30P: Uncommon EGFR Kinase Domain Mutations and Responses to EGFR Inhibitors: A Systematic Review

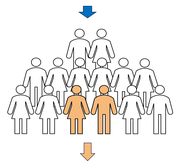
Maxime Borgeaud[1], Kaushal Parikh[2], Giuseppe Luigi Banna[3], Floryane Kim[1], Timothée Olivier[1], Xiuning Le[4], Alfredo Addeo[1]

1. Oncology Department, University Hospital Geneva, Switzerland ; 2. Division of Medical Oncology, Mayo Clinic, Rochester, USA ; 3. Portsmouth Hospitals University NHS Trust, Portsmouth, UK ; 4. Department of Thoracic Head and Neck Medical Oncology, MD Anderson Cancer Center, Houston, USA.

Introduction

Uncommon EGFR mutations represent a rare subgroup of Non-small-Cell Lung Cancer (NSCLC). Data on the efficacy of different generations of tyrosine kinase inhibitors (TKIs) in these rare mutations is limited to mostly retrospective small cohorts, as these patients were usually excluded from clinical trials.

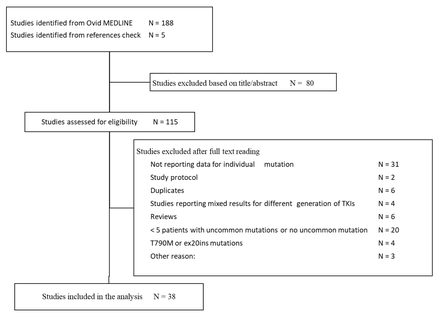
Patients with EGFR-mutant NSCLC



10-15%
Uncommon EGFR Mutations
(= other than ex20ins or T790M)

Method

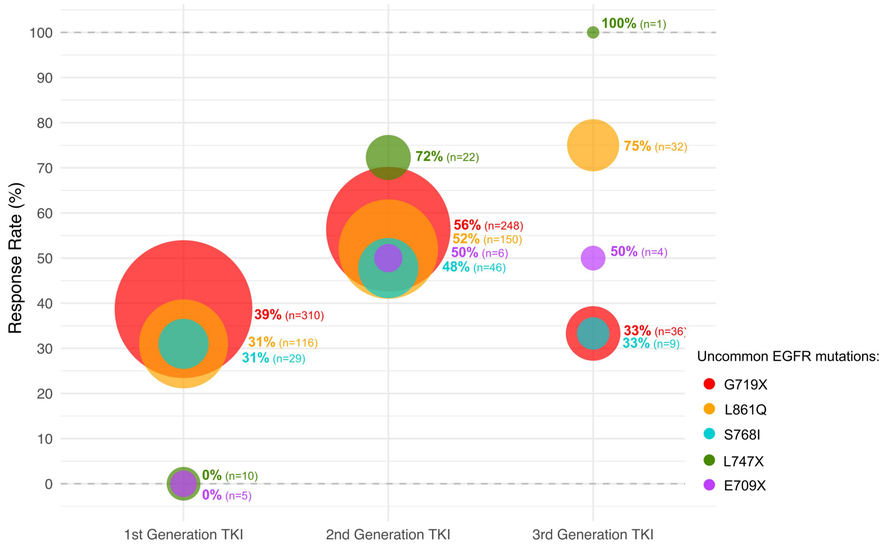
Systematic Review (PRISMA) on the efficacy of TKIs in patients with uncommon EGFR mutations other than ex20ins or T790M. Response rates (RRs) for different generations of TKIs were determined for individual uncommon mutations, compound mutations, and according to classical-like and P-loop alpha helix compressing mutations classes (PACC).



