



ASCO 2024

Investor event

03 June 2024

Forward looking statements

In order, among other things, to utilise the 'safe harbour' provisions of the US Private Securities Litigation Reform Act of 1995, AstraZeneca (hereafter 'the Group') provides the following cautionary statement: This document contains certain forward-looking statements with respect to the operations, performance and financial condition of the Group, including, among other things, statements about expected or targeted revenues, margins, earnings per share or other financial or other measures (including the Financial Ambition Statements described in this presentation). Although the Group believes its expectations and targets are based on reasonable assumptions and has used customary forecasting methodologies used in the pharmaceutical industry and risk-adjusted projections for individual medicines (which take into account the probability of success of individual clinical trials, based on industry-wide data for relevant clinical trials at a similar stage of development), any forward-looking statements, by their very nature, involve risks and uncertainties and may be influenced by factors that could cause actual outcomes and results to be materially different from those predicted. The forward-looking statements reflect knowledge and information available at the date of preparation of this document and the Group undertakes no obligation to update these forward-looking statements. The Group identifies the forward-looking statements by using the words 'anticipates', 'believes', 'expects', 'intends' and similar expressions in such statements. Important factors that could cause actual results to differ materially from those contained in forward-looking statements, certain of which are beyond the Group's control, include, among other things: the risk of failure or delay in delivery of pipeline or launch of new medicines; the risk of failure to meet regulatory or ethical requirements for medicine development or approval; the risk of failures or delays in the quality or execution of the Group's commercial strategies; the risk of pricing, affordability, access and competitive pressures; the risk of failure to maintain supply of compliant, quality medicines; the risk of illegal trade in the Group's medicines; the impact of reliance on third-party goods and services; the risk of failure in information technology or cybersecurity; the risk of failure of critical processes; the risk of failure to collect and manage data in line with legal and regulatory requirements and strategic objectives; the risk of failure to attract, develop, engage and retain a diverse, talented and capable workforce; the risk of failure to meet regulatory or ethical expectations on environmental impact, including climate change; the risk of the safety and efficacy of marketed medicines being questioned; the risk of adverse outcome of litigation and/or governmental investigations; intellectual property-related risks to the Group's products; the risk of failure to achieve strategic plans or meet targets or expectations; the risk of failure in financial control or the occurrence of fraud; the risk of unexpected deterioration in the Group's financial position; the impact that global and/or geopolitical events may have, or continue to have, on these risks, on the Group's ability to continue to mitigate these risks, and on the Group's operations, financial results or financial condition. There can be no guarantees that the conditions to the closing of the proposed transaction with Fusion will be satisfied on the expected timetable, or at all, or that "FPI-2265" (Ac225-PSMA I&T) or any combination product will receive the necessary regulatory approvals or prove to be commercially successful if approved. There can be no guarantees that the conditions to the closing of the proposed transaction with Amolyt Pharma will be satisfied on the expected timetable, or at all, or that eneboparatide ('AZP-3601') will receive the necessary regulatory approvals or prove to be commercially successful if approved.

This presentation includes references to new molecular entities and life-cycle management programmes that are being investigated in current or future clinical trials, and as such have not been approved by any regulatory agency. For a list of new molecular entities and indications in development, see pages 7-11 of the Clinical Trials Appendix that accompanied AstraZeneca's Q1 2024 results.

Basis of AstraZeneca ambitions, forecasts and targets

AstraZeneca ambitions, forecasts and targets in this presentation (the "Financial Ambition Statements") are derived from AstraZeneca's most recent risk-adjusted mid- and long-term plans, adjusted for developments in the business since those plans were finalised. Financial Ambition Statements presented are based on management's risk-adjusted projections for individual medicines and individual clinical trials. Estimates for these probabilities are based on industry-wide data for relevant clinical trials in the pharmaceutical industry at a similar stage of development adjusted for management's view on the risk profile of the specific asset. The peak year revenue (PYR) potential for individual medicines referred to in this presentation are the maximum estimated Total Revenue to be recognised by AstraZeneca in a single calendar year, during the lifecycle of the medicine, and are based on management's latest non-risk adjusted forecast estimates. Estimates are based on customary forecasting methodologies used in the pharmaceutical industry. Peak year revenue may occur in different years for each NME depending on trial outcomes, approval label, competition, launch dates and exclusivity periods, amongst other variables. The peak year revenue figures are derived from net sales at nominal values and are not risk-adjusted or time-value discounted. The development of pharmaceutical products has inherent risks given scientific experimentation and there are a range of possible outcomes in clinical results, safety, efficacy and product labelling. Clinical results may not achieve the desired product profile and competitive environment, pricing and reimbursement may have material impact on commercial revenue forecasts. By their nature, forecasts are based on a multiplicity of assumptions and actual performance in future years may vary, significantly and materially, from these assumptions. The Financial Ambition Statements in this presentation are based on Q1 2024 exchange rates; AZ undertakes no obligation to update those statements based on future currency movements

AstraZeneca @ ASCO 2024

Agenda

CEO opening remarks – *Pascal Soriot, CEO*

AstraZeneca presence at ASCO 2024 – *Susan Galbraith, EVP, Oncology R&D*

Clinical Impressions Lung – *Leora Horn, Late Clinical Development and Global Clinical Strategy Lead, Lung Cancer, R&D (moderator)*

Dr Charu Aggarwal, University of Pennsylvania

Clinical Impressions Breast – *Ingrid Mayer, VP, Breast and Gynecologic Cancers, R&D (moderator)*

Dr Rebecca Dent, National Cancer Center Singapore

Strengthening leadership in lung and breast cancer – *Dave Fredrickson, EVP, Oncology*

Q&A session

AstraZeneca @ ASCO 2024

Speakers and panelists

ASTRAZENECA LEADERSHIP



Pascal Soriot
CHIEF EXECUTIVE OFFICER



Dave Fredrickson
EXECUTIVE VICE PRESIDENT,
ONCOLOGY BUSINESS



Susan Galbraith
EXECUTIVE VICE PRESIDENT,
ONCOLOGY R&D



Leora Horn
LATE CLINICAL DEVELOPMENT
AND GLOBAL CLINICAL
STRATEGY LEAD, LUNG
CANCER



Ingrid Mayer
VICE PRESIDENT, BREAST AND
GYNECOLOGIC CANCERS, R&D

KEY EXTERNAL EXPERTS



Dr Charu Aggarwal
THORACIC MEDICAL ONCOLOGIST,
UNIVERSITY OF PENNSYLVANIA
SCHOOL OF MEDICINE



Dr Rebecca Dent
HEAD OF THE DEPARTMENT OF MEDICAL
ONCOLOGY AND CHIEF OF THE BREAST
MEDICAL ONCOLOGY SERVICE AT THE
NATIONAL CANCER CENTER SINGAPORE

Furthering our oncology ambition at ASCO 2024

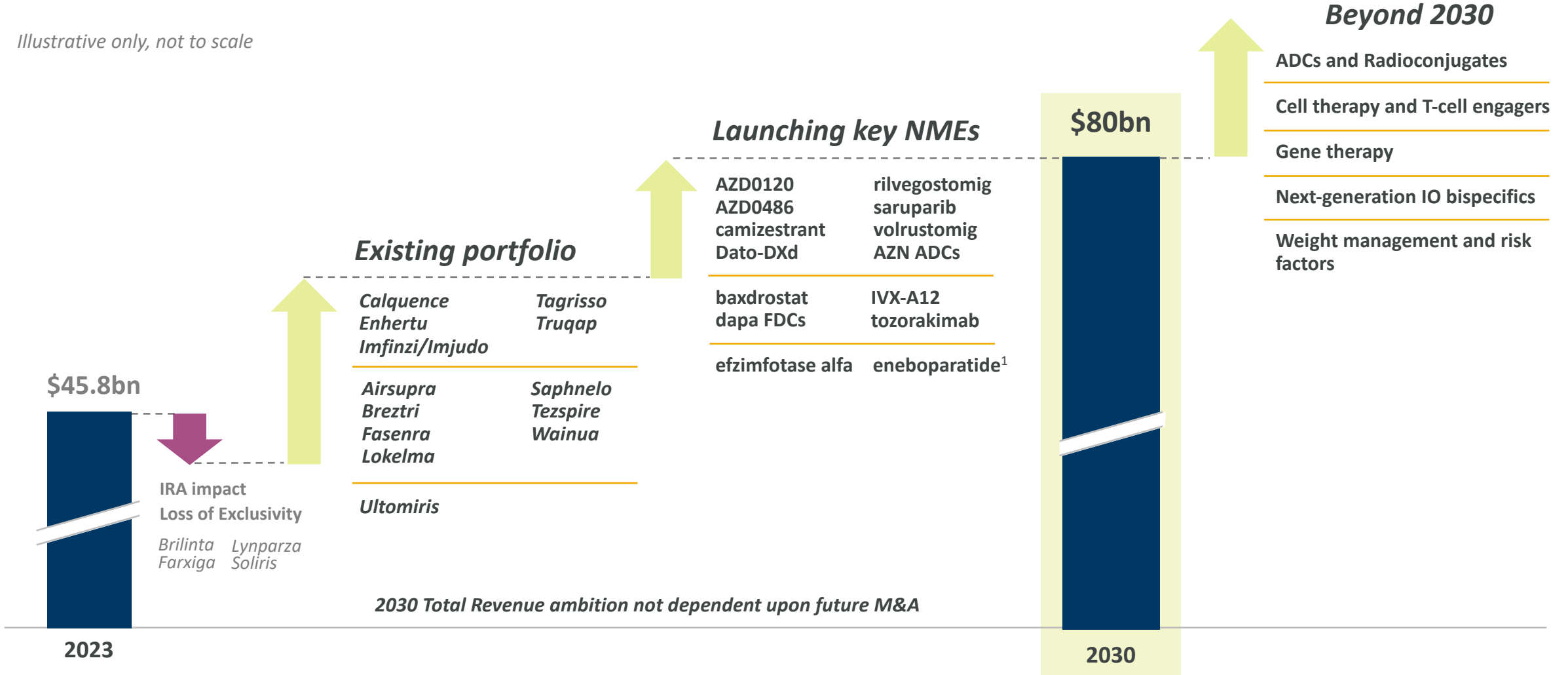
Pascal Soriot

CHIEF EXECUTIVE OFFICER

Ambition – \$80bn Total Revenue by 2030 & sustained 2030+ growth

Working on “today, tomorrow and the day after”

Illustrative only, not to scale



Note: Ambition to achieve \$80bn in Total Revenue by 2030 is risk-adjusted, based on latest long-range plan – see slide 3 for details.

Medicines and assets listed reflect key contributors to 2030 Total Revenue ambition; however, this list is not exhaustive. Medicines and assets listed in alphabetical order and sorted by therapy area.

1. Amolyt Pharma acquisition remains subject to customary external clearances; all clinical development plans mentioned herein subject to deal closure.

Collaboration partners: Daiichi Sankyo (Enhertu, Dato-DXd), Amgen (Tezspire), Ionis (Wainua), Compugen (rilvegostomig), Merck & Co., Inc. (Lynparza).

Investing in disruptive categories to drive 2030+ growth

Weight management and risk factors	ADCs and Radioconjugates	Next-gen IO bispecifics	Cell therapy and T-cell engagers	Gene therapy and gene editing
<p>Establish and lead in new weight management paradigm</p>	<p>Replace systemic chemotherapy and radiotherapy</p>	<p>Replace existing PD-1/PD-L1 inhibitors</p>	<p>Develop scalable cell therapies and T-cell engagers across therapy areas</p>	<p>Make cure possible for a range of rare diseases</p>
<p>oGLP-1 mono and FDCs</p> <hr/> <p>Long-acting amylin</p> <hr/> <p>GLP-1/glucagon</p>	<p>Six clinical-stage ADCs</p> <hr/> <p>FPI-2265¹</p>	<p>volrustomig (PD-1/CTLA-4)</p> <hr/> <p>rilvegostomig (PD-1/TIGIT)</p>	<p>AZD0120 (BCMA/CD19)</p> <hr/> <p>Solid tumour cells</p> <hr/> <p>AZD0486 (CD19/CD3 TCE)</p>	<p>sAAVv and AAV capsid</p> <hr/> <p>TALEN technology</p>

1. Fusion Pharmaceuticals acquisition remains subject to customary external clearances; all clinical development plans mentioned herein subject to deal closure.

7 Collaboration partners: Compugen (rilvegostomig).

AstraZeneca – six years in a row of plenary presentations



ASCO 2024 | DESTINY-Breast06 granted special oral LBA session

Significant news flow across key medicines through 2025

2024

Imfinzi ✓
ADRIATIC
ASCO plenary (June 2024)

Tagrisso ✓
LAURA
ASCO plenary (June'24)

Enhertu ✓
DESTINY-Breast06
ASCO LBA (June 2024)

Calquence ✓
ECHO
MCL updated data cut

Dato-DXd ✓
TROPION-Lung01
OS data, regulatory decision¹

Dato-DXd
TROPION-Breast02
1L TNBC data readout

Truqap
CAPitello-281
dPTEN prostate
data readout

Imfinzi
BR.31
Adjuvant NSCLC
data readout

volrustomig + CTx
AZ FIH Phase I/II
updated data cut

rilvegostomig
Phase I/II ARTEMIDE-01
1L PD-L1>1% NSCLC update

rilvegostomig + CTX
Phase I/II GEMINI
1L gastric data cut

2025

Dato-DXd
TROPION-Breast01
regulatory decision

Dato-DXd + Imfinzi
AVANZAR
1L NSCLC data readout

Imfinzi + ceralasertib
LATIFY
2L NSCLC data readout

Imfinzi
MATTERHORN
early-stage gastric
data readout

Imfinzi
EMERALD-2
adj. HCC
data readout (≥2025)

Imfinzi
EMERALD-3
locoregional HCC
data readout (>2025)

Enhertu
DESTINY-Breast09
1L HER2+ breast
data readout

Enhertu
DESTINY-Breast11
early-stage HER2+
breast data readout

camizestrant
SERENA-4/6
1L HR+ HER2- breast
data readout (>2025)

Enhertu
DESTINY-Lung04
1L HER2m NSCLC
data readout

Calquence
AMPLIFY
1L CLL data readout

Tagrisso + savolitinib
SAFFRON
2L MET+ EGFRm
data readout

Multiple Phase III trial initiations planned with IO bispecifics and ADC combinations over next 12-18 months

1. Regulatory decision anticipated H2 2024.

Collaboration partners: Daiichi Sankyo (*Enhertu*, *Dato-DXd*), CompuGen (*rilvegostomig*).

AstraZeneca presence at ASCO 2024

Susan Galbraith

EVP, HEAD OF ONCOLOGY R&D

119 abstracts accepted
73 poster presentations
16 oral presentations
2 Plenary presentations
1 special LBA session

Key data highlights

- LAURA (Plenary LBA4)
- ADRIATIC (Plenary LBA5)
- DESTINY-Breast06 (LBA1000)
- AZD7003¹ Phase I (4019)
- TROPION-Lung02 additional follow-up (8617)
- I-SPY 2.2 (LBA501 and LBA509)
- TROPION-Breast01 PROs (1006)

Key ASCO 2024 data furthers our ambition to become the leading Oncology company by 2030

Strengthening tumour area leadership

BREAST • LUNG

LAURA

Tagrisso Stg III u/r *EGFR*m NSCLC

DESTINY-Breast06

Enhertu 2L HR+, HER2-low and -ultralow

ADRIATIC

Imfinzi post-CRT LS-SCLC

TROPION-Breast01

Dato-DXd in HR+ HER2- adv. BC

Powerful combinations

ADC + IO

I-SPY 2

Dato-DXd + *Imfinzi* neoadjuvant TNBC

TROPION-Lung02

Dato-DXd + IO ± CTx

Advancing medicines in disruptive categories

CAR-T • ADCs

AZD7003¹ | armoured GPC3 CAR-T
FIH in late line liver cancer

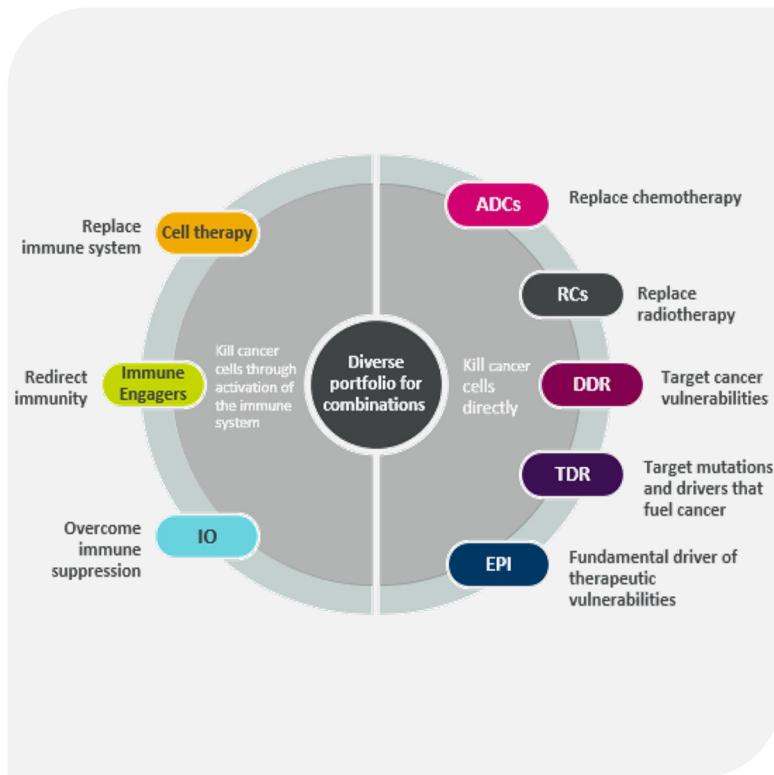
AZD0901 | CLDN18.2
Pre-treated CLDN18.2+ gastric/GEJ

1. Also known as C-CAR031.

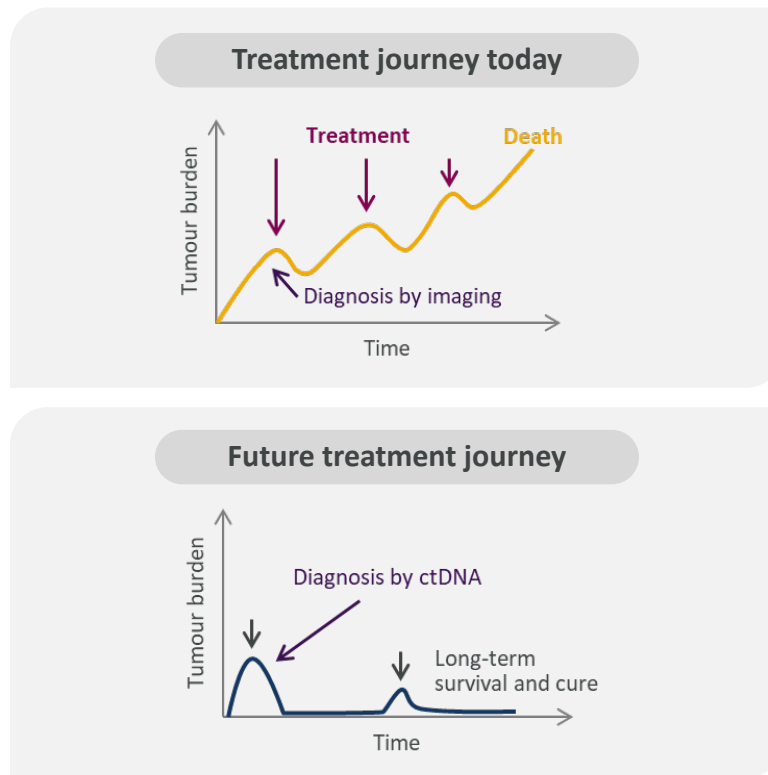
Collaboration partners: Daiichi Sankyo (*Enhertu*, Dato-DXd).

