BACKGROUND
In May 2008, the European Medicines Agency (EMA) granted authorization to Pemetrexed as a first-line treatment for locally advanced or metastatic non-small cell lung cancer (NSCLC), other than predominantly squamous cell (non-SC) histology patients. A phase III trial compared Pemetrexed with Gemcitabine, both in association with cisplatin, and found a similar overall survival between both groups (10.3 months). The EMA authorization was based in a subgroup analysis of this phase III trial. In late 2008, the first Gemcitabine generic drug was commercialized.

PURPOSE
Our aim was to highlight the limited evidence considered on pemetrexed’s approval and the impact on it’s use.

MATERIAL AND METHODS
The literature was reviewed and a retrospective analysis of the first-line treatment options in non-SC NSCLC in our hospital was made, between July 2013 and June/2017.

RESULTS
An opinion article was published in January 2018 in JAMA Oncology. It discussed if an approval based in a subgroup analysis of a clinical trial, predefined but never tested in a phase III trial design for its validation, was strong enough to influence clinical practice.

It is well known that any data retrieved from a clinical trial subgroup analysis is indicative and non-conclusive. It is uncertain when a subgroup analysis should influence clinical practice.

Almost at the same time Gemcitabine generic drug was arriving on the market, all the non-SC NSCLC treatment guidelines replace Gemcitabine for Pemetrexed as a first option, with evidence level II, using efficacy and not safety as a reason, which could be an argument.

In Portugal, Pemetrexed was considered cost-effective compared with Gemcitabine, based on the same limited efficacy data, and considering the cost of the original gemcitabine drug, instead of the generic drug.

In our hospital, in the 4 years analysed, 71 non-small cell lung cancer, patients, with non-squamous cell histology, were treated with Pemetrexed, whereas 22 were treated with Gemcitabine, both associated with platin. The cost difference per patient (six cycles considered) was 10.554€ , with a direct budget impact of 749.334€ for the 71 patients.

CONCLUSION
Pemetrexed was preferred to Gemcitabine as a first-line treatment of non-SC NSCLC, beside its limited evidence quality. A change in clinical practice should require better evidence levels. In our hospital, this change in clinical practice had a relevant economic impact.

REFERENCES