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

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Introduction

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

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 1st- and 2nd-gen TKIs)

Exon 18	Exon 19	Exon 20	Exon 21
E709X	Del19	Ex20ins	L858R
G719X	L747P/S	S768I	L861Q
		T790M	

*EGFR*m+, 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

Aims (uncommon mutations cohort)

1) Investigate real-world treatment patterns in patients with uncommon *EGFR* mutations

2) Assess the efficacy of EGFR TKIs in each uncommon mutation category

3) Assess how *EGFR* mutations are detected in real-world practice

Patients (N=246)

- All had at least one uncommon mutation
- All received an EGFR TKI (afatinib, gefitinib, erlotinib or osimertinib) in 1st- or 2nd-line

Key exclusion criteria

- Treated in a clinical trial
- Active brain metastases
- Patients with acquired T790M only and treated with osimertinib

Patients were categorised hierarchically according to tumour mutation

T790M → Ex20ins → Major uncommon → Other

Primary objective: TTF

Secondary objectives: ORR, OS, DoR

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

Results

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

	All (N=246)	1st-gen TKIs (n=106*)	Afatinib (n=132)	Osimertinib (n=7)
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 1st-line treatment of choice in everyday clinical practice; afatinib was the most commonly used EGFR TKI

ECOG PS remained stable in patients from 1st- to 2nd-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

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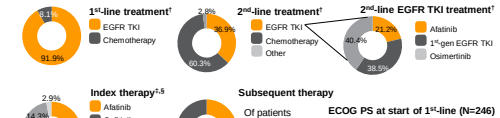
Results (cont'd)

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

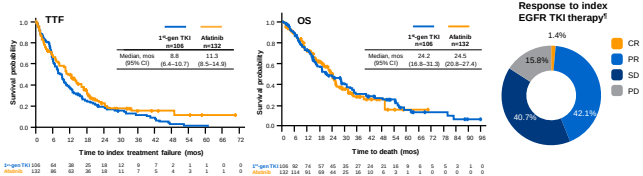


†An additional patient was treated with chemotherapy plus bevacizumab; ‡Includes one patient treated with gefitinib/erlotinib; §Includes one patient treated with afatinib/gefitinib

Data were originally presented at WCLC 2021. *Corresponding author email address: miusat1118@niigata-cc.jp

Results (cont'd)

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



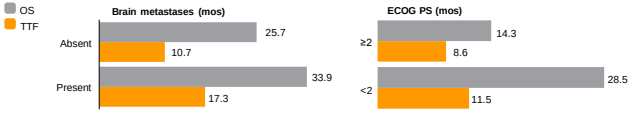
CI, confidence interval; CR, complete response; mos, months; PR, partial response; PD, progressive disease; SD stable disease

Clinical outcomes varied according to mutation category**

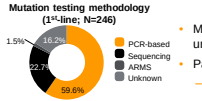
	Any TKI (N=246)				1st-gen EGFR TKIs (n=106)				Afatinib (n=132)			
	TTF, mos	OS, mos	ORR¶, %	DoR¶, mos	TTF, mos	OS, mos	ORR¶, %	DoR¶, mos	TTF, mos	OS, mos	ORR¶, %	DoR¶, mos
All patients	9.9	24.4	43.4	10.0	8.8	24.2	44.1	6.0	11.3	24.5	43.8	12.0
Major uncommon	11.3	25.7	49.1	10.0	9.8	28.5	47.3	6.5	14.3	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	-	33.3	6.0
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



- Mutations were mainly detected from tissue biopsy (86%); liquid biopsies were uncommon (1%)
- Pathology reports varied in quality with many mutations undefined
  - Only 28% of ex20ins and 79% of exon 18 mutations were precisely defined

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

References

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

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