87 82 76 71 68 64 59 56 55 50 47 43 43 42 35 31 25 16 13 11 9 7 5 2 2 2 1 0

All Patients



Patients still at risk:

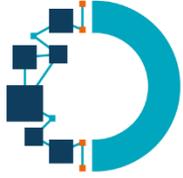
T-DXd (n = 373) 373 366 363 355 350 342 337 325 314 308 295 285 276 269 257 254 240 231 217 205 199 191 182 168 160 145 137 122 107 94 81 75 62 52 48 39 28 21 15 11 7 6 5 3 1 1 1 0
TPC (n = 184) 184 170 165 160 156 152 145 137 127 119 113 107 105 100 95 88 81 75 69 64 59 56 53 49 45 45 44 37 33 27 18 15 12 12 10 8 5 2 2 2 1 0

- ➔ Bénéfice en SG de 31% se maintenant dans le temps dans la cohorte RH+ et dans la population totale, de même que dans l'ensemble des sous-groupes
- ➔ Pas de nouveau signal d'alerte en termes de toxicité (12% d'ILD)



Cancer du sein métastatique

Triple négatif



MADRID
2023

ESMO

congress

Datopotamab Deruxtecan (Dato-DXd) + Durvalumab (D) as First-Line (1L) Treatment for Unresectable Locally Advanced/Metastatic Triple-Negative Breast Cancer (a/mTNBC)

Updated Results From BEGONIA, a Phase 1b/2 Study

Professor Peter Schmid, FRCP, MD, PhD

Barts Cancer Institute, Queen Mary University of London, London, UK

P. J. Wysocki,¹ C. X. Ma,² Y. H. Park,³ R. Fernandes,⁴ S. Lord,⁵ R. D. Baird,⁶ C. Prady,⁷ K. H. Jung,⁸ J. Asselah,⁹ R. Huisden,¹⁰ R. Stewart,¹⁰ K. Heider,¹⁰ P. Vukovic,¹⁰ N. Denduluri,¹¹ Z. Nowecki¹²

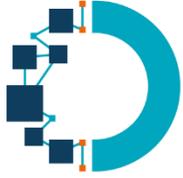
Follow the QR or link to access the presentation and a plain language summary.

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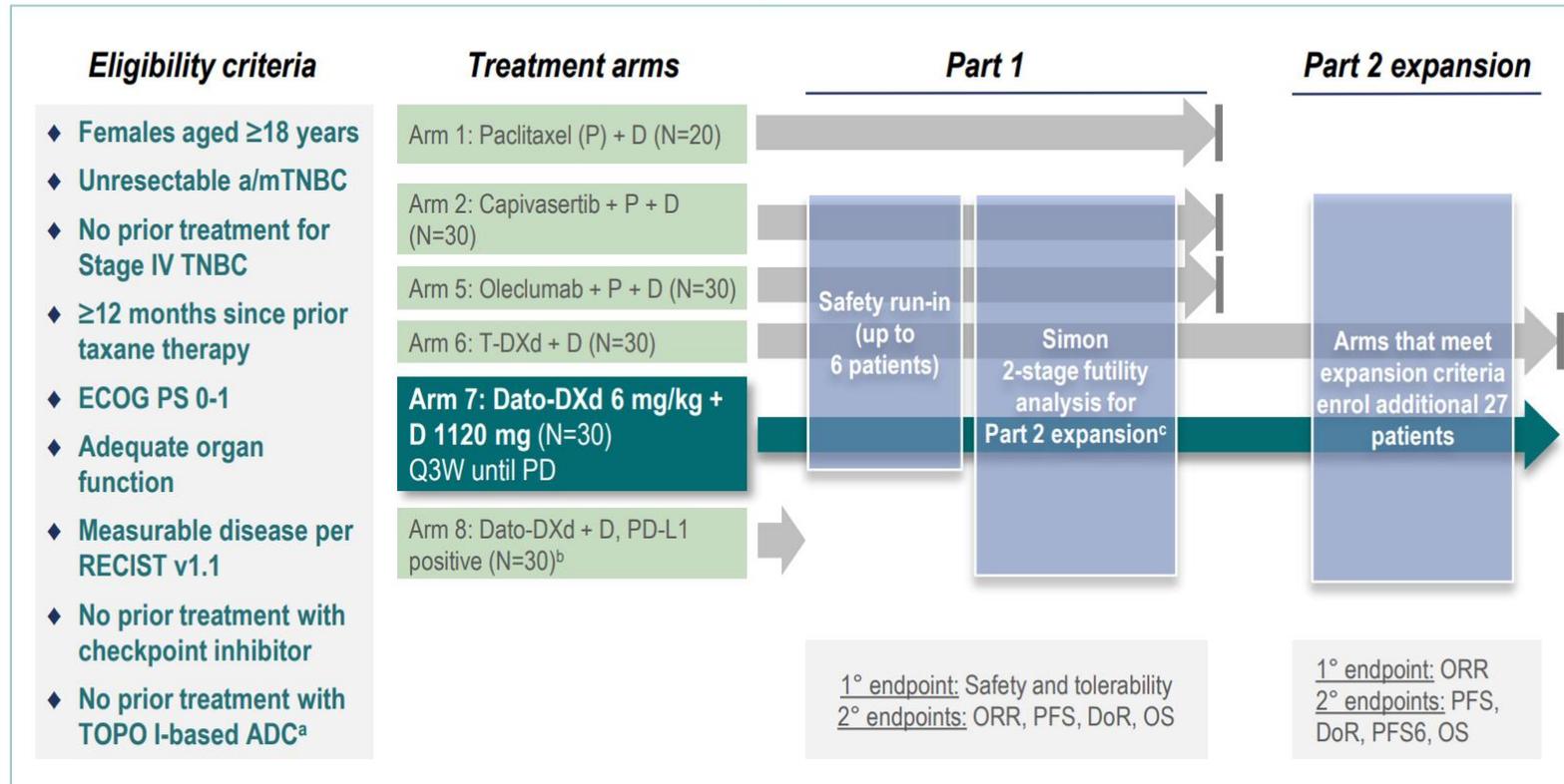
<https://bit.ly/45YZac9>

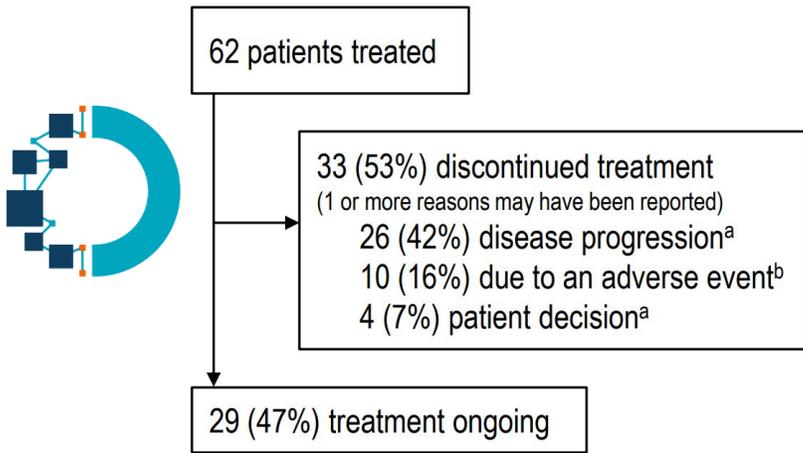




The BEGONIA Study (NCT03742102)

