The therapeutic superiority of neratinib in combination with trastuzumab compared to pertuzumab plus trastuzumab in HER2-positive \( \beta \)-vivo breast cancer models

**Introduction**

The therapeutic efficacy of neratinib (N) in combination with trastuzumab (T) for early stage HER2+ breast cancer and has shown greater potency compared to lapatinib (L) in established cell line- and patient-derived xenograft (PDX) models. (N+T) and how it compares to pertuzumab (P) +T (without chemotherapy) has not been well studied. Here, we evaluate the therapeutic efficacy of N, P, and T, either alone or in combination, with a primary focus on comparing N+T vs. P+T in established cell line- and patient-derived xenograft (PDX) models.

**Experimental Plan**

**Results**

- **Hypothesis**
  - Dual HER2 inhibition using N+T will be highly efficacious and equally potent or more than P alone, due to more complete blockade of the HER pathway.

**Dual HER2 inhibition using N+T will be highly efficacious and equally potent or more than P alone, due to more complete blockade of the HER pathway.**

**Conclusions and clinical significance**

- N significantly improved tumor growth compared to both N+T and P+T alone or in combination.
- N+T significantly improved tumor growth compared to both N and P+T alone or in combination.
- P+T significantly improved tumor growth compared to both N and P alone.
- The combination of N with T in a neoadjuvant setting is feasible and yields complete tumor eradication in xenograft models.
- Our findings strongly support future clinical investigations of the combination of N with T in breast cancer patients.