VERITAC-2: A Phase III Study of Vepdegestrant, a PROTAC ER Degrader, vs Fulvestrant in ER+/HER2- Advanced Breast Cancer

Erika P Hamilton, Cynthia Ma, Michelino De Laurentiis, Hiroji Iwata, Sara A Hurvitz, Seth Wander, Michael Danso, Dongrui R Lu, Julia Perkins Smith, Yuan Liu, Lana Tran, Sibyl Anderson, Mario Campone

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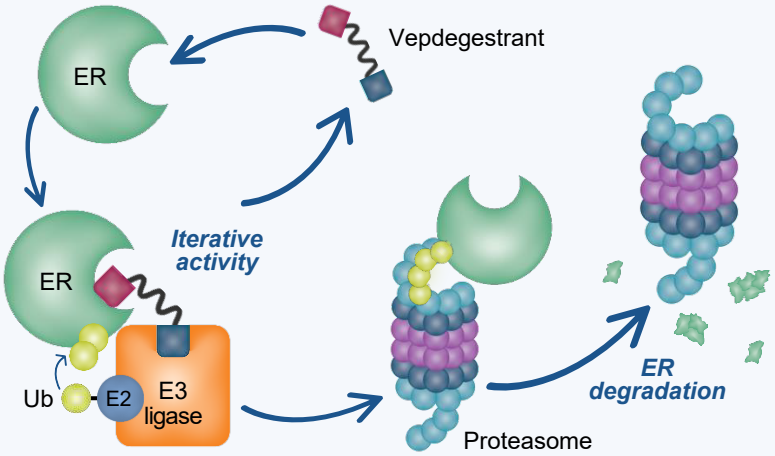
INTRODUCTION

The majority of breast cancers are estrogen receptor positive/human epidermal growth factor receptor 2 negative (ER+/HER2-)

There is a high **unmet need** in the second-line setting for treatments with **distinct mechanisms of action**

Vepdegestrant Mechanism of Action



Vepdegestrant is an oral PROTAC ER degrader that degrades wild-type and clinically relevant mutants of ER in **ER+ breast cancer**

In a first-in-human phase I/II study, **vepdegestrant** monotherapy was **well tolerated** and **showed clinical activity** in heavily pretreated patients with ER+/HER2- advanced breast cancer

VERITAC-2 STUDY DESIGN

VERITAC-2 is an open-label, randomized, global, multicenter, phase III study comparing the efficacy and safety of vepdegestrant and fulvestrant

≈560 patients

>250 sites

>25 countries

Previously treated adult patients with ER+/HER2- advanced breast cancer

Randomize 1:1

28-Day Treatment Cycles

Vepdegestrant
200 mg orally daily
n≈280

Fulvestrant
500 mg intramuscularly
days 1 and 15 of cycle 1 and
day 1 of subsequent cycles
n≈280

Stratification factors
- *ESR1* mutation (yes vs no)
- Visceral disease (yes vs no)

Primary end point: PFS in the overall population and *ESR1* mutant subpopulation

Secondary end points: OS (key secondary), ORR, DOR, CBR, safety and tolerability, PK, PROs, circulating tumor biomarkers

KEY INCLUSION CRITERIA

- Confirmed ER+/HER2- recurrent or metastatic breast cancer
- Radiological progression during or after the last line of therapy
- 1 prior line of CDK4/6 inhibitor + ET and ≤1 additional ET
- Most recent ET regimen given for ≥6 months prior to disease progression
- ECOG PS of 0 or 1

Glossary: CDK4/6=cyclin-dependent kinase 4/6; CBR=clinical benefit rate; DOR=duration of response; ECOG PS=Eastern Cooperative Oncology Group performance status; ER=estrogen receptor; *ESR1*=estrogen receptor 1 gene; ET=endocrine therapy; HER2=human epidermal growth factor receptor type-2; OS=overall survival; ORR=objective response rate; PFS=progression-free survival; PK=pharmacokinetics; PRO=patient-reported outcome; PROTAC=PROteolysis TArgeting Chimera; Ub=ubiquitin