AstraZeneca

ESMO Poster Sessions

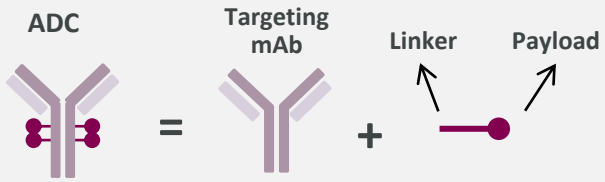
23 October 2023

For distribution to, and usage with, financial/investment analysts and investors only


AstraZeneca
ADCs in focus

ADC revolution: potential to replace conventional chemotherapy

ABCs of ADCs

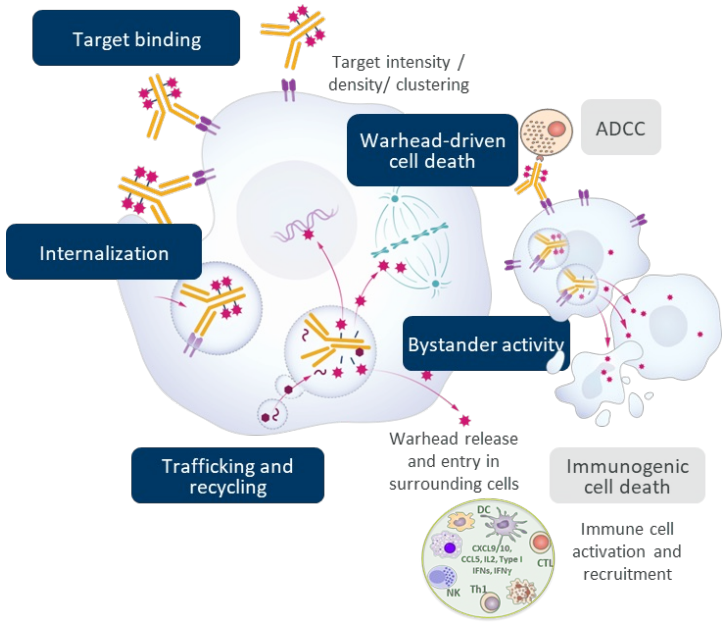


ADCs consist of :

(1) Highly selective mAb against a target antigen overexpressed on tumour cells relative to normal cells

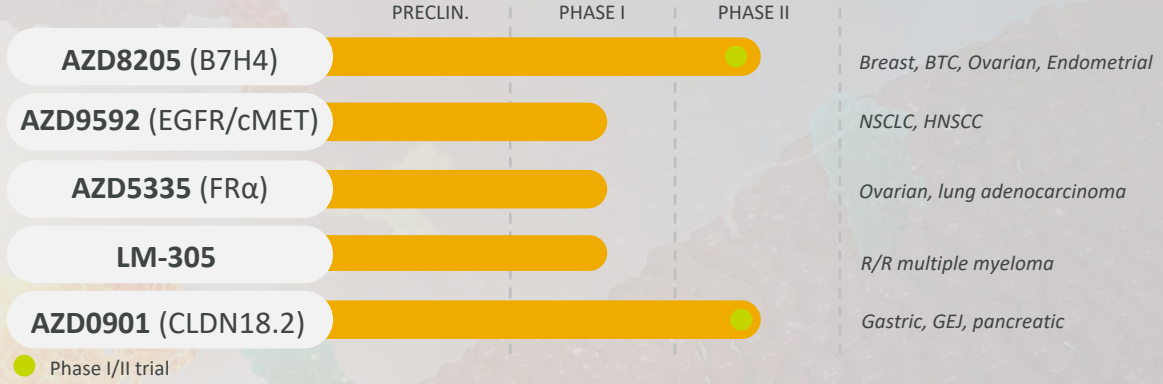
(2) Potent cytotoxic payload designed to induce target cell death

(3) Linker connecting mAb to payload



Optimised ADC technology and biology must align to build successful ADC

AstraZeneca disclosed in-house ADC portfolio



AstraZeneca in-house capabilities | Proprietary ADC platform

>100 dedicated scientists

Efforts focused on:

- novel linker conjugation
- proteomics platform
- warhead toolbox

ADC = antibody drug conjugate; mAb = monoclonal antibody; EGFR = epidermal growth factor receptor; cMET = mesenchymal-epithelial transition factor; FRα = folate receptor alpha; CLDN18.2 = Claudin 18.2; BTC = biliary tract cancer; NSCLC = non-small cell lung cancer; HNSCC = head and neck squamous cell carcinomas; GEJ = gastroesophageal junction adenocarcinoma.
Collaboration partners = AZD0901 partnered with Keymed Biosciences

AstraZeneca novel ADC programmes

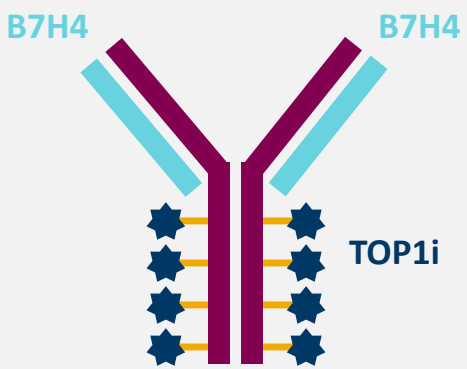
ADC design through optimal combinations

1 Targets & Antibodies
Efficient delivery of ADC payload

2 Conjugation chemistry & linkers
Overcome potential off-target toxicity

3 Payloads
Enable biology-driven combinations and overcome payload resistance

AZD8205 (B7H4)



DAR 8

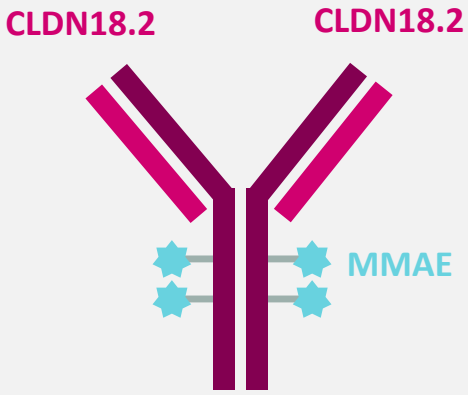
AZD9592 (EGFR/cMET)

DAR 6

AZD5335 (FRα)

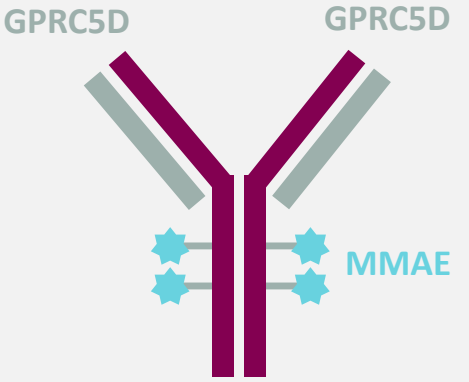
DAR 8

AZD0901 (CLDN18.2)



DAR 4

LM-305 (GPRC5D)



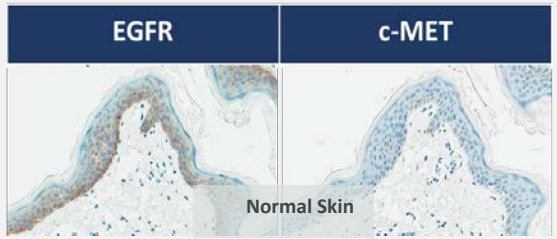
DAR 4

Image is for illustrative purposes only; actual drug positions may vary. ADC = antibody drug conjugate; B7H4 = B7 homolog 4; *EGFRm* = epidermal growth factor receptor mutation; cMET = mesenchymal-epithelial transition factor; FRα = folate receptor α; CLDN18.2 = Claudin 18.2; GPRC5D = G protein-coupled receptor, class C group 5 member D; DAR = drug antibody ratio.
Collaboration partners = AZD0901 partnered with Keymed Biosciences

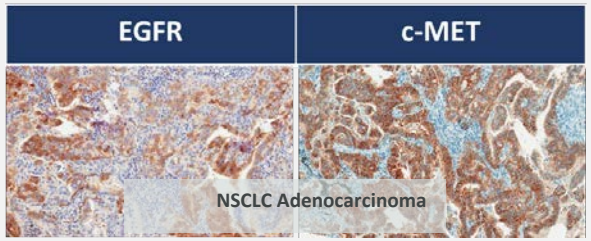
AZD9592 (EGFR/cMET)

Rationale for EGFR-cMET ADC

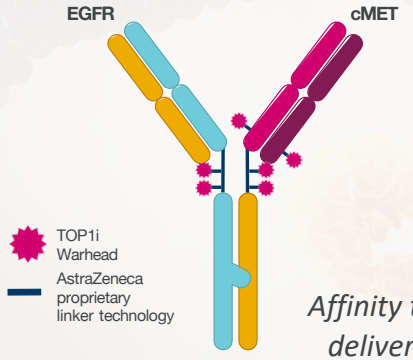
EGFR & cMET co-expression is limited in normal tissue



