Big Data Supporting Public Health Policies

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Lung Cancer KPI analysis report

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Executive summary

This report presents the outcomes of the descriptive and predictive analysis performed in iASiS, in order to achieve the basic Key Performance Indicators for the Lung Cancer use case.

IASIS Lung Cancer descriptive/predictive models aimed at a profiling of our study population, gathering the following information:

- Patient events: in terms of symptoms and diseases, drugs, and surgical procedures accumulated over time in the EHRs.
- The most common symptoms and diseases.
- The most common drugs and medication
- The most common surgical procedures.
- The most common symptoms and diseases reported prior to cancer diagnoses and from cancer to death.

Covering all of those relevant aspects of the patient´s clinical status, we then wanted to proceed to further analysis of these data in order to achieve the proposed KPIs and analyse:

- percentage of patients overtreated: compare those until December 2017 with those post-IASIS specific interventions (2018-2019).
- percentage of patients seen by palliative care service in the month prior to death
- percentage of patients seen by palliative care service > 1 month prior to death
- survival of patients after first line of treatment

KPI1: Data Sources

Description of KPI 1: Large and shared data repository for lung cancer and dementia with data of at least 25,000 patients, from at least 5 different, heterogeneous sources

A total of 1,051 lung cancer patients diagnosed and treated at Puerta de Hierro-Majadahonda University Hospital (HUPHM) have been recruited in the Project. Their demographic, clinical and treatment information and its follow-up data until 31st january 2020 have been analyzed in the project.

The project analysis also included 422 patients from NSCLS-Radiomics images dataset.

KPI2: Overtreatments

Description of KPI 2: Decisions about the accuracy of diagnosis, treatment and prognosis of the disease (measured in the validation activities) will increase by 10% over conventional ways and/or if only one source of data was available.

In lung cancer new treatments are continuously being developed, giving oncologists different treatment options until the end of the patient´s life. This implies an increasing number of overtreatments and a worsening of the quality of life, and as a result, a decrease in overall survival.

By reducing overtreatments, the number of long survivors, quality of life and overall survival will be improved in mutated population and healthcare policies could be modified. In HUPHM the percentage of overtreatments has never been studied. In the literature, it is described between 10-50% overtreatments and there are no clear parameters to help clinicians decide when to stop an active treatment and prioritize palliative care.

Big Data techniques in IASIS platform were used for:

I.   Measuring overtreatments in HUPHM from the years prior to the beginning of the IASIS project
II. Measuring overtreatments after the implementation of the IASIS knowledge in the last year of the project, obtaining a 10% decrease.

RESULTS:

- Patients in advanced stage are usually candidates to receive palliative care (PC). 59.7% of these patients receive PC. We are increasing interconsultations with palliativists in order to provide PC earlier to a greater percentage of patients and prevent overtreatments in the end of life.
- 11% of our patients in advanced stage had received overtreatments before iASiS implementation. Since 2018 we have reduced overtreatments to 10% by identifying patients that won´t benefit from treatments in the end of life and will benefit from early palliative care.
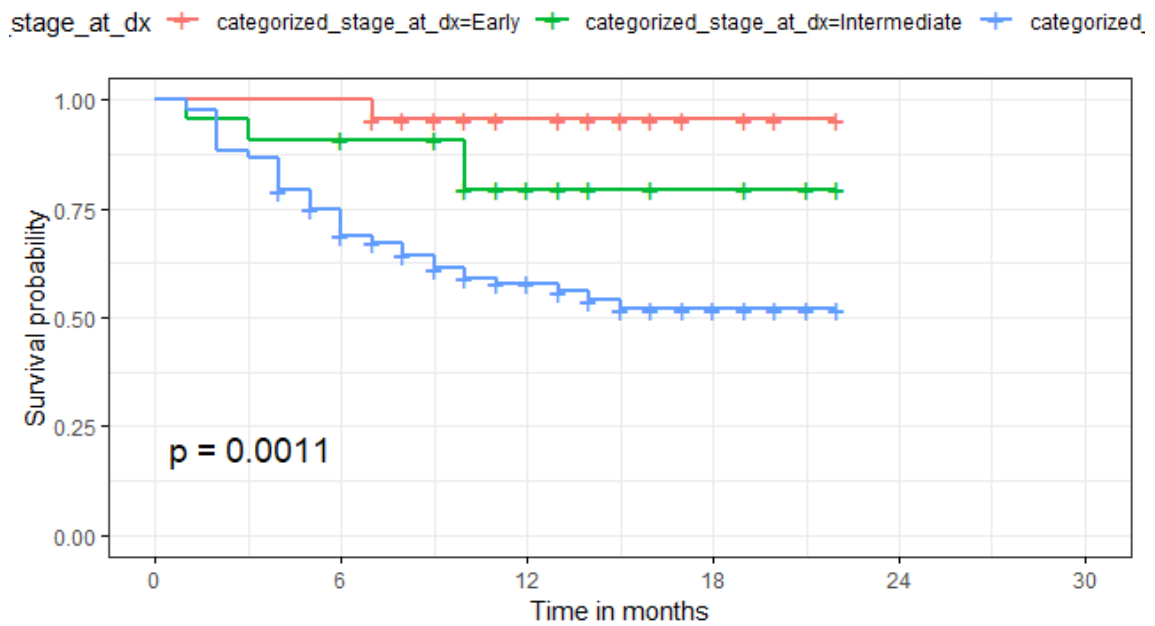
As shown in the survival curves below, we have also increased survival of our patients in all stages. This is of great importance specially in advanced stages, which not only are 60% of our patients but usually have the worst outcome.