Our R&D strategy to transform patient outcomes

Attack cancer from multiple angles



Treat earlier and smarter



Lead with innovative technology

Data and AI in clinical trials

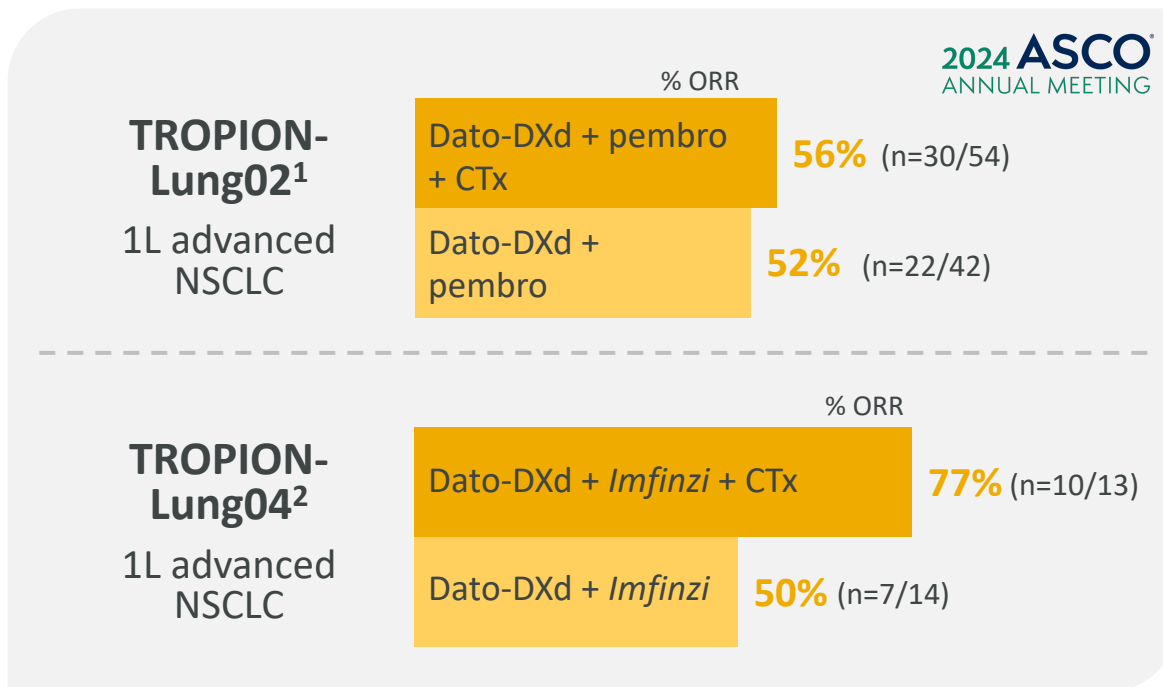
HER2 Accelerating computational pathology

TROP2

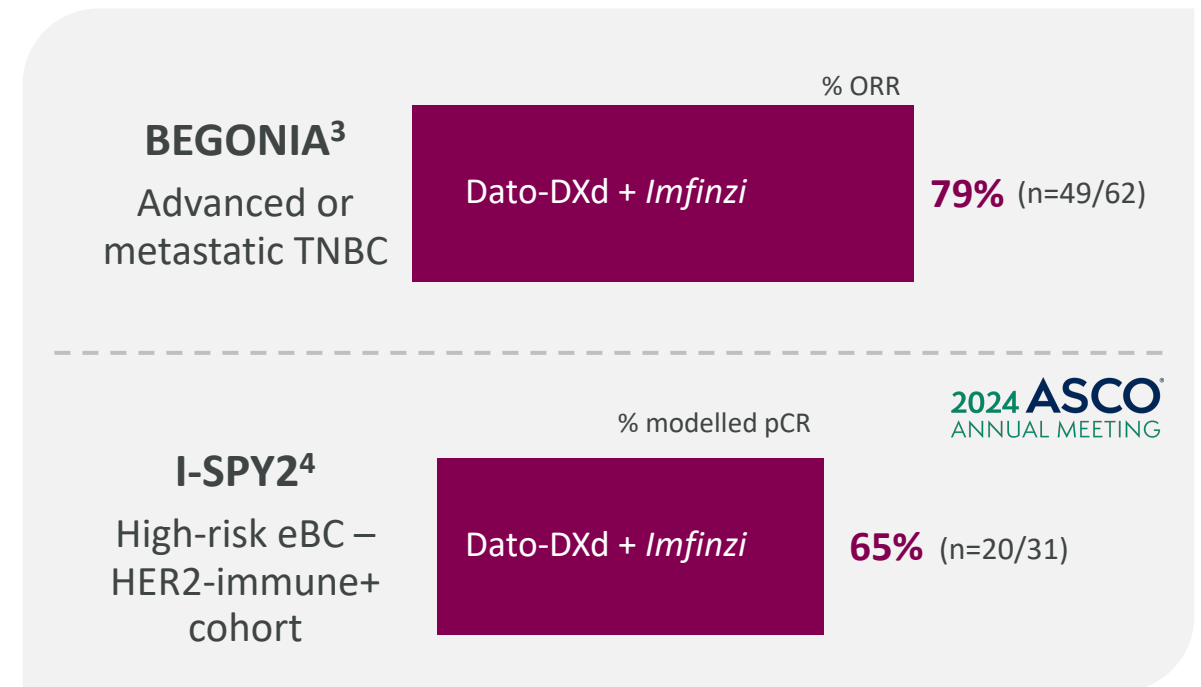
Improving patient outcomes through digital health

Phase I/II efficacy data reinforce Dato-DXd + IO potential in Phase III combination trials

Strong efficacy demonstrated across doublet and triplet combinations in NSCLC



Strong and consistent efficacy observed in breast cancer

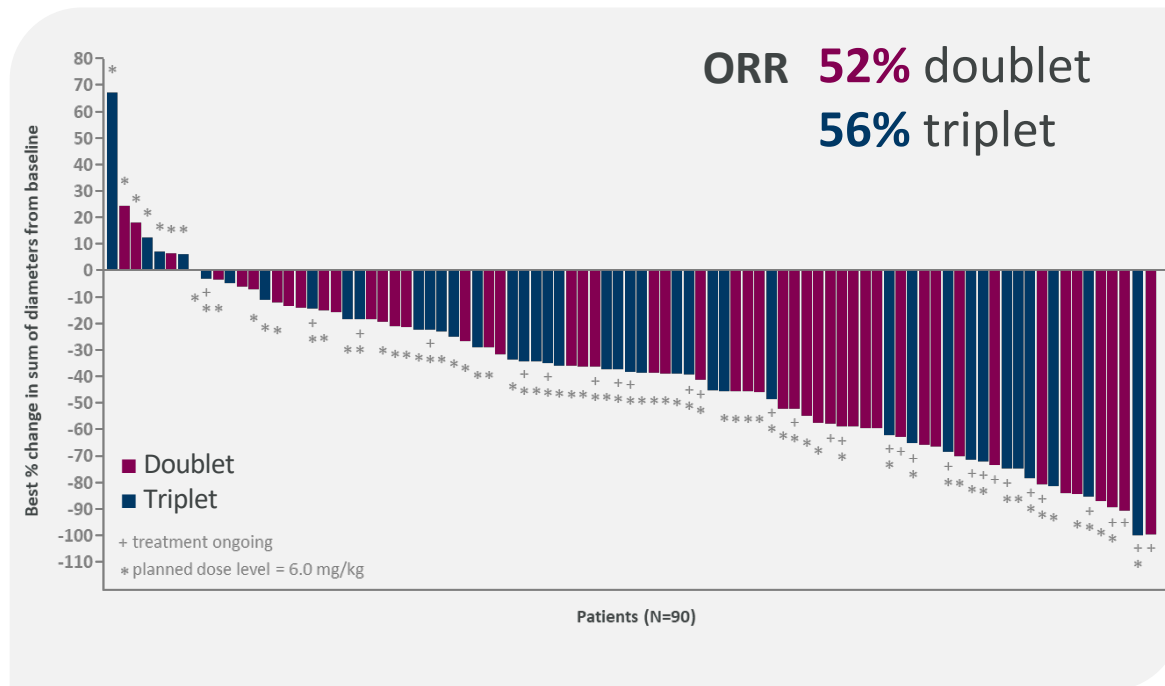


Data for neoadjuvant/adjuvant Dato-DXd + Imfinzi + platinum from NeoCOAST2.0 to be presented at upcoming 2024 congress

1. Levy BP et al. Abstract 8617 presented at American Society of Clinical Oncology 2024. 2. Papadopoulos KP et al. Abstract OA05.06 presented at World Conference on Lung Cancer 2023. 3. Schmid P et al. Abstract 379MO presented at European Society of Medical Oncology 2023. 4. Shatsky RA et al. Abstract LBA501 presented at American Society of Clinical Oncology 2024.
Collaboration partner: Daiichi Sankyo (Dato-DXd).

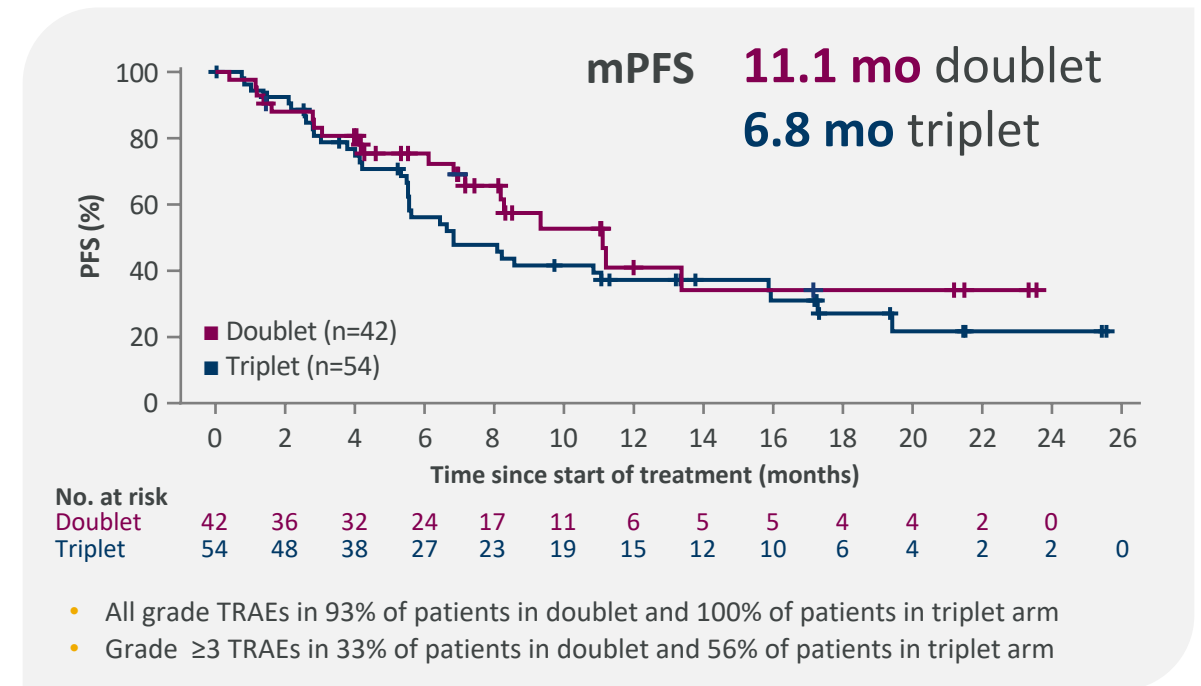
TROPION-Lung02 – Updated data support ongoing Phase III trials of Dato-DXd + IO ± CTx in 1L setting

Durable clinical response for both doublet and triplet



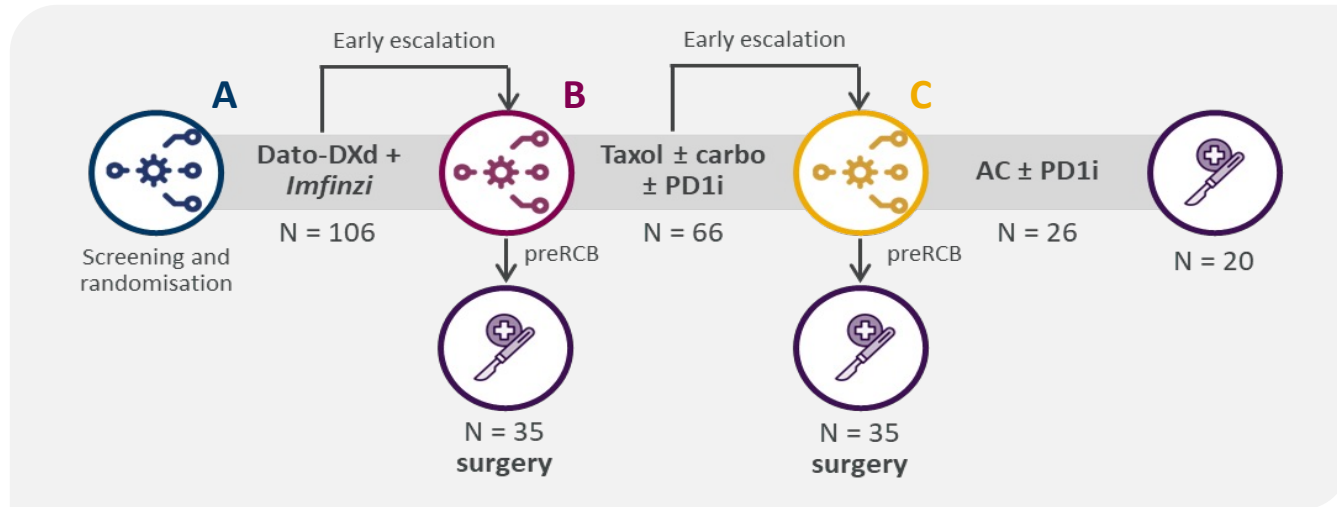
69% patients with non-squamous histology

Encouraging PFS for doublet and triplet independent of PD-L1 status



43% of patients in the doublet and 30% in the triplet arm had PD-L1 expression <1%

I-SPY 2 – First IO + ADC combination showing strong pCR rates in HR+ and HR- patients with breast cancer



Efficacy of Block A only (4 cycles of Dato-DXd + Imfinzi)

Subtype ¹	N	pCR	Non-pCR	Modeled Rate (95% CI)	Threshold	P (>Thr)
HER2-Immune+	47	20	11	65% (47%-83%)	40%	0.99

- Phase II trial in neoadjuvant breast cancer
- Strong efficacy in neoadjuvant, Immune+ breast cancer with only 4 cycles of Dato-DXd + Imfinzi
- ~30% patients went to surgery at end of Block A for Dato-DXd ± Imfinzi cohorts, sparing subsequent chemo
- No new safety signals were observed
- Together with BEGONIA, supportive of ongoing Phase III Dato-DXd + Imfinzi trials
 - TROPION-Breast04, -03, -05

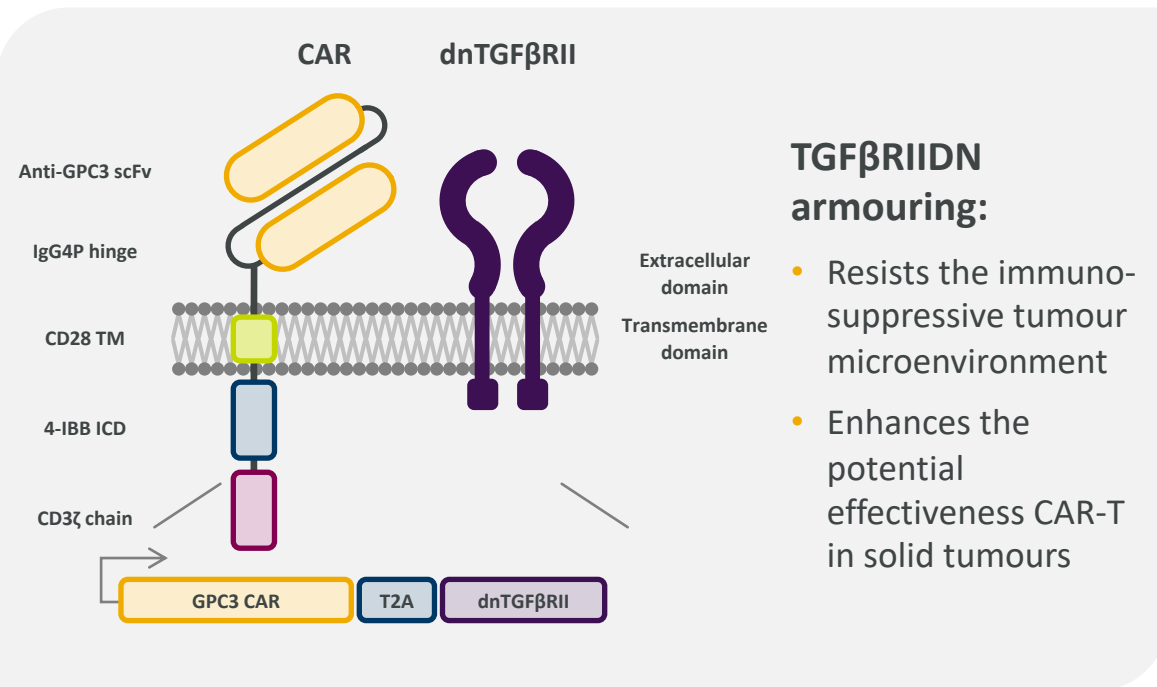
Reinforces potential to replace chemotherapy with Dato-DXd + IO, with reduced toxicity

AZD7003 – GPC3-specific TGFβRIIDN armoured CAR-T

First clinical data in liver cancer, highlights potential of CAR-T in solid tumours

Differentiated vs other GPC3 CAR-Ts

Only clinical-stage CAR-T armoured with TGFβRIIDN



FIH data from Phase I, open-label, dose escalation and expansion study conducted in China

GPC3-positive HCC



Heavily pre-treated patients

Relapsed/progressed/intolerant to HCC systemic therapies (≥1 line)

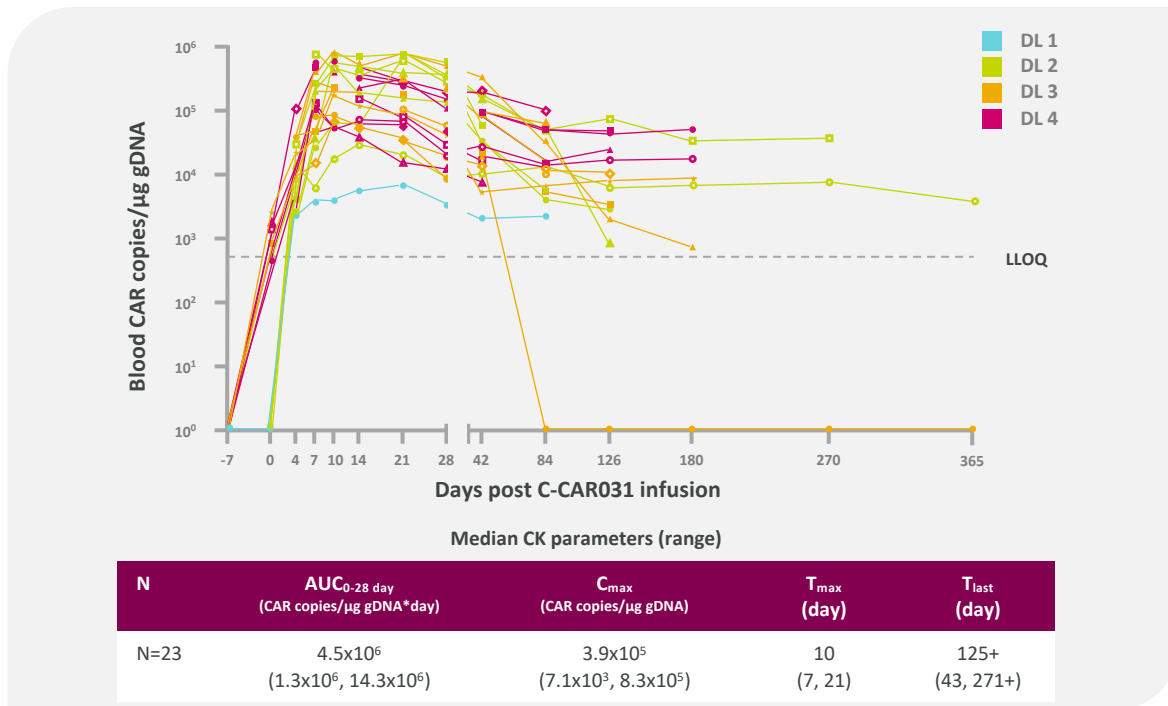
Summary of baseline characteristics	N = 24
ECOG PS, n (%)	
0	2 (8.3)
1	22 (91.7)
Median SLD (mm) ¹ , (range)	73.8 (12.9, 179.4)
Median number of prior lines of therapies, (range)	3.5 (1,6)
≥ 3, n (%)	18 (75)
Received both IO and VEGF(R) inhibitors ²	23 (95.8)

Part of AstraZeneca's innovative in-house CAR-T programme for solid tumours
AZD7003 | GPC3 | **AZD0754** | STEAP2 | **AZD4622** | Claudin 18.2

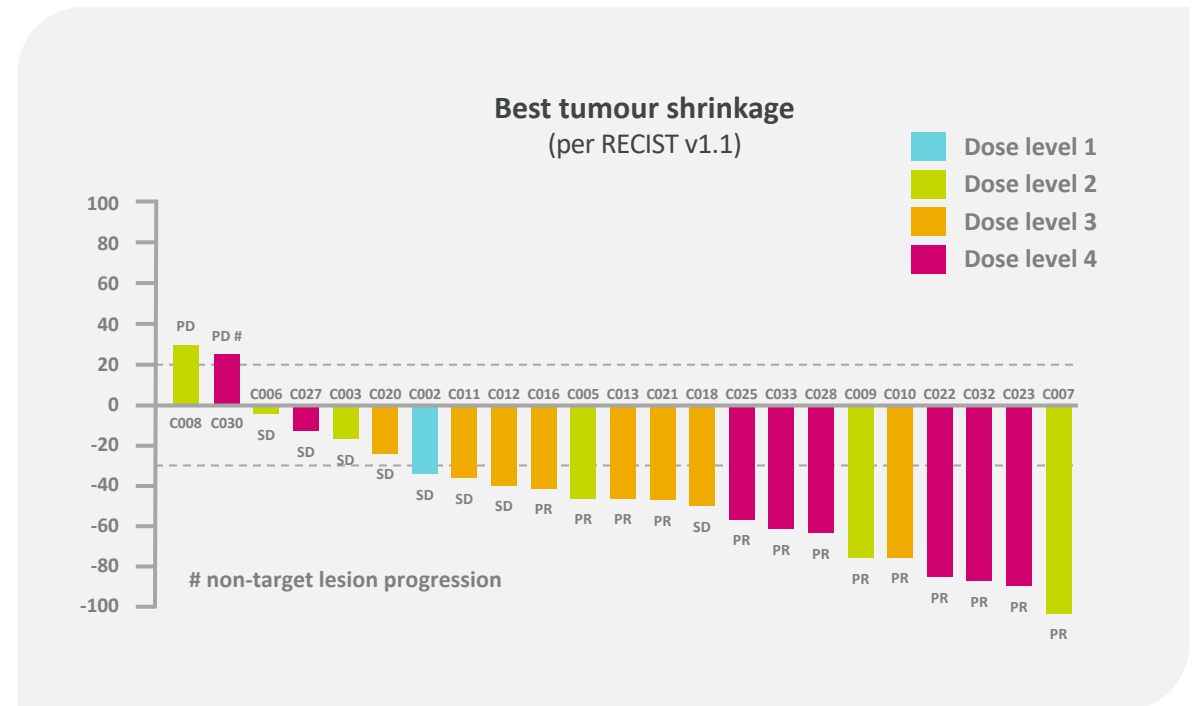
1. Per RECIST 1.1. 2. IO defined as immune checkpoint inhibitors and VEGF(R) inhibitors defined as anti-angiogenesis agents such as Bevacizumab (or its biosimilars), Tyrosine kinase inhibitors such as sorafenib, Lenvatinib, apatinib and etc. Zhang Q et al. Abstract 4019 presented at American Society of Clinical Oncology 2024.

