San Antonio Breast Cancer Symposium®, December 6-10, 2022

Camizestrant, a next-generation oral SERD *vs* fulvestrant in post-menopausal women with advanced ER-positive HER2-negative breast cancer: Results of the randomized, multi-dose Phase 2 SERENA-2 trial

Mafalda Oliveira, MD, PhD[1], Denys Pominchuk, PhD[2], Zbigniew Nowecki MD[3], Erika Hamilton, MD[4], Yaroslav Kulyaba, MD[5], Timur Andabekov, PhD[6], Yevhen Hotko, MD[7], Tamar Melkadze, MD[8], Gia Nemsadze, MD, PhD[9], Patrick Neven, MD[10], Yuriy Semegen, MD[11], Vladimir Vladimirov, MD[12], Claudio Zamagni, MD[13], Hannelore Denys, MD, PhD[14], Frédéric Forget, MD[15], Zsolt Horvath, MD, PhD[16], Alfiya Nesterova, MD, PhD[17], Maxine Bennett, PhD[18], Bistra Kirova, MBChB, MSc[19], Teresa Klinowska, PhD[20], Justin P O Lindemann, MBChB, MB[18], Delphine Lissa, PharmD, PhD[18], Alastair Mathewson, PhD[18], Christopher J Morrow, PhD[18], Zuzana Traugottova, MD[21], Ruaan van Zyl, PhD[22], Ekaterine Arkania, MD[23]

[1]Medical Oncology Department, Vall d'Hebron University Hospital and Breast Cancer Group, Vall d'Hebron Institute of Oncology, Barcelona, Spain; [2]Medical Center Verum, Kyiv, Ukraine; [3]The Maria Sklodowska Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland; [4]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; [5]Makiivka City Hospital of Donetsk Region, Makiivka, Ukraine; [6]AV Medical Group, St Petersburg, Russian Federation; [7]Central City Hospital, Uzhgorod National University, Uzhgorod, Ukraine; [8]Oncology and Hematology Department, Academician Fridon Todua Medical Center – Research Institute of Clinical Medicine Tbilisi, Georgia; [9]The Institute of Clinical Oncology, Tbilisi, Georgia; [10]Multidisciplinary Breast Center, University Hospitals Leuven – Campus Gasthuisberg, Leuven, Belgium; [11]Bukovynsky Clinical Oncology Center, Chernivtsi, Ukraine; [12]Pyatigorsky Oncology Dispensary, Pyatigorsk, Russia; [13]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [14]Department of Medical Oncology, Ghent University Hospital, Belgium; [15]Centre Hospitalier de l'Ardenne-Site de Libramont, Libramont-Chevigny, Belgium; [16]Center of Oncoradiology, Bács-Kiskun County Teaching Hospital, Kecskemét, Hungary; [17]Republican Clinical Oncology Dispensary of the Ministry of Health of the Republic of Tatarstan, Russian Federation; [18]Research and Early Development, Oncology R&D, AstraZeneca, Cambridge, UK; [19]Oncology Patient Safety, Oncology R&D, AstraZeneca, Cambridge, UK; [20]Late Development, Oncology R&D, AstraZeneca, Cambridge, UK; [21]Parexel International, Prague, Czech Republic; [22]Parexel International, Bloemfontein, South Africa; [23]Helsicore Israeli Georgian Medical Research Clinic, Tbilisi, Georgia.

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

Disclosure information

Mafalda Oliveira MD, PhD

I have the following relevant financial relationships to disclose:

Employee of: Vall d'Hebron University Hospital, Barcelona, Spain

Consultant for: AstraZeneca, Gilead, GSK, iTEOS, MSD, Pierre Fabre, Roche and SeaGen

Speaker’s Bureau for: AstraZeneca, Eisai, Novartis, Roche and SeaGen

Grant/Research support from: AstraZeneca, Boehringer-Ingelheim, Genentech, Gilead, GSK, Immunomedics, Novartis, Roche, SeaGen and Zenith Epigenetics

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

Background

- Camizestrant is a next-generation oral SERD and pure ER antagonist[1]
- SERENA-1 (NCT03616587) demonstrated the safety, tolerability, and preliminary clinical efficacy of a range of doses of camizestrant as monotherapy, with dose-dependent exposure[2,3]
- SERENA-2 (NCT04214288) was designed to explore the efficacy and safety of a range of camizestrant doses administered once daily as a monotherapy in comparison with fulvestrant, the current SERD standard of care

ER: estrogen receptor; SERD: selective estrogen receptor and degrader

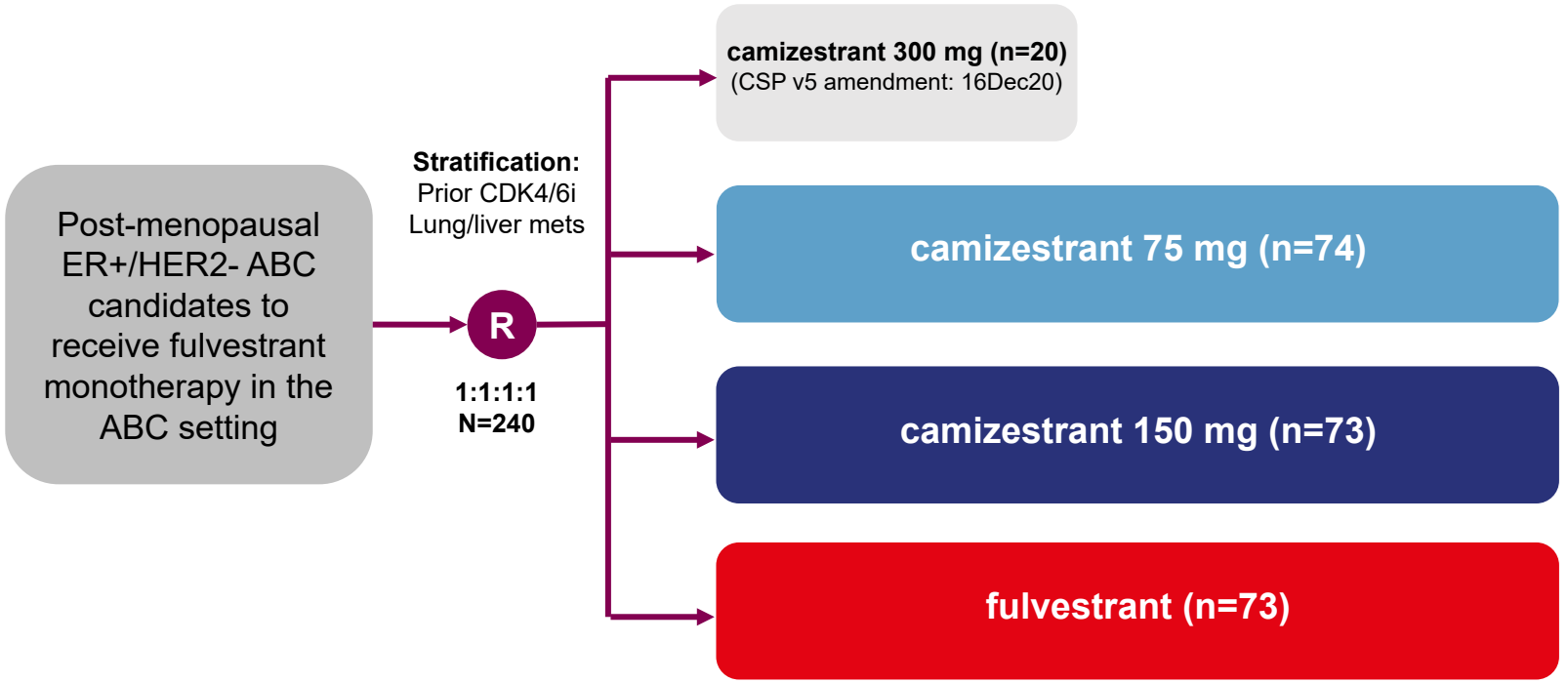
1. Scott JS *et al. J Med Chem* 2020; **63:** 14530–59
2. Hamilton EP *et al. J Clin Oncol* 2020;38 (15 suppl) [abstract 1024]
3. Baird R e*t al*. *Cancer Res* 2021;81(suppl 4) [abstract PS11-05]

