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The *PIK3CA*-ML retrospective analysis

Prediction of *PIK3CA* mutational status through a machine learning approach in patients with endocrine-resistant HR+ HER2- aBC: a retrospective analysis based on data from the GIM-14 trial

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BACKGROUND

- In luminal-like mBC SoC first-line treatment has been based for many years on the combination of ET + CDK4/6i
- The treatment landscape has recently evolved following the results of the INAVO-120 trial, which included patients with endocrine-resistant disease harbouring a *PIK3CA* mutation
- The majority of patients enrolled in INAVO-120 had not previously received a CDK4/6i in the adjuvant setting
- The ongoing INAVO-121 trial allowed the inclusion of patients who progressed on adjuvant ET + CDK4/6i
- **Knowledge gap**: it remains unclear whether continuing CDK4/6 inhibition in patients who progress after receiving these agents in the adjuvant setting could provide an additional benefit when added on treatment with fulvestrant and a PI3K inhibitor

AIM OF THE STUDY

To define the proportion of patients who, in the near future, may fall into the clinical scenario previously described

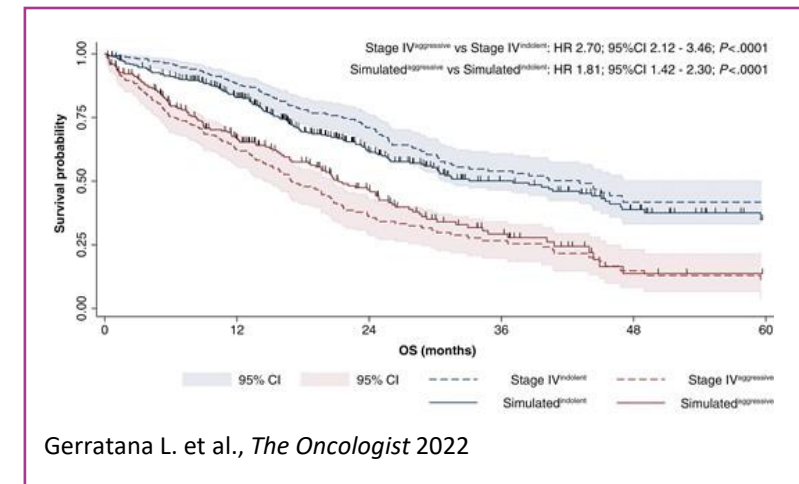
METHODS

- Analysis of data already collected in the GIM-14 trial, focusing on endocrine-resistant patients treated with fulvestrant plus a CDK4/6i as first-line therapy for advanced disease

- *PIK3CA* mutational status is unknown for most of candidate cases

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machine learning approach able to make a prediction based on baseline clinic-molecular characteristics:

- a K-nearest neighbor and a random forest machine learning model will be trained on the PMAC cohort
- the model showing the best performance will be applied to the GIM-14 population selecting patients treated with fulvestrant plus a CDK4/6i
- For patients predicted to harbour a *PIK3CA* mutation, we will assess whether they would have received a CDK4/6i in accordance with current clinical indications, simulating a real-world future scenario



KEY INCLUSION CRITERIA

- Pts enrolled in the GIM-14 trial
- HR+, HER2- aBC pts with endocrine-resistant disease as defined by ESMO guidelines
- First-line treatment for advanced disease with fulvestrant + CDK4/6i
- Availability of complete clinicopathological data from the early-stage setting