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IMLUNESTRANT

SELECTIVE ER DEGRADER

The safety and efficacy of the agents for uses under investigation have not been established. Pipeline molecules may not receive regulatory approval and become commercially available for the uses being investigated. The information provided about new molecules being studied is for scientific information exchange purposes only with no commercial intent. For more information on our pipeline, please visit lillyloxooncologypipeline.com.

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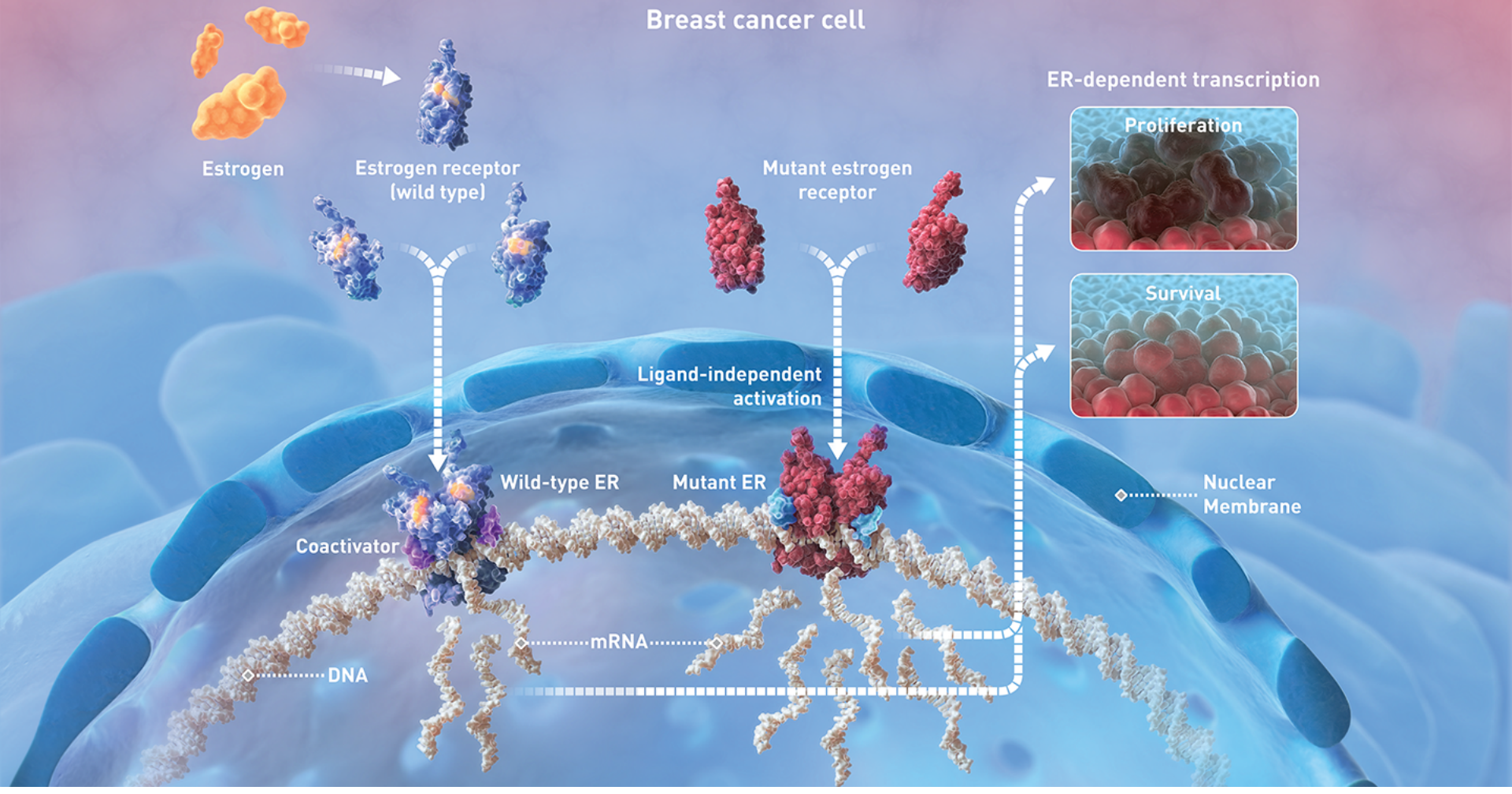
IMLUNESTRANT | MECHANISM OF ACTION[1-4]



References: 1. Gladden AB, Diehl JA. *J Cell Biochem*. 2005;96(5):906-913. **2.** Patel HK, Bihani T. *Pharmacol Ther*. 2018;186:1-24. **3.** Tecalco-Cruz AC, et al. *Cell Signal*. 2017;34:121-132. **4.** Wardell SE, et al. *Clin Cancer Res*. 2015;21(22):5121-5130.

