Poster #

Budget Impact Analysis Of Brigatinib For First-Line Treatment Of ALK-Positive Advanced Non-Small Cell Lung Cancer (NSCLC) In Italy

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Background

- In Italy, lung cancer is the leading cause of death among men and the second among women, with non-small-cell lung cancer (NSCLC) representing 80-90% of all malignant pulmonary neoplasms[1,2]
- In patients with advanced/metastatic stages of NSCLC, several genetic alterations have been identified as driver mutations underlying the development of NSCLC, including anaplastic lymphoma kinase (ALK) which represents approximately 3–7% of all NSCLC[2]
- The oral targeted therapies available for patients with NSCLC exhibiting ALK rearrangements are first generation (i.e. crizotinib) and second generation (i.e. alectinib, ceritinib and brigatinib) ALK-inhibitors[3]
- After brigatinib was reimbursed by AIFA as a second-line therapy (2L) in October 2020, reimbursement as a first-line therapy (1L) was extended in December 2020. Brigatinib thus represents a new therapeutic option reimbursed by the Italian National Health System (NHS) for the treatment of patients with ALK + NSCLC *naïve* to ALK inhibitors[4,5]
- Brigatinib complements the therapeutic possibilities already available in 1L (crizotinib, alectinib and ceritinib) and is characterized by a manageable toxicity profile with great ability to penetrate the blood-brain barrier, able both to act against any localization already present and to prevent brain colonization by the disease[6,7]

Objectives

- This study estimated the impact of brigatinib as monotherapy for the 1L treatment of adult patients with ALK+ advanced NSCLC, naïve to ALK inhibitors, on the Italian NHS budget.

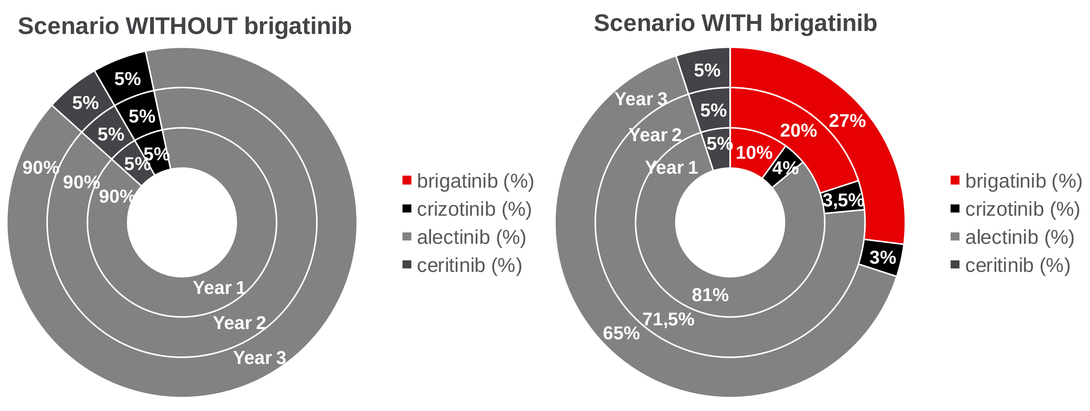
Methods

- A dynamic budget impact model, based on a partitioned survival structure considering four health states and carry-over patients, was developed from the NHS perspective to assess the impact of introducing brigatinib on the Italian budget over a 3-year time horizon
- The analysis compared a scenario where brigatinib is not available (i.e. without brigatinib) and a scenario where brigatinib is reimbursed and progressively replaces crizotinib, alectinib and ceritinib (i.e. with brigatinib). A progressive increase of brigatinib market share of 10%, 20% and 27% was estimated over 3-years, eroding mainly alectinib and crizotinib market shares compared to those of ceritinib
- At year 1, the number of patients with ALK+ NSCLC eligible for ALK-inhibitors were identified with a mixed incidence/prevalence model
- For subsequent years, *carryovers* (i.e. patients continuing previous therapy) were also considered
- Resource consumption varied according to four different health states:
  - Progression-free (i.e. patients treated with molecules in scope who remain with progression-free disease)
  - Post progression without intracranial involvement (i.e. patients treated with molecules in scope who have a disease progression without intracranial involvement based on PFS data, [progression-free survival])
  - Post progression with intracranial involvement (i.e. patients treated with molecules in scope who have a disease progression with intracranial involvement based on CNS-PFS data, [central nervous system PFS])
  - Death (i.e. patients treated with palliative care; all costs in this state were considered as one-off costs)
- A partitioned survival model was used to distribute patients among health states, assuming all patients were progression-free at year one
- Efficacy data of brigatinib and crizotinib have been obtained from Kaplan-Meier curves of the ALTA-1L study[7]
- Relative efficacy of brigatinib vs. alectinib and vs. ceritinib were estimated through Indirect Treatment Comparisons (ITCs) based on the ALEX and ASCEND-4 clinical trials, respectively[7-10]
- Patient resource use was validated by national experts in oncology area
- Unit costs were retrieved from the Italian official drug pricing list (including law discounts where applied) and legislation, guidelines and published literature[11,12]
- The costs included:
  - Drug acquisition and administration for the molecules in scope both in 1L and 2L (applied to progression-free patients)
  - Drug acquisition and administration for the oncologic subsequent therapies (applied to progressing patients with and without intracranial involvement)
  - Costs of managing progression-free disease or patients progressing without intracranial involvement (assumed equal to progression-free patients)
  - Costs of managing patients progressing with intracranial involvement
  - Management of adverse events
  - Palliative care
- All costs were weighted for a 4-week cycle

