

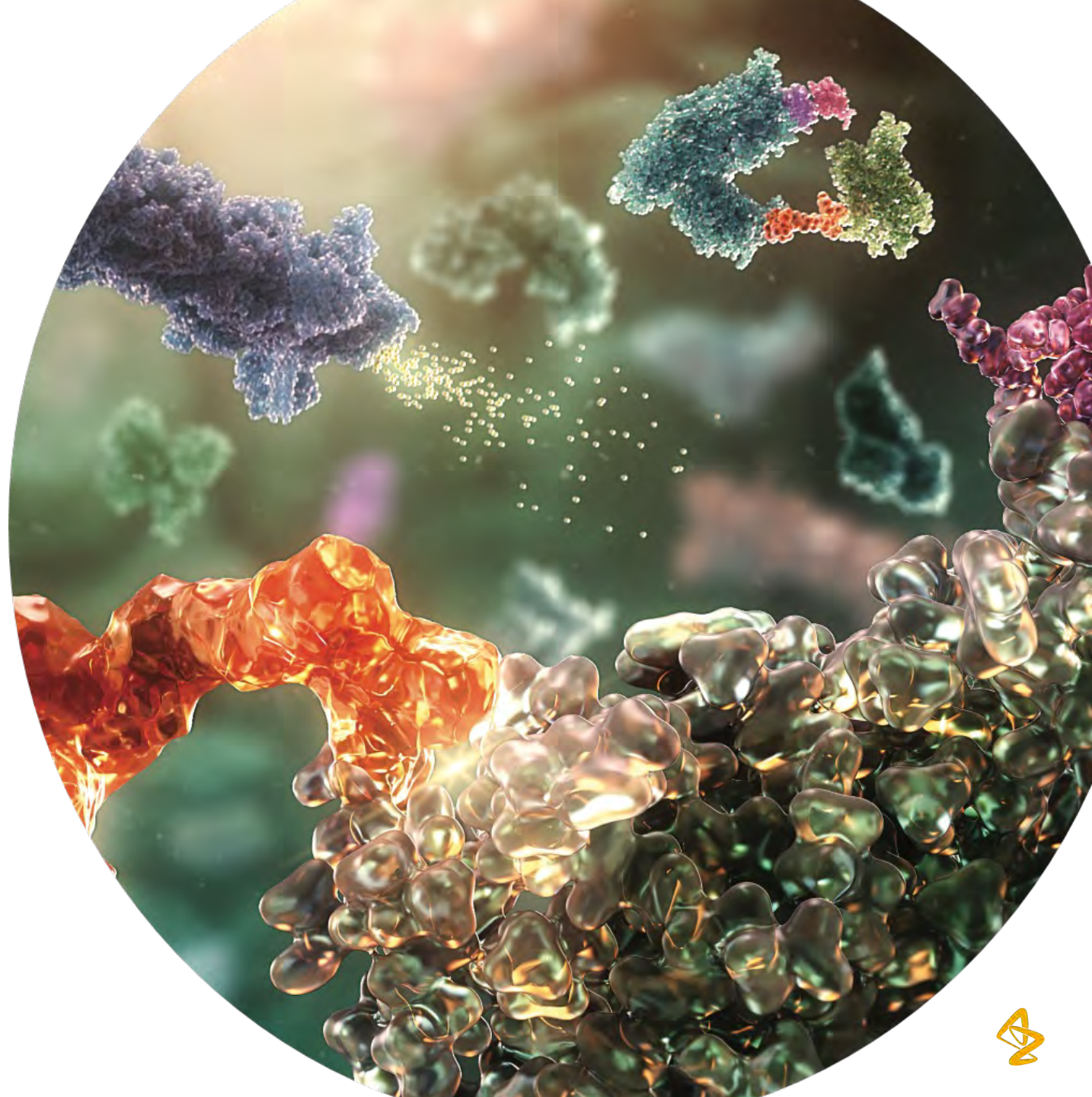


ASCO 2023

Meet AZN Management

For investors and analysts

05 June 2023



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AstraZeneca @ ASCO 2023

AGENDA |

Furthering our oncology ambition @ ASCO 2023 – *Pascal Soriot, CEO*

Strengthening our presence in lung cancer
& advancing emerging portfolio

–

Susan Galbraith, EVP, Oncology R&D
Dave Fredrickson, EVP, Oncology Business
Dr Roy Herbst, Deputy Director, Yale Cancer Center

Q&A session I – Focus on lung cancer

Investigating novel combinations
in ovarian cancer

–

Susan Galbraith, EVP, Oncology R&D
Dave Fredrickson, EVP, Oncology Business

Expanding *Enhertu* beyond
breast, lung and gastric

–

Susan Galbraith, EVP, Oncology R&D
Dave Fredrickson, EVP, Oncology Business

Reinforcing *Calquence* positioning
in BTKi class

–

Anas Younes, SVP, Haematology

Q&A session II – AZN management



AstraZeneca @ ASCO 2023

Speakers and panelists



KEY EXTERNAL EXPERT

Dr Roy Herbst,
Deputy Director, Yale Cancer Center



Dave Fredrickson,
*Executive Vice President
Oncology Business*



Pascal Soriot,
Chief Executive Officer



Sunil Verma,
*Global Head of Oncology,
Medical*



Susan Galbraith,
*Executive Vice President
Oncology R&D*

THERAPEUTIC AREA LEADERSHIP



Leora Horn,
*Global Clinical Head, Lung Cancer
and Lung Cancer Strategy*



Ingrid Mayer,
*Global Clinical Strategy Head,
Breast Cancer*



Osama Rahma,
*Global Clinical Strategy Head,
GI Cancer*



Ashok Gupta,
*Global Clinical Strategy Head,
GU/GYN Cancer*

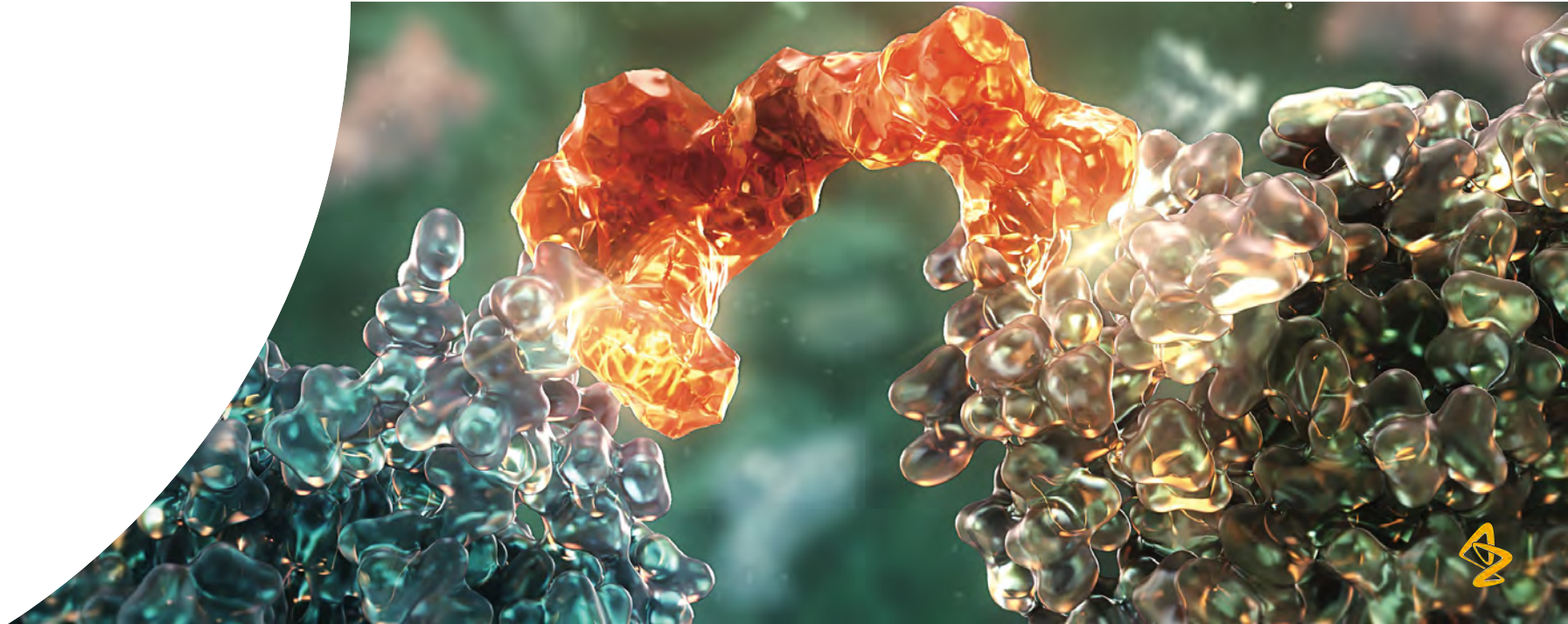


Anas Younes,
Senior Vice President, Hematology



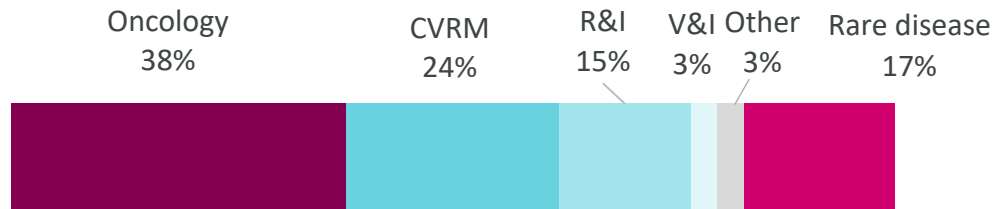
Furthering our oncology ambition *@* ASCO 2023

Pascal Soriot
CHIEF EXECUTIVE OFFICER

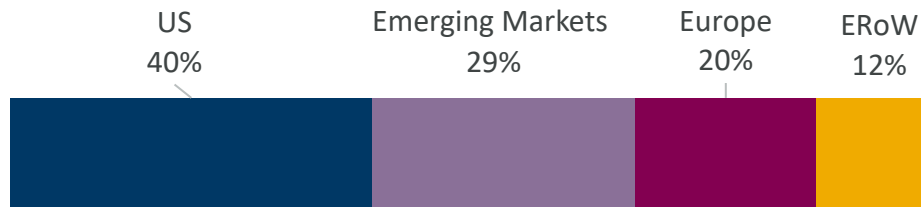


Broad-based, diverse source of revenue

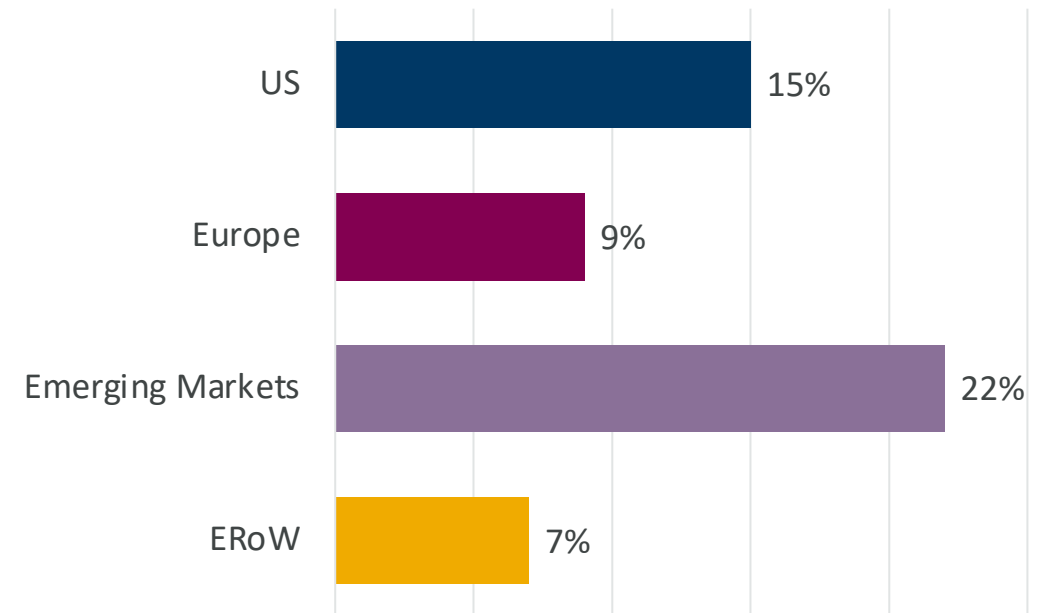
Q1 2023 | % Total Revenue by therapy area



Q1 2023 | % Total Revenue by geography



Q1 2023 | % YoY growth by region, ex. COVID



Industry-leading outlook underpinned by broad portfolio and geographic footprint



134 abstracts with 12 oral presentations

1 plenary presentation

11 oral presentations

6 poster discussions

87 posters

29 online publications

5 years of Plenary Presentations

2019
POLO

2020
ADAURA

2021
OlympiA

2022
DB04

2023
ADAURA
OS

>40% more abstracts vs ASCO 2019

Key data highlights

ADAURA OS (LBA3)

DUO-O (LBA5506)

DESTINY-PanTumor02 (LBA3000)

TROPION-Lung02 (9004)

Calquence r/r MAIC (7540)

ARTEMIDE-01 (9050)

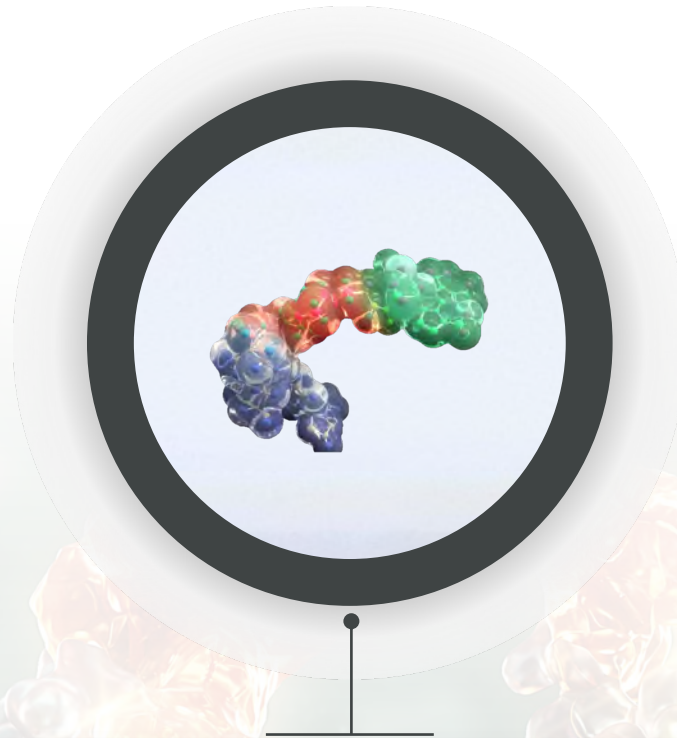


AstraZeneca 2023 – oncology outlook

Strengthening existing leadership positions and expanding innovative pipeline



Reinforce tumour area leadership



Advance novel modalities



Pursue innovative combinations



AstraZeneca in oncology

Diverse portfolio of novel modalities and medicines, supporting potential combinations

Cell therapy

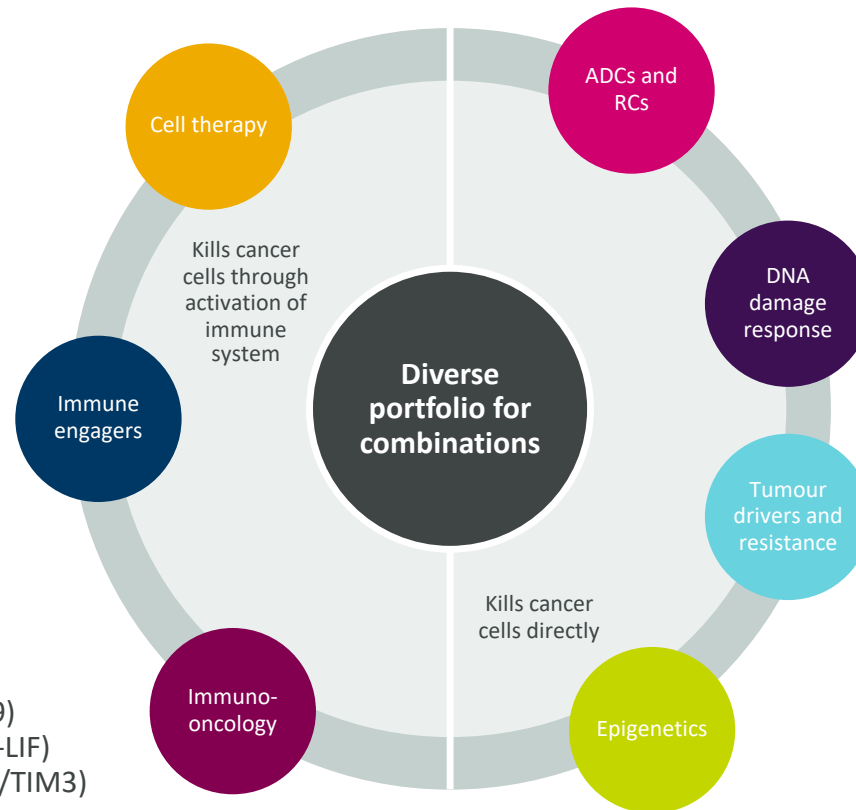
- armoured GPC3 CAR-T
- NT-125 (TCR-T)

Immune engagers

- AZD0486 (CD19xCD3)

Immuno-oncology

- oleclumab
- monalizumab
- volrustomig (PD1/CTLA4)
- rilvegostomig (PD1/TIGIT)
- IPH5201 (CD39)
- AZD0171 (anti-LIF)
- AZD7789 (PD1/TIM3)



ADCs + RCs

- Dato-DXd
- AZD8205 (B7-H4)
- AZD9592 (EGFR/cMET)
- AZD0901 (CLDN18.2)

DNA Damage Response

- ceralasertib (ATR)
- AZD9574 (PARP1BBB)
- saruparib (PARP1sel)
- AZD1390 (ATM)

Tumour Drivers and Resistance

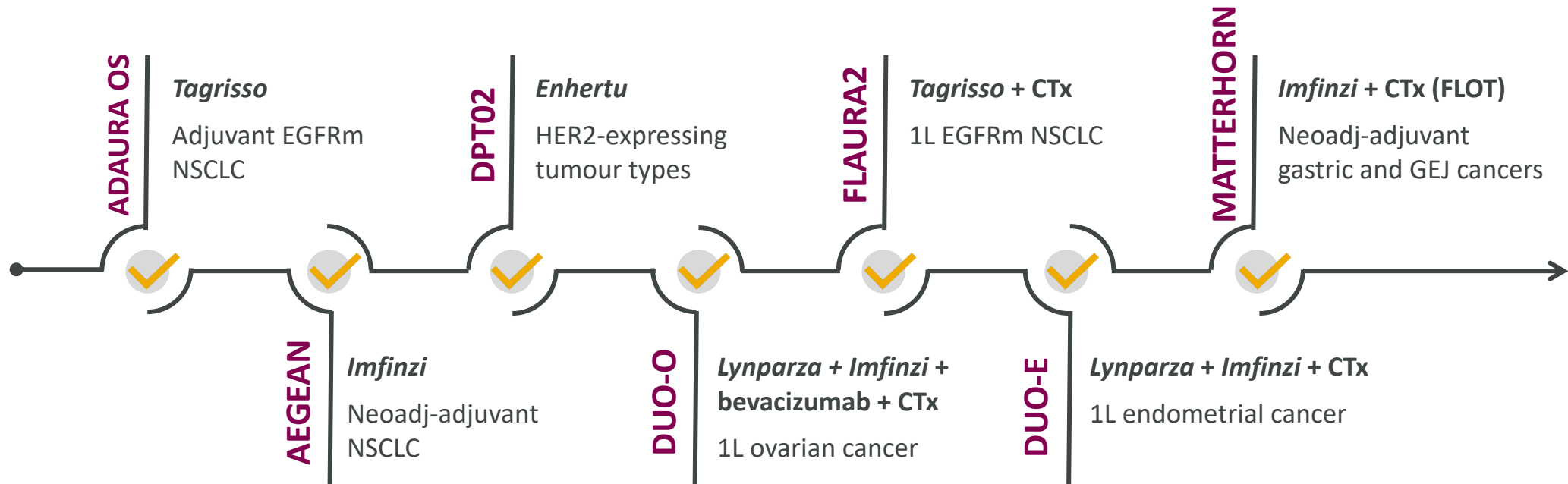
- capivasertib (AKT)
- camizestrant (SERD)
- AZD4573 (CDK9)
- AZD0466 (BCL2-xL)

Epigenetics



AstraZeneca oncology momentum in 2023

Pipeline news flow continues with early efficacy signal in Phase III MATTERHORN trial



