

# Enzalutamide (Xtandi) in High-Risk BCR nmCSPC

## EMBARC Topline Results - Overall Survival

Enzalutamide + Leuprolide vs. Placebo + Leuprolide and  
Enzalutamide Monotherapy vs. Placebo + Leuprolide

Data Cutoff Date: **27 May 2025**



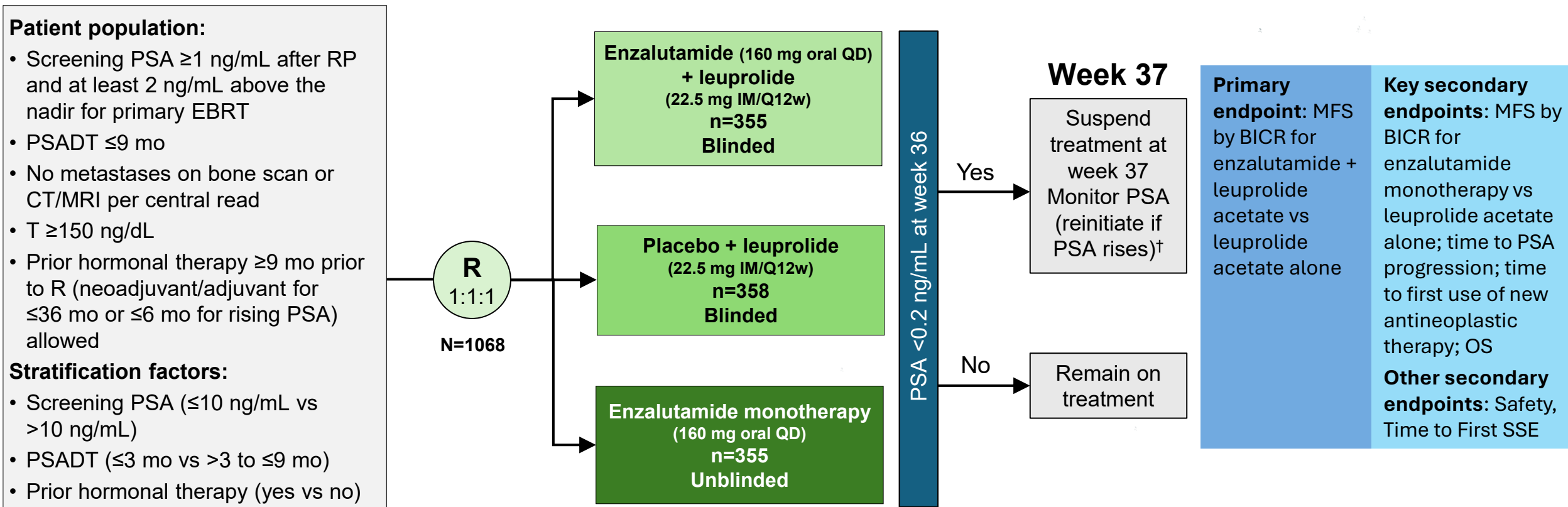
8 July 2025



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# EMBARC study design



<sup>†</sup>Study treatment was suspended once at week 37 if PSA was  $<0.2$  ng/mL and restarted when PSA was  $\geq 5.0$  ng/mL without prior RP or  $\geq 2$  ng/mL with prior RP.

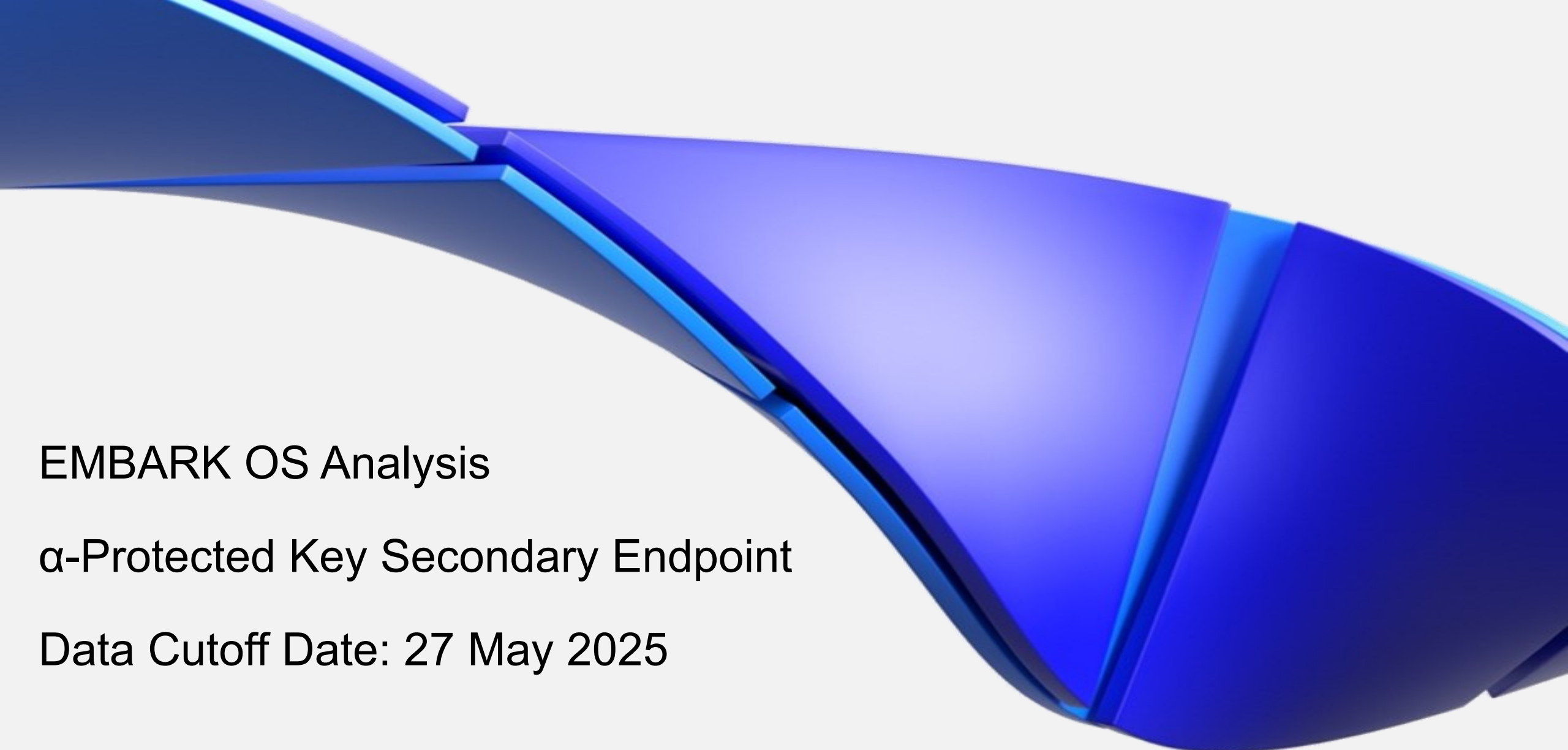
BICR, blinded independent central review; CT, computed tomography; D, day; EBRT, external beam radiotherapy; IM, intramuscular; MFS, metastasis-free survival; mo, month; MRI, magnetic resonance imaging; OS, overall survival; PSA, prostate-specific antigen; PSADT, PSA doubling time; Q, every; R, randomization; RP, radical prostatectomy; T, testosterone; w, weeks.

## Interim OS analyses – PCD, 31 January 2023

	Enza+Leu vs. Placebo+Leu	Enza vs. Placebo+Leu
HR (95% CI)	<b>0.589</b> (0.382, 0.908)	<b>0.782</b> (0.523, 1.170)
2-sided p value	0.0153	0.2304

# EMBARC Executive Summary

- At primary MFS analysis (2023):
  - 1° endpoint met with significantly improved MFS with enzalutamide (Enza) plus leuprolide (Leu) compared to placebo (P) plus Leu]
  - All key 2° endpoints [except overall survival (OS)], including MFS comparing Enza monotherapy vs. P + Leu as well as time to PSA progression and time to first antineoplastic therapy comparing Enza + Leu and Enza monotherapy vs. P + Leu were met
- At this final prespecified analysis (2025):
  - **Statistically significant and clinically meaningful** Improvement in OS with Enza + Leu compared with P + Leu (**40.3% reduction in risk of death**)
  - Trend (not statistically significant) towards improvement in OS with Enza monotherapy compared to P + Leu (17.0% reduction in risk of death)
  - Both the Enza + Leu combination and Enza monotherapy prolonged median time to first new antineoplastic therapy, symptomatic skeletal events (SSE), and PFS2 compared to P + Leu.
  - Safety profile for Enza with/without Leu overall consistent with data based on 2023 MFS data cutoff.
- Updated data solidify Enza's position as the only medicine approved in the HR BCR nmCSPC space

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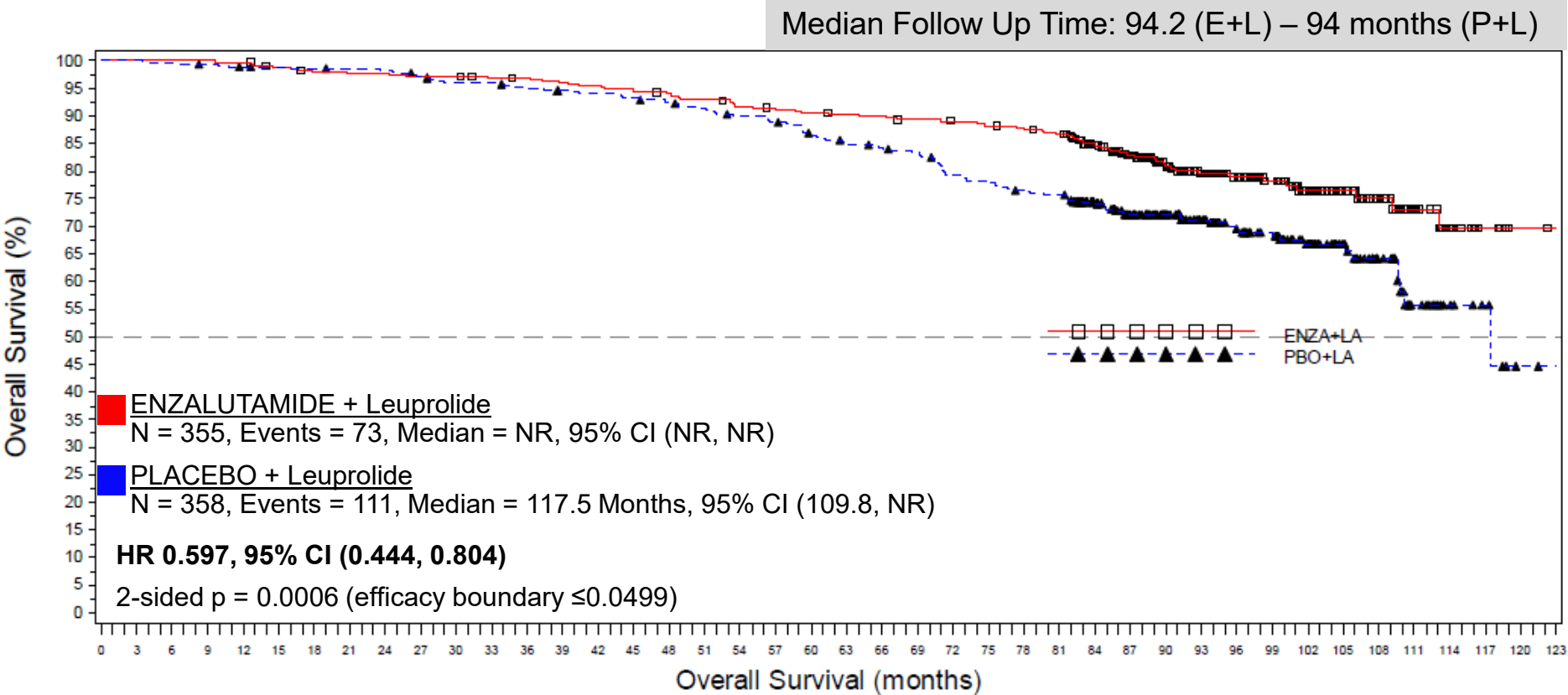
# EMBARC OS Analysis

