A real-world cohort study of EGFR TKIs in patients with NSCLC with uncommon *EGFR* mutations (UpSwinG)

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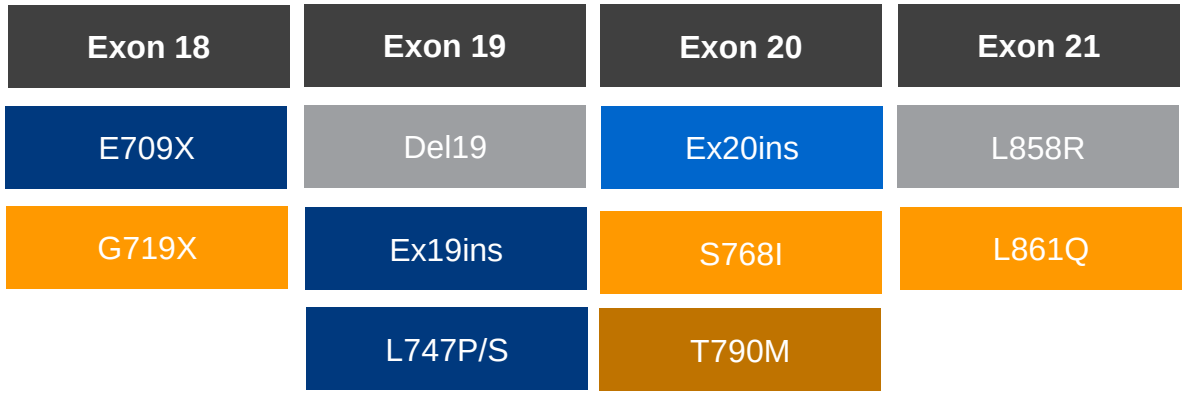
Presenter DISCLOSURES

Ineligible Company (formerly: Commercial Interest)	**Relationship(s)**
Boehringer Ingelheim Inc.	Speaker bureau fees/Expert testimony
MSD Inc.	Speaker bureau fees/Expert testimony
Elli Lilly Japan	Speaker bureau fees/Expert testimony
Ono Pharma. Inc.	Speaker bureau fees/Expert testimony
Chugai Pharma Inc.	Speaker bureau fees/Expert testimony

Introduction

While most patients with *EGFR*m+ NSCLC harbor 'common' mutations (Del19/L858R), uncommon mutations are highly heterogeneous; these can be categorized into four groups:



7–23% of *EGFR* mutations are 'uncommon' mutations[1]

- 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)

- Up to 25% of *EGFR*m+ tumors harbor 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]

*EGFR*m+, *EGFR* mutation-positive; gen, generation; TKI, tyrosine kinase inhibitor.

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

Methods

UpSwinG (NCT04179890): non-interventional global study (nine countries*) that assessed medical records of consecutive patients with uncommon *EGFR* mutations treated in real-world practice (max 15 per site)

Aims (uncommon mutations cohort)

1) Investigate the treatment of 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
- *EGFR* mutation detection undertaken locally using different methodologies