7 positive key oncology data read-outs to date in 2023

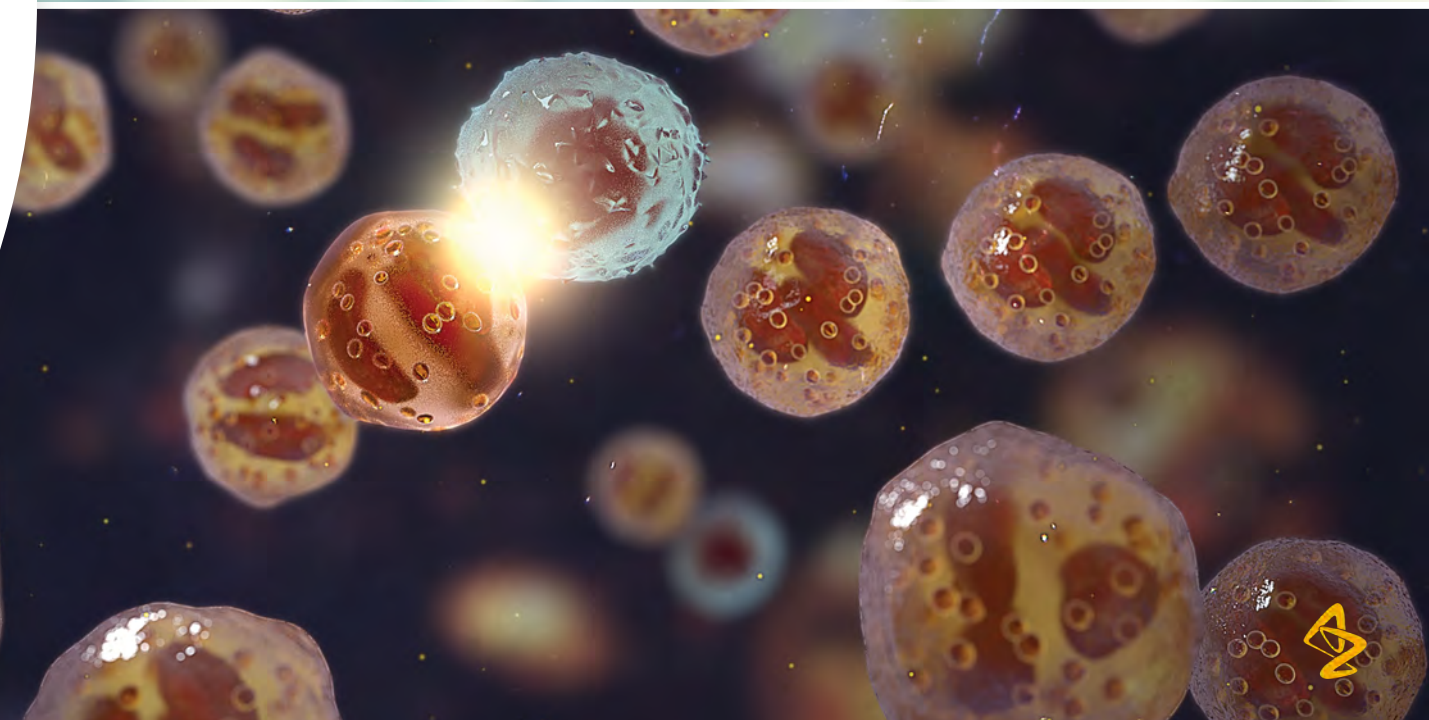


Setting a new milestone in EGFR^m NSCLC

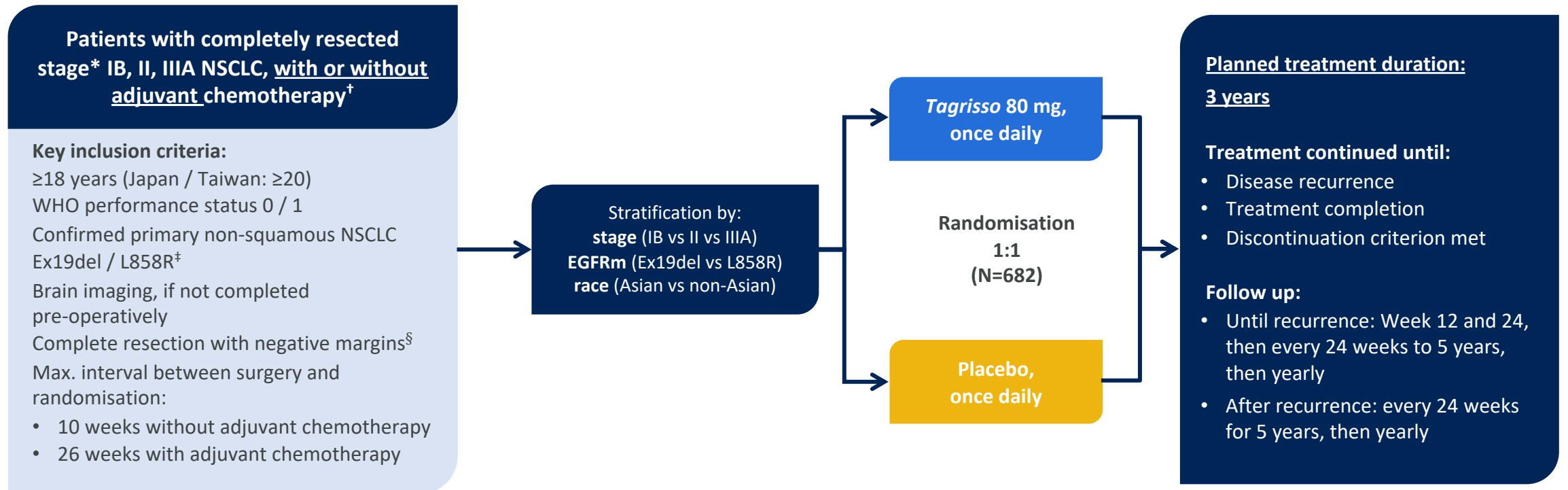
ADAURA OS

Roy Herbst

DEPUTY DIRECTOR, YALE CANCER CENTER
AND SMILOW CANCER HOSPITAL



ADAURA Phase III trial design



Endpoints

- **Primary endpoint:** DFS by investigator assessment in stage II / IIIA patients
- **Key secondary endpoints:** DFS in the overall population (stage IB–IIIA), landmark DFS rates, OS, safety, health-related quality of life

*At the time of recruitment, staging was determined by the AJCC / UICC Staging Manual 7th edition. Patients with stage IB disease were not eligible in Japan. †Pre-operative, post-operative, or planned radiotherapy was not allowed.

‡Centrally confirmed in tissue. §Patients received a CT scan after resection and within 28 days prior to treatment.

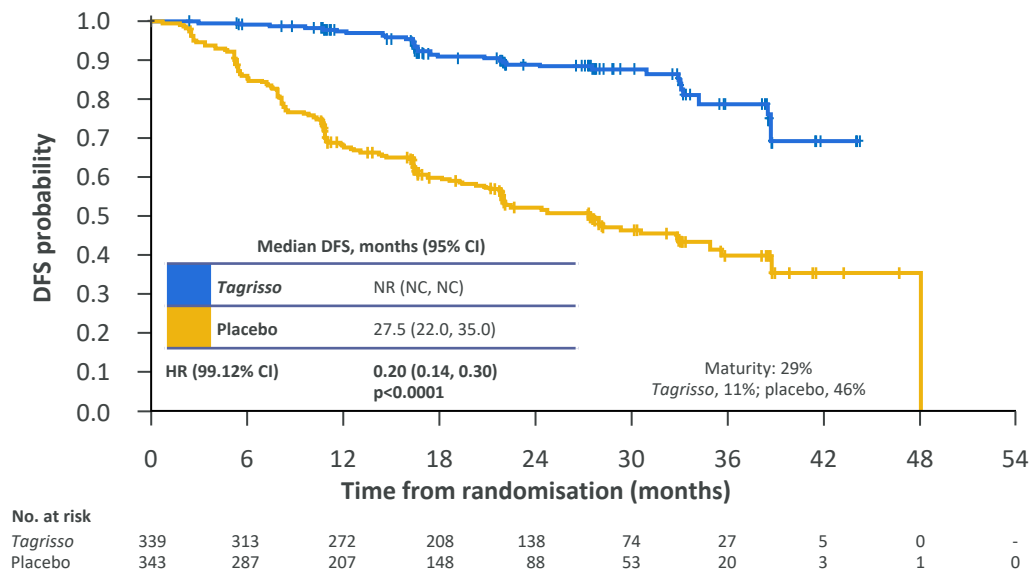
NSCLC = non-small cell lung cancer, EGFRm = epidermal growth factor receptor mutant; DFS = disease-free survival; OS = overall survival.



Adjuvant *Tagrisso* has significantly improved DFS

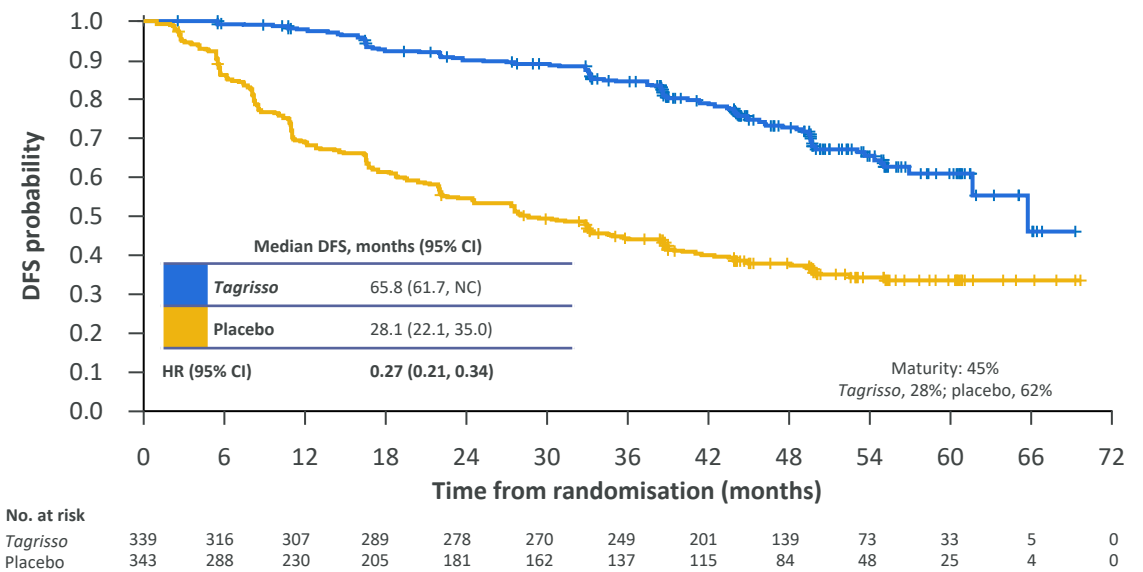
ADAURA primary DFS analysis^{1,2} (stage IB–IIIA)*

Published in NEJM October 2020



ADAURA updated DFS analysis^{3,4} (stage IB–IIIA)[†]

Published in JCO January 2023



- Adjuvant *Tagrisso* has demonstrated a highly statistically significant^{1,2} and clinically meaningful improvement in DFS in completely resected, EGFRm NSCLC vs placebo in both the primary (stage II–IIIA) and overall (IB–IIIA) populations, along with a tolerable safety profile^{1–4}

*Data cut-off: January 17, 2020. † Data cut-off: April 11, 2022.

1. Wu et al. N Engl J Med 2020;383:1711–1723; 2. Herbst et al. J Clin Oncol 2020;38(Suppl 18): abstract / oral LBA5; 3. Herbst et al. J Clin Oncol 2023;41:1830–1840; 4. Tsuboi et al. Ann Oncol 2022;33(Suppl 7): abstract / oral LBA47.

DFS = disease free survival; NEJM = New England Journal of Medicine; JCO = Journal of Clinical Oncology; HR = hazard ratio; CI = confidence interval; NC = not calculable; NR = not reached; no. = number; EGFRm = epidermal growth factor receptor-mutated; NSCLC = non-small cell lung cancer.



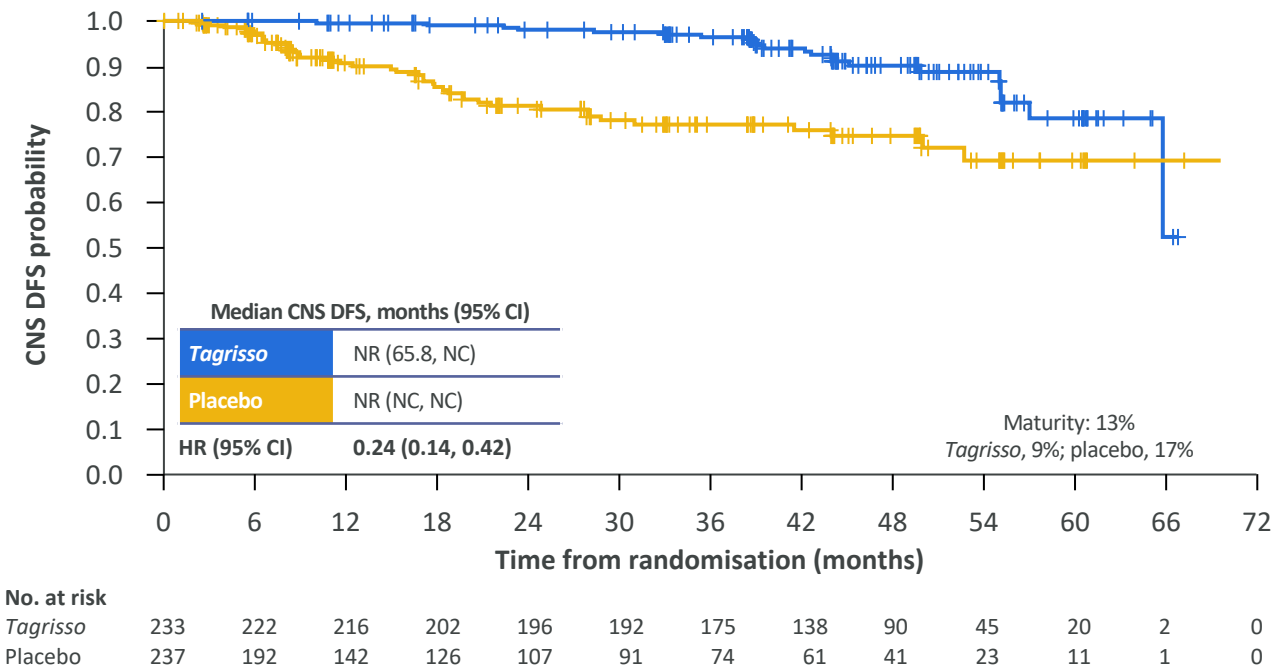
Adjuvant *Tagrisso* has significantly improved CNS DFS

Improved CNS efficacy with *Tagrisso* treatment

- *Tagrisso* has been shown to achieve clinically significant exposure in the brain compared with other EGFR-TKIs, and has shown greater penetration of the blood-brain barrier¹⁻³
- Adjuvant *Tagrisso* demonstrated CNS DFS benefit vs placebo in both the Stage II–IIIA and IB–IIIA populations; in the updated CNS DFS analysis, 63 patients (*Tagrisso* n=22, placebo n=41) had CNS DFS events^{4,5*}

ADAURA updated CNS DFS analysis^{4,5} (stage II–IIIA)

Published in JCO January 2023



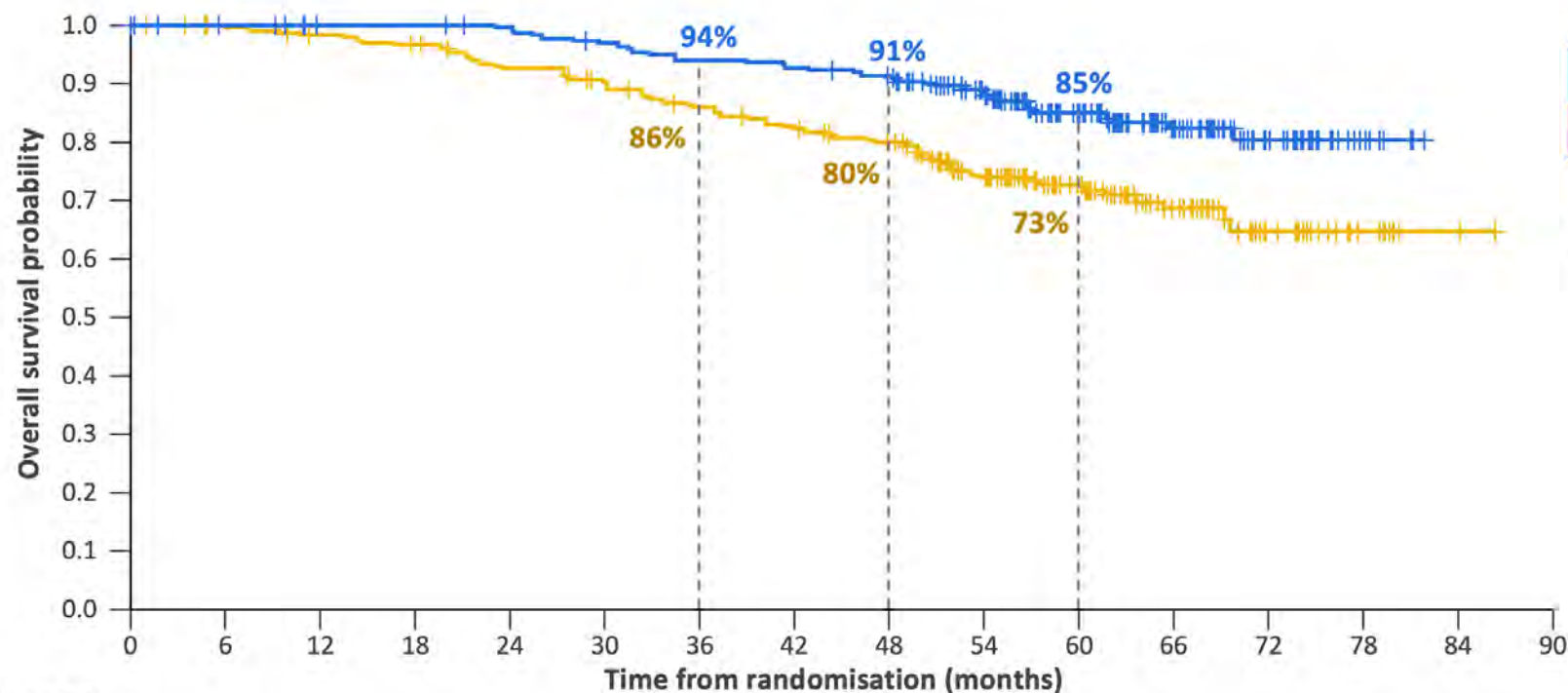
CNS metastases are a poor prognostic factor among patients with NSCLC, associated with deterioration in quality of life⁶

Data cut-off: April 11, 2022. *Defined as CNS as the first site of disease recurrence, or death without any disease recurrence.

Colclough et al. Eur J Cancer 2016;69:S28; 2. Ballard et al. Clin Cancer Res 2016;22:5130–5140; 3. Vishwanathan et al. Cancer Res 2018; 78:CT013; 4. Herbst et al. J Clin Oncol 2023;41:1830–1840; 5. Tsuboi et al. Ann Oncol 2022;33(Suppl 7): abstract / oral LBA47; 6. Peters et al. Cancer Treat Rev 2016;45:139–162.