Study Design

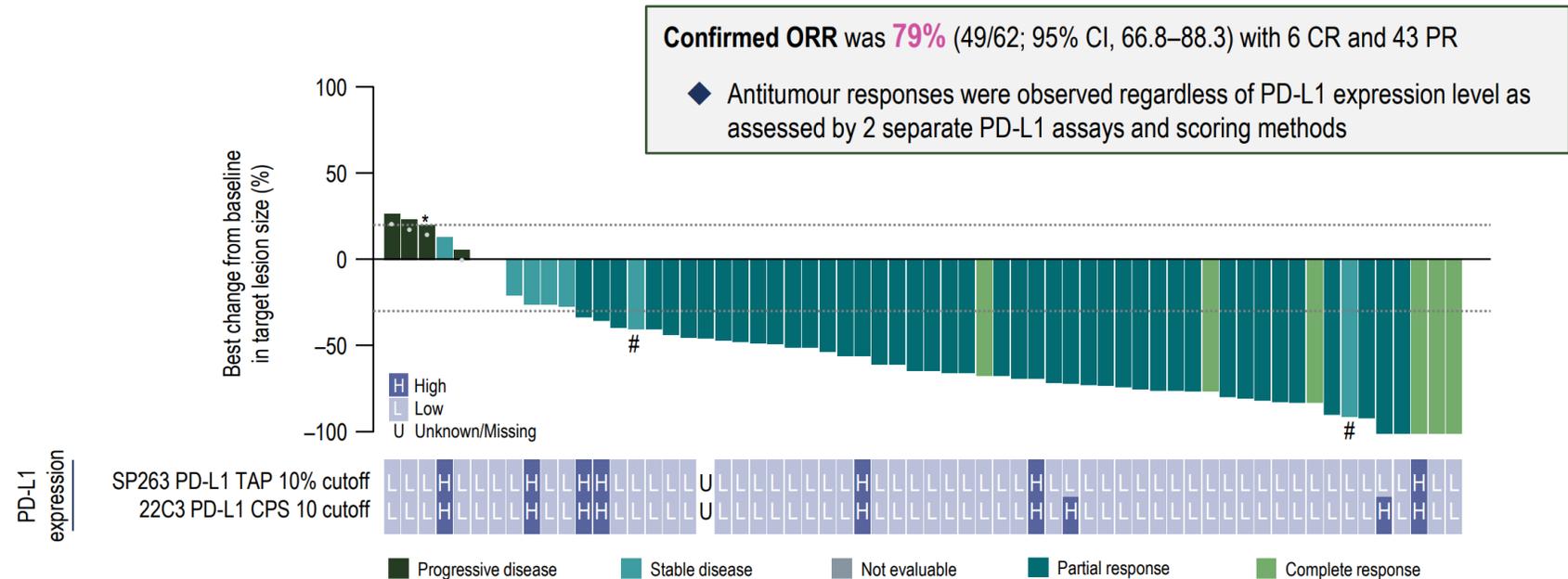


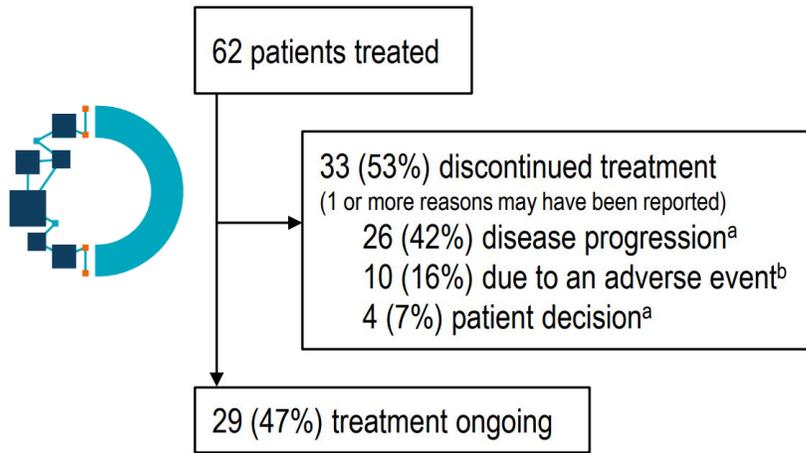


Median follow-up: 11.7 (range, 2–20) months

BEGONIA Arm 7: Dato-DXd + Durvalumab

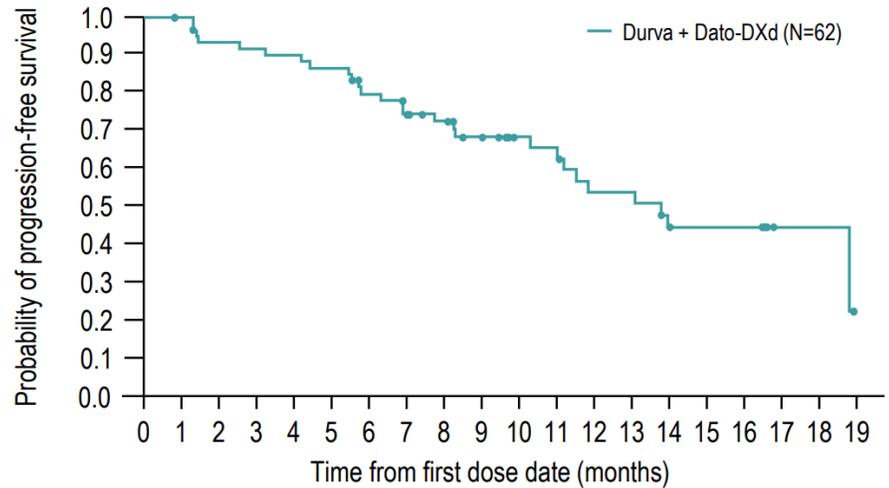
Antitumour Responses in 1L a/mTNBC





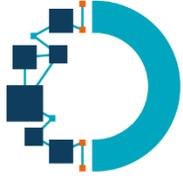
Median follow-up: 11.7 (range, 2–20) months

Median PFS was 13.8 months (95% CI, 11.0–NC)



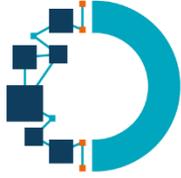
Number of patients at risk

Durva + Dato-DXd	62	61	56	55	54	52	45	40	37	32	24	23	18	18	14	13	13	2	2	0
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Most frequently reported adverse events ($\geq 15\%$) (N=62)

AE preferred term	Any grade, n (%)	Grade 3/4, n (%)
Nausea	40 (65)	0
Stomatitis	40 (65)	7 (11)
Alopecia	31 (50)	0
Constipation	29 (47)	1 (2)
Fatigue	28 (45)	1 (2)
Rash	20 (32)	0
Vomiting	16 (26)	1 (2)
Amylase increased	13 (21)	11 (18)
COVID-19	13 (21)	0
Dry eye	13 (21)	0
Decreased appetite	12 (19)	1 (2)
Pruritus	10 (16)	0
Cough	10 (16)	0