$\alpha$ -Protected Key Secondary Endpoint

Data Cutoff Date: 27 May 2025

# Enza+Leu Treatment Resulted in a **40.3% Reduction** in Risk of Death – ITT

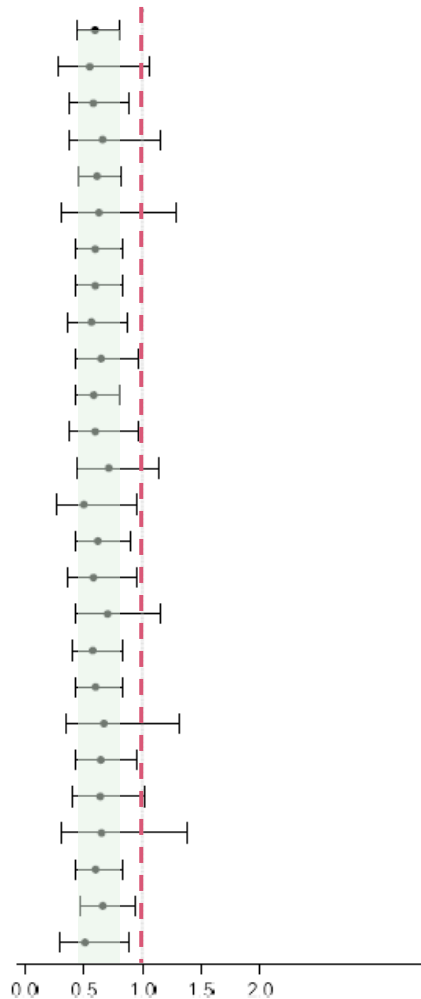
Final Analysis:  $\alpha$ -Protected Key Secondary Endpoint of Overall Survival



Interim analysis, 31JAN2023  
**HR 0.589**  
95% CI (0.382, 0.908)  
2-sided p = 0.0153

ENZA+LA:				0/0	0/0	0/0	0/0	1/1	3/4	3/7	1/8	0/8	2/10	0/10	1/11	0/11	3/14	2/16	3/19	2/21	3/24	5/29	1/30	3/33	1/34	1/35	2/37	1/38	3/41	2/43	3/46	6/52	6/58	5/63	3/66	1/67	1/68	2/70	0/70	1/71	1/72	1/73	0/73	0/73	0/73
Patients at Risk	355	355	355	355	354	349	345	344	344	342	342	339	338	335	333	330	327	324	318	316	313	311	310	307	305	302	299	295	262	235	190	159	126	106	81	60	41	25	12	5	1	0			
PBO+LA:				0/0	0/0	1/1	1/2	2/4	0/4	1/5	0/5	1/6	4/10	4/14	0/14	4/18	1/19	2/21	3/24	3/27	3/30	5/35	4/39	8/47	5/52	3/55	3/58	13/71	5/76	5/81	3/84	5/89	6/95	0/95	2/97	3/100	1/101	3/104	0/104	2/106	4/110	0/110	0/110	1/111	0/111
Patients at Risk	358	358	357	355	352	351	350	349	348	343	338	338	333	331	329	326	322	318	312	308	298	292	288	284	270	265	259	256	228	199	171	140	117	104	81	56	39	18	10	6	1	0			

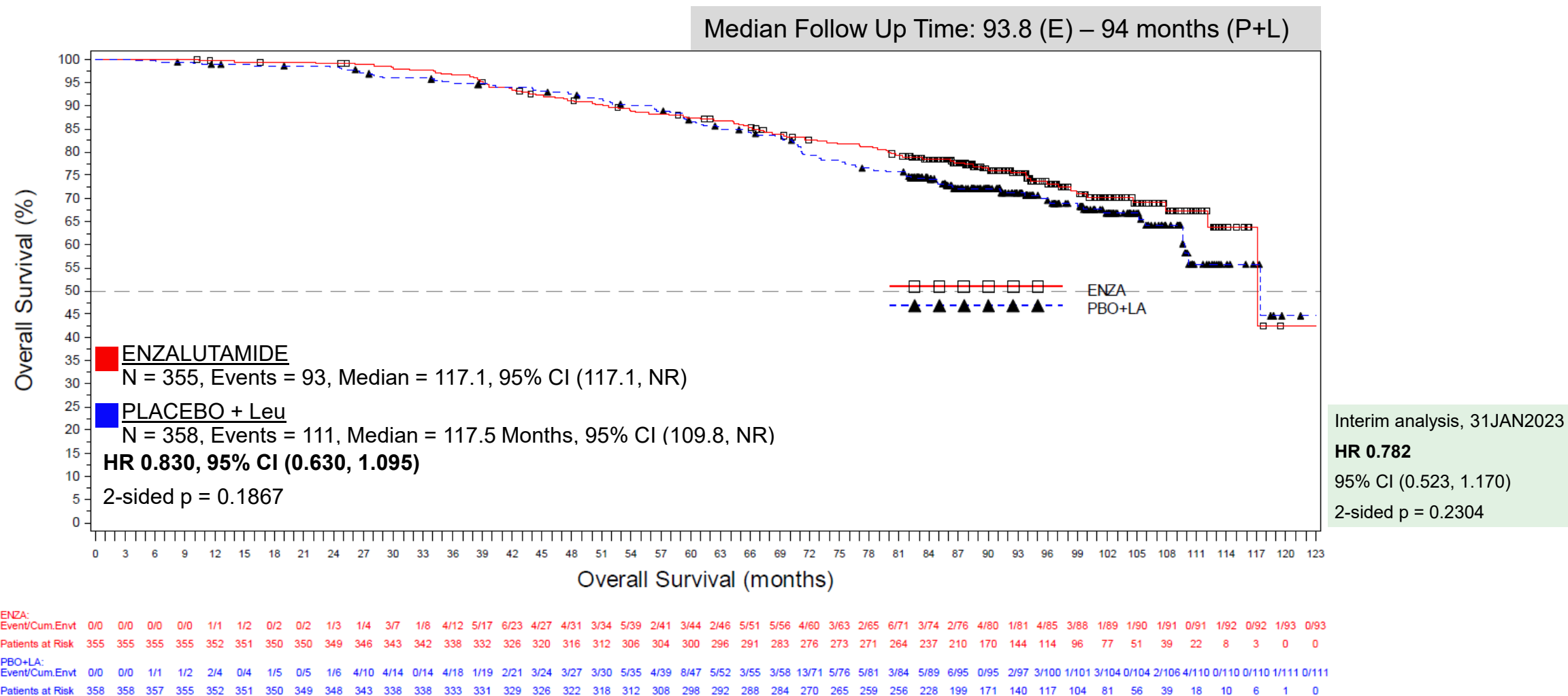
# Pre-Specified Subgroup Analysis of OS Demonstrated a Highly Consistent Treatment Effect in Favor of Enza + Leu

Subgroup	Number of Patients ENZA+LA / PBO+LA	Number of Events ENZA+LA / PBO+LA	Hazard Ratio for OS 	(95% CI)
All Patients	355 / 358	73 / 111	0.597	(0.444,0.804)
PSA Doubling Time (<=3 Months)	69 / 80	14 / 25	0.552	(0.287,1.064)
PSA Doubling Time (>3 to <=6 Months)	187 / 142	39 / 47	0.583	(0.381,0.891)
PSA Doubling Time (>6 to <=9 Months)	98 / 135	19 / 39	0.661	(0.381,1.148)
Baseline Use of a Bone Targeting Agent (No)	355 / 358	73 / 111	0.614	(0.457,0.825)
Baseline Age Category (<65 Years)	81 / 91	12 / 21	0.631	(0.310,1.282)
Baseline Age Category (>=65 Years)	274 / 267	61 / 90	0.599	(0.433,0.829)
Race (White)	293 / 301	60 / 96	0.599	(0.434,0.827)
Body Mass Index Calculated from Height and Weight (<=Median)	173 / 179	32 / 55	0.566	(0.366,0.876)
Body Mass Index Calculated from Height and Weight (>Median)	180 / 175	41 / 56	0.648	(0.433,0.971)
ECOG Performance Status at Baseline (0)	328 / 337	63 / 102	0.586	(0.428,0.803)
Geographic Region (North America)	144 / 137	28 / 42	0.599	(0.371,0.966)
Geographic Region (Europe)	130 / 128	31 / 40	0.715	(0.447,1.142)
Geographic Region (Rest of the World)	81 / 93	14 / 29	0.502	(0.265,0.952)
Total Gleason Score at Baseline (<=7) at Diagnosis	234 / 244	46 / 71	0.621	(0.428,0.900)
Total Gleason Score at Baseline (>=8) at Diagnosis	120 / 113	27 / 40	0.584	(0.358,0.951)
Prior Hormonal Therapy (Yes)	107 / 114	27 / 38	0.704	(0.429,1.157)
Prior Hormonal Therapy (No)	248 / 244	46 / 73	0.578	(0.399,0.836)
Prior Radiation Therapy (Yes)	265 / 283	57 / 92	0.602	(0.432,0.838)
Prior Radiation Therapy (No)	90 / 75	16 / 19	0.674	(0.346,1.311)
Prior Prostatectomy (Yes)	269 / 254	44 / 60	0.646	(0.438,0.953)
Prior Prostatectomy (No)	86 / 104	29 / 51	0.642	(0.407,1.013)
History of Cardiovascular Disease (Yes)	42 / 42	12 / 16	0.653	(0.308,1.382)
History of Cardiovascular Disease (No)	313 / 316	61 / 95	0.602	(0.436,0.831)
PSA Value at Baseline (<=10 ng/mL)	278 / 273	53 / 74	0.663	(0.466,0.944)
PSA Value at Baseline (>10 ng/mL)	77 / 83	20 / 37	0.512	(0.297,0.883)