Overall survival: patients with stage II/IIIA disease



5-year OS rate, % (95% CI)	
Tagrisso (n=233)	85 (79, 89)
Placebo (n=237)	73 (66, 78)

Overall OS HR (95.03% CI) 0.49 (0.33, 0.73); p=0.0004

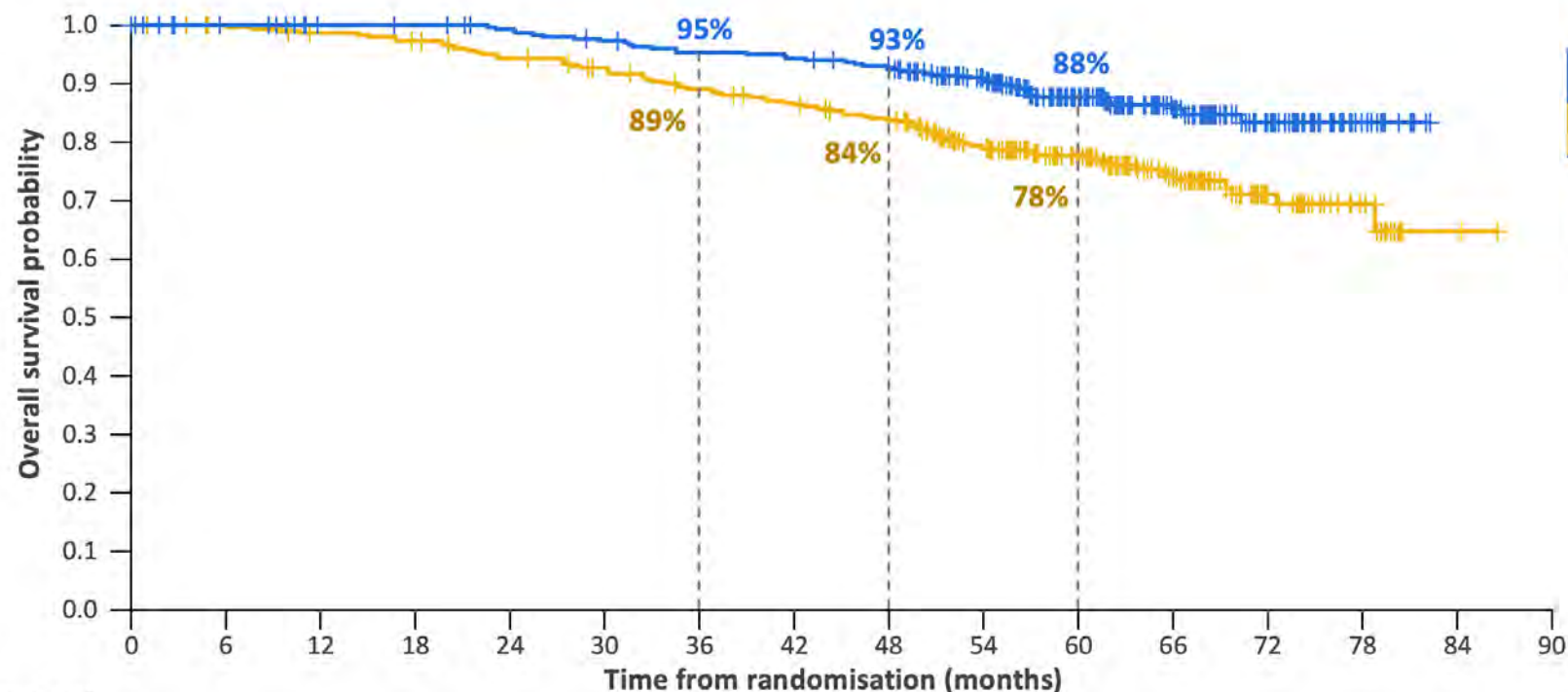
Maturity: 21%
Tagrisso 15%, placebo 27%

Median follow-up for OS* (censored patients):
Tagrisso 61.7 months, placebo 60.4 months

No. at risk		0	6	12	18	24	30	36	42	48	54	60	66	72	78	84	90
Tagrisso	233	229	224	224	221	214	208	205	200	170	115	69	33	9	0	-	
Placebo	237	232	226	221	210	202	190	182	171	138	94	53	25	8	2	0	



Overall survival: overall population (stage IB/II/IIIA disease)



5-year OS rate, % (95% CI)	
Tagrisso (n=339)	88 (83, 91)
Placebo (n=343)	78 (73, 82)

Overall OS HR **0.49 (0.34, 0.70);**
(95.03% CI) **p<0.0001**

Maturity: 18%
 Tagrisso 12%, placebo 24%

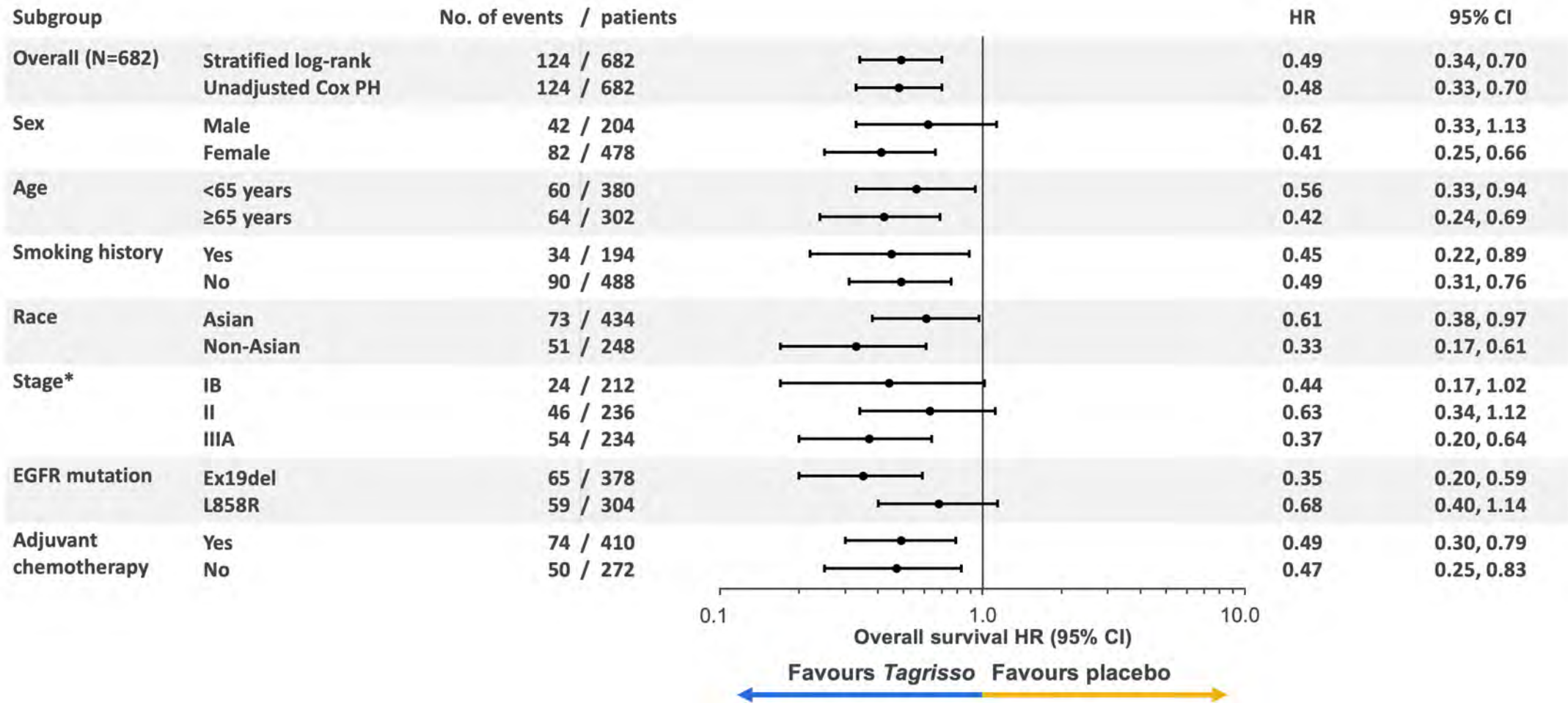
Median follow-up for OS* (censored patients):
Tagrisso 61.5 months, placebo 61.5 months

No. at risk		0	6	12	18	24	30	36	42	48	54	60	66	72	78	84	90
Tagrisso	339	332	325	324	319	311	304	301	294	252	176	108	50	15	0	-	-
Placebo	343	338	332	326	314	304	290	281	267	223	164	97	44	17	3	0	0

- Adjuvant *Tagrisso* demonstrated a statistically and clinically significant improvement in OS vs placebo in the overall population of stage IB-III A disease



OS across subgroups: overall population (stage IB/II/IIIA)



Safety summary

- At the final DFS analysis (data cut-off: 11 April 2022), all patients had completed or discontinued study treatment; the safety profile of adjuvant *Tagrisso* with extended follow-up^{1,2} was consistent with the ADAURA primary analysis³

AE, any cause*, n (%)	Tagrisso (n=337)	Placebo (n=343)
Any AE	330 (98)	309 (90)
Any AE Grade ≥3	79 (23)	48 (14)
Any AE leading to death	1 (<1)	2 (1)
Any serious AE	68 (20)	47 (14)
Any AE leading to discontinuation	43 (13)	9 (3)
Any AE leading to dose reduction	42 (12)	3 (1)
Any AE leading to dose interruption	91 (27)	43 (13)
AE, possibly causally related*†, n (%)		
Any AE	308 (91)	199 (58)
Any AE Grade ≥3	36 (11)	7 (2)
Any AE leading to death	0	0
Any serious AE	10 (3)	2 (1)

- At the time of the current data cut-off (27 January 2023), one additional serious AE (COVID-19 pneumonia) had been reported, which occurred >28 days after treatment discontinuation; the investigator determined that this was not treatment-related and the patient made a full recovery

*Data cut-off: April 11, 2022. Patients with multiple events in the same category counted only once in that category. Patients with events in more than one category 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. †As assessed by the investigator.

1. Herbst et al. J Clin Oncol 2023;41:1830–1840; 2. John et al. J Thorac Oncol 2023; accepted and under revision; 3. Wu et al. N Engl J Med 2020;383:1711–1723.

DFS = disease-free survival; AE = adverse event; COVID-19 = coronavirus disease 2019.



Conclusions

- In the ADAURA primary analysis, adjuvant *Tagrisso* demonstrated a statistically significant¹ and clinically meaningful DFS benefit vs placebo in resected EGFRm stage IB–IIIA NSCLC, along with improved CNS DFS and a tolerable safety profile^{1,2}
- **DFS benefit in ADAURA has translated into a statistically significant OS benefit with adjuvant *Tagrisso* vs placebo**
 - **Primary (stage II–IIIA) population, OS HR 0.49; 95.03% CI 0.33, 0.73; p=0.0004**
 - **Overall (stage IB–IIIA) population, OS HR 0.49; 95.03% CI 0.34, 0.70; p<0.0001**
- OS benefit with adjuvant *Tagrisso* vs placebo was generally consistent across subgroups, including by disease stage (IB / II / IIIA) and prior adjuvant chemotherapy use (yes / no)
- **ADAURA is the first global Phase III study to demonstrate statistically significant and clinically meaningful OS benefit with targeted treatment in this patient population, reinforcing adjuvant *Tagrisso* as the standard of care for patients with resected EGFRm stage IB–IIIA NSCLC**

Data cut-off: January 27, 2023.

20 1. Wu et al. N Engl J Med 2020;383:1711-1723; 2. Herbst et al. J Clin Oncol 2023; 41: 1830-1840.

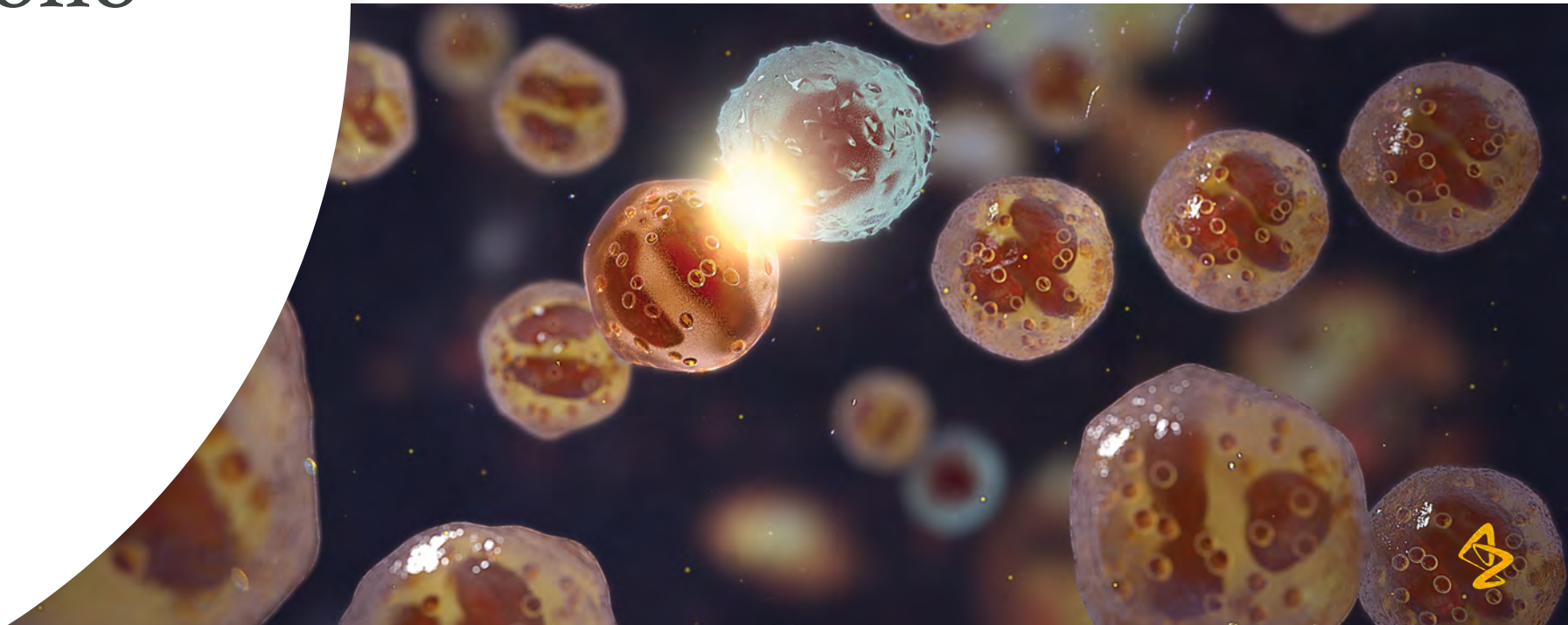
DFS = disease-free survival; EGFRm = epidermal growth factor receptor-mutated; NSCLC = non-small cell lung cancer; CNS = central nervous system; OS = overall survival; HR = hazard ratio.



Strengthening presence in lung cancer & advancing emerging portfolio

Susan Galbraith
ONCOLOGY R&D

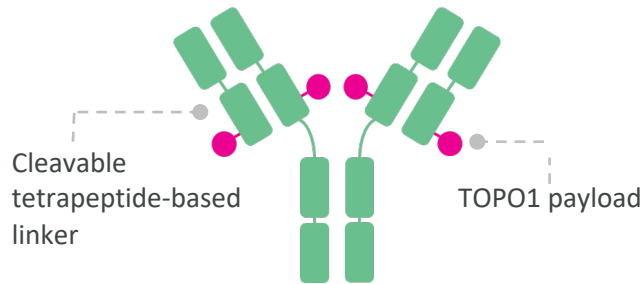
Dave Fredrickson
ONCOLOGY BUSINESS



Dato-DXd

Best-in-class TROP2 ADC investigated in monotherapy and novel combinations

Dato-DXd



- High-potency TOPO1 payload
- Payload with short systemic half-life
- Optimised DAR ~4
- Tumour-selective cleavable linker
- Bystander anti-tumour effect

Clinical development programme supports Dato-DXd strategy

> Potential to replace CTx as monotherapy and as backbone

- First Phase III trials in lung and breast HLR anticipated 2023
- Ongoing signal generation in multiple tumour types beyond lung and breast

> Further outcomes with novel combination regimens

- Emerging IO combination efficacy with studies in 1L metastatic and earlier-line setting
- Signal-finding with other assets ongoing (e.g., *Tagrisso*)

> Assess predictive value of TROP2 biomarker

7 ongoing Phase III trials across NSCLC and breast cancer



Lung

- TROPION-Lung01 (HLR H1 2023)
- TROPION-Lung07 (HLR >2024)
- TROPION-Lung08 (HLR >2024)
- AVANZAR (HLR >2024)



Breast

- TROPION-Breast01 (HLR H2 2023)
- TROPION-Breast02 (HLR 2024)
- TROPION-Breast03 (HLR >2024)

Data-driven Phase III opportunities across multiple tumour areas



TROPION-Lung02

Phase Ib investigating Dato-DXd + pembrolizumab ± PDx in 1L/2L+ mNSCLC

Key eligibility criteria

- Advanced/metastatic NSCLC
- **Dose escalation**^a: ≤2 lines of prior therapy^b
- **Dose expansion**
 - ≤1 line of platinum-based CTx (cohorts 1 and 2)^b
 - Treatment naive (cohort 2; enrollment after Jun 30, 2022)^b
 - Treatment naive (cohorts 3-6)^b

Cohort 1 (n=20):

Dato-DXd IV Q3W + pembro IV Q3W + platinum CT IV Q3W

4 mg/kg + 200 mg

Cohort 2 (n=44):

6 mg/kg + 200 mg

Doublet

Cohort 3 (n=20):

4 mg/kg + 200 mg + carboplatin AUC 5

Cohort 4 (n=30):

6 mg/kg + 200 mg + carboplatin AUC 5

Cohort 5 (n=12):

4 mg/kg + 200 mg + cisplatin 75 mg/m²

Cohort 6 (n=10):

6 mg/kg + 200 mg + cisplatin 75 mg/m²

Triplet

- **Primary objectives:** safety and tolerability
- **Secondary objectives:** efficacy, pharmacokinetics, and antidrug antibodies

^aThe first 3 to 6 patients in each cohort were enrolled to confirm acceptable safety/DLT rate; the remaining patients are considered part of dose expansion (for which enrollment was ongoing at the time of data cutoff). ^bPrior therapy requirements are for treatment in the advanced/metastatic setting.

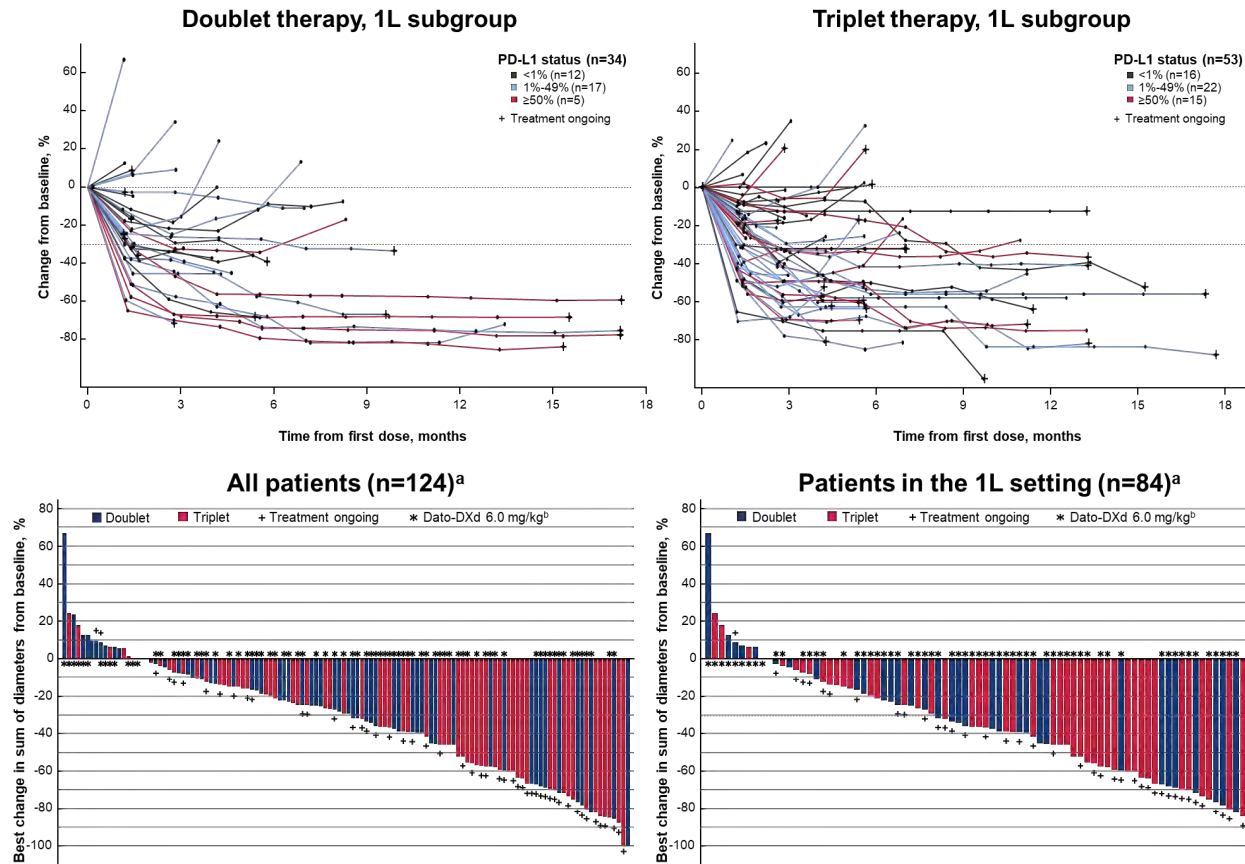
Dato-DXd = datopotamab deruxtecan; pembro = pembrolizumab; PDx = platinum chemotherapy; 1L = 1st-line; 2L = 2nd-line; mNSCLC = metastatic non-small cell lung cancer; CTx = chemotherapy; IV = intravenous; Q3W = every three weeks; AUC = area under the free carboplatin plasma concentration versus time curve.

