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Introduction

- Around 7–23% of patients with *EGFR* + NSCLC have tumours harbouring uncommon mutations (non-Del19/L858R); up to 25% of *EGFR* + tumours harbour compound mutations (>1 *EGFR* mutation)¹
- There is a lack of clinical data assessing the activity of *EGFR* TKIs in patients with NSCLC harbouring uncommon *EGFR* mutations
- Increased use of NGS for mutation detection and plasma-based assays will increase identification of uncommon *EGFR* mutations in everyday clinical practice²
- Previously, we developed a database of 693 patients with NSCLC and uncommon *EGFR* mutations treated with afatinib in RCTs and real-world practice (https://www.uncommonegfrmutations.com). Here we provide an update of >1000 patients, with more data on specific mutations

EGFR +, epidermal growth factor receptor mutation positive; NGS, next generation sequencing; NSCLC, non-small cell lung cancer; RCTs, randomised controlled trials; TKI, tyrosine kinase inhibitor

Methods

Aims

- 1) Investigate afatinib as a treatment for patients with uncommon *EGFR* mutations
- 2) Update the uncommon mutations database with new findings, with a focus on individual ex20ins and 'other' uncommon mutations

Patients categorised into four groups



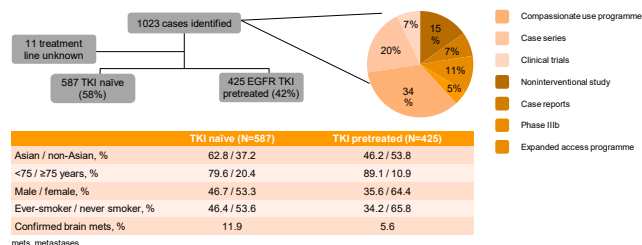
Key endpoints

- TTF
- ORR

*Any mutation not represented in the other groups; †Defined as ≥2 mutations with at least one uncommon mutation. ex20ins, exon 20 insertions; ORR, objective response rate; TTF, time to treatment failure

Results

1023 patients were identified, with most patients treated in clinical studies/compassionate use programmes



Key findings and conclusions

- Data are in line with previously published data
- Afatinib demonstrated strong activity against major uncommon, compound, and 'other' uncommon mutations
- Afatinib showed excellent activity against E709X and L747X mutations in TKI-naïve patients
- Afatinib demonstrated activity against certain exon 20 insertions at residues A763, M766, N771, and V769
- Afatinib showed activity against the osimertinib resistance mutations G724S, L718Q, L718V, and C797S

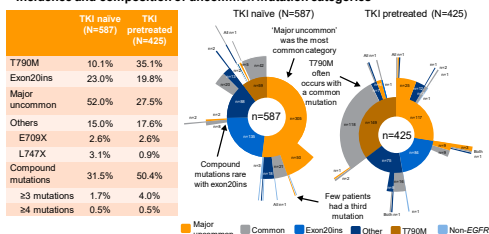


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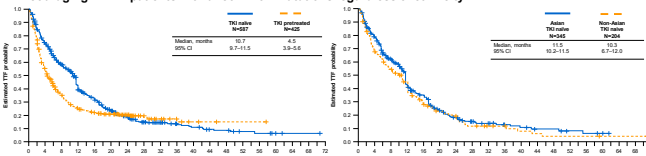
Results (cont'd)

Incidence and composition of uncommon mutation categories



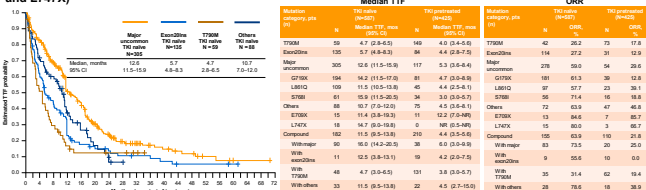
Results (cont'd)

Encouraging TTF in patients with uncommon mutations regardless of ethnicity



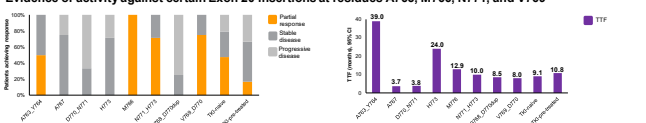
• TTF was also encouraging in patients with uncommon mutations, regardless of presence of brain metastases: 8.2 months (95% CI: 5.5–12.0)

Strong TTF and ORRs against major uncommon, compound and 'other' uncommon mutations (including E790X and L747X)



CI, confidence interval; pts, patients; NR, not reached

Evidence of activity against certain Exon 20 insertions at residues A763, M766, N771, and V769



Evidence of activity against osimertinib resistance mechanisms

Patients with known osimertinib resistance mutations



*Two patients received afatinib combined with osimertinib. ORR, overall response rate; DCR, disease control rate

Evidence of activity of afatinib after osimertinib

- In the 15 pts who received afatinib after osimertinib, ORR was 36% and DCR was 100%



References

1. Yang JC, et al. J Thorac Oncol 2020;15:803-15; 2. Kobayashi Y & Mitsudomi T. Cancer Sci 2016;107:1179-86