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

SERENA-2 study overview

Key inclusion/exclusion criteria:

- Recurrence or progression on at least one line of ET
- No prior fulvestrant or oral SERD in ABC
- No more than one line of ET in ABC setting
- No more than one line CT in ABC setting
- Measurable and non-measurable disease



- **Primary endpoint:** PFS (investigator assessment*)
- **Secondary endpoints:** CBR24, ORR, OS, safety
- **Translational endpoints:** serial ctDNA analysis including *ESR1*m, serial CTCs analysis

*disease progression assessed by the Investigator and defined using RECIST, version 1.1
ABC: advanced breast cancer; CBR24: clinical benefit rate at 24 weeks; CDK4/6i: CDK4/6 inhibitor; CT: chemotherapy; CTC: circulating tumor cells; ctDNA: circulating tumor DNA; ER: estrogen receptor; *ESR1*m: mutation in estrogen receptor 1 gene; ET: endocrine therapy; HER2: human epidermal growth factor; PFS: progression-free survival; R: randomization; RECIST: Response Evaluation Criteria for Solid Tumors; SERD: selective estrogen receptor degrader

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

Statistical considerations

- SERENA-2 was designed to compare each of the camizestrant 75, 150 and 300 mg doses with fulvestrant
- No formal analyses of camizestrant 300 mg versus fulvestrant were conducted since enrolment to camizestrant 300 mg was stopped early (n=20 patients)
- SERENA-2 was not powered to compare between camizestrant doses
- 108 events for the pairwise comparison versus fulvestrant provided 86% power at the 2-sided 10% significance level assuming the true hazard ratio was 0.59 and the median PFS in the control arm was 5 months
- Primary analysis was triggered in August 2022 when 108 progression events (75% maturity) had occurred in the best performing pair (camizestrant 75 or 150 mg versus fulvestrant)
- Primary analyses used a stratified Cox proportional hazards model to compare PFS, adjusting for prior use of CDK4/6i and presence of lung and/or liver metastases
- No multiplicity adjustments were made for multiple comparisons in this Phase 2 study

CDK4/6i: CDK4/6 inhibitor; PFS: progression-free survival

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

Key baseline patient characteristics

	C 75 (n=74)	C 150 (n=73)	F (n=73)	Total (n=240)
Age (median, range)	61.0 (37-89)	60.0 (42-84)	60.0 (35-84)	60.0 (35-89)
Gender, F (%)[a]	100	100	100	100
Race, White (%)	95.9	95.9	89.0	94.2
ER+ (%)	100	100	100	100
PgR+ (%)	81.1	84.9	79.5	79.6
ECOG 0 (%)	62.2	57.5	58.9	58.8
Lung/liver metastasis Y (%)	58.1	58.9	58.9	58.3
Liver metastasis (%)	31.1	41.1	47.9	40.8
Bone only disease (%)	14.9	19.4	17.8	17.6
***ESR1*m detectable (%)[b]**	29.7	35.6	47.9	36.7
D538G	18.9	19.2	31.5	22.9
Y537N	14.9	15.1	15.1	13.8
Y537S	6.8	13.7	19.2	12.5
E380Q	9.5	8.2	8.2	8.3
L536H	1.4	8.2	4.1	4.6
Y537C	4.1	4.1	2.7	3.3

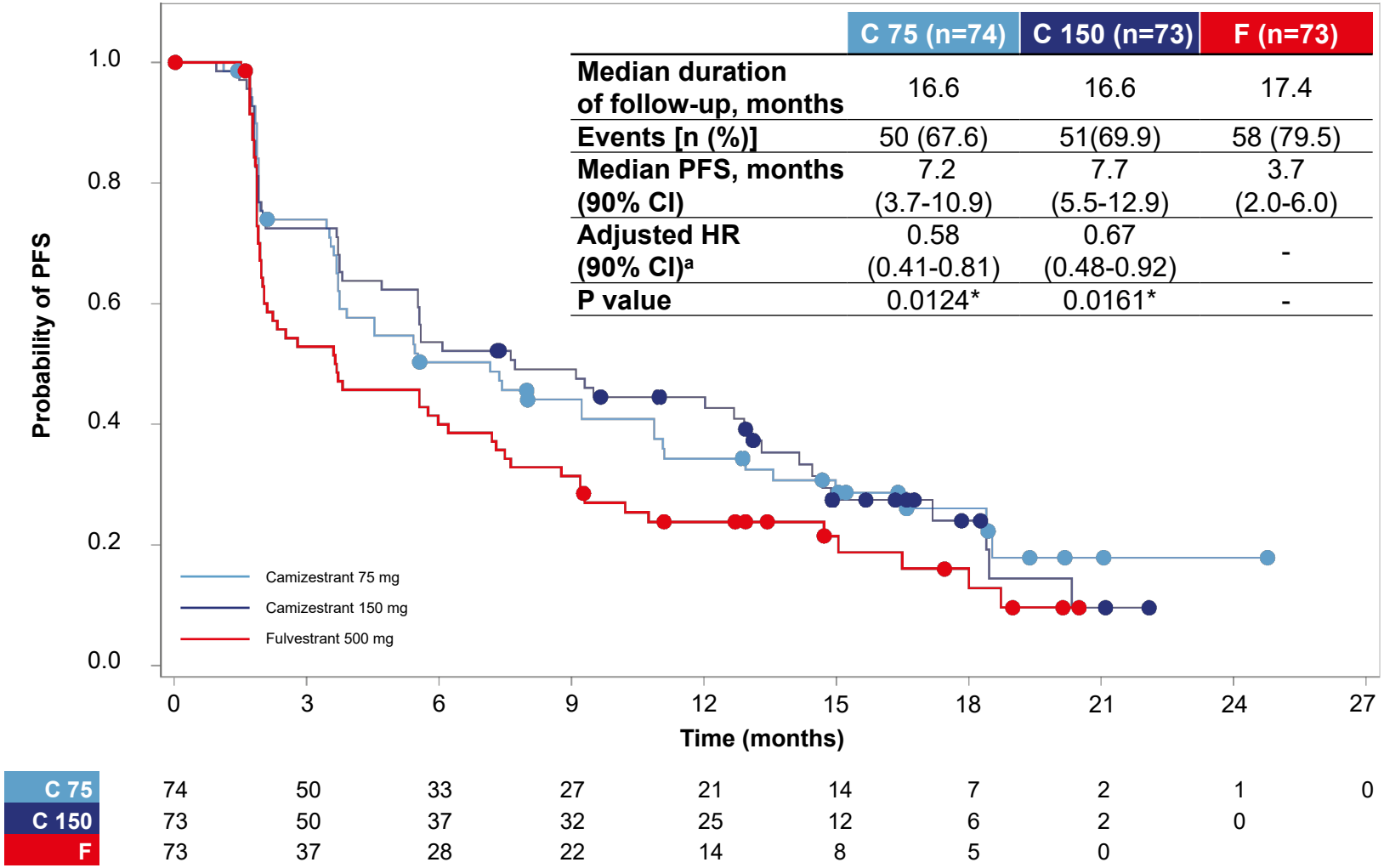
	C 75 (n=74)	C 150 (n=73)	F (n=73)	Total (n=240)
CT adjuvant, Y (%)	54.1	53.4	52.1	52.1
CT in ABC, Y (%)	21.6	12.3	26.0	19.2
ET overall, lines (%)				
0	1.4	1.4	0	0.8
1	81.1	72.6	76.7	77.1
2	16.2	24.7	19.2	20.0
3	1.4	1.4	4.1	2.1
ET adjuvant, Y (%)	66.2	71.2	60.3	66.7
AI	40.5	35.6	31.5	35.8
SERM	32.4	45.2	43.8	41.7
ET in ABC, lines (%)				
0	37.8	28.8	26.0	31.3
1	62.2	71.2	74.0	68.8
AI	55.4	67.1	67.1	63.3
SERM	6.8	2.7	6.8	5.0
Prior CDK4/6i Y (%)[c]	51.4	50.7	50.7	49.6
Palbociclib	21.6	31.5	30.1	27.9
Ribociclib	23.0	19.2	16.4	18.3
Abemaciclib	5.4	1.4	4.1	3.8