Survival of patients diagnosed before 2018 & after 2018

Before 2018 (pre-IASIS interventions)
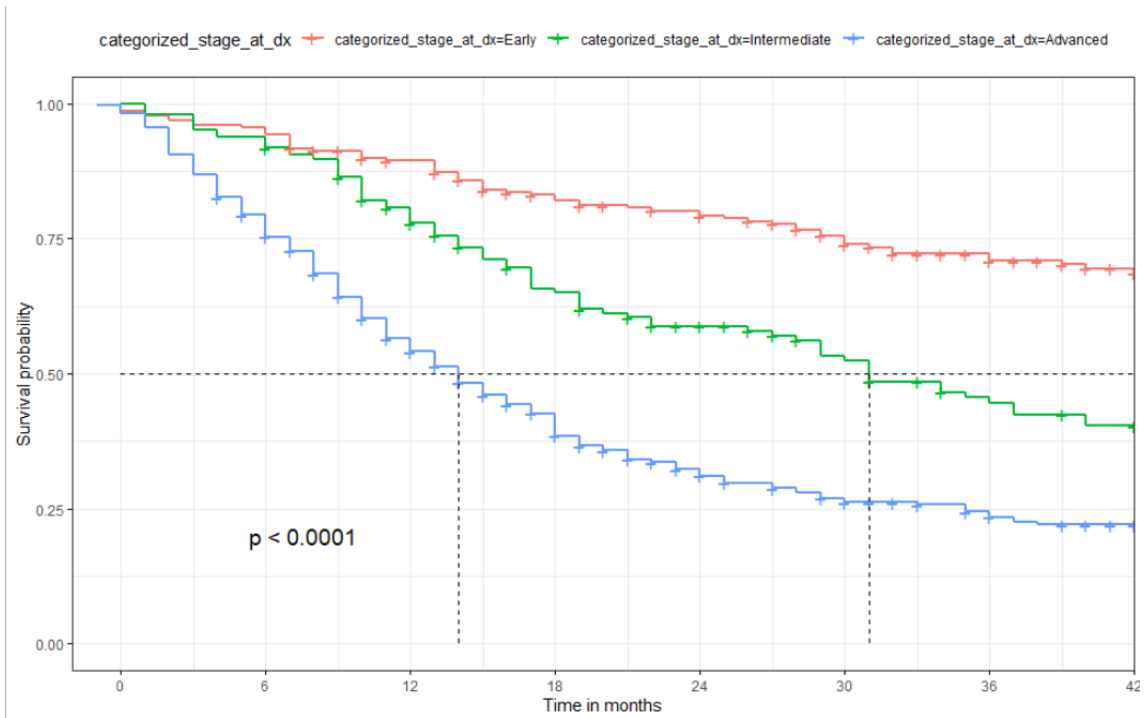
From 2018 (post-IASIS interventions)

KPI3: Toxicities

Description of KPI 3: patient's risk status (measured in the validation activities) will produce a 10% decrease in toxicities related to treatments, with the consequent, improvement in quality of life and prognosis.