A First-in-Human Phase I Trial of HS-20089, a B7-H4 ADC, in Patients with Advanced Solid Tumors

J. Wu^{1,2,*}, J. Zhang^{1,3,*}, H. Li⁴, X. Wang⁵, Q.Y. Zhang⁶, Y. Shi⁷, M. yan⁸, Y. Pan⁹, A. Shen¹⁰,
Q. Chen¹¹, Q.Rao¹¹, H. Wei¹², C. Li¹², L. Yang¹², Q. Huang¹², Z. Cao¹², Q. Wu¹²

¹Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China, ²Department of Breast Surgery, Fudan University Shanghai Cancer Center, Shanghai, China, ³Phase I Clinical Trial Center, Fudan University Shanghai Cancer Center, Shanghai, China, ⁴Medical Oncology, Peking University Cancer Hospital and Institute, Beijing, China, ⁵Medical Oncology, Zhejiang Cancer Hospital – Cancer Research Institute, Hangzhou, China, ⁶Medical Oncology, 3rd Affiliated Hospital of Harbin Medical University, Harbin, China, ⁷Medical oncology department of breast cancer, TMUCIH - Tianjin Medical University Cancer Institute and Hospital, Tianjin, China, ⁸Medical Oncology, Henan Cancer Hospital/Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou, China, ⁹Oncology Dept, Anhui Provincial Hospital, Hefei, China, ¹⁰Clinical Research, The First Affiliated Hospital of USTC/ Anhui Provincial Hospital, Hefei, China, ¹¹Medical Oncology, Sun Yat-Sen Memorial Hospital, Guangzhou, China, ¹²Department of Oncology Medicine, Hansoh Pharma Group CO.,LTD., Shanghai, China

* Contributed equally

Dr Jian Zhang

Madrid Spain, 21. 10. 2023



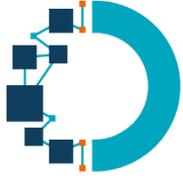
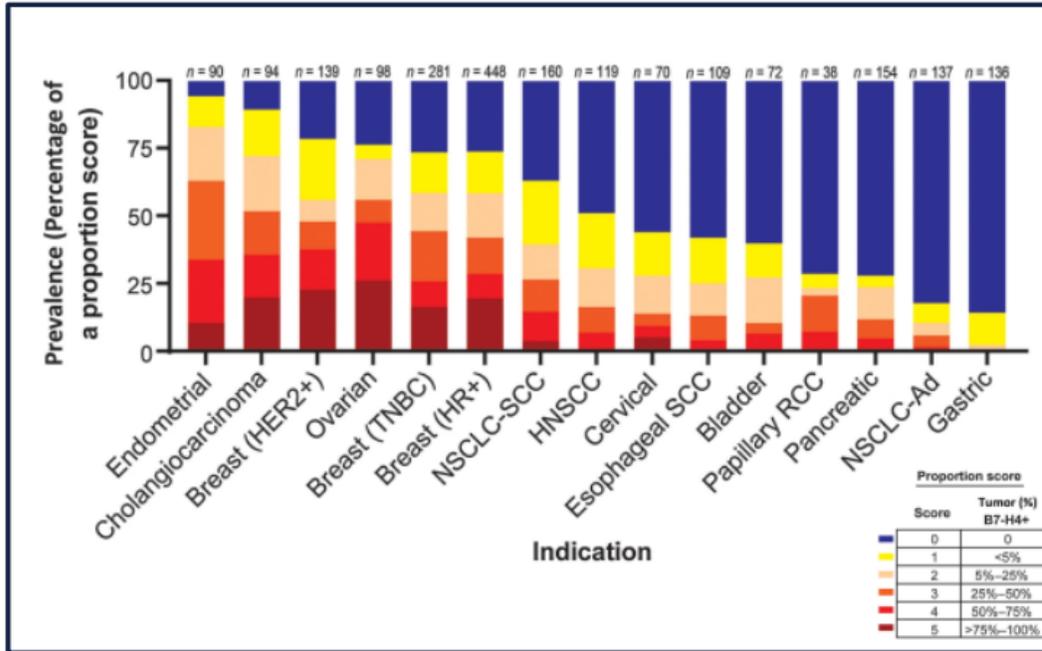
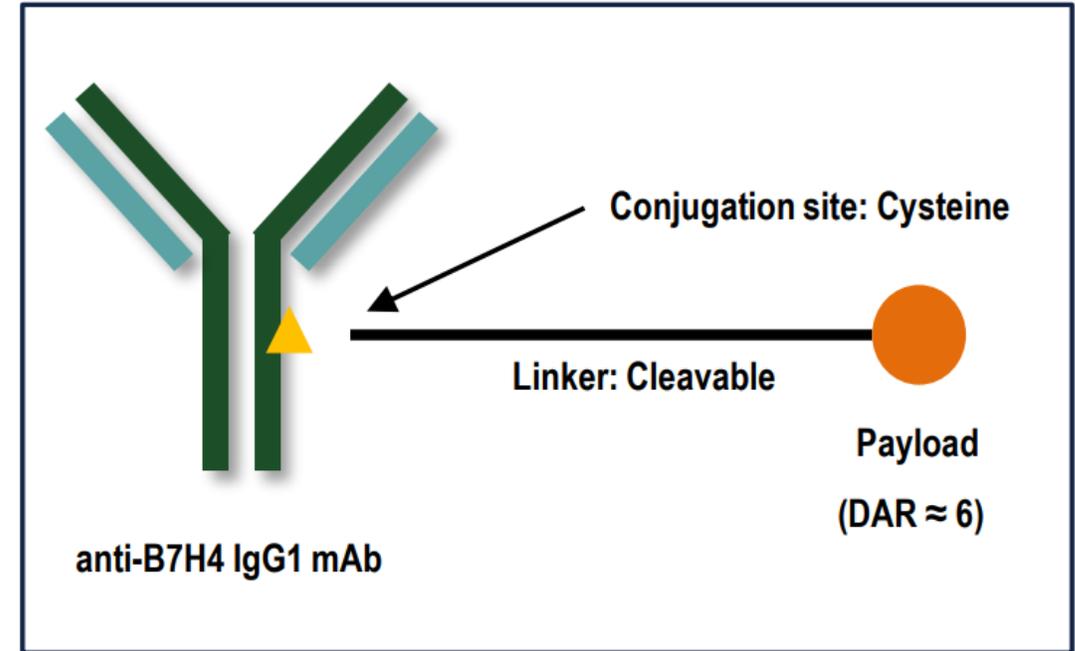