…but highly co-expressed in many tumor types



AZD5952 engineered to maximise efficacy and improve safety



Affinity tuned to deliver TOP1i

Modulate affinity for EGFR

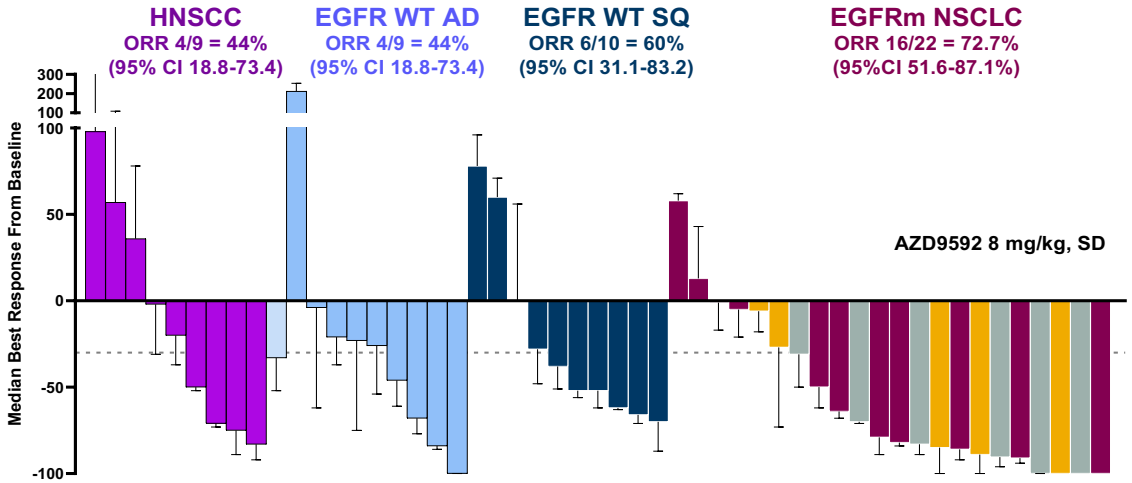
Broaden therapeutic index, safety

Add TOP1i ADC warhead

Direct tumor-killing by TOP1i

Extends benefit beyond signaling-dependent tumors

ADC activity is independent of EGFR and MET driver alterations (mut/amp), oncogenic drivers, and prior treatments

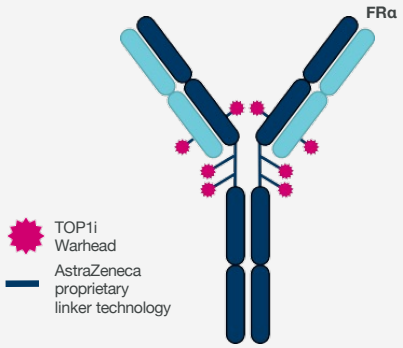


Phase I EGRET first-in-human dose-escalation and dose-expansion trial of AZD9592 in advanced solid tumours ongoing

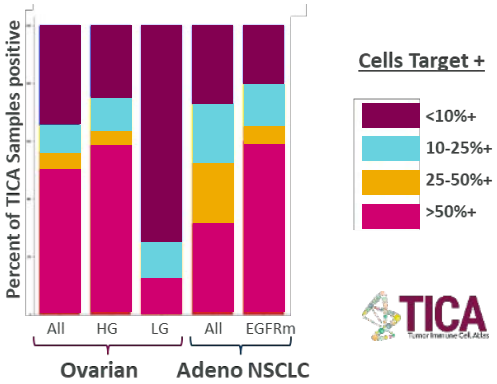
Image is for illustrative purposes only; actual drug positions may vary. 1. Models established from pts with L858R/Ex19 del that progressed on *Tagrisso;* Comer F, et al. Presented at AACR 2023 (Abstract 5736).; McGrath L, et al. Presented at AACR 2023 (Abstract 5737); Sapra, P, Presented at AACR 2023 (Plenary Session); EGFR = epidermal growth factor receptor; cMET = mesenchymal-epithelial transition factor; ADC = antibody drug conjugate; TOP1i = topoisomerase I inhibitor; NSCLC = non-small cell lung cancer; ORR = objective response rate; HNSCC = head and neck squamous cell carcinomas.

AZD5335 (FRα)

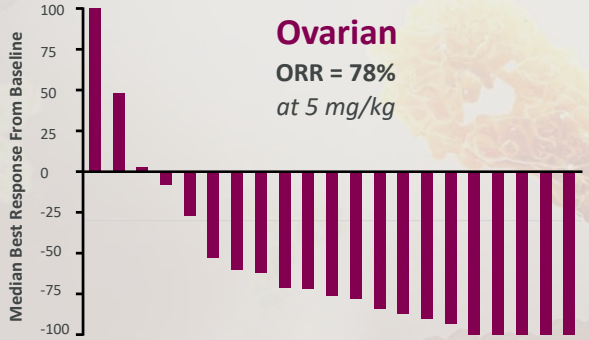
AZD5335: FRα TOP1i



FRα is a validated ADC target expressed in ovarian cancer and NSCLC



Highly active in ovarian cancer PDXs



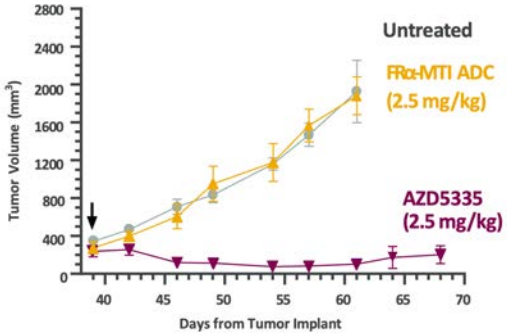
Ovarian
ORR = 78%
at 5 mg/kg

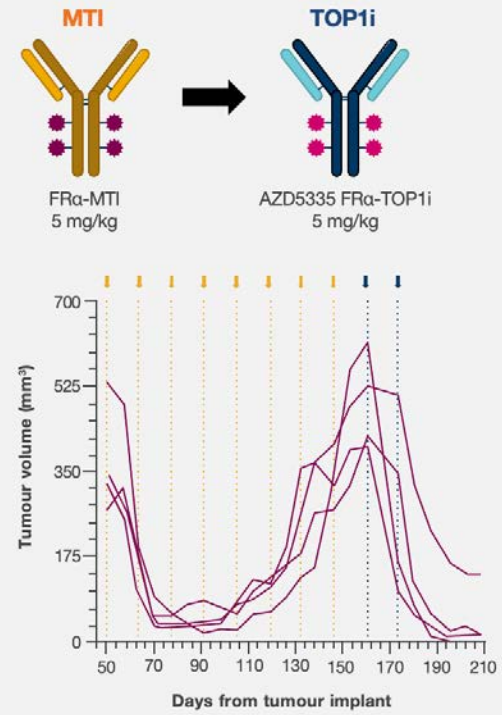
- Similar activity at 2.5 mg/kg

AZD5335 demonstrated superior activity over FRα-MTI ADC

Elahere (FRα-MTI) approved in 3+ FRα ovarian cancer

IHC: 2+ PDX model





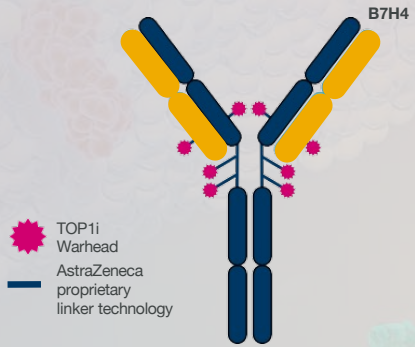
AZD5335 is active in FRα-MTI-refractory CDX

AZD5335 has best-in-class potential for over-expressing solid tumours with clear differentiation from other FRα ADCs

Image is for illustrative purposes only; actual drug positions may vary. Gymnopolous, M et al. Presented at AACR 2023 Abstract #LB025. FRα = folate receptor α; TOP1i = topoisomerase I inhibitor; ADC = antibody drug conjugate; NSCLC = non-small cell lung cancer; TICA = Tumor Immune Cell Atlas; PDXs = patient models; ORR = overall response rate; IHC = immunohistochemistry.

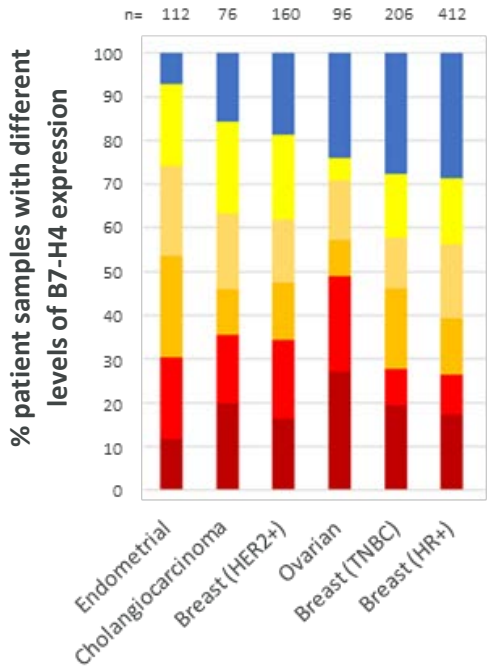
AZD8205 (B7H4)

AZD8205: B7H4



AZD8205 is the first-in-clinic anti-B7-H4 ADC and the first ADC to incorporate AstraZeneca's proprietary TOP1i

