Abstract #1060
Poster Board #39

Imlunestrant With or Without Abemaciclib in Advanced Breast Cancer (ABC): Safety Analyses From the Phase III EMBER-3 Trial

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Study was sponsored by Eli Lilly and Company

OBJECTIVES

- To characterize the incidence, timing, duration, and management of the most common TEAEs of **imlunestrant monotherapy** and in **combination with abemaciclib** in the EMBER-3 trial
- To assess the safety profile of **imlunestrant** in different age groups

CONCLUSIONS

- **Imlunestrant monotherapy** had a favorable safety profile, with generally low grade and manageable side effects
- The incidence and severity of AEs in the **imlunestrant+abemaciclib** arm were consistent with the known safety profile of abemaciclib+fulvestrant and manageable with supportive medications and dose adjustments
- The most frequent TEAEs in both **imlunestrant** arms were generally low grade, reversible, occurred early in treatment, and resulted in few treatment discontinuations
- Incidence of VTE, ILD, dyslipidemia, bradycardia, and photopsia were relatively low or not observed in both **imlunestrant** arms
- In general, the safety profiles of **imlunestrant monotherapy** and **imlunestrant+abemaciclib** were consistent across age groups, with numerical differences in select TEAEs

American Society of Clinical Oncology (ASCO) 61st Annual Meeting; Chicago, USA; May 30 – June 3, 2025

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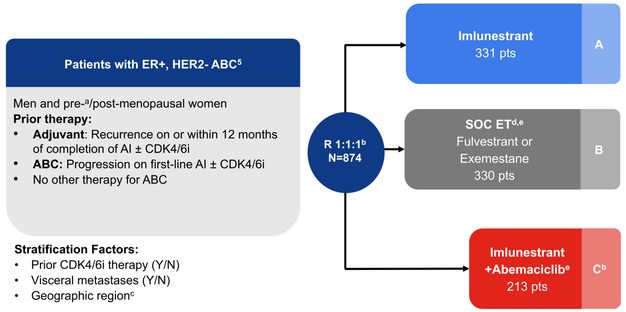
BACKGROUND

- **Imlunestrant** is a next-generation, brain-penetrant, oral SERD and pure ER antagonist that delivers continuous ER inhibition[1]
- In EMBER-3, at the primary outcome analysis[2]:
  - **Imlunestrant** alone significantly improved PFS vs **SOC ET** (fulvestrant or exemestane) in patients with *ESR1*m (5.5 vs 3.8 months; HR=0.62; 95% CI: 0.46–0.82; p<0.001) while **imlunestrant+abemaciclib** significantly improved PFS vs **imlunestrant** alone in all patients (9.4 vs 5.5 months; HR=0.57; 95% CI: 0.44–0.73; p<0.001) regardless of *ESR1*m status
  - **Imlunestrant** demonstrated favorable safety, with generally low-grade and manageable AEs:
    - In the **imlunestrant arm**, fatigue, diarrhea, and nausea were most frequently reported
    - In the **imlunestrant+abemaciclib arm**, diarrhea, nausea, and neutropenia were most frequently reported and incidences were similar to those previously reported for abemaciclib+fulvestrant[3,4]

STUDY DESIGN AND METHODS



Imlunestrant (400 mg QD). Exemestane (25 mg QD). Fulvestrant (500mg IM on days 1 and 15 of cycle 1 and on day 1 of subsequent 28-day cycles). Abemaciclib (150 mg BID). Enrolled October 2021 to November 2023 across 195 sites in 22 countries. [a] A GnRH agonist was required in men and premenopausal women; [b] Arm C enrolled with Protocol Amendment A (at which point 122 pts had been randomized across Arms A and B); [c] East Asia vs United States/European Union vs others; [d] Investigator's choice; [e] Labeled dose

- Safety population: All pts who received **at least one dose of any study drug**
- TEAEs were assessed for severity per **CTCAE v5.0** at baseline and at every visit throughout the study
- Labs were assessed at **baseline, at every cycle,** and approximately **30 days after discontinuation of study therapy**

Dose Adjustment	Imlunestrant Dose
1	200 mg QD

Dose Adjustment	Abemaciclib Dose
1	100 mg BID
2	50 mg BID

Pts receiving **imlunestrant+abemaciclib** could discontinue either drug and continue the other and still be considered on study treatment

RESULTS

Summary of Select TEAEs

Diarrhea		Imlu N=327	SOC ET N=324	Imlu+Abema N=208
% pts	Any grade	21	12	86
	G1 AE	18	9	50
	G2 AE	3	3	28
	G≥3 AE	<1	0	8
	Pts with >1 occurrences of AE	5	1	34
	Pts with >1 occurrences of G≥3 AE	0	0	<1
	Dose interruption/reduction/discontinuation	<1/0/0	0/0/0	19[a]/18[b]/<1[c,d]
	Antidiarrheal medication[e]	10	7	68
Median days	Time to onset (Q1-Q3)	30 (15–129)	52 (17–132)	5 (2–17)
	Duration of G2 AE (range)	3 (1–28)	5 (1–55)	13 (1–87)
	Duration of G≥3 AE (range)	8 (8–8)	–	9 (1–47)

[a] 14 (6.7%) pts had only abemaciclib interrupted and 3 (1.4%) pts had only imlunestrant interrupted; [b] 29 (14%) pts had only abemaciclib reduced; [c] Pts who discontinued both drugs; [d] One (0.5%) more pt discontinued only abemaciclib. [e] Proportion of total safety population treated.

