

# EGFR TKIs in patients with NSCLC with uncommon EGFR mutations: a real-world study (UpSwing)

#1217P

Satoru Miura,<sup>1\*</sup> Te-Chun Hsia,<sup>2</sup> Jen-Yu Hung,<sup>3</sup> Hyun Ae Jung,<sup>4</sup> Jin-Yuan Shih,<sup>5</sup> Cheol-Kyu Park,<sup>6</sup> Seung Hyeon Lee,<sup>7</sup> Tatsuro Okamoto,<sup>8</sup> Jean-Bernard Auliac,<sup>9</sup> Hee Kyung Ahn,<sup>10</sup> Yong Chul Lee,<sup>11</sup> Yuki Sato,<sup>12</sup> Sung Sook Lee,<sup>13</sup> Céline Mascua,<sup>14</sup> Hasan Daoud,<sup>15</sup> Angela Märten,<sup>15</sup> Sanjay Papat<sup>16,17</sup>

<sup>1</sup>Department of Internal Medicine, Niigata Cancer Center Hospital, Niigata, Japan; <sup>2</sup>Department of Internal Medicine, China Medical University Hospital, Taichung, Taiwan; <sup>3</sup>Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan; <sup>4</sup>Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; <sup>5</sup>Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan; <sup>6</sup>Department of Internal Medicine, Chonnam National University Medical School and Hwasun Hospital, Hwasun, Republic of Korea; <sup>7</sup>Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Kyung Hee University Medical Center, Kyung Hee University School of Medicine, Seoul, Republic of Korea; <sup>8</sup>Department of Thoracic Oncology, National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan; <sup>9</sup>Service de Pneumologie, Centre Hospitalier de Mantes la Jolie, Mantes la Jolie, France; <sup>10</sup>Division of Internal Oncology, Gachon University Gil Medical Center, Incheon, Republic of Korea; <sup>11</sup>Department of Internal Medicine, Research Institute of Clinical Medicine of Chonbuk National University Hospital, Biomedical Research Institute of Chonbuk National University Hospital, Chonbuk National University Hospital, Chonbuk National University Medical School, Jeonju, Republic of Korea; <sup>12</sup>Department of Respiratory Medicine, Kobe City Medical Center General Hospital, Hyogo, Japan; <sup>13</sup>Tenjo University Hosotatei Paik Hospital, Niigata University College of Medicine, Busan, Republic of Korea; <sup>14</sup>Pulmonary Department, Strasbourg University, Strasbourg University Hospital, Strasbourg, France; <sup>15</sup>Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; <sup>16</sup>Lung Unit, Royal Marsden National Health Service Foundation Trust, London, United Kingdom; <sup>17</sup>The Institute of Cancer Research, London, United Kingdom

## Introduction

- ~7-23% of EGFR mutations are 'uncommon' mutations (not Del19 or L858R)<sup>1</sup>
- Around a quarter to a third of EGFRm+ tumours harbour compound mutations<sup>1</sup>
- Increased use of sensitive sequencing-based detection methods and liquid biopsy will increase the frequency of uncommon mutations detected in real-world clinical practice<sup>2</sup>

## Categories of uncommon EGFR mutations in lung cancer, with illustrative examples

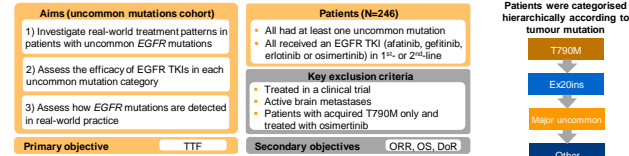
- Common (sensitive to all TKIs; afatinib approved in this setting)
- Major uncommon (sensitive to TKIs; afatinib approved in this setting)
- Ex20ins (considered resistant to TKIs but highly heterogeneous)
- Others (little data on TKI sensitivity; highly heterogeneous)
- T790M (resistant to 1<sup>st</sup>- and 2<sup>nd</sup>-gen TKIs)

Exon 18	Exon 19	Exon 20	Exon 21
E709K	Del19	Ex20ins	L858R
G719X	L747P/S	S768I	L861Q
		T790M	

EGFRm+, epidermal growth factor receptor mutation-positive; ex20ins, exon 20 insertion; gen, generation; TKI, tyrosine kinase inhibitor

## Methods

UpSwing: Real-world, non-interventional, global study of consecutive EGFR TKI-naïve patients with NSCLC



DoR, duration of response; ORR, overall response rate; OS, overall survival; TTF, time-to-treatment failure

## Results

Patients characteristics were similar regardless of EGFR TKI received as index therapy

	All (n=245)	1 <sup>st</sup> -gen TKIs (n=109)	Afatinib (n=132)	Osimertinib (n=17)
Median age, years (range)	69.5 (27.0-93.0)	70.5 (42.0-91.0)	68.5 (27.0-93.0)	71.0 (56.0-85.0)
Female, n (%)	138 (56.1)	66 (62.3)	67 (50.8)	5 (71.4)
Asian, n (%)	206 (83.7)	87 (82.1)	114 (86.4)	5 (71.4)
Brain metastases, n (%)	17 (6.9)	5 (4.7)	12 (9.1)	0
ECOG PS ≥2, n (%)	31 (12.6)	14 (13.2)	17 (12.9)	0
Mutation status, n (%)				
Major uncommon	179 (72.8)	80 (75.5)	94 (71.2)	4 (57.1)
Exon 20 insertion	29 (11.8)	10 (9.4)	18 (13.6)	1 (14.3)
T790M	17 (6.9)	4 (3.8)	11 (8.3)	2 (28.6)
Other	21 (8.5)	12 (11.3)	9 (6.8)	0
Compound	82 (33.3)	32 (30.2)	46 (34.8)	4 (57.1)