Collaboration partners: Daiichi Sankyo (Dato-DXd).



TROPION-Lung02

Further follow-up reinforces encouraging efficacy with doublet and triplet regimens



- Overall DCR 84% (doublet), 87% (triplet)
 - In 1L setting DCR 91% (doublet and triplet)
- In 1L, ORR 50% (doublet) and 57% (triplet)
- mPFS 8.3 months (doublet), 7.8 months (triplet)^c
- TROPION-Lung02 findings supportive of ongoing pivotal Phase III 1L trials:
 - TROPION-Lung07 (non-squamous w/o AGA, PD-L1 <50%)
 - TROPION-Lung08 (w/o AGA, PD-L1 ≥ 50%)
 - AVANZAR (w/o AGA)

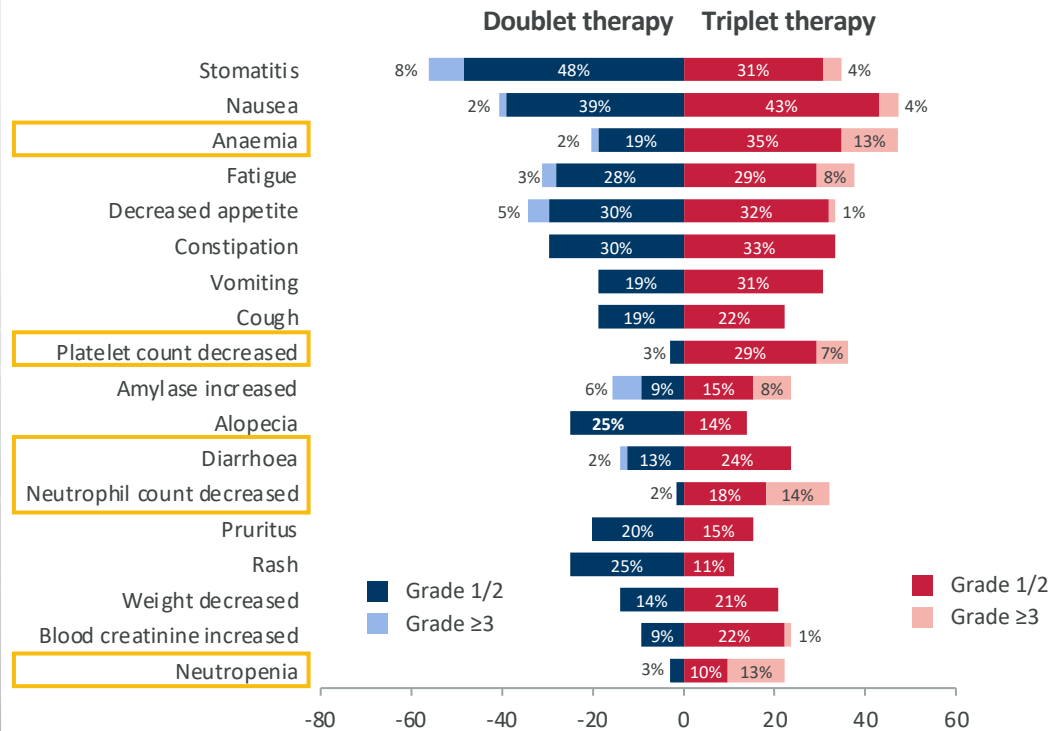
^aPatients with no baseline target lesions or no postbaseline tumor assessments were excluded from the waterfall plots. ^bPlanned dose level; ^cPreliminary PFS is limited by immature duration of follow-up. Dato-DXd = datopotamab deruxtecan; pembro = pembrolizumab; PDx = platinum chemotherapy; 1L = 1st-line; 2L = 2nd-line; mNSCLC = metastatic non-small cell lung cancer; PD-L1 = programmed cell death ligand 1; DCR = disease control rate; ORR = objective response rate; mPFS = median progression-free survival; AGA = actionable genomic alterations. Collaboration partners: Daiichi Sankyo (Dato-DXd).



TROPION-Lung02

Safety and tolerability profile supports dose for ongoing Phase III 1L trials

TEAEs occurred in $\geq 20\%$ of patients



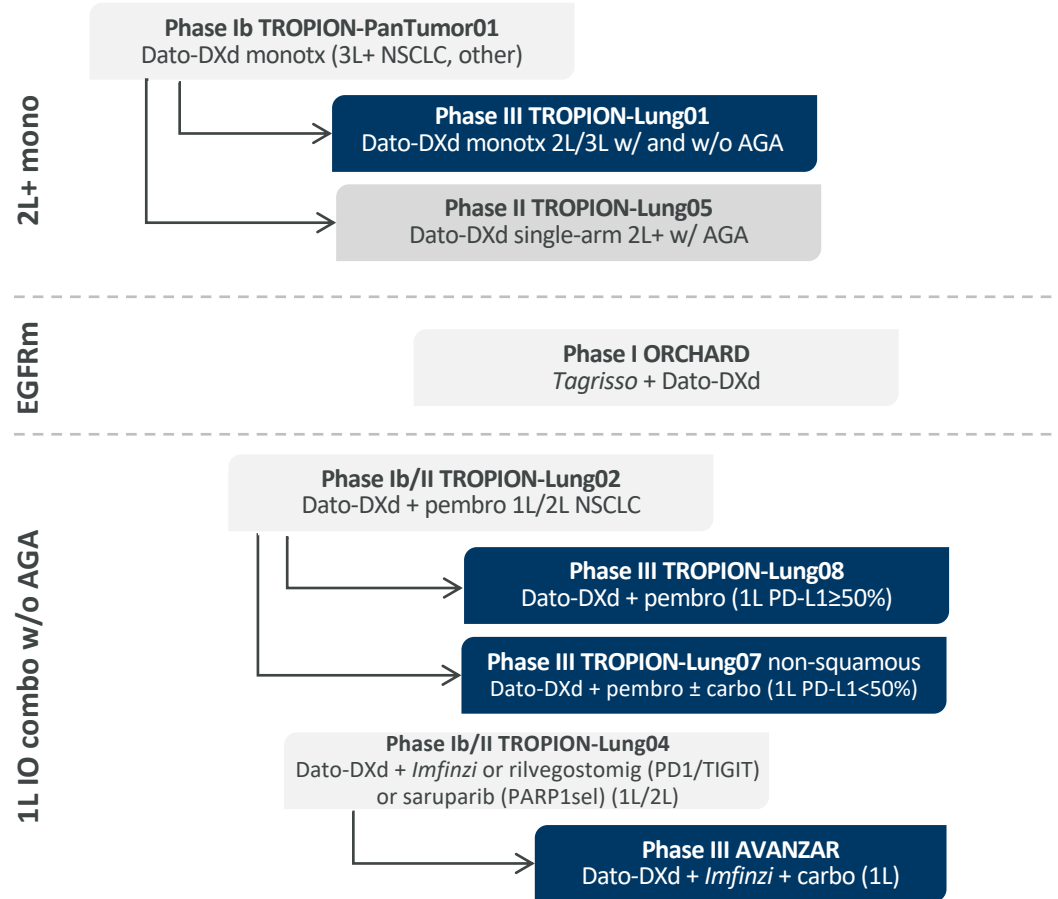
Safety summary

- No new safety signals were observed
- No adjudicated Grade 4 or 5 ILDs attributable to Dato-DXd
- Grade ≥ 3 ILD 3% for both doublet and triplet; similar rates to existing SoC
- Haematological toxicity was manageable with lower rates observed in doublet arm
- Safety data supports use of 6mg/kg dose in 1L NSCLC pivotal Phase III trials (TROPION-Lung07 and TROPION-Lung08)



Dato-DXd in NSCLC

Potential to replace current SoC CTx in 2L+ and establish Dato-DXd as backbone in 1L



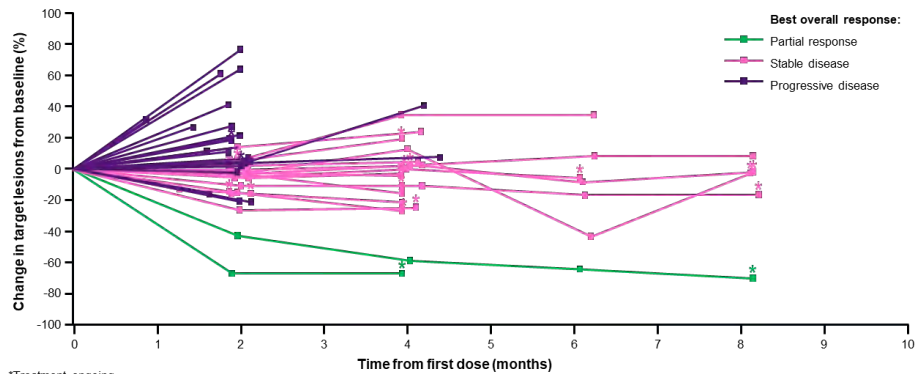
- Replace current chemotherapy as monotherapy
- Pursue novel combinations based on supportive evidence (TROPION-PanTumor01)
- Move Dato-DXd earlier in treatment paradigm in combinations to improve outcomes
- Provide evidence across spectrum of PD-L1 levels
- Assess predictive value of TROP2 biomarker



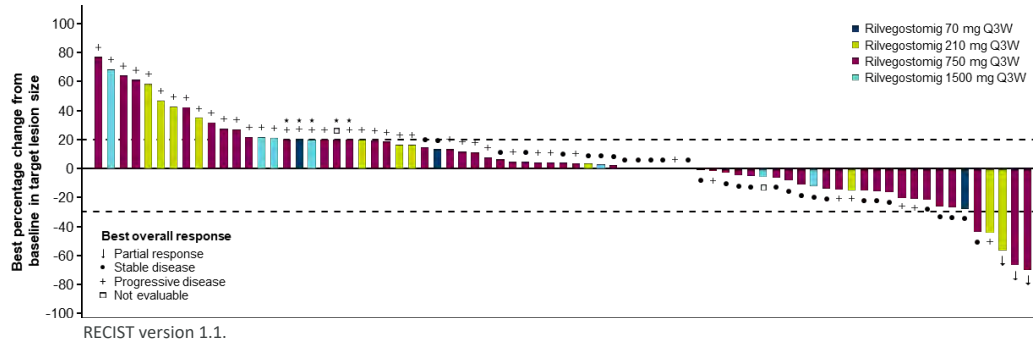
ARTEMIDE-01

Rilvegostomig showed encouraging preliminary anti-tumour activity in CPI-experienced NSCLC

Percentage change from baseline in target lesion size over time at RP2D (750mg IV Q3W)



Best percentage change from baseline in target lesion size, all doses¹



Summary and key conclusions

- Demonstrated encouraging preliminary anti-tumour activity as 2L+ in pre-treated mNSCLC
- Rationale to further test rilvegostomig in CPI-naïve mNSCLC patients (expansion Part C and D)
- Safety established at all doses in patients previously treated with CPI and PDx
- No DLTs observed during dose escalation

Planning to initiate Phase III trial in 2023

1. Imputed data: If best percentage change cannot be calculated due to missing data (including if the patient has no TLs at baseline), a value of +20% is imputed in the following situations: if a patient has no post baseline assessment and has died, if a patient has new lesions or progression of NTLs or TLs, or if a patient has withdrawn due to progressive disease and has no evaluable TL data before or at progression

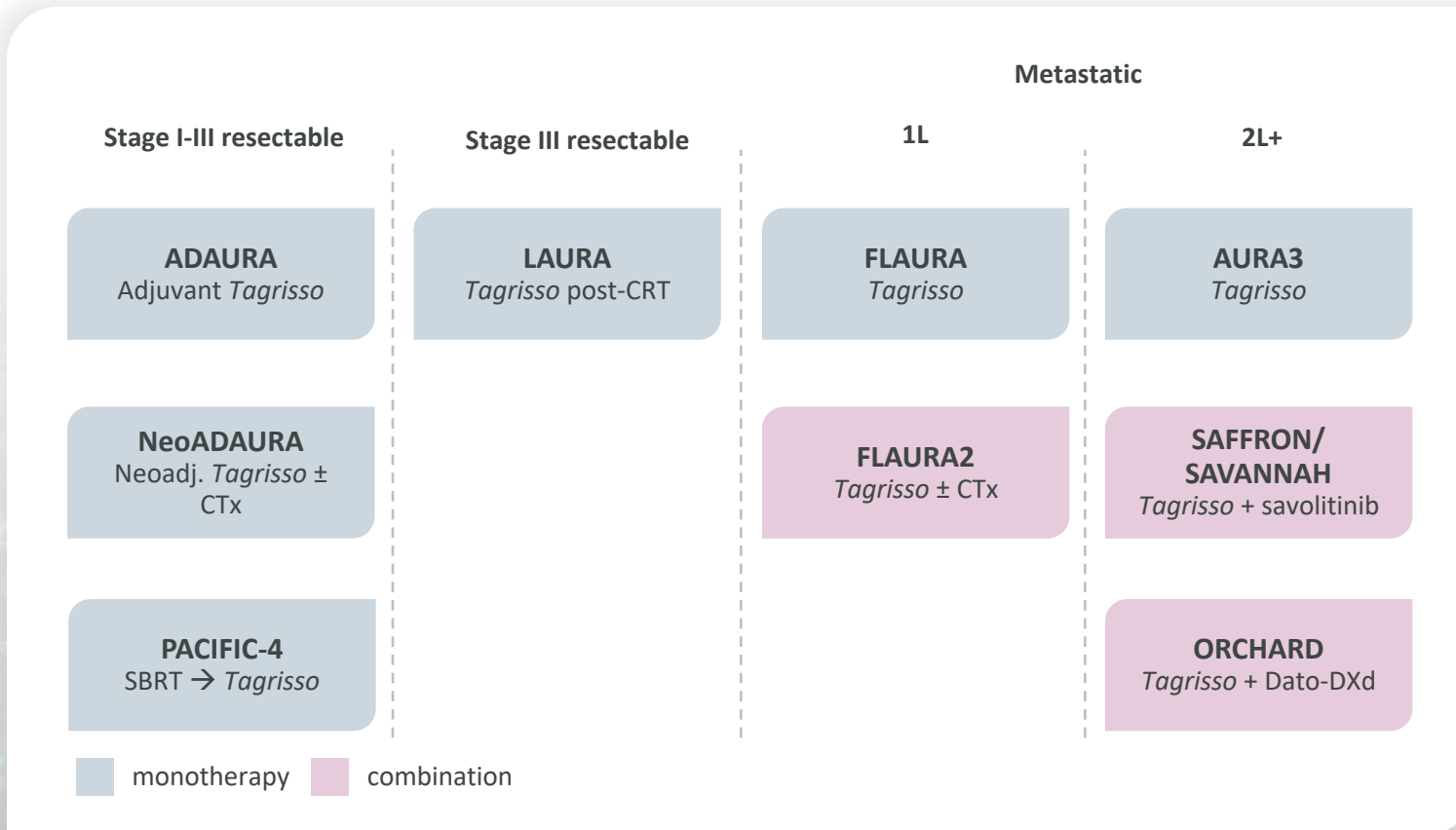
PD1 = programmed cell death protein 1; TIGIT = T cell immunoreceptor with Ig and ITIM domains; (m)NSCLC = (metastatic) non-small cell lung cancer; RP2D = recommended Phase II dose; IV = intravenous; Q3W = every 3 weeks; RECIST = response evaluation criteria in solid tumours; NTL = non-target lesion; TL = target lesion; CPI = checkpoint inhibitor; PDx = platinum chemotherapy; DLTs = dose limiting toxicities.

Collaboration partners: Compugen (rilvegostomig).



Tagrisso

On track to establish *Tagrisso* as backbone TKI for the treatment of EGFRm NSCLC



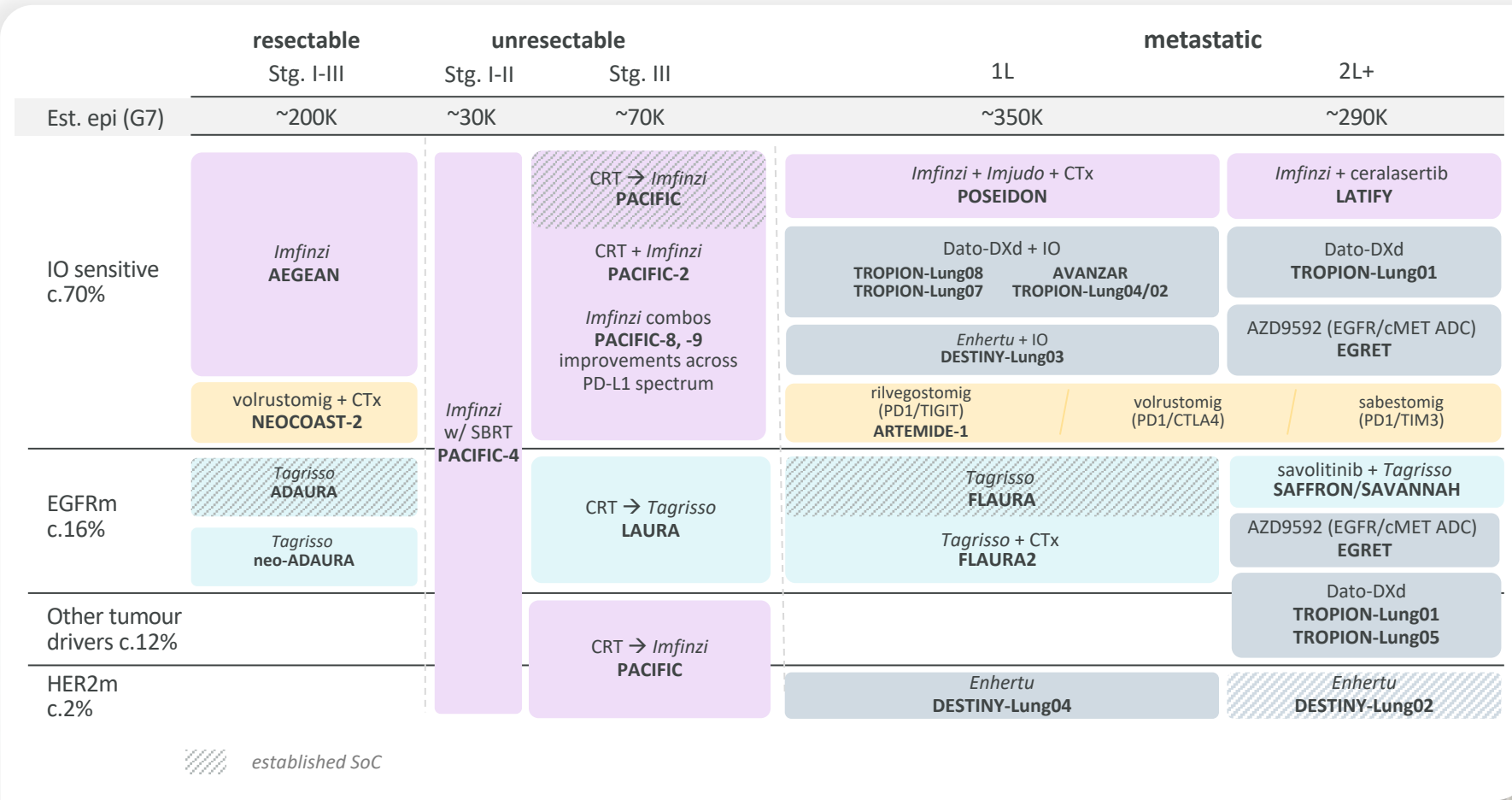
- ADAURA OS expands potential geographic reach in adjuvant
 - Closing care caps
 - Reimbursement
- Anticipate FLAURA remains SoC in 1L EGFRm NSCLC; FLAURA2 offers CTx combination approach
- Address biomarker-driven resistance and advance novel combinations

ADAURA OS data, FLAURA2 Phase III HLR expands patient reach



AstraZeneca in Lung Cancer

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



Leading the future of lung cancer treatment

- *Tagrisso* established TKI backbone in EGFRm
- *Imfinzi* leading IO in unresectable
- Advancing best-in-class ADCs to replace systemic chemotherapy
- Delivering next-wave bispecifics to improve on PD1/PD-L1
- Developing novel combinations, including IO + ADC
- Investing behind new technologies and platforms, including cell therapy, testing/screening

Est epi (G7) = estimated epidemiology across G7 (US, EU5, JP); Stg. = stage; CTx = chemotherapy; SBRT = stereotactic body radiation therapy; CRT = chemoradiotherapy; pembro = pembrolizumab; IO = immunotherapy; ADC = antibody-drug conjugate; PD1 = programmed cell death protein 1; EGFR = epidermal growth factor receptor; c-MET = mesenchymal-epithelial transition factor; TIGIT = T-cell immunoreceptor with immunoglobulin and ITIM domains; CTLA4 = cytotoxic T-lymphocyte associated protein 4;

TIM3 = T-cell immunoglobulin and mucin domain-containing protein 3; SoC = standard of care; TKI = tyrosine kinase inhibitor.