Nausea		Imlu N=327	SOC ET N=324	Imlu+Abema N=208
% pts	Any grade	17	13	49
	G1 AE	14	8	31
	G2 AE	3	5	15
	G≥3 AE	<1	0	2
	Pts with >1 occurrences of AE	2	1	14
	Pts with >1 occurrences of G≥3 AE	0	0	<1
	Dose interruption/reduction/discontinuation	0/<1/0	0/0/0	6[a]/5[b]/0[c,d]
	Antiemetic medication[e]	10	10	21
Median days	Time to onset (Q1-Q3)	20 (4–56)	57 (10–147)	15 (3–48)
	Duration of G2 AE (range)	16 (4–89)	10 (1–90)	19 (2–266)
	Duration of G≥3 AE (range)	24 (24–24)	–	7 (6–13)

[a] One (0.5%) pt each had either imlunestrant or abemaciclib interrupted; [b] Two (1%) pts had imlunestrant reduced and 5 (2.4%) pts had abemaciclib reduced; [c] Pts who discontinued both drugs; [d] One (0.5%) more pt discontinued only abemaciclib; [e] Proportion of total safety population treated.

Fatigue[a]		Imlu N=327	SOC ET N=324	Imlu+Abema N=208
% pts	Any grade	23	13	39
	G1 AE	17	9	20
	G2 AE	5	3	14
	G≥3 AE	<1	<1	5
	Pts with >1 occurrences of AE	2	<1	8
	Pts with >1 occurrences of G≥3 AE	0	0	0
	Dose interruption/reduction/discontinuation	<1/<1/<1	<1/0/0	3[b]/4[c]/<1[d,e]
Median days	Time to onset (Q1-Q3)	42 (14–86)	29 (13–124)	16 (3–49)
	Duration of G2 AE (range)	43 (7–529)	98 (9–232)	28 (4–428)
	Duration of G≥3 AE (range)	7 (7–7)	N/A[f]	15 (3–72)

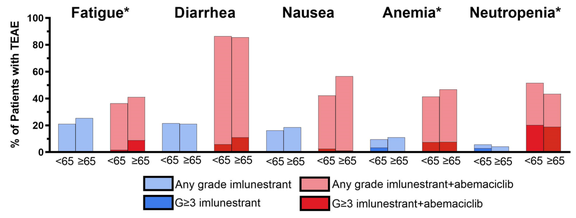
[a] Includes both asthenia and fatigue; [b] Three (1.4%) pts had only abemaciclib interrupted; [c] One (0.5%) pt had only imlunestrant reduced and 7 (3.4%) pts had only abemaciclib reduced; [d] Pts who discontinued both drugs; [e] One (0.5%) more pt discontinued only abemaciclib; [f] Not available due to missing end date.

Elevated Transaminases[a]		Imlu N=327	SOC ET N=324	Imlu+Abema N=208
% pts	Any grade	16	15	20
	G1 AE	11	9	12
	G2 AE	3	5	3
	G≥3 AE	1	1	5
	Pts with >1 occurrences of AE	8	9	12
	Pts with >1 occurrences of G≥3 AE	<1	<1	2
	Dose interruption/reduction/discontinuation	2/1/1	<1/0/0	3[b]/2[c]/2[d,e]
Median days	Time to onset (Q1-Q3)	58 (16–197)	43 (15–185)	66 (29–195)
	Duration of G2 AE (range)	27 (11–97)	29 (5–86)	19 (3–82)
	Duration of G≥3 AE (range)	5 (4–27)	2 (2–2)	9 (2–58)

[a] Includes increased ALT, AST, and hepatic enzymes, drug induced liver injury, hypertransaminasemia, and hepatotoxicity; [b] All 6 (2.9%) pts had both study drugs interrupted; [c] All 5 (2.4%) pts had both study drugs reduced; [d] Pts who discontinued both drugs; [e] One additional pt (0.5%) each discontinued only one of the study drugs and continued the other.