Nowadays there are no guidelines to classify patients objectively according to their risk of developing treatment toxicities. These guidelines are necessary as tools that would help oncologists to improve their understanding and deliver appropriate treatments to patients with cancer, reducing toxicities. These new sources of information will serve to create predictive and stratification models which will help to provide personalized treatments reducing toxicities and therefore achieving better health outcomes. In the literature, the percentage of toxicities is described between 40-85%.

The following clinical issues regarding our patients were to be addressed by IASIS platform:

- Implementation of algorithms that suggest drug interactions: Drug-Drug Interactions (DDIs) are a major cause of morbidity and mortality in lung cancer patients and lead to increased health care costs. DDIs make up nearly 3% of all hospital admissions and 3% to 5% of all inpatient medication errors.
- Toxicity ratio will be measured from the years prior to the beginning of the project and compared with the last year of the project, after obtaining all the important knowledge from the platform.

By reducing toxicities, the number of long survivors' quality of life and overall survival will be improved in mutated population and healthcare policies could be modified. In view of the analysed descriptive data, we considered performing the following analyses within IASIS framework:

- Measuring toxicities in HUPHM from the years prior to the beginning of the IAISIS project
- Measuring toxicities after the implementation of the IASIS knowledge in the last 2 years of the project, obtaining a 10% decrease.

RESULTS: After 2018, patients with 1-2 toxicities have increased from 8.6% to 31.2%, patients with 3-4 toxicities have decreased in 6% (from 57% to 51,8%) and number of patients with 5-10 toxicities have decreased by 17,8% (from 34% to 16%).

REDUCTION IN 3-4 AND 5-10 TOXICITIES: This reduction has been achieved by reviewing iASiS DDI indications and closer follow-up in order to treat patients earlier; better dose adjustment of treatments and closer and more efficient collaboration and communication with other hospital departments, in order to treat those toxicities promptly, and closer collaboration with primary care doctors.

INCREASE IN 1-2 TOXICITIES: This increase should not be seen as a negative result because it means that we are identifying earlier these toxicities. This results in a better overall management of the patient and in an improvement in QoL.