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



AstraZeneca @ ASCO 2023

Q&A Session I: Focus on Lung Cancer

KEY EXTERNAL EXPERT



Roy Herbst

DEPUTY DIRECTOR,
YALE CANCER CENTER AND
SMILOW CANCER HOSPITAL

ABBREVIATED BIOGRAPHY

Dr Herbst is nationally recognised for his leadership and expertise in lung cancer treatment and research. He is best known for his work in developmental therapeutics and the personalised therapy of non-small cell lung cancer, in particular the process of linking genetic abnormalities of cancer cells to novel therapies.

Prior to his appointment at Yale, Dr Herbst was the Barnhart Distinguished Professor and Chief of the Section of Thoracic Medical Oncology in the Department of Thoracic/Head and Neck Medical Oncology, at The University of Texas M.D. Anderson Cancer Center (UT-MDACC) in Houston, Texas. He also served as Professor in the Department of Cancer Biology and Co-Director of the Phase I Clinical Trials Program.

MODERATORS



Susan Galbraith,
*Executive Vice President,
Oncology R&D*

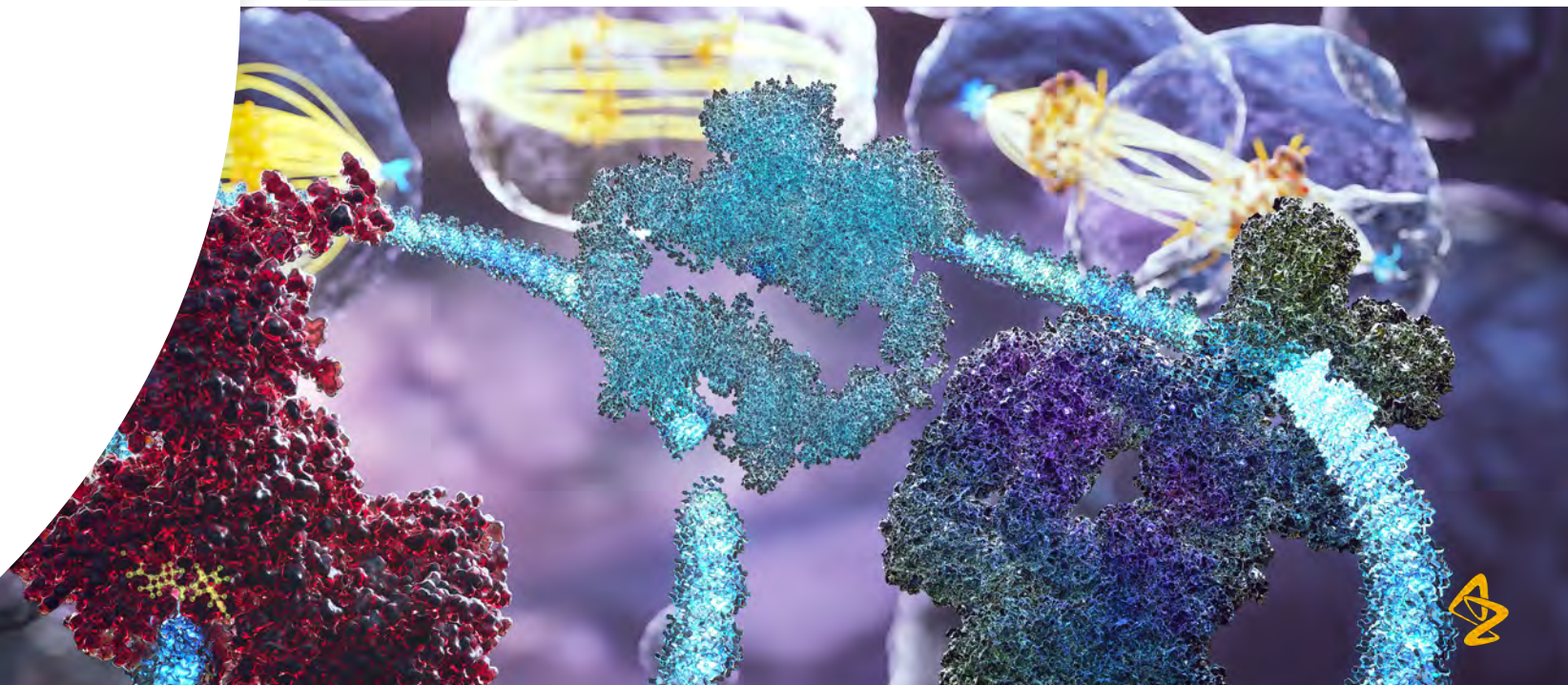


Dave Fredrickson,
*Executive Vice President,
Oncology Business*



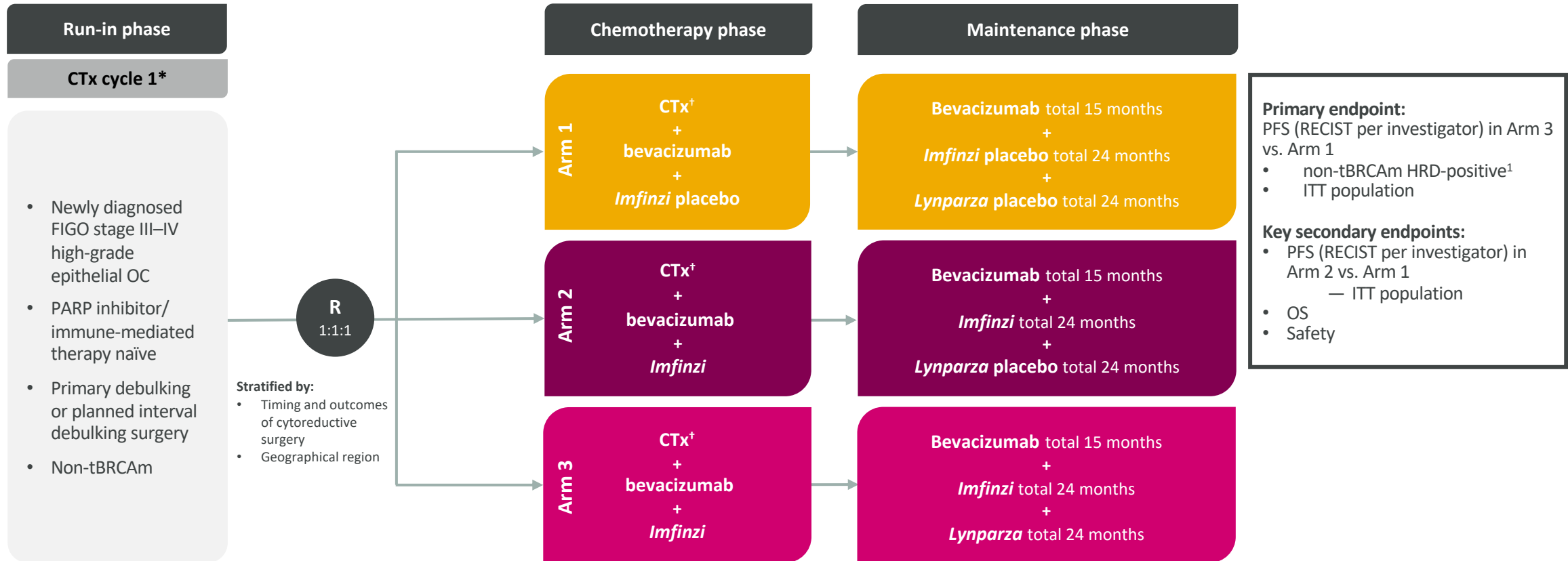
Investigating novel combinations in ovarian cancer

Susan Galbraith
ONCOLOGY R&D



DUO-O Phase III

Investigating combination of *Lynparza*, *Imfinzi*, chemotherapy and bevacizumab



Treatment continued until disease progression, study treatment was complete or other discontinuation criteria were met

DCO: December 5, 2022. DUO-O also included an independent single arm open label tBRCAm cohort – results are not presented.

*With or without bevacizumab according to local practice; †Cycles 2–6; ‡Genomic instability score ≥42 assessed by Myriad MyChoice CDx assay.

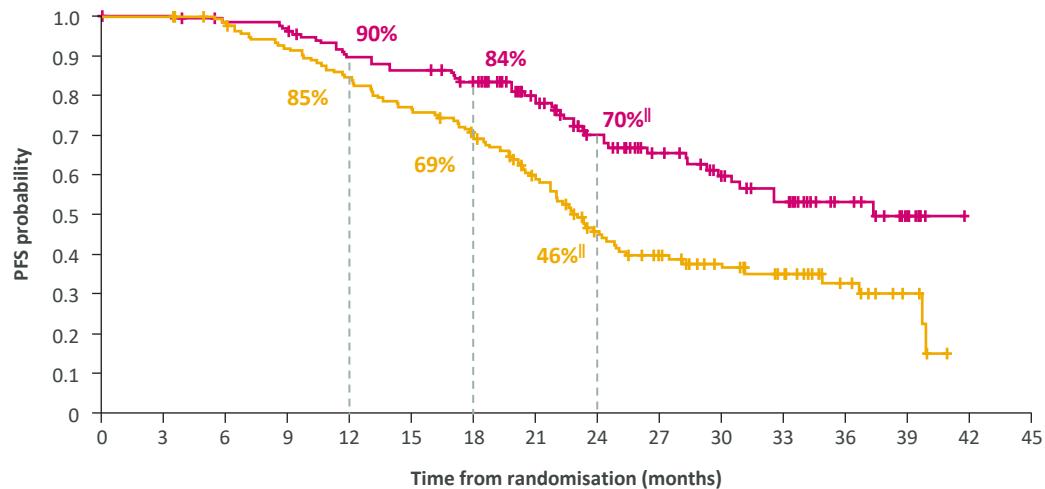
CTx, chemotherapy; FIGO, International Federation of Gynecology and Obstetrics; OC = ovarian cancer; tBRCAm = tumour BRCA-mutated; R = randomisation; PC = paclitaxel/carboplatin; bev = bevacizumab; PFS = progression-free survival; RECIST = Response Evaluation Criteria for Solid Tumours; HRD = homologous recombination deficiency; ITT = intent-to-treat; OS = overall survival.



DUO-O Phase III

Significant improvement in HRD-positive and overall population vs chemotherapy + bevacizumab

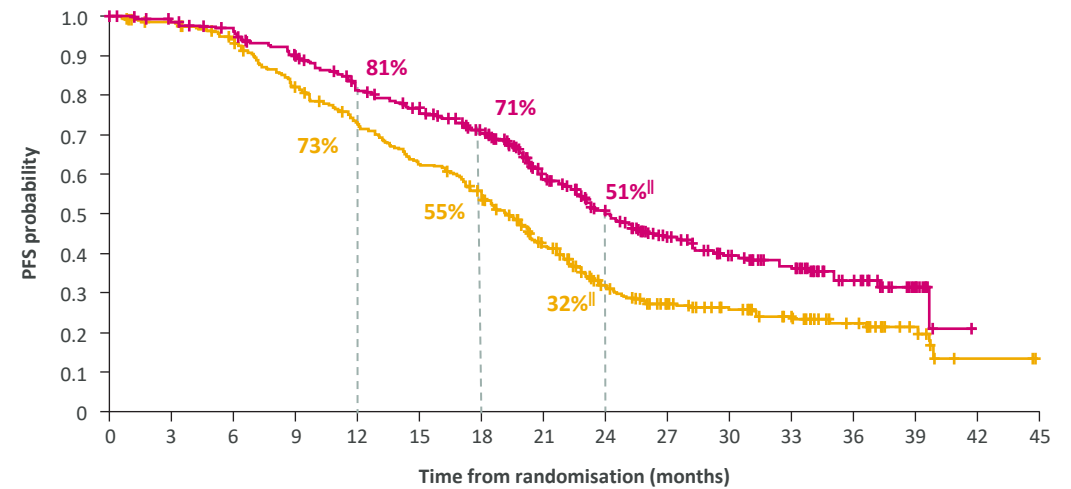
PFS: HRD-positive subgroup (n=431, 38% population*)



No. at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45
Arm 1	143	141	136	126	116	105	93	73	52	41	31	22	13	6	0	
Arm 3	140	138	135	131	120	116	107	84	63	49	39	32	17	6	0	

	Arm 1 PC + bev N=143	Arm 3 PC + bev + Imfinzi + Lyn N=140
Events, n (%)	86 (60)	49 (35)
Median PFS, [†] m	23.0	37.3 [‡]
HR (95% CI) vs Arm 1	0.49 (0.34–0.69) [§] P<0.0001	

PFS: ITT (n=1130)



No. at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45
Arm 1	378	363	341	297	260	223	189	130	87	63	51	35	23	11	2	0
Arm 3	378	366	351	323	286	266	228	163	123	84	65	52	27	9	0	

	Arm 1 PC + bev N=378	Arm 3 PC + bev + Imfinzi + Lyn N=378
Events, n (%)	259 (69)	193 (51)
Median PFS, [†] m	19.3	24.2
HR (95% CI) vs Arm 1	0.63 (0.52–0.76) [§] P<0.0001	

Median follow-up in HRD-positive subgroup: Arm 1 28.8 months, Arm 3 25.6 months; ITT: Arm 1 25.5 months, Arm 3 23.3 months (median follow up in censored patients).

*n=434 includes patients in all arms, Arm 1 n=144, Arm 2 n=150, Arm 3 n=140; [†]Medians and rates were estimated by KM method; [‡]24-month PFS rates unstable. Median PFS in Arm 3 unstable. [§]HR and CI were estimated from a stratified Cox proportional hazards model. P value from a stratified log rank test. Model stratified by timing and outcome of cytoreductive surgery.

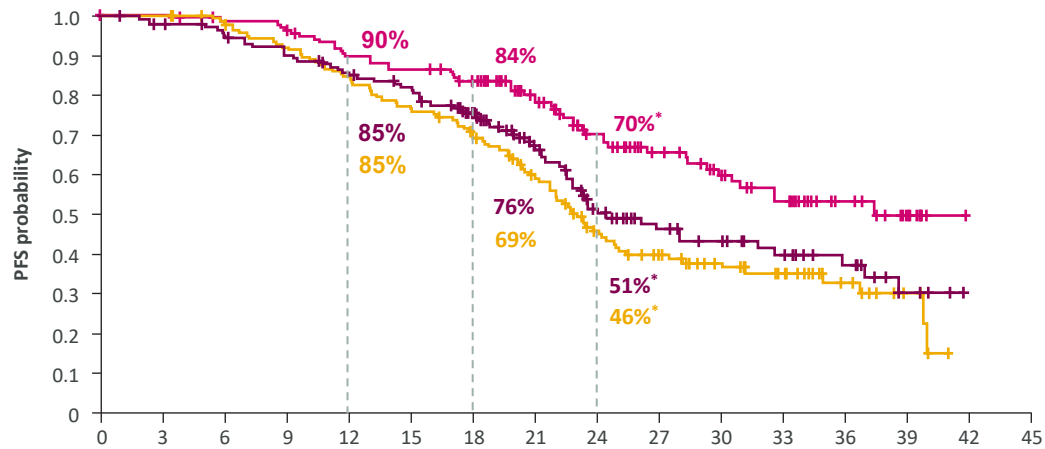
PFS = progression-free survival; HRD = homologous recombination deficient; ITT = intent-to-treat; no. = number; PC = paclitaxel/carboplatin; bev = bevacizumab; Lyn = Lynparza; m = months; HR = hazard ratio; CI = confidence interval; KM = Kaplan–Meier.



DUO-O Phase III

PFS benefit observed across HRD subgroups

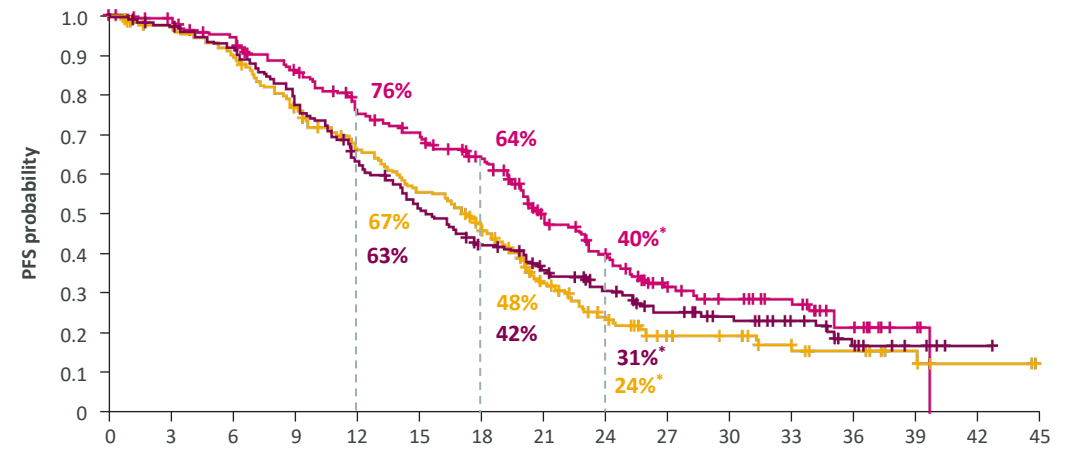
PFS: HRD-positive subgroup (n=431, 38% population)



No. at risk	Time from randomisation (months)														
Arm 1	143	141	136	126	116	105	93	73	52	41	31	22	13	6	0
Arm 2	148	142	137	128	118	112	94	66	45	34	28	21	15	7	0
Arm 3	140	138	135	131	120	116	107	84	63	49	39	32	17	6	0

	Arm 1 PC + bev N=143	Arm 2 PC + bev + Imfinzi N=148	Arm 3 PC + bev + Imfinzi + Lyn N=140
Events, n (%)	86 (60)	69 (47)	49 (35)
Median PFS, [†] m	23.0	24.4 [‡]	37.3 [‡]
HR (95% CI) vs Arm 1		0.82 (0.60–1.12) [§]	0.51 (0.36–0.72) [§]

PFS: HRD-negative subgroup (n=626, 55% population)



No. at risk	Time from randomisation (months)															
Arm 1	216	203	188	159	135	112	92	55	34	21	19	12	9	5	2	0
Arm 2	199	189	177	153	120	97	76	59	45	33	25	17	8	4	1	0
Arm 3	211	202	190	169	145	132	111	75	57	33	26	20	10	3	0	0

	Arm 1 PC + bev N=216	Arm 2 PC + bev + Imfinzi N=199	Arm 3 PC + bev + Imfinzi + Lyn N=211
Events, n (%)	157 (73)	142 (71)	127 (60)
Median PFS, [†] m	17.4	15.4	20.9
HR (95% CI) vs Arm 1		0.94 (0.75–1.18) [§]	0.68 (0.54–0.86) [§]



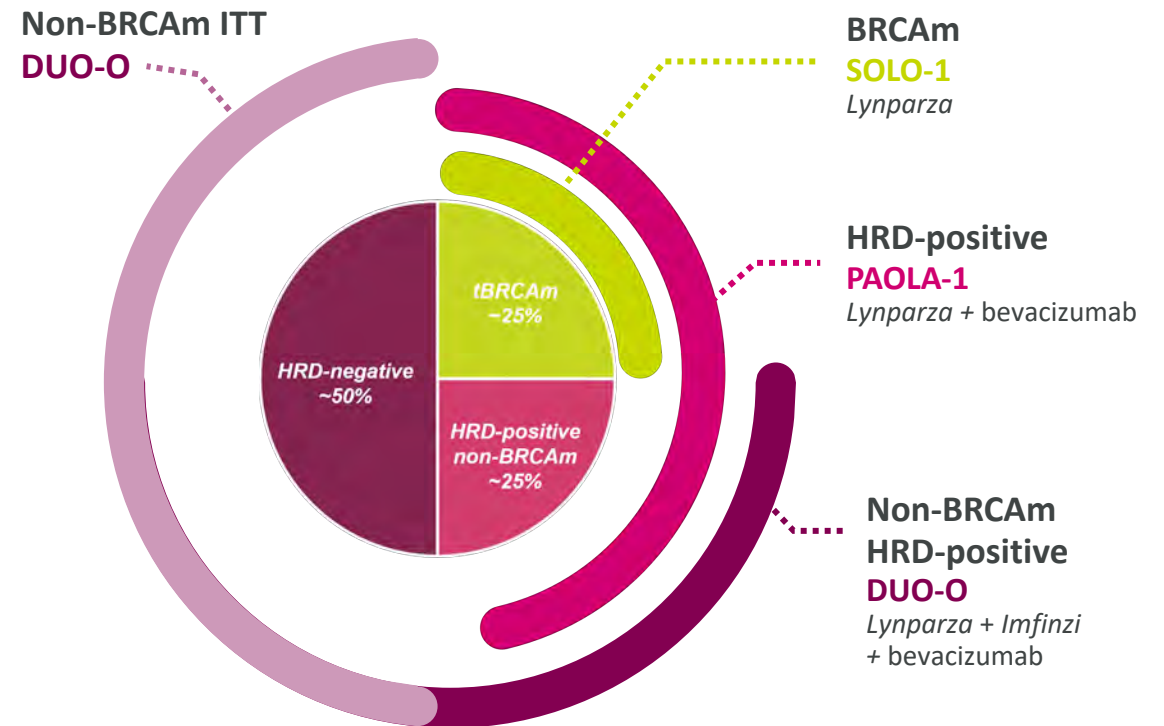
DUO-O Phase III

Imfinzi + *Lynparza* added to CTx + bevacizumab potential new option for patients

