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Current and Future Use of Oral Selective Estrogen Receptor Degraders (SERDs) in the Management of ER-Positive (ER+), HER2-Negative (HER2-neg) Metastatic Breast Cancer (mBC): A Survey of 20 Breast Cancer Research Leaders (RLs)

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BACKGROUND:

The January 2023 approval of elacestrant (E) for patients with ER+ HER2-neg mBC and an ESR1 mutation (ESR1mut) with disease progression (PD) on endocrine therapy introduced new considerations for biomarker-guided decision-making. In the past year, numerous seminal Phase III trials reported potentially practice-changing findings with novel SERD-based strategies. We sought to determine the current and potential use of these agents.

METHODS:

In September 2025, 20 US and international RLs completed a case-based survey on the management of ER+ HER2-neg ESR1mut mBC. For each case, a number of clinical factors (age, sites/extent of metastases, symptom burden, duration of benefit with first-line treatment, PIK3CA mutation status) were varied. A modest honorarium was offered.

RESULTS:

All RLs employ ESR1mut testing, with 7 first doing so at metastatic diagnosis, 10 at PD on first-line treatment and the rest customizing their approach **(Figure 1)**. Twelve favor circulating tumor DNA and 8 have no preference between tissue and liquid ESR1 assays **(Figure 2)**.

For a 65-y-old patient with ESR1mut disease, PD 2.5 y after first-line CDK4/6 inhibitor (CDKi)/aromatase inhibitor (AI), and minimally symptomatic bone mets, 16 of 20 RLs recommend E **(Figure 3)**. For the same patient with symptomatic visceral mets, only 4 would deploy the oral SERD **(Figure 4)**. For the same patient but with a coexisting PIK3CA mutation, E was preferred by 12 RLs in cases with bone-only mets **(Figure 5)** but only by 3 for symptomatic visceral disease **(Figure 6)**. Other factors, including age and shorter duration on CDKi/AI, affected treatment preferences across various situations, with somewhat more RLs turning to E for an 80-y-old and fewer for a 65-y-old with PD after 10 mo of first-line treatment.

Half of the RLs view select other SERDs as equivalent to E in efficacy and tolerability **(Figures 7 & 8)**, and 17 of 20 consider imlunestrant clinically equivalent whenever E is employed **(Figure 9)**. Sixteen of the RLs would consider using imlunestrant with abemaciclib in select situations in the first-line setting, and all would consider using the combination in select situations in the second-line or later setting **(Figure 10)**.

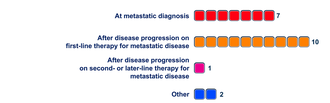
Regarding serial monitoring for ESR1mut during first-line treatment and early switching to a SERD (camizestrant) for patients with "molecular progression" (as in SERENA-6), 13 RLs believe more data are required but 7 endorse this approach now **(Figure 11)**.

CONCLUSIONS:

RLs have rapidly incorporated E into the management of progressive ER+ HER2-neg ESR1mut mBC, but the decision to employ this agent appears to be heavily influenced by the global disease burden and the duration of benefit from first-line treatment. Most RLs consider the newly approved imlunestrant largely equivalent to E, and all would also consider its use in combination with abemaciclib in certain situations. Many fewer would use camizestrant for patients found to have an ESR1mut without clinical PD, but an important and significant minority believe this option should be available to select patients. These practice patterns are likely to rapidly evolve given the continued emergence of new data with this class of therapy.

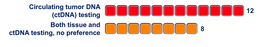
1 TIMING OF ESR1 MUTATION TESTING

At what point do you typically first assess ESR1 mutation status in your patients with ER-positive, HER2-negative breast cancer?



2 PREFERRED ESR1 TESTING METHODOLOGY

Which ESR1 testing methodology do you employ in your practice?

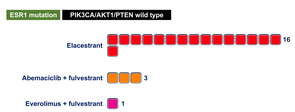


How would you compare the sensitivity of blood-based ctDNA testing to that of tissue testing in assessing for the presence of ESR1 mutations?



3 SECOND-LINE THERAPY FOR ESR1-MUTANT, PIK3CA WILD-TYPE MBC WITH BONE METASTASES

A 65-year-old woman (PS 0) with ER-positive, HER2-negative (IHC 0/null) de novo mBC receives ribociclib + letrozole for 2.5 years followed by disease progression with multiple minimally symptomatic bone metastases



4 SECOND-LINE THERAPY FOR ESR1-MUTANT, PIK3CA WILD-TYPE MBC WITH VISCERAL METASTASES

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7 COMPARATIVE EFFICACY OF AVAILABLE AND INVESTIGATIONAL ORAL SERDS

Based on published research data and your own clinical experience, how would you indirectly compare the global efficacy of elacestrant, imlunestrant, camizestrant and giredestrant when administered as monotherapy for endocrine therapy-pretreated ER-positive, HER2-negative mBC with an ESR1 mutation?

8 COMPARATIVE TOLERABILITY OF AVAILABLE AND INVESTIGATIONAL ORAL SERDS

How would you indirectly compare the global tolerability/toxicity of elacestrant, imlunestrant, camizestrant and giredestrant when administered as monotherapy for endocrine therapy-pretreated, ER-positive, HER2-negative mBC with an ESR1 mutation?

9 POTENTIAL CLINICAL ROLE OF IMLUNESTRANT MONOTHERAPY

If imlunestrant were available, in which situations, if any, would you use this agent as monotherapy?*

* This question was asked prior to the FDA approval of imlunestrant.

10 POTENTIAL CLINICAL ROLE OF IMLUNESTRANT/ABEMACICLIB

Regulatory and reimbursement issues aside, are there situations in which you would employ the combination of imlunestrant/abemaciclib as first-line treatment for ER-positive, HER2-negative mBC?*

Regulatory and reimbursement issues aside, are there situations in which you would employ the combination of imlunestrant/abemaciclib as second- or later-line treatment for ER-positive, HER2-negative mBC?*

* This question was asked prior to the FDA approval of imlunestrant.

11 CURRENT ROLE OF SERIAL CTDNA MONITORING DURING FIRST-LINE THERAPY

Regulatory and reimbursement issues aside, do you believe that the results from the SERENA-6 study justify the routine use of serial ctDNA monitoring for early detection of ESR1 mutations in patients with ER-positive, HER2-negative mBC receiving first-line therapy?

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