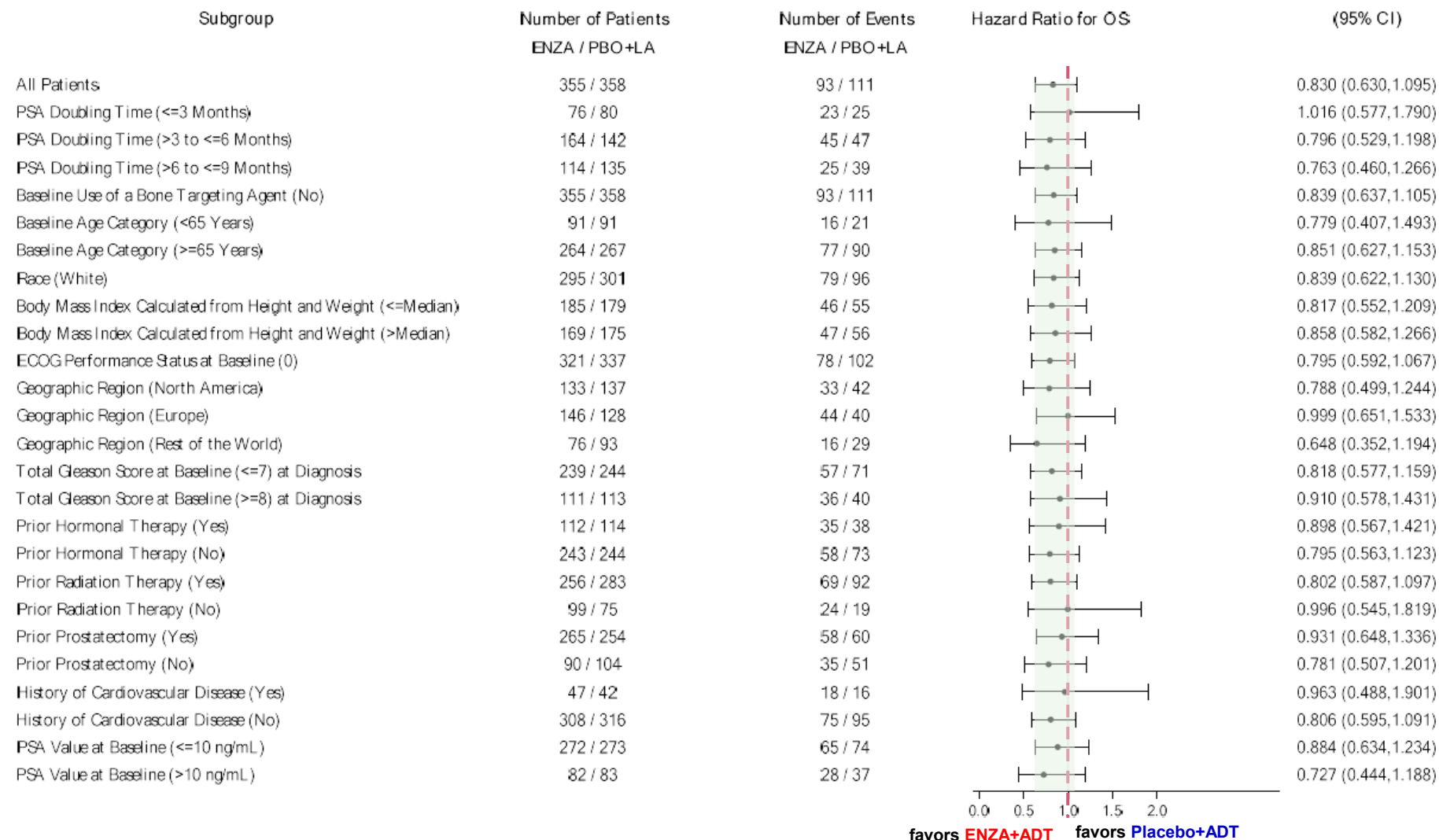
# Enza Mono Treatment Resulted in a **17.0% Reduction** in Risk of Death – ITT

Final Analysis:  $\alpha$ -Protected Key Secondary Endpoint Overall Survival (trend only)





# Pre-Specified Subgroup Analysis of OS Demonstrated a Consistent Treatment Effect in Favor of Enza monotherapy





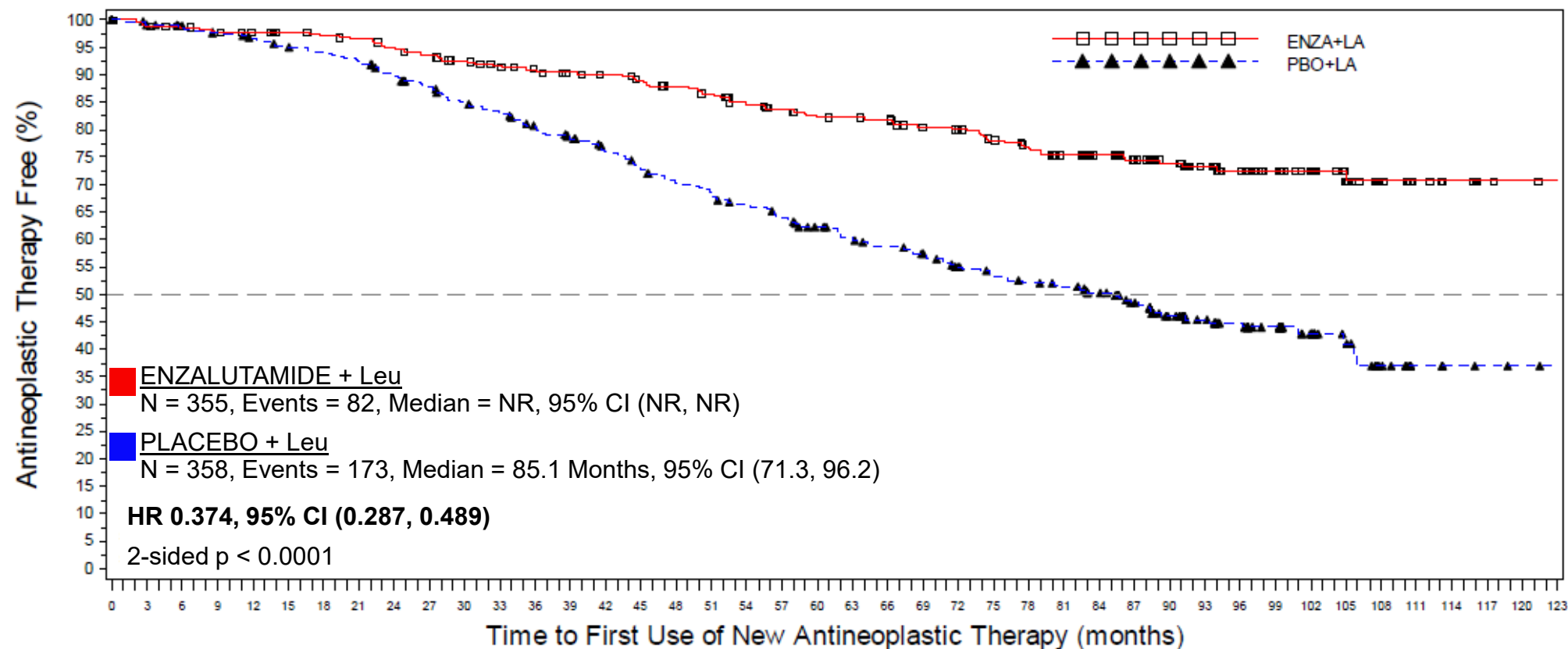
# EMBARC Time to First Use of New Antineoplastic Therapy Analysis

