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ORIGINAL ARTICLE

Imlunestrant with or without abemaciclib in advanced breast cancer: updated efficacy results from the phase III EMBER-3 trial

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Background: At the primary progression-free survival (PFS) analysis, the phase III EMBER-3 trial in endocrine therapy-pretreated patients with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer (ABC) demonstrated significant PFS benefit with imlunestrant versus standard of care (SOC: fulvestrant or exemestane) in patients with *ESR1* mutations (*ESR1*m) and with imlunestrant—abemaciclib versus imlunestrant in all patients, regardless of *ESR1*m. In this article, we report updated efficacy from a prespecified interim overall survival (OS) analysis.

Patients and methods: Patients with ER-positive, HER2-negative ABC previously treated with aromatase inhibitors ± cyclin-dependent kinase 4 and 6 inhibitors were randomly assigned (1 : 1 : 1) to receive imlunestrant, SOC, and imlunestrant—abemaciclib. Primary endpoints were PFS in imlunestrant versus SOC in patients with *ESR1*m and all patients, and versus imlunestrant—abemaciclib in all concurrently randomized patients. OS was a key secondary endpoint (tested if the corresponding PFS was statistically significant). Due to only two of three PFS endpoints being met, a limited significance level was passed to the OS comparisons. Exploratory endpoints included time to chemotherapy, chemotherapy-free survival, and PFS2.

Results: A total of 874 patients were randomized (imlunestrant, $n = 331$; SOC, $n = 330$; imlunestrant—abemaciclib, $n = 213$). Median follow-up was 28.5 months; 10.1% of patients remained on treatment (data cut-off: 18 August 2025).In patients with *ESR1*m, median OS (mOS) was 34.5 months for imlunestrant versus 23.1 months for SOC [hazard ratio (HR) 0.60, 95% confidence interval (CI) 0.43-0.86, $P = 0.0043$, boundary for significance not reached]. In all patients regardless of *ESR1*m, mOS was not reached with imlunestrant—abemaciclib versus 34.4 months with imlunestrant (HR 0.82, 95% CI 0.59-1.16, $P = 0.2622$). Updated PFS demonstrated sustained benefit. Notably, in all patients regardless of *ESR1*m, the median PFS of imlunestrant—abemaciclib versus imlunestrant was 10.9 versus 5.5 months (HR 0.59, 95% CI 0.47-0.74, nominal $P < 0.0001$). All prespecified exploratory endpoints favored imlunestrant-based regimens. Safety remains consistent with prior reports.

Conclusions: These findings reinforce the clinical benefit of imlunestrant-based regimens as a potential all-oral, chemotherapy-free treatment option for endocrine-pretreated patients with ER-positive, HER2-negative ABC.

Key words: SERD, ER positive, *ESR1* mutation, EMBER-3, updated OS

INTRODUCTION

Estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer represents the most common subtype, accounting for ∼70% of all breast cancer cases.[1] Despite therapeutic advances, ER-positive, HER2-negative advanced breast cancer (ABC)

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remains incurable, and patients treated with first-line aromatase inhibitors (AIs) and cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitors will experience disease progression after a median progression-free survival (PFS) of 25-28 months.[2-4]

Selective ER degraders (SERDs), fulvestrant, with or without CDK4/6 inhibitor, have become foundational in the management of AI-resistant ER-positive, HER2-negative ABC. Imlunestrant is a next-generation oral SERD and pure ER antagonist with demonstrated efficacy in overcoming *ESR1* mutation (*ESR1*m)-driven resistance.[5] Abemaciclib, an oral, selective CDK4/6 inhibitor, has improved survival in both advanced and high-risk early breast cancer settings.[6]

In the phase III EMBER-3 trial, imlunestrant demonstrated statistically significant and clinically meaningful improvement in PFS compared with standard of care (SOC: fulvestrant or exemestane) in patients with an *ESR1*m. The combination of imlunestrant—abemaciclib further improved PFS over imlunestrant alone, regardless of *ESR1*m status.[5] At the primary PFS analysis, median follow-up was 15.7 months, and several secondary endpoints were immature.

Here, we present updated results from the prespecified interim overall survival (OS) analysis with 14 months of additional follow-up on all endpoints, including PFS, OS, and other clinically relevant exploratory endpoints such as time to chemotherapy (TTC), chemotherapy-free survival (CFS), and time to second disease progression (PFS2).

PATIENTS AND METHODS

Trial oversight

EMBER-3 (NCT04975308) was funded by the sponsor, Eli Lilly and Company, and designed together with the global steering committee. The trial was conducted in accordance with the principles of the Declaration of Helsinki, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice guidelines, and applicable laws and regulations. The study protocol and amendments were approved by the relevant ethical and institutional review boards. All participants provided written informed consent.

Trial design and patients

EMBER-3 is a global, open-label, randomized phase III trial that enrolled patients with ER-positive, HER2-negative ABC with prior exposure to AI with or without a CDK4/6 inhibitor. The study design has been previously described and is provided in the Supplementary Methods, available at https://doi.org/10.1016/j.annonc.2025.11.018.[5]

Eligible patients included adults with locally confirmed disease progression or recurrence during or within 12 months of prior AI therapy, either alone or with a CDK4/6 inhibitor. No prior chemotherapy for ABC was permitted.

Patients were randomly assigned in a 1 : 1 : 1 ratio to receive either imlunestrant, SOC (fulvestrant or exemestane), or imlunestrant—abemaciclib. Randomization was stratified by previous CDK4/6 inhibitor treatment (yes versus no), visceral metastases (yes versus no), and geographic region (East Asia versus North America or Western Europe versus other). The trial was initially designed as a two-arm study (imlunestrant versus SOC) and was amended early in enrollment to include an imlunestrant—abemaciclib arm.

Endpoints

The primary endpoints were investigator-assessed PFS of imlunestrant compared with SOC among patients with an *ESR1*m and among all patients, and of imlunestrant—abemaciclib compared with imlunestrant among all concurrently randomized patients. OS was a key secondary endpoint.

Prespecified exploratory endpoints included TTC, CFS, and PFS2. TTC was defined as the time from randomization to the start of the first chemotherapy (censoring patients who died before initiation of chemotherapy). CFS was defined as the time from randomization to initiation of first chemotherapy or death, whichever occurred first. PFS2 was defined as the time from randomization to progression on the next line of therapy or death from any cause.

Statistical analysis

A graphical testing procedure evaluated OS for statistical significance only if the corresponding PFS was statistically significant.[5] Due to only two of three PFS endpoints being met at the primary analysis, a minimal fraction of the significance level was passed to the OS comparison of imlunestrant versus SOC in patients with an *ESR1*m (with a two-sided significance level of 5.5×10^{-6}), and of imlunestrant—abemaciclib versus imlunestrant in all concurrently randomized patients (with a two-sided significance level of 1.6×10^{-6}).

This prespecified interim OS analysis (data cut-off: 18 August 2025) was triggered after ~255 OS events had occurred among patients in the imlunestrant and SOC arm. The *P* value boundary for each OS endpoint at the interim was determined by the O'Brien—Fleming type spending function. PFS and OS were estimated using the Kaplan—Meier method and tested with a stratified log-rank test, stratified by randomization factors (region was excluded for analyses in patients with an *ESR1*m). Hazard ratio (HR) and 95% confidence interval (CI) were estimated using the stratified Cox regression model. All reported *P* values are two-sided. Subgroup analyses were carried out for clinically relevant factors and are presented as forest plots. The analyses on exploratory endpoints (TTC, CFS, PFS2) and subgroup analyses were unstratified.