[a]All post-menopausal women; [b]*ESR1*m assessed in plasma samples at screening (GuardantOMNI™) and Cycle 1 Day 1 (Guardant360®), *ESR1*m defined as E380Q, V422del, S463P, L536H/P/R, Y537C/D/N/S, D538G, individual mutations present in >2% total cases reported; [c]Missing or not specified in 3 patients

ABC: advanced breast cancer; AI: aromatase inhibitor; C: camizestrant; CDK4/6i: CDK4/6 inhibitor; CT: chemotherapy; ECOG: Eastern Cooperative Oncology Group; ER: estrogen receptor; *ESR1*m: mutation in estrogen receptor 1 gene; ET: endocrine therapy; F: female; PgR: progesterone receptor; SERM: selective estrogen receptor modulator (tamoxifen or toremifene)

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

Primary endpoint: PFS by investigator assessment



	C 75 (n=74)	C 150 (n=73)	F (n=73)
Median duration of follow-up, months	16.6	16.6	17.4
Events [n (%)]	50 (67.6)	51(69.9)	58 (79.5)
Median PFS, 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)[a]	0.58 (0.41-0.81)	0.67 (0.48-0.92)	-
P value	0.0124*	0.0161*	-

C 75	74	50	33	27	21	14	7	2	1	0
C 150	73	50	37	32	25	12	6	2	0	
F	73	37	28	22	14	8	5	0		

In the overall population, camizestrant produces a statistically significant and clinically meaningful improvement in PFS for both 75 and 150 mg camizestrant doses over fulvestrant

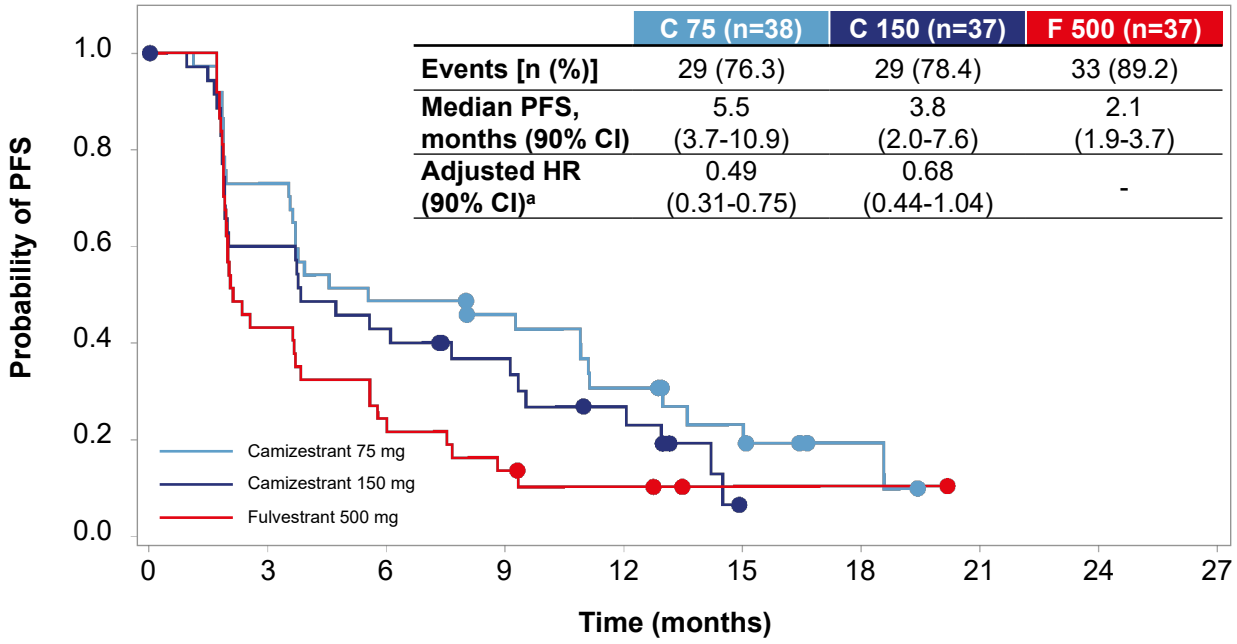
*Statistically significant; [a]HRs adjusted for prior use of CDK4/6i and liver/lung metastases

CDK4/6i: CDK4/6 inhibitor; CI: confidence interval; HR: hazard ratio; PFS: progression-free survival

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

PFS in patients by prior use of CDK4/6i

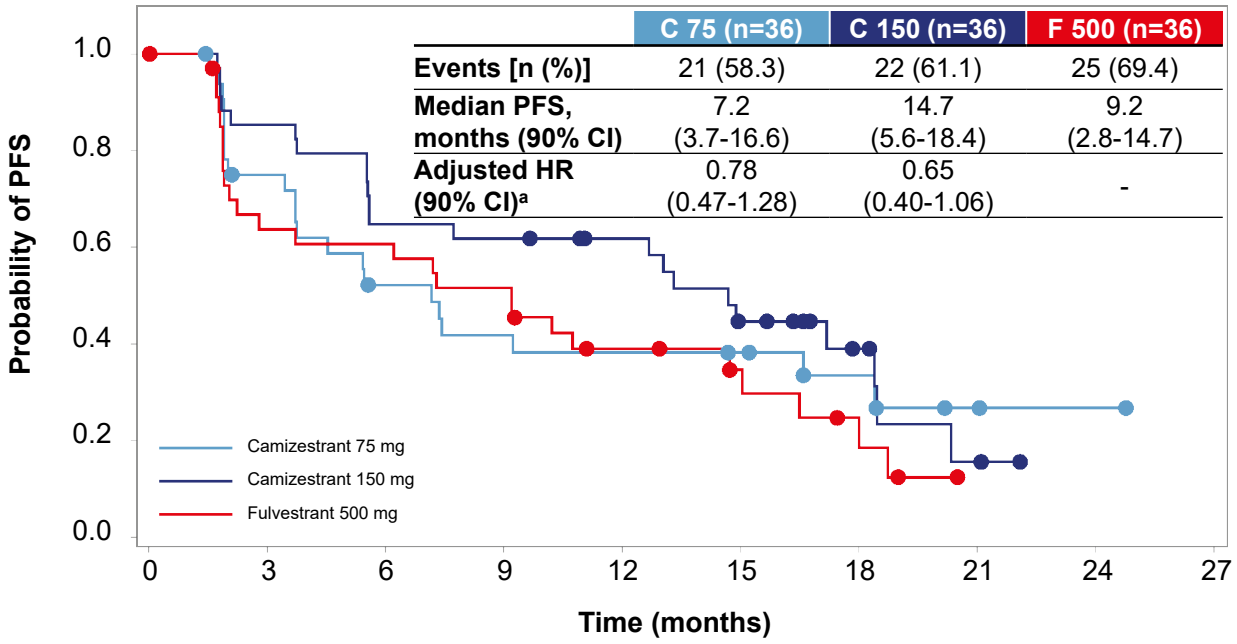
Prior CDK4/6i



	C 75 (n=38)	C 150 (n=37)	F 500 (n=37)
Events [n (%)]	29 (76.3)	29 (78.4)	33 (89.2)
Median PFS, months (90% CI)	5.5 (3.7-10.9)	3.8 (2.0-7.6)	2.1 (1.9-3.7)
Adjusted HR (90% CI)[a]	0.49 (0.31-0.75)	0.68 (0.44-1.04)	-

C 75	38	27	18	15	10	5	2	0
C 150	37	21	15	11	7	0		
F	37	16	8	5	3	1	1	0

No prior CDK4/6i



	C 75 (n=36)	C 150 (n=36)	F 500 (n=36)
Events [n (%)]	21 (58.3)	22 (61.1)	25 (69.4)
Median PFS, months (90% CI)	7.2 (3.7-16.6)	14.7 (5.6-18.4)	9.2 (2.8-14.7)
Adjusted HR (90% CI)[a]	0.78 (0.47-1.28)	0.65 (0.40-1.06)	-

C 75	36	23	15	12	11	9	5	2	1	0
C 150	36	29	22	21	18	12	6	2	0	
F	36	21	20	17	11	7	4	0		

- In the sub-population of patients previously treated with CDK4/6i + endocrine therapy, camizestrant at both doses produces a clinically meaningful improvement in PFS over fulvestrant

