

# DISTRIBUTION AND DETECTABILITY OF *EGFR* EXON 20 INSERTION VARIANTS IN NON-SMALL CELL LUNG CANCER

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# Presenter DISCLOSURES

<b>Ineligible Company</b> (formerly: Commercial Interest)	<b>Relationship(s)</b>
Pfizer	Personal fees
AstraZeneca	Personal fees
Takeda/ARIAD	Personal fees
Roche/Genentech	Personal fees
Daiichi Sankyo	Personal fees
Janssen/J&J	Personal fees
Turning Point Therapeutics	Stock ownership
Elevation Oncology	Stock ownership

# Introduction

- *EGFR* ex20ins mutations comprise a diverse array of insertion variants and represent 5%–10% of *EGFR* mutations in NSCLC<sup>1-4</sup>
- Mobocertinib is a first-in-class, potent, oral TKI designed to target *EGFR* ex20ins mutations<sup>5</sup>
- Identifying patients with *EGFR* ex20ins is challenging due to the limited coverage of PCR assays
- Use of NGS to identify *EGFR* ex20ins is relatively recent but will become increasingly important as more treatments targeting *EGFR* ex20ins are developed
- We describe the distribution of *EGFR* ex20ins variants in NSCLC patients in a global clinical trial and from real-world data in the United States, Germany, and Japan, and evaluate the ability of PCR versus NGS to identify *EGFR* ex20ins in NSCLC

*EGFR*, epidermal growth factor receptor gene; ex20ins, exon 20 insertion; NGS, next-generation sequencing; NSCLC, non-small cell lung cancer; PCR, polymerase chain reaction; TKI, tyrosine kinase inhibitor

1. O'Kane GM, et al. *Lung Cancer*. 2017;109:137-144. 2. Oxnard GR, et al. *J Thorac Oncol*. 2013;8:179-184. 3. Kosaka T, et al. *Cancer Res*. 2017;77:2712-2721. 4. Jorge SE, et al. *Braz J Med Biol Res*. 2014;47:929-939. 5. Gonzalez F, et al. *Cancer Discov*. 2021 Feb 25; candisc.1683.2020. doi: 10.1158/2159-8290.CD-20-1683.

# Methods

- A retrospective analysis was conducted in patients with NSCLC whose *EGFR* ex20ins mutations were identified by sequencing tests, including NGS, from 1 global mobocertinib trial (NCT02716116) and 3 real-world data sources:

## Global Mobocertinib Study 101

- This phase 1/2 study was conducted to evaluate the safety, pharmacokinetics, and anti-tumor activity of mobocertinib in participants with NSCLC (n=157; Data cutoff: 1 Nov 2020)

## German Chart Review Study

- Data on patients with NSCLC Stage IV with *EGFR* ex20ins mutations were collected from 12 academic thoracic oncology centers across Germany (n=80)

## US COTA EHR Database

- The COTA database comprises longitudinal data abstracted from EHRs of healthcare provider sites in routine practice in the United States (n=30; Data cutoff: 30 Nov 2020)

## Japan LC-SCRUM Registry

- The LC-SCRUM is a cancer genome screening project to construct a large-scale patient registry of rare subtypes of lung cancer in Japan (n=95; Data cutoff: 31 Dec 2019)

- Frequencies and percentages were calculated for each unique variant
- Proportions of patients with *EGFR* ex20ins variants identifiable by 6 commercially available PCR kits were projected based on manufacturer-provided coverage information
  - Roche cobas® *EGFR* Mutation Test v2
  - QIAGEN therascreen *EGFR* RGQ PCR Kit v2
  - AmoyDx *EGFR* 29 Mutations Detection Kit
  - PANAGENE PNAClamp™ *EGFR* Mutation Detection Kit v2
  - DIACARTA QClamp® *EGFR* Mutation Detection Test
  - BIOCARTIS Idylla™ *EGFR* Mutation Assay