RESULTS

Patients

Overall, 874 patients were randomly assigned to imlunestrant ($n = 331$), SOC ($n = 330$), or imlunestrant—abemaciclib ($n = 213$) arms between October 2021 and

November 2023. At the data cut-off of this updated analysis (18 August 2025), the median follow-up was 28.5 months across all arms.

The majority of patients had discontinued study treatment by the data cut-off, with 10% in the imlunestrant arm, 5% in the SOC arm, and 18% in the imlunestrant—abemaciclib arm remaining on therapy. The most frequent reason for treatment discontinuation was progressive disease, accounting for 81% for the imlunestrant arm, 85% for the SOC arm, and 67% for the imlunestrant—abemaciclib arm. Other reasons for discontinuation included adverse events (AEs), death (2%-3% across three arms), and patient withdrawal (Supplementary Figure S1, available at https://doi.org/10.1016/j.annonc.2025.11.018). Baseline demographics and clinical characteristics were well balanced across treatment arms (Supplementary Table S1, available at https://doi.org/10.1016/j.annonc.2025.11.018).

Overall survival

With a median follow-up of 29.5 months, 128 OS events occurred among 256 patients with *ESR1*m [imlunestrant, $n = 57$ (41%); SOC, $n = 71$ (60%)]. The HR for death was 0.60 (95% CI 0.43-0.86, $P = 0.0043$). The threshold for significance was not achieved with an overall two-sided alpha allocation of 5.5×10^{-6}, and the P value boundary at this interim was 4×10^{-7} with a corresponding HR boundary of 0.41. Median OS was 34.5 months in the imlunestrant arm and 23.1 months in the SOC arm, with an absolute difference of 11.4 months (Figure 1C). The 24-month OS rates were 63.8% for the imlunestrant arm and 48.9% for the SOC arm. Consistent OS effect sizes were observed across prespecified subgroups (Figure 2), including patients who had previously received treatment with a CDK4/6 inhibitor (HR 0.67, 95% CI 0.44-1.02), with a numerically greater effect observed in patients without a phosphoinositide 3-kinase (PI3K) pathway alteration (HR 0.41, 95% CI 0.25-0.69) compared with those with a PI3K pathway alteration (HR 0.87, 95% CI 0.53-1.43).

In all patients, 263 OS events had occurred among 661 patients [imlunestrant arm, $n = 122$ (37%); SOC arm, $n = 141$ (43%)]. The HR for death was 0.86 (95% CI 0.68-1.10, nominal $P = 0.2343$); median OS was 37.1 months in the imlunestrant arm and 32.3 months in the SOC arm (Supplementary Figure S2C, available at https://doi.org/10.1016/j.annonc.2025.11.018). The 24-month OS rates were 69.2% for imlunestrant and 62.5% for SOC. Exploratory OS analyses in patients without *ESR1*m (33% maturity) are shown in Supplementary Figure S3A, available at https://doi.org/10.1016/j.annonc.2025.11.018.

With a median follow-up of 27 months, 140 OS events had occurred among all 426 patients in the combination comparison [imlunestrant—abemaciclib, $n = 64$ (30%); imlunestrant, $n = 76$ (36%)]. The HR for death was 0.82 (95% CI 0.59-1.16, $P = 0.2622$).

Median OS was not reached in the imlunestrant—abemaciclib arm and was 34.4 months in the imlunestrant arm (Figure 3C). Exploratory OS analyses in patients with and without *ESR1*m (at 35% and 31% maturity, respectively) are shown in Supplementary Figure S4A and B, available at https://doi.org/10.1016/j.annonc.2025.11.018. In the exploratory analysis comparing imlunestrant—abemaciclib with SOC, the HR for death was 0.80 (95% CI 0.57-1.12) (Supplementary Figure S5C, available at https://doi.org/10.1016/j.annonc.2025.11.018).

Updated progression-free survival

The updated PFS of imlunestrant versus SOC was sustained in patients with an *ESR1*m (HR 0.62, 95% CI 0.47-0.82, nominal $P = 0.0007$; median PFS 5.5 months versus 3.8 months) (Figure 1A). The PFS benefit was consistent across subgroups and with prior reports. PFS in all patients is shown in Supplementary Figure S2A, available at https://doi.org/10.1016/j.annonc.2025.11.018. Exploratory analysis of PFS in patients without *ESR1*m is shown in Supplementary Figure S3B, available at https://doi.org/10.1016/j.annonc.2025.11.018 (interaction test P value between *ESR1*m status and treatment was 0.119).

In all patients, PFS was significantly improved with the addition of abemaciclib to imlunestrant (HR 0.59, 95% CI 0.47-0.74, nominal $P < 0.0001$) with a continued separation of the curves. Median PFS was 10.9 months in the imlunestrant—abemaciclib arm versus 5.5 months in the imlunestrant arm (absolute difference 5.4 months; Figure 3A). PFS benefit was consistent across subgroups and with prior report, including patients who had previously received treatment with a CDK4/6 inhibitor (Figure 3B) and regardless of *ESR1*m (Figure 4A and B) or PI3K pathway mutation status (Figure 5A and B).

In subgroup analyses of patients previously treated with a CDK4/6 inhibitor (Supplementary Figure S6A, available at https://doi.org/10.1016/j.annonc.2025.11.018), imlunestrant—abemaciclib demonstrated a consistent benefit over imlunestrant alone, including in patients with high-risk disease (visceral, liver, multiple metastases) and regardless of biomarker status (Supplementary Figure S6B-F, available at https://doi.org/10.1016/j.annonc.2025.11.018), prior duration of CDK4/6 inhibitor, or choice of CDK4/6 inhibitor therapy.

Similarly, in the exploratory analysis of imlunestrant—abemaciclib compared with SOC, consistent benefit was seen in PFS, TTC, CFS, and PFS2, along with a favorable trend in OS (Supplementary Figure S5, available at https://doi.org/10.1016/j.annonc.2025.11.018).

Updated objective response rate

In the updated secondary analysis of overall response rate among patients with measurable disease, imlunestrant demonstrated a higher response rate compared with SOC, particularly in patients with *ESR1*m (Supplementary Table S2, available at https://doi.org/10.1016/j.annonc.2025.11.018). Furthermore, the addition of abemaciclib to imlunestrant resulted in a more than twofold increase in response rate versus imlunestrant (Supplementary

