Fulvestrant +/- palbociclib *vs* everolimus + exemestane in ESR1 or Rb mutated MBC HR+/HER2- patients. A multicentric phase II trial with adaptive randomization. The CONQUER Trial

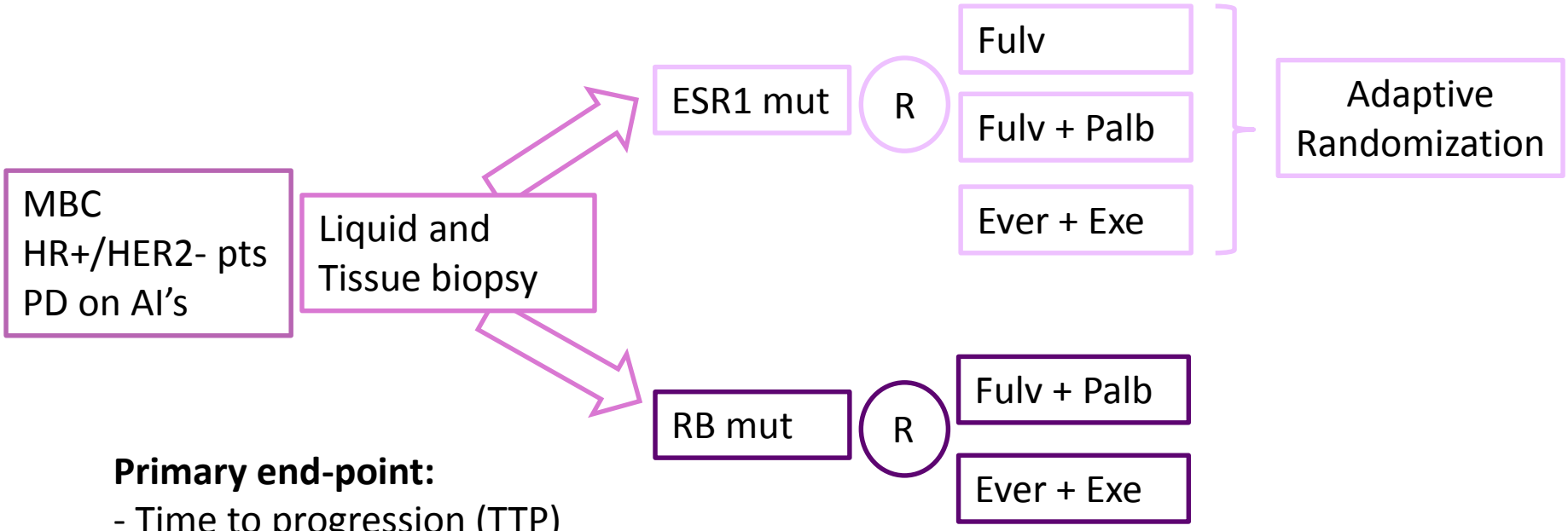
Background

- ESR1 and RB mutations are recognized frequently in patients with MBC progressed after AIs
- ESR1 mutations are relatively resistant to AIs therapy but not to fulvestrant
- Preclinical evidences suggested that patients with RB mutation may have a better outcome to palbociclib

1. Sporke et al., Nat Commun 2016; 2. Lefevre et al., Plos Med 2016

Study design

Ph II trial with adaptive randomization on fulvestrant +/- palbociclib *vs* everolimus + exemestane in ESR1 or Rb mutated MBC HR+/HER2- pts



Primary end-point:

- Time to progression (TTP)

Secondary end-point:

- Overall Survival (OS)
- Concordance between tissue and liquid biopsy
- Feasibility

Main inclusion criteria

- ✓ Age ≥ 18 years
- ✓ Signed informed consent
- ✓ Histologically proven diagnosis of HR+/HER2- metastatic breast cancer
- ✓ Oligometastatic disease (ABC-3 definition)
- ✓ Measurable disease
- ✓ Progression during or after AI's therapy
  - ➢ Adjuvant setting: after 24 months from the beginning and no more than 12 months from the end
  - ➢ Metastatic setting: no more than 1 line of endocrine treatment is allowed

Statistical plan

- 283 biomarker positive patients per Arm are needed to demonstrate a HR 0.7 with 5% alpha and 80% power

- Assuming positivity for ESR1=10% and Rb = 10%, the number needed to molecularly screen (NNMS) is 2830

Financial plan

- Molecular screening = 350.000,00 Euro
- CRO = 150.000,00 Euro
- Patient insurance= 50.000,00 Euro
- 2 Biologist = 180.000,00 Euro
- Statistics= 50.000,00 Euro
- Overheads 10%= 80.000,00 Euro

- **Total = 860.000,00 Euro**