AZD7003 – Encouraging early efficacy in heavily pre-treated HCC patients with ORR 56.6% across dose levels

Robust cellular expansion and persistence in patients



Encouraging tumour responses with mDoR of 7.36 months after median follow-up of 9.03 months



Well tolerated across all four dose levels – no incidence of ICANS and only one case of Grade 3 CRS in dose level 4



Clinical impressions

Lung cancer

Physician fireside



Leora Horn

Global Clinical Head for Lung Cancer and Lung Cancer Strategy, AstraZeneca



Charu Aggarwal

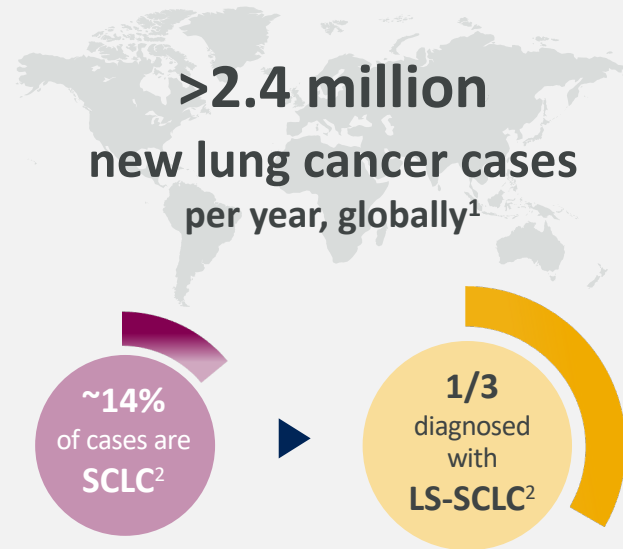
Thoracic Medical Oncologist, University of Pennsylvania School of Medicine

ADRIATIC

Randomised, double-blind, placebo-controlled, multi-centre global Phase III trial evaluating *Imfinzi* monotherapy and *Imfinzi* plus *Imjudo* vs placebo in limited stage SCLC

ADRIATIC Phase III first potential major advancement in systemic treatment for LS-SCLC for several decades

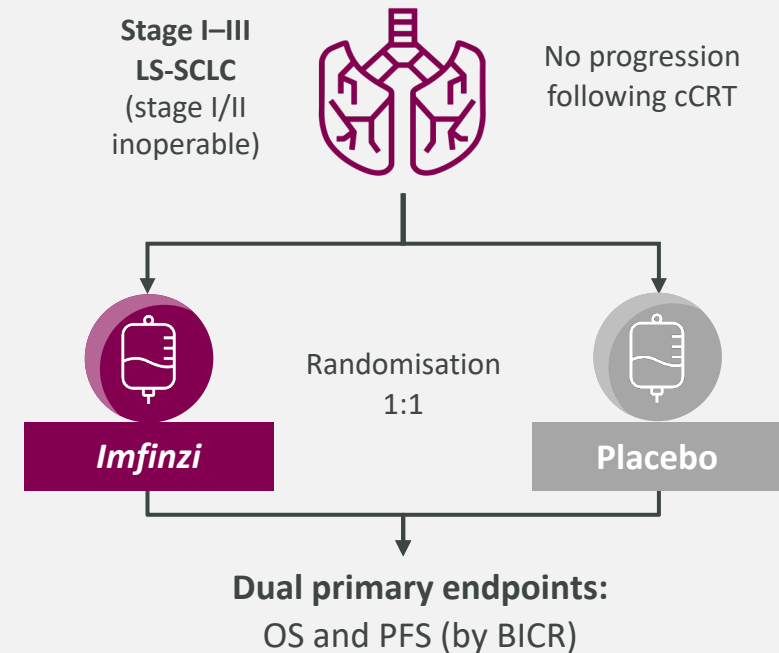
High unmet need in SCLC



SoC is cCRT, followed by PCI if indicated, then observation³

Majority experience disease relapse within 2 years^{4,5}

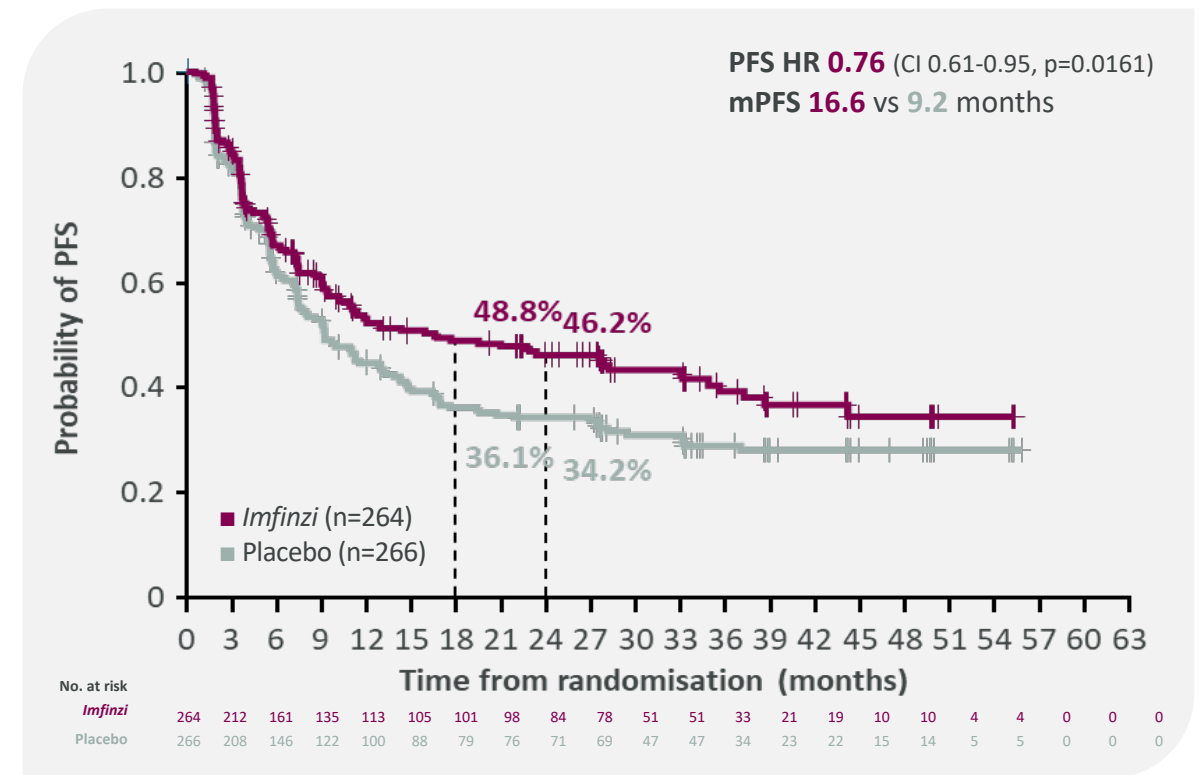
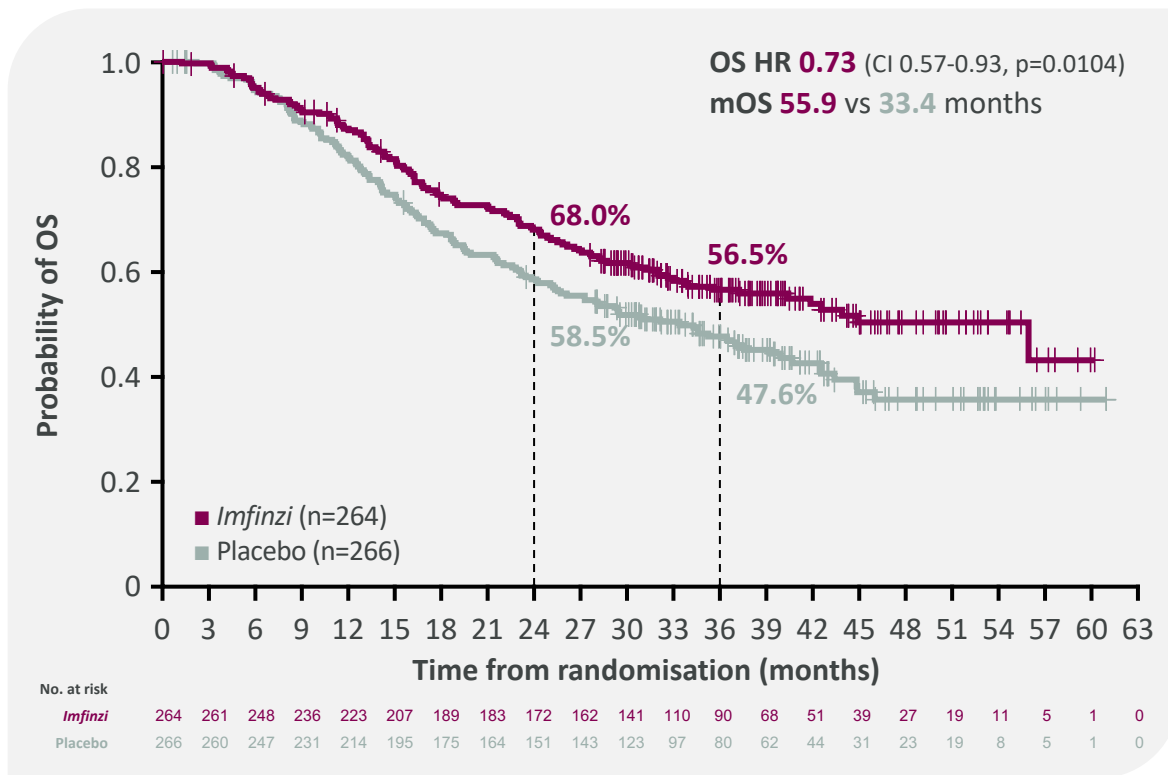
ADRIATIC Phase III addresses limited stage-SCLC



Imfinzi first and only immunotherapy to show survival benefit in limited-stage SCLC in global Phase III trial

~57% of patients treated with *Imfinzi* alive at three years

~46% of patients treated with *Imfinzi* had not experienced disease progression at two years



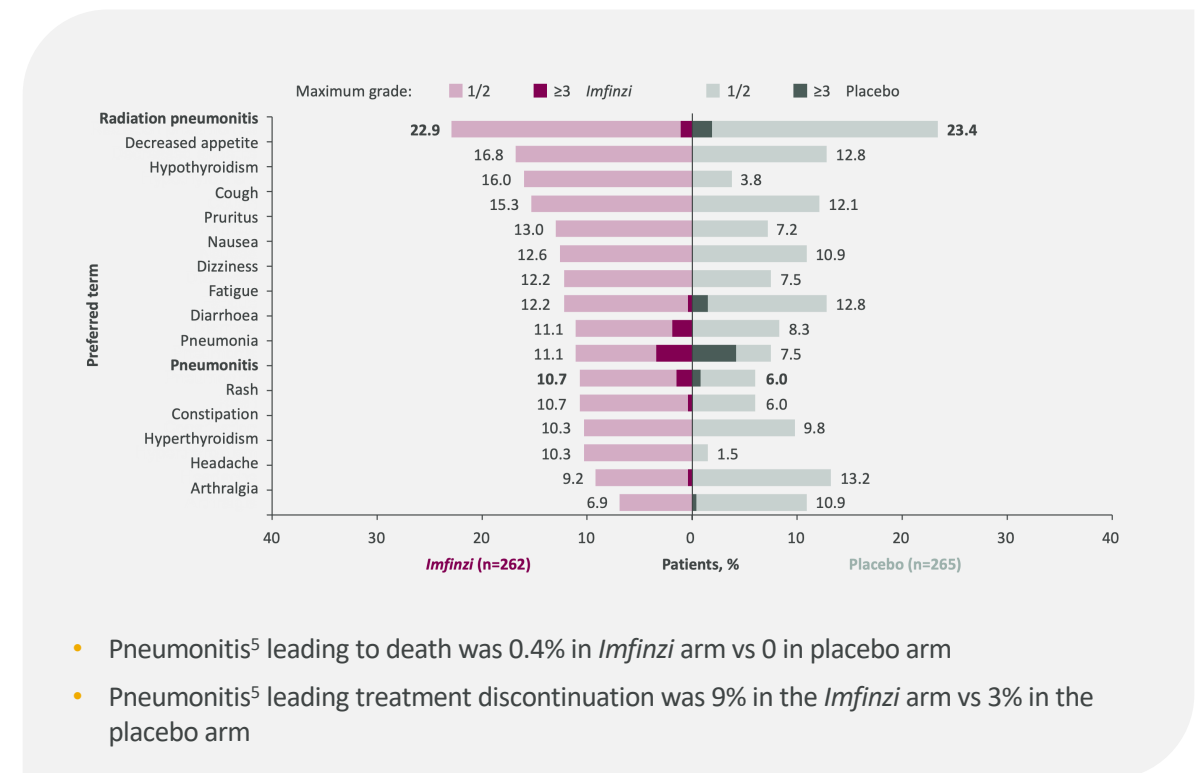
OS was analysed using a stratified log-rank test adjusted for receipt of PCI (yes vs no). The significance level for testing OS at this interim analysis was 0.01679 (2-sided) at the overall 4.5% level, allowing for strong alpha control across interim and final analysis timepoints. PFS assessed by BICR per RECIST, v1.1. PFS was analysed using a stratified log-rank test adjusted for disease stage (stage I/II vs III) and receipt of PCI (yes vs no). The significance level for testing PFS at this interim analysis was 0.00184 (2-sided) at the 0.5% level, and 0.02805 (2-sided) at the overall 5% level. Statistical significance for PFS was achieved through the recycling MTP framework and testing at the 5% (2-sided) alpha level (adjusted for an interim and final analysis).

Safety profile for *Imfinzi* generally manageable and consistent with known profile

Similar rate of Grade ≥ 3 AEs between arms

AEs, n (%)	<i>Imfinzi</i> (n=263)	Placebo (n=265)
All grade	247 (94.3)	234 (88.3)
Grade ≥ 3	64 (24.4)	64 (24.2)
Serious	78 (29.8)	64 (24.2)
Leading to discontinuation	43 (16.4)	28 (10.6)
Leading to death	7 (2.7)	5 (1.9)
Leading to death	2 (0.8) ³	0
Treatment-related ¹ leading to death	84 (32.1)	27 (10.2)
Grade ≥ 3 immune-mediated ²	14 (5.3)	4 (1.5)

Common AEs⁴ consistent with previous trials of *Imfinzi*



1. Assessed by investigator. 2. Defined as an AE of special interest (excluding infusion related/hypersensitivity/anaphylactic reaction) that is consistent with an immune-mediated mechanism that required treatment with systemic corticosteroids, other immunosuppressants, or endocrine therapy. 3. Causes of death were encephalopathy and pneumonitis. 4. Displayed are most common AEs occurring in $\geq 10\%$ of patients in either treatment arm. 5. Includes radiation pneumonitis. Includes the preferred terms of immune-mediated lung disease, interstitial lung disease, pneumonitis, radiation fibrosis – lung, and radiation pneumonitis. Events are included irrespective of aetiology and AE management. Spigel DR et al. Abstract LBA5 presented at American Society of Clinical Oncology 2024.

LAURA

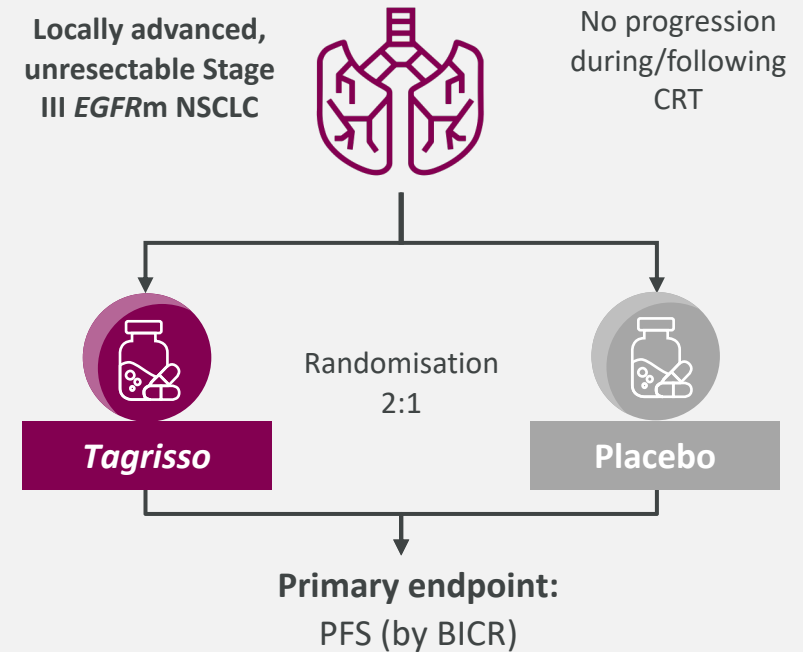
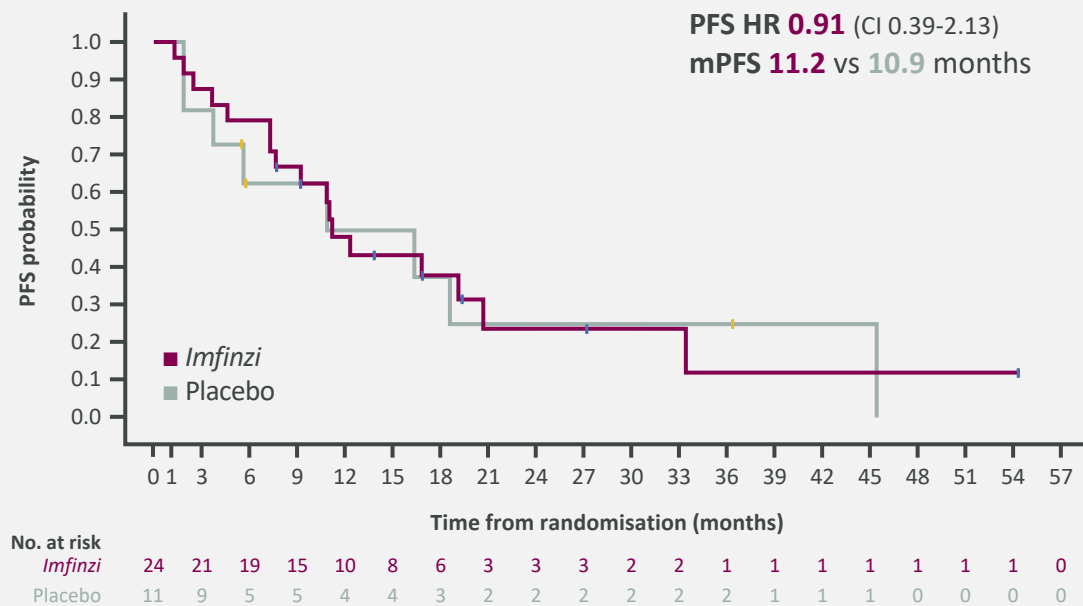
Randomised, double-blind, placebo-controlled, multi-centre, global Phase III trial evaluating *Tagrisso* vs placebo in patients with unresectable, Stage III *EGFRm* NSCLC whose disease has not progressed following definitive platinum-based CRT

LAURA Phase III opportunity to bring *Tagrisso* to population with poorer outcomes on current SoC