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TARGET

Estrogen signaling plays an important role in organ development and growth. In certain cancers, abnormal estrogen signaling via the estrogen receptor is a component of tumor growth.[1] Disruption of estrogen signaling by selective estrogen receptor degraders (SERDs) is one of the treatment options for patients with estrogen-receptor-positive (ER+) cancers.

MOLECULE

Imlunestrant is an orally available SERD that suppresses estrogen signaling and subsequently inhibits cell proliferation in ER-expressing tumor models.[2,3]

CLINICAL DEVELOPMENT

Imlunestrant is being investigated in clinical trials in patients with ER+ breast cancer or endometrial cancer.

References: 1. Lee HR, et al. *Int J Mol Med*. 2012;29:883-890. **2.** Bhagwat SV, et al. *Cancer Res*. 2021;81(13_Suppl):1236. **3.** VandeKopple M, et al. ESMO Breast Cancer Annual Congress; May 11-13, 2023; Berlin, Germany. Abstract 41P.

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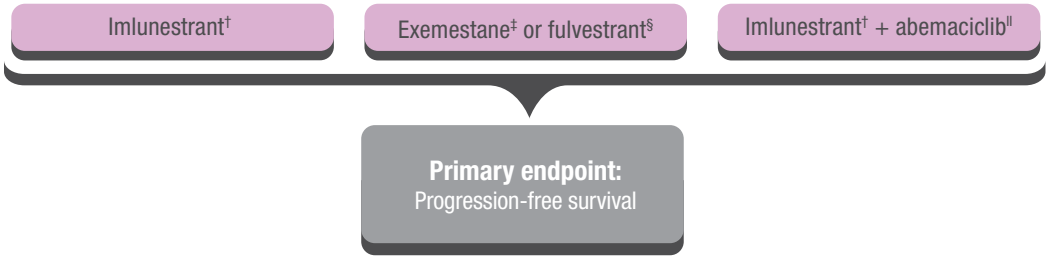
ember-3 CLINICAL TRIAL

A Phase 3, Randomized, Open-Label Study of Imlunestrant, Investigator's Choice of Endocrine Therapy, and Imlunestrant Plus Abemaciclib in Patients With Estrogen-Receptor-Positive, HER2-Negative Locally Advanced or Metastatic Breast Cancer Previously Treated With Endocrine Therapy*



* This clinical trial is being conducted globally.
† Imlunestrant is administered PO.
‡ Exemestane is administered PO.
§ Fulvestrant is administered intramuscularly.
ǁ Abemaciclib is administered PO.

Please visit clinicaltrials.gov for more information on this clinical trial [NCT04975308].

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ember-3 CLINICAL TRIAL

A Phase 3, Randomized, Open-Label Study of Imlunestrant, Investigator's Choice of Endocrine Therapy, and Imlunestrant Plus Abemaciclib in Patients With Estrogen-Receptor-Positive, HER2-Negative Locally Advanced or Metastatic Breast Cancer Previously Treated With Endocrine Therapy (cont.)

KEY INCLUSION CRITERIA

- Diagnosis of estrogen-receptor-positive (ER+), HER2-negative locally advanced or metastatic breast cancer
- Disease that has demonstrated progression on or after an aromatase inhibitor alone or in combination with a cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor
  - Patients are expected to have received prior treatment with a CDK4/6 inhibitor if this treatment is approved and can be reimbursed
- Must be deemed appropriate for treatment with endocrine therapy
- Response Evaluation Criteria in Solid Tumors (RECIST) evaluable disease (measurable disease and/or nonmeasurable bone-only disease)
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Adequate renal, hematologic, and hepatic organ function
- If female, have a postmenopausal status by natural or surgical means or by ovarian function suppression
- Able to swallow capsules/tablets

KEY EXCLUSION CRITERIA

- Prior treatment with chemotherapy (except for neoadjuvant/adjuvant chemotherapy), fulvestrant, or any investigational ER-directed therapy (including SERDs and non-SERDs), any PI3K, mTOR, or AKT inhibitor
- Visceral crisis, lymphangitic spread within the lung, or any evidence of leptomeningeal disease
- Symptomatic or untreated brain metastasis
- Serious preexisting medical conditions
- Known allergic reaction against any of the components of the study treatment

Please visit clinicaltrials.gov for more information on this clinical trial [NCT04975308].

