

COST ANALYSIS OF THE MANAGEMENT OF CNS METASTASES IN PATIENTS WITH ADVANCED ALK+ NSCLC: ALECTINIB VS CRIZOTINIB

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INTRODUCTION

- Lung cancer is the most commonly diagnosed cancer (11,6% of all cases), as well as the leading cause of cancer death (18,4% of total cases of cancer deaths) worldwide¹ in Spain, accounting for up to 22.121 deaths in 2016.²
- Within advanced non-small-cell lung carcinoma (NSCLC) close to 5% of patients present rearrangements in the anaplastic lymphoma kinase (ALK) gene³. Central Nervous System (CNS) metastases represent a very common complication in NSCLC ALK+, appearing at least in 60% of patients along the course of the disease⁴.
- The high prevalence of CNS metastases in NSCLC ALK+ leads to a significant clinical and economic burden for patients and the national health system⁵.
- Alectinib, kinase protein inhibitor and ALK blocker, has demonstrated to reduce the disease progression in the CNS as well as having superior efficacy in its treatment versus crizotinib, the old standard of care^{6,7}. **Because of this preventive effect, alectinib could reduce the healthcare resource utilization and, therefore, the brain-metastases related costs in this pathology.**
- The primary endpoint of this study was to estimate the cost associated with the management of patients with advanced ALK+ NSCLC with and without CNS metastases (Phase I). The secondary objective was to perform an analysis of the annual cost comparing patients treated with alectinib vs crizotinib (Phase II).

METHODS

- A cost analysis was done focused on comparing the annual costs related with the management of patients with advanced NSCLC ALK+ treated with alectinib vs crizotinib. For the analysis, we considered as the main basis the difference between the healthcare resource utilization in patients with and without CNS metastases, and the incidence of brain metastases related to each treatment.

- The analysis was divided into **two phases**:

Phase I. Disaggregated information about healthcare resource utilization in patients with advanced NSCLC ALK+ with and without CNS metastases, taking into account an annual period.

- Estimation of healthcare resources needed could be made thanks to a panel of expert oncologists, specialists in lung cancer, who provided the disaggregated information for both groups of patients (advanced NSCLC ALK+ with and without CNS metastases) (Figure 1).
- The estimation of the annual cost of management per patient was made by multiplying the annual healthcare resource utilization by each unit cost.
- The unit costs (€, 2018) were obtained from a national cost data base⁸.