## Descriptive Update

### Data Cutoff Date: 27 May 2025

# Enza + Leu Treatment Resulted in Longer Median Time to First Use of New Antineoplastic Therapy

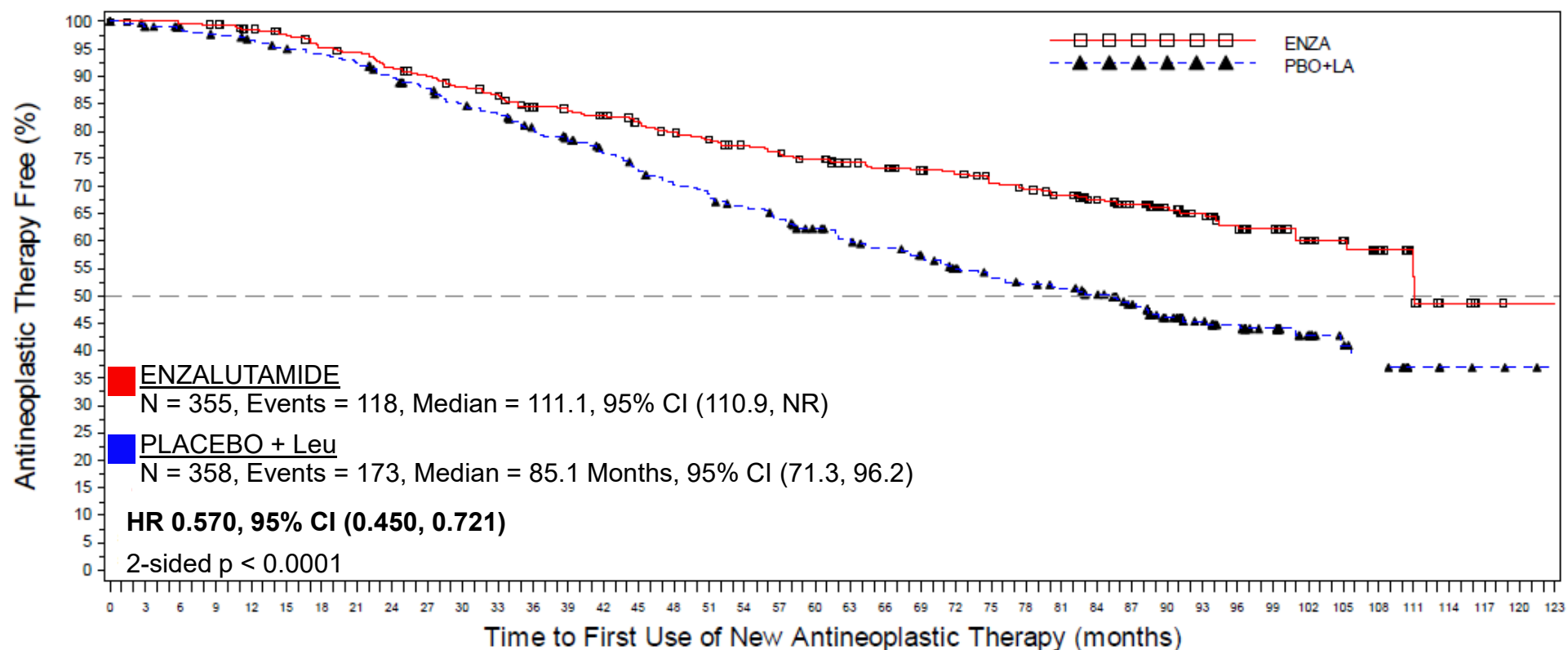
Final Analysis: Descriptive Update



ENZA+LA:	0/0	4/4	1/5	3/8	0/8	0/8	2/10	2/12	5/17	4/21	4/25	3/28	2/30	2/32	1/33	4/37	3/40	4/44	6/50	2/52	5/57	0/57	1/58	4/62	1/63	6/69	4/73	3/76	0/76	2/78	1/79	1/80	1/81	0/81	0/81	1/82	0/82	0/82	0/82	0/82	0/82	0/82
Event/Cum. Envt	0/0	4/4	1/5	3/8	0/8	0/8	2/10	2/12	5/17	4/21	4/25	3/28	2/30	2/32	1/33	4/37	3/40	4/44	6/50	2/52	5/57	0/57	1/58	4/62	1/63	6/69	4/73	3/76	0/76	2/78	1/79	1/80	1/81	0/81	0/81	1/82	0/82	0/82	0/82	0/82	0/82	0/82
Patients at Risk	355	346	341	337	334	330	327	323	317	312	301	295	290	285	282	276	270	265	254	249	242	241	239	230	224	216	208	199	175	152	126	106	90	77	62	38	24	15	6	2	1	0
PBO+LA:	0/0	3/3	2/5	3/8	4/12	5/17	3/20	6/26	9/35	7/42	9/51	6/57	8/65	8/73	7/80	10/90	8/98	5/103	7/110	8/118	5/123	6/129	4/133	4/137	7/144	5/149	3/152	2/154	3/157	4/161	5/166	1/167	1/168	1/169	1/170	1/171	2/173	0/173	0/173	0/173	0/173	0/173
Event/Cum. Envt	0/0	3/3	2/5	3/8	4/12	5/17	3/20	6/26	9/35	7/42	9/51	6/57	8/65	8/73	7/80	10/90	8/98	5/103	7/110	8/118	5/123	6/129	4/133	4/137	7/144	5/149	3/152	2/154	3/157	4/161	5/166	1/167	1/168	1/169	1/170	1/171	2/173	0/173	0/173	0/173	0/173	0/173
Patients at Risk	358	348	342	338	332	326	322	316	304	292	281	274	262	251	240	229	219	214	205	196	186	178	172	166	153	146	142	138	124	107	86	72	58	50	34	22	13	5	3	2	1	0

# Enza Mono Treatment Resulted in Longer Median Time to First Use of New Antineoplastic Therapy

Final Analysis: Descriptive Update



ENZA:																																												
Event/Cum.Event	0/0	0/0	1/1	1/2	3/5	3/8	8/16	3/19	10/29	5/34	7/41	4/45	8/53	2/55	3/58	4/62	6/68	4/72	3/75	4/79	4/83	2/85	3/88	1/89	2/91	5/96	3/99	3/102	2/104	2/106	1/107	2/109	3/112	1/113	2/115	0/115	1/116	1/117	1/118	0/118	0/118	0/118		
Patients at Risk	355	353	352	350	341	335	326	322	312	305	297	292	278	273	268	260	253	247	241	237	231	222	218	212	207	198	194	188	167	150	124	100	83	71	56	39	24	11	4	1	0	0		
PBO+LA:																																												
Event/Cum.Event	0/0	3/3	2/5	3/8	4/12	5/17	3/20	6/26	9/35	7/42	9/51	6/57	8/65	8/73	7/80	10/90	8/98	5/103	7/110	8/118	5/123	6/129	4/133	4/137	7/144	5/149	3/152	2/154	3/157	4/161	5/166	1/167	1/168	1/169	1/170	1/171	2/173	0/173	0/173	0/173	0/173	0/173		
Patients at Risk	358	348	342	338	332	326	322	316	304	292	281	274	262	251	240	229	219	214	205	196	186	178	172	166	153	146	142	138	124	107	86	72	58	50	34	22	13	5	3	2	1	0		