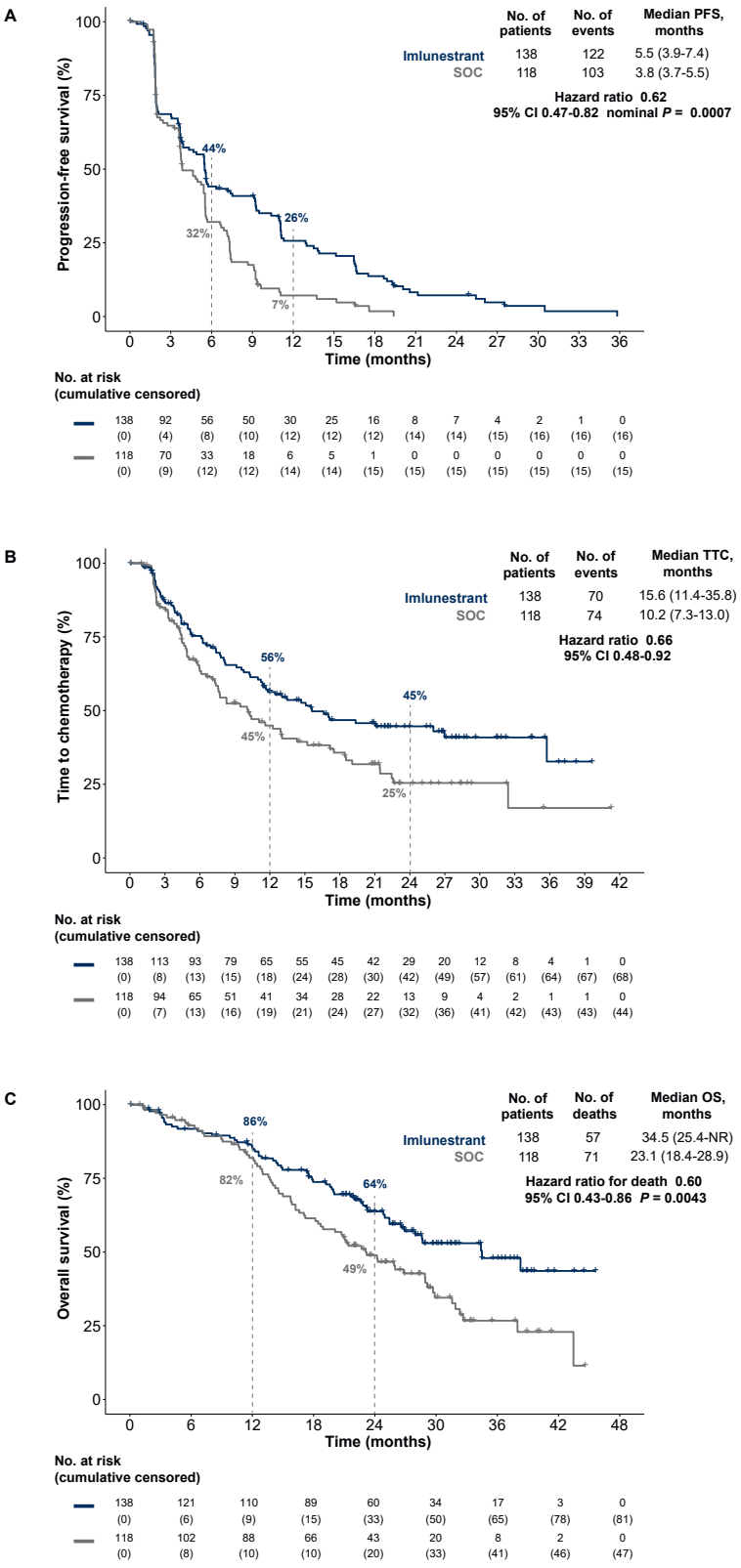

Figure 1. Efficacy for imlunestrant versus SOC in patients with an *ESR1* mutation. (A) Investigator-assessed progression-free survival, (B) time to chemotherapy, and (C) overall survival.
CI, confidence interval; NR, not reached; SOC, standard of care.

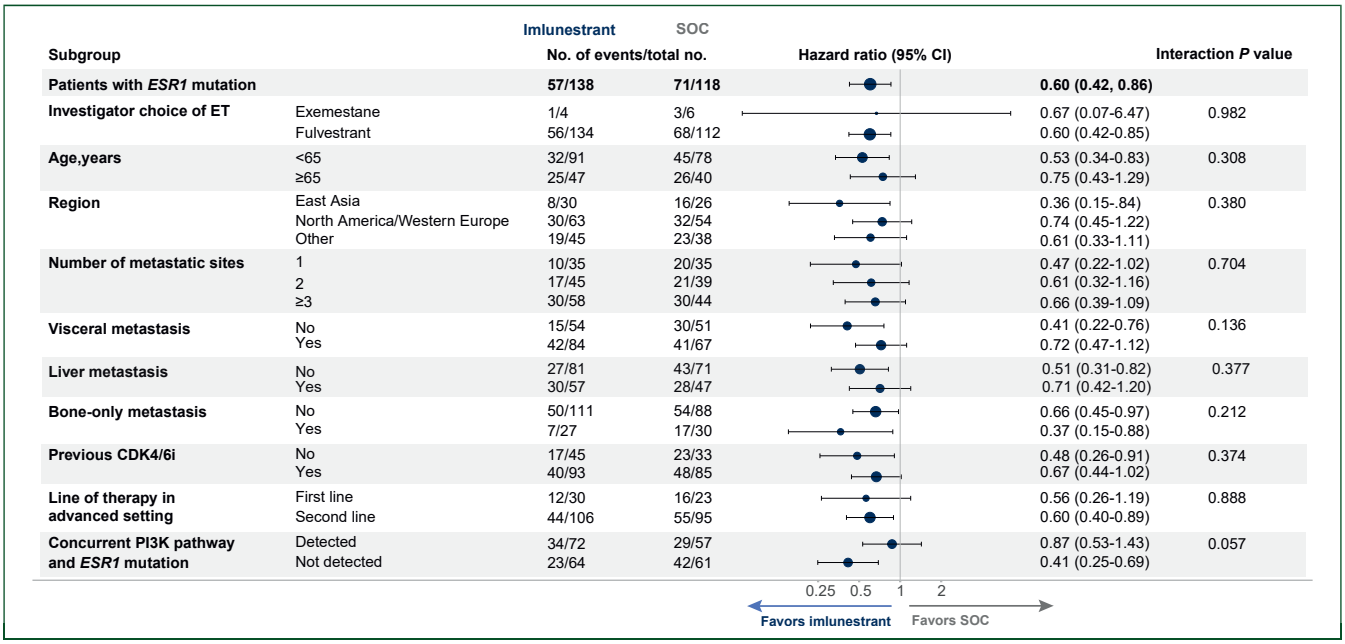

Figure 2. Subgroup analysis of overall survival for imlunestrant versus SOC in patients with an *ESR1* mutation. Bold values indicate overall results.
CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; CI, confidence interval; ET, endocrine therapy; PI3K, phosphoinositide 3-kinase; SOC, standard of care.

Table S3, available at https://doi.org/10.1016/j.annonc.2025.11.018).

Subsequent therapy

Most patients who entered the post-treatment discontinuation follow-up received additional therapies after progression (Table 1, Supplementary Table S4, available at https://doi.org/10.1016/j.annonc.2025.11.018). In total, 37% of patients in the imlunestrant arm, 35% in the SOC arm, and 39% in the imlunestrant—abemaciclib arm received chemotherapy as their first anticancer therapy post-treatment discontinuation.