- The majority of clinically relevant TEAEs were G1, single occurrences that occurred early in treatment and led to few discontinuations across all arms
- In the **imlunestrant arm** few dose adjustments were required
- Similar antidiarrheal and antiemetic use in **imlunestrant** and **SOC ET** arms
- In the **imlunestrant+ abemaciclib** arm, clinically relevant TEAEs were well managed with dose adjustments and concomitant medications
- In the **imlunestrant+ abemaciclib** arm, characteristics of clinically relevant TEAEs were similar to prior experiences with abemaciclib[6]
- Three pts in **imlunestrant arm** had post-baseline ALT/AST increases >3×ULN and total bilirubin increases >2×ULN. All 3 pts had alkaline phosphatase >3×ULN and other risk factors for elevated laboratory values

Safety by Age



AEs, %	Imlu N=327		Imlu+Abema N=208	
	<65 yrs n=209	≥65 yrs n=118	<65 yrs n=118	≥65 yrs n=90
Patients with ≥1 TEAE	82	83	98	99
Patients with ≥1 G≥3 TEAE	19	14	46	52
Patients with ≥1 SAE[a]	12	9	16	18
Dose interruption/reduction/ discontinuation[a] due to TEAE	11/2/4	9/3/4	49/32/4	63/49/9

* Consolidated terms; [a] Deaths were included as SAEs and discontinuations due to AE.

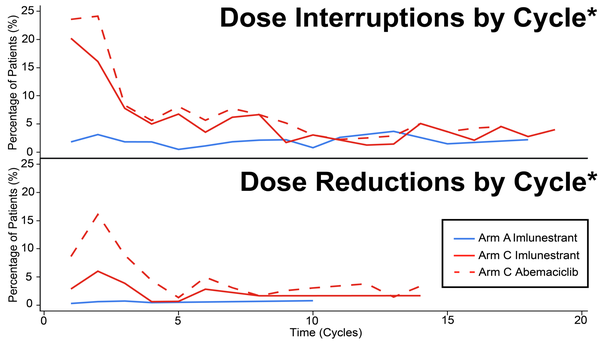
In the **imlunestrant+abemaciclib** arm, consistent with previous abemaciclib experience[7], patients aged ≥65 years had:

- higher incidence of fatigue, nausea, anemia, and G≥3 diarrhea
- lower incidence of neutropenia
- higher rates of dose adjustments

Dose Modifications Due to TEAEs

Patients, %	Imlu N=327	SOC ET N=324	Imlu+Abema N=208
Discontinuations	80	87	64
Discontinuations due to PD	73	80	54
Discontinuations due to TEAE[a]	4	1	6[b]
Dose adjustments due to TEAE	10	7	61
Dose interruptions/delays	10	7	55[c]
Dose reductions	2	0	39[d]

Dose delays of fulvestrant occurred in 7% pts. [a] Dose discontinuations include fatal AEs; [b] One (0.5%) more pt discontinued only imlunestrant and 6 (2.9%) more pts discontinued only abemaciclib. [c] 92 (44.2%) pts had both drugs interrupted, 20 (9.6%) pts had only abemaciclib interrupted, and 3 (1.4%) pts had only imlunestrant interrupted; [d] 30 (14.4%) pts had both drugs dose reduced, 48 (23.1%) pts had only abemaciclib reduced, and 4 (1.9%) pts had only imlunestrant reduced.



- Frequency of discontinuations due to AEs were low. Few dose reductions occurred with **imlunestrant monotherapy**
- In the **imlunestrant+abemaciclib** arm most dose adjustment occurred in the first few months of treatment
- Dose adjustments due to AEs on **abemaciclib** for the **imlunestrant+abemaciclib arm** were similar to prior experiences with **abemaciclib**[3,4]

*SOC not shown. No dose adjustment allowed for exemestane per protocol. Dose delays of fulvestrant occurred in 7% pts

Incidence of TEAEs of Interest

TEAE, Consolidated terms, %	Imlu+Abema N=208	
	Any Grade	G≥3
Neutropenia[a]	48	20
Infection[b]	31	4
ILD[c]	2	0
VTE[d]	3	<1

[a] Includes both neutropenia and neutrophil count decreased; [b] Includes all infections and infestations system organ class; [c] Includes interstitial lung disease, pneumonitis, pulmonary fibrosis, and pulmonary toxicity; [d] Includes central venous catheterization, deep vein thrombosis, pelvic venous thrombosis, peripheral vein thrombosis, portal vein thrombosis, pulmonary embolism, and superficial vein thrombosis.

TEAE, %	Imlu N=327		SOC ET N=324		Imlu+Abema N=208	
	Any Grade	G≥3	Any Grade	G≥3	Any Grade	G≥3
Bradycardia[a]	2	0	0	0	1	0
Photopsia	0	0	0	0	0	0
Dyslipidemia[b]	7	<1	9	0	8	0
Pts receiving lipid-modifying agents[c]	6		4		2	

[a] Includes bradycardia and sinus bradycardia; [b] Includes dyslipidaemia, hypercholesterolaemia, hyperlipidaemia, hypertriglyceridaemia, and low-density lipoprotein increased; [c] Patients who started lipid-modifying agents while on study treatment.

