Study design

Phase 3 giredestrant vs fulvestrant (+CDK4/6i) in 1L ETR ER+ HER2- aBC

pionERA
Breast Cancer
NCT06065748

N~1050 (420 *ESR1*m [40%], 630 *ESR1*nmd [60%])

- > post- or pre/perimenopausal[1] women, men[1]
- > ER+ HER2- LA/mBC; confirmed *ESR1* status[2]
- > resistant to adjuvant ET (± CDK4/6i): relapse
  - on-treatment after ≥12 mo *OR*
  - off-treatment within ≤12 mo (TFI)
  - if CDK4/6i, ≥ 12 mo since its completion
- > no prior systemic treatment for LA/mBC (1L)

R 1:1

- giredestrant 30 mg PO QD + CDK4/6i[3] PO QD/BID
- fulvestrant[4] IM Q4W + CDK4/6i[3] PO QD/BID

Survival Follow-up

Endpoints

co-primary PFS *ESR1*m & FAS

secondary[5] PFS *ESR1*nmd, OS, cORR, DoR, CBR, TTCtx, safety, PROs

stratification: non-/visceral, *ESR1* mutational status, intended CDK4/6i choice, prior adj CDK4/6i

[1]pre/perimenopausal women and men should also receive LHRH agonist for the duration of study treatment in both arms

[2]valid results *ESR1*m vs. *ESR1*nmd (cap 60%) from central testing of baseline blood ctDNA by F1LCDx assay

[3]CDK4/6i of investigator's choice - palbociclib 125 mg QD D1−21 (cap 20%), ribociclib 600 mg QD D1−21, or abemaciclib 150 mg BID D1−28, of each 28-day cycle

[4]fulvestrant 500 mg IM administered on C1D1&D15, C2D1 and every 4 weeks thereafter

[5]secondary efficacy endpoints will be assessed in *ESR1*m and *ESR1*nmd subgroups and in FAS/ITT