B7H4 highly expressed in ovarian, breast, cholangiocarcinoma and endometrial

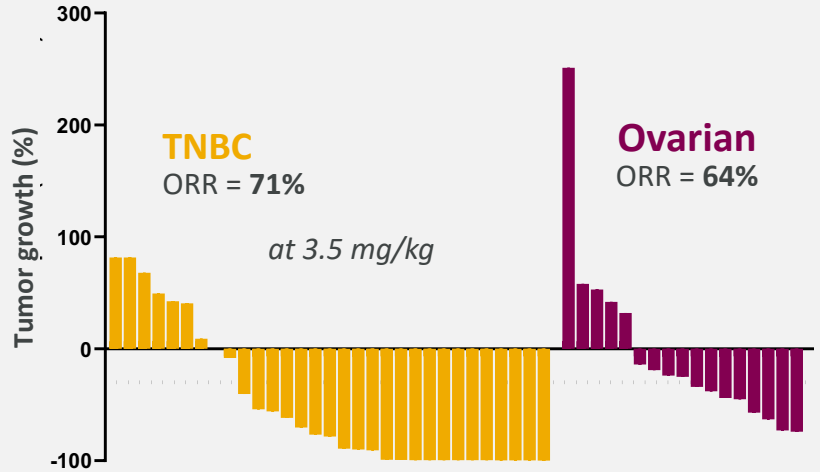


B7-H4 expression was scored in patient samples as % tumour cells expressing B7-H4

Proportion Score

Score	% Tumor
0	0
1	<5%
2	5-25%
3	25-50%
4	50-75%
5	75-100%

Robust activity in patient derived xenograft models



Pre-clinical efficacy demonstrated in breast and ovarian

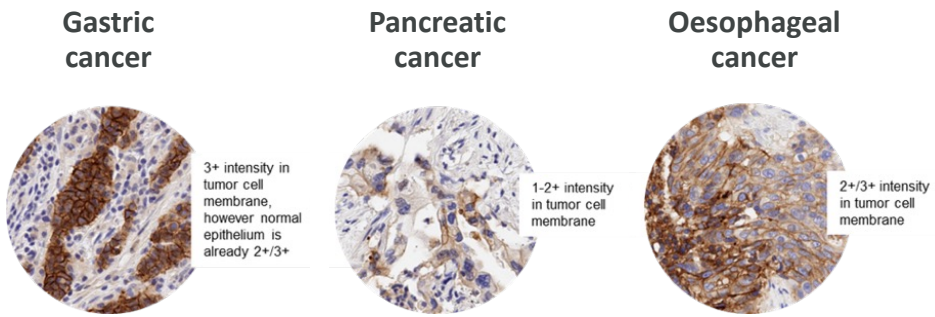
Phase I/II solid tumour dose-escalation and dose-expansion trial (breast, biliary tract, ovarian, endometrial cancers) ongoing

Image is for illustrative purposes only; actual drug positions may vary. Kinneer, K et al. 2023. Clinical Cancer Research, 29(6): 1086-1109. Cazes, A et al. Presented at AACR 2023 Abstract #2947. B7H4 = B7H4 homolog; ADC = antibody drug conjugate; TOP1i = topoisomerase I inhibitor; Pos = positive; TNBC = triple negative breast cancer; HER2 = human epidermal growth factor receptor 2; HR+ = hormone receptor positive; ORR = overall response rate.

AZD0901 (Claudin 18.2)

AZD0901: Claudin 18.2

Claudin 18.2 is expressed in gastric, pancreatic and oesophageal cancers



- Expression appears to be independent of other biomarkers in gastric cancer
- Expression maintained across disease stages, including in metastatic lesions

AZD0901 response in Claudin 18.2-positive gastric / GEJ cancer (N=8)

75%	**ORR** (n=6/8)
100%	**DCR** (n=8/8)
NR	**median PFS**
NR	**median OS**

AZD0901 is showing promising efficacy in 2L+ gastric cancer

Image is for illustrative purposes only; actual drug positions may vary. Xu RH et al. Presented at ASCO GI 2023 Abstract #352.

2L = 2nd-line; P1 = Phase I; GEJ = gastroesophageal junction adenocarcinoma; ORR = objective response rate; DCR = disease control rate; NR = not reached; PFS = progression-free survival; OS = overall survival.
Collaboration partners = AZD0901 partnered with Keymed Biosciences.

Next-wave IO bispecifics

LCM and next-wave bispecifics support continued IO leadership

>70% of global growth driven by new launches:

HIMALAYA (unresectable HCC), **TOPAZ-1** (1L BTC), **POSEIDON** (1L NSCLC)

Imfinzi LCM support further expansion in key tumor areas

NSCLC

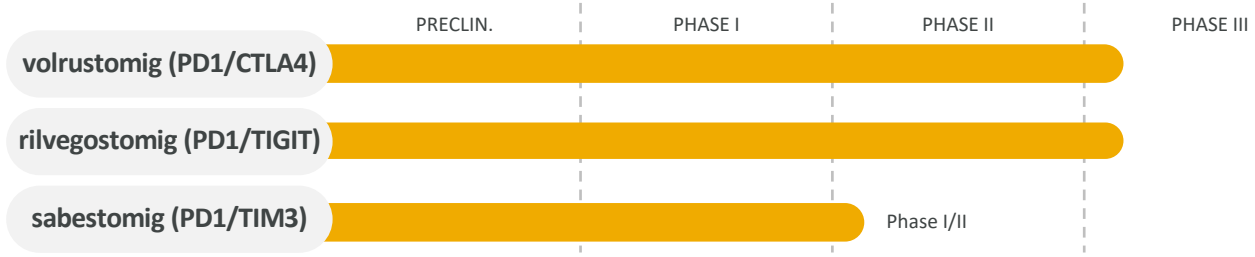
- **PACIFIC trials**
- **AVANZAR** 1L NSCLC
- **ADRIATIC** limited-stage SCLC
- **AEGEAN** Neo/adjuvant NSCLC

GI

GU

- **DUO-O** ovarian cancer
- **DUO-E** endometrial cancer
- **MATTERHORN** gastric/GEJ cancer
- **POTOMAC** Non-muscle invasive bladder cancer
- **EMERALD-1** locoregional liver cancer
- **EMERALD-2** adjuvant liver cancer

Next-wave bispecifics drive IO growth beyond 2025

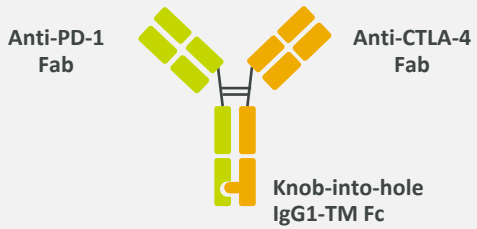


- eVOLVE-Lung02, eVOLVE-cervical
- *Plans to initiate Phase III trial* (potential areas of focus include NSCLC, Gastric cancer, HCC, BTC)
- NSCLC, R/R classical Hodgkin lymphoma

Collaboration partner: Daiichi Sankyo (Dato-DXd).

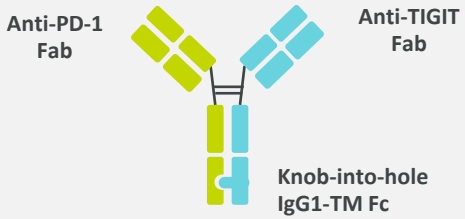
Leading next-wave IO with novel bispecifics portfolio

volrustomig
(PD1/CTLA4)



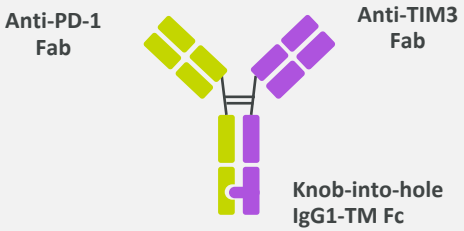
Specifically designed to enhance CTLA-4 blockade on PD-1+ activated T-cells to widen therapeutic index

rilvegostomig
(PD1/TIGIT)



Designed to maximise effect of PD-1 and TIGIT blockade through cooperative binding

sabestomig
(PD1/TIM3)



Binds to unique TIM3 epitope and exerts differentiated T-cell and myeloid/dendritic cell engagement

Image is for illustrative purposes only; actual drug positions may vary. Lee, et al. J Immunother Cancer. 2022;10: doi: 10.1136/jitc-2022-SITC2022.0469 (presented at SITC 2022)
Collaboration partner: Compugen (rilvegostomig).

ESMO2023: volrustomig (PD1/CTLA4) in 1L advanced ccRCC (N=65)

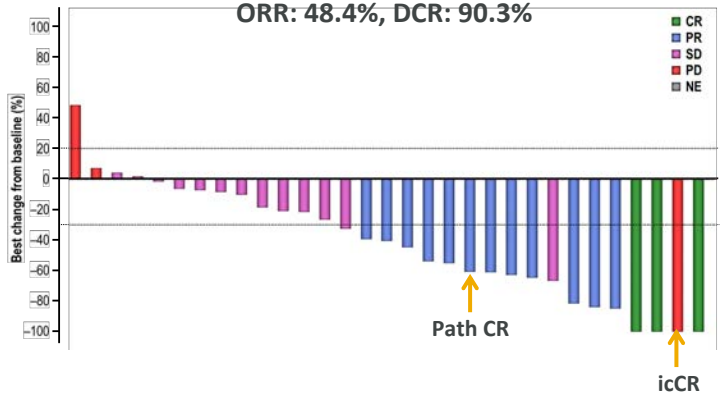
Volrustomig is a monovalent PD-1/CTLA-4 bispecific which achieves full PD-1 blockade and preferential CTLA-4 inhibition on activated PD-1+ T cells.