Imlunestrant delayed the TTC in patients with an *ESR1*m. Median TTC was 15.6 months in the imlunestrant arm and 10.2 months in the SOC arm (HR 0.66, 95% CI 0.48-0.92) (Figure 1B). Median CFS in patients with *ESR1*m was 12.5 months with the imlunestrant arm and 7.7 months with the SOC arm (HR 0.65, 95% CI 0.49-0.86) (Supplementary Figure S7A, available at https://doi.org/10.1016/j.annonc.2025.11.018). PFS2 in patients with *ESR1*m was also extended, with a median of 19.2 months in the imlunestrant arm and 13.5 months in the SOC arm (HR 0.71, 95% CI 0.53-0.95) (Supplementary Figure S7B, available at https://doi.org/10.1016/j.annonc.2025.11.018). In all patients, the addition of abemaciclib to imlunestrant numerically extended the TTC (HR 0.78, 95% CI 0.59-1.03) versus the imlunestrant arm. Median TTC was 27.8 months in the imlunestrant—abemaciclib arm versus 15.5 months in the imlunestrant arm (Supplementary Figure S8A, available at https://doi.org/10.1016/j.annonc.2025.11.018). Median CFS was 19.6 months in the combination arm versus 12.6 months in the imlunestrant arm (HR 0.80, 95% CI 0.63-1.03) (Supplementary Figure S8B, available at https://doi.org/10.1016/j.annonc.2025.11.018). PFS2 was numerically extended by the combination (HR 0.79, 95% CI 0.61-1.02). Median PFS2 was 22.6 months in the imlunestrant—abemaciclib arm and 18.5 months in the imlunestrant arm (Supplementary Figure S8C, available at https://doi.org/10.1016/j.annonc.2025.11.018).

Safety

With most patients off study treatment, updated safety outcomes are reported in Supplementary Table S5, available at https://doi.org/10.1016/j.annonc.2025.11.018. The safety profile remained consistent with the known characteristics of imlunestrant and abemaciclib. The incidence of grade $\geq$3 AEs, treatment discontinuations, and dose reductions due to AEs was similar to the primary analysis, and no new safety signals were detected. Most grade $\geq$3 events in the combination were reversible or manageable by dose modification and uncommonly led to treatment discontinuation. The most common AEs for imlunestrant (fatigue, diarrhea, and nausea) and the imlunestrant—abemaciclib combination (diarrhea, nausea, and neutropenia) were consistent with earlier analyses and remained predominantly low grade. No cases of photopsia were observed.

DISCUSSION

In the EMBER-3 trial, in AI $\pm$ CDK4/6 inhibitor-resistant patients with ER-positive, HER2-negative ABC, a clinically meaningful and statistically significant prolongation of PFS was seen with imlunestrant over SOC in patients with an *ESR1*m, as well as with imlunestrant—abemaciclib over imlunestrant in all patients, regardless of *ESR1*m status.

OS was a key secondary endpoint, tested only if the corresponding PFS endpoint achieved statistical significance. Notably, because only two of the three PFS

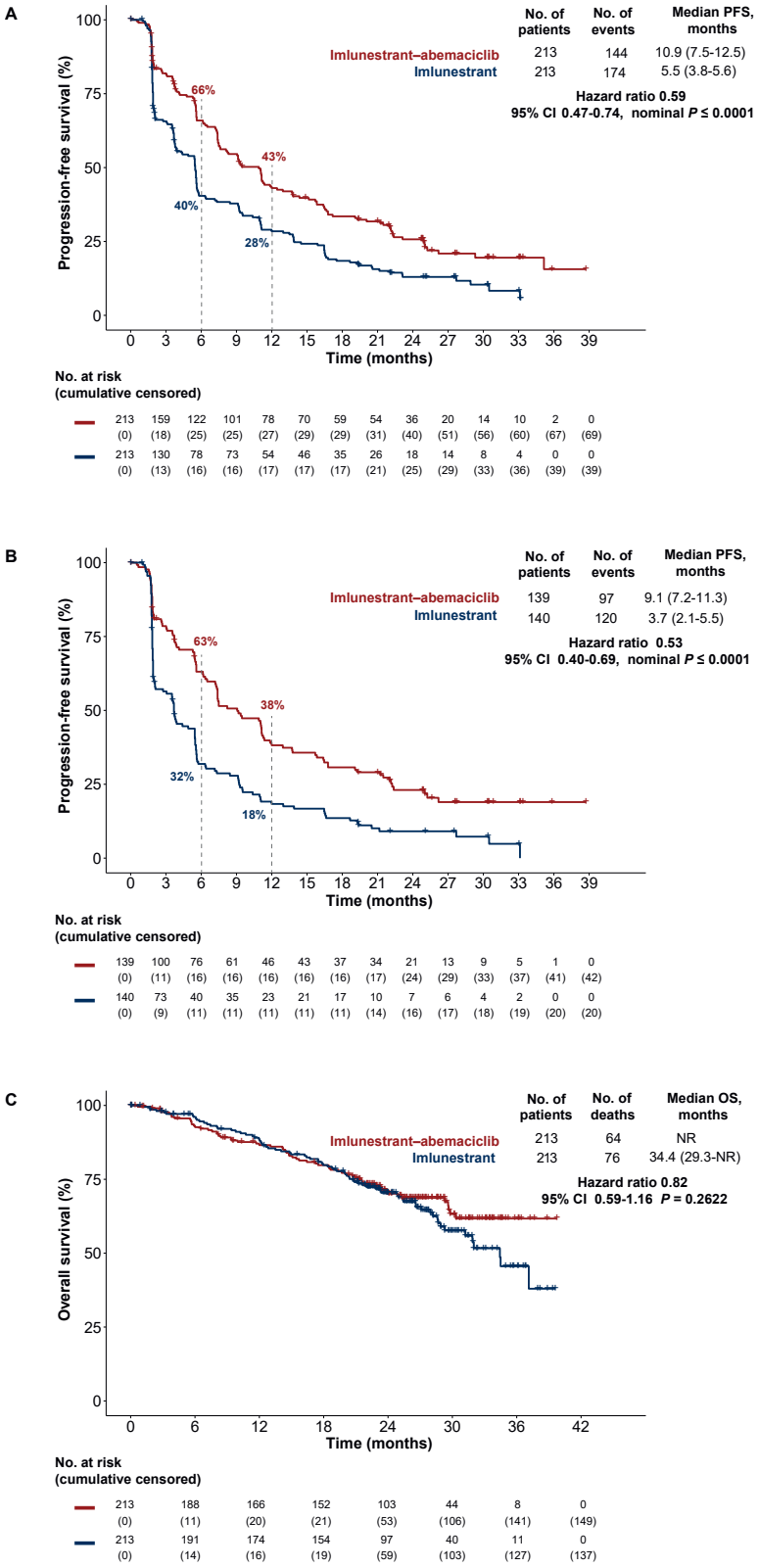

Figure 3. Efficacy for imlunestrant–abemaciclib versus imlunestrant alone in all patients. (A) Investigator-assessed progression-free survival, (B) investigator-assessed progression-free survival in patients previously treated with a CDK4/6i, and (C) overall survival.
CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; CI, confidence interval; NR, not reached.