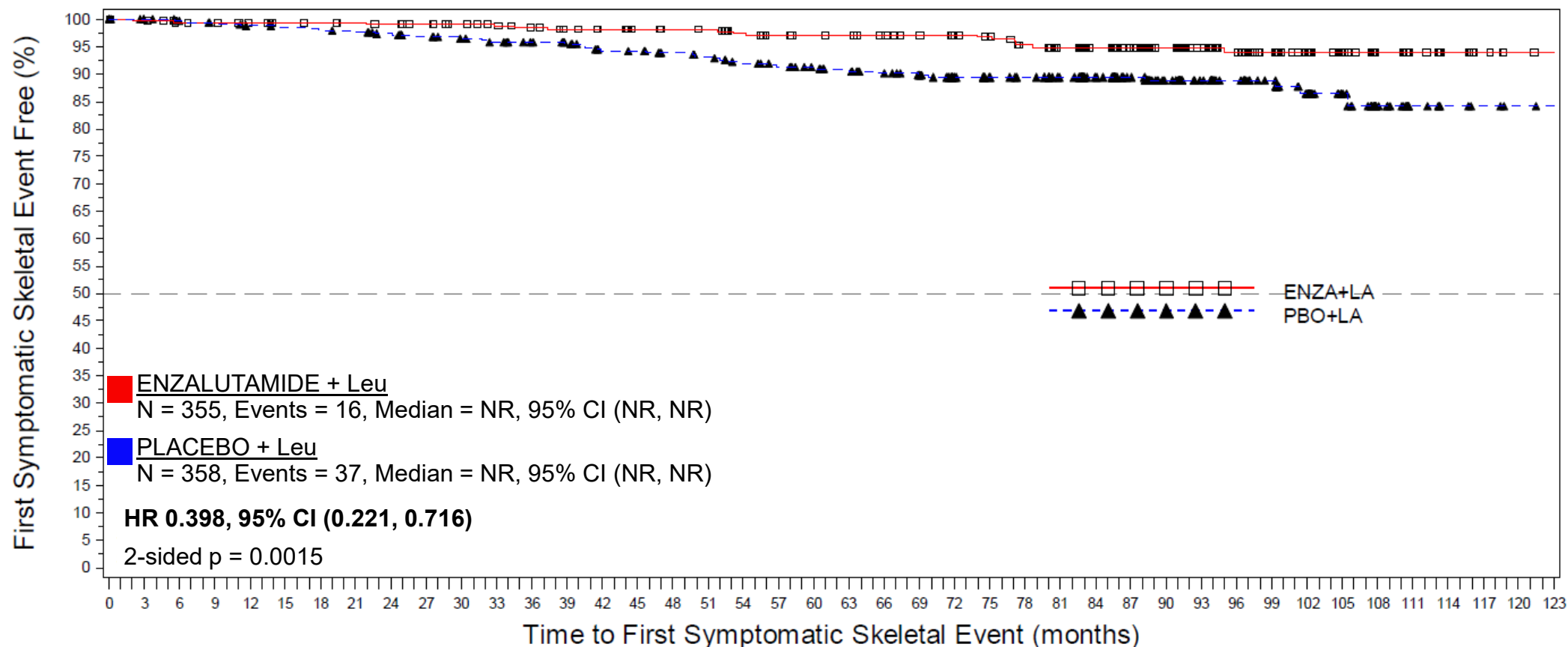
EMBARC Time to First SSE

Descriptive Update

Data Cutoff Date: 27 May 2025

# Enza + Leu Treatment Resulted in Longer Median Time to First Symptomatic Skeletal Event (SSE)

Final Analysis: Descriptive Update

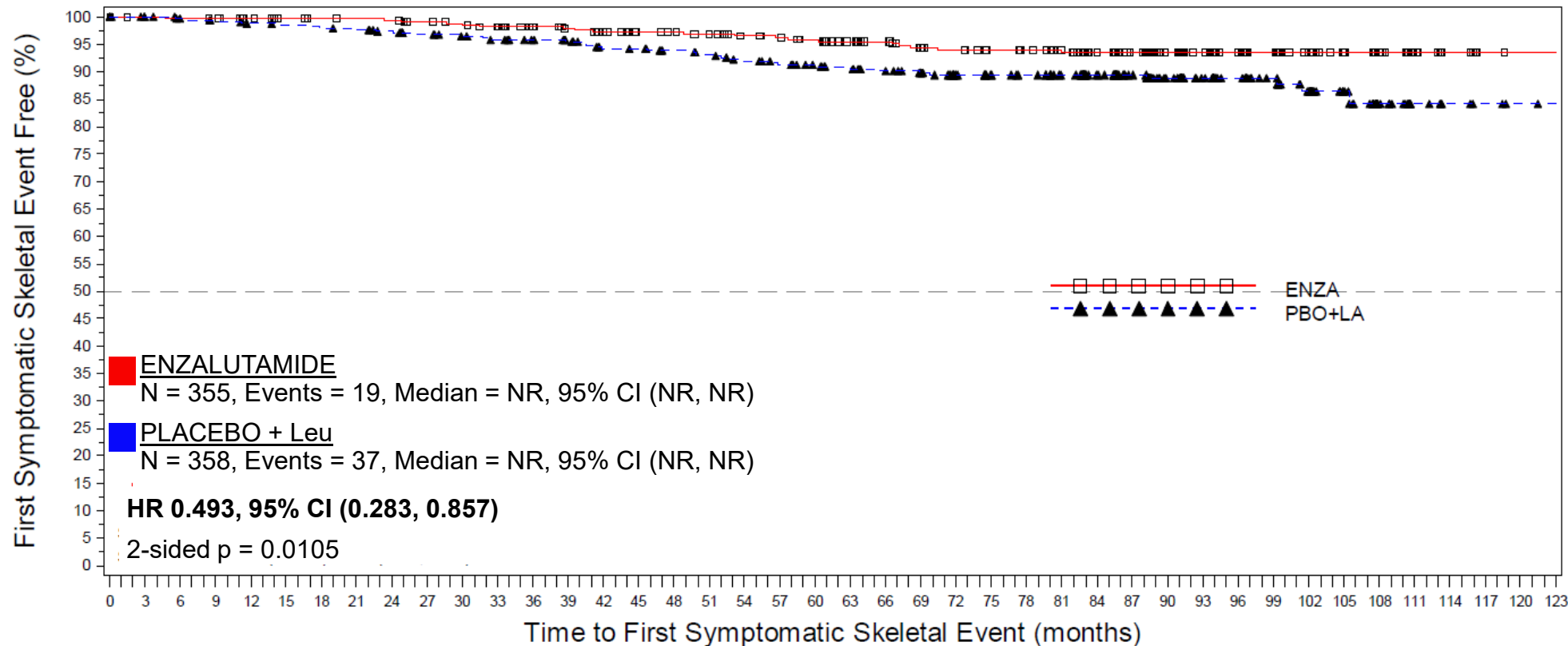


ENZA+LA:																																											
Event/Cum. Env	0/0	1/1	1/2	0/2	0/2	0/2	0/2	0/2	1/3	0/3	0/3	1/4	1/5	1/6	0/6	0/6	0/6	0/6	2/8	1/9	0/9	0/9	0/9	0/9	0/9	1/10	4/14	1/15	0/15	0/15	0/15	0/15	1/16	0/16	0/16	0/16	0/16	0/16	0/16	0/16	0/16		
Patients at Risk	355	350	345	344	341	336	335	333	331	328	321	317	313	309	306	302	298	297	286	282	279	278	274	267	259	256	246	238	211	187	150	124	102	86	65	43	29	19	8	4	1	0	
PBO+LA:																																											
Event/Cum. Env	0/0	0/0	1/1	1/2	2/4	1/5	2/7	1/8	1/9	2/11	1/12	2/14	0/14	1/15	4/19	0/19	1/20	2/22	4/26	2/28	0/28	2/30	1/31	1/32	1/33	0/33	0/33	0/33	0/33	0/33	0/33	1/34	0/34	0/34	0/34	2/36	0/36	1/37	0/37	0/37	0/37	0/37	0/37
Patients at Risk	358	352	347	344	340	338	336	334	329	321	316	312	307	302	292	291	285	280	272	267	260	254	248	241	226	220	216	207	184	162	135	109	92	81	63	41	22	9	5	3	1	0	



# Enza Mono Treatment Resulted in Longer Median Time to First Symptomatic Skeletal Event (SSE)

Final Analysis: Descriptive Update



ENZA:																																										
Event/Cum. Env	0/0	0/0	1/1	0/1	0/1	0/1	0/1	1/2	1/3	1/4	2/6	0/6	1/7	2/9	0/9	0/9	1/10	1/11	1/12	1/13	1/14	0/14	3/17	1/18	0/18	0/18	0/18	1/19	0/19	0/19	0/19	0/19	0/19	0/19	0/19	0/19	0/19	0/19	0/19	0/19	0/19	
Patients at Risk	355	353	352	351	345	341	339	338	337	332	329	324	315	308	301	292	290	286	280	277	273	262	256	246	241	232	229	221	197	175	146	122	100	83	66	42	28	14	5	1	0	0
PBO+LA:																																										
Event/Cum. Env	0/0	0/0	1/1	1/2	2/4	1/5	2/7	1/8	1/9	2/11	1/12	2/14	0/14	1/15	4/19	0/19	1/20	2/22	4/26	2/28	0/28	2/30	1/31	1/32	1/33	0/33	0/33	0/33	0/33	0/33	1/34	0/34	0/34	0/34	2/36	0/36	1/37	0/37	0/37	0/37	0/37	0/37
Patients at Risk	358	352	347	344	340	338	336	334	329	321	316	312	307	302	292	291	285	280	272	267	260	254	248	241	226	220	216	207	184	162	135	109	92	81	63	41	22	9	5	3	1	0





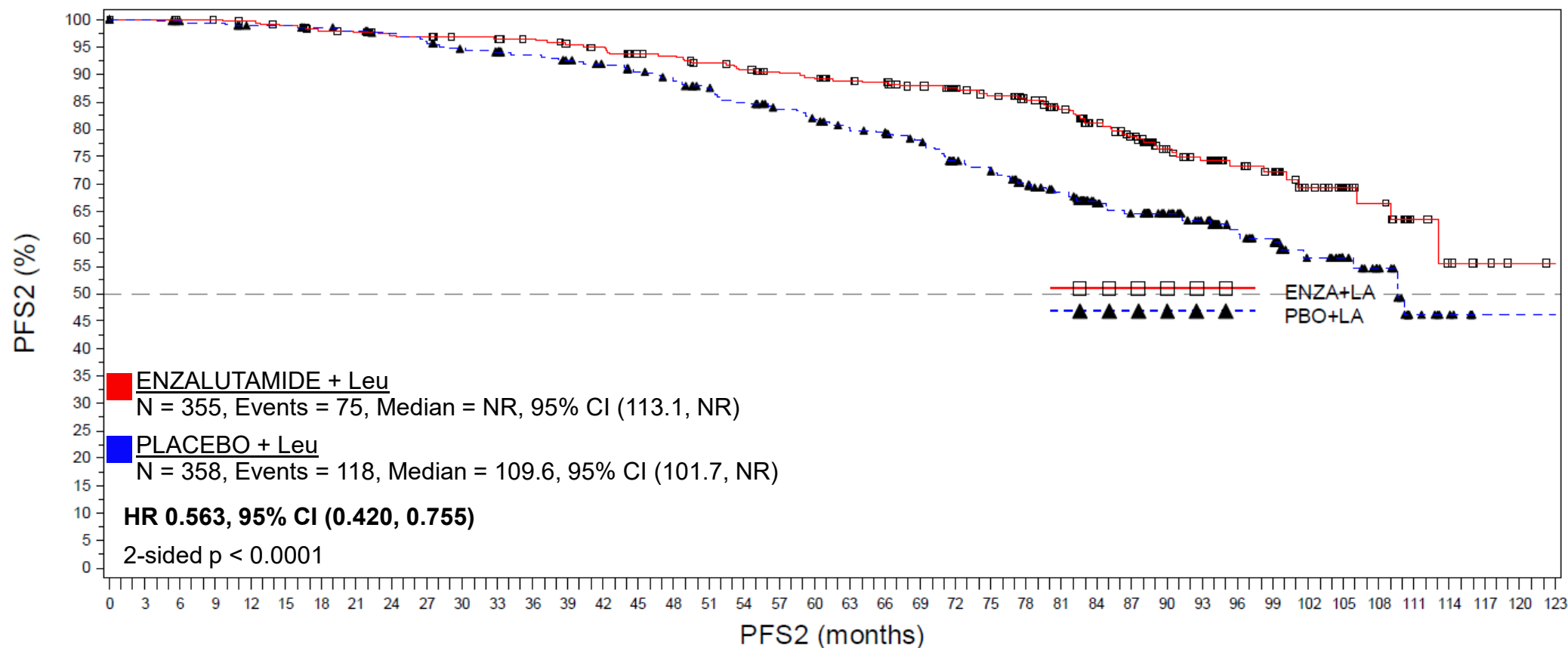
EMBARK PFS2

Descriptive Update

Data Cutoff Date: 27 May 2025

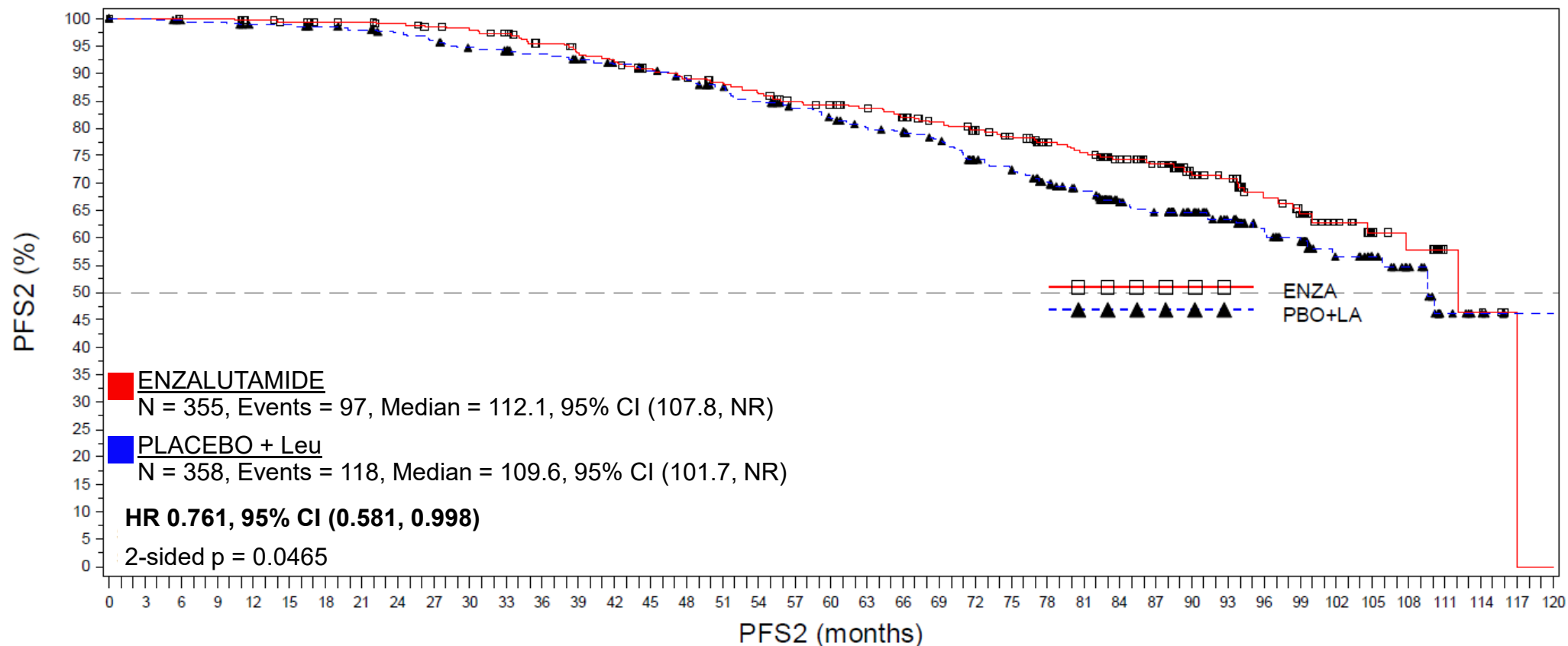
# Enza + Leu Treatment Resulted in Longer Median Progression-Free Time on First Subsequent Therapy (PFS2)