Volrustomig 750mg and 500mg Q3W demonstrated deep and durable response in treatment-naïve advanced ccRCC patients. Maturing data at 750mg show promising DOR and PFS with PFS-12 of 51.7%.

Both the 500mg and 750mg doses showed an improved safety profile compared to 1500mg. A Phase Ib combination trial of volrustomig and lenvatinib is ongoing in 1L RCC.

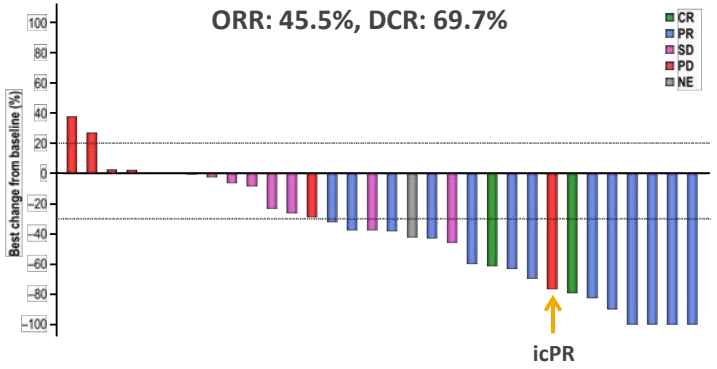
volrustomig 750mg (N = 32)

ORR: 48.4%, DCR: 90.3%

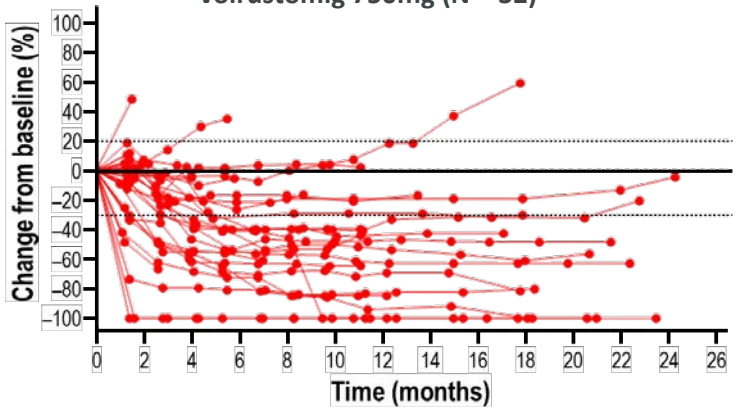


volrustomig 500mg (N = 33)

ORR: 45.5%, DCR: 69.7%

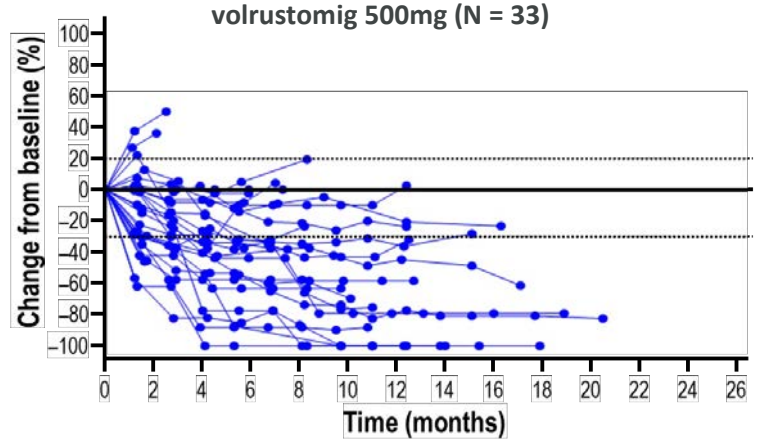


volrustomig 750mg (N = 32)



Median DoR, months (95% CI)	17.0 (9.8-NE)
Median PFS, months (95% CI)	12.3 (8.1-22.8)
PFS-12 (%)	51.7

volrustomig 500mg (N = 33)



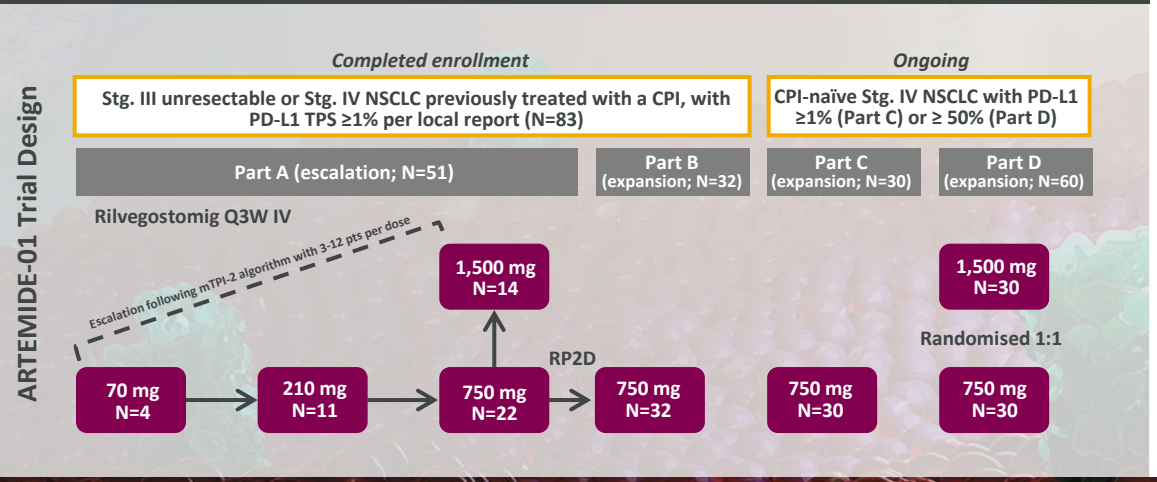
Median DoR, months (95% CI)	11.5 (5.8–NE)
Median PFS, months (95% CI)	9.7 (3.9-NE)
PFS-12 (%)	43.8

ccRCC = clear cell renal carcinoma.

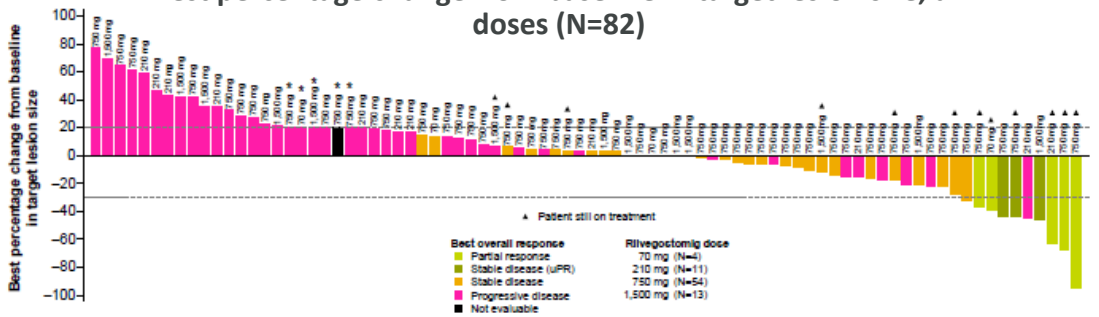
ESMO2023: rilvegostomig in CPI-experienced mNSCLC (ARTEMIDE-01, updated data from Parts A and B)

Rilvegostomig is a bispecific targeting PD-1 and TIGIT, designed to maximise effect of PD-1 and TIGIT blockade through cooperative binding. ARTEMIDE-01 is an ongoing dose-escalation and dose-expansion trial to evaluate the safety and efficacy of rilvegostomig in patients with Stg. III or IV NSCLC.

Updated data from Parts A and B at ESMO 2023 show rilvegostomig was well tolerated across all doses with no DLTs observed during dose escalation. Antitumour activity was observed in heavily pre-treated patients with CPI-resistant mNSCLC. Expansion (Part C) and dose optimisation (Part D) in CPI-naïve patients with NSCLC are currently enrolling.