Conclusions

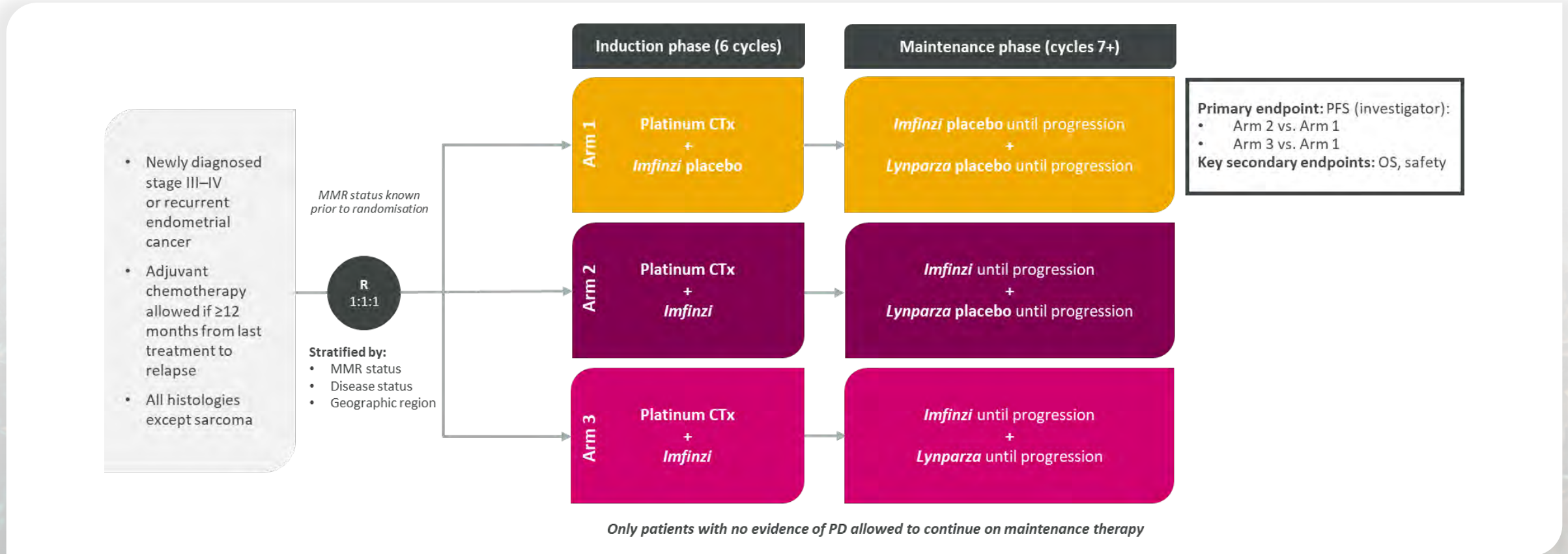
- Statistically significant and clinically meaningful improvement in PFS with addition of *Imfinzi* + *Lynparza* to CTx + bevacizumab vs CTx + bevacizumab in advanced OC patients
- PFS benefit observed across subgroups, including those patients with HRD-negative disease
- Numerical, but not statistical improvement in PFS for addition of *Imfinzi* to chemotherapy + bevacizumab in ITT
- Safety generally consistent with the known profiles of each individual agent
- DUO-O Phase III trial follow-up continues

Lynparza data across the entire newly diagnosed ovarian cancer space



DUO-E Phase III in advanced endometrial cancer

Imfinzi plus *Lynparza* and *Imfinzi* alone significantly improved PFS when added to chemotherapy



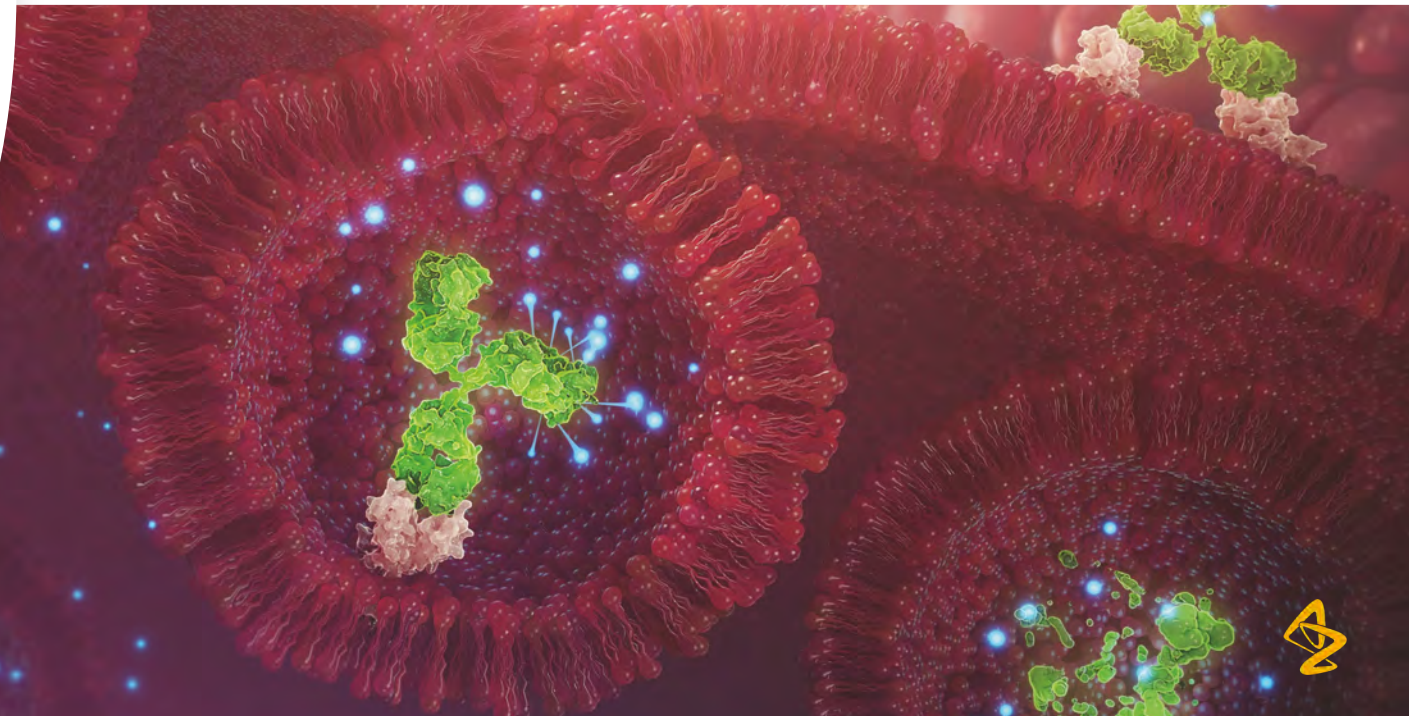
DUO-E Phase III results to be presented at upcoming medical congress



Expanding *Enhertu* beyond breast, lung and gastric

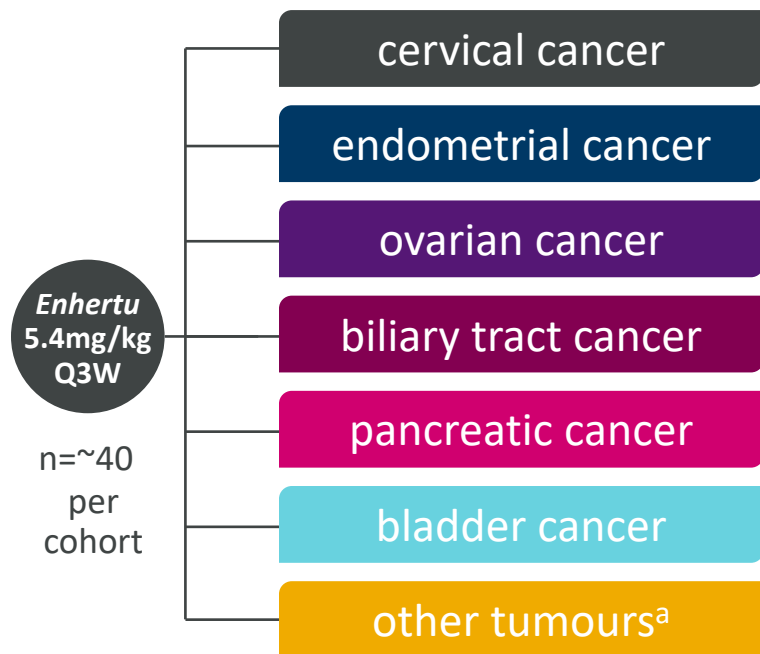
Susan Galbraith
ONCOLOGY R&D

Dave Fredrickson
ONCOLOGY BUSINESS



DESTINY-Pantumor02 Phase II

Enhertu for HER2-expressing solid tumors



Primary endpoint

- Confirmed ORR (investigator)^b

Secondary endpoints

- DoR^b
- DCR^b
- PFS^b
- OS
- Safety/ tolerability

Data cut-off for analysis:

- 16 November 2022

Key trial criteria

- Advanced solid tumours not eligible for curative therapy
- 2L+ patient population
- HER2 expression (IHC 3+ or IHC 2+)
 - Local testing or central testing by Herceptest if local testing not feasible (ASCO/CAP gastric cancer guidelines¹)^c
- Prior HER2-targeting therapy allowed
- ECOG/WHO PS 0-1

1. Hofmann M, et al. Histopathology 2008;52:797-805.

^aPatients that express HER2, excluding the tumors in the tumor-specific cohorts, and breast cancer, non-small cell lung cancer, gastric cancer, and colorectal cancer; ^bInvestigator-assessed per Response Evaluation Criteria In Solid Tumors version 1.1; ^cPatients were eligible by either test. All patients were centrally confirmed.

HER2 = human epidermal growth factor receptor 2; Q3W = every three weeks; ORR = objective response rate; DoR = duration of response; DCR = disease control rate; PFS = progression-free survival; OS = overall survival; 2L = 2nd-line; IHC = immunohistochemistry; ASCO = American Society of Clinical Oncology; CAP = College of American Pathologists; ECOG/WHO PS = Eastern Cooperative Oncology Group / World Health Organisation performance status.

Collaboration partners: Daiichi Sankyo (*Enhertu*).



DESTINY-Pantumor02 Phase II

Clinically meaningful activity observed across broad range of HER2-expressing solid tumours

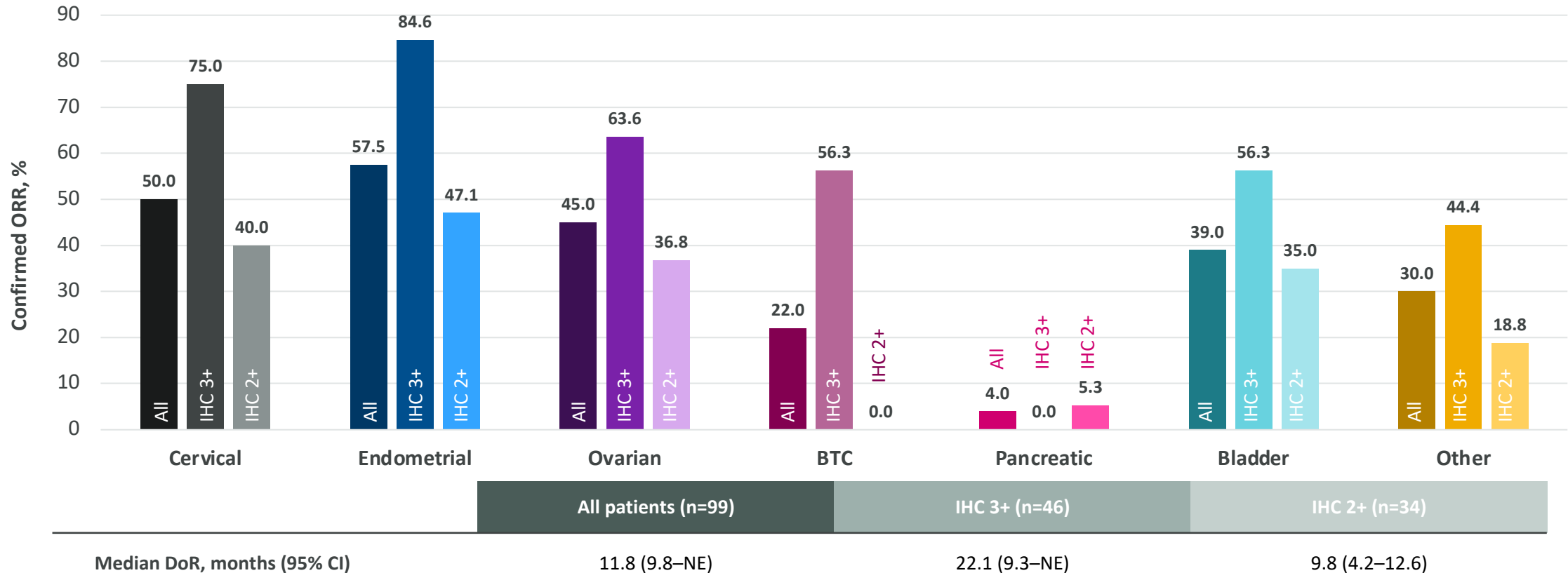
	Cervical (n=40)	Endometrial (n=40)	Ovarian (n=40)	BTC (n=41)	Pancreatic (n=25)	Bladder (n=41)	Other (n=40)	All patients (n=267)
ORR, n (%)	20 (50.0)	23 (57.5)	18 (45.0)	9 (22.0)	1 (4.0)	16 (39.0)	12 (30.0)	99 (37.1)
Best overall response, n (%)								
Complete response	2 (5.0)	7 (17.5)	4 (10.0)	1 (2.4)	0	1 (2.4)	0	15 (5.6)
Partial response	18 (45.0)	16 (40.0)	14 (35.0)	8 (19.5)	1 (4.0)	15 (36.6)	12 (30.0)	84 (31.5)
Stable disease	11 (27.5)	12 (30.0)	13 (32.5)	23 (56.1)	16 (64.0)	16 (39.0)	20 (50.0)	111 (41.6)
Progressive disease	7 (17.5)	4 (10.0)	7 (17.5)	7 (17.1)	7 (28.0)	7 (17.1)	3 (7.5)	42 (15.7)
Not evaluable	1 (2.5)	0	1 (2.5)	0	0	0	1 (2.5)	3 (1.1)
DCR^a, n (%)	27 (67.5)	32 (80.0)	28 (70.0)	27 (65.9)	9 (36.0)	29 (70.7)	30 (75.0)	182 (68.2)
Median DoR, months (95% CI)	9.8 (4.2–NE)	NR (9.9–NE)	11.3 (4.1–NE)	8.6 (2.1–NE)	NR	8.7 (4.3–11.8)	NR (4.1–NE)	11.8 (9.8–NE)

^aConfirmed complete response, confirmed partial response or stable disease at or after 11 weeks.



DESTINY-Pantumor02 Phase II

Responses observed in both IHC 3+ and IHC 2+ populations



IHC based on central HER2 testing; 67 patients had IHC 1+ (n=25), IHC 0 (n=30) or unknown IHC status (n=12) by central testing. Other includes responses in extramammary Paget disease, head and neck cancer, oropharyngeal neoplasm, and salivary gland cancer.

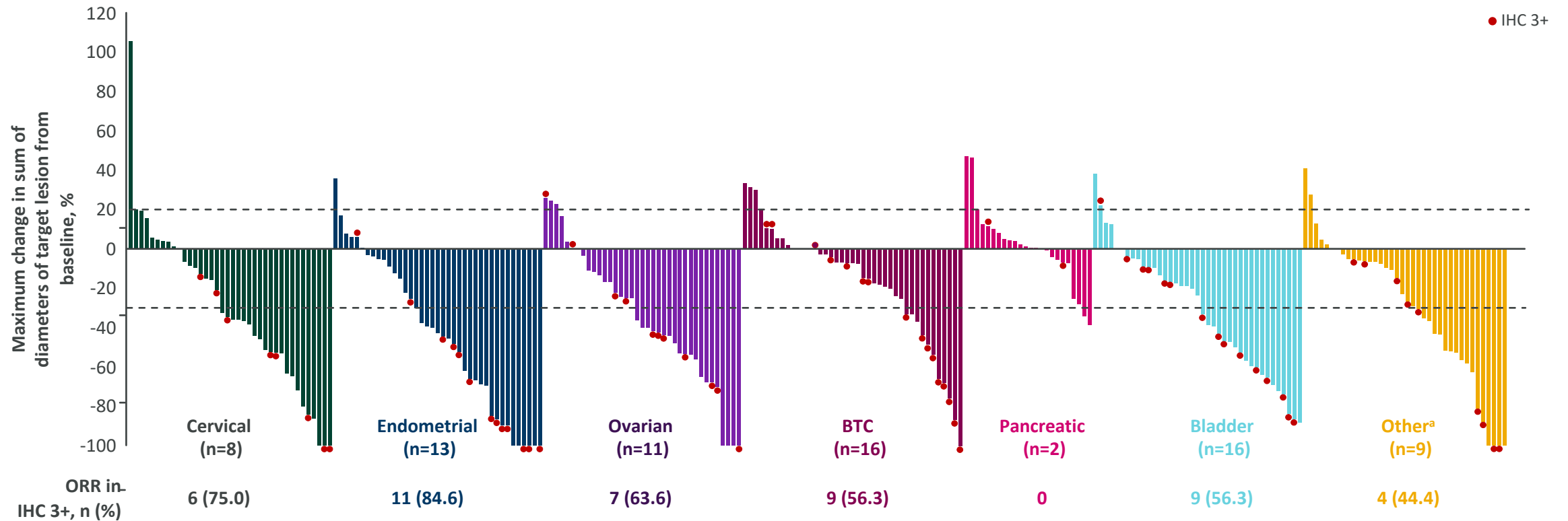
IHC = immunohistochemistry; ORR = objective response rate; BTC = biliary tract cancer; DoR = duration of response; CI = confidence interval; NE = non estimable.

Collaboration partners: Daiichi Sankyo (*Enhertu*).



DESTINY-Pantumor02 Phase II

Best percentage change in target lesion from baseline demonstrates depth of response



DPT02 trial follow-up continues (PFS and OS)

Analyses were performed in patients who received ≥ 1 dose of *Enhertu* (n=267). Analysis of ORR in IHC 3+ was performed in patients with centrally confirmed HER2 status (n=75).

^aResponses in extramammary Paget's disease, head and neck cancer, oropharyngeal neoplasm, and salivary gland cancer.