Unmet need in unresectable Stage III *EGFRm* NSCLC

LAURA Phase III addresses Stage III unresectable setting

PACIFIC *EGFRm* post-hoc subgroup analysis¹

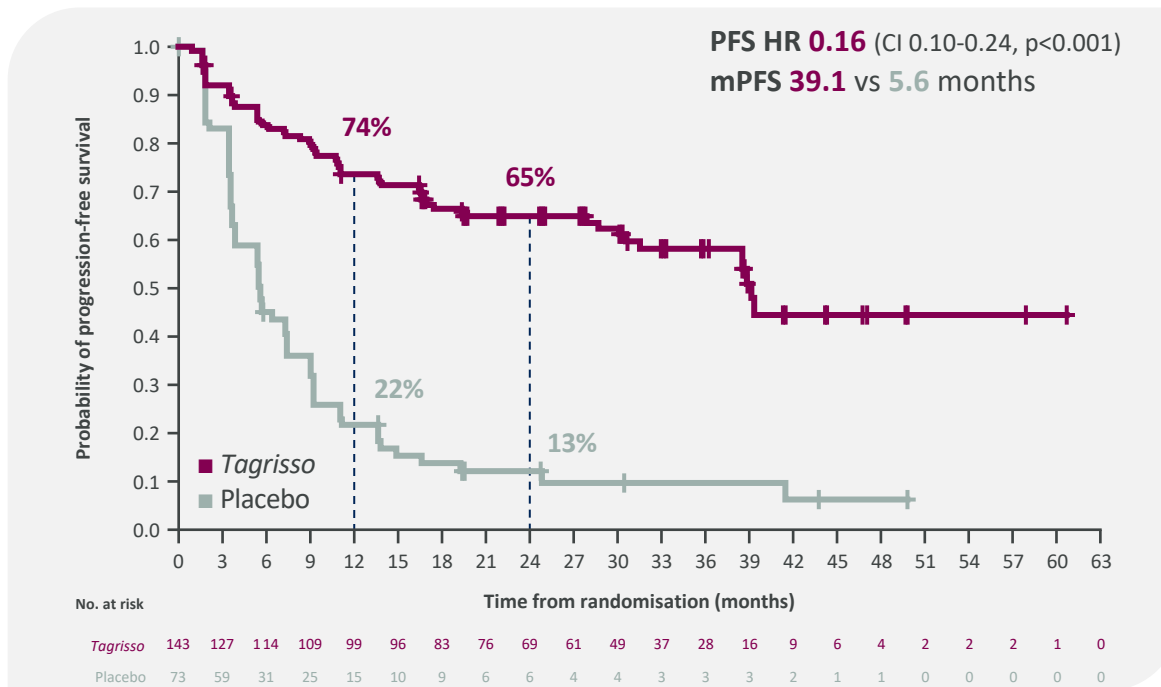


1. Naidoo et al. J Thorac Oncol 2023;18:657-663.

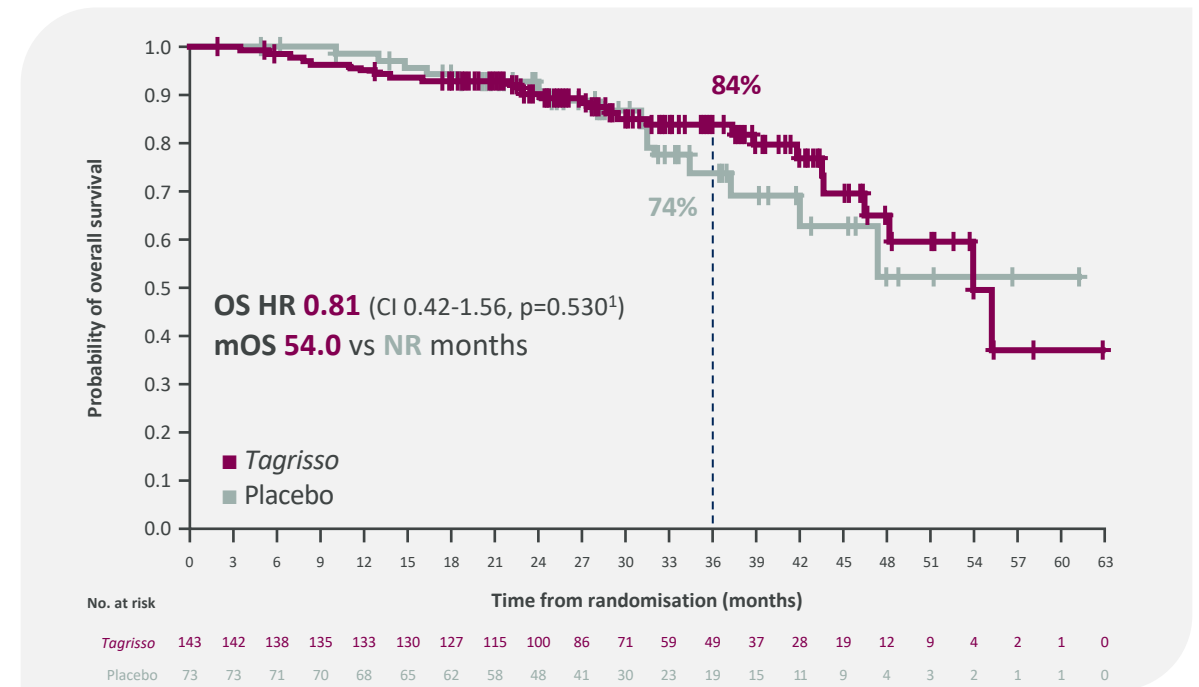
25 Ramalingam SS et al. Abstract LBA4 presented at American Society of Clinical Oncology 2024.

Tagrisso demonstrated overwhelming efficacy benefit in LAURA Phase III trial

Statistically significant and clinically meaningful improvement in PFS with *Tagrisso* vs placebo



Early trend to OS benefit with *Tagrisso* vs placebo



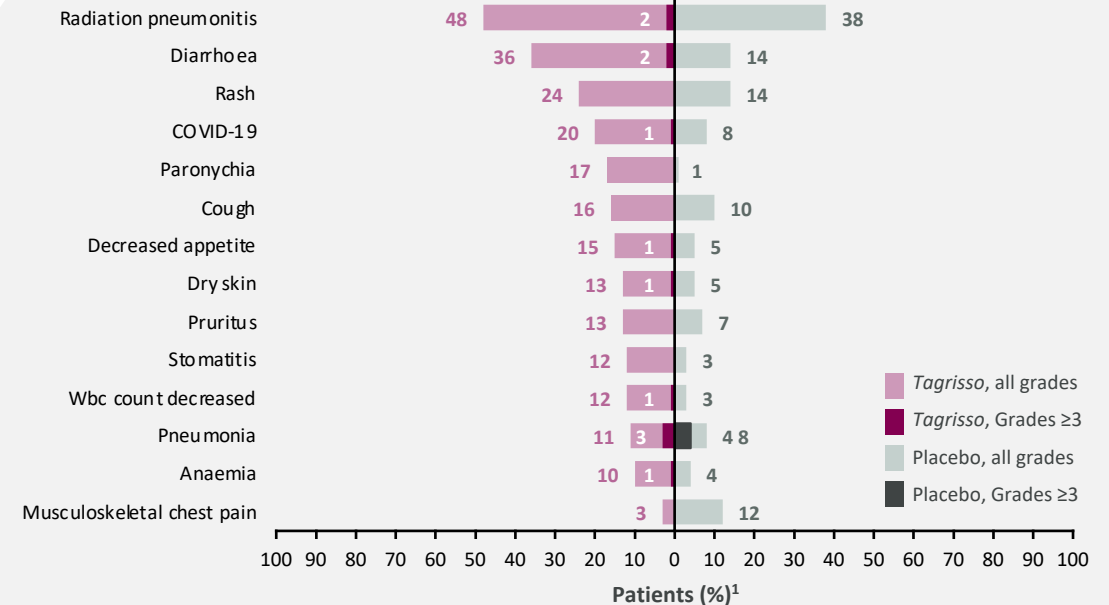
81% of patients in the placebo arm with BICR-confirmed progression crossed over to *Tagrisso*

Safety profile of *Tagrisso* post-CRT was as expected and manageable

Low discontinuation rate for *Tagrisso*

	<i>Tagrisso</i> (n=143)	Placebo (n=73)
Any AE	140 (98)	64 (88)
Any AE Grade ≥ 3	50 (35)	9 (12)
Any AE leading to death	3 (2)	2 (3)
Any serious AE	55 (38)	11 (15)
Any AE leading to discontinuation	18 (13)	4 (5)
Any AE leading to dose reduction	12 (8)	1 (1)
Any AE leading to dose interruption	80 (56)	18 (25)

Consistent AE profile with previous *Tagrisso* trials



- ILD² was reported in 11 (8%) patients in the *Tagrisso* arm. The majority were Grades 1/2; Grade 5 (n=1)

1. Median duration of exposure: *Tagrisso* 24.0 months, placebo 8.3 months. AEs with incidence of 10% or more in either treatment arm are shown. Patients with multiple events in the same category counted only once in that category. Patients with events in more than one category are counted once in each of those categories. Includes AEs with an onset date on or after the date of first dose and up to and including 28 days following the discontinuation of study treatment and before starting subsequent cancer therapy.

2. Interstitial lung disease (grouped term) was reported in 1 patient (1%) in placebo arm; AE was pneumonitis, Grade 1.

Ramalingam SS et al. Abstract LBA4 presented at American Society of Clinical Oncology 2024.



Clinical impressions

Breast cancer

Physician fireside



Ingrid Mayer

Global Clinical Strategy Head,
Breast and Gynaecological Cancers
AstraZeneca



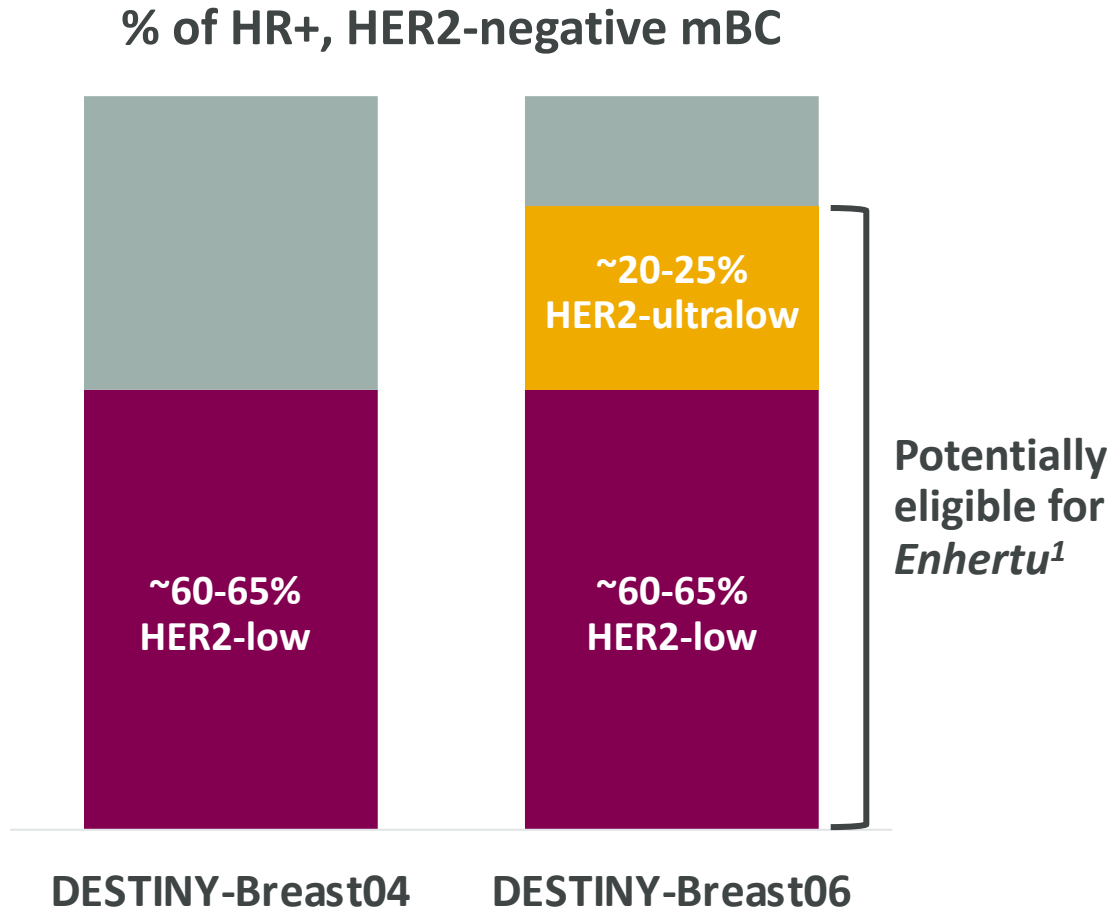
Rebecca Dent

Head of the Department of Medical
Oncology and Chief of the Breast
Medical Oncology Service at the
National Cancer Center Singapore

DESTINY-Breast06

Randomised, open-label, Phase III trial in patients with HR-positive, HER2-low or HER2-ultralow advanced or metastatic breast cancer evaluating *Enhertu* vs investigator's choice of chemotherapy

Enhertu demonstrated efficacy in HER2-low mBC in an earlier line of treatment to DESTINY-Breast04



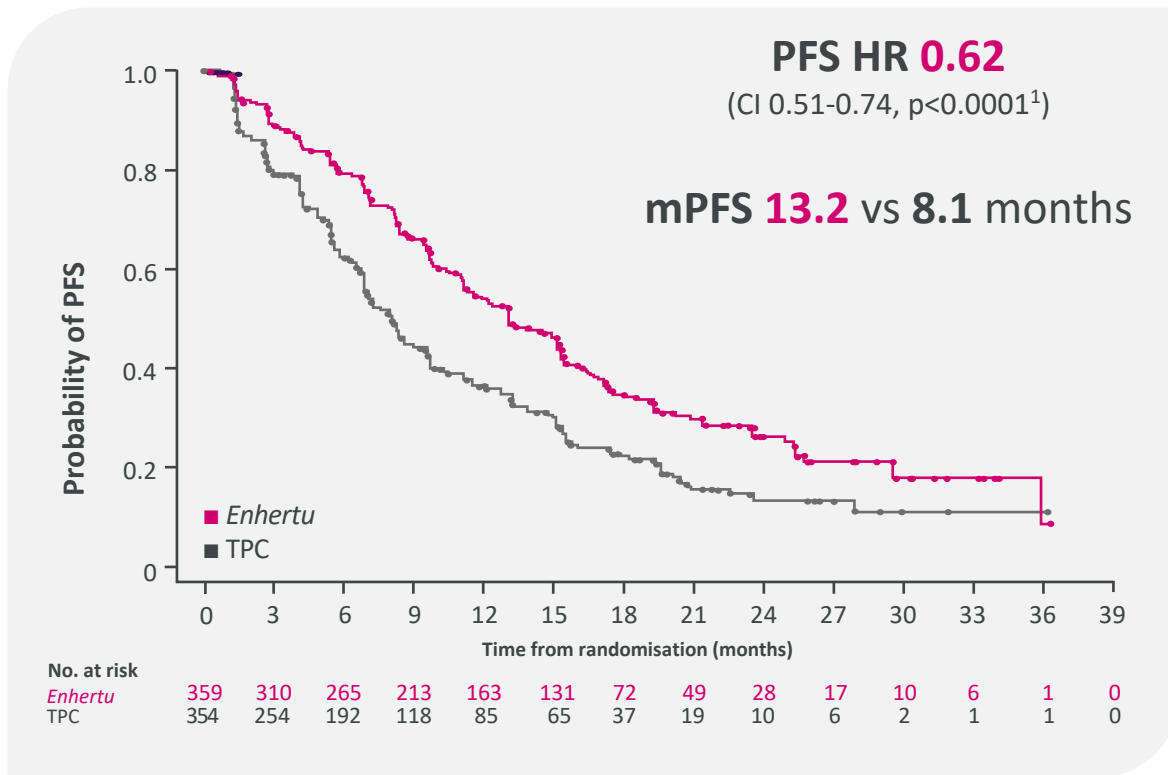
- *Enhertu* demonstrated efficacy in **HER2-low mBC** in an **earlier line of treatment** to DESTINY-Breast04
- Including HER2-ultralow, the proportion of patients who could benefit from *Enhertu* is **~85% of HR+, HER2-negative mBC** after DESTINY-Breast06

In DESTINY-Breast06, *Enhertu* demonstrated a statistically significant and clinically meaningful PFS benefit vs TPC (CTx) in HR+, HER2-low mBC after ≥ 1 endocrine-based therapy, with consistent results in HER2-ultralow mBC

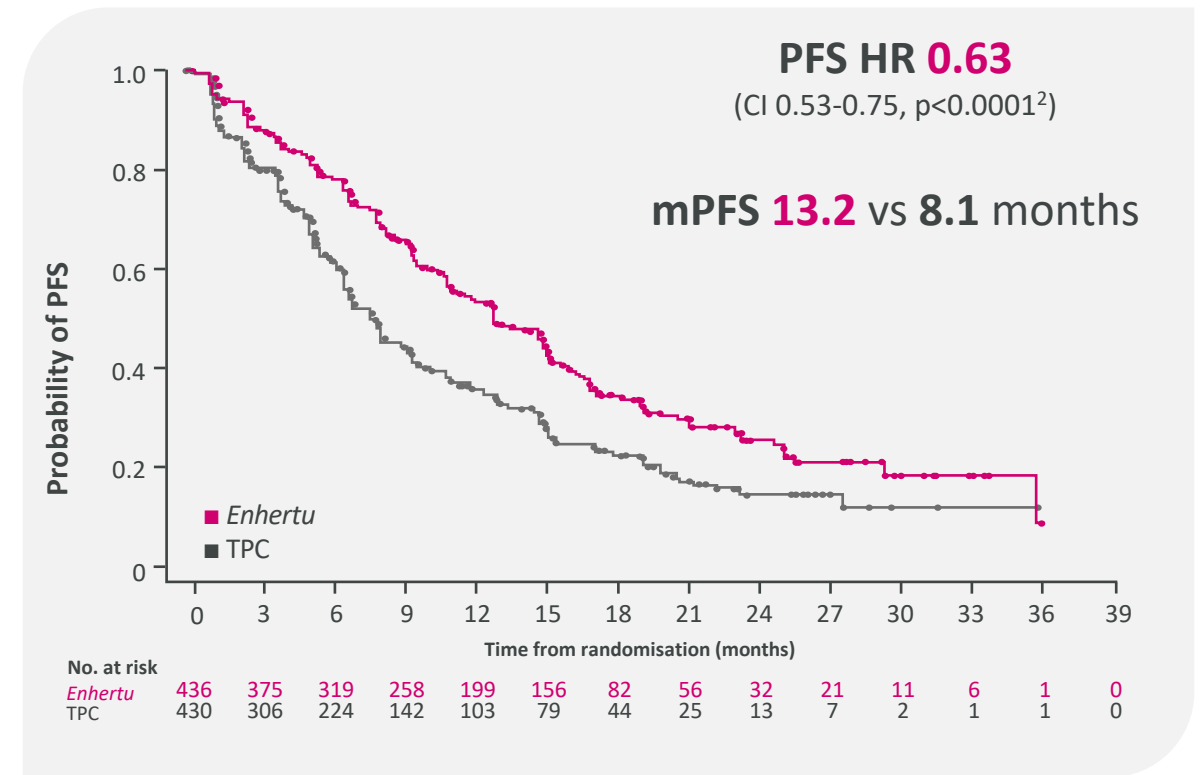
1. As a percentage of HR+, HER2-negative mBC.