- Incidence of VTE, ILD, dyslipidemia, bradycardia, and photopsia were relatively low or not observed in both **imlunestrant arms**
- The use of lipid-modifying agents was generally similar between the **imlunestrant** and **SOC ET** arms

ABBREVIATIONS

ABC, advanced breast cancer; Abema, abemaciclib; AE, adverse event; AI, aromatase inhibitor; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; CI, confidence interval; CTCAE, Common Terminology Criteria for Adverse Events; ER, estrogen receptor; *ESR1*m, *ESR1* mutation; G, grade; GnRH, gonadotropin-releasing hormone; HER2-, human epidermal growth factor receptor 2-negative; HR, hazard ratio; ILD, interstitial lung disease; IM, intramuscular; Imlu, imlunestrant; med, median; N, number of patients in total safety population; n, number of patients in specified category; PD, progressive disease; PFS, progression-free survival; pts, patients; Q, quartile; QD, once daily; R, randomized; SAE, serious adverse event; SERD, selective estrogen receptor degrader; SOC ET, standard of care endocrine therapy; TEAE, treatment-emergent adverse event; ULN, upper limit of normal; VTE, venous thromboembolism

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ACKNOWLEDGMENTS

- We would like to thank the support staff who contributed to this study.
- We are very grateful for the time and efforts of the EMBER-3 Steering Committee.
- We thank the 874 clinical trial participants and their families/caregivers from 195 sites in 22 countries for participating in this trial.
- Medical writing support was provided by Preethi Govindarajan of Syneos Health.

ASCO 61st Annual Meeting
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Background and Objectives

Background

- **Imlunestrant** is a next-generation, brain-penetrant, oral SERD and pure ER antagonist that delivers continuous ER inhibition[1]
- In EMBER-3, at the primary outcome analysis[2]:
  - **Imlunestrant** alone significantly improved PFS vs **SOC ET** (fulvestrant or exemestane) in patients with *ESR1*m (5.5 vs 3.8 months; HR=0.62; 95% CI: 0.46–0.82; p<0.001) while **imlunestrant+abemaciclib** significantly improved PFS vs **imlunestrant** alone in all patients (9.4 vs 5.5 months; HR=0.57; 95% CI: 0.44–0.73; p<0.001) regardless of *ESR1*m status
  - **Imlunestrant** demonstrated favorable safety, with generally low-grade and manageable AEs:
    - In the **imlunestrant arm**, fatigue, diarrhea, and nausea were most frequently reported
    - In the **imlunestrant+abemaciclib arm**, diarrhea, nausea, and neutropenia were most frequently reported and incidences were similar to those previously reported for abemaciclib+fulvestrant[3,4]

Objectives

- To characterize the incidence, timing, duration, and management of the most common TEAEs of **imlunestrant monotherapy** and in **combination with abemaciclib** in the EMBER-3 trial
- To assess the safety profile of **imlunestrant** in different age groups

Methods – Study Design

Patients with ER+, HER2- ABC[5]