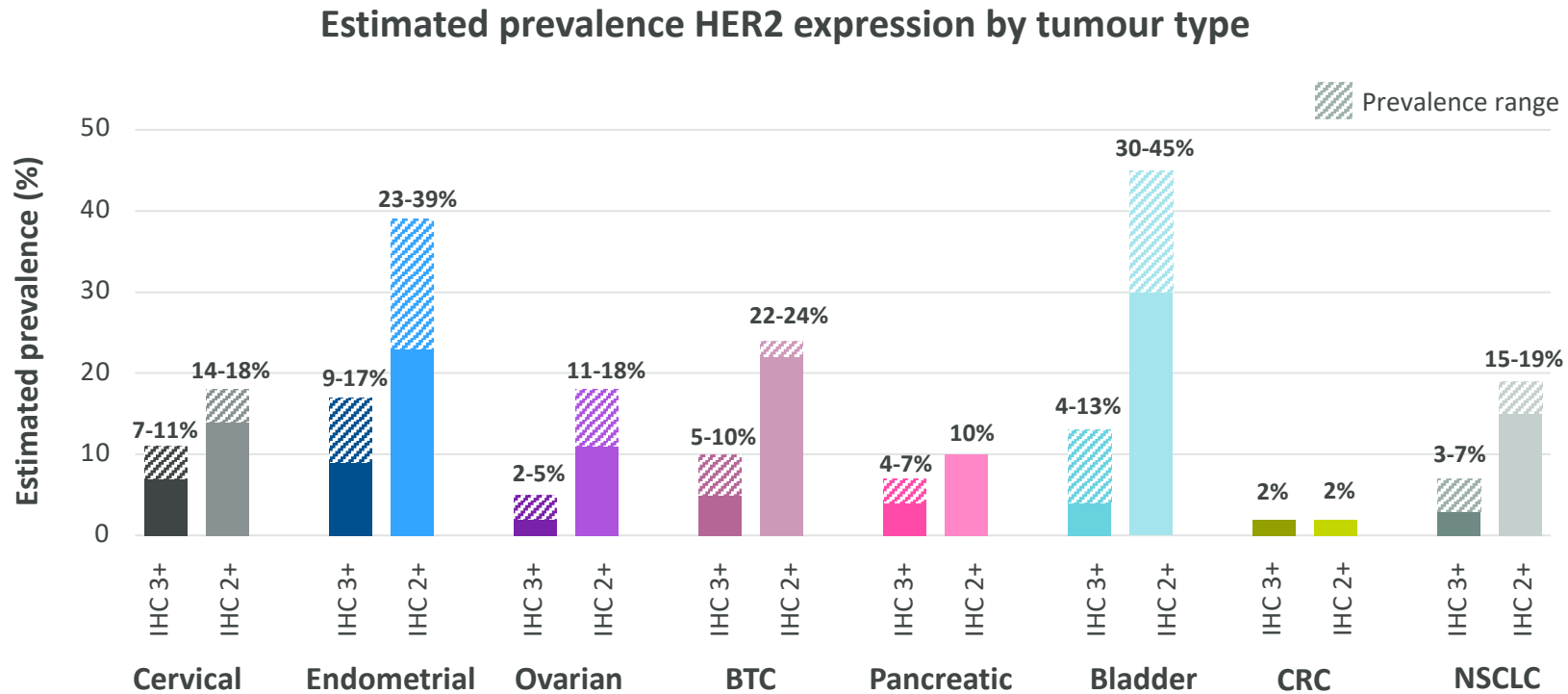
ORR = objective response rate; BTC = biliary tract cancer; IHC = immunohistochemistry; PFS = progression-free survival; OS = overall survival.

Collaboration partners: Daiichi Sankyo (*Enhertu*).



DESTINY-Pantumor02 in HER2-expressing cancers

Targeting tumours with HER2-expression beyond breast and gastric



- Levels of HER2 expression differ by tumour type
- Variability in prevalence influenced by timing of biopsy (primary vs metastatic)
- IHC 3+ shows greatest magnitude and consistency of benefit

Planned discussions with regulatory agencies

c.8,000-12,000 3L+ patients with HER2-expressing tumours in the US*

*Includes solid tumours beyond those in DESTINY-Pantumor02

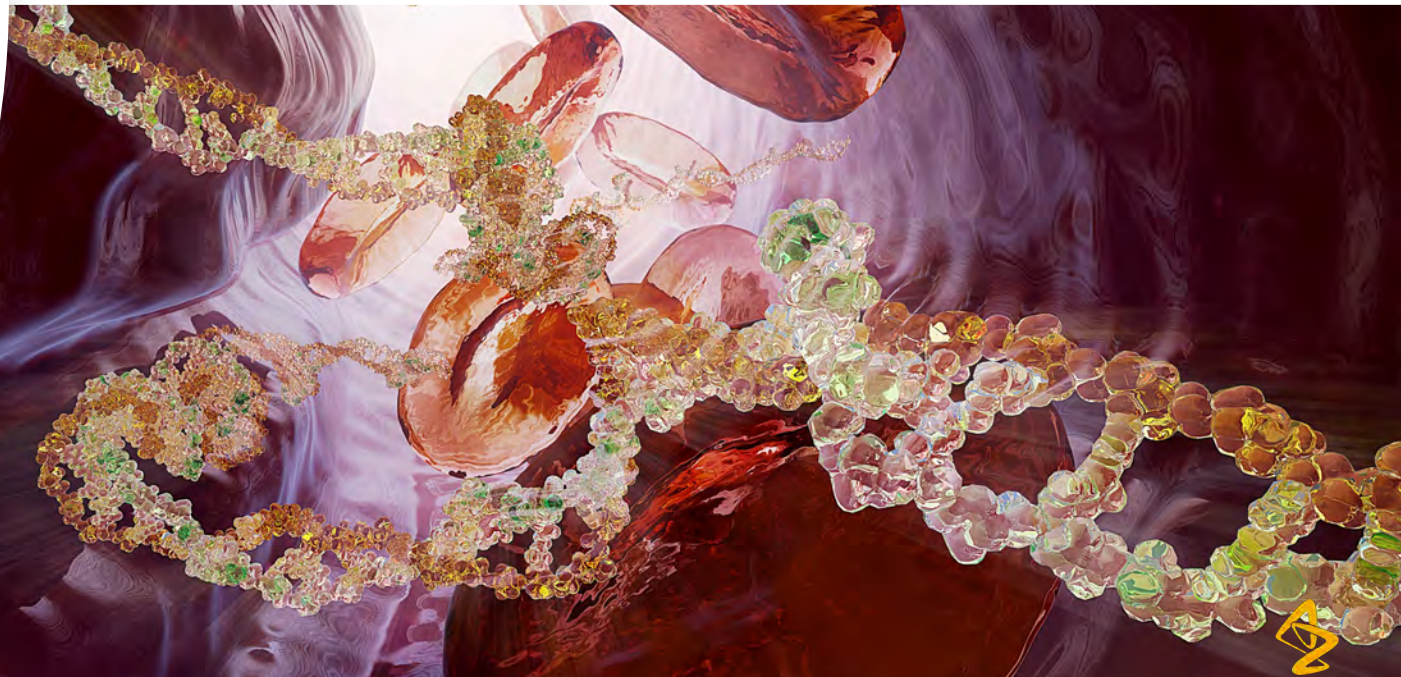
Estimates uncertain based on literature and AstraZeneca in-house data. No HER2 IHC assay has been approved or tested for these indications, (caveat with antibody-related possible artifacts used for scoring, especially for the assessment of HER2 2+; different algorithms can provide different results) and data / references used for estimates were not specifically designed to evaluate HER2 prevalence.

HER2 = human epidermal growth factor receptor 2 = IHC, immunohistochemistry; BTC = biliary tract cancer.



Reinforcing *Calquence* positioning in BTKi class

Anas Younes
SVP, Haematology



Calquence MAIC

Methodology uses weighting equation to exactly match baseline characteristics

ASCEND vs ALPINE compared through unanchored MAIC

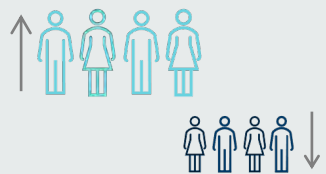
ASCEND trial population



Calquence

Weighting equation matches baseline characteristics*

ASCEND reweighted



Calquence

ALPINE (recovered)

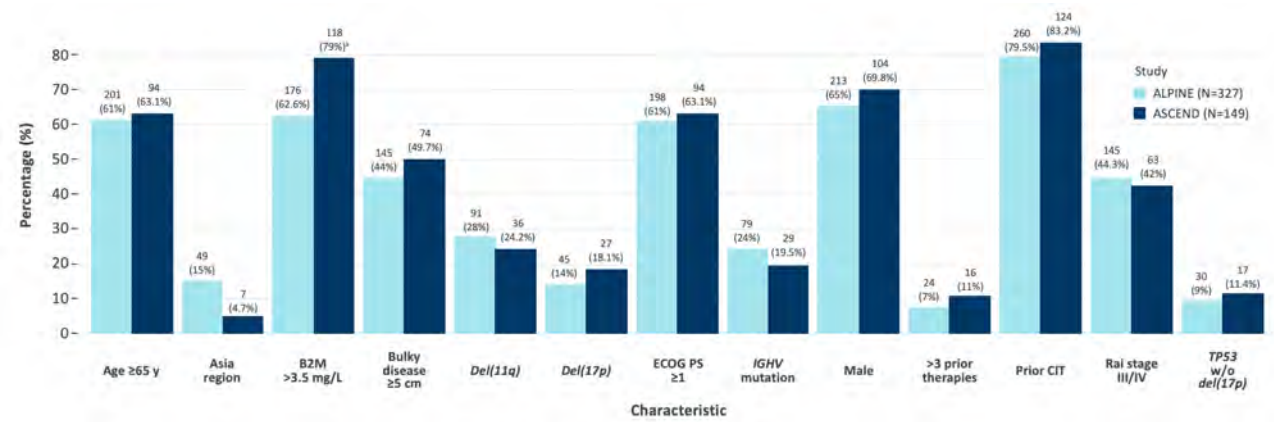


zanubrutinib

vs

□ Non-ALPINE-like patients □ ALPINE-like patients

Similar baseline characteristics of ASCEND and ALPINE



Inclusion, baseline characteristics enable comparison and reduce selection bias risk

- Unselected for mutation status
- Median one prior line of treatment
- Consistent endpoint definitions

*Percentages for B2M were calculated based on those with complete information only (14% of patients had missing data).

*Variables included in matching analysis: gender, bulky disease, prior chemoimmunotherapy, Del(11q), TP53 without del(17p), Del(17p), region, age, ECOG, prior lines of therapy, IGHV, Rai stage.

1. Ghia P, et al. *J Clin Oncol*. 2020; 38: 2849–2861. 2. Brown JR, et al. *New Engl J Med*. 2023; 388: 319–332.

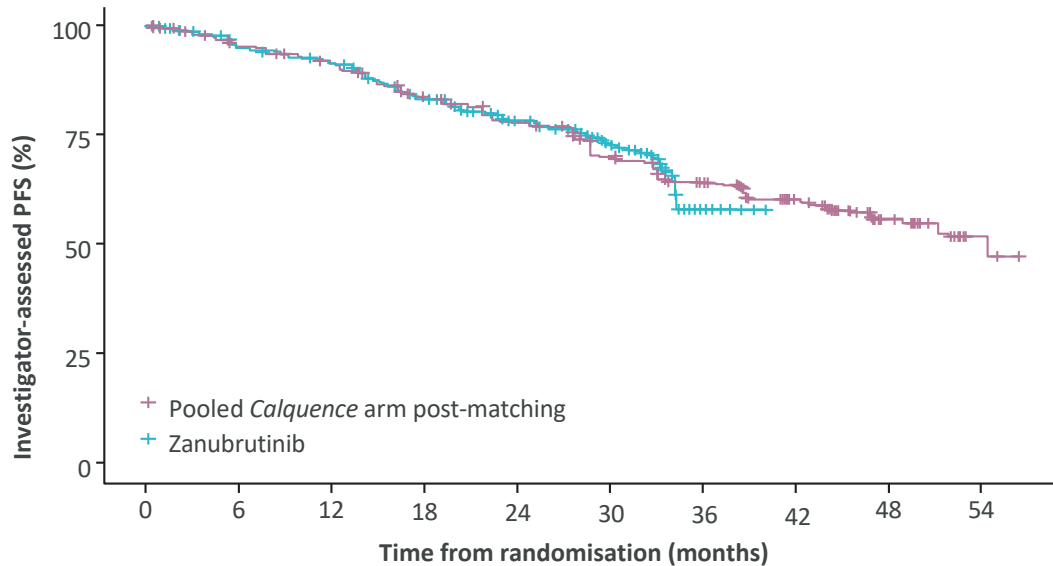
MAIC = matched-adjusted indirect comparison; ECOG = Eastern Cooperative Oncology Group; IGHV = immunoglobulin heavy variable.



Calquence MAIC

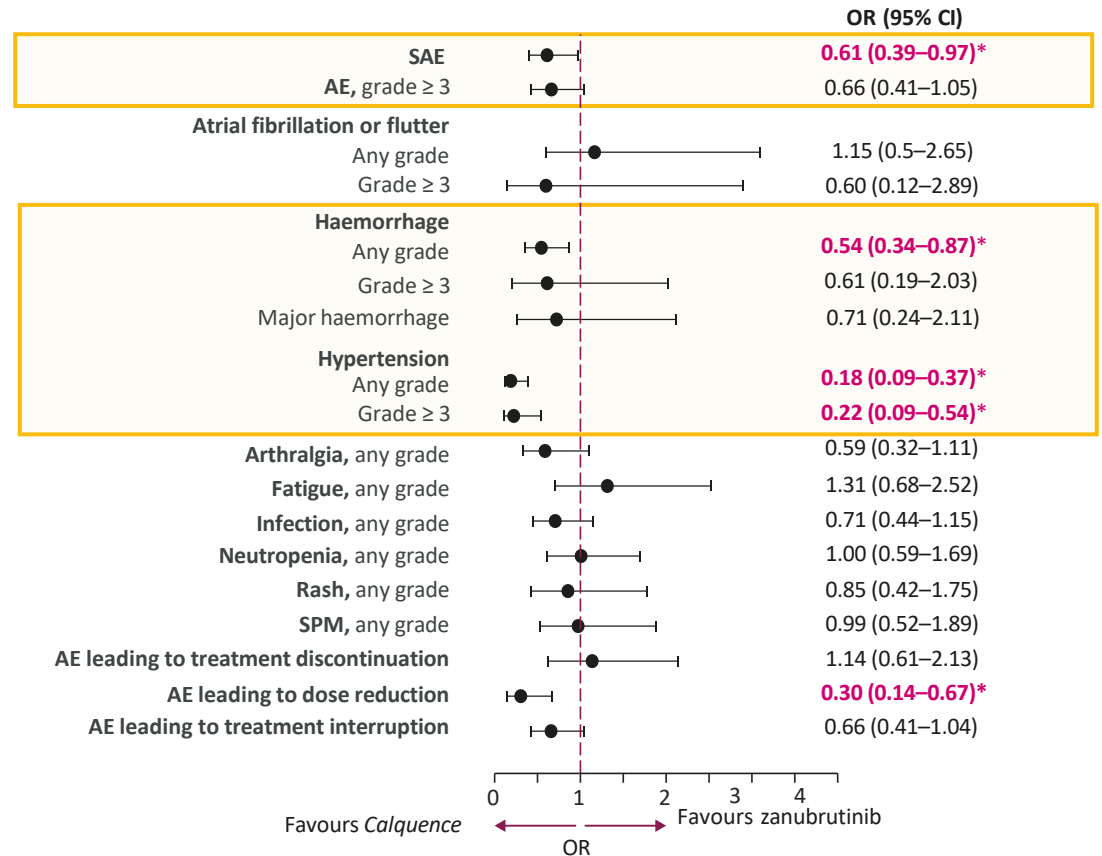
MAIC demonstrates equivalent PFS in r/r CLL but *Calquence* more favourable safety

Calquence vs zanubrutinib PFS



Analysis set	HR for <i>Calquence</i> vs. zanubrutinib (CI)	HR for <i>Calquence</i> vs. ibrutinib (CI)
Weighted (matched to ALPINE)	0.90 (0.60–1.36)	0.60 (0.40–0.90)

Calquence vs zanubrutinib safety



AstraZeneca @ ASCO 2023

Q&A session



Pascal Soriot,
Chief Executive Officer



Dave Fredrickson,
*Executive Vice President
Oncology Business*



Susan Galbraith,
*Executive Vice President
Oncology R&D*



Sunil Verma,
*Global Head of Oncology,
Medical*

THERAPEUTIC AREA LEADERSHIP



Leora Horn,
*Global Clinical Head,
Lung Cancer and Lung Cancer Strategy*



Ingrid Mayer,
*Global Clinical Strategy Head,
Breast Cancer*



Osama Rahma,
*Global Clinical Strategy Head,
GI Cancer*



Ashok Gupta,
*Global Clinical Strategy Head,
GU/GYN Cancer*



Anas Younes,
*Senior Vice President,
Haematology*



Strengthening oncology leadership

ASCO 2023 data reinforces potential to transform patient outcomes in key tumour areas

Lung



TAGRISSO
osimertinib

IMFINZI durvalumab **IMJUDO** tremelimumab-act

ENHERTU fam-trastuzumab deruxtecan-nxki

Orpathys

Dato-DXd

volrustomig

rilvegostomig

ceralasertib

AZD9592 (EGFR-cMET ADC)

38

Breast



ENHERTU fam-trastuzumab deruxtecan-nxki

Lynparza olaparib

IMFINZI durvalumab

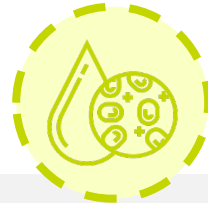
Dato-DXd

capiasertib

camizestrant

16

Haematology



CALQUENCE (acalabrutinib) 100mg capsules

AZD0486 (CD3xCD19 TCE)

AZD4573 (CDK9)

capiasertib (AKTi)

AZD0466 (BCL2-xL)

sabestomig (PD1/TIM3)

6

GI



IMFINZI durvalumab

IMFINZI durvalumab **IMJUDO** tremelimumab-act

Lynparza olaparib

ENHERTU fam-trastuzumab deruxtecan-nxki

IMFINZI durvalumab **Orpathys**

Orpathys

AZD5851 (GPC3 CAR-T)

21

GYN/GU



Lynparza olaparib

IMFINZI durvalumab

IMFINZI durvalumab **IMJUDO** tremelimumab-act

ENHERTU fam-trastuzumab deruxtecan-nxki

capiasertib (AKTi)

29

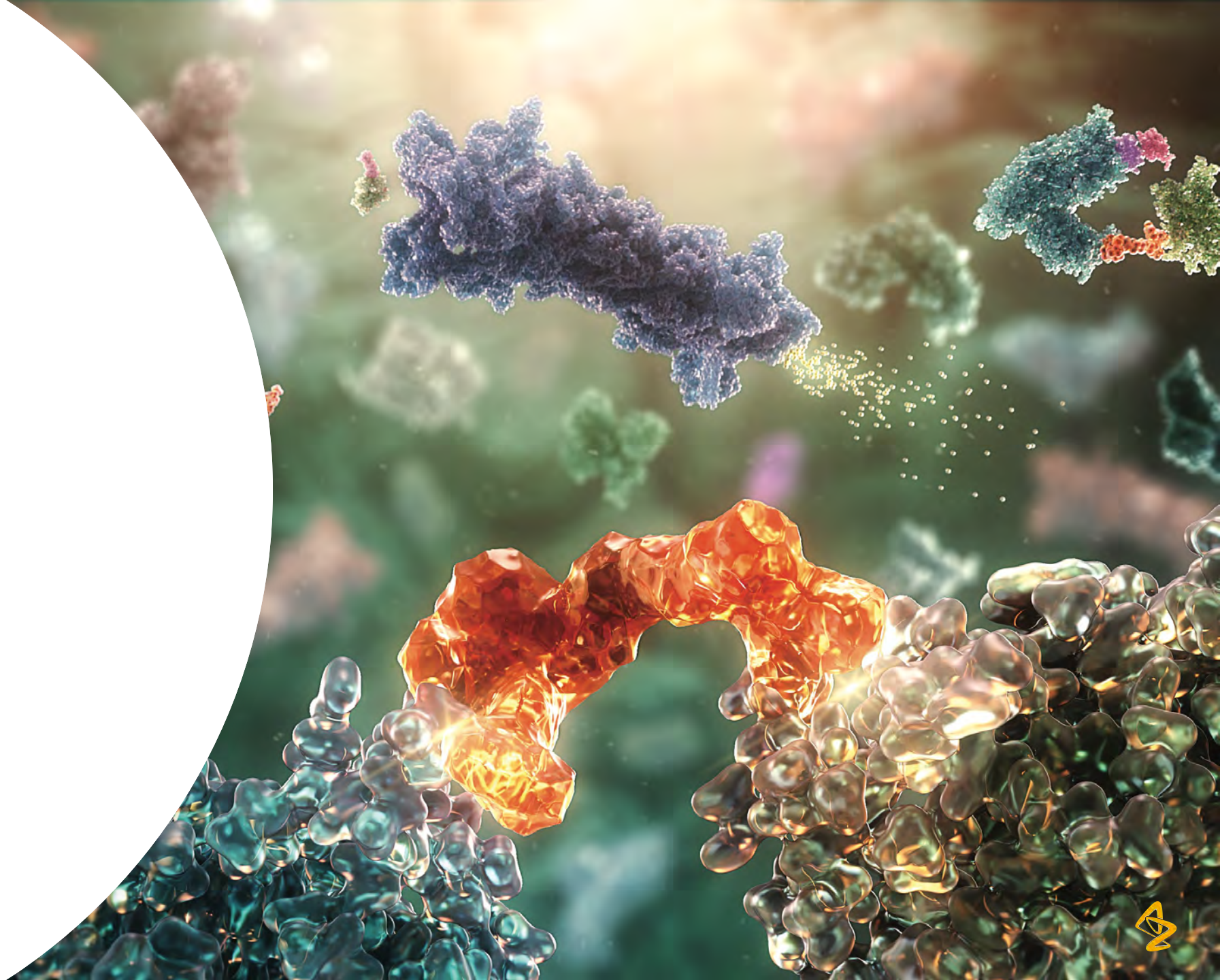
DATA PRESENTATIONS BY TUMOUR AREA

2023 **ASCO**
ANNUAL MEETING

Dato-DXd = datopotamab deruxtecan; EGFR = epidermal growth factor receptor; c-MET = mesenchymal-epithelial transition factor; ADC = antibody-drug conjugate; PARP1sel = poly ADP ribose polymerase-1 selective; CD3xCD19 = cluster of differentiation 3 and cluster of differentiation 19 bispecific; TCE = T cell engager; CDK9 = cyclin-dependent kinase 9; AKTi = protein kinase B inhibitor; BCL2-xL = B-cell lymphoma-extra large; PD1 = programmed cell death protein 1; TIM3 = T-cell immunoglobulin and mucin domain-containing protein 3; GPC3 = glypican 3 protein; CAR-T = chimeric antigen receptor t-cell; CLDN18.2 = Claudin-18.2. Collaboration partners: Daiichi Sankyo (*Enhertu*, Dato-DXd), Merck & Co., Inc. (*Lynparza*); Compugen (rilvegostomig).