Key exclusion criteria

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

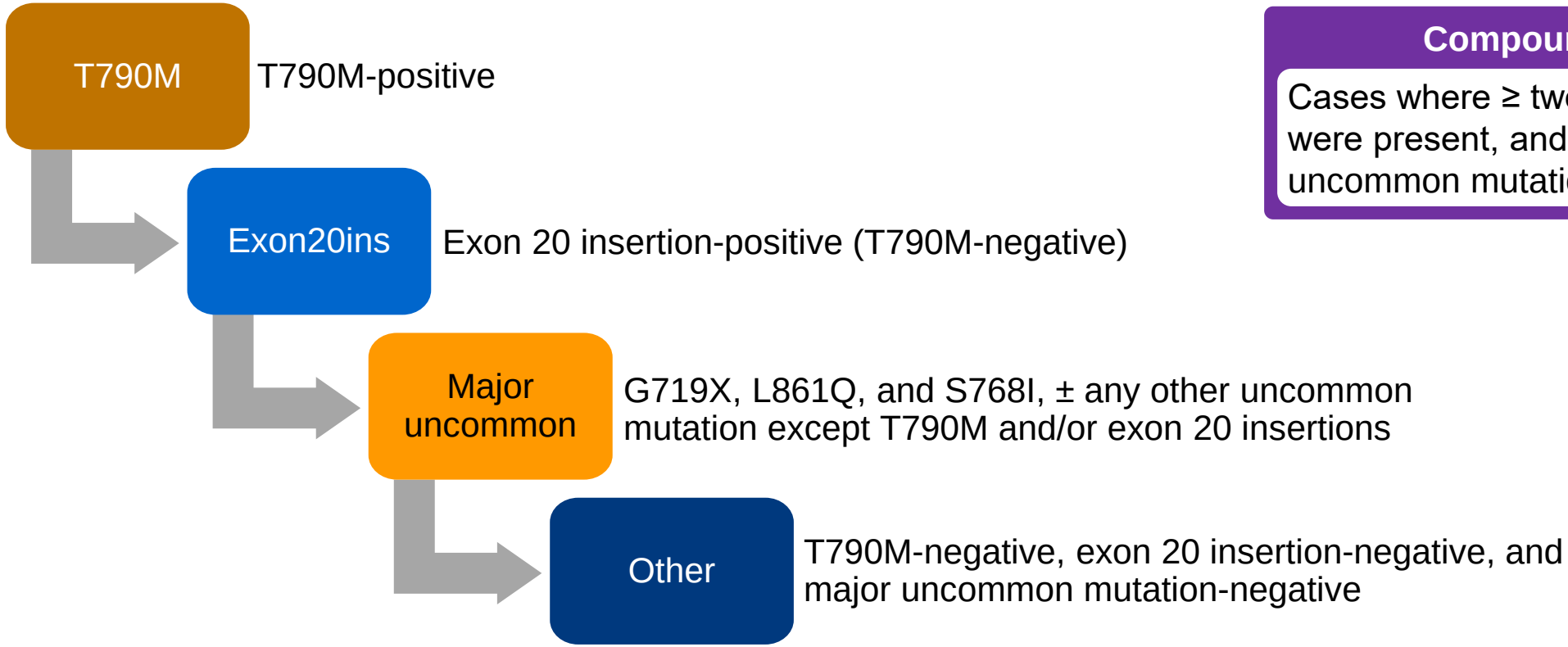
Primary objective: TTF

Secondary objectives: ORR, OS, DoR

DoR, duration of response; ORR, overall response rate; OS, overall survival; TTF, time-to-treatment failure.
*Austria, France, Germany, Italy, Japan, South Korea, Spain, Taiwan, United Kingdom

Methods (continued)

Patients were categorized hierarchically according to tumor mutation



Compound mutations

Cases where ≥ two *EGFR* mutations were present, and ≥ one was an uncommon mutation

Results

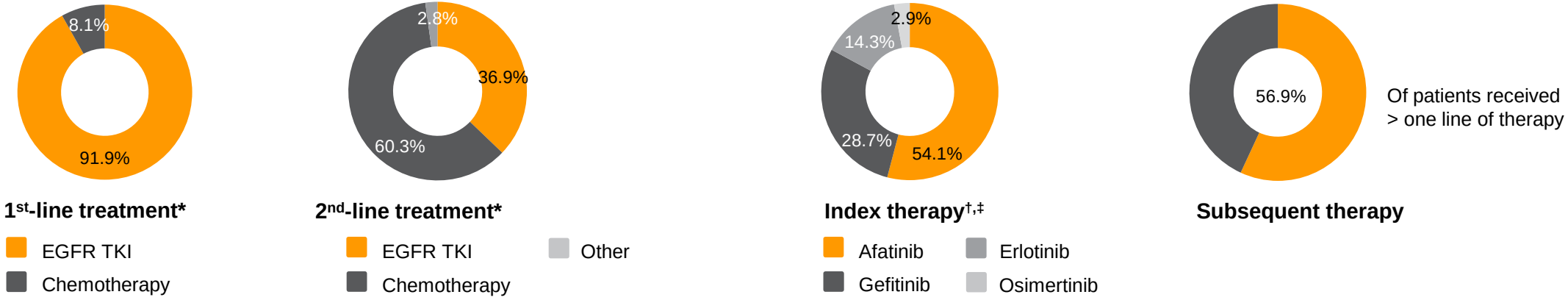
Patient characteristics were generally similar regardless of which EGFR TKI was received as index therapy