Statistically significant and clinically meaningful PFS improvement with *Enhertu* vs TPC in HER2-low and ITT

HER2-low PFS



ITT PFS (HER2-low + HER2-ultralow)

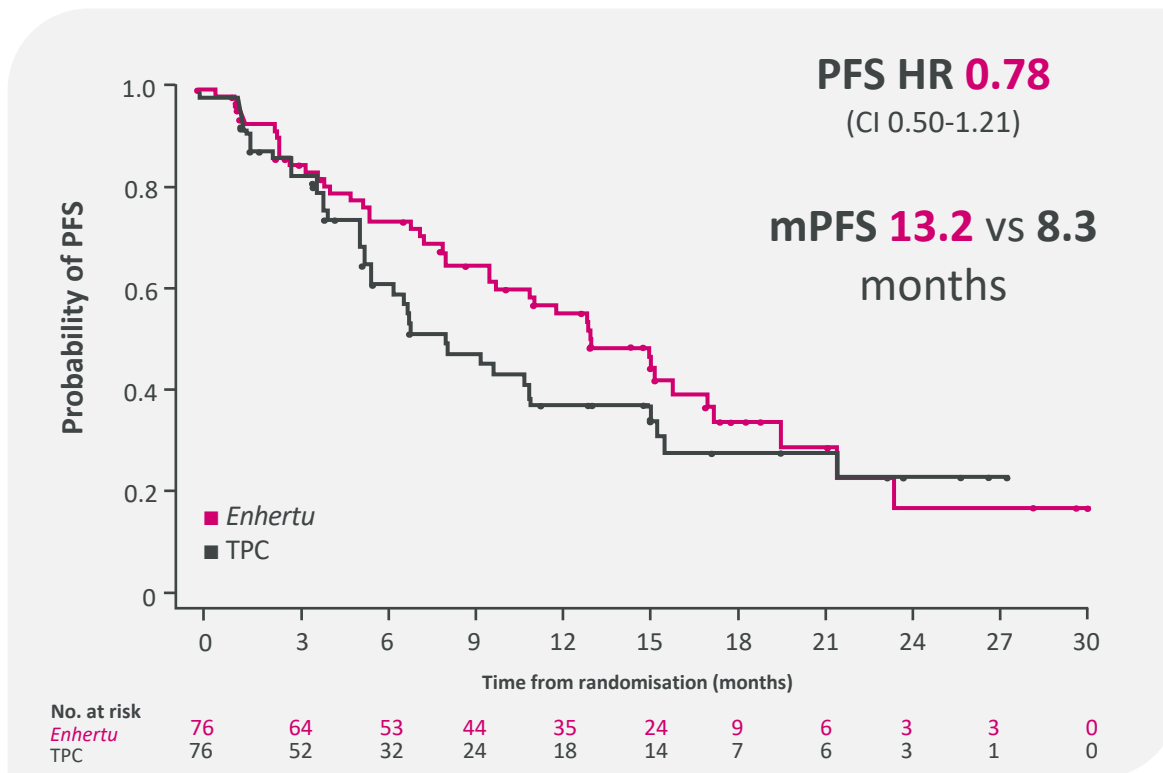


1. P-value of <0.05 required for statistical significance. 2. P-value of <0.015 required for statistical significance.

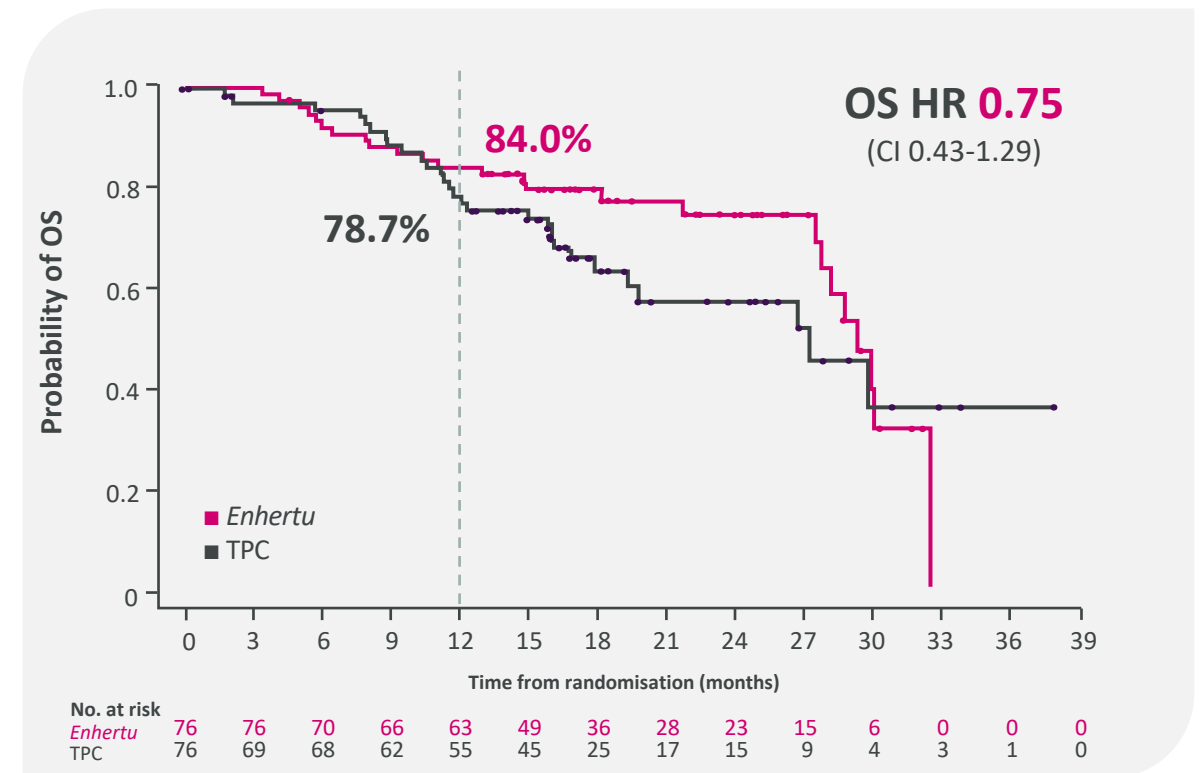
Curigliano G et al. Abstract LBA1000 presented at American Society of Clinical Oncology 2024. Collaboration partners: Daiichi Sankyo (*Enhertu*).

Clinically meaningful PFS improvement with *Enhertu* vs TPC consistent between HER2-low and -ultralow disease

HER2-ultralow PFS (BICR) (N=152)



HER2-ultralow OS¹ (N=152)



1. 34.9% maturity (of total N for population) at this first interim analysis; median duration of follow up was 16.8 months.

Enhertu safety profile consistent with known profile; details of the *Enhertu* safety and tolerability profile in DESTINY-Breast06 can be found in the Appendix of this presentation.

Curigliano G et al. Abstract LBA1000 presented at American Society of Clinical Oncology 2024. Collaboration partners: Daiichi Sankyo (*Enhertu*).

Strengthening our leadership in lung and breast

Dave Fredrickson

EVP, HEAD OF ONCOLOGY

Our commercial strategy to transform cancer outcomes

Medicines that matter

Building transformative brands



Zoladex



Leveraging scale

Tumour area leadership



Lung



Haematology



GYN/GU



Breast



Gastrointestinal

Transforming patient care

Closing the care gap



Early detection



Precision diagnostics



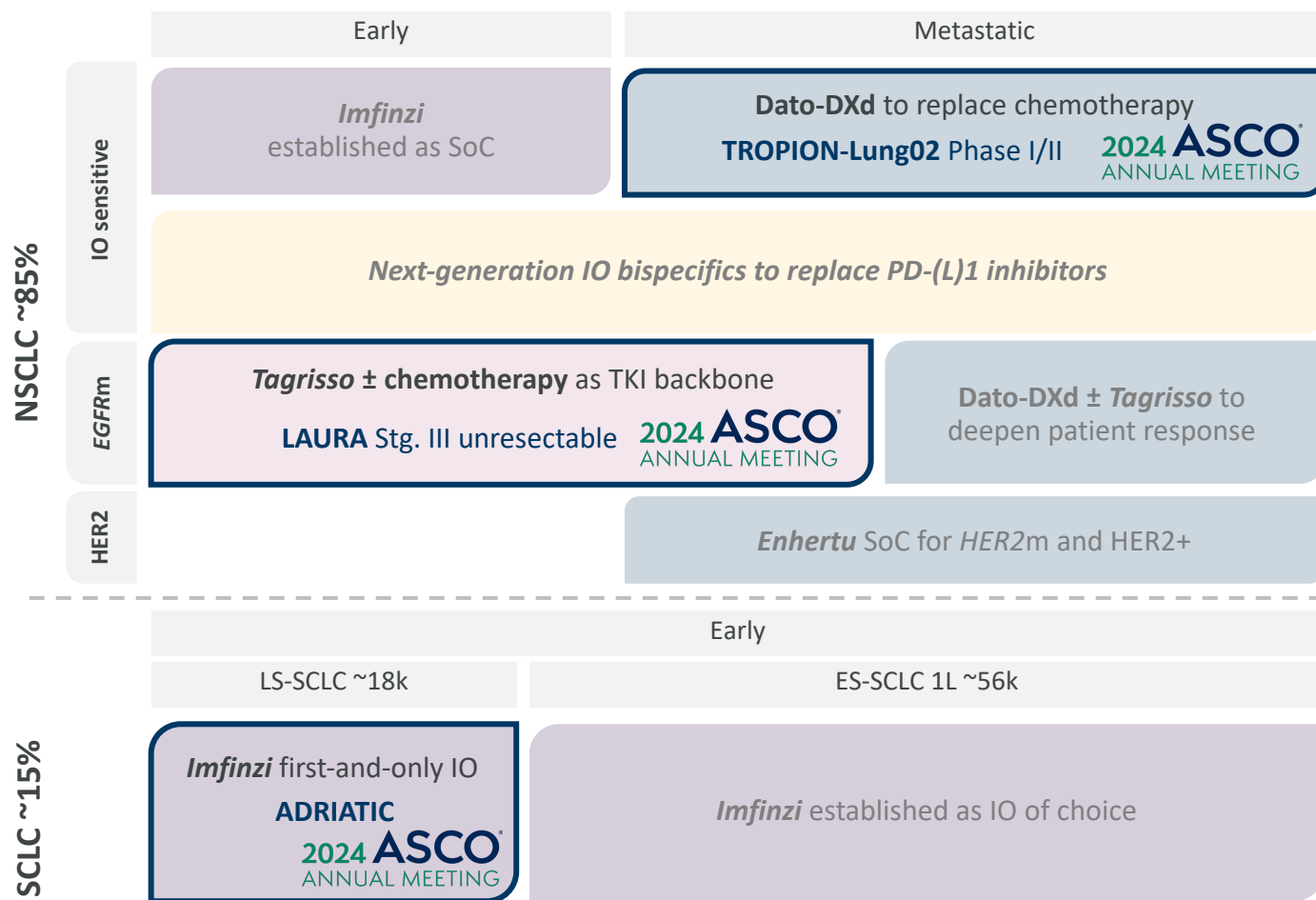
Guideline-based treatment



Patient experience

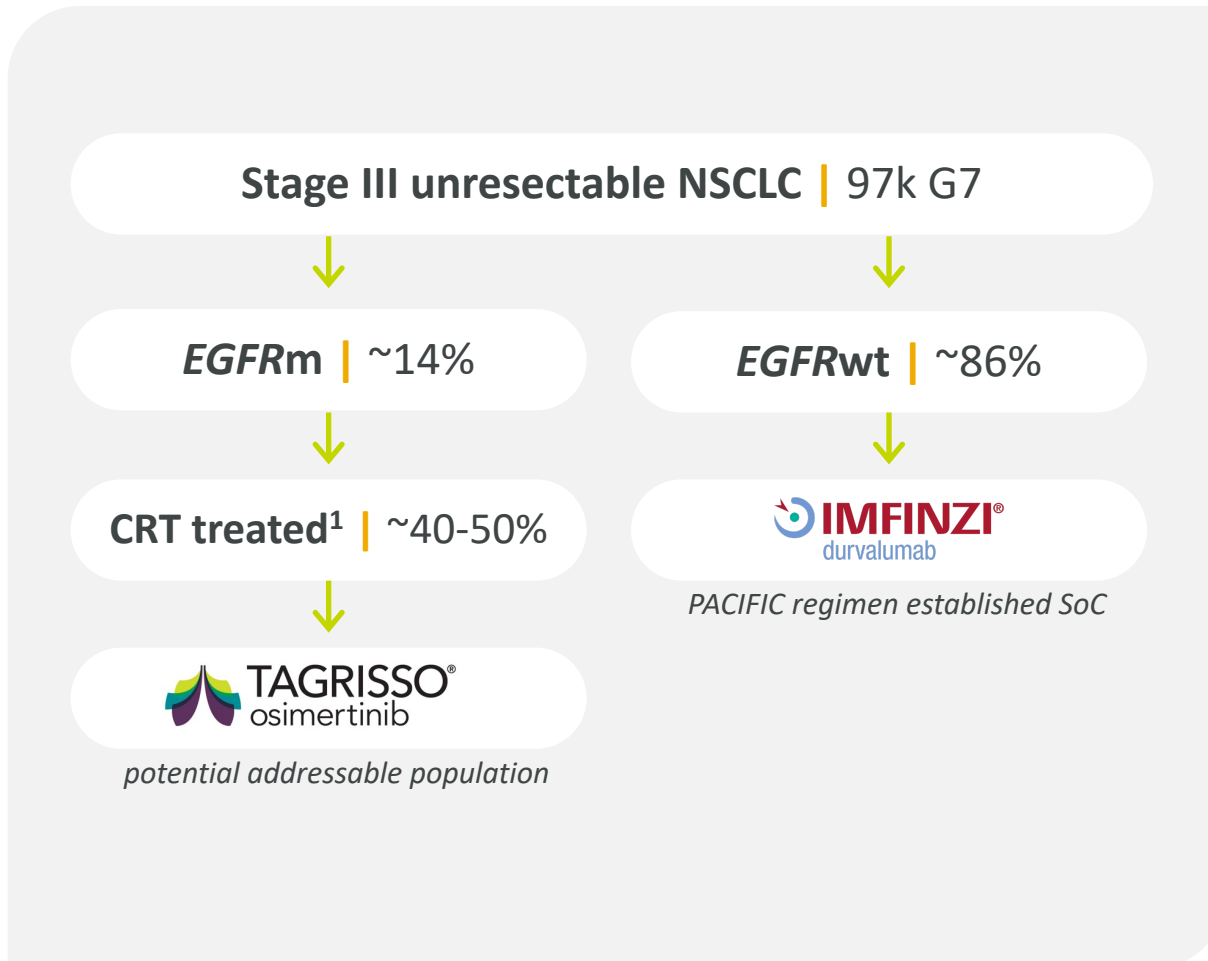
AstraZeneca @ ASCO 2024

Key data furthers ambition to redefine treatment of lung cancer



- I. Replace systemic chemotherapy with ADCs
 - **TROPION-Lung02 updated data cut reinforce confidence in 1L Phase III trials**
- II. Replace PD-(L)1 with next-generation IO bispecifics
- III. Leverage biomarker understanding to drive adoption of targeted medicines
 - **LAURA expands in early-stage and strengthens *Tagrisso* as backbone TKI**
- IV. Establish *Imfinzi* as IO of choice in SCLC
 - **ADRIATIC first innovation in >3 decades, establishes IO post-CRT**

LAURA – *Tagrisso* expanding presence in early-stage, potential SoC Stg. III unresectable EGFRm NSCLC



- **Significant unmet need in *EGFRm* patients**
 - CRT alone has increased risk of distant recurrence
 - IO post-CRT limited additional benefit in *EGFRm*
- **Clear path to unlock value and drive new SoC**
 - Maximise *EGFRm* testing rates at diagnosis
 - Drive engagement and LAURA adoption across multi-disciplinary teams
 - Reinforce treatment to progression, maximise patient adherence

LAURA represents potential blockbuster opportunity

ADRIATIC – *Imfinzi* first-and-only IO in LS-SCLC and first novel innovation in over three decades



cCRT is SoC, survival outcomes remain poor

50% thoracic recurrence at 2 years³

19% CNS recurrence at 2 years³

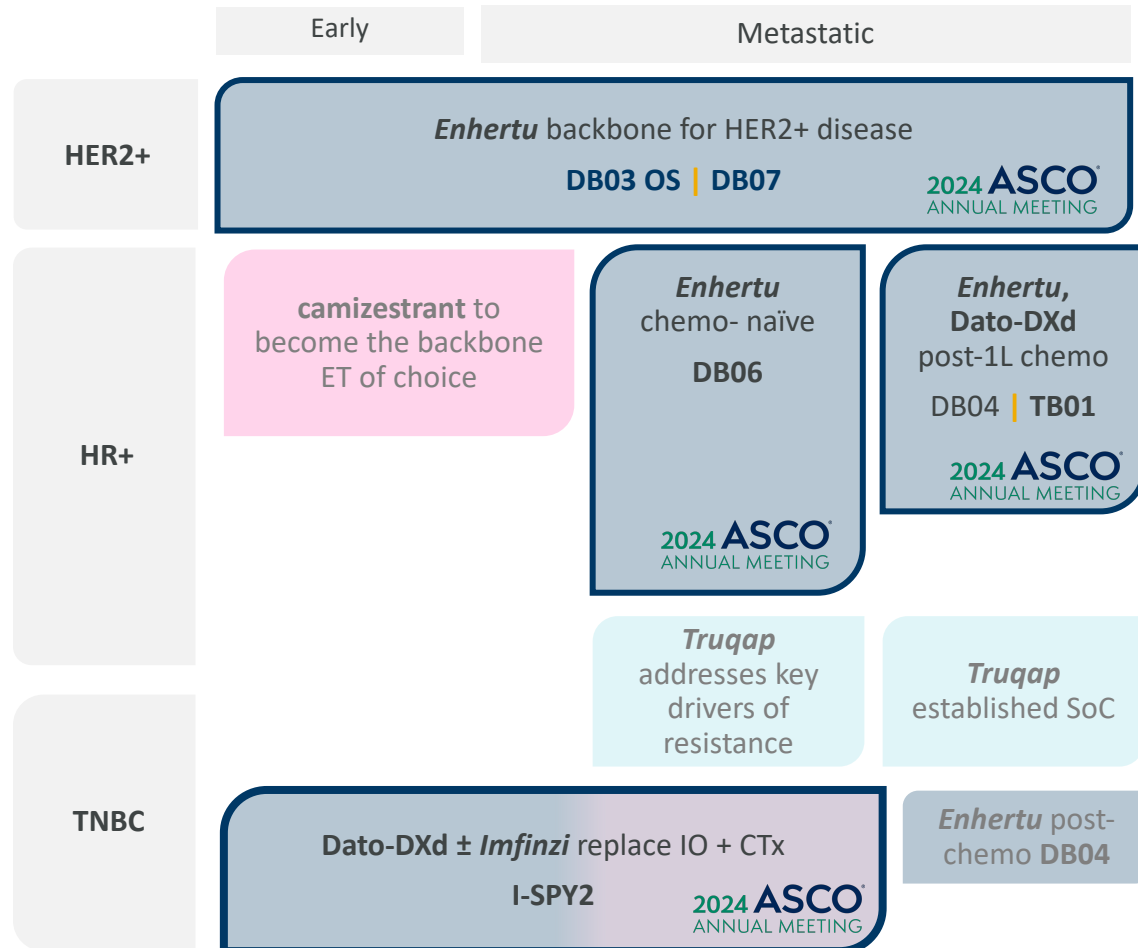
ADRIATIC reinforces *Imfinzi* foundation in SCLC, built on support from CASPIAN, PACIFIC



- PACIFIC (u/r Stg. III NSCLC) *Imfinzi* post-CRT showed significant improvement in OS
- CASPIAN (ES-SCLC) supported rationale for *Imfinzi* monotherapy arm in ADRIATIC
- ADRIATIC (OS HR, 0.73, PFS HR, 0.76) *Imfinzi* potential SoC in LS-SCLC

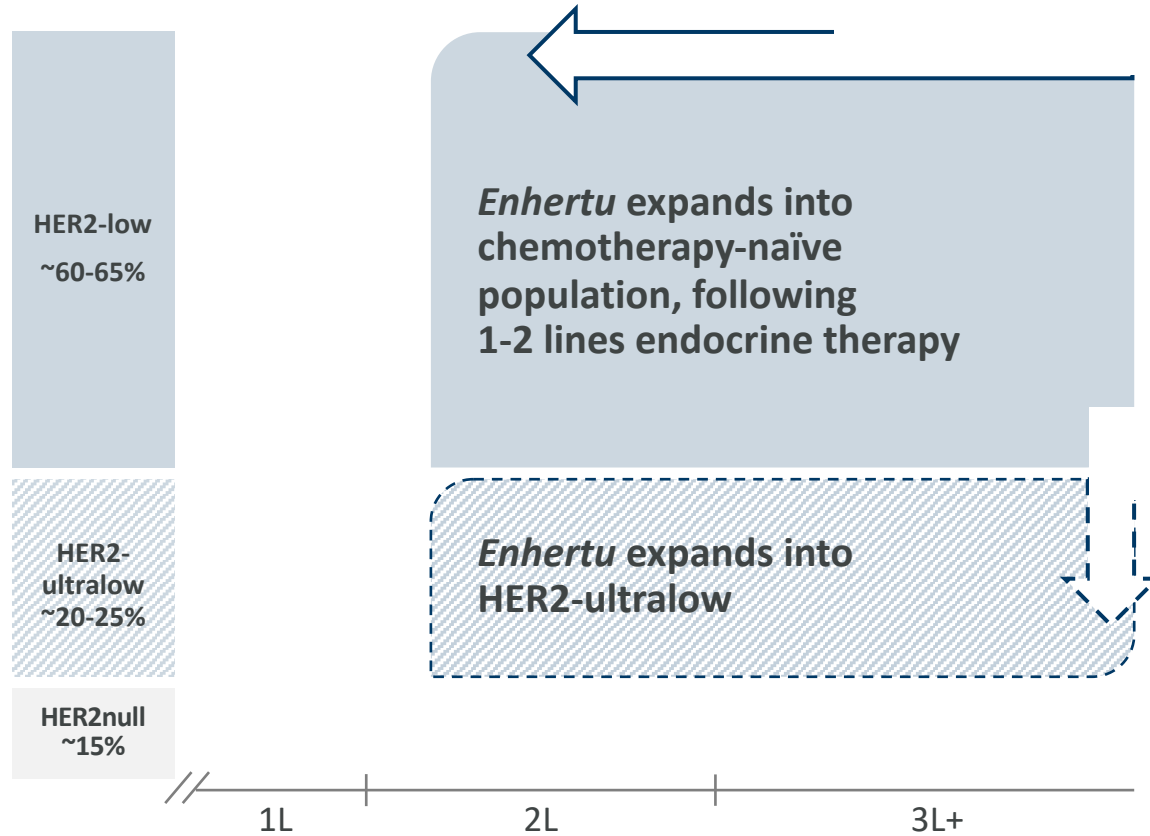
AstraZeneca @ ASCO 2024

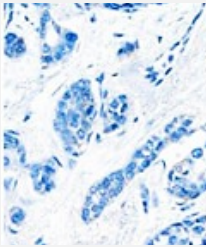
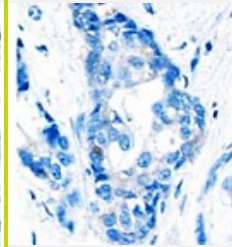
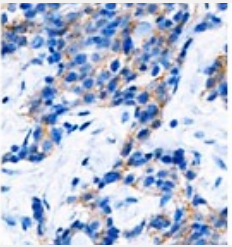
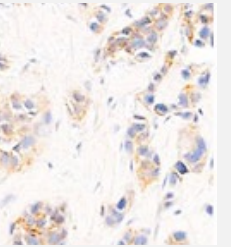
Key data furthers ambition to redefine treatment of breast cancer



- I. Address full spectrum of HR+ disease through targeted medicines and novel combinations
 - ER drive exists – deliver best-in-class ET, seek to extend benefit of ET
 - ER-driven disease is absent – replace systemic chemotherapy with ADCs
 - **DESTINY-Breast03 OS**
 - **DESTINY-Breast07** benefit in HER2+ mBC, support for ongoing DESTINY-Breast09
 - **DESTINY-Breast06** moves *Enhertu* earlier, expands into HER2-ultralow
 - **TROPION-Breast01** Patient Reported Outcomes
- II. Redefine TNBC – identifying subsets of patients with actionable features
 - **I-SPY 2** benefit of *Imfinzi* ± Dato-DXd in neoadjuvant, support for TROPION-Breast04

DESTINY-Breast06 – *Enhertu* moving into 2L and expanding into HER2-ultralow breast cancer



HER2 IHC 0	HER2-ultralow	HER2-low	
			
IHC 0 ~20k receptors per cell	IHC >0 <1+ 20-100k receptors per cell	IHC 1+ ~100-200k receptors per cell	IHC 2+ ~200-500k receptors per cell

Opportunity to build understanding of HER2-ultralow pathology to reach full addressable population

55-60k patients with HER2-low or -ultralow HR+ mBC that have received prior ET and are chemotherapy-naïve¹

1. Estimated for G7 countries. All numbers are approximate. Illustrative settings and populations, not to scale. AstraZeneca data on file; Tarantino P, et al. J Clin Oncol. 2020; Schettini F, et al. NPJ Breast Cancer. 2021; Owens et al., Clinical Breast Cancer 2004; Lambein et al., American Journal of Clinical Pathology 2013, CancerMPACT (2017); Schettini et al. ESMO BC 2020; Nuciforo et al., Molec Onc. 10, 2016; Scott et al. ASCO 2021 Abstract #1021. Collaboration partner: Daiichi Sankyo (*Enhertu*).