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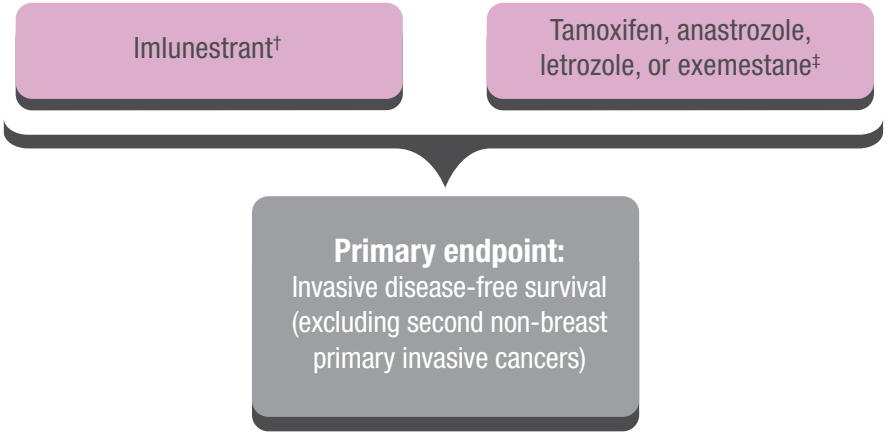
A Randomized, Open-Label, Phase 3 Study of Adjuvant Imlunestrant vs Standard Adjuvant Endocrine Therapy in Patients Who Have Previously Received 2 to 5 Years of Adjuvant Endocrine Therapy for ER+, HER2- Early Breast Cancer With an Increased Risk of Recurrence*



* This clinical trial is being conducted globally.
† Imlunestrant is administered PO.
‡ Endocrine therapy (investigator's choice of tamoxifen, anastrozole, letrozole, or exemestane) is administered per local approved label.

Please visit clinicaltrials.gov for more information on this clinical trial [NCT05514054].

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ember-4 CLINICAL TRIAL

A Randomized, Open-Label, Phase 3 Study of Adjuvant Imlunestrant vs Standard Adjuvant Endocrine Therapy in Patients Who Have Previously Received 2 to 5 Years of Adjuvant Endocrine Therapy for ER+, HER2- Early Breast Cancer With an Increased Risk of Recurrence (cont.)

KEY INCLUSION CRITERIA

- Diagnosis of estrogen-receptor-positive (ER+), HER2-negative (HER2-) early-stage, resected, invasive breast cancer without evidence of distant metastasis
- Participants must have received at least 24 months, but not more than 60 months, of any adjuvant endocrine therapy (ET) from time of adjuvant ET initiation
- Participants may have received neoadjuvant chemotherapy and/or targeted therapy with a cyclin-dependent kinase 4 and 6 (CDK4/6)- or poly adenosine diphosphate-ribose polymerase (PARP)- inhibitor
- Must have an increased risk of disease recurrence based on clinical-pathological risk features
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Adequate organ function

KEY EXCLUSION CRITERIA

- Any evidence of metastatic disease (including contralateral axillary lymph node [ALN]) or inflammatory breast cancer at primary breast cancer diagnosis
- Greater than a 6-month consecutive gap in therapy during prior adjuvant ET
- Participants who have completed or discontinued prior adjuvant ET >6 months prior to screening
- History of previous breast cancer are excluded, except for ipsilateral ductal carcinoma in situ (DCIS) treated by locoregional therapy alone ≥5 years ago
- Pregnant, breastfeeding, or expecting to conceive or father children within the projected duration of the trial, starting with the screening visit through 180 days after the last dose of study intervention
- Prior ET of any duration for breast cancer prevention (tamoxifen or aromatase inhibitors [AIs]) or raloxifene
- History of any other cancer
- Serious preexisting medical conditions

Please visit clinicaltrials.gov for more information on this clinical trial [NCT05514054].

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ACTIVE TRIAL CURRENTLY NOT ENROLLING

[NCT04188548] Breast Cancer

EMBER: A Study of LY3484356 for Patients With ER+, Locally Advanced or Metastatic Breast Cancer and Other Select Non-breast Cancers

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Pipeline information is current through February 6, 2024.

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