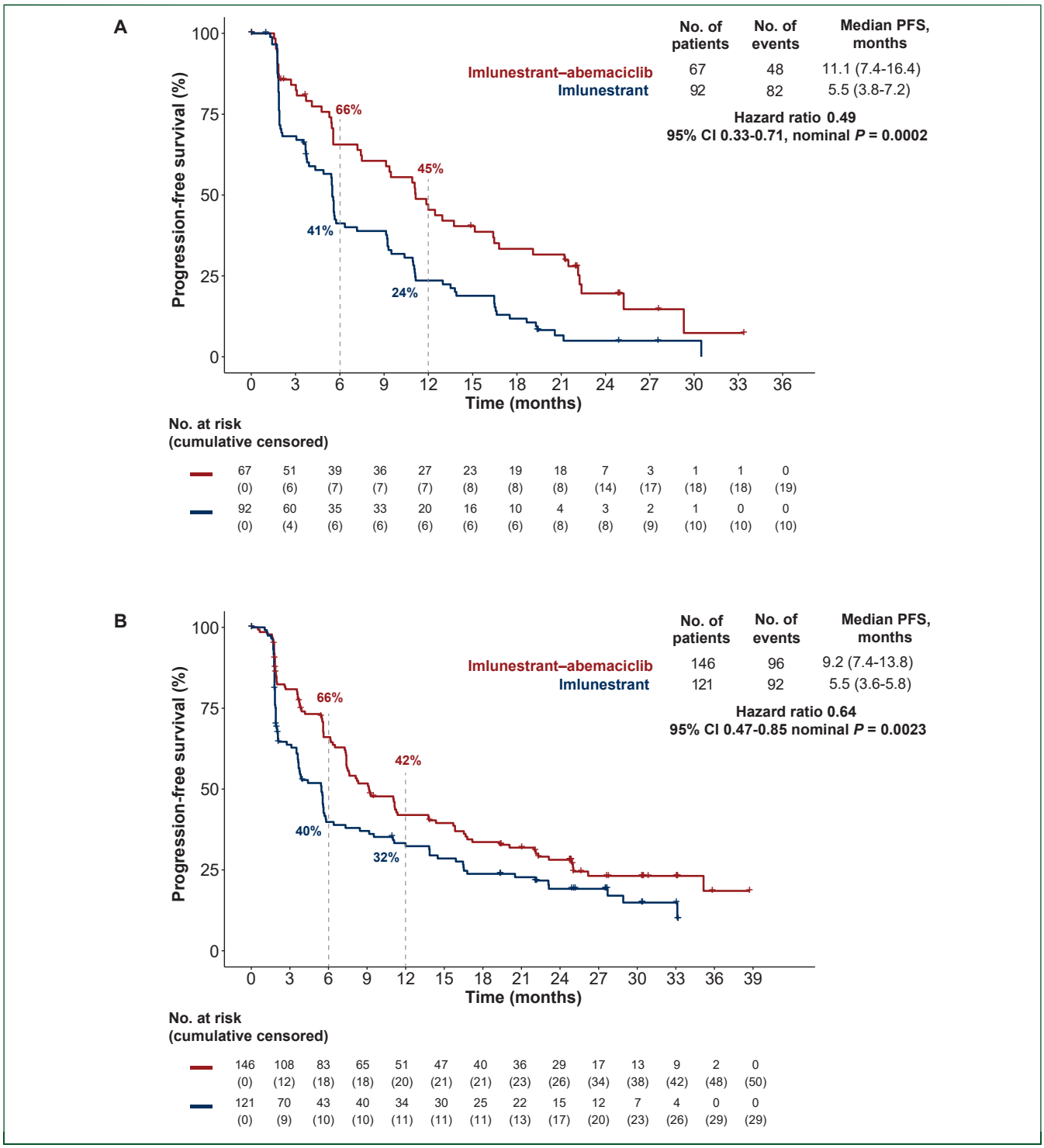

Figure 4. Investigator-assessed progression-free survival for imlunestrant–abemaciclib versus imlunestrant alone by *ESR1* mutation status. (A) With *ESR1* mutation and (B) without *ESR1* mutation.
CI, confidence interval.

endpoints were met, a limited significance level was passed to the OS analyses.

At this prespecified interim OS analysis, with a median follow-up of 29.5 months, median OS was numerically longer with imlunestrant versus SOC (difference of 11.4 months; HR 0.60, 95% CI 0.43-0.86, $P = 0.0043$) in patients with an *ESR1*m. Although the prespecified threshold for formal statistical significance (interim P value boundary is 4×10^{-7}) was not met, these results represent a clinically meaningful difference in OS. Additionally, while the OS analysis for the combination remains immature, late separation of the survival curves was observed at ~24 months with imlunestrant–abemaciclib over imlunestrant in all patients (HR 0.82, 95% CI 0.59-1.16, $P = 0.2622$).

The encouraging OS results were further supported, and potentially explained, by consistent improvements in

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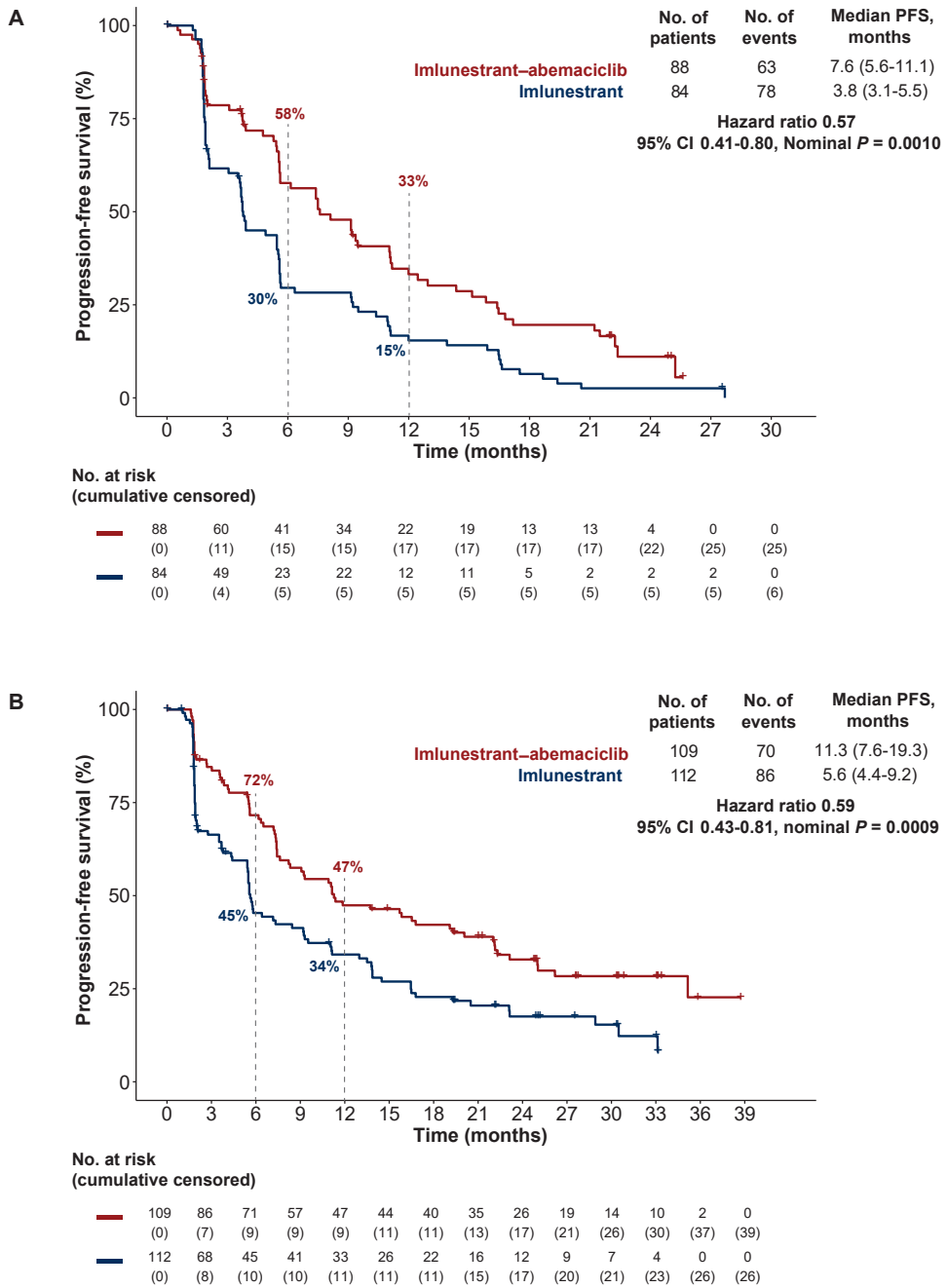