Final Analysis: Descriptive Update



# Enza Mono Treatment Resulted in Longer Median Progression-Free Time on First Subsequent Therapy (PFS2)

Final Analysis: Descriptive Update



ENZA:																																									
Event/Cum. Env	0/0	0/0	0/0	1/1	1/2	0/2	0/2	1/3	2/5	2/7	2/9	6/15	6/21	5/26	4/30	6/36	2/38	7/45	4/49	2/51	2/53	5/58	3/61	4/65	3/68	3/71	5/76	3/79	2/81	3/84	1/85	4/89	3/92	1/93	1/94	1/95	0/95	1/96	0/96	1/97	
Patients at Risk	355	353	352	352	347	344	341	340	337	333	330	326	314	306	301	292	286	281	274	265	261	254	247	235	224	217	203	197	165	155	109	101	69	62	38	23	19	5	4	1	0
PBO+LA:																																									
Event/Cum. Env	0/0	0/0	1/1	1/2	2/4	0/4	1/5	2/7	2/9	5/14	4/18	2/20	2/22	3/25	3/28	4/32	5/37	4/41	8/49	4/53	6/59	5/64	2/66	4/70	11/81	4/85	7/92	4/96	5/104	10/104	10/105	10/107	11/101	11/113	11/140	11/141	11/153	11/180	11/180	11/180	11/18
Patients at Risk	358	353	349	348	343	343	339	336	330	325	317	314	307	301	295	289	282	274	265	255	248	239	236	225	205	200	182	172	141	134	108	96	73	68	40	30	23	9	5	0	0



# EMBARK Safety

## EMBARC – Safety Summary

The safety profile was overall consistent with that observed at the primary analysis and no new safety signals were identified

# Overall Summary of Treatment-Emergent Adverse Events (Safety population)

Number of Patients Reporting at Least One	ENZA + LA (N=353)	PBO + LA (N=354)	ENZA (N=354)
TEAE	346 ( 98.0%)	347 ( 98.0%)	348 ( 98.3%)
TEAE that was Primary Reason for Treatment Discontinuation [1]	97 ( 27.5%)	45 ( 12.7%)	73 ( 20.6%)
TEAE Leading to ENZA / PBO Discontinuation [2]	82 ( 23.2%)	35 ( 9.9%)	65 ( 18.4%)
TEAE Leading to LA Discontinuation [2]	65 ( 18.4%)	36 ( 10.2%)	0 ( 0.0%)
TEAE Leading to Dose Reduction of ENZA / PBO	29 ( 8.2%)	17 ( 4.8%)	64 ( 18.1%)
TEAE Leading to Dose Reduction of LA	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)
TEAE Leading to Dose Interruption of ENZA / PBO	62 ( 17.6%)	45 ( 12.7%)	74 ( 20.9%)
TEAE Leading to Dose Interruption of LA	16 ( 4.5%)	8 ( 2.3%)	0 ( 0.0%)
TEAE Leading to Death	10 ( 2.8%)	5 ( 1.4%)	12 ( 3.4%)
Non Serious TEAE	342 ( 96.9%)	343 ( 96.9%)	347 ( 98.0%)
Grade 3 or Higher TEAE	185 ( 52.4%)	175 ( 49.4%)	203 ( 57.3%)
Non Serious TEAE Related to Study Drug [3]	304 ( 86.1%)	285 ( 80.5%)	315 ( 89.0%)
TEAE Related to Study Drug [3]	307 ( 87.0%)	286 ( 80.8%)	316 ( 89.3%)
TEAE Related to ENZA / PBO	291 ( 82.4%)	265 ( 74.9%)	316 ( 89.3%)
TEAE Related to LA	287 ( 81.3%)	266 ( 75.1%)	0 ( 0.0%)
Grade 3 or Higher TEAE Related to Study Drug [3]	68 ( 19.3%)	34 ( 9.6%)	72 ( 20.3%)
Grade 3 or Higher TEAE Related to ENZA / PBO	65 ( 18.4%)	32 ( 9.0%)	72 ( 20.3%)
Grade 3 or Higher TEAE Related to LA	42 ( 11.9%)	21 ( 5.9%)	0 ( 0.0%)
Serious TEAE	143 ( 40.5%)	133 ( 37.6%)	154 ( 43.5%)
Serious TEAE Related to Study Drug [3]	30 ( 8.5%)	9 ( 2.5%)	27 ( 7.6%)
Serious TEAE Related to ENZA / PBO	26 ( 7.4%)	9 ( 2.5%)	27 ( 7.6%)
Serious TEAE Related to LA	17 ( 4.8%)	6 ( 1.7%)	0 ( 0.0%)

# Treatment-Emergent Adverse Events of Special Interest (Safety Population)

TEAE of Special Interest	ENZA + LA (N=353)		PBO + LA (N=354)		ENZA (N=354)	
	All (a)	Per 100 PY (b)	All (a)	Per 100 PY (b)	All (a)	Per 100 PY (b)
Number of Patients Reporting at Least One TEAE of Special Interest(a) / Total Treatment Emergent Period (Patient-Years) (b)	313 ( 88.7%)	1915.61	289 ( 81.6%)	1663.97	301 ( 85.0%)	1950.09
Convulsion (Seizure)	4 ( 1.1%)	4 (0.2)	0 ( 0.0%)	0 (0.0)	3 ( 0.8%)	4 (0.2)
Hypertension	99 ( 28.0%)	115 (6.0)	81 ( 22.9%)	94 (5.6)	86 ( 24.3%)	95 (4.9)
Neutrophil Count Decreased	4 ( 1.1%)	4 (0.2)	8 ( 2.3%)	10 (0.6)	4 ( 1.1%)	4 (0.2)
Cognitive and Memory Impairment	57 ( 16.1%)	69 (3.6)	24 ( 6.8%)	30 (1.8)	57 ( 16.1%)	72 (3.7)
Ischemic Heart Disease(IHD)	22 ( 6.2%)	37 (1.9)	22 ( 6.2%)	25 (1.5)	38 ( 10.7%)	49 (2.5)
Other Selected Cardiovascular Events	29 ( 8.2%)	32 (1.7)	18 ( 5.1%)	21 (1.3)	15 ( 4.2%)	18 (0.9)
Posterior Reversible Encephalopathy Syndrome (PRES)	0 ( 0.0%)	0 (0.0)	0 ( 0.0%)	0 (0.0)	0 ( 0.0%)	0 (0.0)
Fatigue	183 ( 51.8%)	252 (13.2)	137 ( 38.7%)	158 (9.5)	198 ( 55.9%)	274 (14.1)
Renal Disorder	27 ( 7.6%)	36 (1.9)	13 ( 3.7%)	13 (0.8)	14 ( 4.0%)	22 (1.1)
Second Primary Malignancies	36 ( 10.2%)	37 (1.9)	24 ( 6.8%)	33 (2.0)	23 ( 6.5%)	29 (1.5)
Fall	104 ( 29.5%)	159 (8.3)	60 ( 16.9%)	88 (5.3)	71 ( 20.1%)	113 (5.8)
Fracture [1]	79 ( 22.4%)	115 (6.0)	53 ( 15.0%)	57 (3.4)	50 ( 14.1%)	70 (3.6)
Loss of Consciousness	22 ( 6.2%)	29 (1.5)	15 ( 4.2%)	18 (1.1)	18 ( 5.1%)	21 (1.1)
Thrombocytopenia	4 ( 1.1%)	5 (0.3)	7 ( 2.0%)	8 (0.5)	5 ( 1.4%)	5 (0.3)
Musculoskeletal Events	171 ( 48.4%)	288 (15.0)	150 ( 42.4%)	254 (15.3)	170 ( 48.0%)	266 (13.6)
Severe Cutaneous Adverse Reaction (SCAR)	1 ( 0.3%)	1 (<0.1)	0 ( 0.0%)	0 (0.0)	0 ( 0.0%)	0 (0.0)
Angioedema	12 ( 3.4%)	12 (0.6)	6 ( 1.7%)	7 (0.4)	7 ( 2.0%)	7 (0.4)
Rash	34 ( 9.6%)	46 (2.4)	27 ( 7.6%)	38 (2.3)	31 ( 8.8%)	37 (1.9)
Hepatic Disorder	22 ( 6.2%)	33 (1.7)	32 ( 9.0%)	56 (3.4)	16 ( 4.5%)	25 (1.3)



# Treatment-Emergent Adverse Events by Preferred Term in at least 5% in Any Treatment Arm (Safety Population) 1/3

Preferred Term	ENZA + LA (N=353)		PBO + LA (N=354)		ENZA (N=354)	
	All (a)	Per 100 PY (b)	All (a)	Per 100 PY (b)	All (a)	Per 100 PY (b)
Number of Patients Reporting at Least One TEAE (a) / Total Treatment Emergent Period (Patient-Years) (b)	346 ( 98.0%)	1915.61	347 ( 98.0%)	1663.97	348 ( 98.3%)	1950.09
Hot flush	246 ( 69.7%)	328 (17.1)	206 ( 58.2%)	257 (15.4)	80 ( 22.6%)	90 (4.6)
Fatigue	154 ( 43.6%)	199 (10.4)	119 ( 33.6%)	131 (7.9)	170 ( 48.0%)	226 (11.6)
Arthralgia	104 ( 29.5%)	116 (6.1)	75 ( 21.2%)	84 (5.0)	89 ( 25.1%)	96 (4.9)
Fall	104 ( 29.5%)	159 (8.3)	60 ( 16.9%)	88 (5.3)	71 ( 20.1%)	113 (5.8)
Hypertension	92 ( 26.1%)	107 (5.6)	75 ( 21.2%)	88 (5.3)	76 ( 21.5%)	84 (4.3)
Back pain	62 ( 17.6%)	71 (3.7)	56 ( 15.8%)	67 (4.0)	67 ( 18.9%)	77 (3.9)
Diarrhoea	55 ( 15.6%)	74 (3.9)	31 ( 8.8%)	37 (2.2)	47 ( 13.3%)	57 (2.9)
Constipation	53 ( 15.0%)	58 (3.0)	35 ( 9.9%)	41 (2.5)	38 ( 10.7%)	42 (2.2)
Haematuria	50 ( 14.2%)	69 (3.6)	57 ( 16.1%)	87 (5.2)	53 ( 15.0%)	88 (4.5)
Dizziness	46 ( 13.0%)	54 (2.8)	44 ( 12.4%)	56 (3.4)	47 ( 13.3%)	50 (2.6)
Headache	46 ( 13.0%)	56 (2.9)	36 ( 10.2%)	44 (2.6)	47 ( 13.3%)	57 (2.9)
Insomnia	45 ( 12.7%)	49 (2.6)	40 ( 11.3%)	43 (2.6)	26 ( 7.3%)	26 (1.3)
Nausea	43 ( 12.2%)	56 (2.9)	31 ( 8.8%)	35 (2.1)	57 ( 16.1%)	65 (3.3)
Asthenia	42 ( 11.9%)	53 (2.8)	21 ( 5.9%)	27 (1.6)	41 ( 11.6%)	48 (2.5)
Pain in extremity	42 ( 11.9%)	45 (2.3)	37 ( 10.5%)	39 (2.3)	44 ( 12.4%)	46 (2.4)
COVID-19	38 ( 10.8%)	40 (2.1)	51 ( 14.4%)	59 (3.5)	50 ( 14.1%)	51 (2.6)
Urinary incontinence	38 ( 10.8%)	40 (2.1)	35 ( 9.9%)	36 (2.2)	40 ( 11.3%)	47 (2.4)
Pollakiuria	34 ( 9.6%)	35 (1.8)	33 ( 9.3%)	33 (2.0)	28 ( 7.9%)	28 (1.4)
Dyspnoea	33 ( 9.3%)	35 (1.8)	24 ( 6.8%)	29 (1.7)	20 ( 5.6%)	23 (1.2)
Urinary tract infection	33 ( 9.3%)	61 (3.2)	28 ( 7.9%)	46 (2.8)	46 ( 13.0%)	69 (3.5)
Oedema peripheral	32 ( 9.1%)	40 (2.1)	40 ( 11.3%)	44 (2.6)	37 ( 10.5%)	42 (2.2)
Gynaecomastia	31 ( 8.8%)	31 (1.6)	32 ( 9.0%)	32 (1.9)	163 ( 46.0%)	190 (9.7)