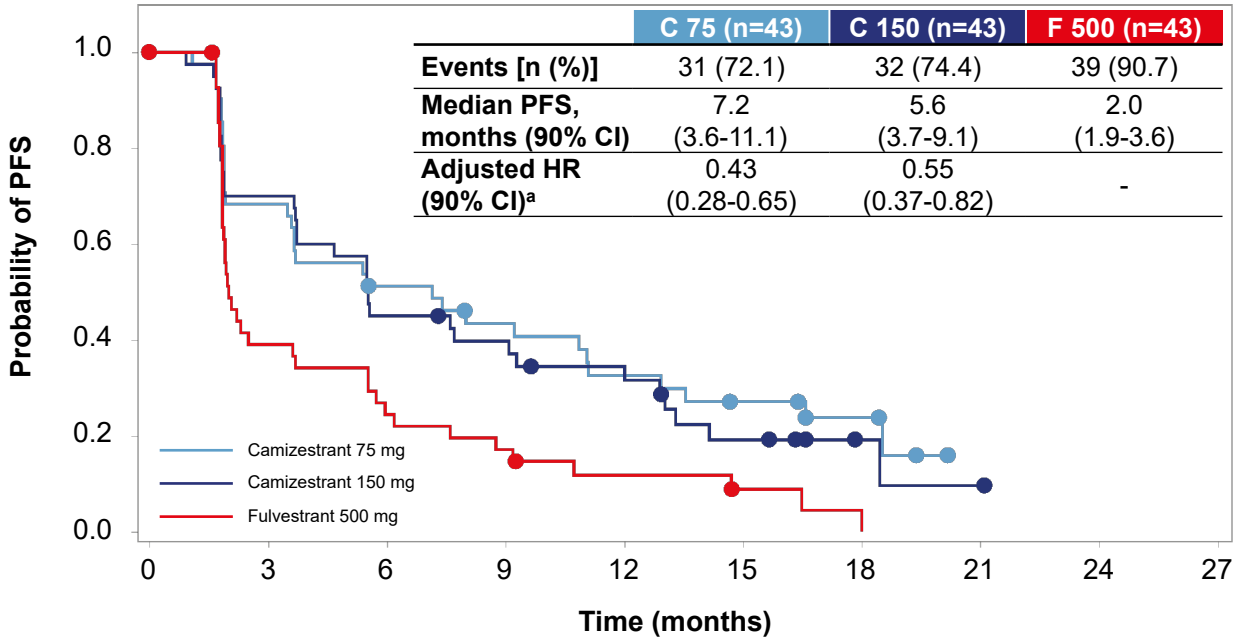
[a]HRs adjusted for liver/lung metastases

CI: confidence interval; CDK4/6i: CDK4/6 inhibitor; HR: hazard ratio; PFS: progression-free survival

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

PFS in patients by lung and/or liver metastases

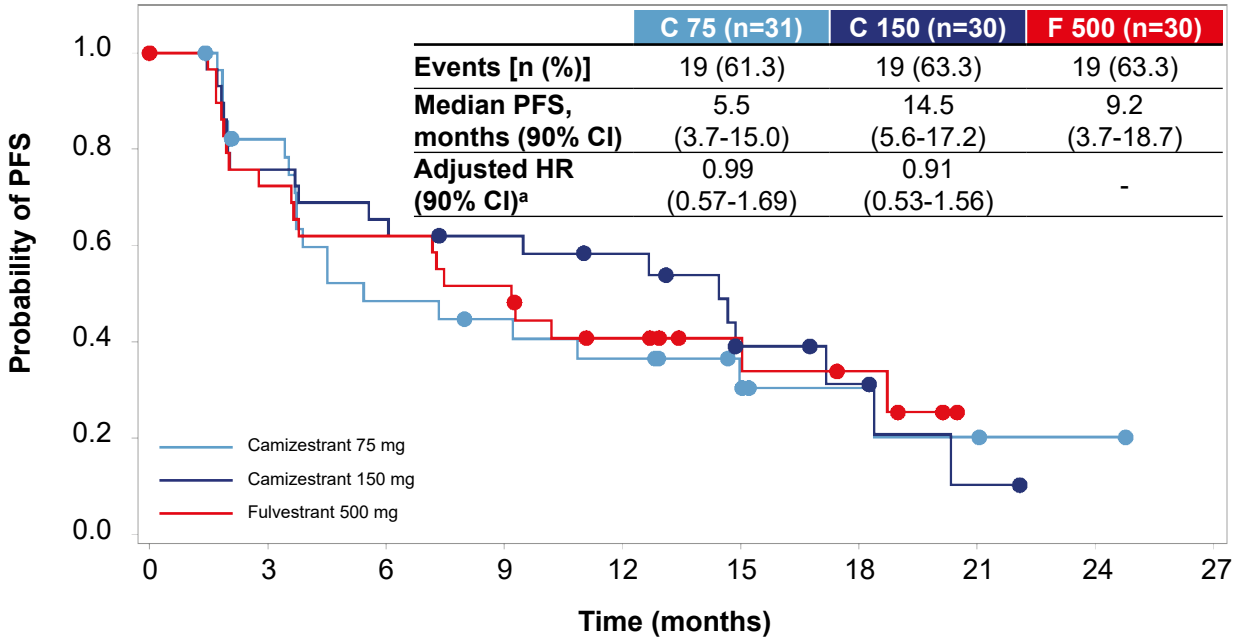
Presence of lung and/or liver metastases



	C 75 (n=43)	C 150 (n=43)	F 500 (n=43)
Events [n (%)]	31 (72.1)	32 (74.4)	39 (90.7)
Median PFS, months (90% CI)	7.2 (3.6-11.1)	5.6 (3.7-9.1)	2.0 (1.9-3.6)
Adjusted HR (90% CI)[a]	0.43 (0.28-0.65)	0.55 (0.37-0.82)	-

C 75	43	28	20	16	12	9	4	0		
C 150	43	28	18	15	12	6	2	1	0	
F	43	16	10	7	4	2	1	0		

No lung or liver metastases



	C 75 (n=31)	C 150 (n=30)	F 500 (n=30)
Events [n (%)]	19 (61.3)	19 (63.3)	19 (63.3)
Median PFS, months (90% CI)	5.5 (3.7-15.0)	14.5 (5.6-17.2)	9.2 (3.7-18.7)
Adjusted HR (90% CI)[a]	0.99 (0.57-1.69)	0.91 (0.53-1.56)	-

C 75	31	22	13	11	9	5	3	2	1	0
C 150	30	22	19	17	13	6	4	1	0	
F	30	21	18	15	10	6	4	0		

- In the sub-population of patients with lung and/or liver metastases, camizestrant at both doses produces a clinically meaningful improvement in PFS over fulvestrant

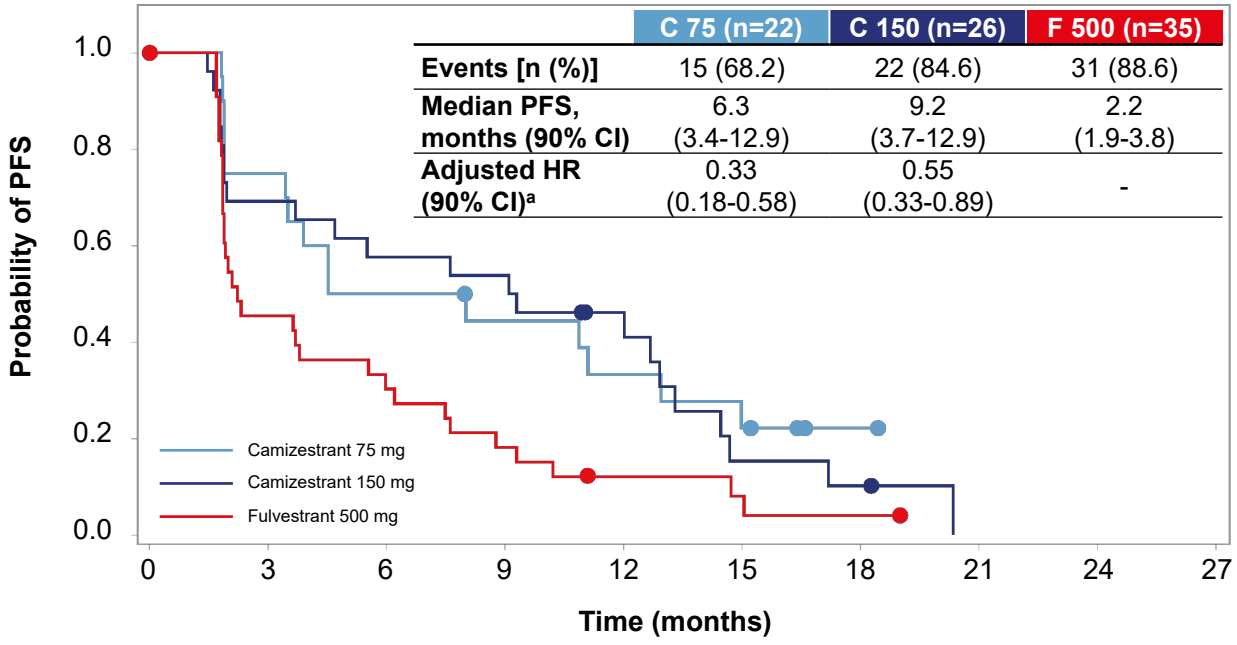
[a]HRs adjusted for prior use of CDK4/6i