Figure 5. Investigator-assessed progression-free survival for imlunestrant–abemaciclib versus imlunestrant alone by PI3K pathway mutation. (A) With PI3K pathway mutation and (B) without PI3K pathway mutation.
CI, confidence interval; PI3K, phosphoinositide 3-kinase.

exploratory endpoints, including TTC, CFS, and PFS2, on top of a sustained improvement in PFS. Collectively, these findings suggest that imlunestrant not only delays disease progression through the subsequent line of therapy but also postpones the need for chemotherapy. Given the historically poor outcomes of endocrine monotherapy following CDK4/6 inhibitor-containing therapy,[7-9] these observations are important and emphasize the clinical benefits of imlunestrant in this population. This delay in chemotherapy initiation is particularly relevant in the ABC setting, where initiation of chemotherapy often negatively impacts quality of life.[10] Notably, at a similar level of OS maturity (~50% event rate) in the EMERALD trial, elacestrant did not demonstrate a similar trend in improved survival versus SOC endocrine therapy (ET) (median OS 24.2 versus 23.5 months, HR 0.90, 95% CI 0.63-1.30) in a CDK4/6 inhibitor-pretreated population.[11] The reasons for the comparatively more favorable OS observed with imlunestrant may stem from differences in the drug, including complete ER antagonism with imlunestrant,[12,13] along with differences in the enrolled populations and trial designs.[9,11]

Given the relatively short PFS follow-up for the imlunestrant combination at the prespecified primary analysis, the additional follow-up here was important to confirm the

Table 1. First subsequent post-discontinuation therapy

n (%)	Imlunestrant −abemaciclib *n* = 213	Imlunestrant *n* = 331	SOC *n* = 330
Discontinued	174	299	313
Any therapya	131 (75)	227 (76)	248 (79)
Endocrine therapy	58 (33)	105 (35)	117 (37)
Chemotherapy	68 (39)	111 (37)	111 (35)
Targeted agent therapyb	36 (21)	84 (28)	89 (28)
CDK4/6 inhibitor	12 (7)	47 (16)	56 (18)
PI3K/AKT/mTOR inhibitorc	25 (14)	38 (13)	34 (11)
ADC	3 (2)	6 (2)	9 (3)
Immunotherapy	1 (1)	2 (1)	0
Otherd	15 (9)	19 (6)	29 (9)

Percentages were calculated based on the number of patients who discontinued.
ADC, antibody–drug conjugate; AE, adverse event; AKT, protein kinase B; CDK4/6i, cyclin-dependent kinase 4 and 6 inhibitor; mTOR, mammalian target of rapamycin; PI3K, phosphoinositide 3-kinase; SOC, standard of care.
[a]180 (22.9%) patients did not receive subsequent therapy, for reasons including (i) death (9.8%), (ii) withdrawal from study (8.4%), (iii) lost to follow-up (1.5%), and (iv) still on follow-up (3.2%). Deaths were balanced across arms, 7.0% due to study disease and 2.8% due to AE.
[b]Some patients were counted more than once due to receiving combinations of listed agents.
[c]PI3K inhibitors given after discontinuation included alpelisib, inavolisib, and LOXO-783.
[d]Other anticancer agents given in >1% include bevacizumab.

benefit previously observed. With this additional follow-up, the median PFS of imlunestrant–abemaciclib was increased to 10.9 months. To our knowledge, the observed median PFS of 10.9 months in all patients—9.1 months in patients previously treated with a CDK4/6 inhibitor and 11.1 months in patients with an *ESR1*m previously treated with a CDK4/6 inhibitor—is among the longest reported for ER-positive, HER2-negative ABC following prior ET plus a CDK4/6 inhibitor. PFS benefit was also consistent across prespecified subgroups, including patients with prior CDK4/6 inhibitor exposure and regardless of *ESR1* or PI3K pathway mutational status. Taken together, these findings—along with improvements in objective response rates and exploratory endpoints such as TTC, CFS, and PFS2—support the clinical value of dual ER and CDK4/6 inhibition in this context.

The majority of patients (65%) in the imlunestrant–abemaciclib arm had previously received a CDK4/6 inhibitor. In a subgroup analysis of patients previously treated with CDK4/6 inhibitors, the combination demonstrated consistent benefit over imlunestrant monotherapy, regardless of clinico-genomic factors such as duration of prior CDK4/6 inhibitor treatment or choice of the CDK4/6 agent. However, <10% of patients had prior exposure to abemaciclib, limiting the interpretation of results in this subgroup. Interestingly, the numerically greatest effect was observed in patients with concurrent *ESR1*m and PI3K pathway mutation (HR 0.29, 95% CI 0.15-0.53, median PFS 16.4 versus 3.8 months; Supplementary Figure S5F, available at https://doi.org/10.1016/j.annonc.2025.11.018), though numbers in this subgroup were again limited.

Consistent with prior reports for available therapies, PI3K pathway mutation status had a clear prognostic impact in this trial. A numerically greater OS effect was observed with imlunestrant versus SOC in patients without a PI3K pathway alteration (HR 0.41, 95% CI 0.25-0.69) compared with those harboring a PI3K pathway alteration (HR 0.87, 95% CI 0.53-1.43). While the combination demonstrated benefit irrespective of PI3K pathway status, the absolute median PFS with imlunestrant plus abemaciclib was longer in patients without a PI3K pathway alteration (11.3 months, 95% CI 7.6-19.3 months; HR 0.59, 95% CI 0.43-0.81) than in those with an alteration (7.6 months, 95% CI 5.6-11.1 months; HR 0.57, 95% CI 0.41-0.80). Given the known outcomes (median PFS 5.5-8 months[14,15]) of available PI3K pathway inhibitors in the second-line (predominantly CDK4/6 inhibitor-pretreated) setting, these findings underscore the poor prognosis associated with PI3K pathway alterations. Further, in light of the notable PFS and OS improvements observed with inavolisib plus palbociclib–fulvestrant[16] in the first-line (CDK4/6 inhibitor naive, endocrine resistant) setting, earlier intervention with triplet strategies may therefore be warranted to improve outcomes in patients harboring PI3K pathway alterations.

The recently reported VIKTORIA-1 trial[17] evaluated the pan-PI3K/mTORC1/2 inhibitor, gedatolisib (administered intravenously, 3 weeks on and 1 week off), as a triplet with palbociclib–fulvestrant or as a doublet with fulvestrant compared with fulvestrant alone. The triplet and doublet yielded median PFS of 9.3 months and 7.4 months, respectively, compared with 2.0 months with fulvestrant alone, in the *PIK3CA*-wild-type population, and results from the *PIK3CA*-mutant population are awaited. Reported toxicities included stomatitis, nausea, vomiting, and rash, consistent with broader pathway inhibition. Differences in route of administration and dosing schedules of the various components of this combination regimen, together with the toxicity profile and pathway selectivity, will be relevant considerations when comparing such regimens with oral targeted combinations.