number Of toxicities before 2018

## number Of toxicities after 2018
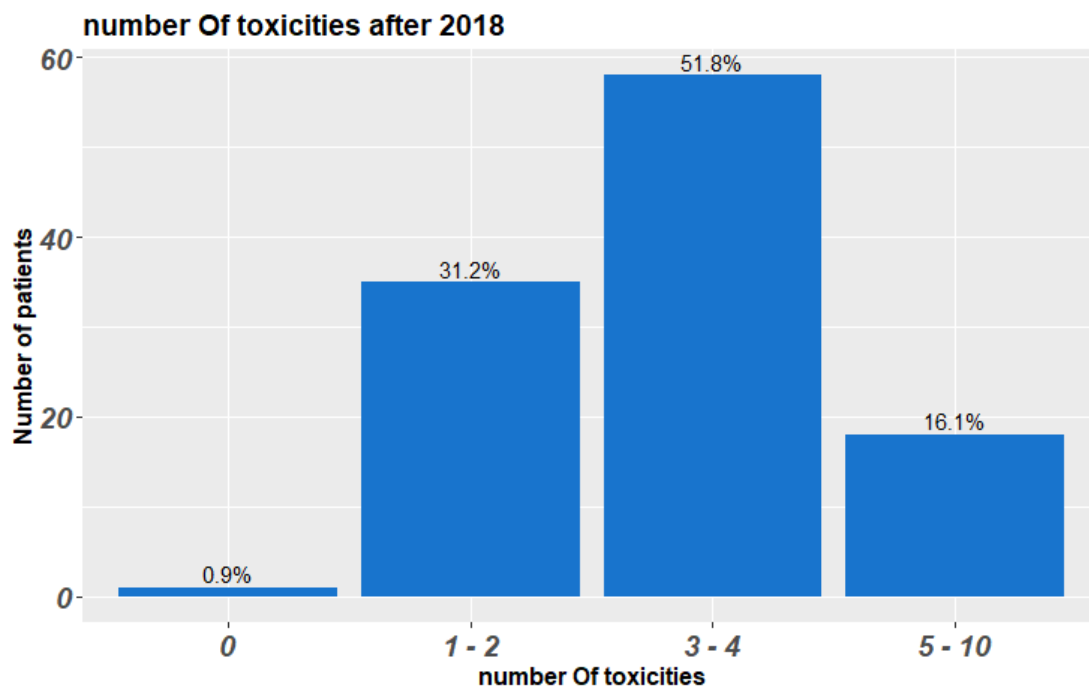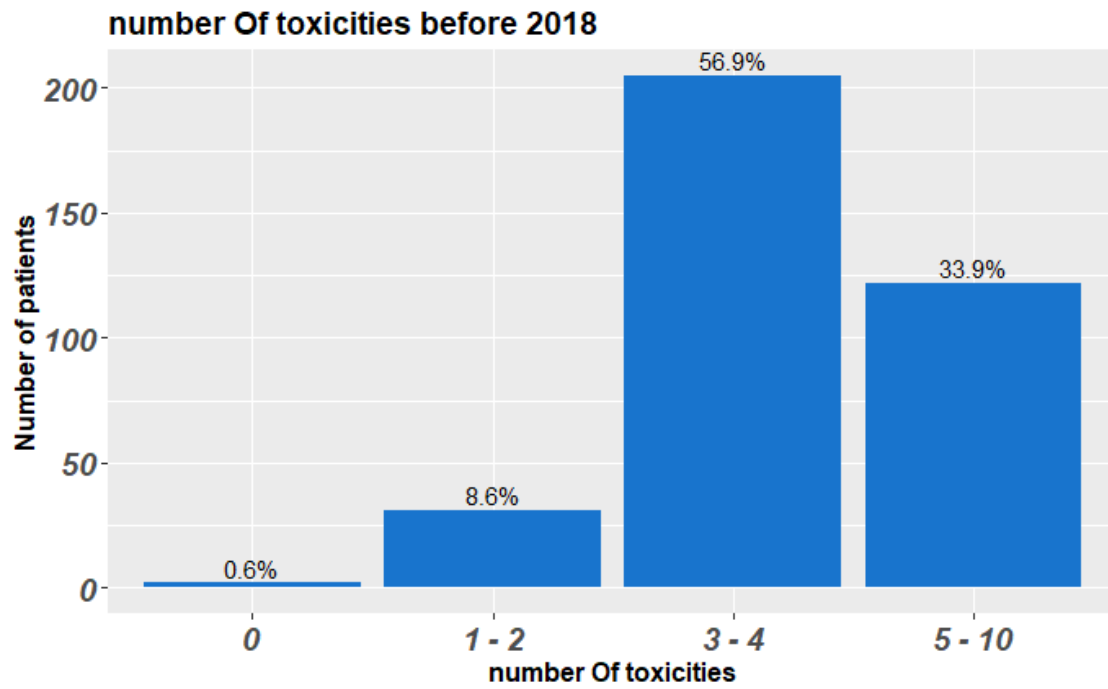
In terms of DDIs, the number of non oncological drugs that the patients took routinely before cancer diagnosis were analysed. This fact is relevant in two ways: the first one because it´s related to the number of comorbidities that the patient previously had, which will impact their prognosis and survival, and secondly, some of these drugs may interact with the oncological treatment decreasing its efficacy or increasing their toxicity so they had to be explored.