Figure 1. Expression of B7-H4 in Multiple Tumors*

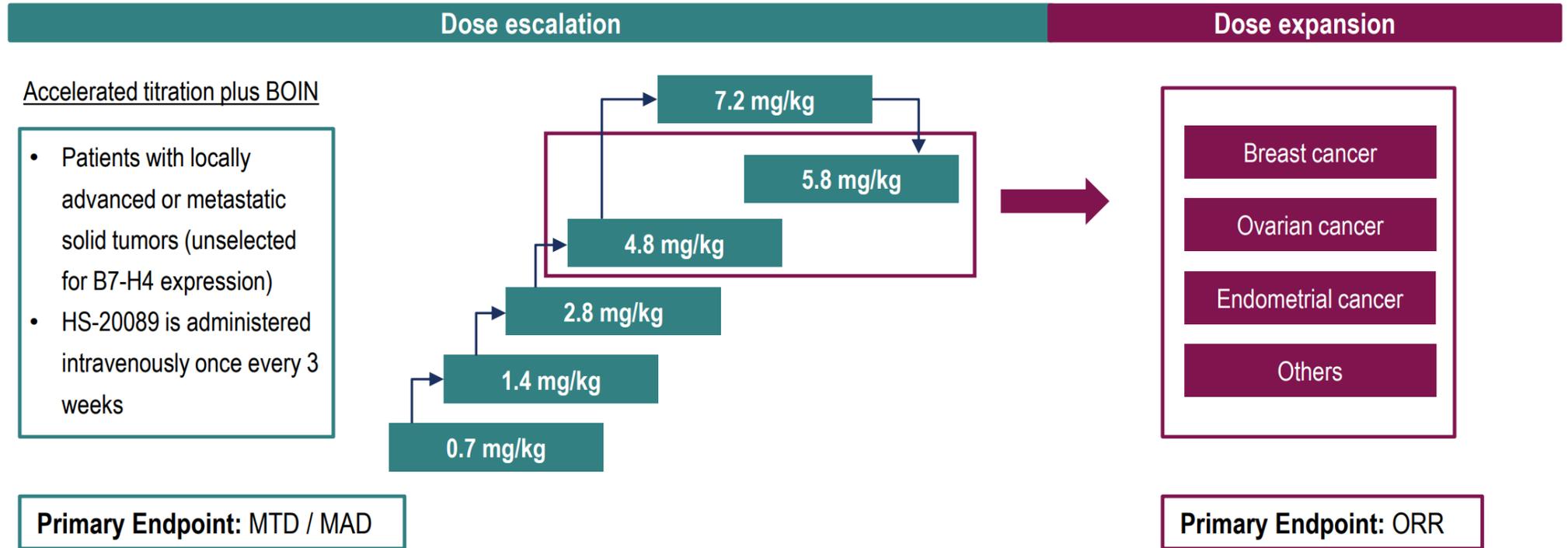
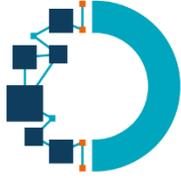


*Reference: Clin Cancer Res . 2022 Dec

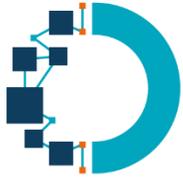
Figure 2. Structure of HS-20089



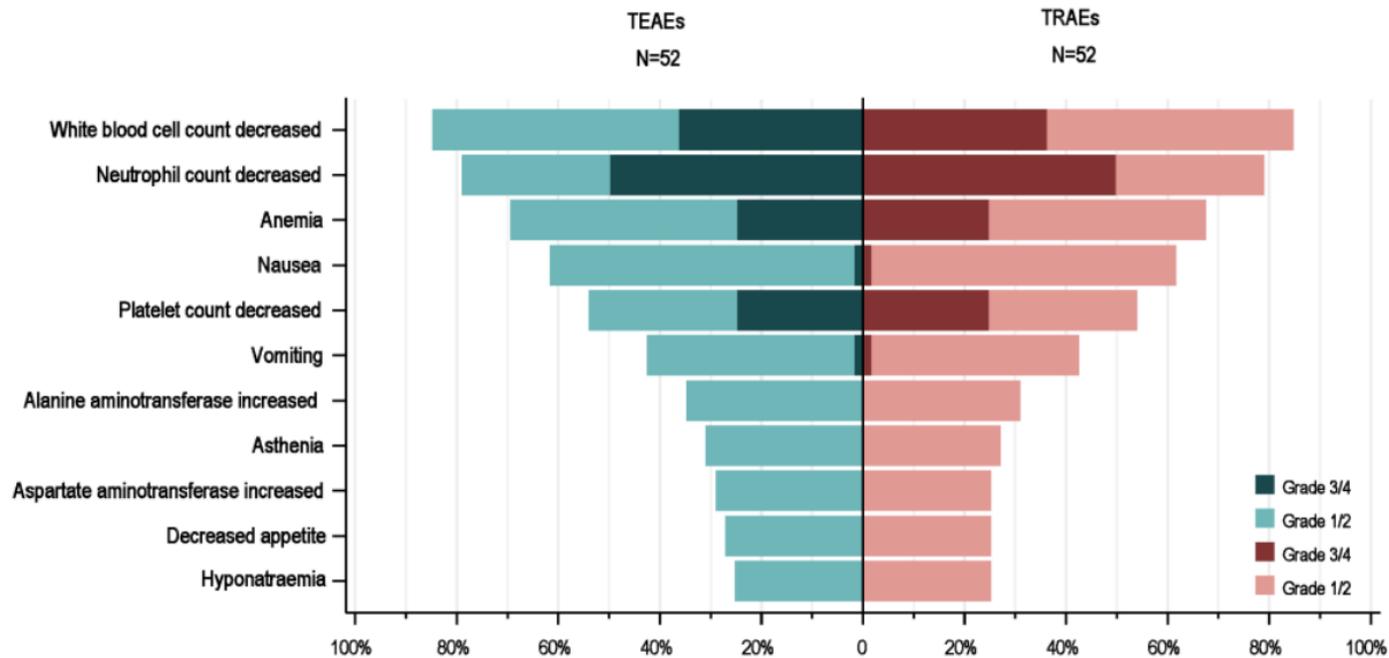
DAR: Drug to antibody ratio.



Résultat phase escalade de dose :
52 patients dont 48 ayant un cancer du sein :
32 TN
12 RH +
4 HER2 +