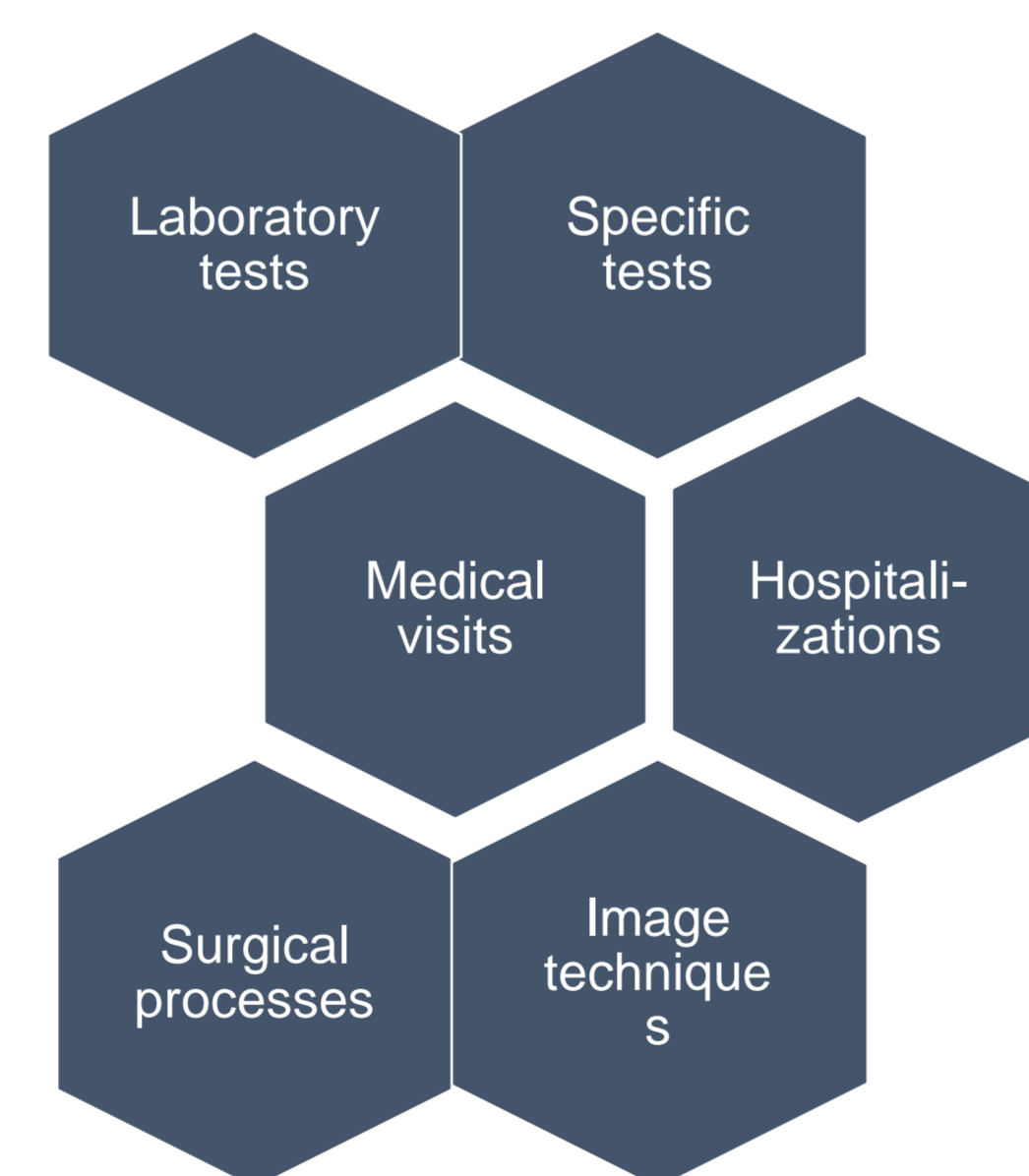


Figure 1. Healthcare resource utilization estimated by the panel of experts.

Phase II. Management annual cost estimation of patients with advanced NSCLC ALK+ treated with alectinib or crizotinib.

- The total annual cost estimated for each alternative was calculated weighting the annual cost of the management of the patients with advanced NSCLC ALK+ (with and without metastases), previously estimated, by the incidence of developing or not the metastases consecutively.
- Thanks to clinical trial ALEX (Phase III, alectinib vs crizotinib) it is possible to estimate the number of patients who would develop CNS metastases after taking one of the pharmacologic treatments (accumulated incidence outcome).
- Of the total patients treated with alectinib, at 12 months, 9,4% had developed CNS metastases compared to 41,1% of the patients treated with crizotinib⁷ (Figure 3).
- As a complementary analysis, we considered the costs related to the management of adverse events (AE) with grades 3-5 in both groups of treatment. The AE frequency for each treatment option was obtained from ALEX clinical trial⁷.

RESULTS

- According to the healthcare resource utilization, estimated by the panel of experts, and its corresponding unit costs, an annual cost of € 6,173.42 per patient with NSCLC ALK+ without CNS metastases, and an annual cost of € 21,637.50 per patient with NSCLC ALK+ with CNS metastases was estimated.
- The presence of brain metastases was considered to be related to an increase of the annual cost of €15,464,08 per patient with NSCLC ALK+ (€ 1,288.67 per month) (Figure 2).
- The costs difference between both subgroups of patients was mainly due to the different frequency of the surgical procedures such as surgical resection, holocraneal radiotherapy or radiosurgery.
- Surgical procedures are necessary to treat CNS metastases and therefore, one of the leading causes of the incremental costs of management in the patient subgroup with CNS metastases.
- Additionally to this, it is important to consider the negative impact these procedures have on patients due to their invasive characteristic.