CI: confidence interval; CDK4/6i: CDK4/6 inhibitor; HR: hazard ratio; PFS: progression-free survival

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

PFS in patients by detectable *ESR1*m

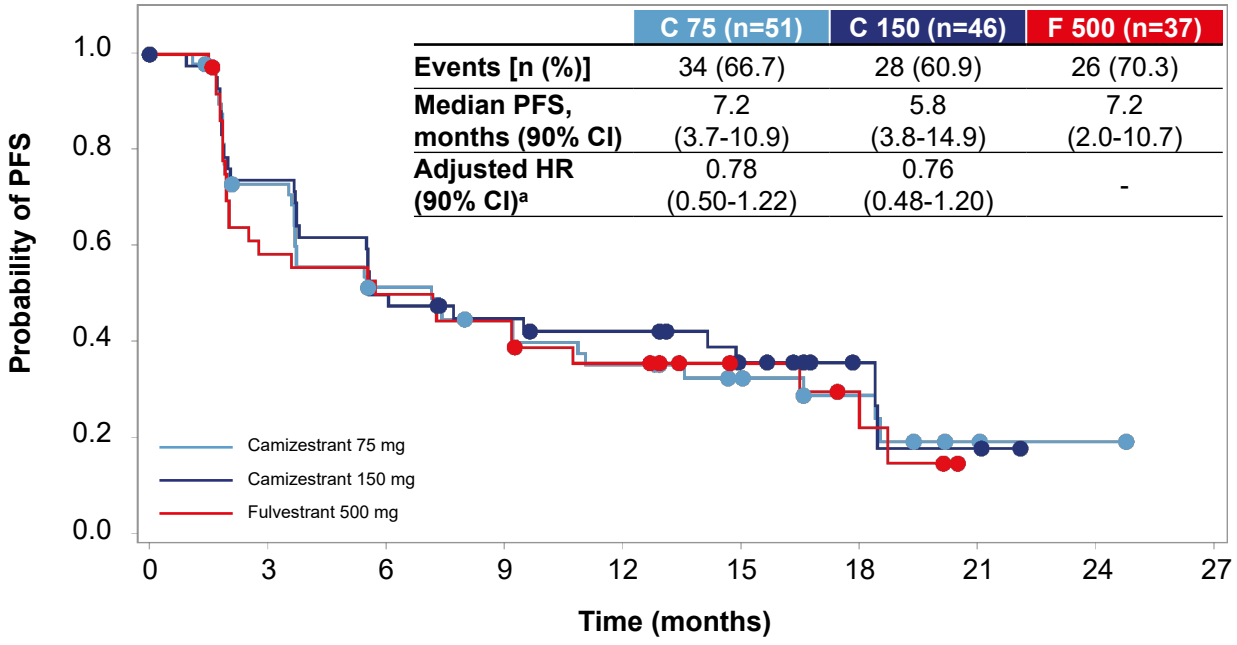
*ESR1*m detectable at baseline



	C 75 (n=22)	C 150 (n=26)	F 500 (n=35)
Events [n (%)]	15 (68.2)	22 (84.6)	31 (88.6)
Median PFS, months (90% CI)	6.3 (3.4-12.9)	9.2 (3.7-12.9)	2.2 (1.9-3.8)
Adjusted HR (90% CI)[a]	0.33 (0.18-0.58)	0.55 (0.33-0.89)	-

C 75	22	15	10	8	6	4	1	0
C 150	26	18	15	14	9	3	2	0
F	35	15	10	6	3	2	1	0

*ESR1*m not detectable at baseline



	C 75 (n=51)	C 150 (n=46)	F 500 (n=37)
Events [n (%)]	34 (66.7)	28 (60.9)	26 (70.3)
Median PFS, months (90% CI)	7.2 (3.7-10.9)	5.8 (3.8-14.9)	7.2 (2.0-10.7)
Adjusted HR (90% CI)[a]	0.78 (0.50-1.22)	0.76 (0.48-1.20)	-

C 75	51	34	23	19	15	10	6	2	1	0
C 150	46	31	21	17	15	9	4	2	0	
F	37	21	18	16	11	6	4	1	0	

- In the sub-population of patients with detectable *ESR1*m at baseline, camizestrant at both doses produces a clinically meaningful improvement in PFS over fulvestrant

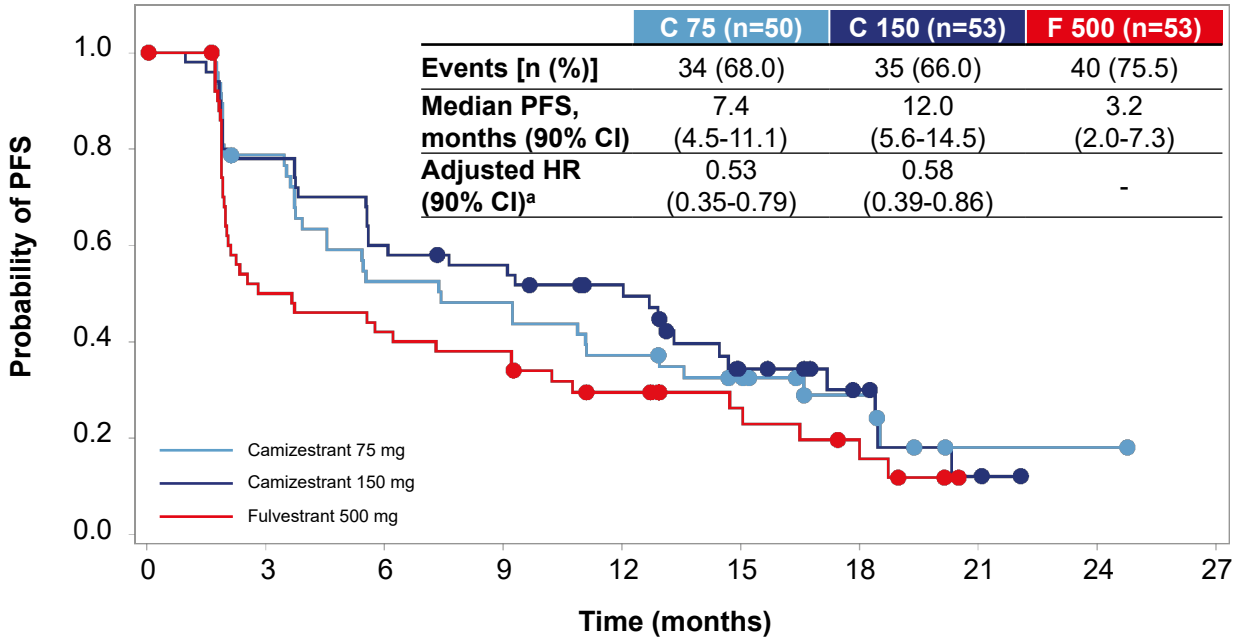
[a]HRs adjusted for prior use of CDK4/6i and liver/lung metastases