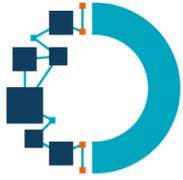
Safety



Clinical cutoff: June 30, 2023

→ suivi median : 5,7 mois

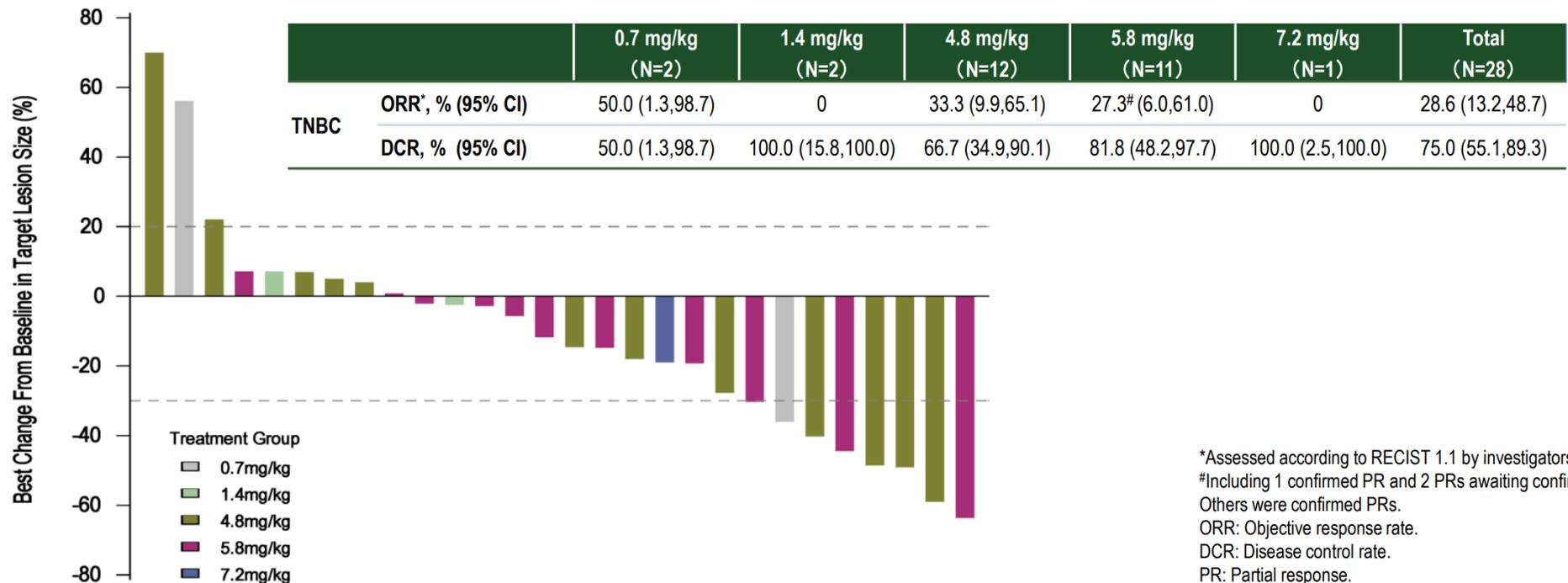
Majorité des effets indésirables de grade 3 et plus : hématologiques



Efficacy - TNBC

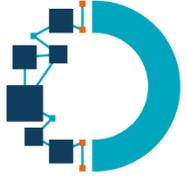
- HS-20089 showed promising anti-tumor activity in triple-negative breast cancer (TNBC).
- At potential target therapeutic doses of 4.8 and 5.8 mg/kg, the ORR were 33.3% and 27.3%, respectively.

Figure 5. Best Percent Change of Target Lesions in TNBC



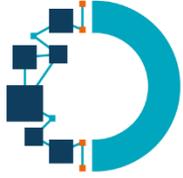
*Assessed according to RECIST 1.1 by investigators.
 #Including 1 confirmed PR and 2 PRs awaiting confirmation.
 Others were confirmed PRs.
 ORR: Objective response rate.
 DCR: Disease control rate.
 PR: Partial response.

Clinical cutoff: August 17, 2023



Cancer du sein métastatique

HER2 + - Métastases cérébrales



MADRID
2023

ESMO congress

A Pooled Analysis of Trastuzumab Deruxtecan in Patients With HER2-Positive Metastatic Breast Cancer With Brain Metastases (BMs) from DESTINY-Breast01, -02, and -03

Presentation 3770

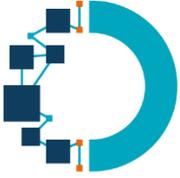
Sara A. Hurvitz¹, Shanu Modi, Wei Li, Yeon Hee Park, Wei-Pang Chung, Sung-Bae Kim, Javier Cortes, Toshinari Yamashita, Jose Luiz Pedrini, Seock-Ah Im, Ling-Ming Tseng, Nadia Harbeck, Ian Krop, Giuseppe Curigliano, Elton Mathias, Jillian Cathcart, Antonio Cagnazzo, Shahid Ashfaq, Anton Egorov, Fabrice André

On behalf of the DESTINY-Breast01, -02, and -03 pooled investigators

¹Fred Hutchinson Cancer Center, University of Washington School of Medicine, Seattle, WA, USA

Madrid, Spain, October 20-24, 2023





Objectif

Analyse exploratoire pour évaluer l'efficacité au niveau cérébral du T-DXD, versus bras comparateur (traitement standard)

2 populations

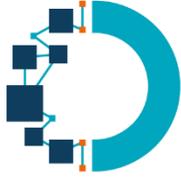
- o Treated/stable BMs (traitement local réalisé, maladie cérébrale stable au baseline)
- o Untreated/active BMs (progression cérébrale non traitée localement, asymptomatique)

DESTINY-Breast01¹

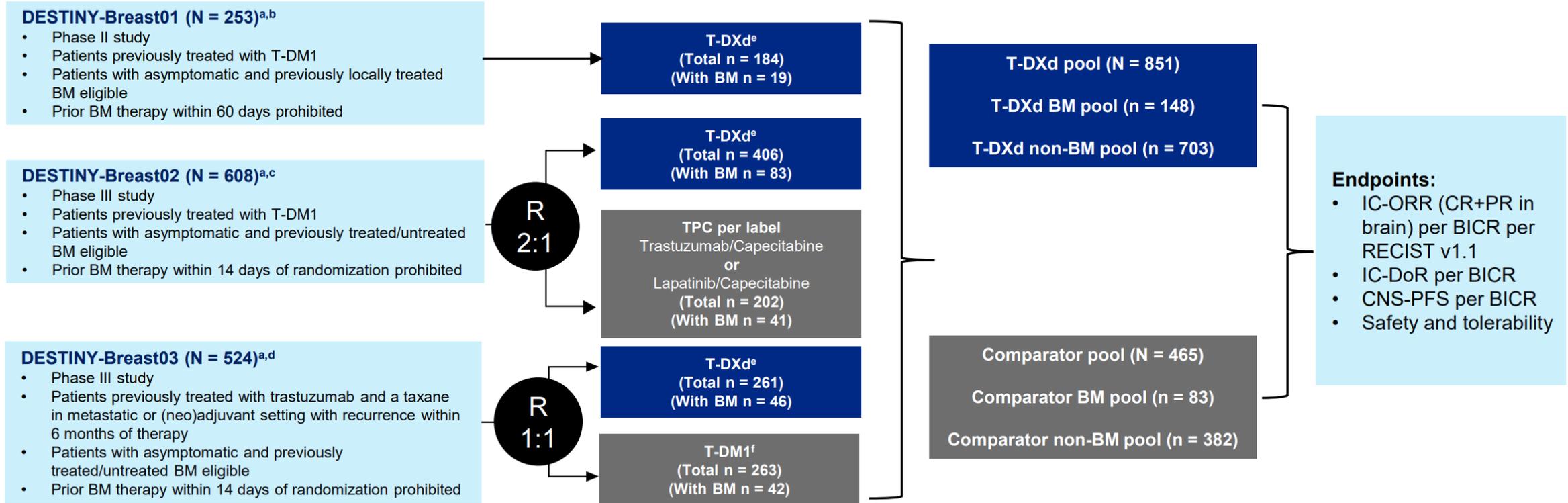
- Patients with asymptomatic, previously locally treated, and stable BMs