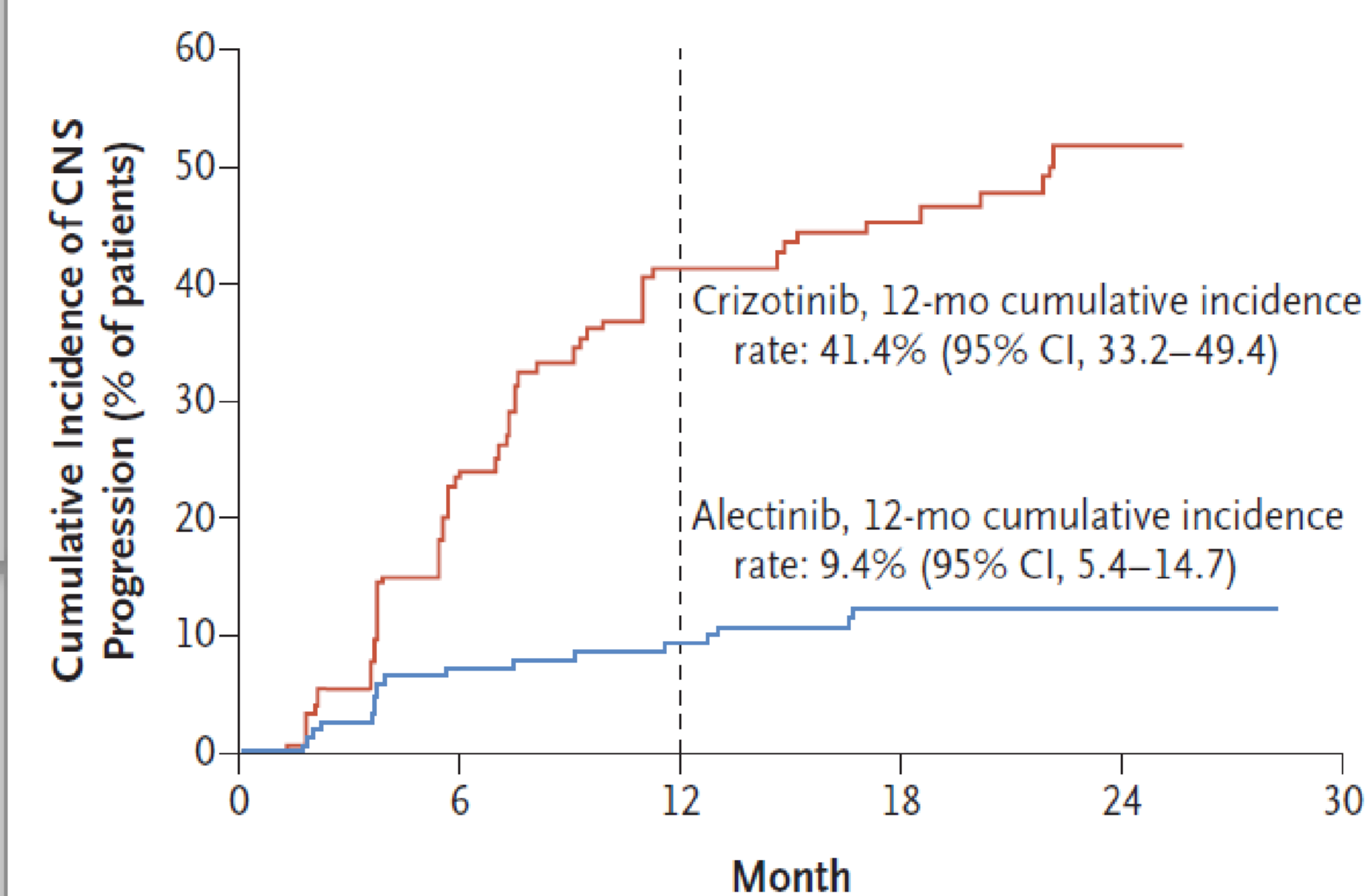


Figure 2. Cumulative Incidence of CNS progression. Data obtained from ALEX study⁷.