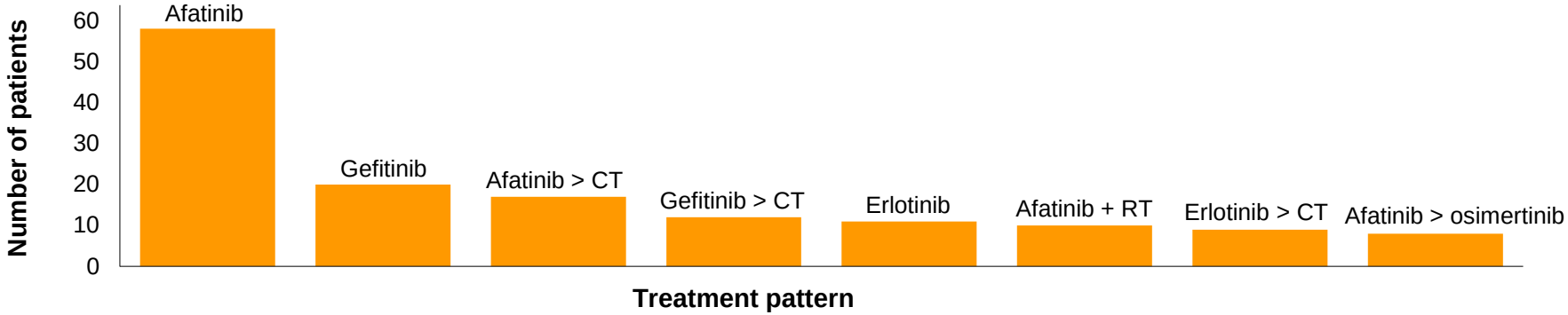
		All (N=246)	1st-gen EGFR TKIs (n=106*)	Afatinib (n=132)
	Female, n (%)	138 (56.1)	66 (62.3)	67 (50.8)
	Median age, years (range)	69.5 (27.0–93.0)	70.5 (42.0–91.0)	68.5 (27.0–93.0)
	Never-smoker, n (%)	129 (52.4)	64 (60.4)	62 (47.0)
BMI, n (%)	Normal	116 (47.2)	42 (39.6)	68 (51.5)
	Underweight	17 (6.9)	9 (8.5)	7 (5.3)
	Overweight/obese	49 (19.9)	21 (19.8)	27 (20.5)
Ethnicity, n (%)	Caucasian	23 (9.3)	8 (7.5)	13 (9.8)
	Asian	206 (83.7)	87 (82.1)	114 (86.4)
	Unknown/not collected	17 (6.9)	11 (10.4)	5 (3.8)
Stage/histology, n (%)	Stage IIIB/C	37 (15.0)	14 (13.2)	22 (16.7)
	Stage IV	209 (85.0)	92 (86.8)	110 (83.3)
	Adenocarcinoma	239 (97.2)	102 (96.2)	129 (97.7)
	Brain metastases	17 (6.9)	5 (4.7)	12 (9.1)
ECOG PS, n (%)	0	35 (14.2)	9 (8.5)	25 (18.9)
	1	124 (50.4)	61 (57.5)	59 (44.7)
	2–4	31 (12.6)	14 (13.2)	17 (12.9)
	Unknown	56 (22.8)	22 (20.8)	31 (23.5)

BMI, body mass index; ECOG PS, Eastern Cooperative Oncology Group performance status

Results (continued)

EGFR TKIs were generally the 1st-line treatment of choice for uncommon mutations



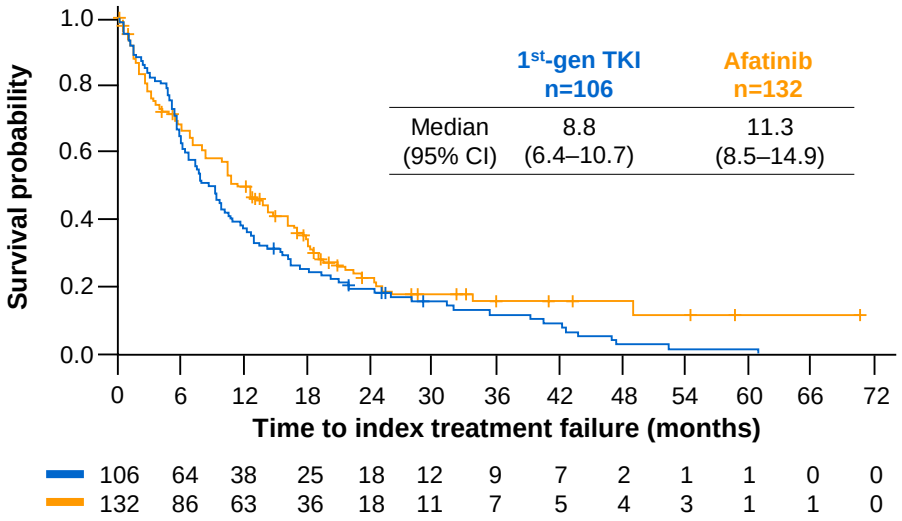


CT, chemotherapy; RT, radiotherapy.
*An additional patient was treated with chemotherapy plus bevacizumab; †Includes one patient treated with gefitinib/erlotinib; ‡Includes one patient treated with afatinib/gefitinib