As depicted in the survival curve below, patients who took less than 3 non oncological drugs before cancer diagnosis live longer than those more complex patients who usually took more than 3 drugs previous to cancer diagnosis.
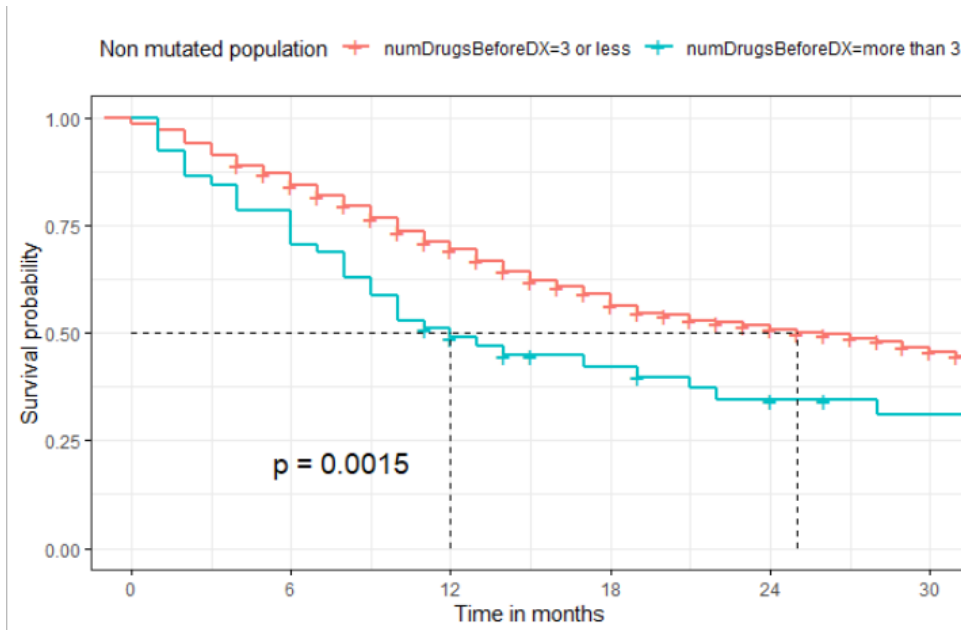
Focusing on treatment in intermediate and advanced stages, in relation to toxicities, DDIs and survival, new schemes that include immunotherapy in monotherapy or combined with chemotherapy, as shown in the figure below, have demonstrated to be the most effective, with less toxicities and which provide a longer survival significantly (p=0.002), compared to non treated patients or to those who received chemotherapy.
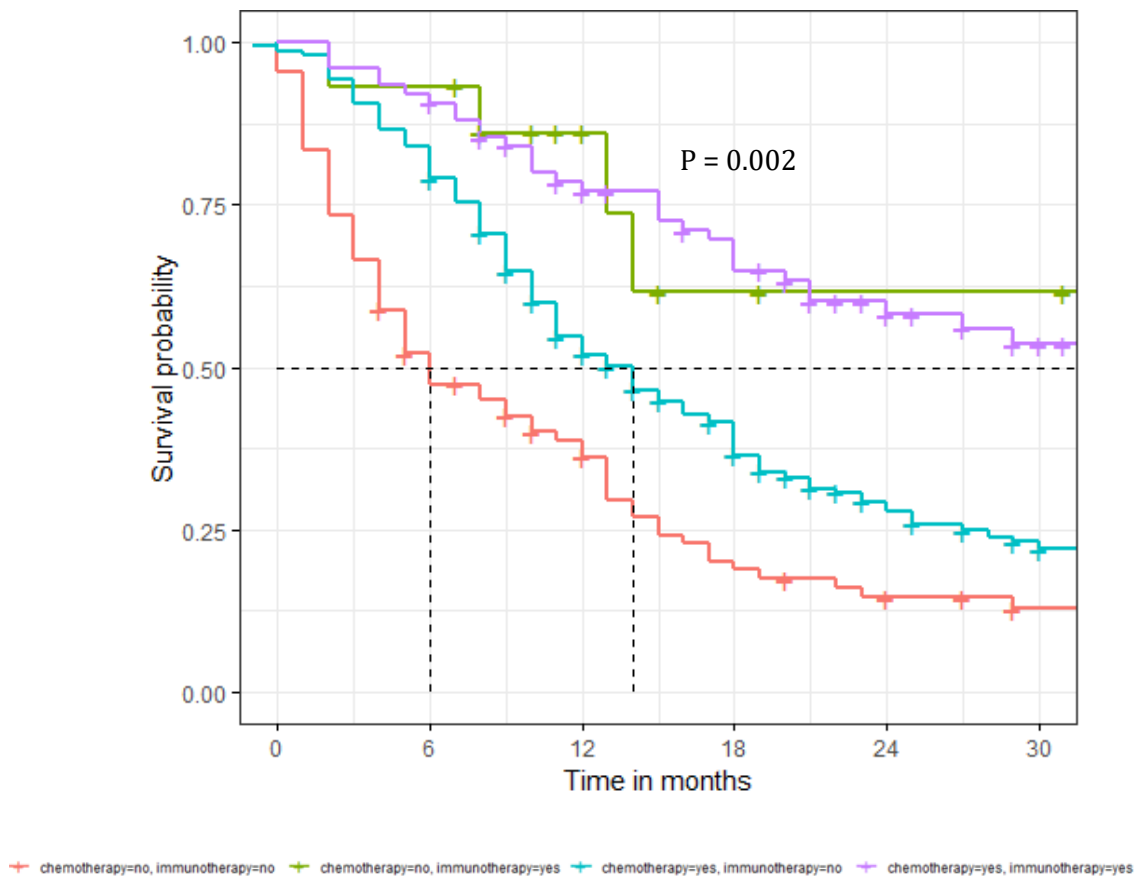
Exploring DDIs identified in IASIS knowledge graph, we observed, with statistical significance ($p<0.05$), a difference among the different chemotherapy schemes, with the combination with vinorelbine and carboplatin being the most effective one in terms of secondary effects and survival. On the other hand, the combination of vinorelbine and cisplatin is the most toxic one for our patients.