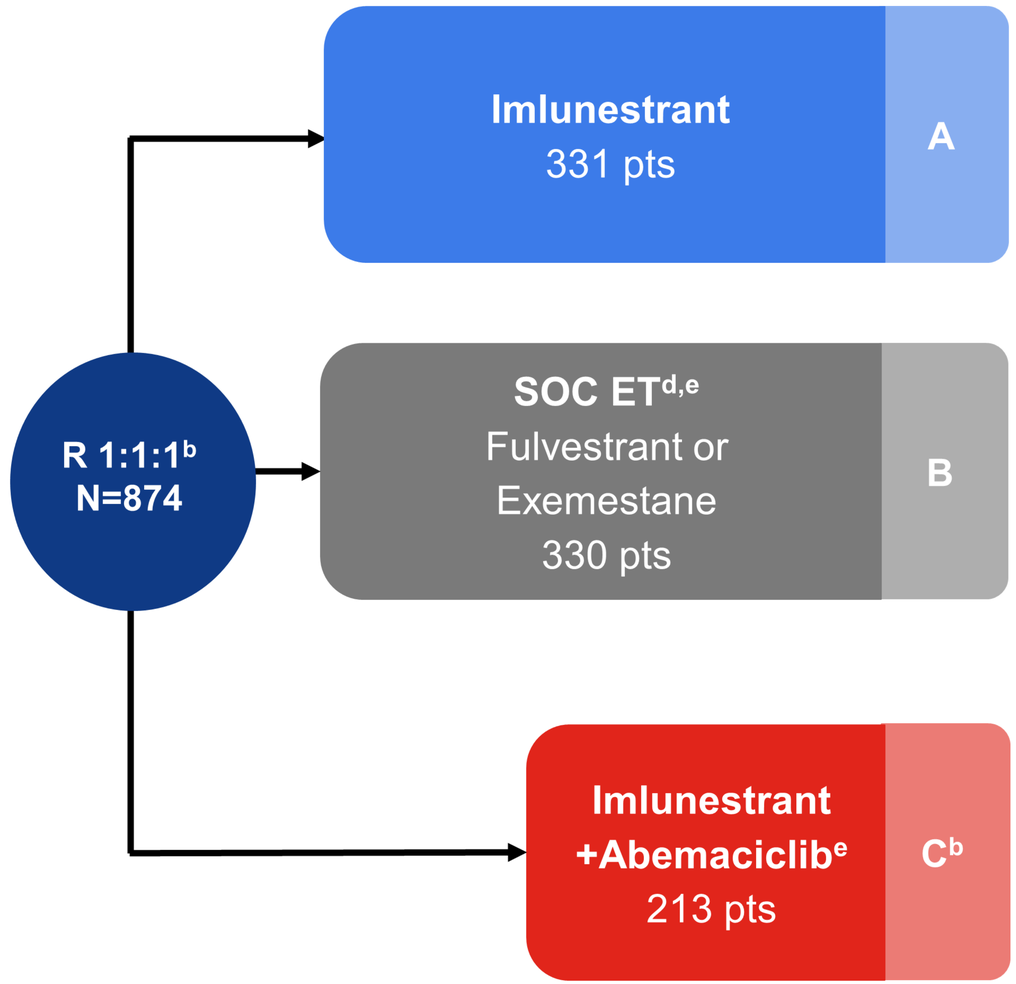
Men and pre-[a]/post-menopausal women

Prior therapy:

- **Adjuvant**: Recurrence on or within 12 months of completion of AI ± CDK4/6i
- **ABC:** Progression on first-line AI ± CDK4/6i
- No other therapy for ABC

Stratification Factors:

- Prior CDK4/6i therapy (Y/N)
- Visceral metastases (Y/N)
- Geographic region[c]



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Methods – Study Design

- Safety population: all patients who received **at least one dose of any study drug**
- TEAEs were assessed for severity per **CTCAE v5.0** at baseline and at every visit throughout the study
- Labs were assessed at **baseline, at every cycle,** and approximately **30 days after discontinuation of study therapy**

Dose Adjustment	Imlunestrant Dose
1	200 mg QD

Dose Adjustment	Abemaciclib Dose
1	100 mg BID
2	50 mg BID

Patients receiving **imlunestrant+abemaciclib** could discontinue either drug and continue the other per investigator's decision

Summary of Diarrhea

Diarrhea		Imlu N=327	SOC ET N=324	Imlu+Abema N=208
% pts	Any grade	21	12	86
	G1 AE	18	9	50
	G2 AE	3	3	28
	G≥3 AE	<1	0	8
	Pts with >1 occurrences of AE	5	1	34
	Pts with >1 occurrences of G≥3 AE	0	0	<1
	Dose interruption/reduction/discontinuation	<1/0/0	0/0/0	19[a]/18[b]/<1[c,d]
	Antidiarrheal medication[e]	10	7	68
Median days	Time to onset (Q1-Q3)	30 (15–129)	52 (17–132)	5 (2–17)
	Duration of G2 AE (range)	3 (1–28)	5 (1–55)	13 (1–87)
	Duration of G≥3 AE (range)	8 (8–8)	–	9 (1–47)

- In both **imlunestrant** arms, the majority of events were G1 and occurred in the first month
- Diarrhea in the **imlunestrant+abemaciclib** arm was comparable to that observed previously with abemaciclib[6] and was well managed with dose adjustments and antidiarrheals

[a] 14 (6.7%) pts had only abemaciclib interrupted and 3 (1.4%) pts had only imlunestrant interrupted; [b] 29 (14%) pts had only abemaciclib reduced; [c] Pts who discontinued both drugs; [d] One (0.5%) more pt discontinued only abemaciclib. [e] Proportion of total safety population treated.

Summary of Nausea

Nausea		Imlu N=327	SOC ET N=324	Imlu+Abema N=208
% pts	Any grade	17	13	49
	G1 AE	14	8	31
	G2 AE	3	5	15
	G≥3 AE	<1	0	2
	Pts with >1 occurrences of AE	2	1	14
	Pts with >1 occurrences of G≥3 AE	0	0	<1
	Dose interruption/reduction/discontinuation	0/<1/0	0/0/0	6[a]/5[b]/0[c,d]
	Antiemetic medication[e]	10	10	21
Median days	Time to onset (Q1-Q3)	20 (4–56)	57 (10–147)	15 (3–48)
	Duration of G2 AE (range)	16 (4–89)	10 (1–90)	19 (2–266)
	Duration of G≥3 AE (range)	24 (24–24)	–	7 (6–13)

- The majority of events across all arms were G1, single occurrences that occurred early in treatment
- Nausea was well managed with few dose adjustments and did not lead to treatment discontinuations in any arm
- Antiemetic use was the same in the **imlunestrant** and **SOC ET** arms

[a] One (0.5%) pt each had either imlunestrant or abemaciclib interrupted; [b] Two (1%) pts had imlunestrant reduced and 5 (2.4%) pts had abemaciclib reduced; [c] Pts who discontinued both drugs; [d] One (0.5%) more pt discontinued only abemaciclib; [e] Proportion of total safety population treated.