DESTINY-Breast02 and DESTINY-Breast03²⁻⁴

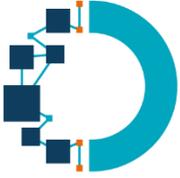
- Initially, patients with previously untreated and asymptomatic BM were eligible
- After protocol amendments, only patients with treated, asymptomatic BMs were allowed



Retrospective Exploratory Pooled Analysis Plan¹⁻³

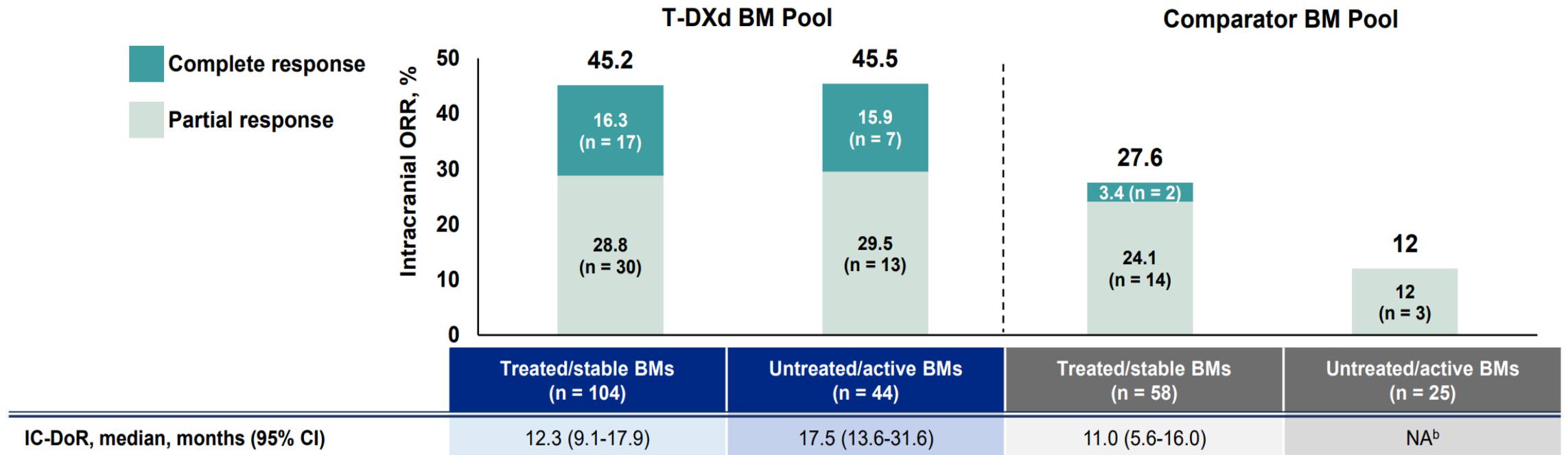


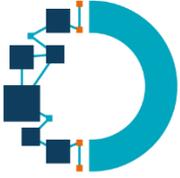
- The BM and non-BM pools were determined by BICR at baseline among all patients based on mandatory brain CT/MRI screening



Exploratory Best IC Response, ORR, and DoR per BICR

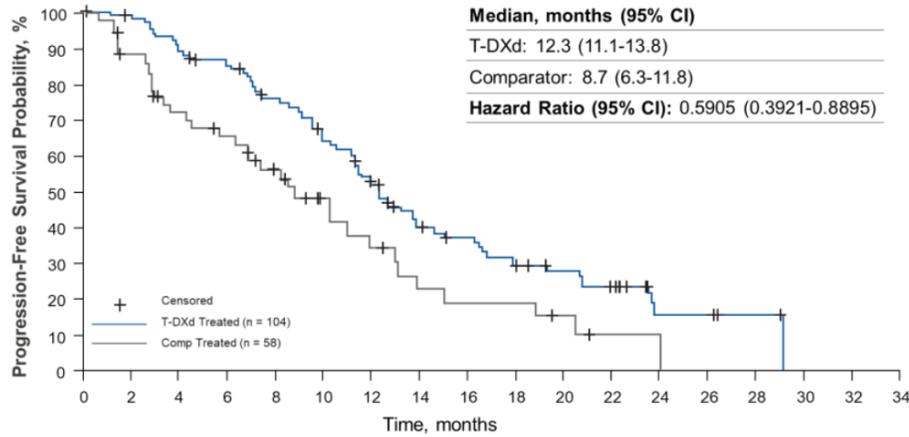
Intracranial ORR^a





Exploratory CNS-PFS per BICR

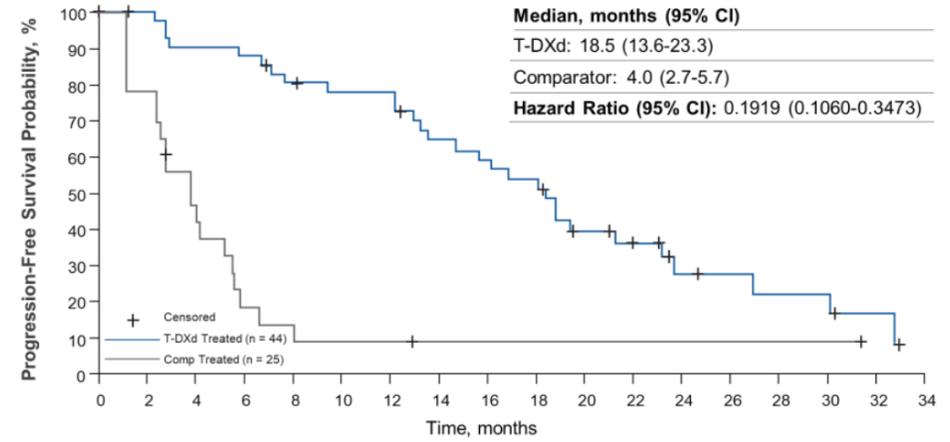
Treated/Stable BMs



Patients still at risk

T-DXd Treated (n = 104)	104	100	89	83	72	58	46	32	28	21	18	12	4	4	2	0	0	0
Comparator Treated (n = 58)	58	44	33	29	22	14	10	6	5	5	3	1	0	0	0	0	0	0

Untreated/Active BMs



Patients still at risk

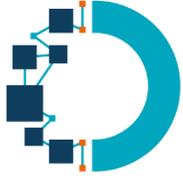
T-DXd Treated (n = 44)	44	41	37	36	32	30	30	24	22	20	13	11	6	5	4	4	2	0
Comparator Treated (n = 25)	25	18	11	5	3	2	2	1	1	1	1	1	1	1	1	1	0	0

- **T-DXd demonstrated a trend towards prolonged CNS-PFS over comparator, with a noticeably greater advantage for patients with untreated/active BMs**



Cancer du sein localisé

EN BREF, dans les RH +



A randomized, double-blind trial of nivolumab vs placebo with neoadjuvant chemotherapy followed by adjuvant endocrine therapy in patients with high-risk, ER+ HER2– primary breast cancer