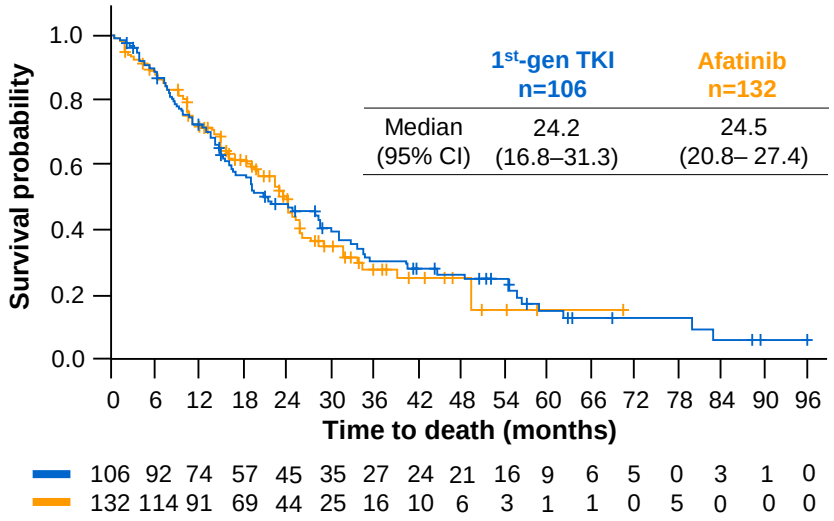
Results (continued)

EGFR TKIs conferred encouraging TTF, ORR and OS; the OS was likely confounded by the high uptake of subsequent treatments and less censoring for the 1st-generation EGFR TKIs due to their longer availability*

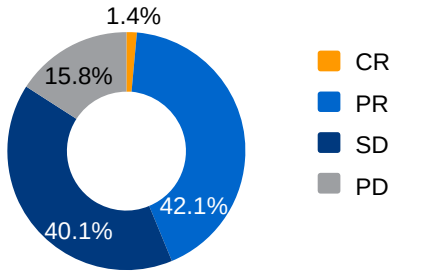
TTF



OS



Response to index EGFR TKI therapy†



CI, confidence interval; CR, complete response; PD, progressive disease; PR, partial response; SD stable disease.
*Results from patients treated with osimertinib not shown due to small sample size; †Evaluable patients

Results (continued)

Clinical outcomes varied according to mutation category in patients treated with EGFR TKIs*

	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

Mos, months.
*Results from patients treated with osimertinib not shown due to small sample size; †Evaluable patients

Results (continued)

Most patients (76.8%) received the approved starting dose of EGFR TKIs (gefitinib 250 mg; erlotinib 150 mg; afatinib 40 mg); outcomes were not affected by starting dose*

	Any TKI (n=189)				1st-gen EGFR TKIs (n=91)				Afatinib (n=93)			
	TTF, mos	OS, mos	ORR†, %	DoR†, mos	TTF, mos	OS, mos	ORR†, %	DoR†, mos	TTF, mos	OS, mos	ORR†, %	DoR†, mos
All patients	10.7	25.6	45.4	10.0	9.3	28.2	47.6	6.0	12.8	24.8	44.2	12.0
Major uncommon	11.9	28.5	50.0	10.0	10.4	30.2	51.5	6.5	15.7	24.5	49.2	12.0
Exon 20 insertion	10.6	22.5	16.7	-	6.0	21.0	0	-	15.5	22.5	22.2	-
T790M	2.8	23.0	21.4	6.0	2.1	14.2	0	-	5.7	-	33.3	6.0
Other	11.5	20.2	50.0	6.0	7.4	13.4	55.6	4.5	13.3	24.8	33.3	12.0
Compound	12.6	30.2	50.0	10.0	14.0	33.0	52.0	4.5	12.6	23.4	51.7	10.0

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

Key findings and conclusions

- EGFR TKIs are 1st-line treatment of choice for uncommon mutations in everyday clinical practice
- Afatinib was the most commonly used EGFR TKI
- Overall, median TTF was 9.9 months and median OS was 24.4 months
- Strongest results were seen in major uncommon and compound mutations
- Treatment with an EGFR TKI should be considered for most patients with uncommon mutations

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