Summary of Fatigue

Fatigue[a]		Imlu N=327	SOC ET N=324	Imlu+Abema N=208
% pts	Any grade	23	13	39
	G1 AE	17	9	20
	G2 AE	5	3	14
	G≥3 AE	<1	<1	5
	Pts with >1 occurrences of AE	2	<1	8
	Pts with >1 occurrences of G≥3 AE	0	0	0
	Dose interruption/reduction/discontinuation	<1/<1/<1	<1/0/0	3[b]/4[c]/<1[d,e]
Median days	Time to onset (Q1-Q3)	42 (14–86)	29 (13–124)	16 (3–49)
	Duration of G2 AE (range)	43 (7–529)	98 (9–232)	28 (4–428)
	Duration of G≥3 AE (range)	7 (7–7)	N/A[f]	15 (3–72)

- Across all arms, the majority of events were low grade, single occurrences, and did not lead to treatment discontinuations
- There were few dose interruptions or reductions due to fatigue

[a] Includes both asthenia and fatigue; [b] Three (1.4%) pts had only abemaciclib interrupted; [c] One (0.5%) pt had only imlunestrant reduced and 7 (3.4%) pts had only abemaciclib reduced; [d] Pts who discontinued both drugs; [e] One (0.5%) more pt discontinued only abemaciclib; [f] Not available due to missing end date.

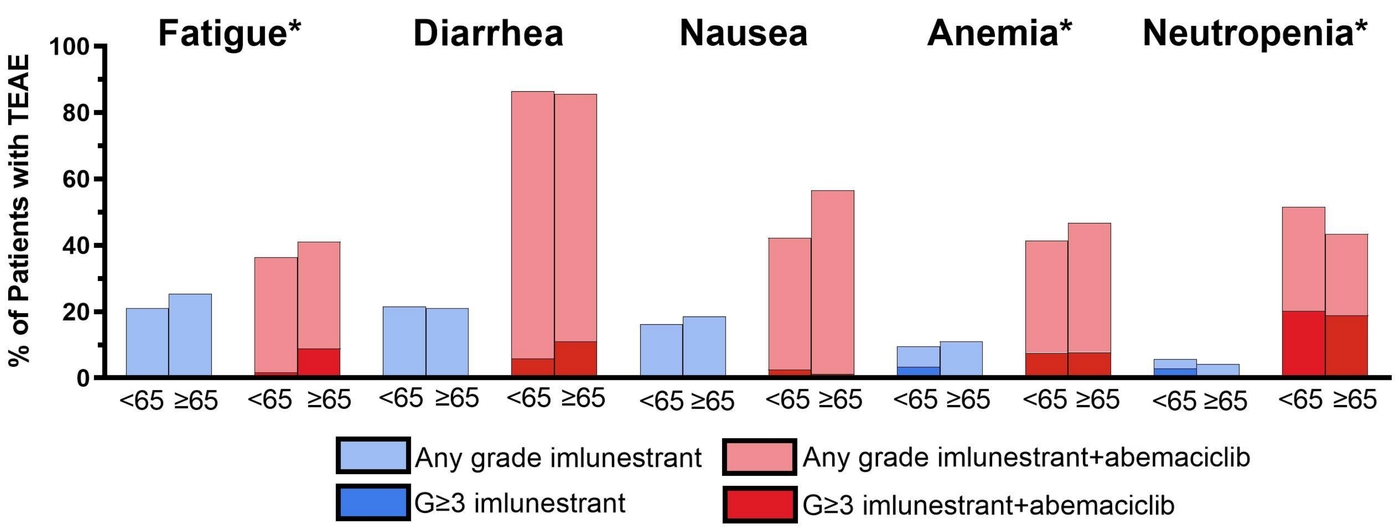
Summary of Transaminase Elevations

Elevated Transaminases[a]		Imlu N=327	SOC ET N=324	Imlu+Abema N=208
% pts	Any grade	16	15	20
	G1 AE	11	9	12
	G2 AE	3	5	3
	G≥3 AE	1	1	5
	Pts with >1 occurrences of AE	8	9	12
	Pts with >1 occurrences of G≥3 AE	<1	<1	2
	Dose interruption/reduction/discontinuation	2/1/1	<1/0/0	3[b]/2[c]/2[d,e]
Median days	Time to onset (Q1-Q3)	58 (16–197)	43 (15–185)	66 (29–195)
	Duration of G2 AE (range)	27 (11–97)	29 (5–86)	19 (3–82)
	Duration of G≥3 AE (range)	5 (4–27)	2 (2–2)	9 (2–58)

