Sequential afatinib and osimertinib in patients with advanced *EGFR*m+ NSCLC and acquired T790M: the real-world UpSwinG study

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Presenter DISCLOSURES

Ineligible Company (formerly: Commercial Interest)	**Relationship(s)**	**Ineligible Company** (formerly: Commercial Interest)	**Relationship(s)**
AstraZeneca	Consulting fees, Corporate-sponsored research	GSK	Consulting fees, Corporate-sponsored research
Roche	Consulting fees, Corporate-sponsored research	BeiGene	Consulting fees
Boehringer Ingelheim	Consulting fees, Corporate-sponsored research	Incyte	Consulting fees
Pfizer	Consulting fees	Eli Lilly	Consulting fees
Novartis	Consulting fees, Corporate-sponsored research	Amgen	Consulting fees
Takeda	Consulting fees, Corporate-sponsored research	Seattle Genetics	Consulting fees
Bristol Myers Squibb	Consulting fees, Corporate-sponsored research	Clovis	Corporate-sponsored research
Merck Sharp & Dohme	Consulting fees, Corporate-sponsored research	Celgene	Corporate-sponsored research
EMD Serono	Consulting fees	Ariad	Corporate-sponsored research
Bayer	Consulting fees	Epizyme	Corporate-sponsored research
Blueprint	Consulting fees	Mirati	Corporate-sponsored research
Daiichi Sankyo	Consulting fees, Corporate-sponsored research	Trizel	Corporate-sponsored research
Guardant Health	Consulting fees, Corporate-sponsored research	Turning Point Therapeutics	Corporate-sponsored research
Janssen	Consulting fees, Corporate-sponsored research		

Introduction

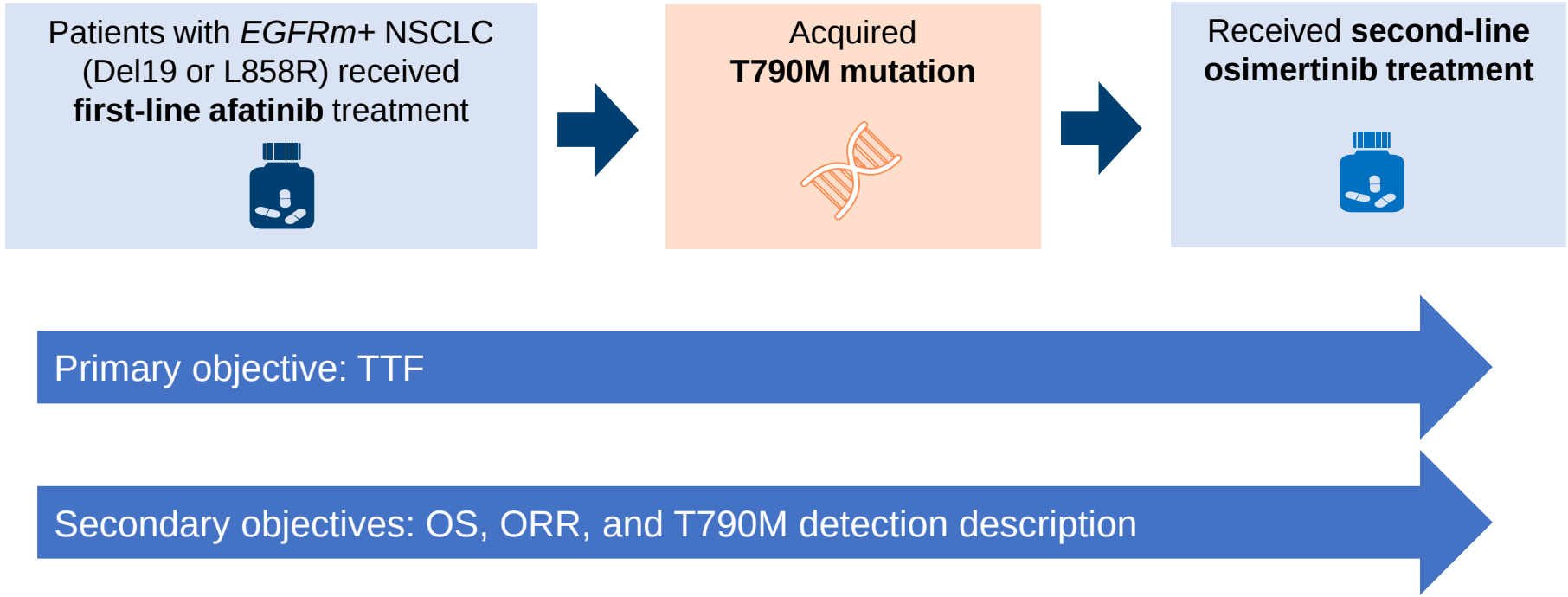
- The ErbB family blockers, afatinib and dacomitinib, and the third-generation EGFR TKI, osimertinib, confer significant clinical benefit versus first-generation EGFR TKIs (erlotinib and gefitinib) in patients with *EGFR*m+ NSCLC. However, no prospective data exist directly comparing afatinib, dacomitinib 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]
- It is possible that reserving osimertinib for second-line use following afatinib could help maximize the duration of targeted treatment 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+, *EGFR* mutation-positive; NSCLC, non-small cell lung cancer; OS, overall survival; TKI, tyrosine kinase inhibitor.