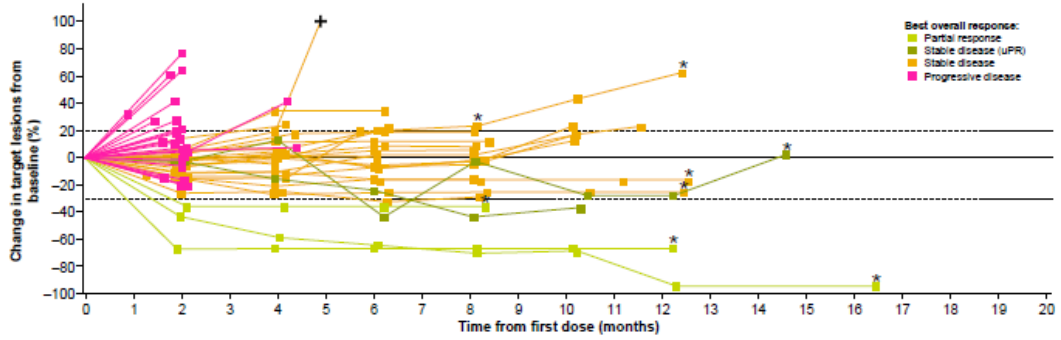


Best percentage change from baseline in target lesion size, all doses (N=82)



RECIST version 1.1.
*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 PD and has no evaluable TL data before or at PD.
NTL, non-target lesion; PD, progressive disease; RECIST, Response Evaluation Criteria in Solid Tumours; TL, target lesion; uPR, unconfirmed partial response

Percentage change from baseline in target lesion size over time at RP2D (750mg Q3W, Parts A and B; N=54)



RECIST version 1.1.
+Percentage change from baseline in tumour lesion size exceeds +100%. Spider plot truncated for the patient at this point.
*Represents patient still on treatment (n=8/54).
RP2D, recommended phase 2 dose; Q3W, every three weeks; uPR, unconfirmed partial response

EGFRm = epidermal growth factor receptor mutation.
Collaboration partner: Compugen (rilvegostomig).

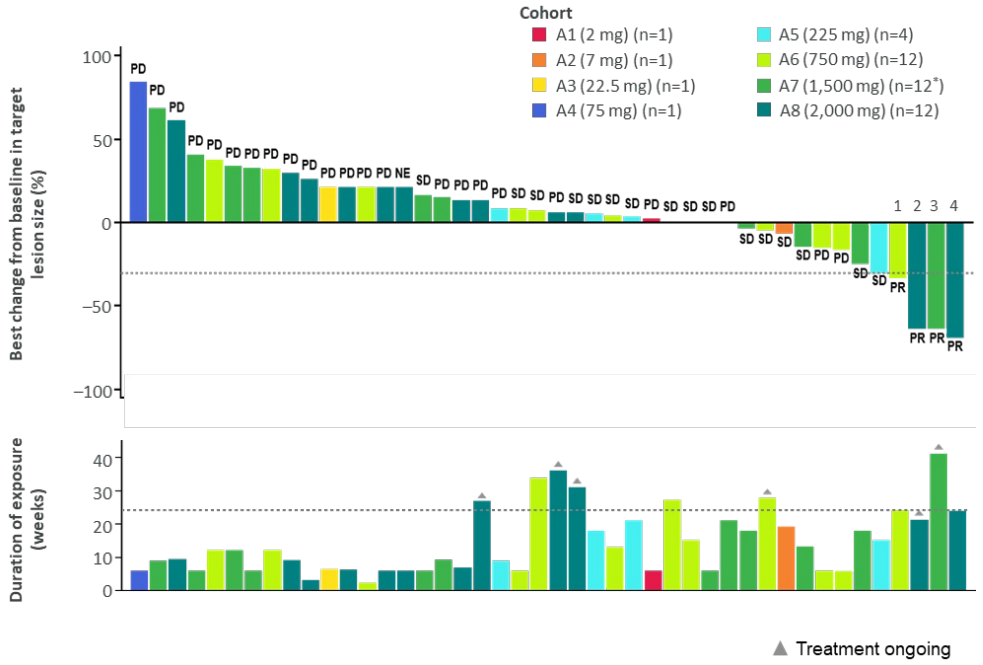
ESMO2023: sabestomig in patients with Stg IIIB-IV NSCLC with prior PD-L1 therapy

Sabestomig is specifically designed to bind to PD-1 and a unique TIM-3 epitope and is believed to act through:

I. Targeting PD-1 and TIM-3 to reinvigorate T-cell function and improve anti-tumour response

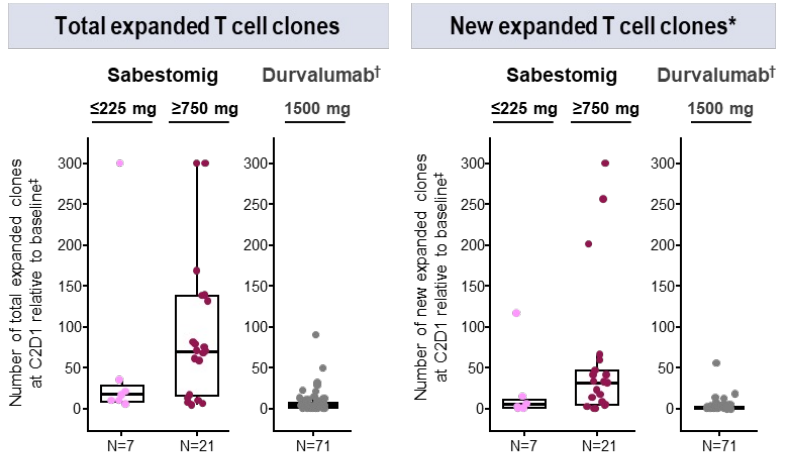
II. Targeting TIM-3 to increase tumour cell phagocytosis and antigen presentation

In first-in-human data presented at ESMO 2023, sabestomig was well tolerated with no dose limiting toxicities and showed clinical activity in Stg. IIIB-IV 2L+ NSCLC patients with primary or acquired resistance to anti-PDL1.



Responses observed at biologically active doses (≥750mg, n=36) in patients with PD-L1 resistant NSCLC, including **four patients with cPR**

Sabestomig drives **expansion of existing and new T cell clones in periphery**, consistent with TIM-3 MoAs



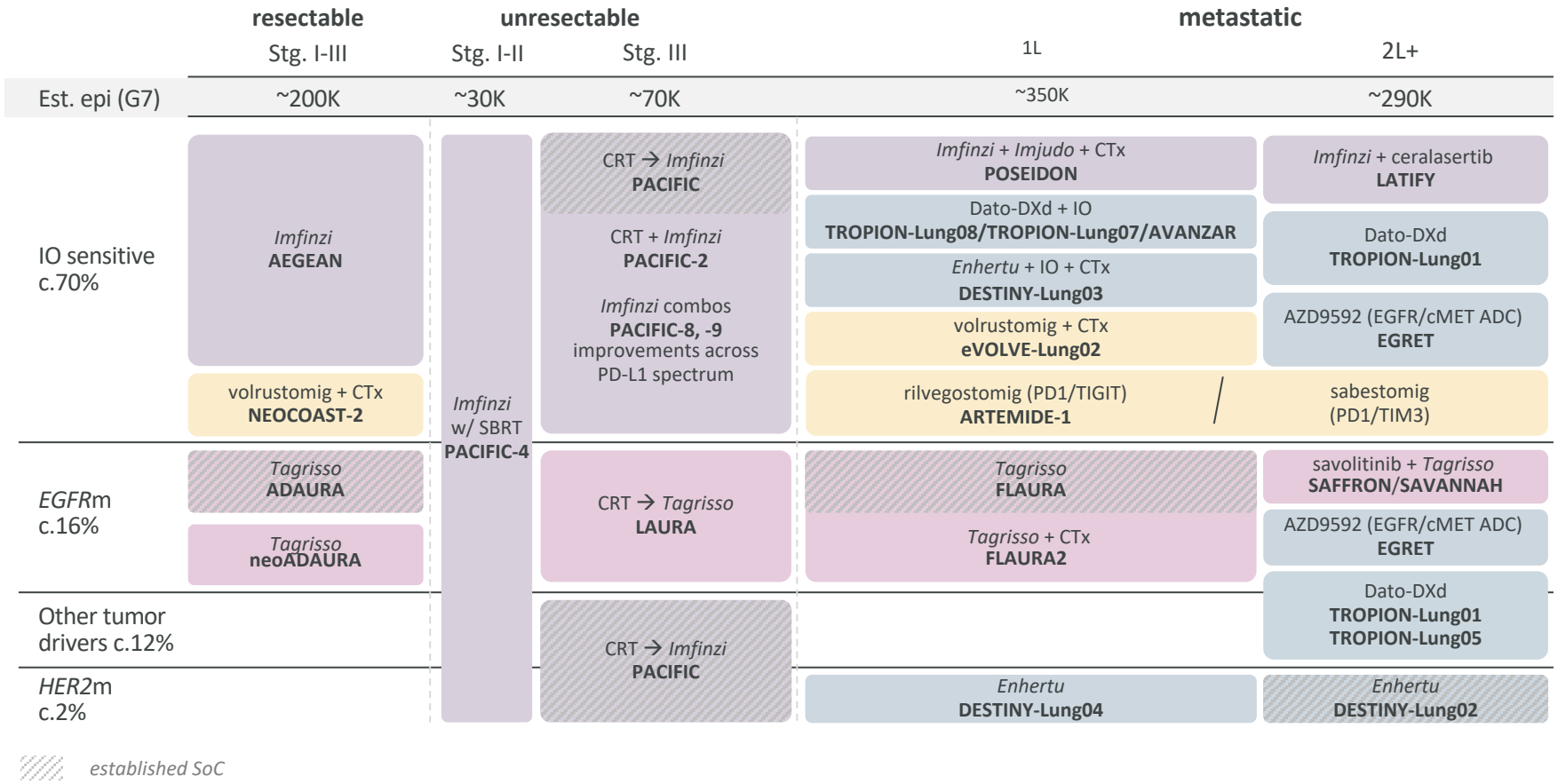
T cell clonal expansion analysis using TCR sequencing. *New expanded T cell clones = unique clones not detected at baseline.
† Cohort was durvalumab + olaparib to represent anti-PD-L1 effect.† ‡Y axis ceiling applied.