### Kaplan-Meier Survival Time Curve Estimate for each DDI Line 1
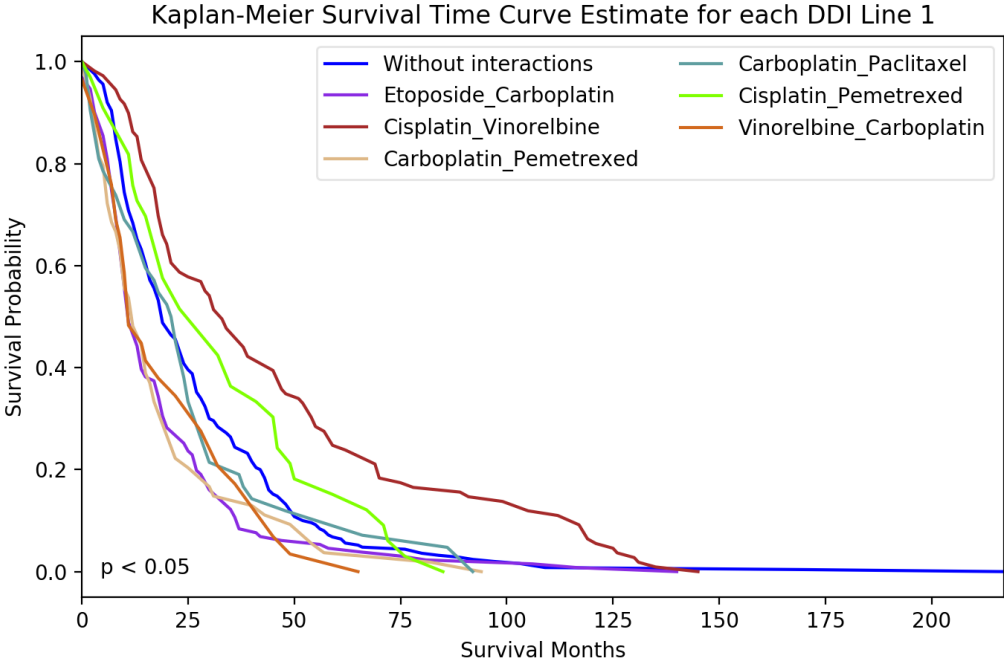
Finally, we explored the most common non oncological drugs taken by our patients, being omeprazol and ranitine (gastric protectors), atorvastatin and simvastatin (statins for hypercholesterolemia treatment) and enalapril and atenolol (antihypertensives).

