BACKGROUND
Metastatic breast cancer represents an incurable disease and the treatments aim at selecting symptoms without toxicity and prolonging survival. The association of 5-FU and vinorelbine is one of the most utilized chemotherapy scheme, but hematologic toxicity remains a major problem. The optimal time for ‘strat by dose’ is defined as the least toxic time and to the most efficient time of administration in animal model (19 HALO).

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OBJECTIVES
Definition of the Least Toxic Time (LTT) of vinorelbine, given in combination with 5-FU in metastatic breast cancer patients.

PATIENTS & METHODS
Key Eligibility Criteria
- Metastatic breast cancer (MBC)
- WHO performance status < 2
- Adequate hematologic, hepatic, renal and cardiac function
- No central nervous system metastasis

Safety assessment
Toxicity was assessed according to the NCI-CTCAE version 2.0. Dose reduction were planned for the following toxicities:
- Grade II–III nephropathy, Grade I–II neuropathy
- 5-FU induced emesis or diarrhea
- 5-FU induced fever

RESULTS
Cycles, with tumour progression problems leading to a more than 25% deviation in the drug dosage or timing, were excluded from the final analysis. At 224 cycles have been analyzed:

Least Toxic Time analysis
The Least Toxic Time was estimated for several toxicity. In the case of 5-FU and vinorelbine, the optimal time of administration at 17:00 (5 p.m.) to reduce the incidence of leucopenia G3-4. This time of administration almost corresponds to the least toxic and to the most efficient time of administration in animal model (19 HALO).

CONCLUSION
Chromophobinolization of vinorelbine in Humans can demonstrate an optimal time of administration at 17:00 (5 p.m.) to reduce the incidence of leucopenia and thrombocytopenia. This study was performed as a randomized trial comparing the conventional administration of 5-FU and vinorelbine with the chronomodulation of 5-FU combined with V30. The main isotonic 5-FU toxicity was gastrointestinal (2% & 4%), other gastrointestinal (5% & 1%), infection (4%), sensory (4%), pulmonary (2% & 6%), alopecia (7%).