Q&A session

ASTRAZENECA LEADERSHIP



Pascal Soriot
CEO, ASTRAZENECA



Susan Galbraith
EVP, ONCOLOGY R&D



Dave Fredrickson
EVP, ONCOLOGY



Cristian Massacesi
CHIEF MEDICAL OFFICER
AND ONCOLOGY CHIEF
DEVELOPMENT OFFICER



Sunil Verna
SVP, GLOBAL HEAD OF
ONCOLOGY, MEDICAL



Leora Horn
LATE CLINICAL DEVELOPMENT
AND GLOBAL CLINICAL
STRATEGY LEAD, LUNG CANCER



Ingrid Mayer
VP, BREAST AND
GYNECOLOGIC CANCERS, R&D

KEY EXTERNAL EXPERTS



Dr Charu Aggarwal
MEDICAL ONCOLOGIST,
LUNG CANCER



Dr Rebecca Dent
MEDICAL ONCOLOGIST,
BREAST CANCER



Appendix

Lung and breast tumour maps

AstraZeneca in lung cancer

Ambition for >50% of lung cancer patients to be eligible for AZN medicine by 2030

	resectable	unresectable		metastatic	
	Stg. I-III	Stg. I-II	Stg. III	1L	2L+
Est. epi (G7)	~200K	~30K	~70K	~350K	~290K
IO sensitive c.70%	Imfinzi AEGEAN	Imfinzi / Osi w/ SBRT PACIFIC-4	CRT → Imfinzi PACIFIC	Imfinzi + Imjudo + CTx POSEIDON	Imfinzi + ceralasertib LATIFY
	volrustomig + CTx Imfinzi + Dato + plat NEOCOAST-2		Imfinzi combos PACIFIC-8, -9 improvements across PD-L1 spectrum	Dato-DXd + IO +/- Platinum TROPION-Lung08/TROPION-Lung07/AVANZAR	Dato-DXd TROPION-Lung01
				Dato-DXd + Rilvegostomig TROPION-Lung10	AZD9592 (EGFR/cMET ADC) EGRET
EGFRm c.16%	Tagrisso ADAURA	Imfinzi / Osi w/ SBRT PACIFIC-4	CRT → Tagrisso LAURA	Tagrisso FLAURA	savolitinib + Tagrisso SAFFRON/SAVANNAH
	Tagrisso neoADAURA			Tagrisso + CTx FLAURA-2	Dato-DXd +/- Tagrisso TROPION-Lung15/ 01
Other tumour drivers c.12%		Imfinzi / Osi w/ SBRT PACIFIC-4		Dato-DXd + Tagrisso TROPION-Lung14	AZD9592 (EGFR/cMET ADC) EGRET
HER2m c.2%			CRT → Imfinzi PACIFIC	Enhertu DESTINY-Lung04	Enhertu DESTINY-Lung02

Established SoC

Leading the future of lung cancer treatment

- Establishing *Tagrisso* as backbone TKI in *EGFRm*
- *Imfinzi* leading IO in unresectable
- Advancing best-in-class ADCs to replace systemic chemotherapy
- Delivering next-wave bispecifics to improve on PD-(L)1
- Developing novel combinations, including IO & *Tagrisso* + ADCs
- Investing behind new technologies and platforms, including cell therapy and testing/screening

AstraZeneca in breast cancer

Ambition to eliminate breast cancer as a cause of death

Established SoC	Early		RECURRENCE	Metastatic			
	Noadjuvant	Adjuvant		1st line	2nd line	3rd line	4th line +
Est. epi (G7)	540k			125k	90k	65k	55k
HER2-positive 15-20%	<i>Enhertu</i> ± THP DESTINY-Breast11	NST → residual disease → <i>Enhertu</i> DESTINY-Breast05		<i>Enhertu</i> ± pertuzumab DESTINY-Breast09	<i>Enhertu</i> DESTINY-Breast03	<i>Enhertu</i> DESTINY-Breast02	
HR-positive 65-75%		Low risk Good outcomes with current SoC CTx → camizestrant (± CDK4/6i) CAMBRIA-2 CTx → AI (± CDK4/6i) 2-5 yrs → camizestrant CAMBRIA-1		camizestrant + CDK4/6i SERENA-4 AI + CDK4/6i → camizestrant + CDK4/6i SERENA-6 <i>ESR1m</i> 35% <i>Truqap</i> + <i>Faslodex</i> + CDK4/6i CAPitello292 saruparib + camizestrant EvoPAR-Breast01 <i>tBRCAm, PALB2m</i> 9%	<i>Truqap</i> + <i>Faslodex</i> CAPitello291 <i>PIK3CA, AKT1, PTEN</i> alt.40% <i>Enhertu</i> DESTINY-Breast06 HER2-low (1+, 2+) 60% HER2-ultralow (0-1+) 25%	Dato-DXd TROPION-Breast01 <i>Enhertu</i> DESTINY-Breast04 HER2-low (1+, 2+) 60%	
TNBC 10-15%	Dato-DXd + <i>Imfinzi</i> TROPION-Breast04	NST → residual disease → Dato-DXd ± <i>Imfinzi</i> TROPION-Breast03		<i>Truqap</i> + paclitaxel CAPitello290 PD-L1+ 40% Dato-DXd + <i>Imfinzi</i> TROPION-Breast05 PD-L1- 60% Dato-DXd TROPION-Breast02	HER2-low (1+, 2+) 35%		
gBRCAm 5% of HR-positive 15% of TNBC		CTx → <i>Lynparza</i> OlympiA		<i>Lynparza</i> OlympiAD			



Appendix

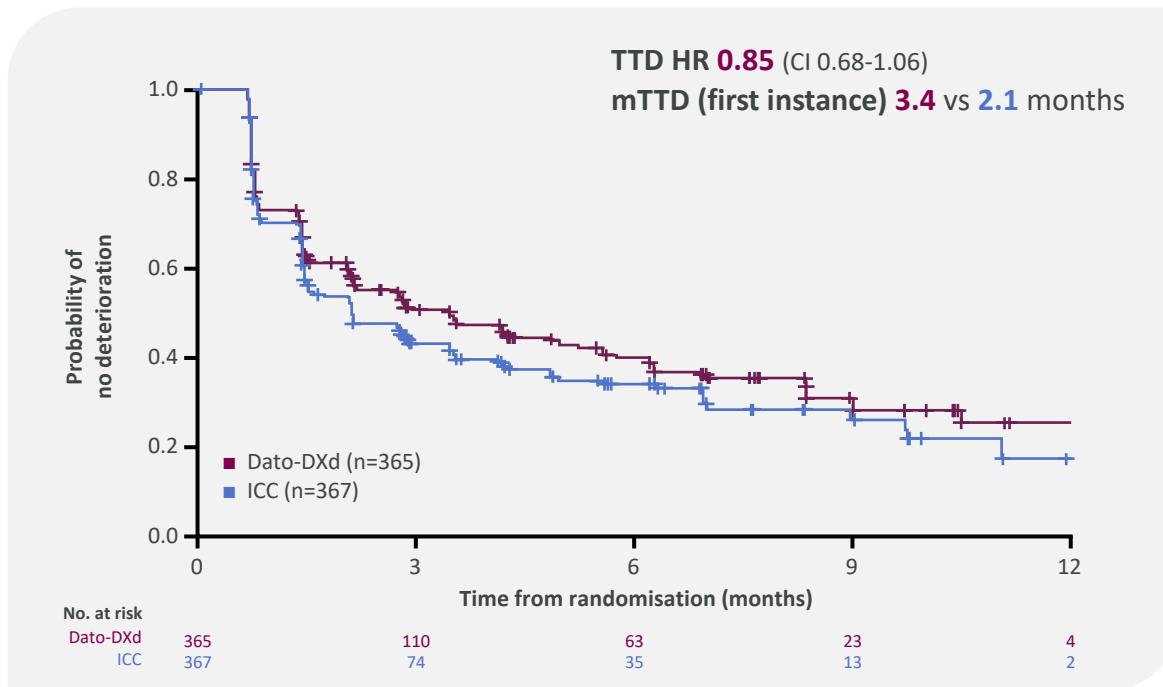
Key data at ASCO 2024

TROPION-Breast01

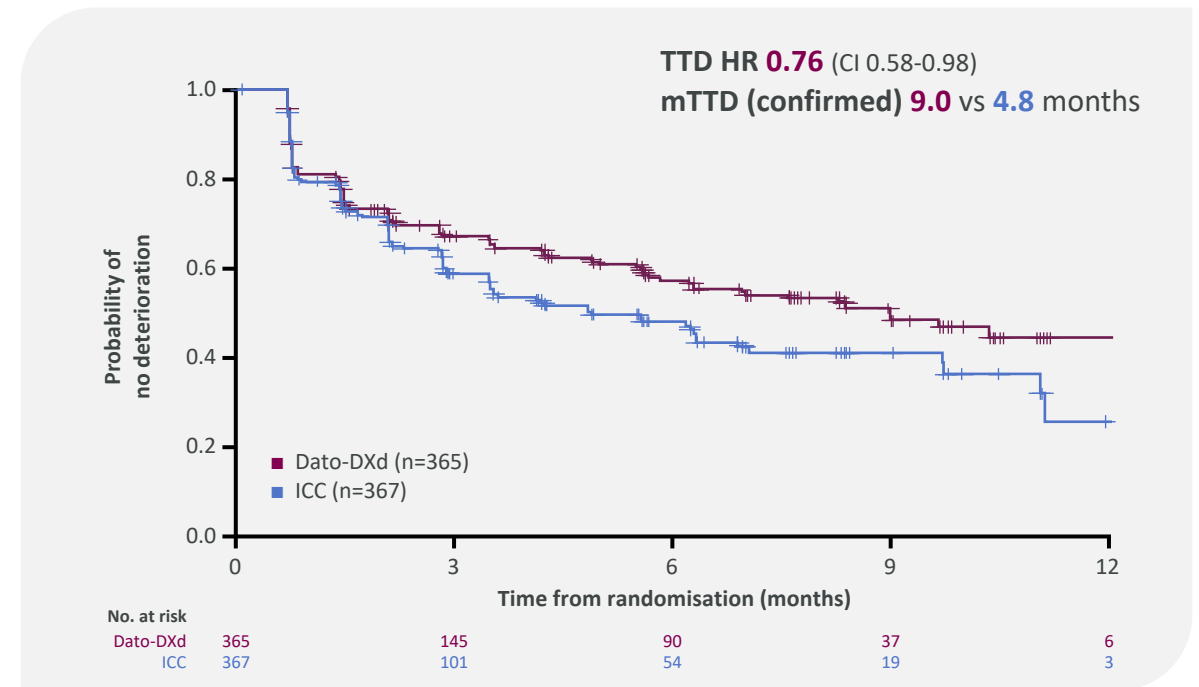
Randomised, open-label, Phase III trial evaluating *Enhertu* vs T-DM1 in patients with HER2-positive unresectable and/or metastatic breast cancer previously treated with trastuzumab and a taxane

PRO data support Dato-DXd as a potential new, well-tolerated therapeutic option for HR+ HER2- adv. BC

Time to deterioration¹ in GHS/QoL (first instance)



Time to deterioration¹ in GHS/QoL (confirmed)



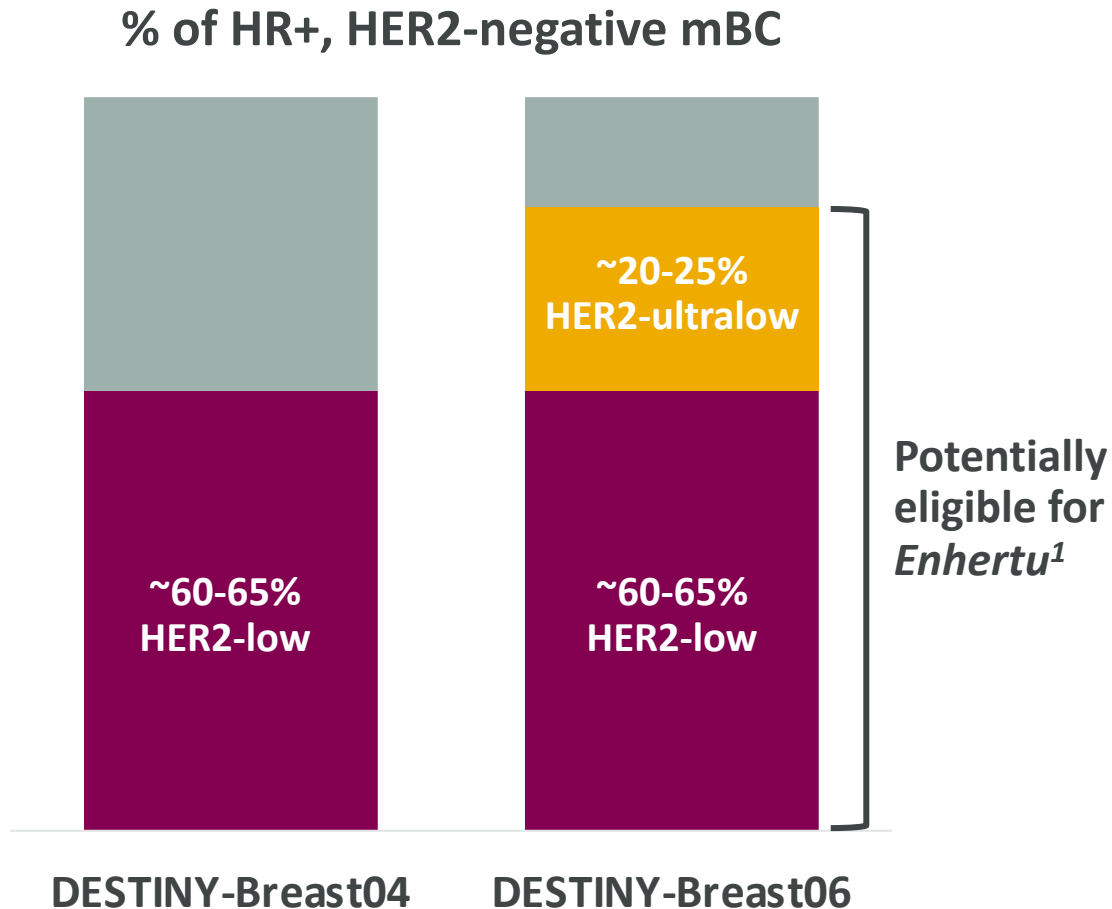
Patient-reported symptomatic AEs generally consistent with clinician-reported safety data, without showing major impact on patients' functioning and health-related quality of life

1. TTD in GHS/QoL, pain, and physical functioning are secondary endpoints and were measured using EORTC QLQ-C30. Time to first deterioration (primary analysis) was defined as the time from date of randomization to date of first deterioration. Time to confirmed deterioration (sensitivity analysis) required deterioration to be confirmed at a subsequent timepoint. Deterioration was defined as a change from baseline that reached a clinically meaningful deterioration threshold of 16.6.

DESTINY-Breast06

Randomised, open-label, Phase III trial in patients with HR-positive, HER2-low or HER2-ultralow advanced or metastatic breast cancer evaluating *Enhertu* vs investigator's choice of chemotherapy

Enhertu demonstrated efficacy in HER2-low mBC in an earlier line of treatment to DESTINY-Breast04



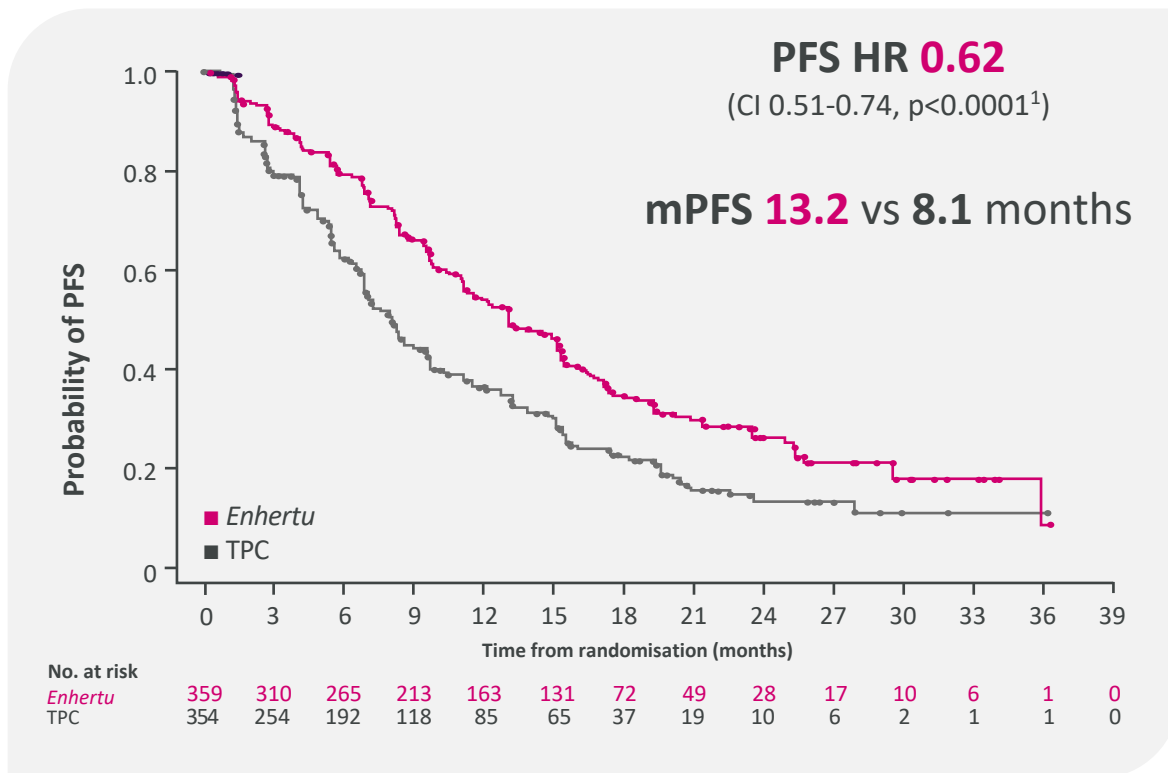
- *Enhertu* demonstrated efficacy in **HER2-low mBC** in an **earlier line of treatment** to DESTINY-Breast04
- Including HER2-ultralow, the proportion of patients who could benefit from *Enhertu* is **~85% of HR+, HER2-negative mBC** after DESTINY-Breast06

In DESTINY-Breast06, *Enhertu* demonstrated a statistically significant and clinically meaningful PFS benefit vs TPC (CTx) in HR+, HER2-low mBC after ≥ 1 endocrine-based therapy, with consistent results in HER2-ultralow mBC

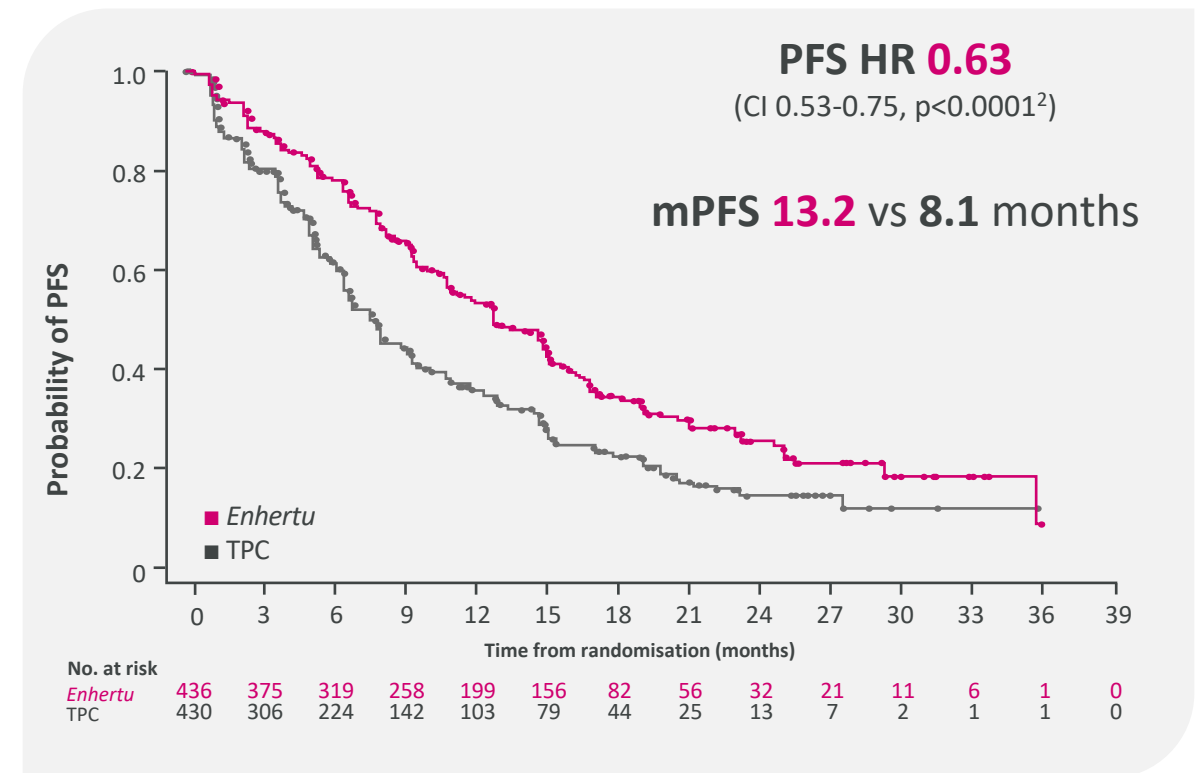
1. As a percentage of HR+, HER2-negative mBC.