At the time of the previous report, EMBER-3 was the first phase III trial of an oral SERD in combination with a CDK4/6 inhibitor. Since then, the SERENA-6 trial evaluated a switch strategy at the time of molecular (*ESR1*m) progression—in the absence of radiologic progression—in patients with ER-positive, HER2-negative ABC who had received first-line AI plus CDK4/6 inhibition for at least 6 months. Switching to camizestrant with continued CDK4/6 inhibition significantly prolonged PFS (16.0 months) compared with continued AI + CDK4/6 inhibition (9.2 months), an absolute improvement of 6.8 months; OS data remain immature.[18] The trial did not include a comparator arm evaluating therapy switch (to camizestrant or SOC) at the time of radiologic progression and patients were not crossed over to camizestrant at radiologic progression. Of note, median time to *ESR1*m detection was ∼23 months,[18] suggesting that *ESR1*-mutant resistance typically emerges late during first-line treatment (historic median PFS for AI + CDK4/6

inhibition is ~25-28 months).[2-4] Long-term follow-up, together with the practical reliance on serial circulating tumor DNA monitoring, will be important considerations in determining the clinical utility of this approach,[19,20] particularly as additional oral SERD—combination data emerge in ET-pretreated ABC.[21-23]

Recently presented data from the evERA trial further support the evolving role of oral SERDs in this setting, showing median PFS improvements with giredestrant + everolimus versus SOC ET (predominantly AI) + everolimus in both the intention-to-treat (8.77 versus 5.49 months) and *ESR1*m populations (9.99 versus 5.45 months). Reported toxicities included stomatitis, diarrhea, and anemia, consistent with the known profiles of everolimus and giredestrant.

Collectively, these findings highlight that, for patients previously treated with CDK4/6 inhibition, multiple oral SERD-based options and other novel targeted therapeutics are now emerging. Careful consideration of key patient factors—including prior therapies, disease biology and burden, baseline comorbidities, toxicity differences, and patient preference—will be essential to guide optimal therapy selection and sequencing in this setting.

Importantly, no new safety signals were identified with longer follow-up of EMBER-3 and the safety profile of both monotherapy and the combination remained consistent with previous findings. Notably, lower frequencies of bradycardia, dyslipidemia, and photopsia were observed than with other new SERDs.[11,18,24] As expected, the incidence of treatment-related grade ≥3 AEs was highest with imlunestrant plus abemaciclib (43%) versus imlunestrant (5%) or SOC (2%), leading to treatment discontinuation in 5%, 2%, and 0% of patients, respectively (Supplementary Table S5, available at https://doi.org/10.1016/j.annonc.2025.11.018).

Limitations of these EMBER-3 analyses should be acknowledged. These are interim OS data, and it will be important and clinically meaningful to further characterize the OS and other exploratory efficacy endpoints. Fulvestrant—abemaciclib was not considered standard therapy for CDK4/6 inhibitor-pretreated patients at the time of EMBER-3 study design and enrollment (2021-2023). Subsequent data from the postMONARCH trial, conducted in a CDK4/6 inhibitor-pretreated population and reported in 2024, have since supported its use in this setting.[6] Thus, another limitation is the lack of a direct comparison with fulvestrant—abemaciclib. An indirect treatment comparison of patient-level data from EMBER-3, MONARCH 2, and postMONARCH was conducted to contextualize outcomes. While limitations of such analyses are acknowledged, imlunestrant—abemaciclib showed numerical PFS benefit compared with fulvestrant—abemaciclib (HR ranged from 0.77 to 0.83 across different methods).[25]

Looking ahead, with multiple adjuvant trials ongoing,[26-30] oral SERDs may ultimately have their greatest impact in early breast cancer by reducing recurrence risk in intermediate- and high-risk populations. With adjuvant CDK4/6 inhibition established as SOC since 2021—and the demonstrated OS benefit of abemaciclib in patients with high-risk disease—it will be essential to understand the role of oral SERDs against the backdrop of CDK4/6 inhibition and specifically their incremental benefit within a CDK4/6 inhibitor-treated landscape.

Conclusion

In this updated analysis of the phase III EMBER-3 trial, imlunestrant continues to demonstrate clinically meaningful improvements in PFS, along with a numerically longer survival over SOC ET in patients with ER-positive, HER2-negative ABC with an *ESR1*m. The addition of abemaciclib to imlunestrant expands the benefit to patients regardless of *ESR1*m status, achieving one of the longest PFS durations reported among phase III randomized studies in the ET-pretreated setting.

Importantly, the observed delay in chemotherapy initiation reinforces the value of dual inhibition with an oral SERD and a CDK4/6 inhibitor, delivered in an all-oral regimen with a favorable safety profile. These findings position imlunestrant, both as monotherapy and in combination with abemaciclib, as a promising, chemotherapy-free, all-oral treatment option for patients with limited alternatives.

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DATA SHARING

Eli Lilly provides access to all individual participant data collected during the trial, after anonymization, with the exception of pharmacokinetic or genetic data. Data are available to request 6 months after the indication studied has been approved in the USA and European Union (EU) and after primary publication acceptance, whichever is later. No expiration date of data requests is currently set once data are made available. Access is provided after a proposal has been approved by an independent review committee identified for this purpose and after receipt of a signed data sharing agreement. Data and documents, including the study protocol, statistical analysis plan, clinical study report, and blank or annotated case report forms, will be provided in a secure data sharing environment. For details on submitting a request, see the instructions provided at www.vivli.org.

REFERENCES

1. Howlader N, Altekruse SF, Li CI, et al. US incidence of breast cancer subtypes defined by joint hormone receptor and HER2 status. *J Natl Cancer Inst*. 2014;106(5).
2. Johnston S, Martin M, Di Leo A, et al. MONARCH 3 final PFS: a randomized study of abemaciclib as initial therapy for advanced breast cancer. *NPJ Breast Cancer*. 2019;5:5.
3. Hortobagyi GN, Stemmer SM, Burris HA, et al. Updated results from MONALEESA-2, a phase III trial of first-line ribociclib plus letrozole versus placebo plus letrozole in hormone receptor-positive, HER2-negative advanced breast cancer. *Ann Oncol*. 2019;30(11):1842.
4. Finn RS, Martin M, Rugo HS, et al. Palbociclib and letrozole in advanced breast cancer. *N Engl J Med*. 2016;375(20):1925-1936.
5. Jhaveri KL, Neven P, Casalnuovo ML, et al. Imlunestrant with or without abemaciclib in advanced breast cancer. *N Engl J Med*. 2025;392(12):1189-1202.
6. Kalinsky K, Bianchini G, Hamilton E, et al. Abemaciclib plus fulvestrant in advanced breast cancer after progression on CDK4/6 inhibition: results from the phase III postMONARCH trial. *J Clin Oncol*. 2025;43(9):1101-1112.
7. Kalinsky K, Accordino MK, Chiuzan C, et al. Randomized phase II trial of endocrine therapy with or without ribociclib after progression on cyclin-dependent kinase 4/6 inhibition in hormone receptor—positive, human epidermal growth factor receptor 2—negative metastatic breast cancer: MAINTAIN trial. *J Clin Oncol*. 2023;41(24):4004-4013.