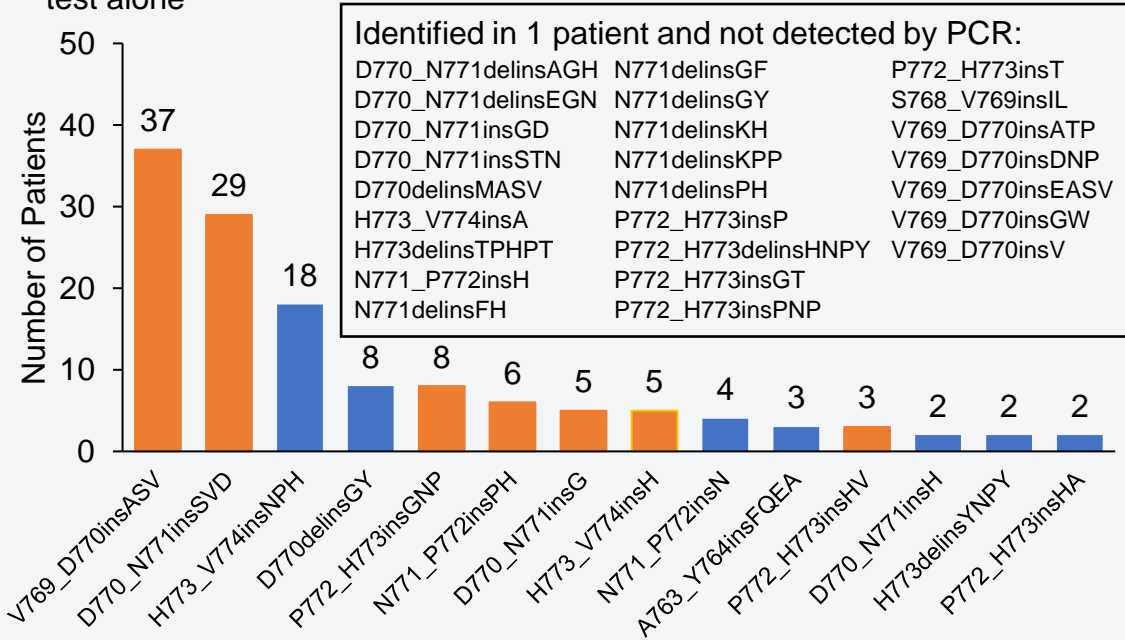
*EGFR*, epidermal growth factor receptor gene; EHR, electronic health records; ex20ins, exon 20 insertion; NGS, next-generation sequencing; NSCLC, non-small cell lung cancer; PCR, polymerase chain reaction

# Identification of *EGFR* ex20ins Variants by Sequencing

- A total of 63 unique *EGFR* ex20ins variants identified across 4 databases
  - The most common variants (V769\_D770insASV and D770\_N771insSVD) accounted for 33%–46% of patients across data sets

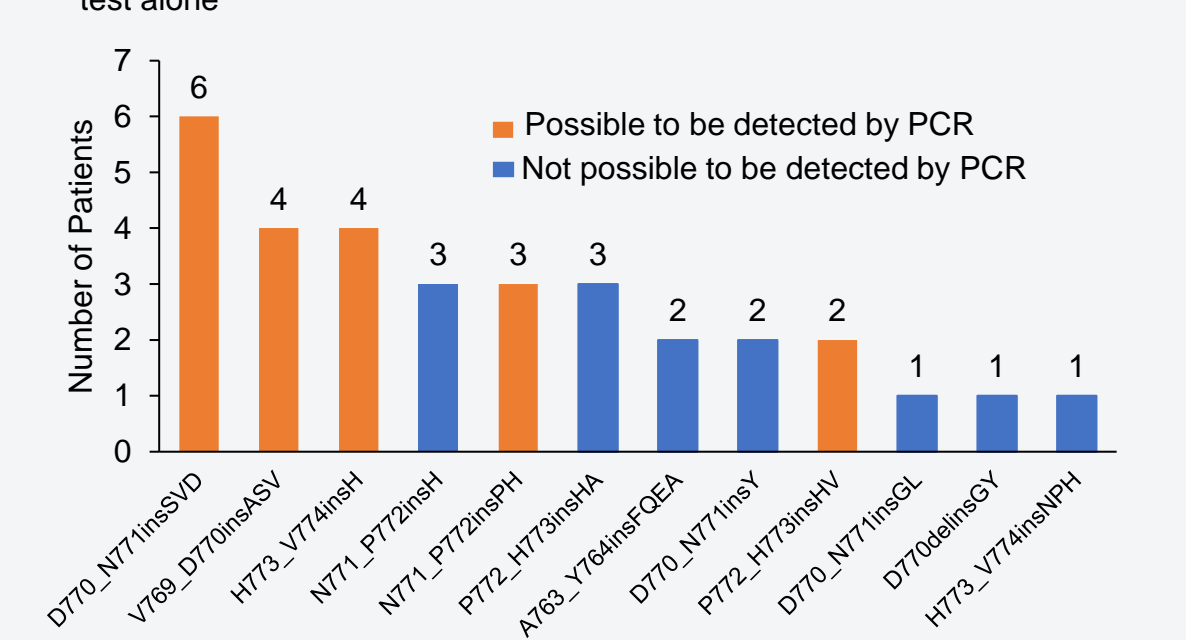
## Global Mobocertinib Study 101 Database (N=157)