Appendix



AstraZeneca in Breast Cancer

Ambition to eliminate breast cancer as a cause of death

 established SoC	Early			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> DESTINY-Breast09	<i>Enhertu</i> DESTINY-Breast03	<i>Enhertu</i> DESTINY-Breast02	
HR-positive 65-75% --- <i>HER2-low</i> 60%		Low risk Current SoC drives good outcomes for patients with low risk HR-positive eBC CTx → AI (+/- CDK4/6i) → camizestrant CAMBRIA-1	RECURRENCE	camizestrant + CDK4/6i SERENA-4 <i>ESR1m</i> CDK4/6i + AI → CDK4/6i + camizestrant SERENA-6	capiasertib + <i>Faslodex</i> CAPitello291	Dato-DXd TROPION-Breast01	
TNBC 10-15% --- <i>HER2-low</i> 35%		NST → residual disease → Dato-DXd +/- <i>Imfinzi</i> TROPION-Breast03		capiasertib + paclitaxel CAPitello290 PD-L1-60% Dato-DXd TROPION-Breast02	<i>HER2-low</i>	<i>HER2-low</i> <i>Enhertu</i> DESTINY-Breast04	
gBRCAm 5% of HR-positive 15% of TNBC		CTx → <i>Lynparza</i> OlympiA			<i>Lynparza</i> OlympiAD		

All numbers are approximate. Illustrative settings and populations, not to scale.

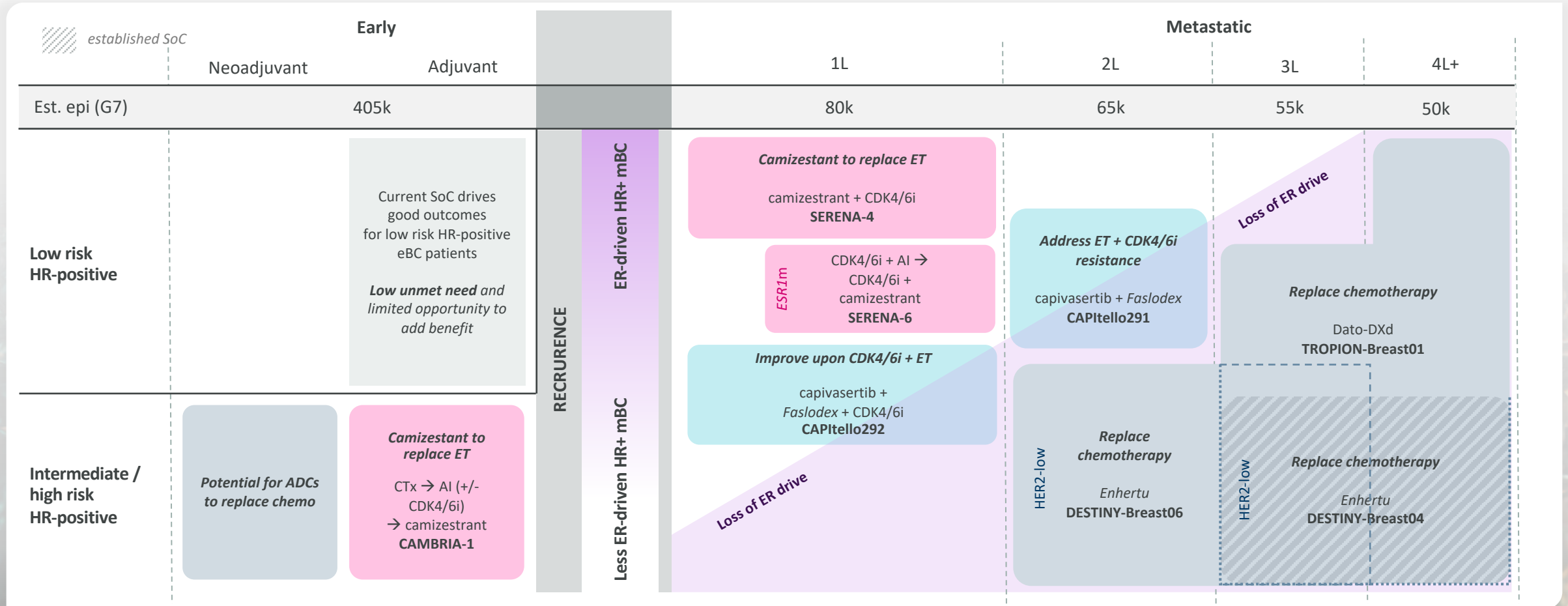
1/2/3/4L = 1st/2nd/3rd/ 4th-line; est epi (G7) = estimated epidemiology across G7 (US, EU5, JP for drug treated patients). **HER2** = human epidermal growth factor receptor 2; THP = docetaxel, trastuzumab, and pertuzumab; NST = neoadjuvant systemic treatment; HR = hormone receptor; SoC = standard of care; CTx = chemotherapy; AI = aromatase inhibitor; CDK4/6i = cyclin-dependent kinase 4 and 6 inhibitor; ESR1m = oestrogen receptor 1 gene mutation; Dato-DXd = datopotamab deruxtecan; TNBC = triple negative breast cancer; PD-L1 = programmed cell death ligand 1; gBRCAm = germline BRCA-mutated.

Collaboration partners: Daiichi Sankyo (*Enhertu*, Dato-DXd), Merck & Co., Inc. (*Lynparza*).



AstraZeneca in HR-positive Breast Cancer

Ambition to eliminate breast cancer as a cause of death



All numbers are approximate. Illustrative settings and populations, not to scale.

HR = hormone receptor; 1/2/3/4L = 1st/2nd/3rd/ 4th-line; est epi (G7) = estimated epidemiology across G7 (US, EU5, JP for drug treated patients; SoC = standard of care; ADC = antibody drug conjugate; ET = endocrine therapy; CTx = chemotherapy; AI = aromatase inhibitor; CDK4/6i = cyclin-dependent kinase 4 and 6 inhibitor; ESR1m = oestrogen receptor 1 gene mutation; ER = oestrogen receptor; Dato-DXd = datopotamab deruxtecan.

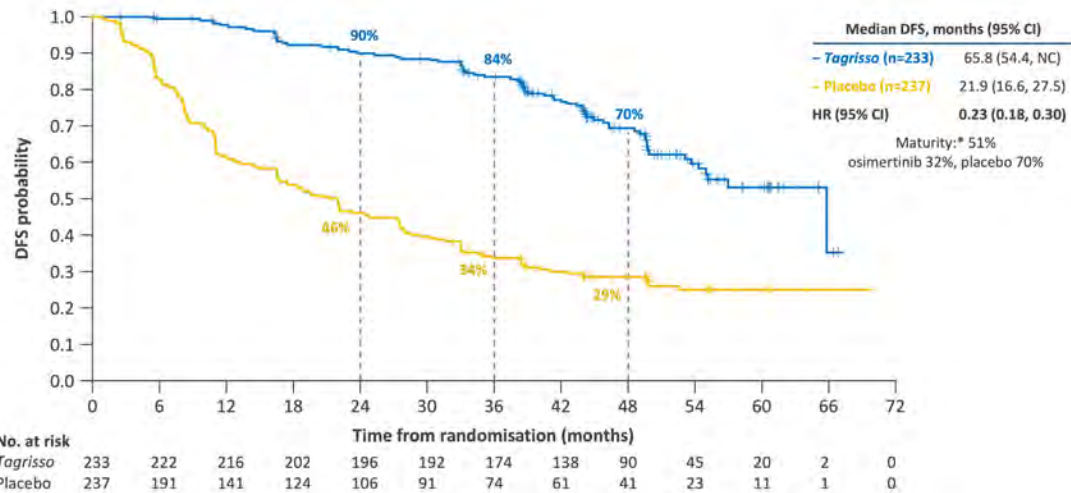
Collaboration partners: Daiichi Sankyo (Enhertu, Dato-DXd).



ADAURA DFS

Updated disease-free survival data presented at ESMO 2022

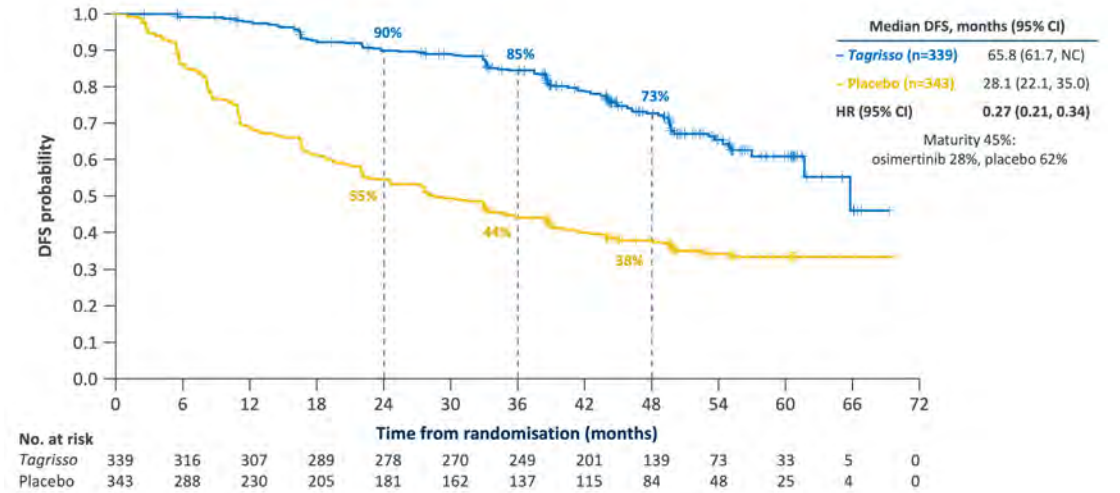
Primary endpoint: updated DFS in Stage II/IIIA



Median follow-up Tagrisso 44.2 months (range 0 to 67), placebo 19.6 months (range 0 to 70); DFS by investigator assessment; Tick marks indicate censored data. *Planned maturity for DFS analysis: 50%.

Data cut-off: April 11, 2022.

Updated DFS in the overall population (Stage IB/II/IIIA disease)



Median follow-up Tagrisso 44.2 months (range 0 to 69), placebo 27.7 months (range 0 to 70); DFS by investigator assessment; Tick marks indicate censored data.

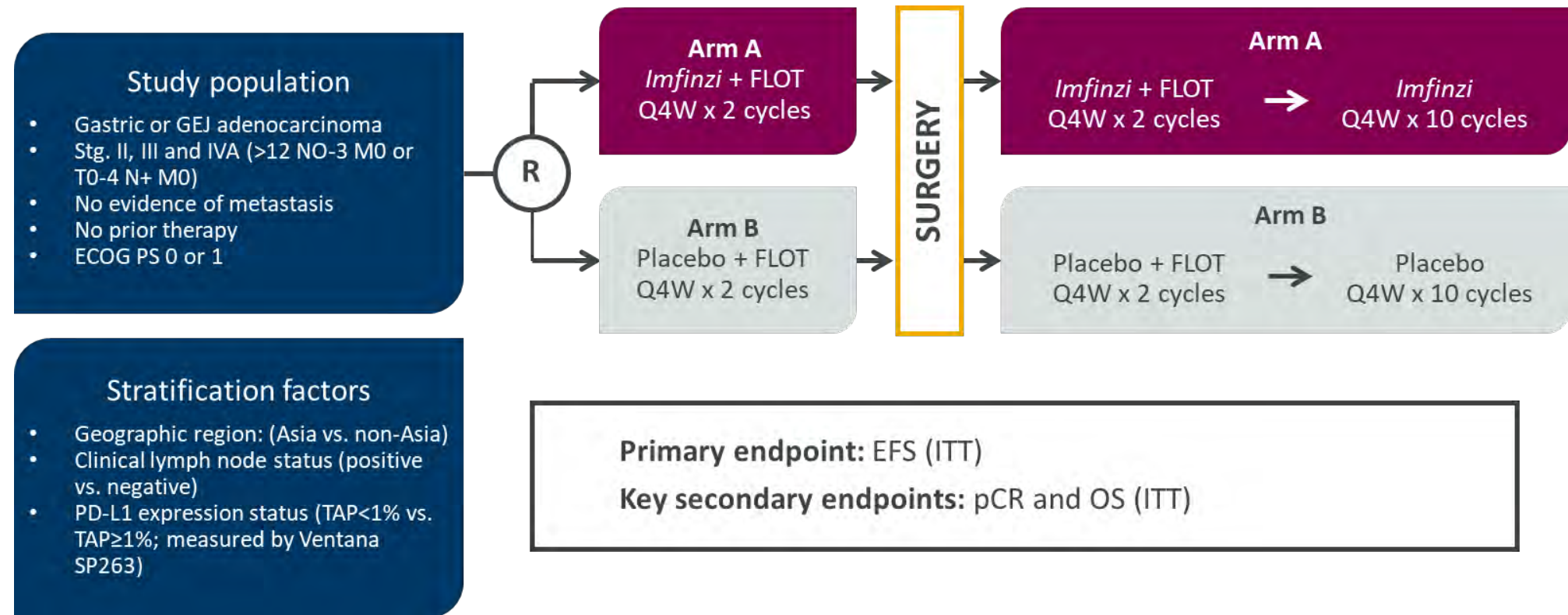
Data cut-off: April 11, 2022.



MATTERHORN

Imfinzi + FLOT showed statistically significant and clinically meaningful pCR improvement

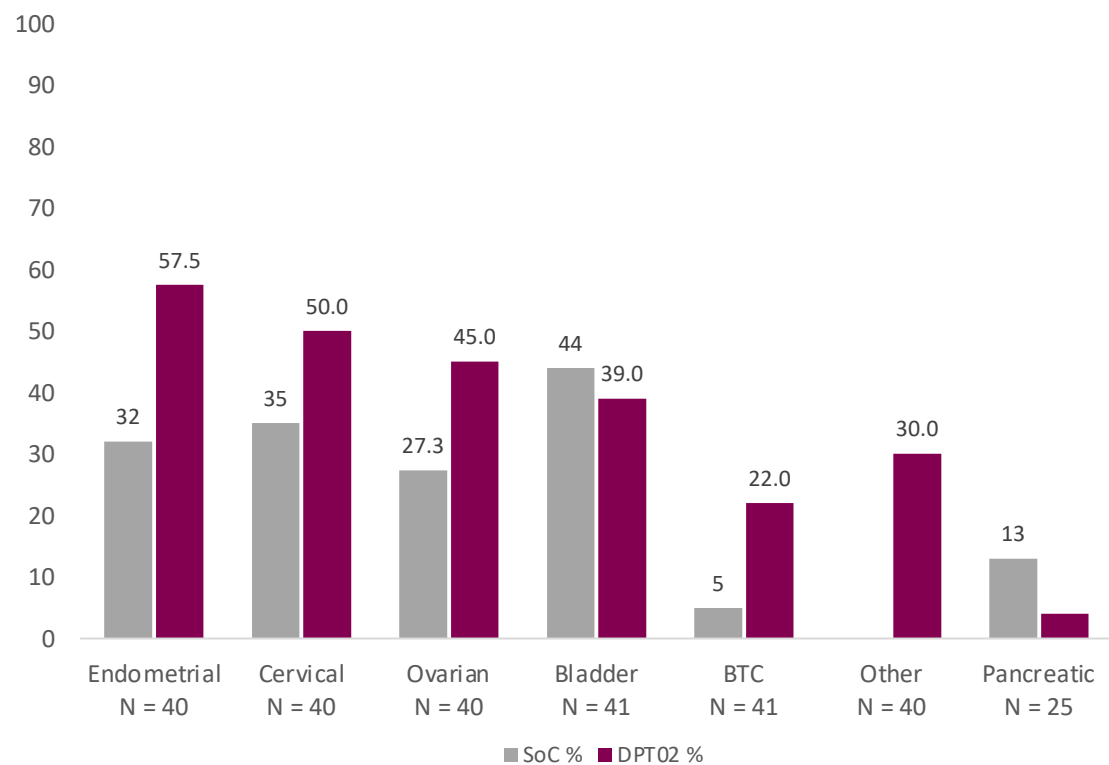
MATTERHORN Phase III trial design



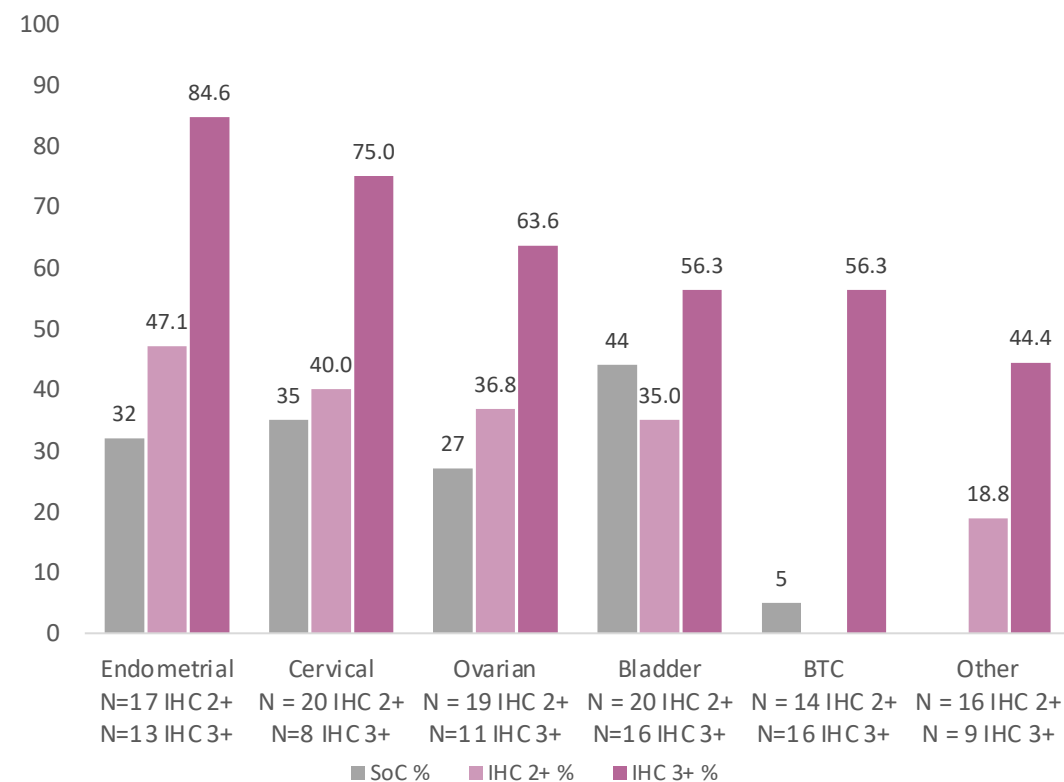
Confirmed ORR in efficacy subset: SoC comparison

Clinically meaningful responses in DESTINY-Pantumor02 vs 2L SoC¹⁻⁶ in nearly all cohorts

DPT02 Confirmed ORR All Patients vs 2L SoC



DPT02 Confirmed ORR by IHC status vs 2L SoC



Note: right graph does not show pancreatic cohort data due to small n (1 patient in IHC 2+ subgroup with response)

Illustrative data only – cross trial comparisons should always be interpreted with caution

1. Makker V et al. *N Engl J Med.* 2022;386(5):437-448; 2. Oaknin A et al. *J Immunother Cancer.* 2022;10(1):e003777; 3. Pujade-Lauraine E et al. *J Clin Oncol.* 2014;32(13):1302-1308; 4. Rosenberg JE et al. *J Clin Oncol.* 2019;37(29):2592-2600; 5. Lamarca A et al. *Lancet Oncol.* 2021;22(5):690-701; 6. Mita N et al. *J Clin Med.* 2019;8(6):761. Published 2019 May 29.

ORR = objective response rate; SoC = standard of care; 2L = 2nd-line; DPT02 = DestinyPantumor02; IHC = immunohistochemistry