8. Llombart-Cussac A, Harper-Wynne C, Perello A, et al. Second-line endocrine therapy with or without palbociclib rechallenge in patients with hormone receptor-positive/human epidermal growth factor receptor 2-negative advanced breast cancer: PALMIRA trial. *J Clin Oncol*. 2025;43(18):2084-2093.
9. Bidard FC, Kaklamani VG, Neven P, et al. Elacestrant (oral selective estrogen receptor degrader) versus standard endocrine therapy for estrogen receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer: results from the randomized phase III EMERALD trial. *J Clin Oncol*. 2022;40(28):3246-3256.
10. Brufsky AM. Delaying chemotherapy in the treatment of hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer. *Clin Med Insights Oncol*. 2015;9:137-147.
11. Shah M, Lingam H, Gao X, et al. US Food and Drug Administration approval summary: elacestrant for estrogen receptor-positive, human epidermal growth factor receptor 2-negative, ESR1-mutated advanced or metastatic breast cancer. *J Clin Oncol*. 2024;42(10):1193-1201.
12. Bhagwat SV, Mur C, Vandekopple M, et al. Imlunestrant is an oral, brain-penetrant selective estrogen receptor degrader with potent antitumor activity in ESR1 wild-type and mutant breast cancer. *Cancer Res*. 2025;85(4):777-790.
13. Wardell SE, Nelson ER, Chao CA, et al. Evaluation of the pharmacological activities of RAD1901, a selective estrogen receptor degrader. *Endocr Relat Cancer*. 2015;22(5):713-724.
14. Turner NC, Oliveira M, Howell SJ, et al. Capivasertib in hormone receptor-positive advanced breast cancer. *N Engl J Med*. 2023;388(22):2058-2070.
15. Chia S, Neven P, Ciruelos EM, et al. Alpelisib + endocrine therapy in patients with *PIK3CA*-mutated, hormone receptor—positive, human epidermal growth factor receptor 2—negative, advanced breast cancer: analysis of all 3 cohorts of the BYLieve study. *J Clin Oncol*. 2023;41(suppl 16). 1078-1078.
16. Turner NC, Im S-A, Saura C, et al. Inavolisib-based therapy in *PIK3CA*-mutated advanced breast cancer. *N Engl J Med*. 2024;391(17):1584-1596.
17. Hurvitz SA, Layman RM, Curigliano G, et al. Gedatolisib plus fulvestrant, with and without palbociclib, vs fulvestrant in patients with HR+/HER2-/PIK3CA wild-type advanced breast cancer: first results from VIKTORIA-1. Presented at: European Society for Medical Oncology (ESMO) Annual Meeting; 2025 October 17-21; Berlin, Germany. LBA #17.
18. Bidard FC, Mayer EL, Park YH, et al. First-line camizestrant for emerging *ESR1*-mutated advanced breast cancer. *N Engl J Med*. 2025;393(6):569-580.
19. Medford AJ, Wander SA. SERENA-6: dynamic ctDNA assessment and the future of precision cancer medicine. *Nat Rev Clin Oncol*. 2025;22(11):804-805.
20. Barreto RB. Assessing the clinical readiness of the SERENA-6 strategy. *Oncologist*. 2025;30(9).
21. Mayer EL, Tolaney SM, Brufsky A, et al. evERA breast cancer (BC): phase III study of giredestrant + everolimus vs exemestane + everolimus in patients (pts) with estrogen receptor-positive, HER2-negative locally advanced or metastatic BC (ER+, HER2− LA/mBC). *J Clin Oncol*. 2023;41(suppl 16):TPS1119.
22. Llombart-Cussac A, Perez-Garcia JM, Lopez-Miranda E, et al. ADELA: a double-blind, placebo-controlled, randomized phase 3 trial of elacestrant (ELA) + everolimus (EVE) versus ELA + placebo (PBO) in ER+/HER2- advanced breast cancer (aBC) patients with ESR1-mutated tumors progressing on endocrine therapy (ET) + CDK4/6i. *J Clin Oncol*. 2025;43(suppl 16):TPS1129.
23. Mayer E, Tolaney SM, Martin M, et al. Giredestrant (GIRE), an oral selective oestrogen receptor (ER) antagonist and degrader, + everolimus (E) in patients (pts) with ER-positive, HER2-negative advanced breast cancer (ER+, HER2− aBC) previously treated with a CDK4/6 inhibitor (i): Primary results of the Phase III evERA BC trial. Presented at: European Society for Medical Oncology (ESMO) Annual Meeting; 2025 October 17-21; Berlin, Germany. LBA #16.
24. Hamilton E, Oliveira M, Turner N, et al. A phase I dose escalation and expansion trial of the next-generation oral SERD camizestrant in women with ER-positive, HER2-negative advanced breast cancer: SERENA-1 monotherapy results. *Ann Oncol*. 2024;35(8):707-717.
25. Jhaveri KL, Bidard F-C, Kalinsky K. 496P Imlunestrant plus abemaciclib versus fulvestrant plus abemaciclib in estrogen receptor positive (ER+), human epidermal growth factor receptor 2 negative (HER2-) advanced breast cancer (ABC): an indirect treatment comparison (ITC) of three phase 3 trials. Presented at: European Society for Medical Oncology (ESMO) Annual Meeting; 2025 October 17-21; Berlin, Germany.
26. Jhaveri K, O'Shaughnessy J, Andre F, et al. Abstract OT1-01-02: EMBER-4: a phase 3 adjuvant trial of imlunestrant vs standard endocrine therapy (ET) in patients with ER+, HER2- early breast cancer (EBC) with an increased risk of recurrence who have previously received 2 to 5 years of adjuvant ET. *Cancer Res*. 2023;83(suppl 5). OT1-01-02.
27. Hamilton E, Loibl S, Niikura N, et al. 354TiP A phase III randomised open-label study of extended adjuvant therapy with camizestrant vs standard endocrine therapy (ET) in patients with ER+/HER2− early breast cancer (BC) and an intermediate or high risk of recurrence (CAMBRIA-1). *Ann Oncol*. 2023;34(suppl 2):S323-S324.
28. Loibl S, Park Y, Tolaney S, et al. Abstract PO4-27-07: a phase 3, randomized, open-label study of upfront camizestrant vs standard endocrine therapy as adjuvant treatment for ER-positive/HER2-negative early breast cancer with intermediate-high or high risk of recurrence (CAMBRIA-2). *Cancer Res*. 2024;84(suppl 9). PO4-27-07.
29. Bardia A, Kaklamani VG, O'Shaughnessy J, et al. ELEGANT: elacestrant versus standard endocrine therapy (ET) in women and men with node-positive, estrogen receptor-positive (ER+), HER2-negative (HER2-), early breast cancer (eBC) with high risk of recurrence in a global, multicenter, randomized, open-label phase 3 study. *J Clin Oncol*. 2025;43(suppl 16):TPS619.
30. Geyer C, Bardia A, Harbeck N, et al. lidERA breast cancer (BC): phase III adjuvant study of giredestrant vs. physician's choice of endocrine therapy (PCET) in patients (pts) with estrogen receptor-positive, HER2-negative early BC (ER+, HER2− eBC). *J Clin Oncol*. 2023;41(suppl 16):TPS616.