→ 38 studies included, 1836 patients

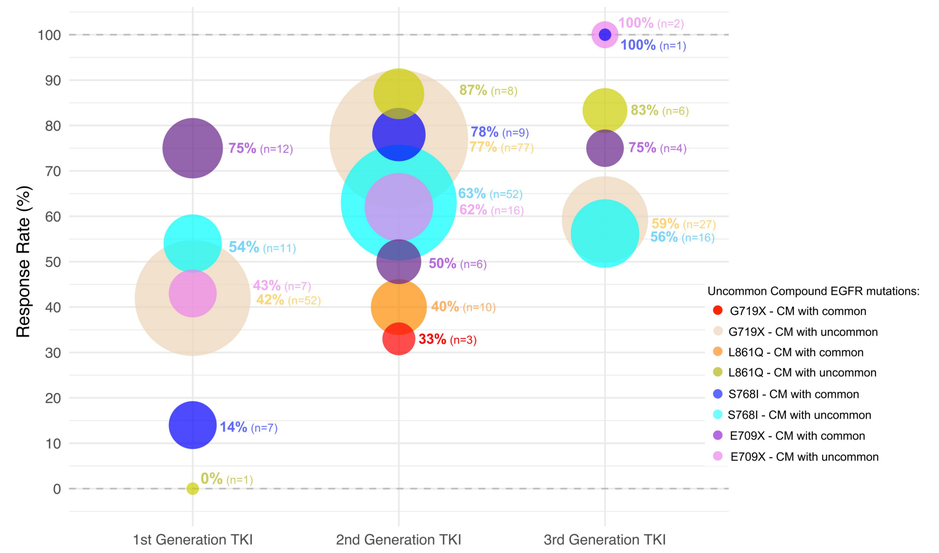
Results

Single Uncommon Mutations



Each bubble represents the response rate for a mutation (color-code) with response rate and number of patients (n). The size of each bubble is proportional to the number of patients.

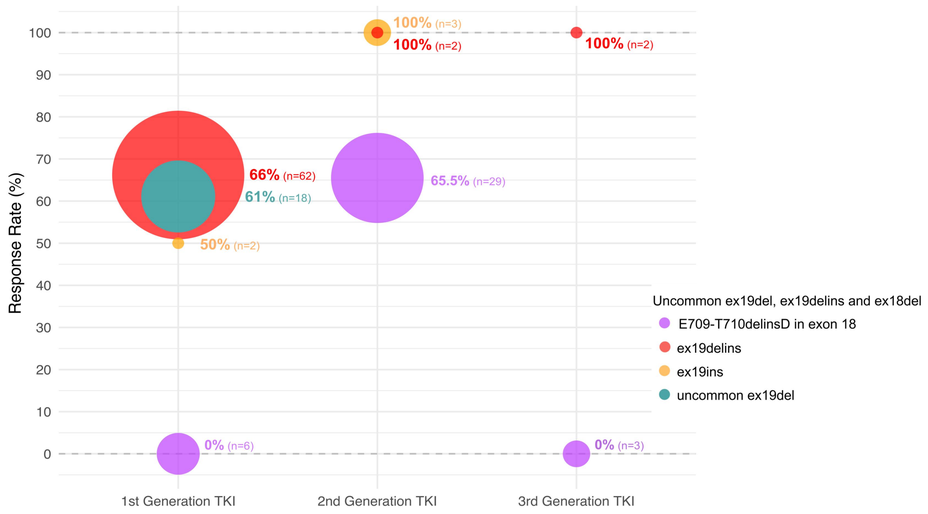
Uncommon Compound Mutations



Response Rates by MDACC - structure-based classification[1]

Generation TKI	1st	2nd	3rd
(Uncommon) Classical-like mutations (N=343)	35.4% (95%CI: 27.2-44.2%)	51.9% (95%CI: 44.4-59.3%)	68.3% (95%CI : 50.6-86%)
PACC mutations (N=811)	37.2% (95%CI: 32.4-42.1%)	59.6% (95%CI: 54.8-64.3%)	45.4% (95%CI : 32.5-58.3%)

Uncommon ex19del, ex19delins and ex18del



CONCLUSION

This systematic review supports the use of 2nd generation TKI afatinib for G719X, S768I, E709X and L747X mutations, as well as for compound uncommon mutations. For other uncommon mutations such as L861Q, 3rd generation TKI, such as osimertinib, seems a reasonable option could also be considered, considering given its activity and toxicity profile.

Reference:
1. Robichaux JP, et al. Nature 2021;597:732–7

Corresponding authors: maxime.borgeaud@hug.ch; alfredo.addeo@hug.ch

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