Prospective efficacy of osimertinib in circulating tumour DNA (ctDNA) *T790M*-mutant non-small cell lung cancer (NSCLC) patients

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BACKGROUND

Liquid biopsy circulating tumor DNA (ctDNA) analysis in advanced *EGFR*-mutant NSCLC patients is an approved tool for molecular profiling and disease surveillance when tissue is not available (1).
Long-term efficacy of osimertinib in patients with the *T790M* resistance mutation positive detected only by ctDNA (without tissue information) has not been fully validated.

OBJECTIVES

The objectives were to assess:

- Proportion of patients with acquired ctDNA-*T790M* positive;
- Overall survival (OS) of the overall advanced *EGFR*-mutant population, as well as, OS comparison for *T790M* positive *vs.* negative.

Also, for those *T790M*-positive NSCLC patients who received osimertinib in a real world data we assessed:

- Response rate (RR) by investigator and,
- Progression free survival (PFS) with osimertinib.

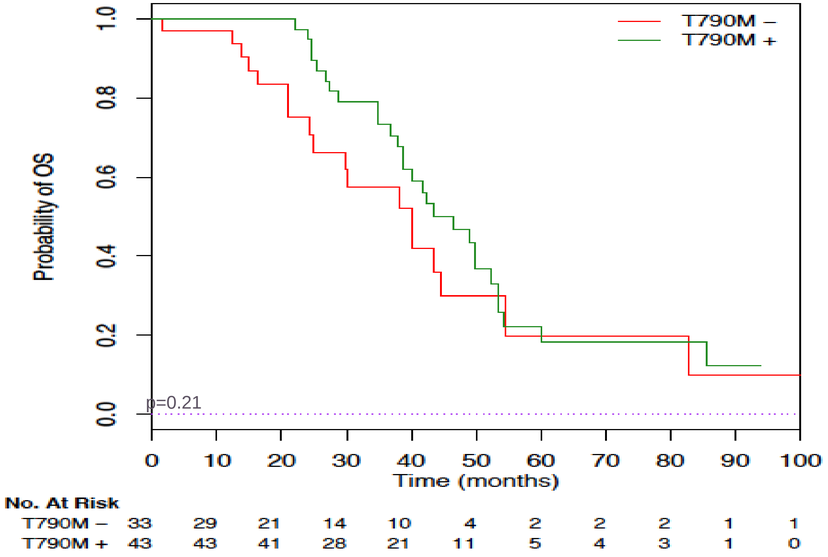
METHODS

Prospective study in non feasible tissue re-biopsy *EGFR*-mutant advanced NSCLC patients with acquired resistance to EGFR TKI who received osimertinib (80 mg daily, EAP or approval) at RECIST progression according to *ct*DNA *T790M* mutational status using InVisionSeq™ results.
The RR was evaluated according to RECIST 1.1 by investigator, and the PFS was calculated from the date of osimertinib initiation until the date of progression or death, or the date of last follow-up.

RESULTS

- We recruited 76 patients (71% female, median age 64 years, 72% *Del19* EGFR mutation, 71% never-smokers).
- The *ct*DNA *T790M* mutation was detected in 56% (N=43) of NSCLC patients.
- Median OS of advanced *EGFR*-mutant population was 42.4 months (mo.) (95% CI:38.6 - 49.8).
  - According to T790M status, median OS was 46.6 mo. (95% CI: 38.8 - 55.5) and 40.0 mo. (95% CI: 29.8 - NR) for *T790M*-positive and *T790M*-negative NSCLC patients, respectively (p=0.21). Both cohorts had already received a median of 3 previous treatment lines (Figure 1).
- In 36 *T790M*-positive NSCLC patients who received osimertinib:
  - The RR was 55% (PR: 55%, SD 27.5% and PD: 12.5%)
  - The median PFS was 7.9 months (95% CI: 5.6-12.3).
  - Median OS on osimertinib among 10 patients with brain and / or leptomeningeal metastases at baseline was of 18 mo. (95%: 12-NR).

Figure 1



CONCLUSIONS

In patients with acquired resistance to first- or second-generation EGFR TKIs, ctDNA *T790M* detection by InVisionSeq™ is equivalent to what has been reported in tissue biopsy. Osimertinib has clinical benefit in patients for which the *T790M* resistance mutation is detected only through a liquid biopsy procedure.

Bibliography: (1) Remon et al. Ann Oncol 2017