Results

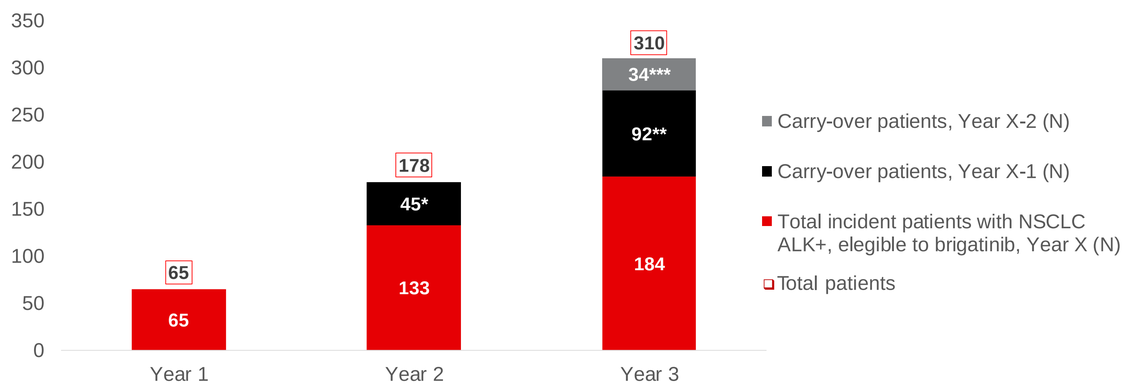
- The target population for ALK inhibitors in scope was estimated at 649, 665 and 681 at year 1, 2 and 3, respectively, considering incident patients
- Patients with ALK+ NSCLC treated in 1L with brigatinib corresponded to 65, 178 and 310 over 3-years, as a result of molecule market shares applied to incident population and carry-over patients added for year 2 and 3 of the analysis
- The NHS expenditure in the scenario without brigatinib resulted in € 27.38 million at year 1, € 67.65 million at year two and € 98.51 million at year 3 compared to € 26.68 million at year 1, € 65.06 million at year 2 and € 93.68 million at year 3 in the new scenario
- Therefore, the introduction of brigatinib is expected to overall reduce the NHS expenditure by € 8.1 million over three years, corresponding to a saving of roughly € 700K at year 1 and € 2.5 million at year 2, and of € 4.8 million at year 3
- Main drivers for savings were the drug acquisition costs
- The introduction of brigatinib could generate savings also in terms of adverse event's management, monitoring for progressing patients, subsequent therapies, and end-of-life care

Figure 1. Number (%) of incident patients with ALK+ NSCLC treated in 1L over 3-years



	Year 1	Year 2	Year 3
Total incident patients ALK+ NSCLC	**649**	**665**	**681**

Figure 2. Brigatinib patient pool considering *carryover* patients



* Calculated as the number of incident patients at Year X-1 (65), multiplied by the percentage of progression-free patients after one year of treatment (69.30%)
** Calculated as the number of incident patients at Year X-1 (133), multiplied by the percentage of progression-free patients after one year of treatment (69.30%)
*** Calculated as the number of incident patients at Year X-2 (65), multiplied by the percentage of progression-free patients after two years of treatment (52.90%)