Statistically significant and clinically meaningful PFS improvement with *Enhertu* vs TPC in HER2-low and ITT

HER2-low PFS



ITT PFS (HER2-low + HER2-ultralow)

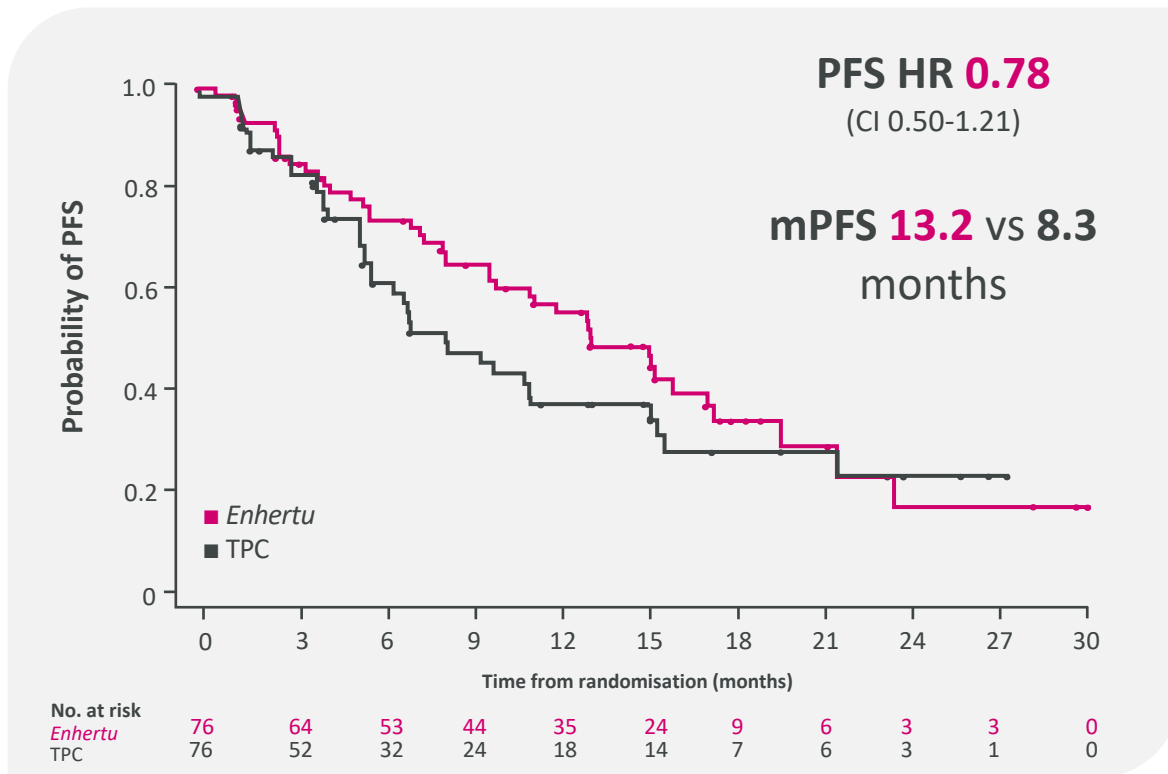


1. P-value of <0.05 required for statistical significance. 2. P-value of <0.015 required for statistical significance.

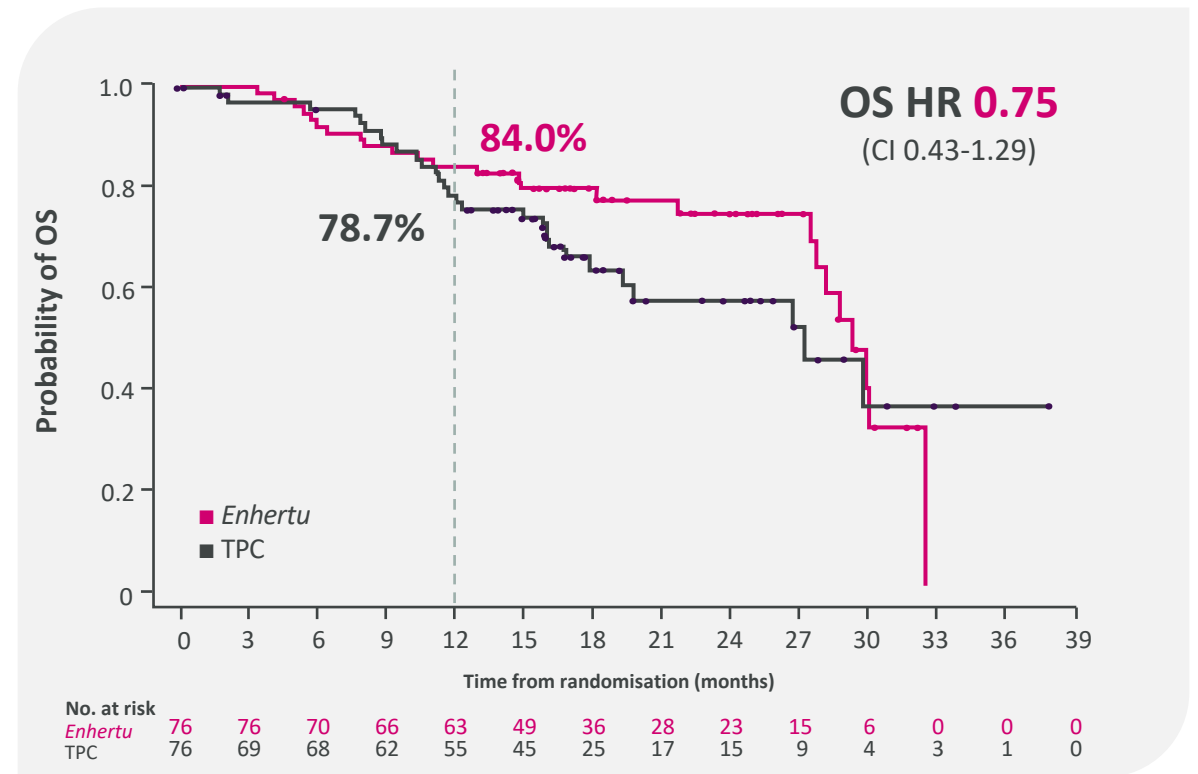
Curigliano G et al. Abstract LBA1000 presented at American Society of Clinical Oncology 2024. Collaboration partners: Daiichi Sankyo (*Enhertu*).

Clinically meaningful PFS improvement with *Enhertu* vs TPC consistent between HER2-low and -ultralow disease

HER2-ultralow PFS (BICR) (N=152)



HER2-ultralow OS¹ (N=152)

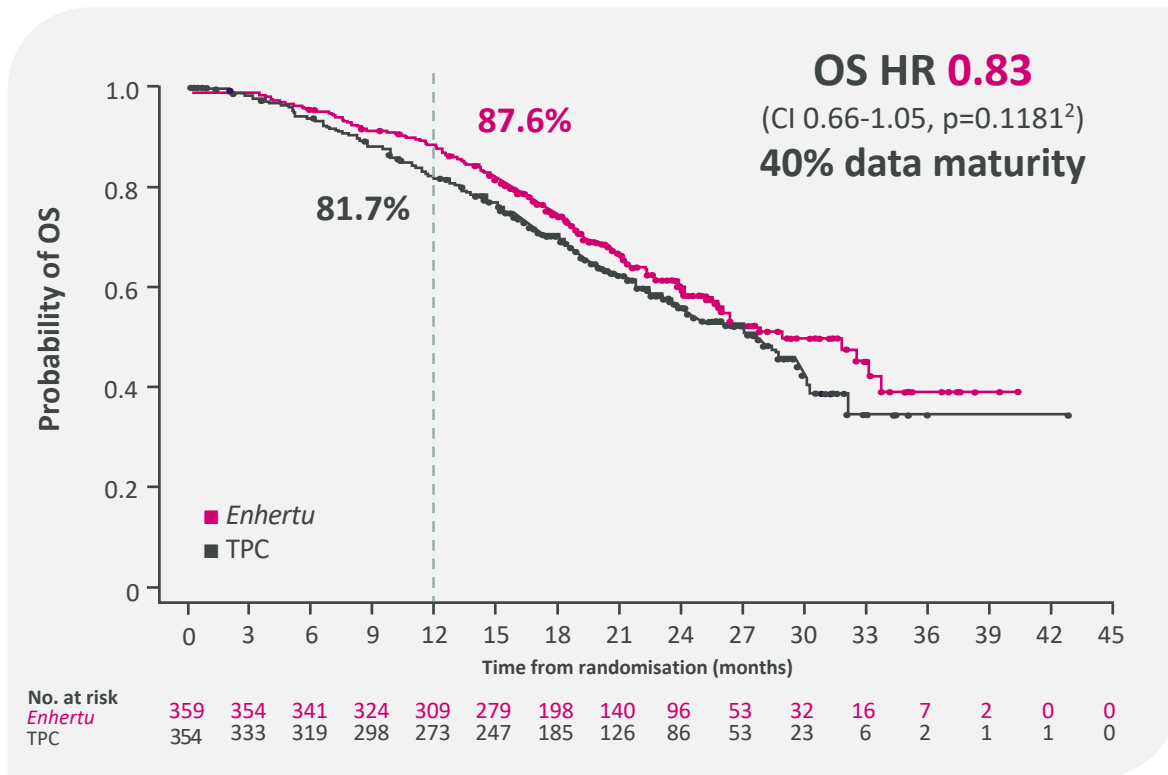


1. 34.9% maturity (of total N for population) at this first interim analysis; median duration of follow up was 16.8 months.

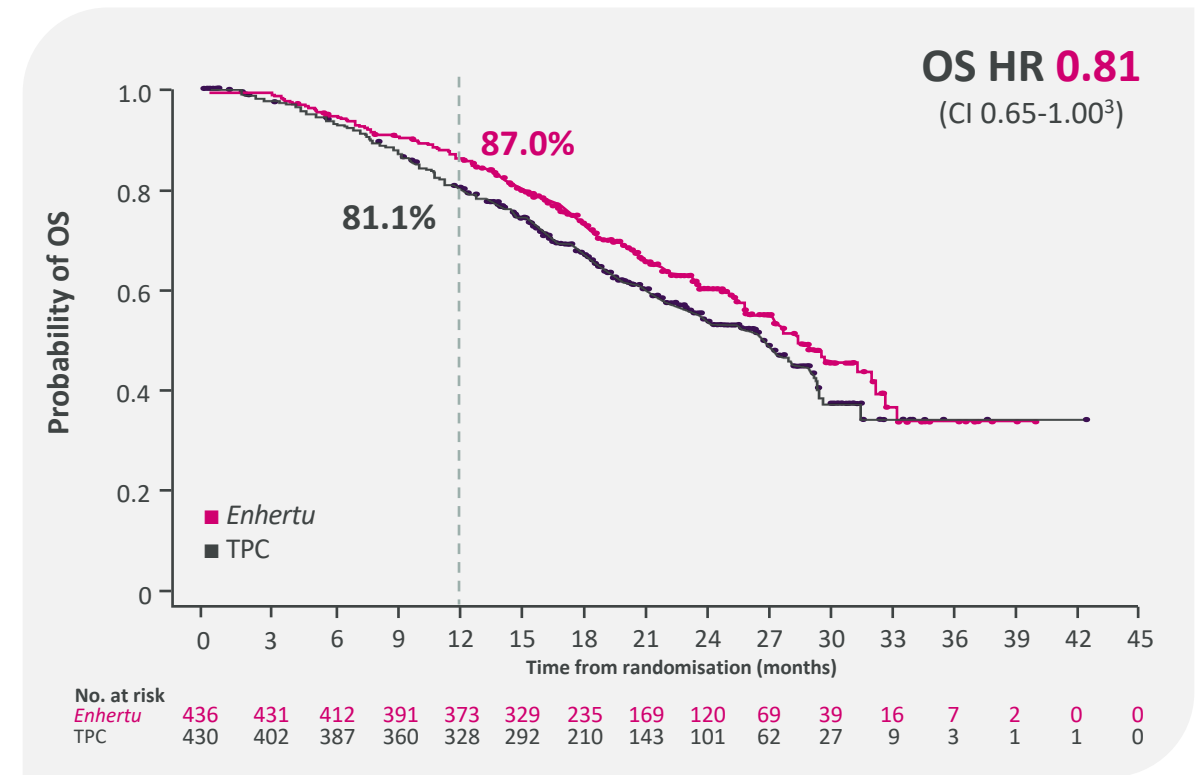
Curigliano G et al. Abstract LBA1000 presented at American Society of Clinical Oncology 2024. Collaboration partners: Daiichi Sankyo (*Enhertu*).

Trend to overall survival benefit with *Enhertu* vs TPC (~40% maturity)

HER2-low OS¹ (N=713)



ITT OS (HER2-low + HER2-ultralow) (N=866)



1. 39.6% maturity (of total N for population) at this first interim analysis; median duration of follow up was 18.6 months (HER2-low). 2. P-value of <0.0046 required for statistical significance. 3. No test of significance was performed in line with the multiple testing procedure; median duration of follow up was 18.2 months (ITT)

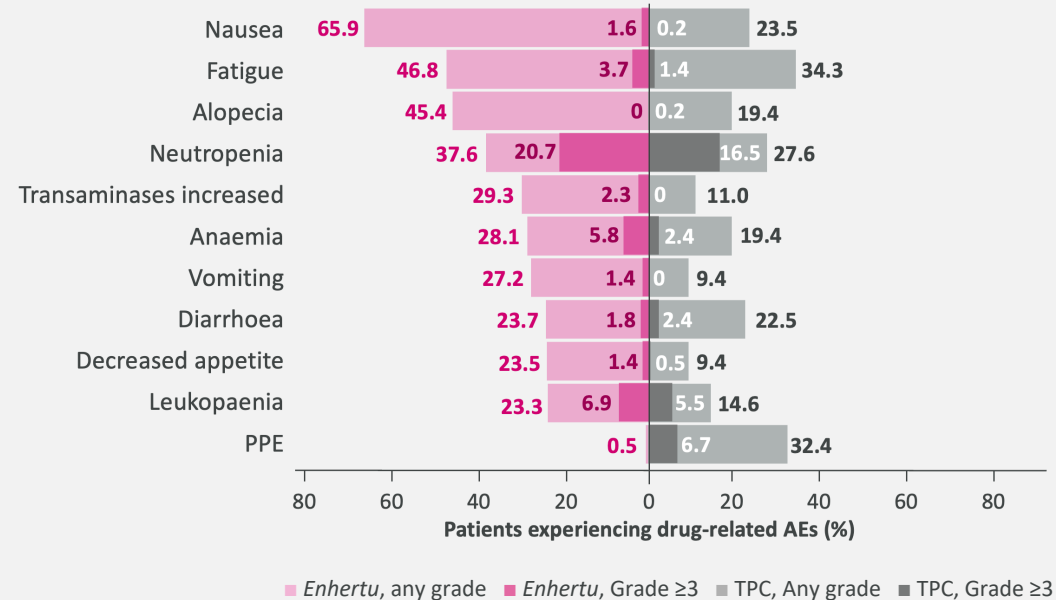
Curigliano G et al. Abstract LBA1000 presented at American Society of Clinical Oncology 2024. Collaboration partners: Daiichi Sankyo (*Enhertu*).

Enhertu safety profile consistent with known profile

Enhertu AE profile generally manageable through dose interruptions and reductions

TEAEs, n (%)	Enhertu (n=434)	TPC (n=417)
Any TEAE	438.5	263.5
	429 (98.8)	397 (95.2)
Treatment-related TEAEs	417 (96.1)	373 (89.4)
Grade ≥3	176 (40.6)	131 (31.4)
Serious TEAEs	88 (20.3)	67 (16.1)
Associated with treatment discontinuation	62 (14.3)	39 (9.4)
Associated with dose interruptions	210 (48.4)	160 (38.4)
Associated with dose reductions	107 (24.7)	161 (38.6)
Leading to death	11 (2.5)	6 (1.4)
Treatment related ¹	5 (1.2)	0

Common AEs consistent with previous trials of Enhertu



- Three cases (0.7%) of adjudicated Grade 5 drug-related interstitial lung disease/pneumonitis¹ in *Enhertu* arm (vs 0 in TPC arm)

1. Reasons were interstitial lung disease (n=2), sepsis (n=1), neutropenic sepsis (n=1) and general physical health deterioration (n=1). 2. Grouped term. Median time to first onset of interstitial lung disease / pneumonitis for patients with *Enhertu* was 141 days (range 37–835). No pending cases of drug-related interstitial lung disease / pneumonitis to be adjudicated. One interstitial lung disease–related death per investigator assessment was upheld by the adjudication committee. An additional two deaths were adjudicated as interstitial lung disease–related by the adjudication committee.

Tornado plot displays drug-related TEAEs in ≥20% of patients (either treatment group).

Curigliano G et al. Abstract LBA1000 presented at American Society of Clinical Oncology 2024. Collaboration partners: Daiichi Sankyo (*Enhertu*).