Sherene Loi,¹ Giuseppe Curigliano,^{2,3} Roberto Salgado,^{1,4} Roberto Iván Romero Díaz,⁵ Suzette Delaloge,⁶ Carlos Ignacio Rojas García,⁷ Marleen Kok,⁸ Cristina Saura,⁹ Nadia Harbeck,¹⁰ Elizabeth A. Mittendorf,¹¹ Denise A. Yardley,¹² Lajos Pusztai,¹³ Alberto Suárez Zaizar,¹⁴ Andrei Ungureanu,¹⁵ Felipe Ades,¹⁶ Rajalakshmi Chandra,¹⁶ Raheel Nathani,¹⁶ Misena Pacius,¹⁶ Jenny Qun Wu,¹⁶ Heather McArthur¹⁷

CHECKMATE 7FL

Abstract LBA20

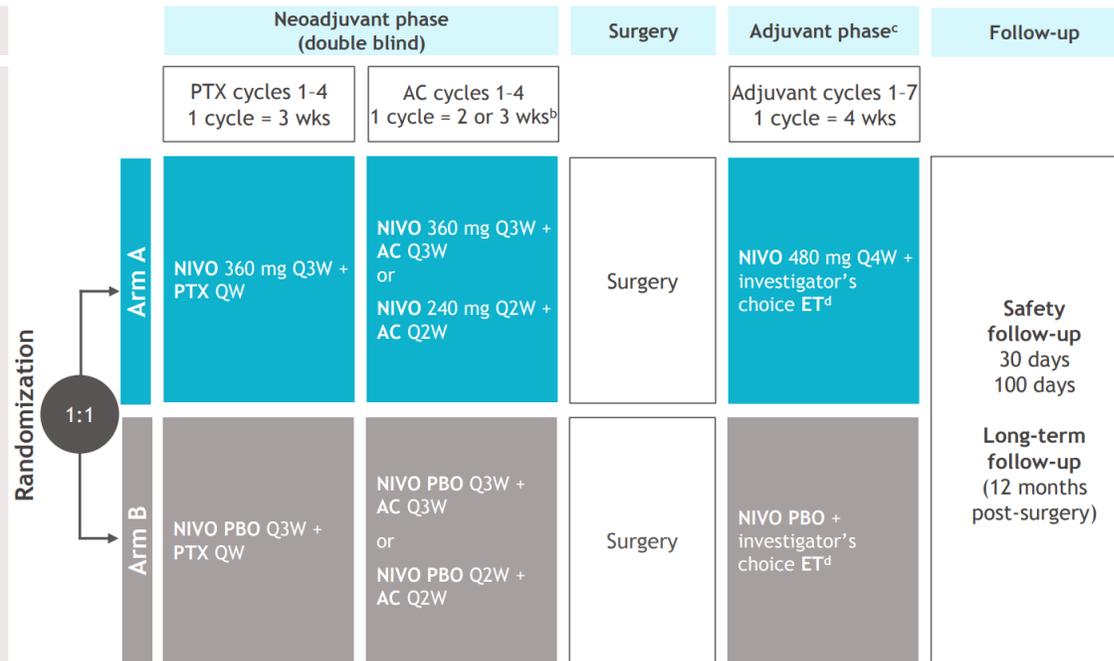
KEYNOTE-756: Phase 3 Study of Neoadjuvant Pembrolizumab or Placebo + Chemotherapy Followed by Adjuvant Pembrolizumab or Placebo + Endocrine Therapy for Early-Stage High-Risk ER+/HER2– Breast Cancer

Fatima Cardoso¹, Heather McArthur², Peter Schmid³, Javier Cortes⁴, Nadia Harbeck⁵, Melinda L Telli⁶, David W. Cescon⁷, Joyce O' Shaughnessy⁸, Peter A. Fasching⁹, Zhimin Shao¹⁰, Delphine Loirat¹¹, Yeon Hee Park¹², Manuel Gonzalez Fernandez¹³, Zhenzhen Liu¹⁴, Hiroyuki Yasojima¹⁵, Yu Ding¹⁶, Liyi Jia¹⁶, Vassiliki Karantza¹⁶, Konstantinos Tryfonidis¹⁶, Aditya Bardia¹⁷

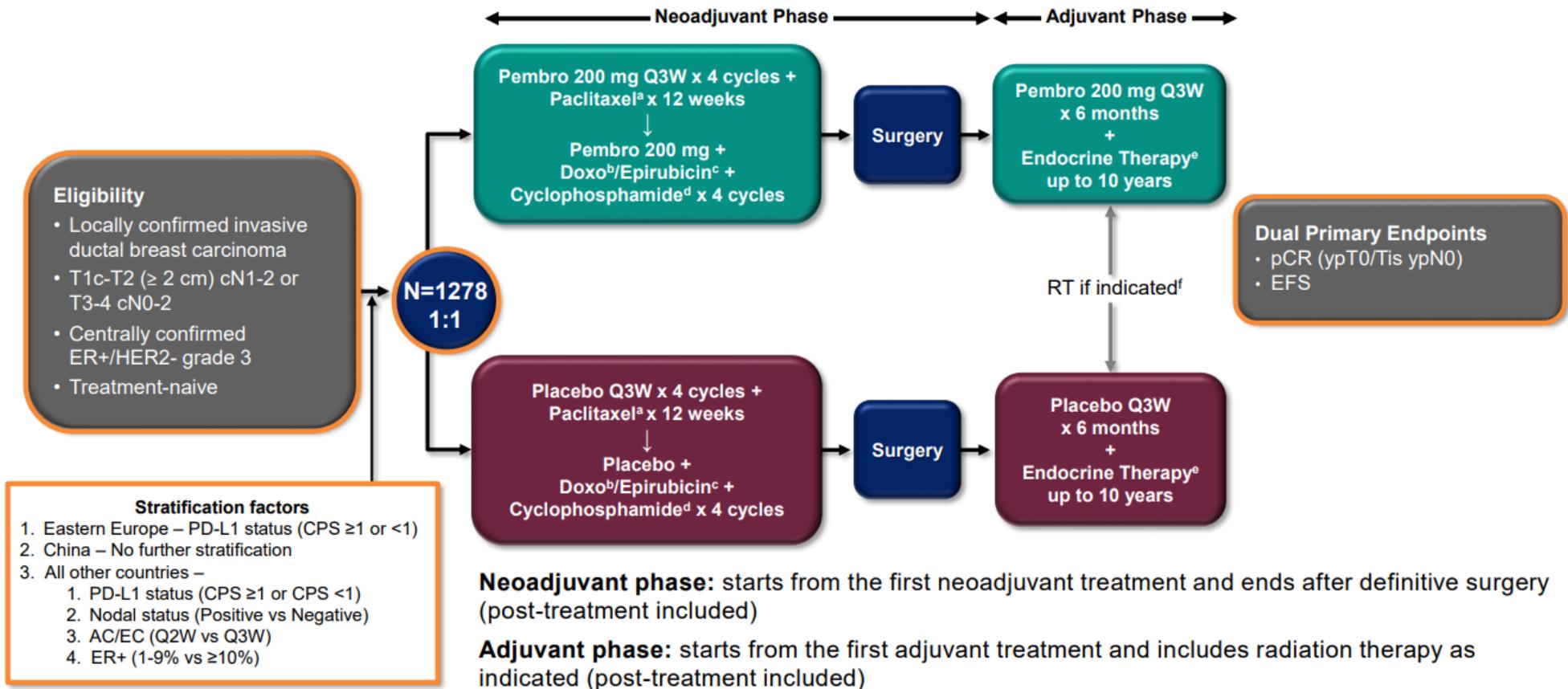
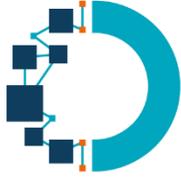
Abstract LBA21