CI: confidence interval; CDK4/6i: CDK4/6 inhibitor; ESR1m: mutation in estrogen receptor 1 gene; HR: hazard ratio; PFS: progression-free survival

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

PFS in patients by ER-driven disease*

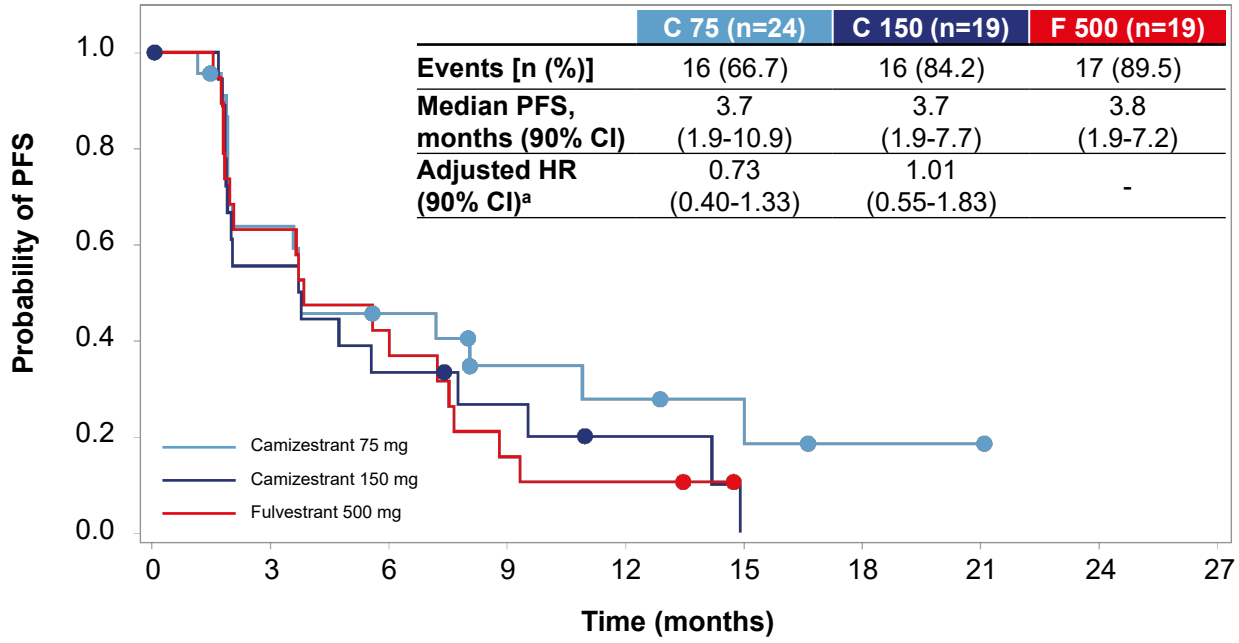
Patients with evidence of ER-driven disease*



	C 75 (n=50)	C 150 (n=53)	F 500 (n=53)
Events [n (%)]	34 (68.0)	35 (66.0)	40 (75.5)
Median PFS, months (90% CI)	7.4 (4.5-11.1)	12.0 (5.6-14.5)	3.2 (2.0-7.3)
Adjusted HR (90% CI)[a]	0.53 (0.35-0.79)	0.58 (0.39-0.86)	-

C 75	50	36	24	22	17	12	6	1	1	0
C 150	53	39	30	27	22	11	6	2	0	
F	53	25	21	19	12	8	5	0		

Patients without evidence of ER-driven disease*



	C 75 (n=24)	C 150 (n=19)	F 500 (n=19)
Events [n (%)]	16 (66.7)	16 (84.2)	17 (89.5)
Median PFS, months (90% CI)	3.7 (1.9-10.9)	3.7 (1.9-7.7)	3.8 (1.9-7.2)
Adjusted HR (90% CI)[a]	0.73 (0.40-1.33)	1.01 (0.55-1.83)	-

C 75	24	14	9	5	4	2	1	1	0	
C 150	19	10	6	4	2	0				
F	19	12	7	3	2	0				

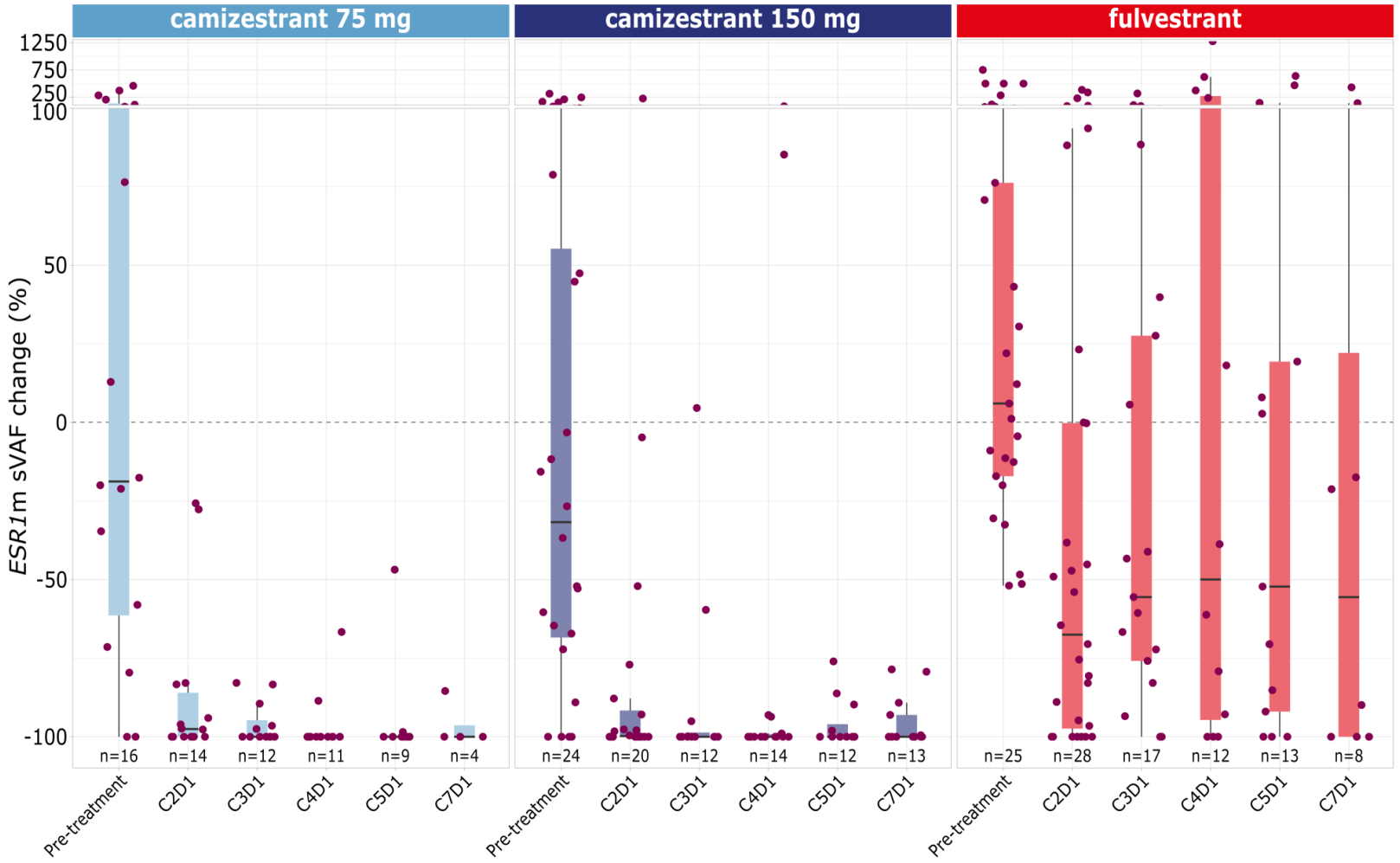
- In the subgroup of patients with evidence of ER-driven disease (71.3% of overall population), both 75 mg (HR 0.53) and 150 mg (HR 0.58) produced a clinically meaningful PFS improvement over fulvestrant
- In the (small, 28.7% of overall population) subgroup patients without evidence of ER-driven disease, 75 mg (HR 0.73) produced a trend to benefit over fulvestrant; the effect for 150 mg (HR 1.01) was less clear