- Once estimated the healthcare resource utilization for both subgroups, and considering the accumulated incidence obtained from the ALEX study (Figure 3), the average annual cost of management according to the develop or not of CNS metastases was estimated.
- The annual average cost of management demonstrated in the study was equal to €7,627,04 per patient with advanced NSCLC ALK+ treated with alectinib and €12,575,55 per patient treated with crizotinib.
- The therapy with alectinib was related to a decrease in the management annual cost of patients with NSCLC ALK+, which would mean a €4,948,51 savings per patient/year (Figure 4).**

- The obtained results from this analysis, taking into consideration its strengths and weaknesses, highlight two relevant points:

- ❖ Developing CNS metastases implies a higher healthcare resource utilization comparing to those patients who do not develop them, taking into account the Spanish health system context.
- ❖ The first line treatment with alectinib in patients with advanced NSCLC ALK+ could mean a saving in the annual management costs of patients, thanks to its protective and preventive effect.

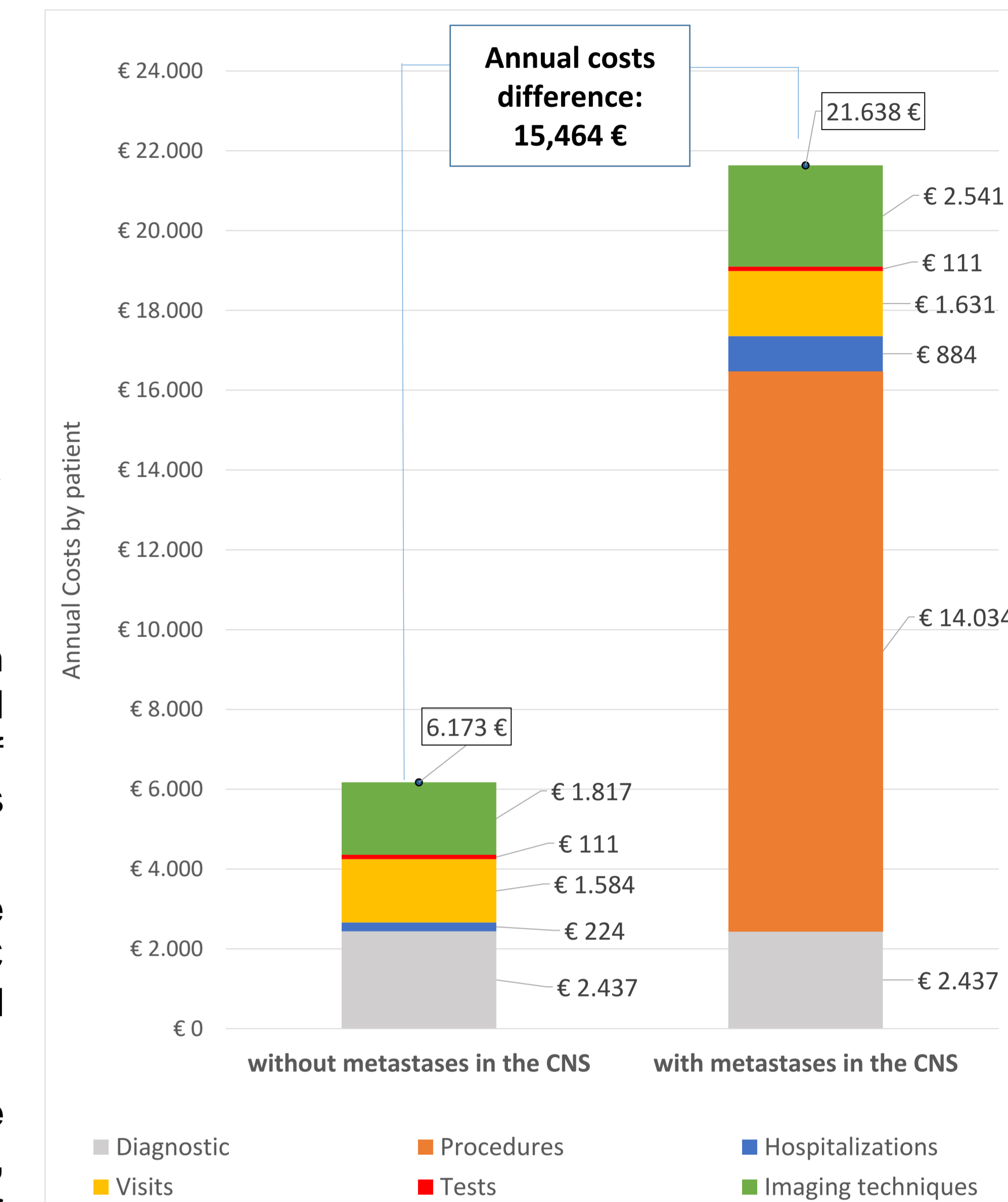


Figure 3. Annual cost related to the management of patients with NSCLC ALK+ without metastases versus patients with CNS metastases.

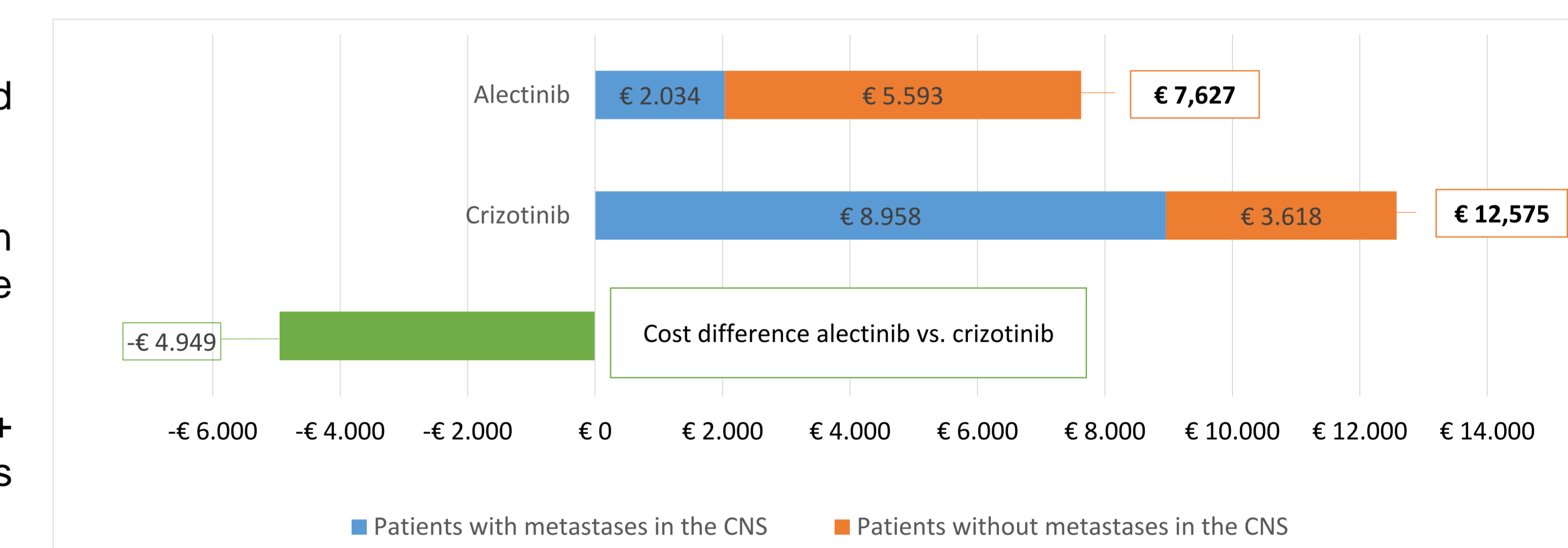


Figure 4. Principal scenario results: average cost per patient treated with alectinib versus crizotinib

CONCLUSIONS

- Noticing the clinical (for the patients), and the economical impact (for the health systems) derived from the appearance of CNS metastases, it is undeniable the necessity to adopt effective strategies to prevent its appearance.
- Starting the treatment of patients with advanced NSCLC ALK+ with a treatment such as alectinib, which has a protective effect against the CNS metastasis appearance, could reduce the annual costs of managing this disease by reducing the healthcare resource utilization related to the CNS metastases.

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