Can sequencing of TKI inhibitors first line advanced non-small cell lung cancer with improve clinical outcomes and cost of treatment in common EGFR+ mutations in Spain?

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OBJECTIVE

The model aims to compare the time on treatment (ToT) and the TKI treatment-related costs of sequential treatment with afatinib vs. first-line osimertinib treatment, in patients with EGFR+ NSCLC in Spain.

METHODS

- **Model design**: A decision-analytic model was developed to compare the results of two treatment options:
  - Sequential treatment with afatinib plus osimertinib (Scenario 1): Patients received first-line afatinib treatment. Upon disease progression, T790M+ patients received second-line osimertinib, and subsequent chemotherapy upon further disease progression. T790M- patients received second-line chemotherapy.
  - First-line osimertinib treatment plus chemotherapy (Scenario 2): Patients received first-line osimertinib treatment. Upon disease progression, patients received second-line chemotherapy.

- **Population**: EGFR+ mutation NSCLC patient12.
- **Time horizon**: Time period from initiation of first-line TKI treatment to best supportive care (BSC) or death.
- **Perspective**: Spanish National Health System (NHS).
- **Model inputs**: EGFR T790M mutation rate and successive-line treatment rates are described in Figure 1.

- **Clinical input**:
  - ToT was estimated using individual patient level data reconstructed from published progression free survival (PFS) curves13,14, using the Gini method15. The relative benefit of re-treatment, costs of TKI inhibitors were included using adjusted indirect treatment comparison (ITC). The mean ToT was extrapolated to a common time horizon using the Weibull distribution.
  - Adverse event (AE) frequencies for anemia, diarrhea, dyspnea, fatigue, leukopenia, neutropenia, paronychia, rash and stomatitis were obtained from the literature16-18. Only grade ≥3 AE were considered.
  - In addition to ToT, the model also calculated quality adjusted life months (QALM). The QALM calculation was based on progression status, treatment line and AE profile.

- **Cost input**: Direct costs were included (Table 1). They were obtained from the literature and updated to €2019 according to the consumer price index6, when applicable.

- **Sensitivity analyses**: A sensitivity analysis was performed to analyze the impact of osimertinib potential price change (25% and 40% discount vs. current list price) expected with the approval of the new indication (1st line in EGFR+ NSCLC patients) in Spain.

INPUT

- **Drug acquisition (first-line)**: afatinib €518,25; osimertinib €688,92; and chemotherapy €1,892,19.
- **Testing**: For all patients progressing on 1st line afatinib.
- **COST** (€ 2019) UNIT REFERENCE
  - T790M test: €90,07 Per test 18
  - AE management: Anemia €111,13 Per episode 19
  - Diarrhea €582,05 Per episode 19
  - Dyspnea €43,95 Per episode 20
  - Fatigue €178,71 Per episode 19
  - Leukopenia €633,78 Per episode 19
  - Neutropenia €914,87 Per episode 19
  - Paronychia €0 Per episode 19
  - Rash €2,15 Per episode 19
  - Stomatitis €376,17 Per episode 19

Table 1. Costs considered in the model (expressed in € 2019). *without drug wastage adjustment.

RESULTS

The model showed that sequential treatment results in:

- A gain in efficacy: sequential treatment may lead to improved tumour control with an additional 4.4 months in expected ToT in patients progressing on afatinib plus chemotherapy (28.1 vs. 24.8 months, respectively) (Figure 2).

- Improved quality and quantity of life: the ToT benefit is translated into a gain of quality-adjusted life months (QALM) (sequential treatment 26.5 vs. first-line osimertinib 17.4 months), suggesting a favourable risk benefit profile for the seqeunce.

- Reduced costs: sequential treatment offers potential cost savings when compared to first-line osimertinib treatment (€37,338 per patient). In the base case scenario, in the sensitivity analyses, cost savings are still observed with sequential treatment (figure 3).

CONCLUSION

The model showed that TKI sequencing could lead to an increase of ToT and QALM in first-line treatment in NSCLC EGFR+. Additionally, utilizing first-line afatinib may result in a total treatment-related cost reduction, generating potential cost savings for the Spanish NHS. Further clinical research is required to assess the relative benefit of the two treatment strategies. In addition, more comprehensive economic evaluations should be considered when mature overall survival is reported for osimertinib.

LIMITATIONS

- There are currently no head-to-head clinical trials comparing the sequential therapy with afatinib vs. first-line osimertinib treatment. Hence, mean PFS data had to be obtained from their respective pivotal trials.

- The model assumed that TKI treatment is discontinued upon disease progression. This may not reflect the clinical practice. Also, ToT may be underestimated.

- The model was based on TKI list price. As hospital drugs have dual price in Spain, cost for TKI treatment could be lower than described.

- An AE rates were not reported by mutation type in the respective trials, the frequency of AE were assumed to be constant across the different EGFR mutation subtypes.

- T790M test was based on data from one region. Cost may vary in other regions.