*Defined in accordance with 5th ESO-ESMO ABC guidelines where the cut-point is increased to 12 months for patients receiving ET+CDK4/6i therapy in the advanced setting

[a]HRs adjusted for prior use of CDK4/6i and liver/lung metastases; CI: confidence interval; CDK4/6i: CDK4/6 inhibitor; ER: estrogen receptor; HR: hazard ratio; PFS: progression-free survival

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

Changes in *ESR1*m ctDNA variant allele frequency



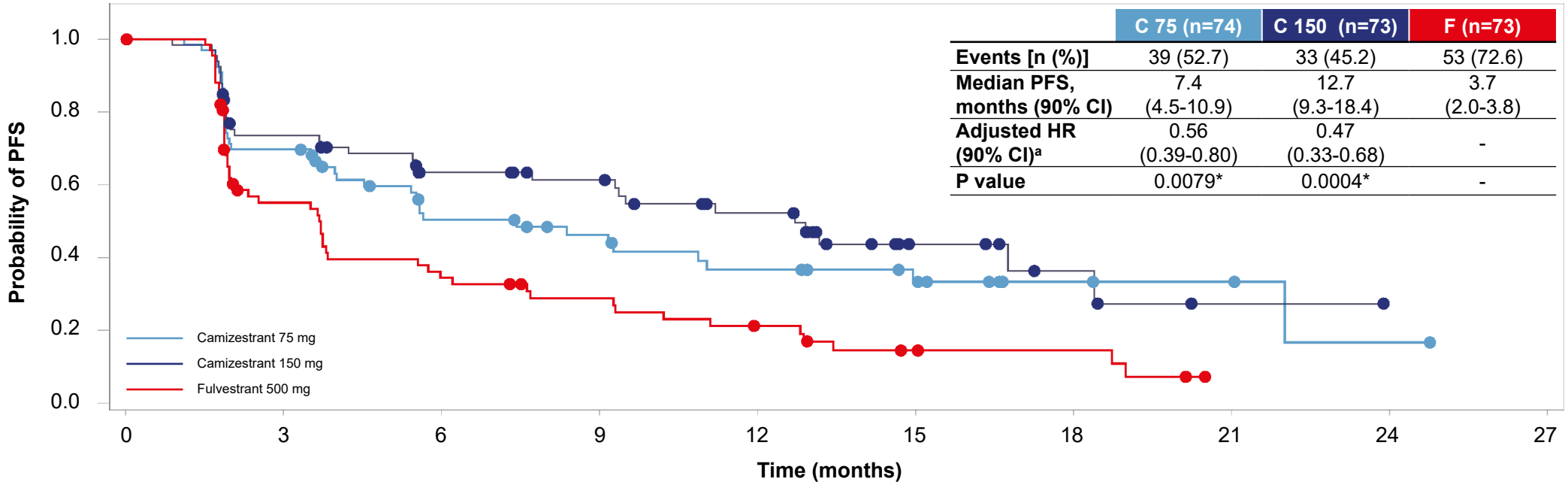
- Treatment with camizestrant 75 and 150 mg reduced the level of *ESR1*m ctDNA to undetectable or near undetectable levels by Cycle 2 Day 1 and maintained this to Cycle 7 Day 1
- Fulvestrant also reduced levels of *ESR1*m ctDNA, but not to the same extent as camizestrant

*ESR1*m classed as E380Q, V422del, S463P, L536H/P/R, Y537C/D/N/S, D538G. Pre-treatment = % change in *ESR1*m sVAF from screening to Cycle 1 Day 1, CXD1 = % change from Cycle 1 Day 1 to Cycle X Day 1

ctDNA: circulating tumor DNA; *ESR1*m: mutation in estrogen receptor 1 gene; *ESR1*m sVAF: Summed variant allele frequency of qualifying *ESR1*m

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

PFS by blinded independent central review



	C 75 (n=74)	C 150 (n=73)	F (n=73)
Events [n (%)]	39 (52.7)	33 (45.2)	53 (72.6)
Median PFS, months (90% CI)	7.4 (4.5-10.9)	12.7 (9.3-18.4)	3.7 (2.0-3.8)
Adjusted HR (90% CI)[a]	0.56 (0.39-0.80)	0.47 (0.33-0.68)	-
P value	0.0079*	0.0004*	-

C 75	74	46	27	21	15	10	4	3	1	0
C 150	73	45	33	29	21	8	4	1	0	
F	73	32	20	15	10	5	4	0		

- BICR assessment conducted as a sensitivity analysis shows a statistically significant benefit in PFS at both doses of camizestrant over fulvestrant, consistent with the investigator assessment
- The camizestrant 150 mg group showed a higher degree of investigator versus BICR discordance than the camizestrant 75 mg and fulvestrant groups, where investigator PD was called more often than BICR PD, 31.5% discordance for 150 versus 18.9% and 15.1% for 75 and F, respectively

*Statistically significant; [a]HRs adjusted for prior use of CDK4/6i and liver/lung metastases

BICR: blinded independent central review; CI: confidence interval; HR: hazard ratio; PFS: progression-free survival

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

Objective response rate and clinical benefit rate at 24 weeks

Group	n	Number (%) of patients with response	Adjusted response rate (%)	Comparison against fulvestrant		
				Odds ratio	90% CI	2-sided p-value
ORR						
Camizestrant 75 mg	70	11 (15.7)	15.7	1.43	0.63-3.33	0.4789
Camizestrant 150 mg	65	13 (20.0)	20.3	1.96	0.88-4.51	0.1675
Fulvestrant	68	8 (11.8)	11.5			
CBR24						
Camizestrant 75 mg	74	35 (47.3)	48.8	1.48	0.84-2.64	0.2554
Camizestrant 150 mg	73	36 (49.3)	51.0	1.62	0.91-2.89	0.1658
Fulvestrant	73	28 (38.4)	39.1			

The analysis was performed using logistic regression with adjustments for prior use of CDK 4/6 inhibitors and presence of lung and/or liver metastasis.
Includes unconfirmed responses.
Objective response determined for patients with measurable disease only.
Clinical benefit defined as patients with best objective response of complete response or partial response in the first 25 weeks or who have stable disease for at least 23 weeks after randomization.

- Camizestrant at 75 and 150 mg increases both ORR and CBR24 over fulvestrant

CBR24: clinical benefit rate at 24 weeks; CI confidence interval; ORR: objective response rate.

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

Patient level safety summary

	C 75 (n=74)	C 150 (n=73)	C 300 (n=20)	F 500 (n=73)
Total duration, months, mean (SD)	8.27 (6.59)	8.91 (6.78)	9.26 (8.19)	7.34 (6.09)
Any treatment-emergent AE (TEAE), n (%)	57 (77.0)	66 (90.4)	19 (95.0)	50 (68.5)
Any treatment-related AE (TRAE), n (%)	39 (52.7)	49 (67.1)	14 (70.0)	13 (17.8)
CTCAE Grade 3 or higher, n (%)	1 (1.4)	2 (2.7)	1 (5.0)	1 (1.4)
serious, n (%)	3 (4.1)	2 (2.7)	1 (5.0)	0
fatal	0	0	0	0
leading to discontinuation of treatment, n (%)	2 (2.7)	0	0	0
TEAE leading to dose reduction, n (%)	1 (1.4)	9 (12.3)	4 (20.0)	0
TEAE leading to dose interruption, n (%)	11 (14.9)	16 (21.9)	4 (20.0)	3 (4.1)
TRAE leading to dose interruption, n (%)	7 (9.5)	8 (11.0)	3 (15.0)	0
Median duration of dose interruption (days)	7.0	7.5	7.0	-

- TRAEs of Grade 3 or higher and TRAEs leading to discontinuation were infrequent across all treatment arms
- TRAEs leading to dose interruptions were numerically similar for camizestrant 75 and 150 mg, and of short duration
- All camizestrant doses are well tolerated

AE: adverse event; CTCAE: common terminology criteria for adverse events; SD: standard deviation; TEAE: treatment-emergent adverse event; TRAE: treatment-related adverse event