- Most transaminase elevations were low grade, reversible, and required few dose adjustments or discontinuations
- Three pts in the imlunestrant arm had post-baseline ALT/AST increases >3×ULN and total bilirubin increases >2×ULN. All 3 patients had alkaline phosphatase >3×ULN and other risk factors for elevated laboratory values

[a] Includes increased ALT, AST, and hepatic enzymes, drug induced liver injury, hypertransaminaesemia, and hepatotoxicity; [b] All 6 (2.9%) pts had both study drugs interrupted; [c] All 5 (2.4%) pts had both study drugs reduced; [d] Pts who discontinued both drugs; [e] One additional pt (0.5%) each discontinued only one of the study drugs and continued the other.

Safety by Age



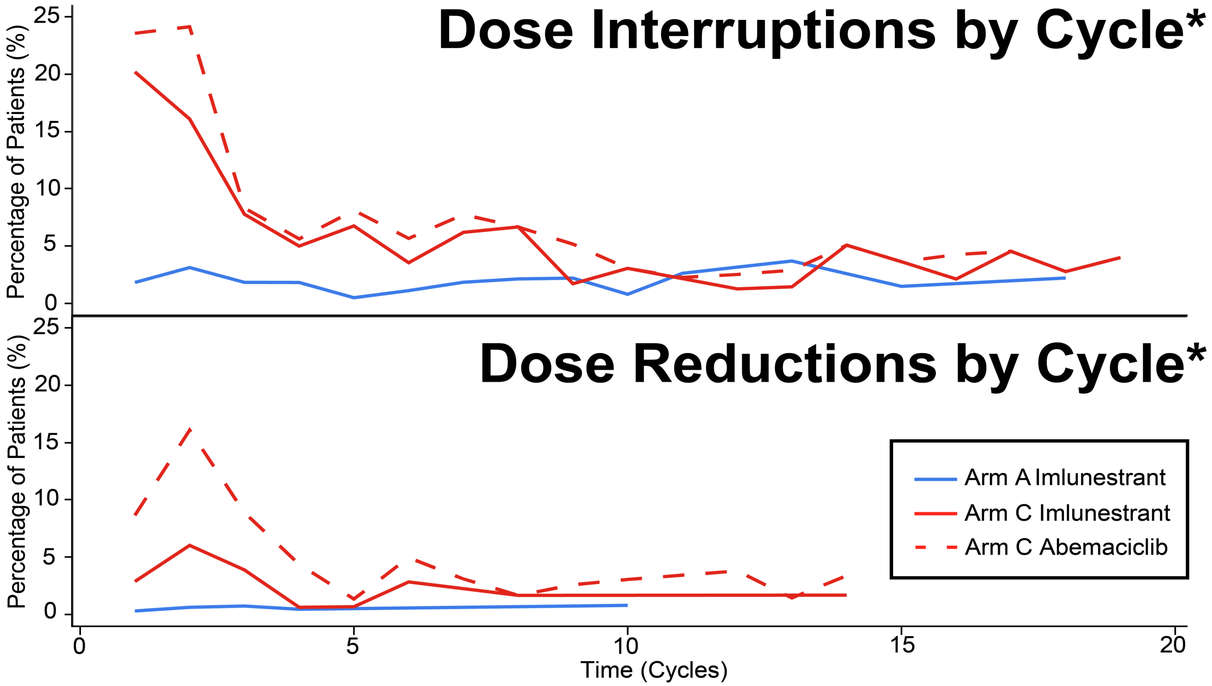
AEs, %	Imlu N=327		Imlu+Abema N=208	
	<65 yrs n=209	≥65 yrs n=118	<65 yrs n=118	≥65 yrs n=90
Patients with ≥1 TEAE	82	83	98	99
Patients with ≥1 G≥3 TEAE	19	14	46	52
Patients with ≥1 SAE[a]	12	9	16	18
Dose interruption/reduction/ discontinuation[a] due to TEAE	11/2/4	9/3/4	49/32/4	63/49/9

In the **imlunestrant+abemaciclib** arm, consistent with previous abemaciclib experience[7], patients aged ≥65 years had:

- higher incidence of fatigue, nausea, anemia, and G≥3 diarrhea
- lower incidence of neutropenia
- higher rates of dose adjustments

* Consolidated terms; [a] Deaths were included as SAEs and discontinuations due to AE.