1. Besse, B., Italiano, A. et al. ESMO 2023. Safety and preliminary efficacy of sabestomig (AZD7789), a bispecific antibody targeting PD-1 and TIM-3, in patients with Stage IIIB–IV non-small-cell lung cancer with previous anti-PD-(L)1 therapy.
EGFRm = epidermal growth factor receptor mutation.

AstraZeneca

Lung Cancer strategy & FLAURA2

AstraZeneca in NSCLC



- Establishing *Tagrisso* as backbone TKI in *EGFR*m
- *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 + ADCs
- Investing behind new technologies and platforms, including cell therapy and testing/screening

Ambition for >50% of all treated lung cancer patients to be eligible for an AstraZeneca medicine by the year 2030

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).

WCLC23: FLAURA2 (Tagrisso + CTx) demonstrates statistically significant, clinically meaningful improvement

FLAURA2 offers unsurpassed efficacy with a novel regimen that builds on clinician experience with *Tagrisso* and chemotherapy.

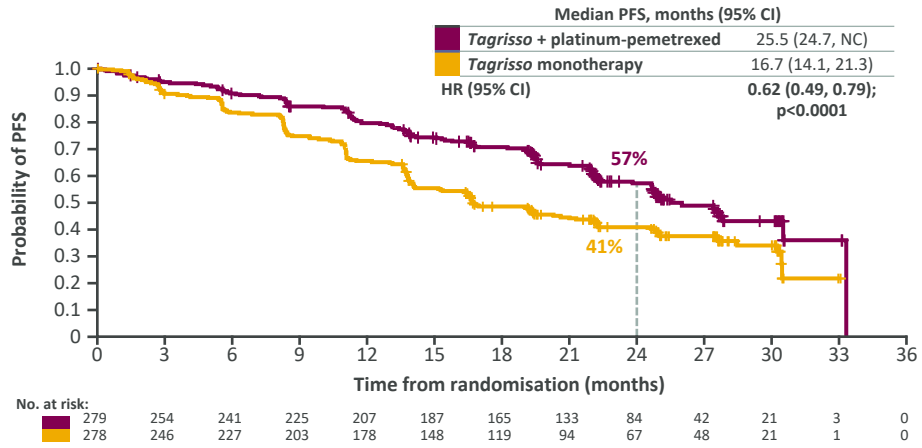
Tagrisso monotherapy is standard of care for 1L *EGFR*m NSCLC. However, despite the observed benefits, most patients will progress following treatment leaving an opportunity for additional 1L treatments.

Data from FLAURA2 demonstrated that *Tagrisso* combined with platinum-pemetrexed resulted in a statistically significant and clinically meaningful improvement in PFS over *Tagrisso* monotherapy in patients with 1L *EGFR*m advanced NSCLC.

In addition, the safety profiles were as expected for each treatment and were manageable with standard medical practice, with only 11% discontinuing *Tagrisso* in the combination arm.

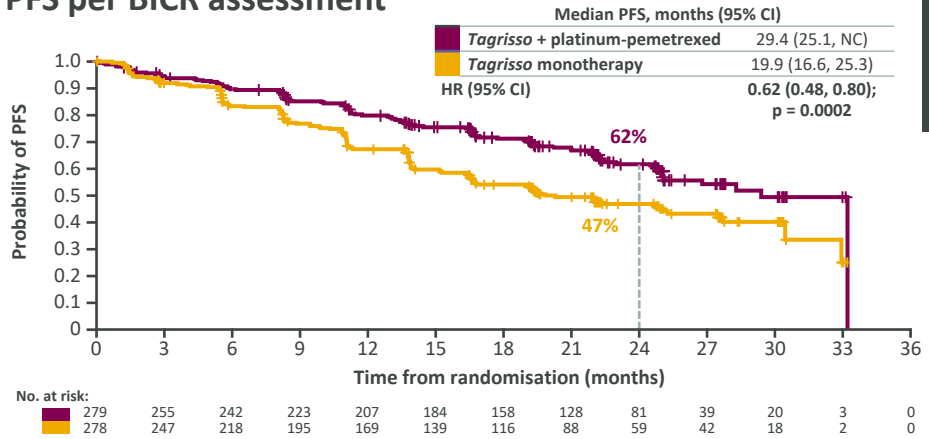
Follow-up continues for PFS2 and OS.

PFS per investigator assessment



mPFS improvement of **8.8 months** per investigator assessment with **HR 0.62**

PFS per BICR assessment



mPFS improvement of **9.5 months** per BICR assessment with **HR 0.62**

Data cut-off: 03 April 2023.

EGFRm = epidermal growth factor receptor mutated; NSCLC = non-small cell lung cancer; 1L = 1st-line; PFS = progression-free survival; PFS2 = progression-free survival 2; OS = overall survival; CI = confidence interval; NC = not calculable; HR = hazard ratio; no. = number.

WCLC23: FLAURA2 (Tagrisso + CTx) demonstrates statistically significant, clinically meaningful improvement

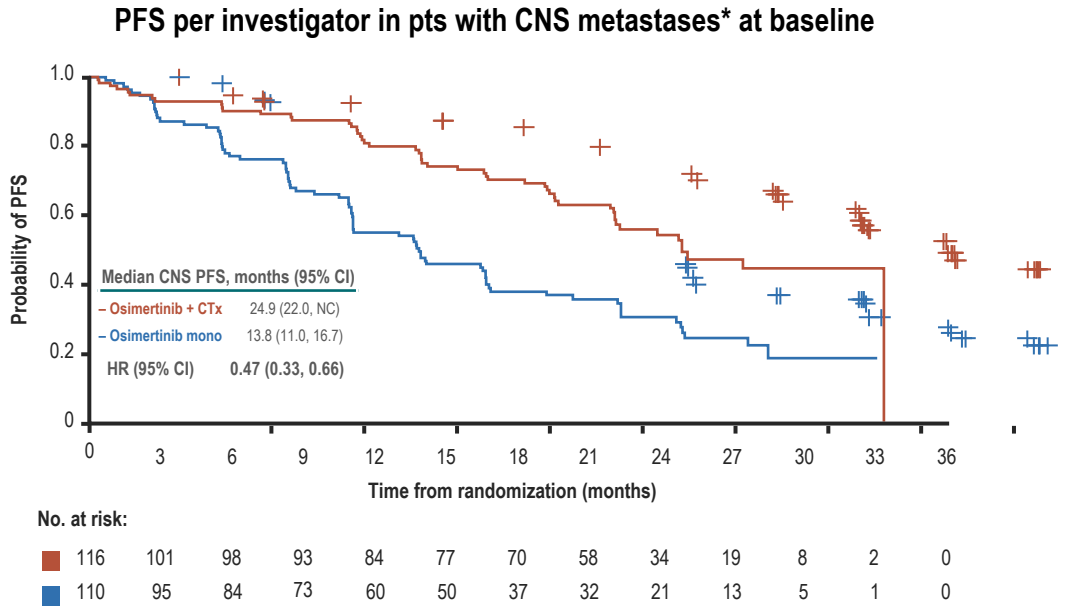
PFS across pre-defined subgroups

Subgroup		*Tagrisso* + platinum-pemetrexed (Events / patients)	*Tagrisso* monotherapy (Events / patients)	HR (95% CI)
All patients	Stratified log-rank	120 / 279	166 / 278	**0.62** (0.49, 0.79)
	Unadjusted Cox PH	120 / 279	166 / 278	**0.62** (0.49, 0.78)
Sex	Male	51 / 106	73 / 109	**0.54** (0.37, 0.77)
	Female	69 / 173	93 / 169	**0.67** (0.49, 0.92)
Race	Chinese Asian	26 / 71	43 / 69	**0.49** (0.30, 0.81)
	Non-Chinese Asian	54 / 107	65 / 107	**0.76** (0.53, 1.09)
	Non-Asian	40 / 101	58 / 102	**0.55** (0.37, 0.83)
EGFR mutation test method	Central	52 / 121	67 / 119	**0.73** (0.51, 1.05)
	Local	68 / 158	99 / 159	**0.55** (0.40, 0.74)
Age at screening	<65 years	73 / 174	97 / 166	**0.59** (0.44, 0.80)
	≥65 years	47 / 105	69 / 112	**0.68** (0.47, 0.98)
Smoking history	Yes	43 / 91	57 / 97	**0.63** (0.42, 0.94)
	No	77 / 188	109 / 181	**0.61** (0.46, 0.82)
EGFR mutation type[1]	Ex19del	65 / 172	94 / 169	**0.60** (0.44, 0.83)
	L858R	55 / 106	70 / 107	**0.63** (0.44, 0.90)
WHO PS	0	48 / 101	57 / 102	**0.79** (0.54, 1.16)
	1	72 / 178	109 / 176	**0.53** (0.39, 0.72)
CNS status at baseline	Yes	52 / 116	79 / 110	**0.47** (0.33, 0.66)
	No	68 / 163	87 / 168	**0.75** (0.55, 1.03)

PFS benefits were consistent across all pre-defined patient subgroups, including in the **~40% of patients with CNS metastases** at baseline as assessed by MRI

