Pharmacokinetic (PK) interactions between lapatinib (LPT) and vinorelbine (VNR) in a phase I study in locally advanced or metastatic breast cancer (LAMBC) patients overexpressing HER2 (HER2-PIK3CA-C) were assessed with the following objectives and endpoints:

**OBJECTIVES & ENDPOINTS**

**Main objectives**
- Assessment of relevant PK interactions between LPT and VNR.
- Individual and population pharmacokinetics of LPT and VNR.
- Exploration of safety and efficacy of LPT and VNR according to the LAMBC population.

**Exploratory endpoints**
- Correlation between drug exposure and adverse events or anti-tumor activity.
- PK interactions with other relevant drugs.

**Eligibility criteria**
- HER2 overexpression confirmed by IHC or FISH.
- Histologically confirmed locally advanced breast cancer (LABC) or metastatic breast cancer (MBC).
- Aged between 18 and 75 years.
- Adequate haematological, liver, renal and cardiac functions.

**Treatment schedule**
- LPT 1,500 mg IV plus VNR 20 mg/m².

**PK samples**
- Collected at doses of 750 mg and 1,250 mg for LPT and VNR.

**Population analysis**
- Total reduction of VNR CL: 26.4% with 1,000 mg of LPT and 41.3% with 1,250 mg of LPT.

**PK parameters of LPT**
- Mean CL of LPT: 1,000 mg = 81.2 ± 31.4 L/h, 1,250 mg = 87.8 ± 31.0 L/h.
- Mean CL of VNR: 1,000 mg = 37.8 ± 16.7 L/h, 1,250 mg = 33.8 ± 14.3 L/h.

**Conclusions**
- There was a drug-drug interaction between LPT and VNR.
- A stepwise dose-escalation method was used.
- A total of 57 patients were enrolled, 28 for LPT and 29 for VNR.
- The recommended dose for phase II studies was 1,250 mg LPT and 20 mg/m² VNR.

**Acknowledgements**
- F. Lokiec, E. Brain, N. Isambert, F. Dalenc, P. Tresca, J. Bonneterre, K. Rezaï, H. Roché, N. Penel, M. Jimenez, V. Diéras, P. Fumoleau
- SABCS December 6-9, 2019