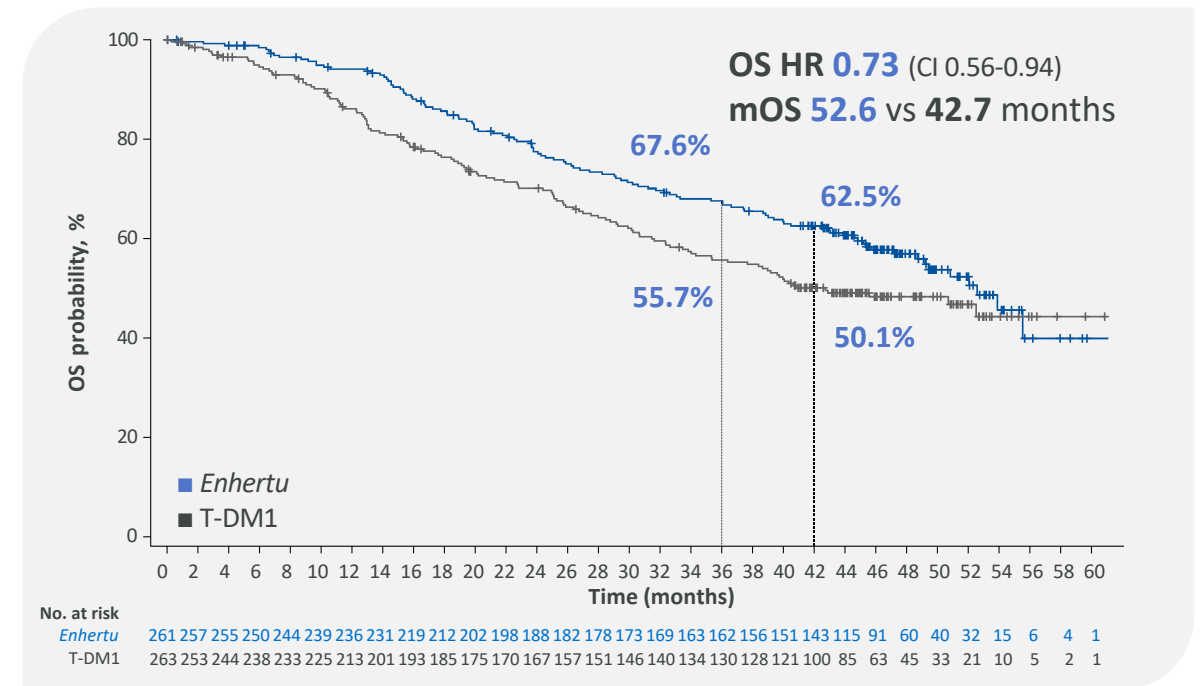
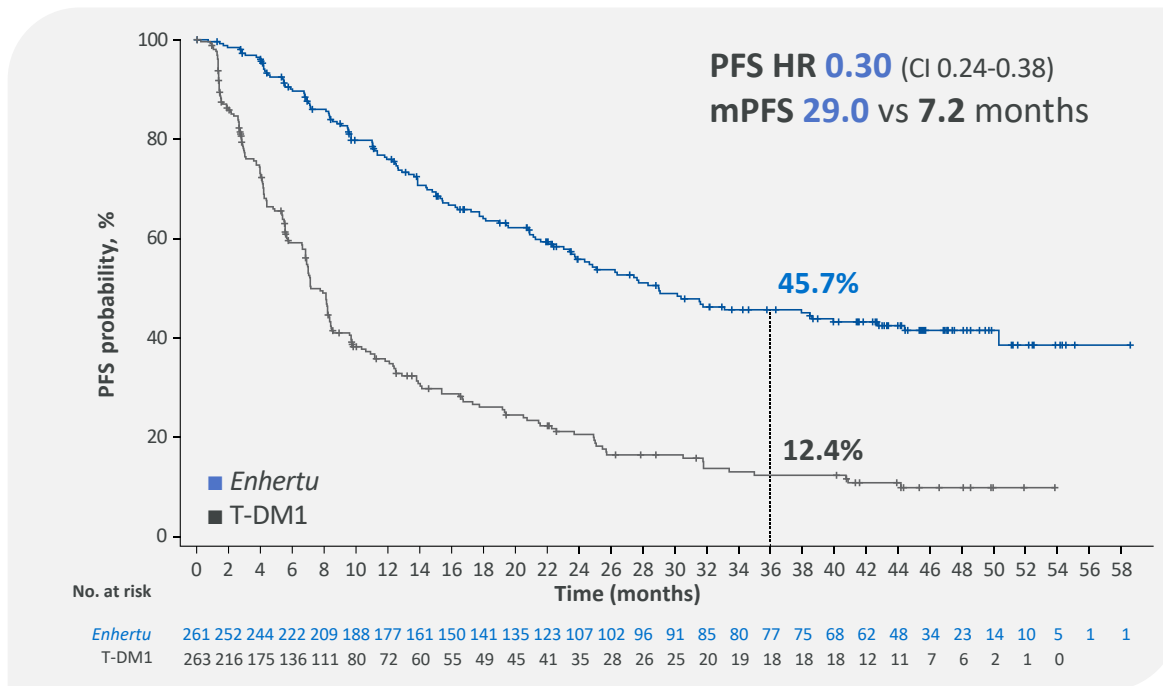
DESTINY-Breast03

Randomised, open-label, Phase III trial evaluating *Enhertu* vs T-DM1 in patients with HER2-positive unresectable and/or metastatic breast cancer previously treated with trastuzumab and a taxane

Long-term follow-up from DESTINY-Breast03 further support superiority of *Enhertu* over T-DM1 2L+ HER2+ mBC

Investigator-assessed mPFS
~4 times longer for *Enhertu* vs T-DM1

Over 4 years median overall survival for patients on *Enhertu*



With longer follow-up *Enhertu* safety profile remained consistent¹ and manageable, with no cumulative toxicities

With longest OS in this setting, data reinforce use of *Enhertu* as SoC for 2L+ HER+ mBC

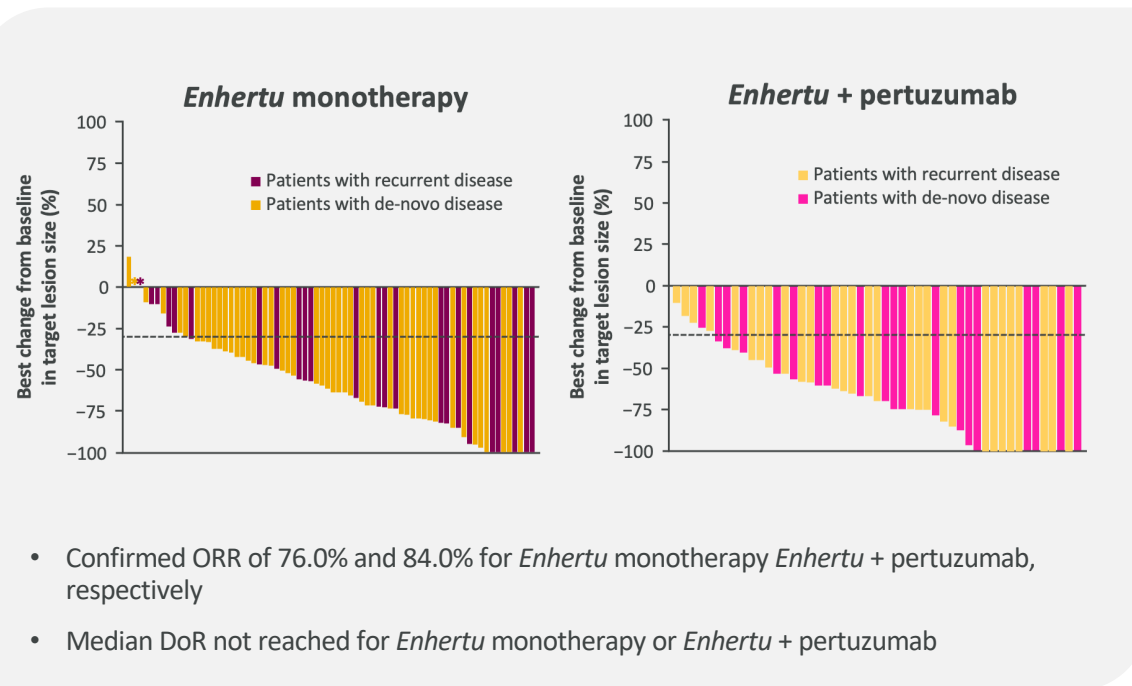
1. With previous analyses.

DESTINY-Breast07

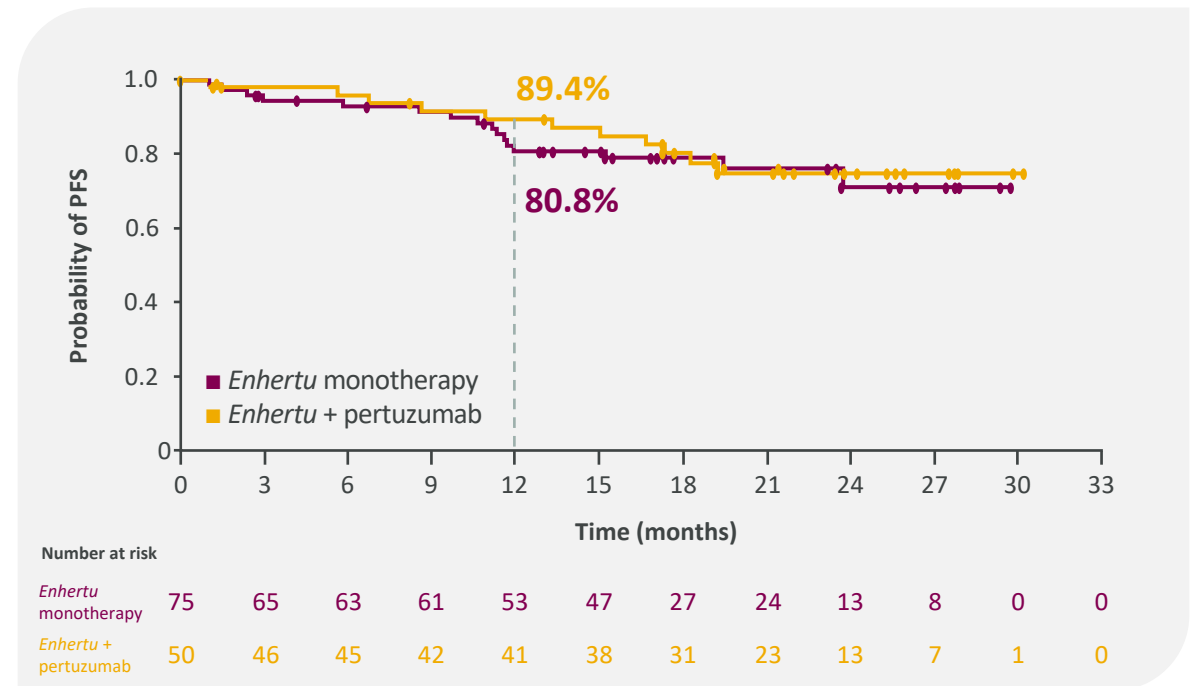
Open-label, Phase Ib/II trial in patients with HER2-positive advanced or metastatic breast cancer evaluating *Enhertu*

DESTINY-Breast07 – first dataset of *Enhertu* ± pertuzumab as 1L treatment for HER2+ mBC

Robust efficacy demonstrated by ORR and mDOR¹



Improved PFS rate at 12 months, further follow-up required²



Safety profiles of *Enhertu* and pertuzumab consistent with their individual known profiles

Enhertu ± pertuzumab being evaluated in patients with 1L HER2+ mBC in the Phase III DESTINY-Breast09 trial

*Patients had 0% change from baseline.

1. Dashed reference line at -30% indicates the threshold for partial response. DCO was December 22, 2023. Median duration of follow up was 23.9 months for *Enhertu* monotherapy and 25.3 months for *Enhertu* + pertuzumab. 2.

Number of PFS events is small and most patients were censored.

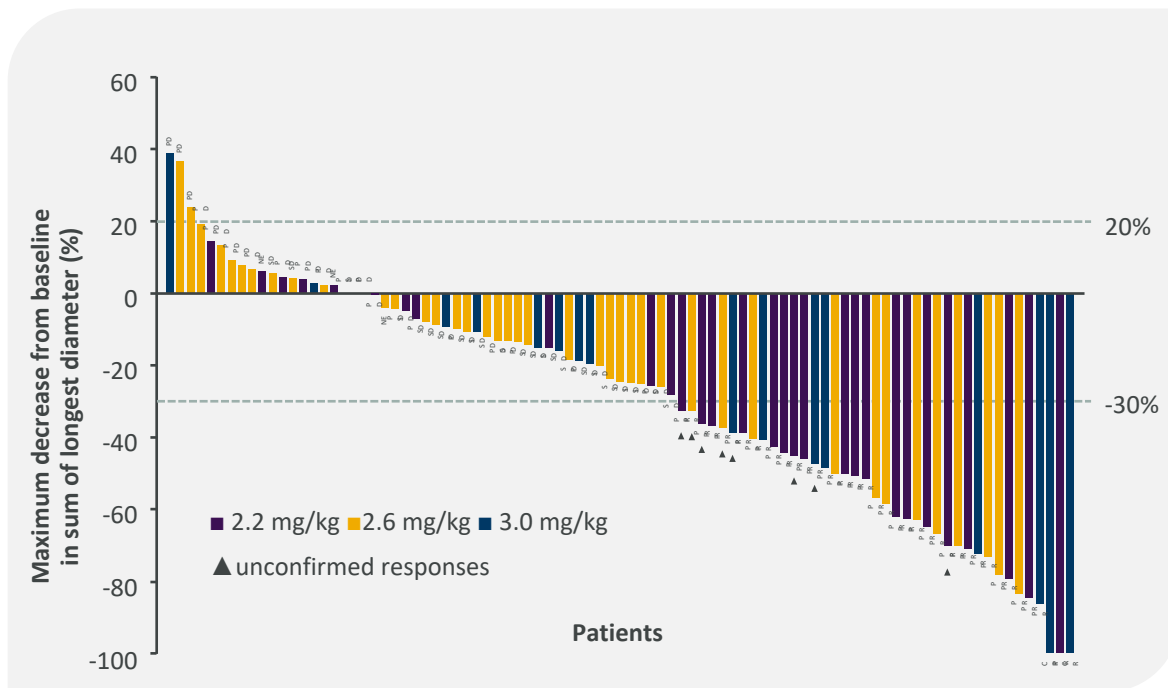
Andre F et al. Abstract 1009 presented at American Society of Clinical Oncology 2024. Collaboration partners: Daiichi Sankyo (*Enhertu*).

AZD0901

Multi-centre, open-label Phase I trial evaluating AZD0901 in relapsed and/or refractory advanced solid tumours

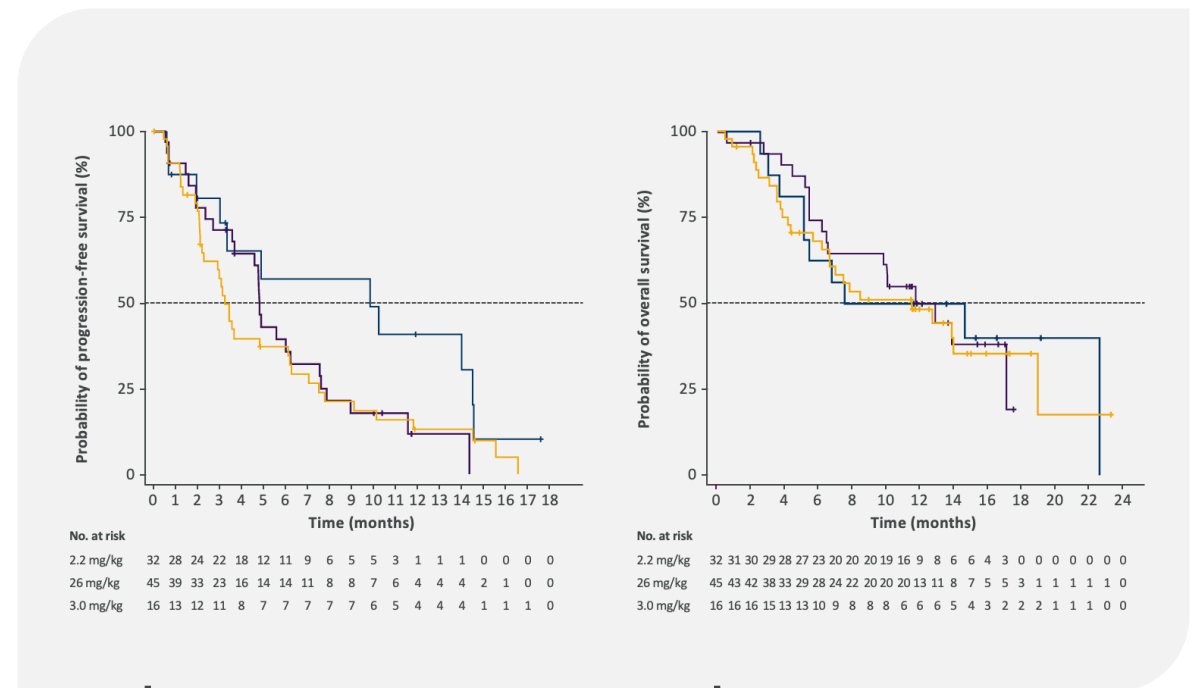
AZD0901¹ – Promising clinical efficacy in pretreated patients with CLDN18.2-high gastric/GEJ cancer

Robust ORR of 48% in 2.2 mg/kg cohort



AZD0901 was generally well-tolerated, with a manageable safety profile

Encouraging mPFS of 4.8 months and mOS of 11.8 months in 2.2 mg/kg cohort



The current clinical program for AZD0901 is expanding for advanced solid tumours expressing CLDN18.2

1. Also known as CMG901

Glossary

1L, 2L, 3L	first-, second-, third-line	ET	endocrine therapy	oGLP-1	oral glucagon-like receptor peptide-1
4-IBB	tumour necrosis factor ligand superfamily member 9	exp.	expressing	ORR	overall response rate
AAV	adeno-associated virus	FDC	fixed dose combination	OS	overall survival
AC	doxorubicin/cytophosphamide	FIH	first-in-human	PCI	prophylactic cranial irradiation
ADC	antibody-drug conjugate	G7	US, Japan, EU5	pCR	pathological complete response
AE	adverse event	GEJ	gastroesophageal junction	PD	Progressive disease
AI	artificial intelligence	GLP-1	glucagon-like receptor peptide-1	PD-1	programmed cell death protein-1
ASCO	American Society of Clinical Oncology	GPC3	glypican-3	PD-1i	programmed cell death protein-1 inhibitor
BC	breast cancer	GU	genitourinary	PD-L1	programmed cell death ligand-1
BCMA	B-cell maturation antigen	GYN	gynaecological	pembro	pembrolizumab
BICR	Blinded Independent Central Review	HCC	hepatocellular carcinoma	PFS	progression-free survival
CAR	chimeric antigen receptor	HER2	human epidermal growth factor receptor 2	PPE	palmar-plantar erythrodysesthesia
carbo	carboplatin	HER2-	human epidermal growth factor receptor 2-negative	PR	partial response
CAR-T	chimeric antigen receptor T-cells	HER2-immune+	human epidermal growth factor receptor 2-immune-positive	preRCB	pre-residual cancer burden
cCRT	concurrent chemoradiotherapy	HER2-low	human epidermal growth factor receptor 2-low	RC	radioconjugate
CD19	cluster of differentiation 19	HER2-negative	human epidermal growth factor receptor 2-negative	RECIST	Response Evaluation Criteria in Solid Tumours
CD28	cluster of differentiation 28	HER2-positive	human epidermal growth factor receptor 2-positive	scFv	single-chain fragment variable
CD3	cluster of differentiation 3	HER2-ultralow	human epidermal growth factor receptor 2-ultralow	SCLC	small-cell lung cancer
CD3ζ	T-cell surface glycoprotein CD3 zeta chain	HR	hazard ratio	SD	standard deviation
CI	confidence interval	HR-	hormone receptor-negative	SD	stable disease
CLDN 18.2	Claudin 18.2	HR+	hormone receptor-positive	SLD	sum of lesion diameters
CRS	cytokine release syndrome	ICANS	immune effector cell-associated neurotoxicity syndrome	SoC	standard-of-care
CRT	chemoradiotherapy	ICD	International Classification of Diseases	STEAP2	six-transmembrane epithelial antigen of prostate-2
ctDNA	circulating tumour DNA	IgG4P	immunoglobulin G4 protein	Stg.	stage
CTLA-4	cytotoxic T-lymphocyte associated protein-4	IHC	immunohistochemistry	T2A	tumor is between 3cm and 4cm
CTx	chemotherapy	ILD	interstitial lung disease	taxol	paclitaxel
Dato-DXd	datopotamab deruxtecan	IO	immuno-oncology	TB01	TROPION-Breast01
DB03	DESTINY-Breast03	ISH	in situ hybridisation	TCE	T-cell engager
DB04	DESTINY-Breast04	ITT	intent to treat	TDR	tumour drivers and resistance
DB06	DESTINY-Breast06	LBA	late-breaking abstract	T-DxD	trastuzumab deruxtecan (Enhertu)
DB07	DESTINY-Breast07	LS	late-stage	TEAE	treatment emergent adverse event
DDR	DNA damage response	LS-SCLC	limited stage small-cell lung cancer	TIGIT	T-cell immunoreceptor with immunoglobulin and ITIM domains
DL	dose level	mBC	metastatic breast cancer	TKI	tyrosine kinase inhibitor
dnTGFβRII	dominant-negative transforming growth factor-beta type II receptor	mDoR	median duration of response	TNBC	triple negative breast cancer
dPTEN	de novo phosphatase and tensin homolog deficient	mo	month	TPC	docetaxel, cisplatin and irinotecan
eBC	early breast cancer	mOS	median overall survival	TROP2	trophoblast cell surface antigen 2
ECOG	Eastern Cooperative Oncology Group	mPFS	median progression-free survival	TTD	time to treatment discontinuation
EGFR	epidermal growth factor receptor	mTTD	median time to treatment discontinuation	u/r	unresectable
EGFRm	epidermal growth factor receptor-mutant	NME	new molecular entity	unresect.	unresectable
EPI	epigenetics	no.	number	VEGF(R)	vascular endothelial growth factor (receptor)
ES-SCLC	early stage small-cell lung cancer	NSCLC	non-small cell lung cancer		