Sequential afatinib and osimertinib in patients with advanced *EGFR* mutation-positive NSCLC who acquire the T790M resistance mutation: a non-interventional cohort study (UpSwinG)

#1223P

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Introduction

- The ErbB family blockers, afatinib and dacomitinib, and third-generation EGFR TKI, osimertinib, confer significant clinical benefit versus first-generation EGFR TKIs (erlotinib and gefitinib) in patients with *EGFR*m+ NSCLC. No prospective data exist directly comparing afatinib, dacomitinib and osimertinib[1]
- Survival outcomes are highly dependent on the availability and implementation of subsequent therapy following acquired resistance to first-line therapy
- Resistance to afatinib caused by the T790M mutation occurs in up to 50–70% of cases.[2] The T790M mutation is highly sensitive to osimertinib[3]
- Reserving osimertinib for second-line use following afatinib may maximise targeted treatment duration in patients with T790M+ disease
- A previous retrospective study (GioTag) demonstrated encouraging OS (>3 years) in patients with acquired T790M treated with sequential afatinib and osimertinib[4]

*EGFR*m+, epidermal growth factor receptor mutation-positive; NSCLC, non-small cell lung cancer; OS, overall survival; TKI, tyrosine kinase inhibitor

Study design

- This non-interventional, global, multicentre study (NCT04179890) investigated health records of EGFR TKI-naïve patients with *EGFR*m+ NSCLC treated in clinical practice (data were analysed descriptively)

ORR, overall response rate; TTF, time-to-treatment failure

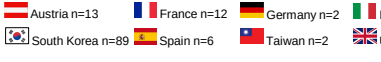
Results

Patients were mostly Asian and female; 13.6% had brain metastases

		Patients (n=191)
Median age, years (range)		62 (34–88)
Smoking status, n (%)	Never	121 (63.4)
	Previous	52 (27.2)
	Current	12 (6.3)
	Unknown	6 (3.1)
Ethnicity, n (%)	Caucasian	55 (28.8)
	Asian	118 (61.8)
	Other	3 (1.6)
	Unknown/not collected	15 (7.9)
Stage, n (%)	IIIB/C	15 (7.9)
	IV	176 (92.1)
Female, n (%)		106 (55.5)
Histology, n (%)	Adenocarcinoma	186 (97.4)
	Other	5 (2.6)
	Brain metastases	26 (13.6)
ECOG PS, n (%)	0	49 (25.7)
	1	90 (47.1)
	≥2	19 (9.9)
	Unknown	33 (17.3)
Mutation type, n (%)	Del19	135 (70.7)
	L858R	56 (29.3)

Austria n=13 | France n=12 | Germany n=2 | Italy n=17 | Japan n=23 | South Korea n=89 | Spain n=6 | Taiwan n=2 | United Kingdom n=27

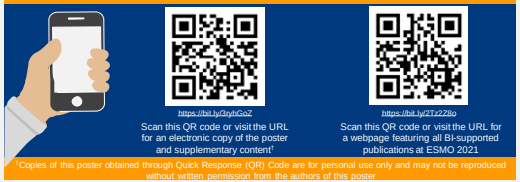
The median observation period was 30 months; median duration of treatment, months



ECOG PS, Eastern Cooperative Oncology Group performance status.

Key findings and conclusions

- Promising activity with sequential afatinib + osimertinib in patients with *EGFR*m+ NSCLC
- Consistent outcomes across subgroups including patients with ECOG PS ≥2 and brain metastases
- Promising OS in Asian patients (42.3 months)
  - Notable because osimertinib did not improve OS versus first-generation TKIs in FLAURA (37.1 vs 35.8 months)[5]
- ECOG PS and incidence of brain metastases remained stable on afatinib treatment
- The data substantiate previous studies, including GioTag[4]
- Use of next-generation sequencing and liquid biopsy is still low in real-world clinical practice
  - Greater use could allow more patients to benefit from targeted therapies
- Sequential afatinib + osimertinib could be considered in everyday clinical practice, especially in Asia



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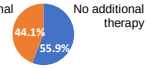
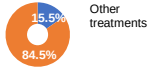
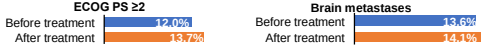
Nearly half of patients had at least one further treatment after afatinib + osimertinib



Further treatment was generally chemotherapy based



Patient fitness remained stable before and after treatment with afatinib



- Median time from end of osimertinib treatment to death was 5.0 months (95% CI 4.2–6.5)

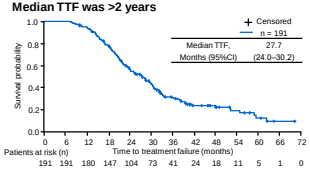
CI, confidence interval

Data were originally presented at WCLC 2021. *Corresponding author email address: Sanjay.Popat@rmh.nhs.uk

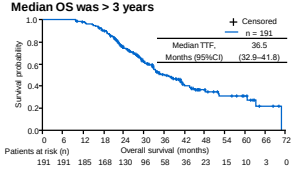
Results (cont'd)

Median TTF and OS were ~2 and 3 years, respectively

Median TTF was >2 years



Median OS was > 3 years



- Outcomes were similar in patients who received the approved starting dose of afatinib (40 mg; n=155): median TTF=27.5 months (23.6–30.1); median OS=36.5 months (32.7–42.3)

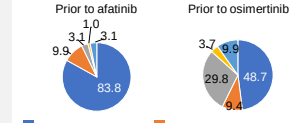
Median OS was longest in Asian patients (42.3 months) and Asian patients with Del19 mutation (43.8 months)

	Median TTF, months (95% CI)	Median OS, months (95% CI)	ORR, % Afatinib	ORR, % Osimertinib
All patients	27.7 (24.0–30.2)	36.5 (32.9–41.8)	73.6	45.2
Mutation type				
Del19	28.6 (24.5–31.2)	38.0 (33.1–44.4)	74.0	47.1
L858R	22.1 (19.8–30.4)	33.1 (24.9–41.8)	72.7	40.4
Ethnicity				
Asian	28.8 (22.4–31.2)	42.3 (33.2–63.5)	79.3	48.0
Non-Asian	25.5 (22.1–28.6)	31.3 (27.2–38.0)	67.3	36.0
Brain metastases present				
No	28.4 (24.3–30.8)	37.6 (33.1–42.3)	71.2	45.8
Yes	21.4 (19.2–30.9)	29.6 (22.4–NR)	91.3	41.7
ECOG PS				
<2	28.5 (24.0–30.9)	39.8 (32.9–45.2)	77.9	47.9
≥2	29.6 (20.5–32.3)	33.1 (21.8–37.6)	70.6	40.0
Asian and Del19	29.7 (23.0–33.0)	43.8 (33.2–71.1)		

NR, not reached

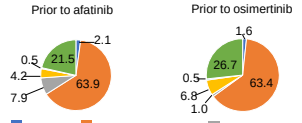
Most patients underwent tissue biopsy; liquid biopsies were uncommon

Sample(s) used for mutation testing (%)



Mutations were mainly detected (63.9% of cases) with PCR-based techniques

Methodology used for mutation testing (%)



ARMS, Amplification Refractory Mutation System; PCR, polymerase chain reaction

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