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Introduction

- EGFR exon 19 deletion can be classified into subtypes based on the specific deletion pattern.
- Only a few studies have investigated the prognostic impact of exon 19 deletion subtypes in patients treated with osimertinib, and their findings have been inconsistent [1,2].
- The biological mechanisms underlying the subtype-specific prognostic differences among *EGFR* exon 19 deletions remain unclear.

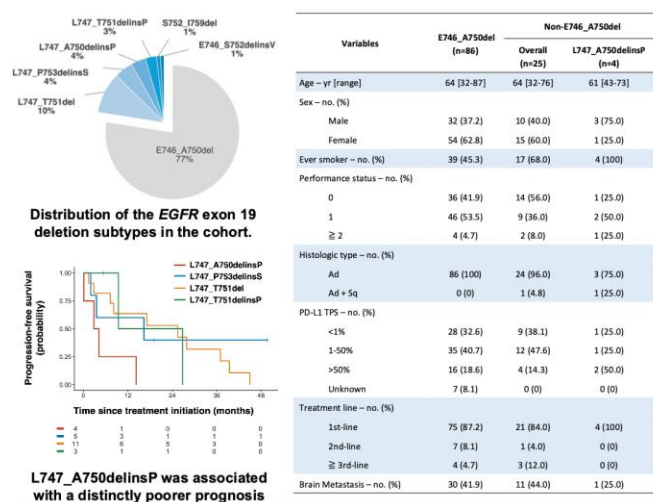
Objectives:

- To compare survival outcomes among *EGFR* exon 19 deletion subtypes in Japanese patients with NSCLC treated with osimertinib.
- To investigate differences in co-occurring genetic alterations among the exon19 deletion subtypes

Methods

- We retrospectively reviewed data from patients with advanced NSCLC harboring *EGFR* exon 19 deletions with confirmed subtypes who were treated with osimertinib at the five national center or university hospitals in Japan.
- Whole-exome sequencing data were collected from AACR GENIE v16.1-public and MSK-CHORD databases.

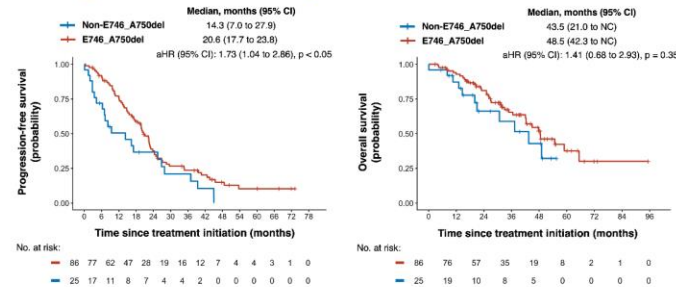
Baseline characteristics



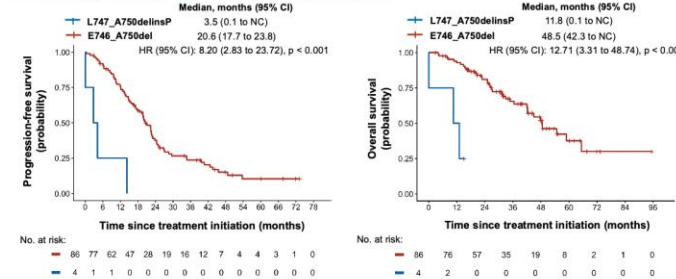
L747_T751delinsP was associated with a distinctly poorer prognosis

Clinical outcomes across exon 19 del subtypes

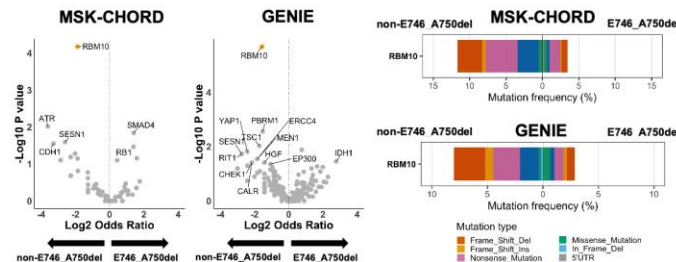
E746_A750del vs. non-E746_A750del



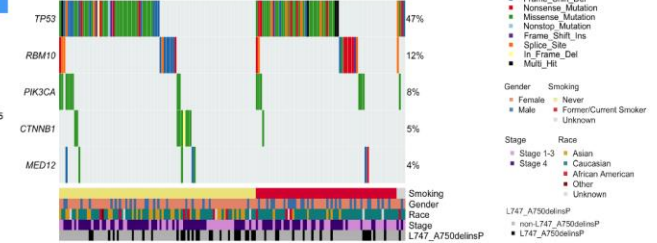
E746_A750del vs. L747_T751delinsP



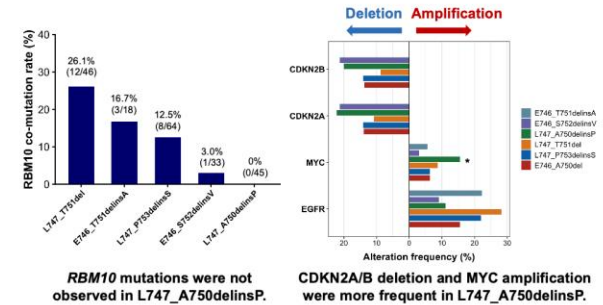
Enrichment of RBM10 mutation in non-E746_A750del



non-E746_A750del patients in MSK-CHORD



RBM10 mutation tended to be mutually exclusive with TP53 mut. No difference in frequencies according to smoking history, gender, race or stage.



RBM10 mutations were not observed in L747_T751delinsP. CDKN2A/B deletion and MYC amplification were more frequent in L747_T751delinsP.

Discussion

- Non-E746_A750del subtypes, especially L747_T751delinsP showed poorer prognosis compared to E746_A750del.
- Increased frequencies of *RBM10* mutation, *CDKN2A/B* deletion and *MYC* amplification might contribute to the poor prognosis in these subtypes.
- Since *RBM10* deficiency confers resistance to apoptosis [3], combination strategies with chemotherapy may need to be selected in these subtypes.
- As treatment options in *EGFR* mut NSCLC continue to expand, further studies are warranted to determine whether exon 19 deletion subtypes remain clinically relevant.

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