Figure 3 Results of Budget Impact Analysis

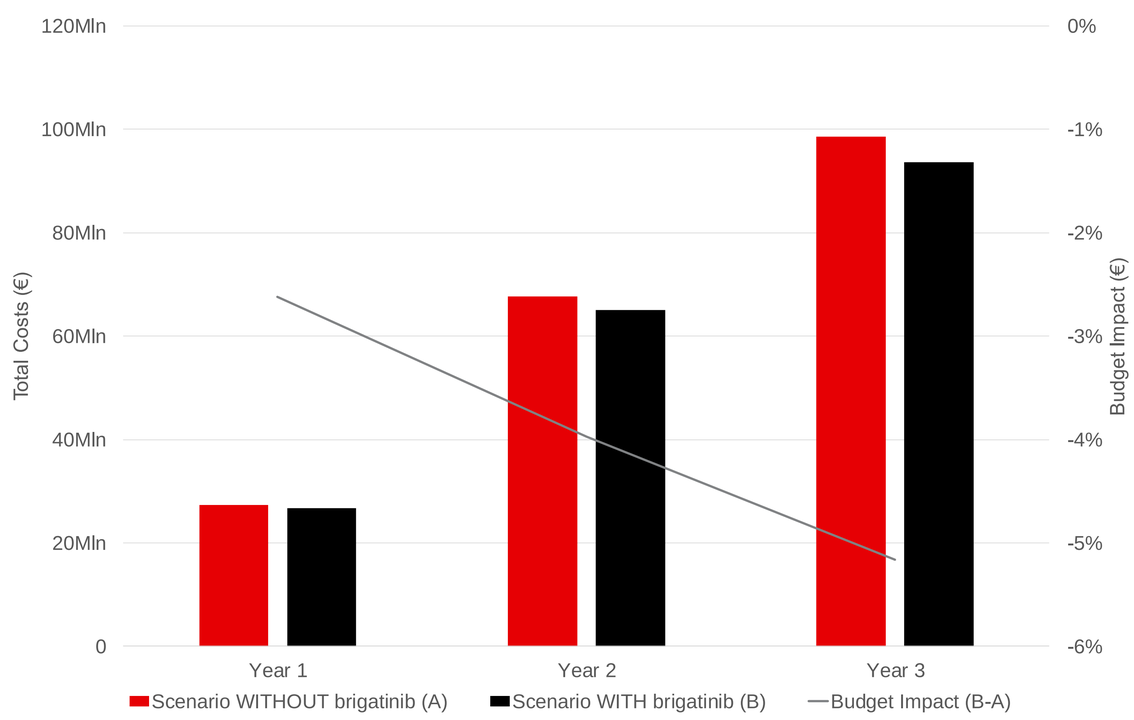
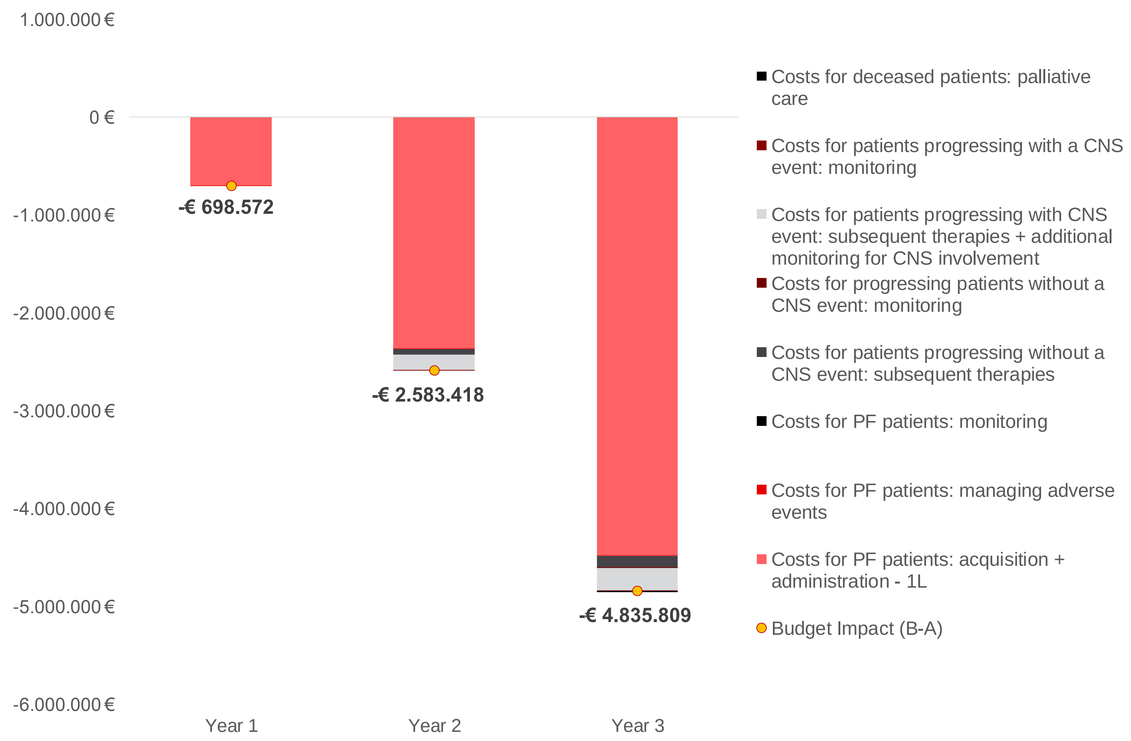


Figure 4. Cost components of Budget Impact



Conclusions

- The introduction and progressive use of brigatinib in Italy is expected to determine an increase in health benefits and generate savings in the expenditure incurred by the NHS for metastatic/advanced ALK+ NSCLC drug therapies
- The cost saving effect is coupled with benefits in terms of clinical efficacy, statistically superior to crizotinib, superior to ceritinib, and comparable to alectinib
- Brigatinib is a convenient dosing regimen with a different tolerability profile to alectinib and offers patients and clinicians another therapeutic choice

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Abbreviations

ALK = Anaplastic Lymphoma Kinase; NSCLC = Non-small Cell Lung Cancer; NHS = National Healthcare System; PFS = Progression Free Survival; CNS = Central Nervous System; ITC = Indirect Treatment Comparison; MAIC = Matched-Adjusted Indirect Comparison; AEs = Adverse Events

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