- 39 unique variants identified in Study 101
- Only 7 variants could have been identified by PCR tests
- Only 14.0%–48.4% of patients could have been detected by any single PCR test alone



## US COTA EHR Database (N=30)<sup>a</sup>

- 12 unique variants identified in the COTA database
- Only 5 variants could have been identified by PCR tests
- Only 13.3%–46.7% of patients could have been detected by any single PCR test alone



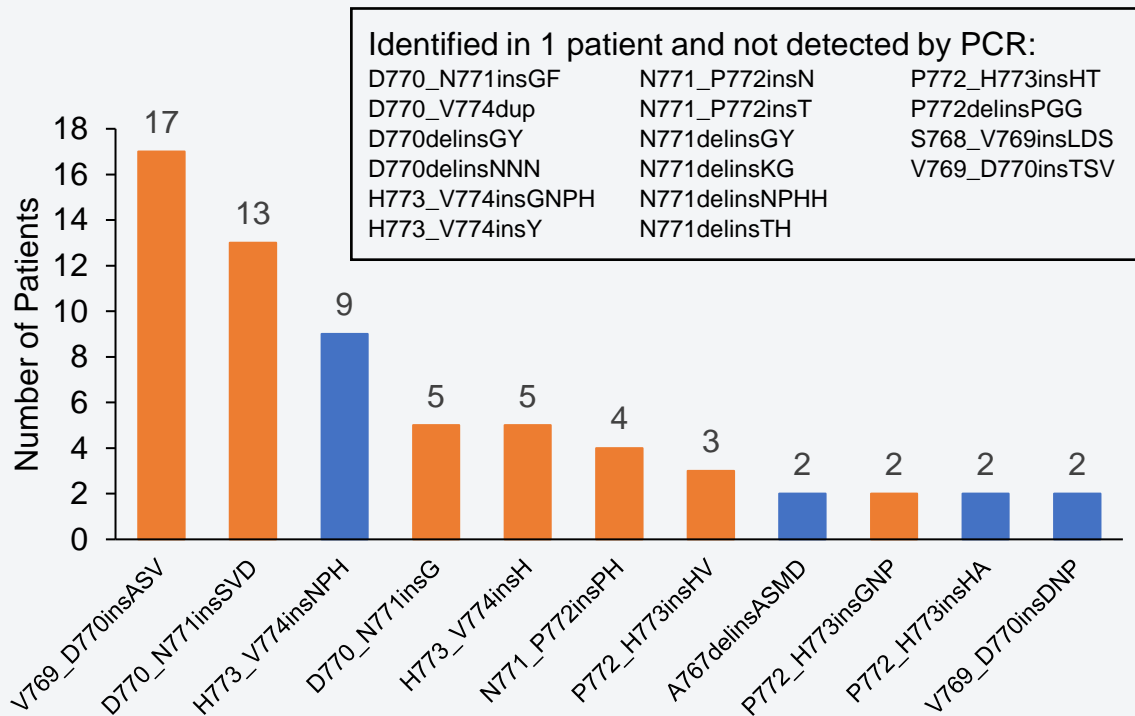
<sup>a</sup> Two patients had 2 ex20ins mutations

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# Identification of *EGFR* ex20ins Variants by Sequencing (con't)

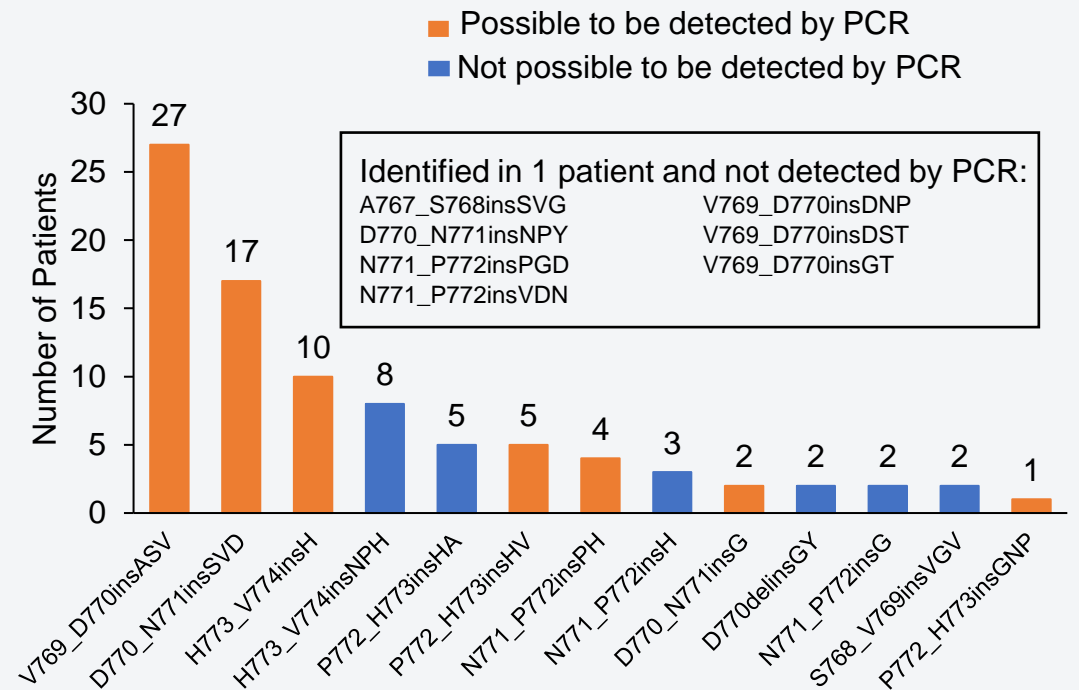
## German Chart Review Study (N=80)