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

All treatment-emergent adverse events

AE, n (%)	C 75 (n=74)		C 150 (n=73)		C 300 (n=20)		F 500 (n=73)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Any AE	57 (77.0)	9 (12.2)	66 (90.4)	16 (21.9)	19 (95.0)	3 (15)	50 (68.5)	10 (13.7)
Photopsia	9 (12.2)	0	18 (24.7)	0	7 (35.0)	0	0	0
(Sinus) bradycardia	4 (5.4)	0	19 (26.0)	0	8 (40.0)	0	0	0
Fatigue	4 (5.4)	0	13 (17.8)	1 (1.4)	4 (20.0)	0	3 (4.1)	0
Anemia	8 (10.8)	0	11 (15.1)	1 (1.4)	1 (5.0)	0	5 (6.8)	2 (2.7)
Asthenia	6 (8.1)	0	11 (15.1)	0	2 (10.0)	0	4 (5.5)	0
Arthralgia	3 (4.1)	0	9 (12.3)	1 (1.4)	2 (10.0)	0	2 (2.7)	0
AST increased	2 (2.7)	0	6 (8.2)	0	2 (10.0)	0	5 (6.8)	1 (1.4)
ALT increased	1 (1.4)	0	6 (8.2)	1 (1.4)	3 (15.0)	0	4 (5.5)	1 (1.4)
Covid-19	4 (5.4)	0	4 (5.5)	0	3 (15.0)	0	3 (4.1)	0
Diarrhea	4 (5.4)	0	4 (5.5)	0	3 (15.0)	1 (5.0)	2 (2.7)	1 (1.4)
Pain in extremity	1 (1.4)	0	4 (5.5)	1 (1.4)	2 (10.0)	0	3 (4.1)	0
Dyspepsia	1 (1.4)	0	3 (4.1)	0	2 (10.0)	0	1 (1.4)	0
Insomnia	1 (1.4)	0	3 (4.1)	0	2 (10.0)	0	1 (1.4)	0
Hyponatremia	0	0	3 (4.1)	1 (1.4)	2 (10.0)	0	1 (1.4)	1 (1.4)
Blood pressure increased	2 (2.7)	1 (1.4)	1 (1.4)	1 (1.4)	2 (10.0)	1 (5.0)	0	0
Cataract	2 (2.7)	0	0	0	2 (10.0)	0	0	0
Vitreous floaters	2 (2.7)	0	0	0	2 (10.0)	0	0	0

Ranked by all grades for the 150 mg dose, ≥10% in any arm, irrespective of causality assessment
AE: adverse event; ALT: alanine transaminase; AST: aspartate aminotransferase

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

Upcoming study analyses

- Overall survival maturity at data cut-off was 24.5% and with approximately 18 events per arm; follow-up and later analysis is planned
- Analyses of intersections and interactions between key subgroups is ongoing, and will include consideration of primary and secondary endocrine resistance
- Analyses of the rich translational dataset including serial ctDNA and CTCs are ongoing

CTC: circulating tumor cells; ctDNA: circulating tumor DNA

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

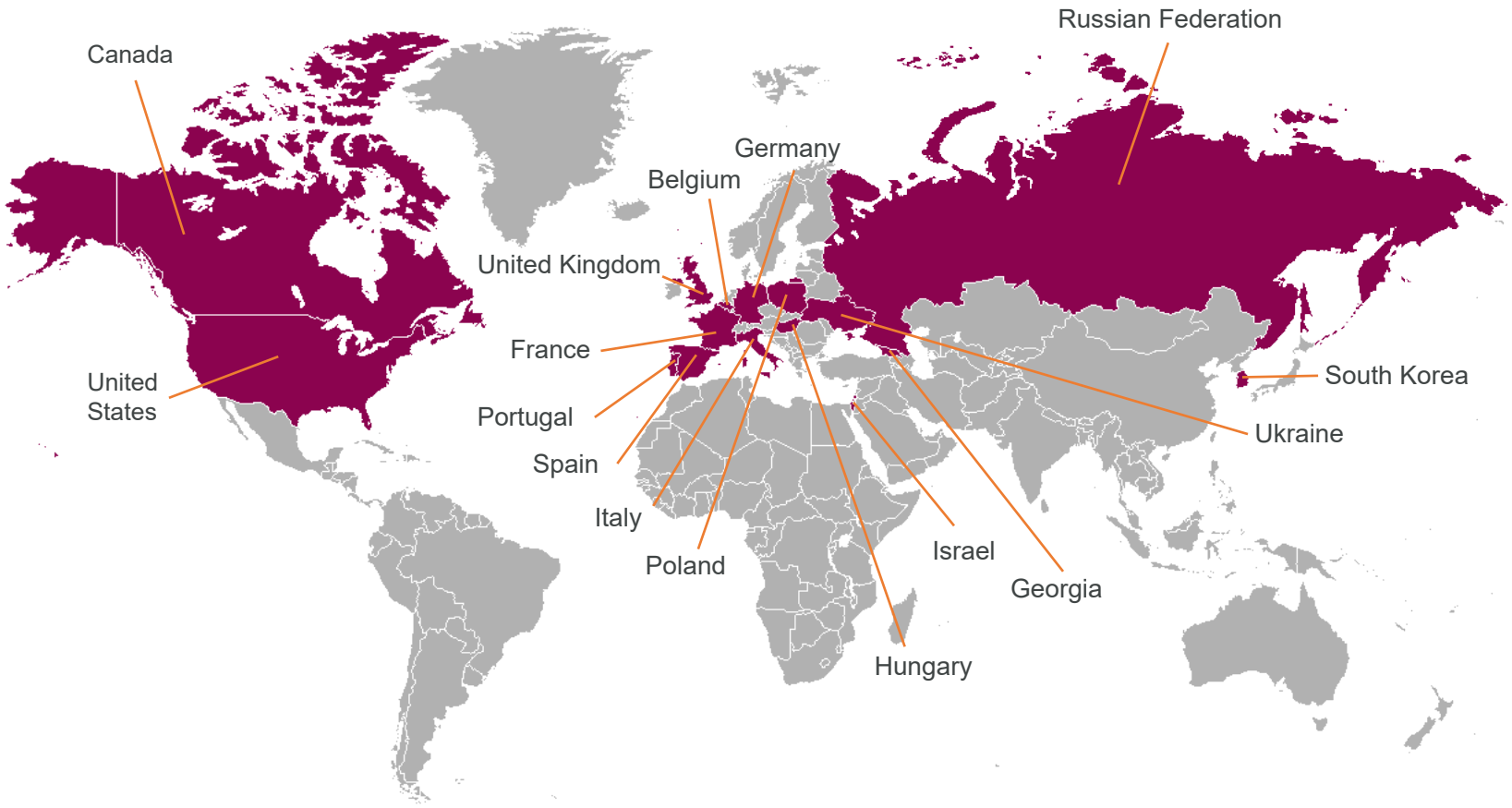
Conclusions

- SERENA-2 met its primary objective: camizestrant at both 75 and 150 mg doses improves PFS over fulvestrant in post-menopausal women with ER+/HER2- ABC
- Camizestrant delivers statistically significant and clinically meaningful PFS benefit at both 75 and 150 mg doses over fulvestrant in the overall population
  - A clinically meaningful PFS benefit was observed across the pre-specified subgroups of unmet medical need (post-CDK4/6i, lung/liver metastases, *ESR1*m and evidence of ER-driven disease)
- Both camizestrant doses are well tolerated, with infrequent Grade ≥3 TRAEs, dose reductions and discontinuations
- The results of SERENA-2 support the further development of camizestrant in ER+ BC
- Recruitment to two Phase 3 studies of camizestrant in ABC, SERENA-4[a] and SERENA-6[b], continues

[a]SERENA-4 NCT04711252; [b]SERENA-6 NCT04964934
ABC: advanced breast cancer; AE: adverse event; CDK4/6i: CDK4/6 inhibitor; *ESR1*m: mutation in estrogen receptor 1 gene; HER2: human epidermal growth factor receptor 2; PFS: progression-free survival; TRAE: treatment-related adverse event

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.

Acknowledgements



- The study was sponsored by AstraZeneca
- Our deepest gratitude is extended to the patients and their families for their participation
- We sincerely thank all the investigators and site staff for their contribution

- Please scan this QR code to view a plain language summary

This presentation is the intellectual property of the author/presenter. Contact them at moliveira@vhio.net for permission to reprint and/or distribute.