\*Includes one patient treated with gefitinib/erlotinib. ECOG PS, Eastern Cooperative Oncology Group performance status

Patients were investigated in 36 sites across nine countries

Austria n=6
France n=12
Germany n=2
Italy n=8
Japan n=45
South Korea n=95
Spain n=5
Taiwan n=67
United Kingdom n=6

## Key findings and conclusions

Real-world study (NCT04179890) in patients with EGFRm+ NSCLC (uncommon mutations)

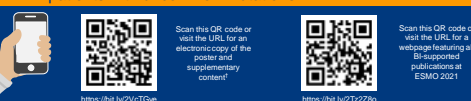
EGFR TKIs are 1<sup>st</sup>-line treatment of choice in everyday clinical practice; afatinib was the most commonly used EGFR TKI

ECOG PS remained stable in patients from 1<sup>st</sup>- to 2<sup>nd</sup>-line, enabling many patients to receive further treatment

Strongest outcomes were observed in major uncommon and compound mutations; activity was observed in patients with poor risk factors

Some patients with 'other' and ex20ins mutations responded to EGFR TKIs, demonstrating the need for precise information on EGFR mutation type

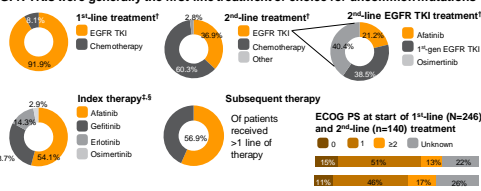
Treatment with an EGFR TKI should be considered for most patients with uncommon mutations



\*Copies of this poster obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without written permission from the authors of this poster

## Results (cont'd)

EGFR TKIs were generally the first-line treatment of choice for uncommon mutations

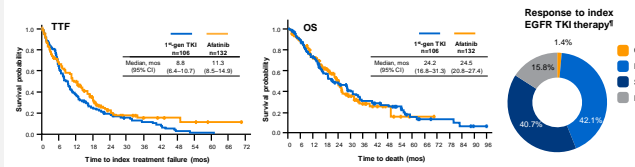


\*An additional patient was treated with chemotherapy plus bevacizumab; †Includes one patient treated with gefitinib/erlotinib; ‡Includes one patient treated with afatinib/erlotinib

Data were originally presented at WCLC 2021. \*Corresponding author email address: miusai1118@niigata-crc.jp

## Results (cont'd)

In patients with uncommon EGFR mutations, EGFR TKIs conferred encouraging TTF, OS and ORR



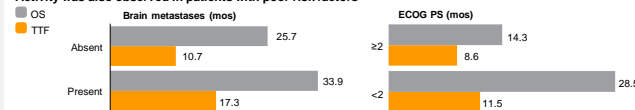
CI, confidence interval; CR, complete response; mos, months; PR, partial response; PD, progressive disease; SD, stable disease

Clinical outcomes varied according to mutation category\*\*

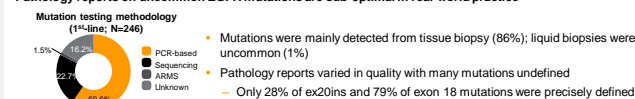
	Any TKI (n=246)				1 <sup>st</sup> -gen EGFR TKIs (n=106)				Afatinib (n=132)			
	TTF, mos	OS, mos	ORR <sup>†</sup> , %	DoR <sup>†</sup> , mos	TTF, mos	OS, mos	ORR <sup>†</sup> , %	DoR <sup>†</sup> , mos	TTF, mos	OS, mos	ORR <sup>†</sup> , %	DoR <sup>†</sup> , mos
All patients	9.9	24.4	43.4	10.0	8.8	24.2	44.1	6.0	11.3	24.5	43.8	12.0
Major uncommon	11.3	25.7	49.1	10.0	9.8	28.5	47.3	6.5	14.3	24.5	50.6	12.0
Exon 20 insertion	5.5	22.5	17.4	19.3	5.2	21.0	16.7	33.0	8.3	22.5	18.8	5.5
T790M	2.8	32.7	20.0	6.0	2.1	14.2	0	5.7	5.7	33.3	6.0	0
Other	7.4	13.4	43.8	7.5	7.3	12.8	55.6	4.5	10.8	20.2	28.6	10.5
Compound	12.3	28.7	48.6	10.0	12.4	31.3	48.3	6.0	12.6	23.4	52.5	10.0

\*\*Evaluable patients; \*\*Results from patients treated with osimertinib not shown due to small sample size

Activity was also observed in patients with poor risk factors



Pathology reports on uncommon EGFR mutations are sub-optimal in real-world practice



ARMS, amplification refractory mutation system; PCR, polymerase chain reaction

## References

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