Drug	Number of Patients taking most common non oncological drugs
Omeprazole	330
Ranitidine	27
Atorvastatin	99
Simvastatin	84
Enalapril	97
Atenolol	50

The only statistical significance was observed with the effect of gastric protectors. Omeprazole, as previously described in the literature since 2017, is known to decrease the efficiency of several

oncological treatments, such as tyrosin-kinase inhibitors, which is why this treatment is either suspended, shortened in time or substituted by ranitidine, an alternative to omeprazole with less impact on the oncological treatment.
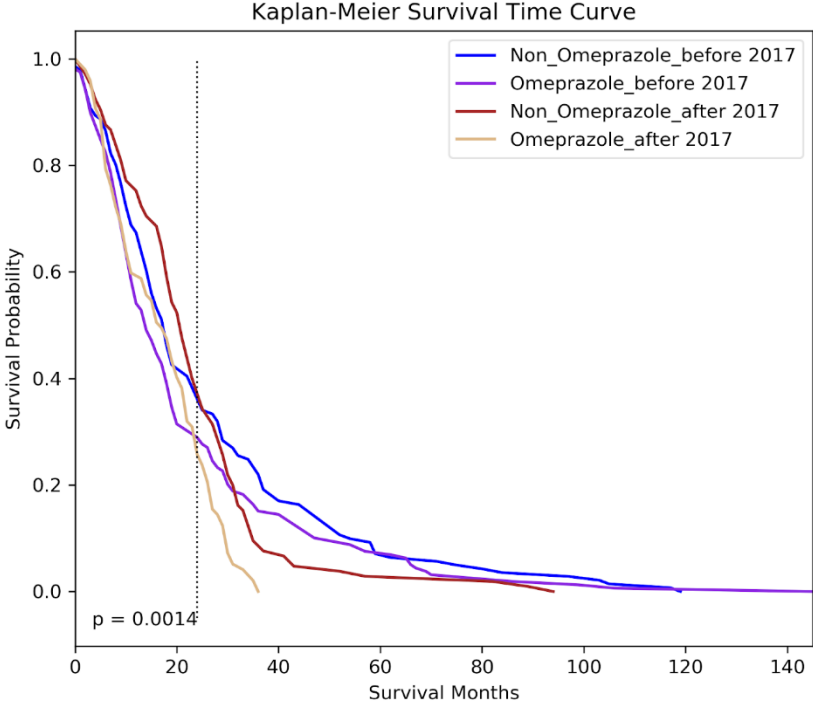
In terms of impact on omeprazol with certain chemotherapy schemes, we observe a better outcome in stage III patients treated with vinorelbine-cisplatin in absence of omeprazol, compared to those taking omeprazol concomitantly to chemotherapy or to other schemes.

Kaplan-Meier Survival Time Curve
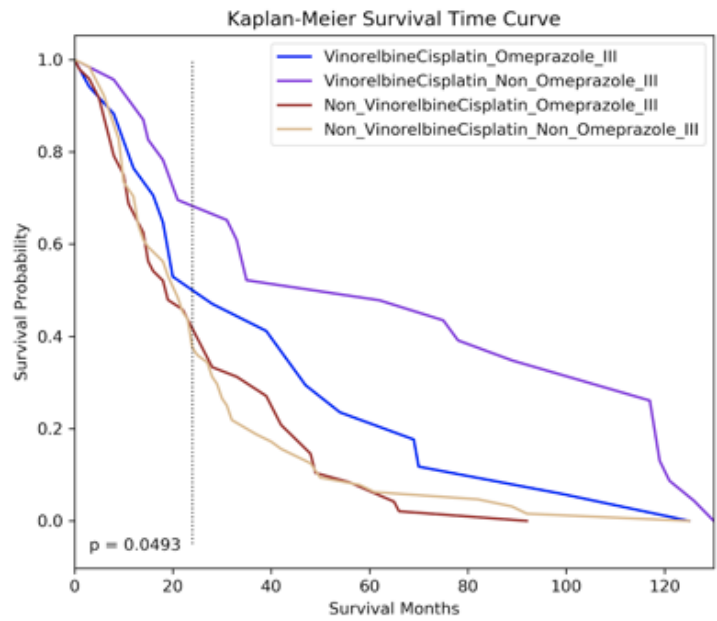
Significant difference (p <0.05) survival time patients in Stage III who take Vinorelbine, Cisplatin, and Omeprazole versus those taking only Vinorelbine, Cisplatin and no Omeprazole

No significant differences are observed for a possible impact of statins or antihypertensives on survival of advanced stage patients when taking these treatments concomitantly with chemotherapy schemes.

Kaplan-Meier Survival Time Curve

Kaplan-Meier Survival Time Curve