- 27 unique variants identified in the Germany study
- Only 7 variants could have been identified by PCR tests
- Only 17.5%–50.0% of patients could have been detected by any single PCR test alone



## Japan LC-SCRUM Study (N=95)

- 20 unique variants identified in the Japan database
- Only 7 variants could have been identified by PCR tests
- Only 21.1%–58.9% of patients could have been detected by any single PCR test alone



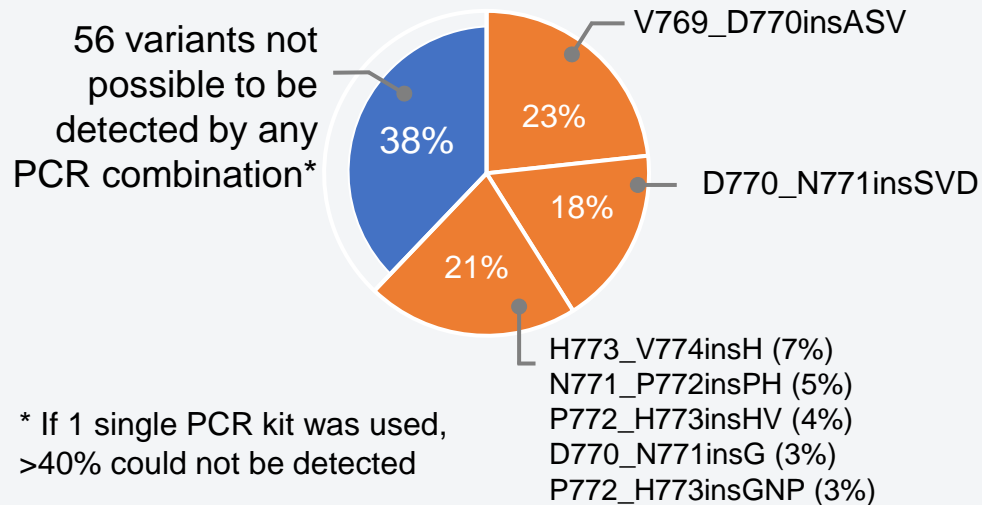
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# Conclusions

- The spectrum of *EGFR* ex20ins variants is diverse, with a total of 63 unique ex20ins variants across data sources

## ex20ins Variant Frequencies in the 4 Pooled Data Sets

- 7 variants possible to be detected by 1 of the PCR tests



- Although commonly used in clinical diagnosis, PCR tests have different and limited coverage for detecting *EGFR* ex20ins
  - There is considerable variability in the sensitivity among 6 PCR kits assessed in this study

Proportion of patients whose ex20ins could have been detected by any PCR test alone

Mobocertinib Trial	US COTA Study	German Study	SCRUM Study
14.0%–48.4%	13.3%–46.7%	17.5%–50.0%	21.1%–58.9%

- Findings of this study suggest that the PCR tests assessed would have missed >40% of patients with NSCLC harboring *EGFR* ex20ins
- Given the diverse profile of *EGFR* ex20ins variants (>100 unique variants reported in the literature<sup>1</sup>), NGS-based genetic testing can substantially improve their identification in NSCLC and is preferable
- It is important for molecular diagnostic laboratories to be knowledgeable about the assay used and include the assay type in the report generated
- Clinicians should be cautious when interpreting “EGFR wild type” reports and to confirm the capabilities of the assay used with molecular diagnostics

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 1. O’Kane GM, et al. *Lung Cancer*. 2017;109:137-144.

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