New at ESMO 2023: FLAURA2 in CNS metastases

CNS ORR 59% (cFAS, N=222) and 48% (cEFR, N=78)

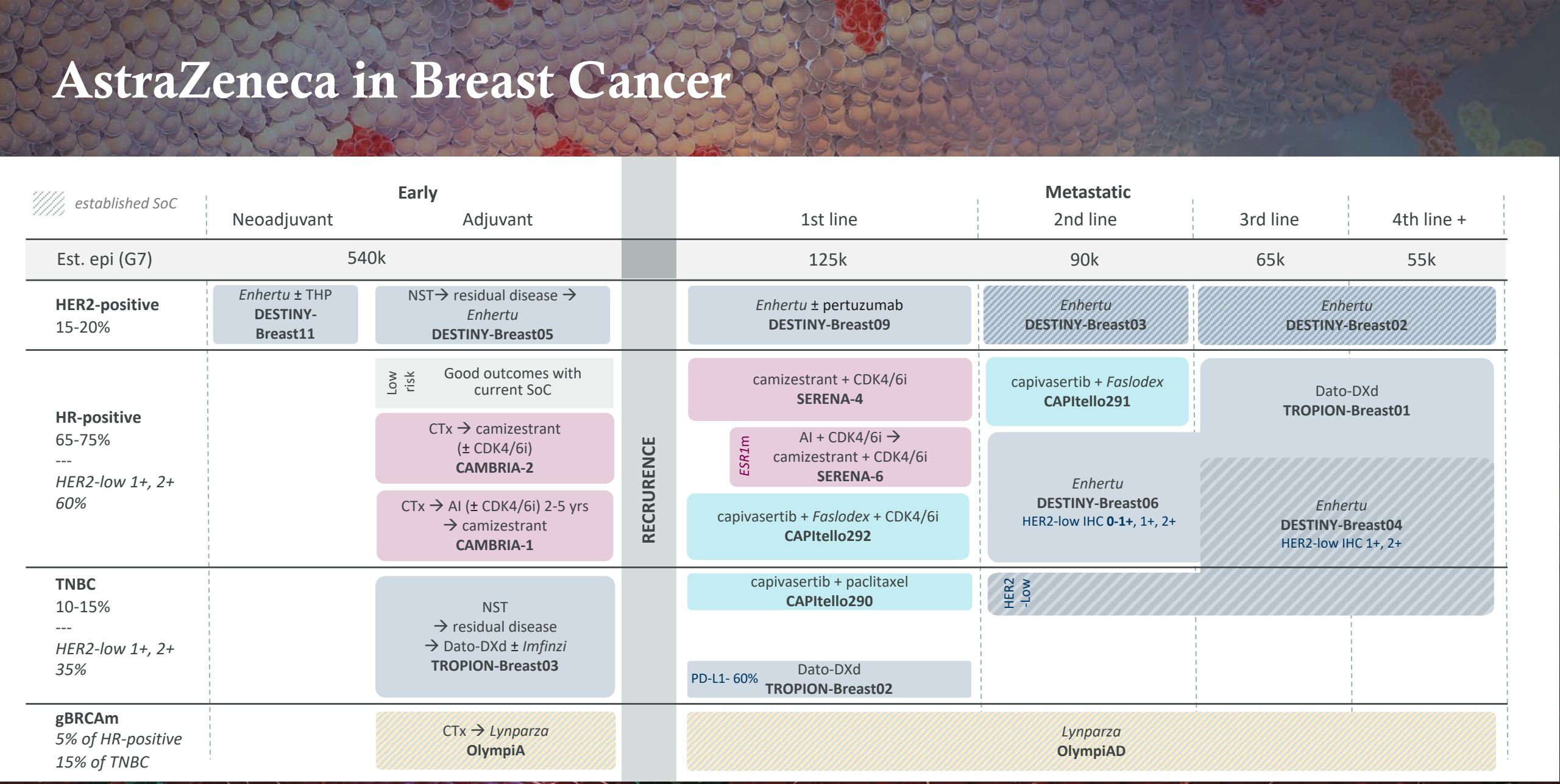


Data cut-off: 03 April 2023. 1.For EGFR mutation type, patients with both Ex19del and L858R were included in Ex19del group.
CTx = chemotherapy; PFS = progression-free survival; CNS = central nervous system; MRI = magnetic resonance imaging; WHO PS = World Health Organisation performance score; EGFRm = epidermal growth factor receptor mutated; NC = not calculable; HR = hazard ratio; CI = confidence interval; no. = number.

AstraZeneca

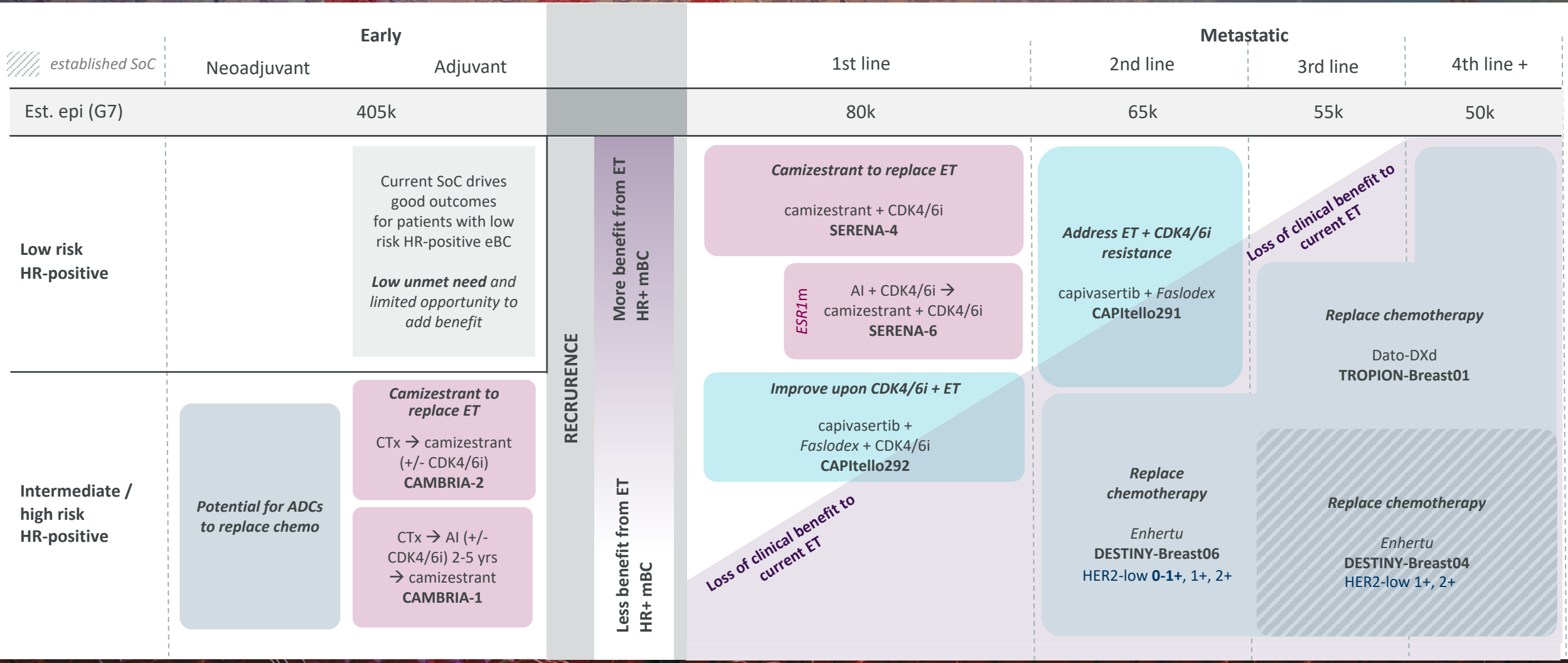
Breast cancer strategy

AstraZeneca in Breast Cancer



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; yrs = years; ESR1m = estrogen 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*).

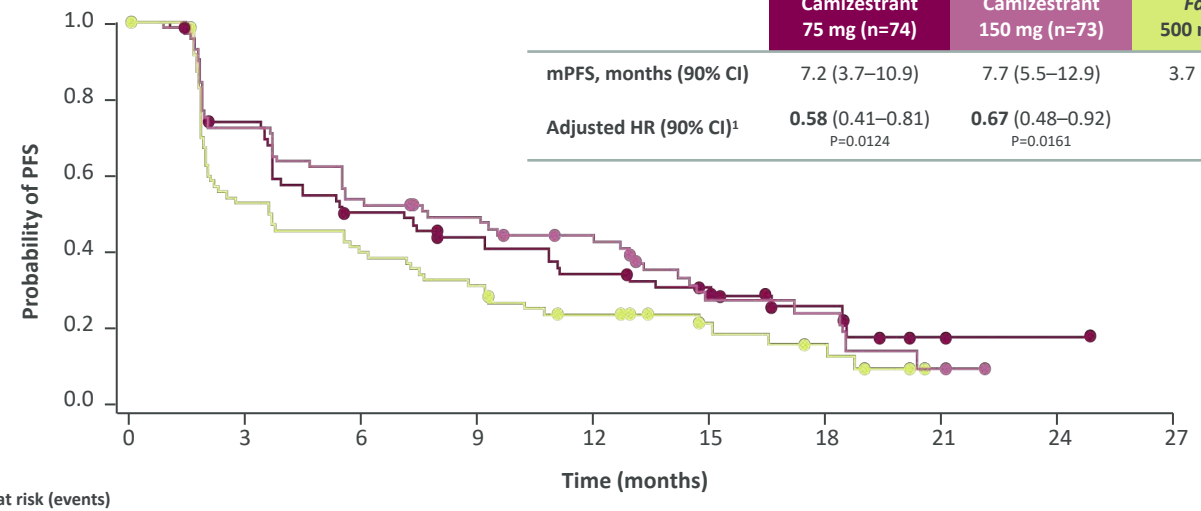
AstraZeneca in HR-positive Breast Cancer



All numbers are approximate. Illustrative settings and populations, not to scale.
HR = hormone receptor; 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; yrs = years; ESR1m = estrogen receptor 1 gene mutation; ER = estrogen receptor; Dato-DXd = datopotamab deruxtecan.
Collaboration partners: Daiichi Sankyo (*Enhertu*, Dato-DXd).

