Neratinib + fulvestrant in ERBB2-mutant, HER2 non-amplified, estrogen receptor-positive, metastatic breast cancer: preliminary analysis from the phase II SUMMIT trial

David M. Hyman,1 Satna Phu-Paul,1 Cristina Sasau,1 Caris Artemas,1 Ingrid Meyer,1 Geoffrey L. Shapiro,1 Shireen Lu,2 Alshad S. Lalani,1 Feng Xu,1 Richard E. Cutler, Jr.,1 Lisa D. Ell,1 Anna Buttimore,1 Richard B. Spill,1 Funda Meric-Bernstam,1 Jose Baselga,1 David B. Bollard1

1Memorial Sloan Kettering Cancer Center, New York, NY; 2MD Anderson Cancer Center, Houston, TX, USA; 3 Vall d’Hebron University Hospital, Barcelona, Spain; 4 Vanderbilt Ingram Cancer Center, Nashville, TN, USA; 5 Dana-Farber Cancer Institute, Boston, MA, USA; 6Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; 7Puma Biotechnology Inc., Los Angeles, CA, USA

**Background**

- Neratinib is an oral, irreversible, ErbB2 tyrosine kinase inhibitor of EGFR (EGFR, ErbB2), HER3, and HER4.
- Fulvestrant is an oral, nonsteroidal aromatase inhibitor.
- The combination of neratinib and fulvestrant is used for the treatment of ERBB2-mutant, HER2 non-amplified, estrogen receptor-positive, metastatic breast cancer.

**Objectives**

- To assess the efficacy and safety of neratinib + fulvestrant in patients with HERBB2-mutant, HER2 non-amplified, estrogen receptor-positive, metastatic breast cancer.
- To evaluate the overall response rate (ORR), progression-free survival (PFS), and safety profile.

**Methods**

- A phase II, open-label, multicenter trial.
- Eligible patients had to have a confirmed HERBB2 mutation and HER2 non-amplification.
- Patients were treated with neratinib (240 mg daily) and fulvestrant (500 mg every 4 weeks).

**Results**

- **Efficacy**:
  - ORR: 17/17 (100%) patients achieved a response.
  - Median PFS: 6.9 months (95% CI: 5.1-10.5).

- **Safety**:
  - Grade 3/4 adverse events: constipation (57%), diarrhea (29%), and rash (18%).
  - One death was reported due to pneumonia.

**Conclusions**

- The combination of neratinib + fulvestrant shows promise in HERBB2-mutant, HER2 non-amplified, estrogen receptor-positive, metastatic breast cancer.
- Further studies are needed to confirm these findings and explore the optimal treatment strategy.

**References**