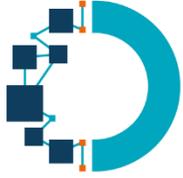


Screening
<p>Key inclusion criteria</p> <ul style="list-style-type: none"> Newly diagnosed ER+ HER2- breast cancer Confirmed ER+ breast cancer T1c-T2, cN1-cN2 or T3-T4, cN0-cN2 Grade 3 with ER \geq 1% or grade 2 with ER 1-10%^a Adequate organ function Tissue available for biomarker assessment ECOG PS 0-1 <p>Stratification factors</p> <ul style="list-style-type: none"> PD-L1 IC (\geq 1% or $<$ 1%) Tumor grade (3 or 2) Axillary nodal status (positive or negative) AC frequency (Q3W or Q2W)

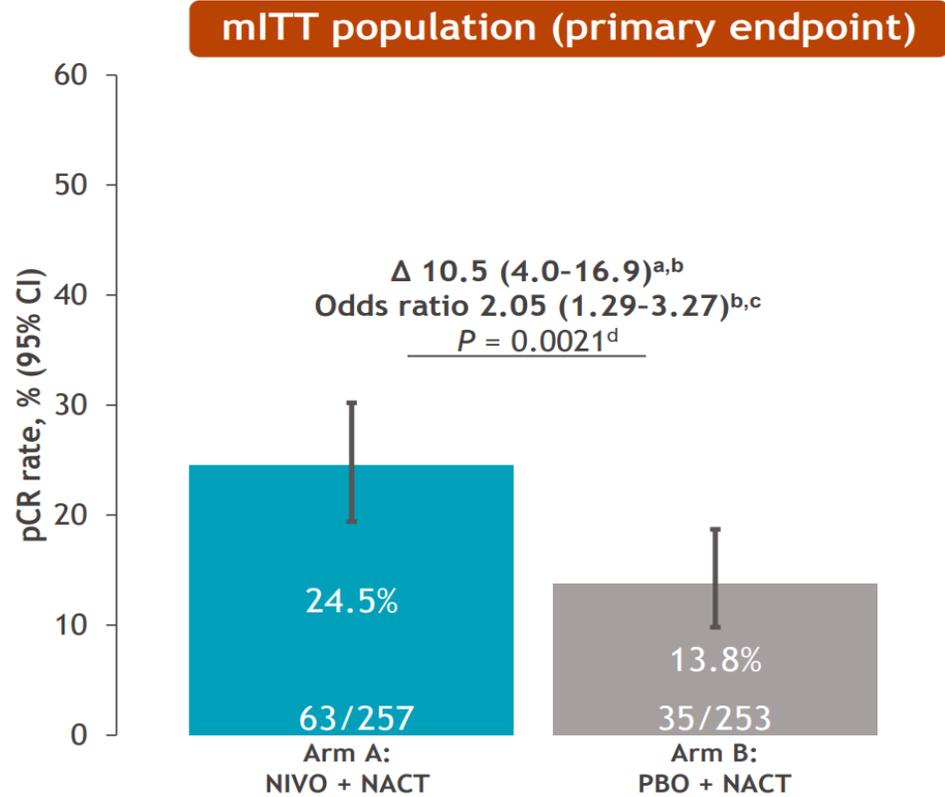


Primary endpoint
<ul style="list-style-type: none"> pCR in the mITT population^a
Secondary endpoints
<ul style="list-style-type: none"> pCR^a in the PD-L1+ population^b RCB class (0/1/2/3) frequency and RCB 0-1 rate RCB class frequency and RCB 0-1 rate in the PD-L1+ population Safety and tolerability
Exploratory endpoint
<ul style="list-style-type: none"> EFS (unavailable for this presentation)

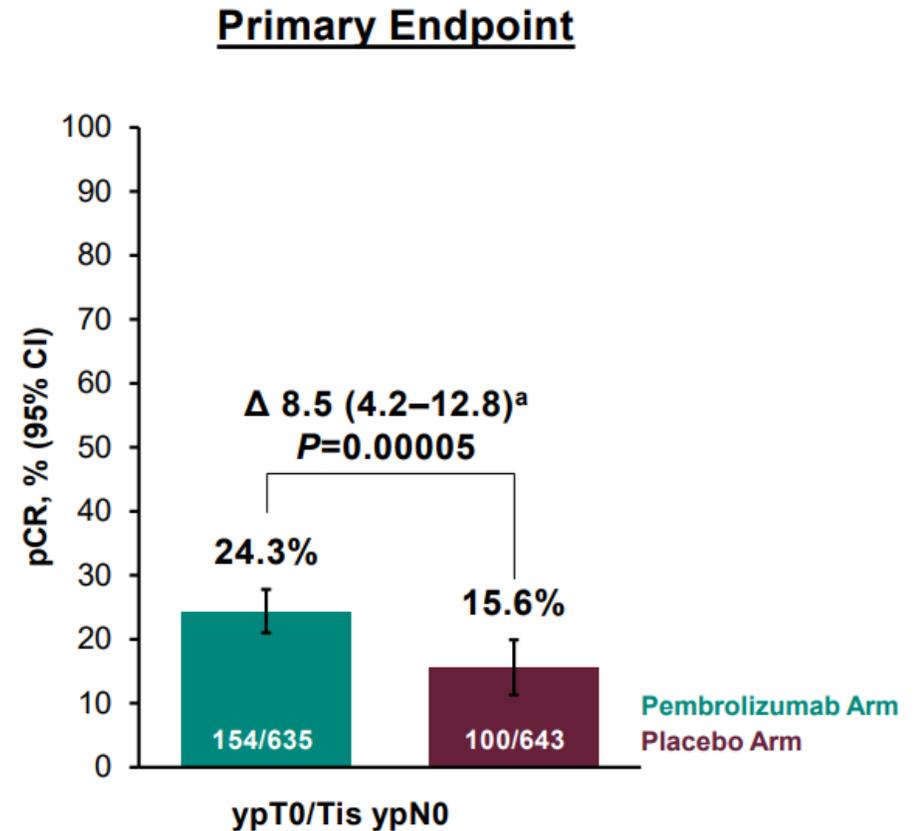


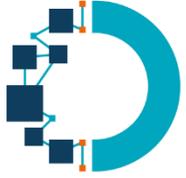


CHECKMATE-7FL



KEYNOTE-756





CONCLUSION

Cancer du sein métastatique :

- Avènement des ADCs
- RH+ HER2 0 ou low et triple négatifs : problématique dans le futur de l'agencement des ADC à disposition (selon profil de tolérance et biomarqueurs ?)
- Triple négatif : BEGONIA prometteur concernant association ADC + immunothérapie
- HER2 + : résultats encourageants sur le contrôle par T-DXD des métastases cérébrales

Cancer du sein localisé :

- Immunothérapie en NA dans les RH+ HER2 nég : à suivre...