Camizestrant: Next-generation oral SERD set to reimagine treatment in both early and advanced HR+ breast cancer

SERENA-2: Phase II trial in advanced ER+ HER2- breast cancer[1]



	Camizestrant 75 mg (n=74)	Camizestrant 150 mg (n=73)	*Faslodex* 500 mg (n=73)
mPFS, months (90% CI)	7.2 (3.7–10.9)	7.7 (5.5–12.9)	3.7 (2.0–6.0)
Adjusted HR (90% CI)[1]	**0.58** (0.41–0.81) P=0.0124	**0.67** (0.48–0.92) P=0.0161	

No. at risk (events)

Cami 75mg	74	50	33	27	21	14	7	2	1	0
Cami 150mg	73	50	37	32	25	12	6	2	0	
Faslodex 500 mg	73	37	28	22	14	8	5	0		

TRAE, n (%)	Camizestrant 75 mg (n=74)	*Faslodex* 500 mg (n=73)
Any AE	57 (77)	50 (68.5)
Grade ≥3 AE	1 (1.4)	1 (1.4)
AE leading to discontinuation of treatment	2 (2.7)	0

Ongoing Phase III trials (>2024)

Adjuvant treatment for early breast cancer

CAMBRIA-1
Pts at high risk of recurrence

Locoregional tx ± CTx
↓
ET ± CDK4/6i
↓
2-5 years
↓
Cami

CAMBRIA-2
Pts at high or intermediate risk of recurrence

Locoregional tx ± CTx
↓
Cami ± CDK4/6i

1st line treatment for advanced breast cancer

SERENA-6
Pts with detected *ESR1*m before progression

AI + CDK4/6i
↓
*ESR1*m detected
↓
Cami + CDK4/6i

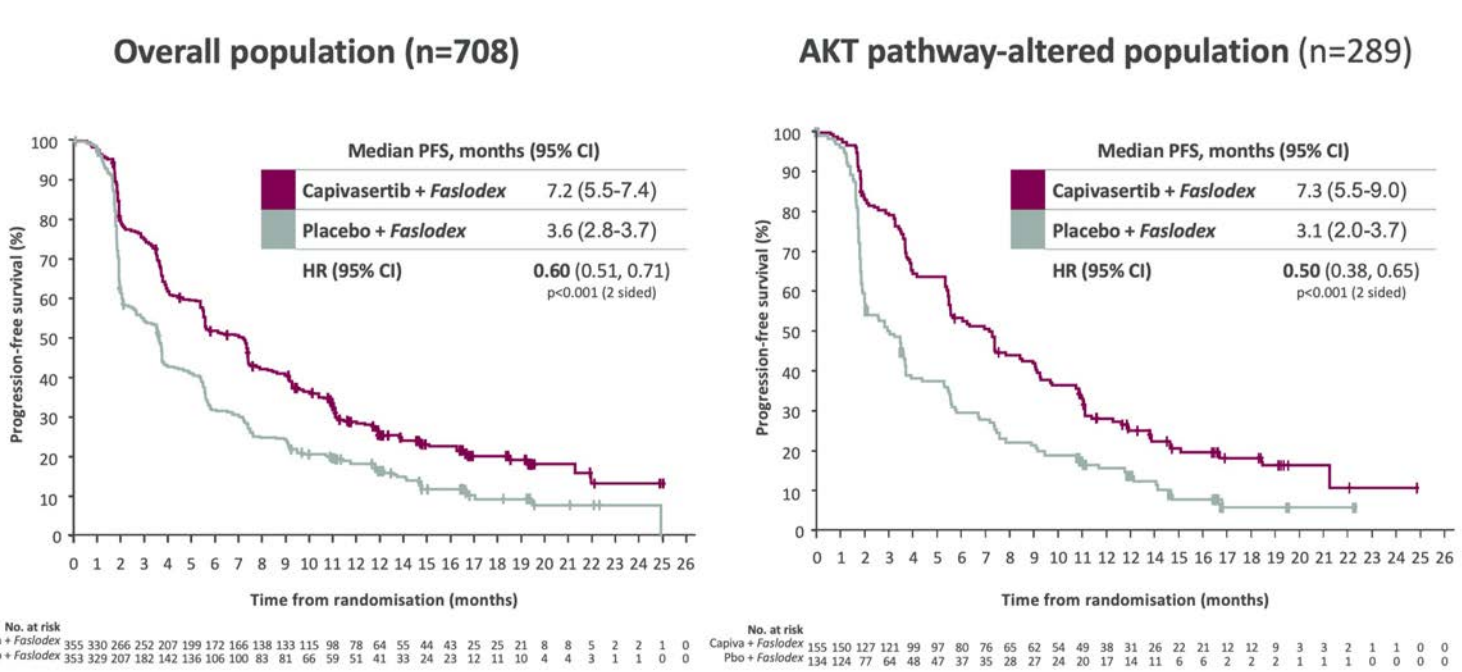
SERENA-4
Pts with no prior treatment for aBC

Cami + CDK4/6i

1. Oliveira M et al. Presented at San Antonio Breast Cancer Symposium, December 6–10, 2022; 2. HR adjusted for prior use of CDK4/6i and liver/lung metastases.
SERD = selective estrogen receptor degrader; HR+ = hormone receptor positive; ER = oestrogen receptor; HER2- = human epidermal growth factor receptor 2 negative; (m)PFS = (median) progression-free survival; no. = number; cami = camizestrant; HR = hazard ratio; CI = confidence interval; (TR)AE = (treatment related) adverse event; pts = patients; tx = treatment; CTx = chemotherapy; ET = endocrine therapy; CDK4/6i = cyclin-dependent kynases 4 and 6 inhibitor; *ESR1*m = oestrogen receptor alpha mutated; aBC = advanced breast cancer.

CAPItello-291: First Phase III for potential first-in-class AKT inhibitor capivasertib[1]

Statistically significant and **clinically meaningful improvements in PFS** with **capivasertib + *Faslodex*** in both **overall** and **AKT pathway-altered populations**



AE, n (%)	Capivasertib + *Faslodex* (n=355)		Placebo + *Faslodex* (n=350)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any AE	343 (96.6)	148 (41.7)	288 (82.3)	54 (15.4)
Diarrhoea[2]	257 (72.4)	33 (9.3)	71 (20.3)	1 (0.3)
Rash[2]	135 (38.0)	43 (12.1)	25 (7.1)	1 (0.3)
Nausea	123 (34.6)	3 (0.8)	54 (15.4)	2 (0.6)
Fatigue	74 (20.8)	2 (0.6)	45 (12.9)	2 (0.6)
Vomiting	73 (20.6)	6 (1.7)	17 (4.9)	2 (0.6)
Headache	60 (16.9)	1 (0.3)	43 (12.3)	2 (0.6)
Hyperglycaemia[2]	60 (16.9)	8 (2.3)	14 (4.0)	1 (0.3)
Decreased appetite	59 (16.6)	1 (0.1)	22 (6.3)	2 (0.6)
Serious AE	57 (16.1)		28 (8.0)	
AE leading to death[3]	4 (1.1)		1 (0.3)	
AE leading to discontinuation	46 (13.0)		8 (2.3)	

Overall safety profile of capivasertib + *Faslodex* consistent with that observed in previous trials evaluating this combination

Granted Priority Review in the US for patients with advanced HR-positive breast cancer

1. Turner NC et al. N Engl J Med. 2023;388(22):2058–2070; 2. Group terms (preferred terms): diarrhea (diarrhea, frequent bowel movements, gastrointestinal hypermotility); rash (rash, rash macular, rash maculo-papular, rash papular, rash pruritic) and hyperglycaemia (blood glucose increased, hyperglycaemia); 3. Grade 5 events included acute myocardial infarction, cerebral hemorrhage, pneumonia aspiration and sepsis (all n=1) in the capivasertib + *Faslodex* group and COVID-19 (n=1) in the placebo + *Faslodex* group. No grade 5 events were classified as related to capivasertib/placebo by local investigator. The safety analysis population included all patients who received at least one dose of the study drug.
AKT = protein kinase B; PFS = progression-free survival; CI = confidence interval; HR = hazard ratio; no. = number; AE = adverse event; HR = hormone receptor.