Dose Discontinuations and Dose Adjustments due to TEAEs



Patients, %	Imlu N=327	SOC ET N=324	Imlu+Abema N=208
Discontinuations	80	87	64
Discontinuations due to PD	73	80	54
Discontinuations due to TEAE[a]	4	1	6[b]
Dose adjustments due to TEAE	10	7	61
Dose interruptions/delays	10	7	55[c]
Dose reductions	2	0	39[d]

- Frequency of discontinuations due to AEs were low. Few dose reductions occurred with **imlunestrant monotherapy**
- In the **imlunestrant+abemaciclib** arm most dose adjustment occurred in the first few months of treatment
- Dose adjustments due to AEs on **abemaciclib** for the **imlunestrant+abemaciclib arm** were similar to prior experiences with **abemaciclib**[3,4]

* SOC ET not shown. No dose adjustment allowed for exemestane per protocol. Dose delays of fulvestrant occurred in 7% pts. [a] Dose discontinuations include fatal AEs; [b] One (0.5%) more pt discontinued only imlunestrant and 6 (2.9%) more pts discontinued only abemaciclib. [c] 92 (44.2%) pts had both drugs interrupted, 20 (9.6%) pts had only abemaciclib interrupted, and 3 (1.4%) pts had only imlunestrant interrupted; [d] 30 (14.4%) pts had both drugs dose reduced, 48 (23.1%) pts had only abemaciclib reduced, and 4 (1.9%) pts had only imlunestrant reduced.

Incidence of TEAEs of Interest

TEAE, Consolidated terms, %	Imlu+Abema N=208	
	Any Grade	G≥3
Neutropenia[a]	48	20
Infection[b]	31	4
ILD[c]	2	0
VTE[d]	3	<1

[a]Includes both neutropenia and neutrophil count decreased; [b]Includes all infections and infestations system organ class; [c]Includes Interstitial lung disease, pneumonitis, pulmonary fibrosis, and pulmonary toxicity; [d]Includes central venous catheterization, deep vein thrombosis, pelvic venous thrombosis, peripheral vein thrombosis, portal vein thrombosis, pulmonary embolism, and superficial vein thrombosis.

TEAE, %	Imlu N=327		SOC ET N=324		Imlu+Abema N=208	
	Any Grade	G≥3	Any Grade	G≥3	Any Grade	G≥3
Bradycardia[a]	2	0	0	0	1	0
Photopsia	0	0	0	0	0	0
Dyslipidemia[b]	7	<1	9	0	8	0
Pts receiving lipid-modifying agents[c]	6		4		2	

[a] Includes bradycardia and sinus bradycardia; [b] Includes dyslipidaemia, hypercholesterolaemia, hyperlipidaemia, hypertriglyceridaemia, and low-density lipoprotein increased; [c] Patients who started lipid-modifying agents while on study treatment.

- Incidence of VTE, ILD, dyslipidemia, bradycardia, and photopsia were relatively low or not observed in both **imlunestrant arms**
- The use of lipid-modifying agents was generally similar between the **imlunestrant** and **SOC ET** arms

O'Shaughnessy, et al.; ASCO 2025

Conclusions

- **Imlunestrant monotherapy** had a favorable safety profile, with generally low grade and manageable side effects
- The incidence and severity of AEs in the **imlunestrant+abemaciclib** arm were consistent with the known safety profile of abemaciclib+fulvestrant and manageable with supportive medications and dose adjustments
- The most frequent TEAEs in both **imlunestrant** arms were generally low grade, reversible, occurred early in treatment, and resulted in few treatment discontinuations
- Incidence of VTE, ILD, dyslipidemia, bradycardia, and photopsia were relatively low or not observed in both **imlunestrant** arms
- In general, the safety profiles of **imlunestrant monotherapy** and **imlunestrant+abemaciclib** were consistent across age groups, with numerical differences in select TEAEs

ABBREVIATIONS

ABC, advanced breast cancer; Abema, abemaciclib; AE, adverse event; AI, aromatase inhibitor; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; CI, confidence interval; CTCAE, Common Terminology Criteria for Adverse Events; ER, estrogen receptor; *ESR1*m, *ESR1* mutation; G, grade; GnRH, gonadotropin-releasing hormone; HER2-, human epidermal growth factor receptor 2-negative; HR, hazard ratio; ILD, interstitial lung disease; IM, intramuscular; Imlu, imlunestrant; med, median; N, number of patients in total safety population; n, number of patients in specified category; PD, progressive disease; PFS, progression-free survival; pts, patients; Q, quartile; QD, once daily; R, randomized; SAE, serious adverse event; SERD, selective estrogen receptor degrader; SOC ET, standard of care endocrine therapy; TEAE, treatment-emergent adverse event; ULN, upper limit of normal; VTE, venous thromboembolism

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ACKNOWLEDGEMENTS

- We would like to thank the support staff who contributed to this study.
- We are very grateful for the time and efforts of the EMBER-3 Steering Committee.
- We thank the 874 clinical trial participants and their families/caregivers from 195 sites in 22 countries for participating in this trial.
- Medical writing support was provided by Preethi Govindarajan of Syneos Health.