# Treatment-Emergent Adverse Events by Preferred Term in at least 5% in Any Treatment Arm (Safety Population) 2/3

Preferred Term	ENZA + LA (N=353)		PBO + LA (N=354)		ENZA (N=354)	
	All (a)	Per 100 PY (b)	All (a)	Per 100 PY (b)	All (a)	Per 100 PY (b)
Nasopharyngitis	31 ( 8.8%)	52 (2.7)	26 ( 7.3%)	37 (2.2)	40 ( 11.3%)	63 (3.2)
Rib fracture	31 ( 8.8%)	39 (2.0)	26 ( 7.3%)	26 (1.6)	26 ( 7.3%)	28 (1.4)
Anaemia	30 ( 8.5%)	40 (2.1)	17 ( 4.8%)	22 (1.3)	26 ( 7.3%)	31 (1.6)
Nocturia	30 ( 8.5%)	33 (1.7)	18 ( 5.1%)	18 (1.1)	13 ( 3.7%)	13 (0.7)
Decreased appetite	29 ( 8.2%)	32 (1.7)	16 ( 4.5%)	19 (1.1)	33 ( 9.3%)	35 (1.8)
Memory impairment	28 ( 7.9%)	29 (1.5)	12 ( 3.4%)	12 (0.7)	24 ( 6.8%)	25 (1.3)
Rash	28 ( 7.9%)	36 (1.9)	23 ( 6.5%)	27 (1.6)	25 ( 7.1%)	26 (1.3)
Weight increased	28 ( 7.9%)	37 (1.9)	30 ( 8.5%)	42 (2.5)	18 ( 5.1%)	28 (1.4)
Upper respiratory tract infection	26 ( 7.4%)	34 (1.8)	25 ( 7.1%)	32 (1.9)	24 ( 6.8%)	29 (1.5)
Weight decreased	25 ( 7.1%)	30 (1.6)	14 ( 4.0%)	16 (1.0)	42 ( 11.9%)	49 (2.5)
Anxiety	24 ( 6.8%)	26 (1.4)	14 ( 4.0%)	15 (0.9)	22 ( 6.2%)	22 (1.1)
Cataract	24 ( 6.8%)	32 (1.7)	21 ( 5.9%)	24 (1.4)	27 ( 7.6%)	30 (1.5)
Dry skin	24 ( 6.8%)	27 (1.4)	11 ( 3.1%)	11 (0.7)	17 ( 4.8%)	17 (0.9)
Osteoporosis	24 ( 6.8%)	24 (1.3)	4 ( 1.1%)	4 (0.2)	4 ( 1.1%)	4 (0.2)
Cough	23 ( 6.5%)	33 (1.7)	26 ( 7.3%)	28 (1.7)	22 ( 6.2%)	24 (1.2)
Depression	23 ( 6.5%)	25 (1.3)	21 ( 5.9%)	23 (1.4)	22 ( 6.2%)	23 (1.2)
Epistaxis	23 ( 6.5%)	27 (1.4)	4 ( 1.1%)	4 (0.2)	18 ( 5.1%)	20 (1.0)
Osteoarthritis	22 ( 6.2%)	24 (1.3)	14 ( 4.0%)	14 (0.8)	22 ( 6.2%)	22 (1.1)
Arthritis	21 ( 5.9%)	21 (1.1)	15 ( 4.2%)	17 (1.0)	27 ( 7.6%)	28 (1.4)
Hypercholesterolaemia	21 ( 5.9%)	21 (1.1)	15 ( 4.2%)	15 (0.9)	8 ( 2.3%)	9 (0.5)
Contusion	20 ( 5.7%)	24 (1.3)	10 ( 2.8%)	13 (0.8)	14 ( 4.0%)	16 (0.8)
Alopecia	19 ( 5.4%)	21 (1.1)	4 ( 1.1%)	4 (0.2)	14 ( 4.0%)	15 (0.8)
Bronchitis	19 ( 5.4%)	22 (1.1)	13 ( 3.7%)	17 (1.0)	12 ( 3.4%)	12 (0.6)
Musculoskeletal chest pain	19 ( 5.4%)	19 (1.0)	15 ( 4.2%)	17 (1.0)	12 ( 3.4%)	12 (0.6)
Syncope	19 ( 5.4%)	23 (1.2)	10 ( 2.8%)	13 (0.8)	13 ( 3.7%)	15 (0.8)

# Treatment-Emergent Adverse Events by Preferred Term in at least 5% in Any Treatment Arm (Safety Population) 3/3

Preferred Term	ENZA + LA (N=353)		PBO + LA (N=354)		ENZA (N=354)	
	All (a)	Per 100 PY (b)	All (a)	Per 100 PY (b)	All (a)	Per 100 PY (b)
Amnesia	18 ( 5.1%)	19 (1.0)	9 ( 2.5%)	9 (0.5)	17 ( 4.8%)	19 (1.0)
Atrial fibrillation	18 ( 5.1%)	20 (1.0)	18 ( 5.1%)	22 (1.3)	10 ( 2.8%)	11 (0.6)
Neck pain	18 ( 5.1%)	18 (0.9)	18 ( 5.1%)	18 (1.1)	16 ( 4.5%)	18 (0.9)
Paraesthesia	18 ( 5.1%)	19 (1.0)	9 ( 2.5%)	9 (0.5)	13 ( 3.7%)	14 (0.7)
Type 2 diabetes mellitus	18 ( 5.1%)	19 (1.0)	20 ( 5.6%)	20 (1.2)	11 ( 3.1%)	12 (0.6)
Dysuria	15 ( 4.2%)	15 (0.8)	22 ( 6.2%)	25 (1.5)	10 ( 2.8%)	12 (0.6)
Muscle spasms	15 ( 4.2%)	19 (1.0)	25 ( 7.1%)	27 (1.6)	10 ( 2.8%)	10 (0.5)
Pneumonia	15 ( 4.2%)	15 (0.8)	19 ( 5.4%)	28 (1.7)	13 ( 3.7%)	13 (0.7)
Erectile dysfunction	14 ( 4.0%)	14 (0.7)	15 ( 4.2%)	15 (0.9)	18 ( 5.1%)	18 (0.9)
Nipple pain	13 ( 3.7%)	13 (0.7)	4 ( 1.1%)	4 (0.2)	54 (15.3%)	59 (3.0)
Overdose	12 ( 3.4%)	19 (1.0)	12 ( 3.4%)	15 (0.9)	22 ( 6.2%)	34 (1.7)
Dyspepsia	7 ( 2.0%)	7 (0.4)	10 ( 2.8%)	10 (0.6)	22 ( 6.2%)	26 (1.3)
Breast pain	4 ( 1.1%)	4 (0.2)	3 ( 0.8%)	3 (0.2)	25 ( 7.1%)	30 (1.5)
Breast tenderness	4 ( 1.1%)	4 (0.2)	4 ( 1.1%)	4 (0.2)	51 (14.4%)	61 (3.1)

## EMBARC – Conclusions

- Statistically significant and clinically meaningful improvement in OS was observed for the Enza + Leu arm compared to P + Leu at the pre-planned final analysis.
- Enza monotherapy did not result in a statistically significant improvement in OS compared with P + Leu, although a trend favorable to Enza monotherapy was observed.
- Updated follow up confirmed longer median time to first use of new antineoplastic therapy, median time to first SSE and median PFS2 for both Enza + Leu and Enza monotherapy compared to P + Leu
- There was no overall change in the safety profile of Enza + Leu or Enza monotherapy.
- These findings should further solidify Enza's position as the only medicine approved in the high-risk BCR nmCSPC space



