

James Chih-Hsin Yang,^{1*} Martin Schuler,² Sanjay Popat,^{3,4} Satoru Miura,⁵ Keunchil Park,⁶ Antonio Passaro,⁷ Filippo De Marinis,⁷ Flavio Solca,⁸ Angela Mårten,⁹ Edward S. Kim¹⁰

¹Department of Medical Oncology, National Taiwan University Cancer Center, Taipei, Taiwan; ²West German Cancer Center, University Duisburg-Essen & German Cancer Consortium (DKTK), Partner site University Hospital Essen, Essen, Germany; ³Lung Unit, Royal Marsden National Health Service Foundation Trust, London, United Kingdom; ⁴The Institute of Cancer Research, London, United Kingdom; ⁵Department of Internal Medicine, Niigata Cancer Center Hospital, Niigata, Japan; ⁶Division of Hematology/Oncology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; ⁷Division of Thoracic Oncology, IEO, European Institute of Oncology IRCCS, Milan, Italy; ⁸Boehringer Ingelheim RCV GmbH & Co KG, Vienna, Austria; ⁹Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; ¹⁰City of Hope National Medical Center, Los Angeles, CA, USA

Introduction

- Around 7–23% of patients with EGFRm + NSCLC have tumours harbouring uncommon mutations (non-Del19/L858R); up to 25% of EGFRm + 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

EGFRm+, 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



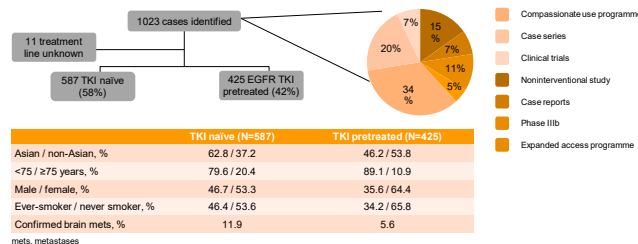
Key endpoints

- 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

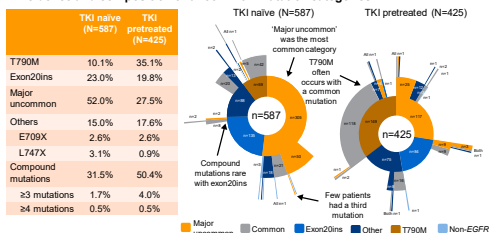


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*Corresponding author email address: chihyang@ntu.edu.tw

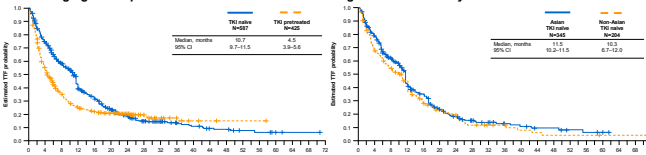
Results (cont'd)

Incidence and composition of uncommon mutation categories



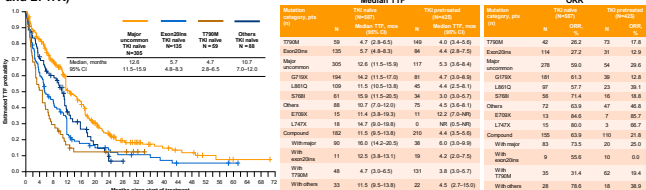
Results (cont'd)

Encouraging TTF in patients with uncommon mutations regardless of ethnicity



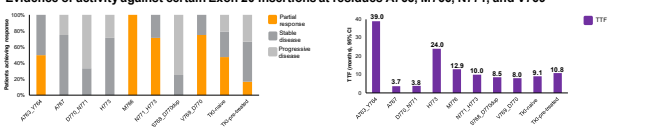
* TTF was also encouraging in patients with uncommon mutations, regardless of presence of brain metastases: 8.2 months (95% CI: 5.5–12.0)

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



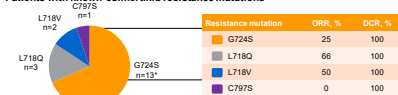
CI, confidence interval; pts, patients; NR, not reached

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