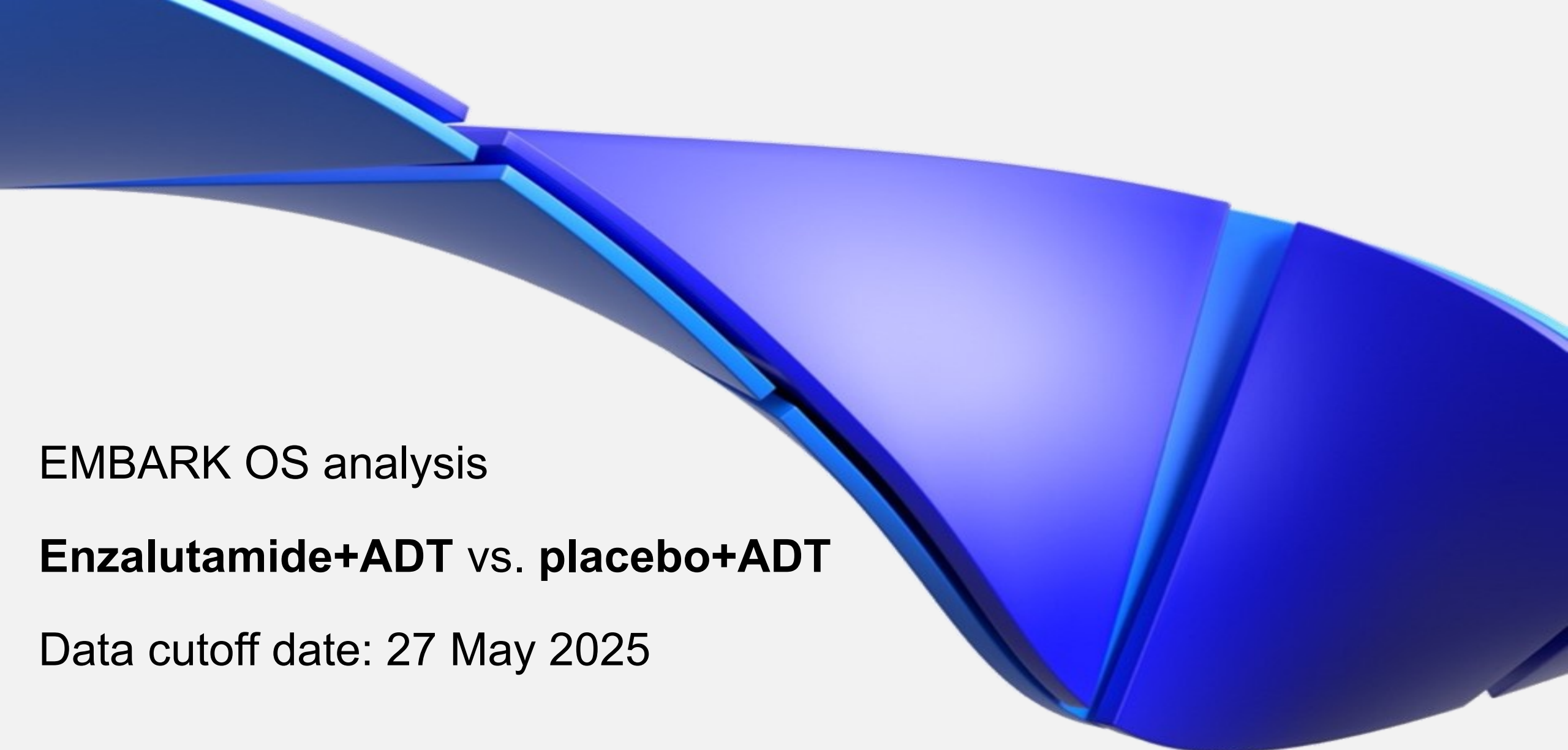
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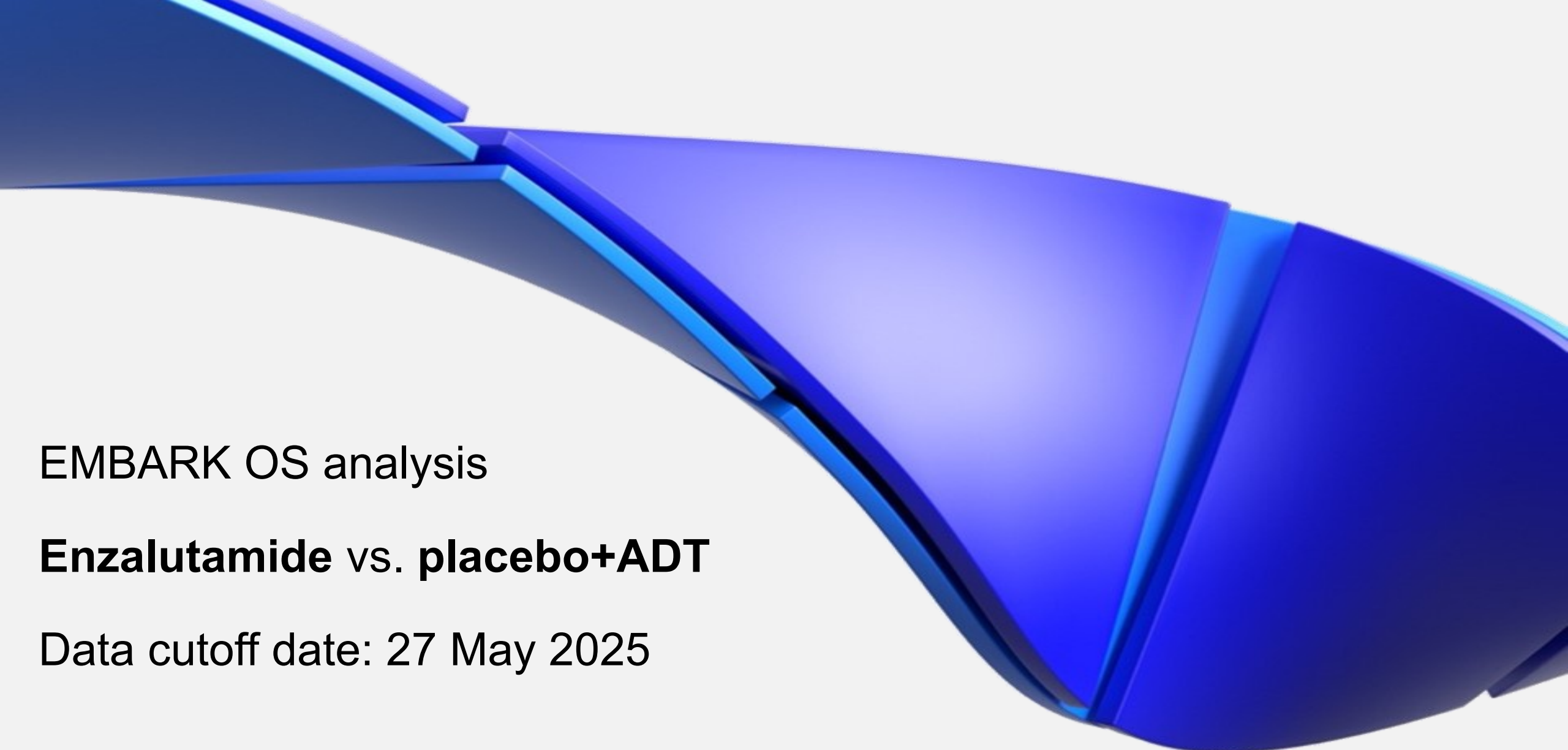
An abstract graphic composed of several overlapping, curved, and faceted planes in various shades of blue, ranging from light sky blue to deep navy blue. The planes are arranged in a way that creates a sense of depth and movement, resembling a stylized, modern architectural structure or a dynamic, flowing shape. The overall effect is clean and professional, typical of corporate branding.

EMBARC OS analysis

**Enzalutamide+ADT vs. placebo+ADT**

Data cutoff date: 27 May 2025



An abstract graphic composed of several overlapping, curved, blue and purple geometric shapes that create a sense of depth and movement, resembling a stylized wave or a series of connected planes.

EMBARC OS analysis

**Enzalutamide vs. placebo+ADT**

Data cutoff date: 27 May 2025

**Treatment-Emergent Adverse Events by Preferred Term in at least 5% of Patients in Any Treatment Group  
(Safety Population)**

Preferred Term	ENZA + LA (N=353)		PBO + LA (N=354)		ENZA (N=354)	
	All (a)	Per 100 PY (b)	All (a)	Per 100 PY (b)	All (a)	Per 100 PY (b)
Number of Patients Reporting at Least One TEAE (a) / Total Treatment Emergent Period (Patient-Years) (b)	346 ( 98.0%)	1915.61	347 ( 98.0%)	1663.97	348 ( 98.3%)	1950.09
Hot flush	246 ( 69.7%)	328 (17.1)	206 ( 58.2%)	257 (15.4)	80 ( 22.6%)	90 (4.6)
Fatigue	154 ( 43.6%)	199 (10.4)	119 ( 33.6%)	131 (7.9)	170 ( 48.0%)	226 (11.6)
Arthralgia	104 ( 29.5%)	116 (6.1)	75 ( 21.2%)	84 (5.0)	89 ( 25.1%)	96 (4.9)
Fall	104 ( 29.5%)	159 (8.3)	60 ( 16.9%)	88 (5.3)	71 ( 20.1%)	113 (5.8)
Hypertension	92 ( 26.1%)	107 (5.6)	75 ( 21.2%)	88 (5.3)	76 ( 21.5%)	84 (4.3)
Back pain	62 ( 17.6%)	71 (3.7)	56 ( 15.8%)	67 (4.0)	67 ( 18.9%)	77 (3.9)
Diarrhoea	55 ( 15.6%)	74 (3.9)	31 ( 8.8%)	37 (2.2)	47 ( 13.3%)	57 (2.9)
Constipation	53 ( 15.0%)	58 (3.0)	35 ( 9.9%)	41 (2.5)	38 ( 10.7%)	42 (2.2)
• Modified						
Hot flush	244 ( 69.1%)	317 (23.6)	204 ( 57.6%)	253 (19.2)	79 ( 22.3%)	88 (5.4)
Fatigue	153 ( 43.3%)	194 (14.5)	117 ( 33.1%)	128 (9.7)	165 ( 46.6%)	219 (13.5)
Fall	87 ( 24.6%)	128 (9.5)	53 ( 15.0%)	70 (5.3)	66 ( 18.6%)	103 (6.3)
Hypertension	80 ( 22.7%)	93 (6.9)	62 ( 17.5%)	72 (5.5)	64 ( 18.1%)	71 (4.4)
Arthralgia	78 ( 22.1%)	87 (6.5)	66 ( 18.6%)	70 (5.3)	78 ( 22.0%)	83 (5.1)
Diarrhoea	46 ( 13.0%)	62 (4.6)	27 ( 7.6%)	30 (2.3)	42 ( 11.9%)	51 (3.1)
Headache	43 ( 12.2%)	51 (3.8)	35 ( 9.9%)	43 (3.3)	44 ( 12.4%)	54 (3.3)
Asthenia	42 ( 11.9%)	51 (3.8)	20 ( 5.6%)	27 (2.0)	41 ( 11.6%)	48 (3.0)
• Reinitiation						
Total Number of Reinitiated Patients	254 ( 72.0%)		207 ( 58.5%)		275 ( 77.7%)	
Hot flush	94 ( 37.0%)	96 (9.3)	54 ( 26.1%)	55 (7.3)	25 ( 9.1%)	25 (2.0)
Fatigue	70 ( 27.6%)	73 (7.1)	32 ( 15.5%)	36 (4.8)	93 ( 33.8%)	103 (8.3)
Fall	63 ( 24.8%)	96 (9.3)	32 ( 15.5%)	47 (6.2)	50 ( 18.2%)	77 (6.2)
Arthralgia	50 ( 19.7%)	54 (5.2)	22 ( 10.6%)	25 (3.3)	52 ( 18.9%)	54 (4.4)
Hypertension	49 ( 19.3%)	52 (5.0)	27 ( 13.0%)	31 (4.1)	39 ( 14.2%)	42 (3.4)
COVID-19	32 ( 12.6%)	34 (3.3)	44 ( 21.3%)	50 (6.6)	43 ( 15.6%)	43 (3.5)
Diarrhoea	26 ( 10.2%)	30 (2.9)	14 ( 6.8%)	16 (2.1)	20 ( 7.3%)	21 (1.7)

- The median duration of treatment (range) was 80.1 months (0.1, 118.2) for enzalutamide plus leuprolide, 55.8 months (0.7, 121.9) for placebo plus leuprolide and 78.5 months (0.4, 120.3) for enzalutamide monotherapy. The median (range) modified duration of treatment, which excludes the protocol-defined treatment suspension period from total duration of treatment, was 44.3 months (0.1, 111.3) for enzalutamide plus leuprolide, 40.7 months (0.7, 111.1) for placebo plus leuprolide and 59.3 months (0.4, 112.2) for enzalutamide monotherapy. The median duration of treatment suspension (range) was 19.3 months (1.4, 109.0) for enzalutamide plus leuprolide, 16.6 months (3.4, 110.9) for placebo plus leuprolide and 9.6 months (1.9, 105.5) for enzalutamide monotherapy.