1. Shah R & Lester JF. Clin Lung Cancer 2020;21:216–28; 2. Girard N. Future Oncol 2019;15:2983–97; 3. Mok et al. N Engl J Med 2017;376:629–40; 4. Hochmair et al. Future Oncol 2020;16:2799–808

Study Design

- This non-interventional, global, multicenter study (NCT04179890) investigated existing medical or electronic health records of EGFR TKI-naïve patients with *EGFR*m+ NSCLC treated in regular clinical practice
- Data were analyzed descriptively



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

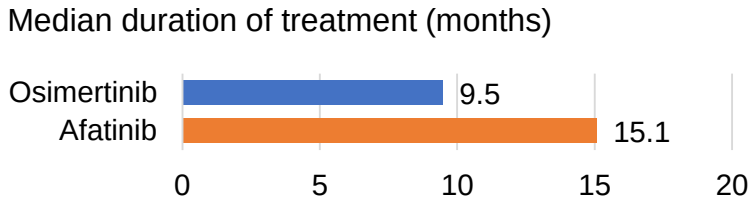
Results

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

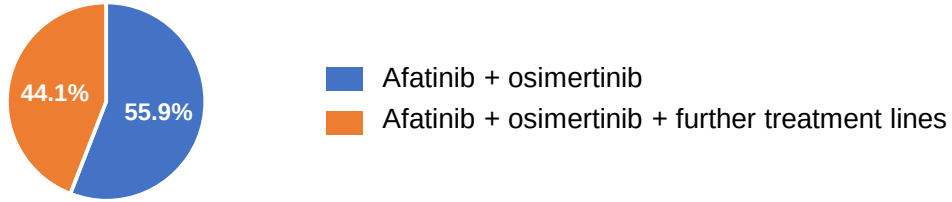
		Patients (n=191)
	Median age, years (range)	62 (34–88)
	Female, n (%)	106 (55.5)
Smoking status, n (%)	Never	121 (63.4)
	Previous	52 (27.2)
	Current	12 (6.3)
	Unknown	6 (3.1)
Ethnicity, n (%)	Caucasian	55 (28.8)
	Asian	118 (61.8)
	Other	3 (1.6)
	Unknown/Not collected	15 (7.9)
Stage, n (%)	IIIB/C	15 (7.9)
	IV	176 (92.1)
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)

ECOG PS, Eastern Cooperative Oncology Group performance status

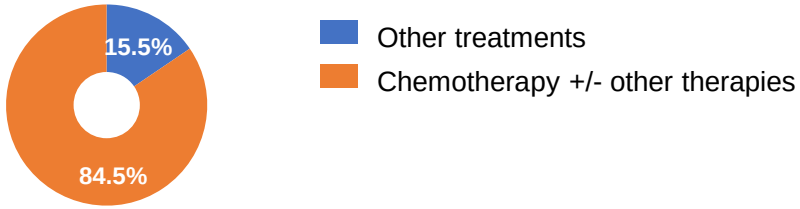
The median observation period was 30 months



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



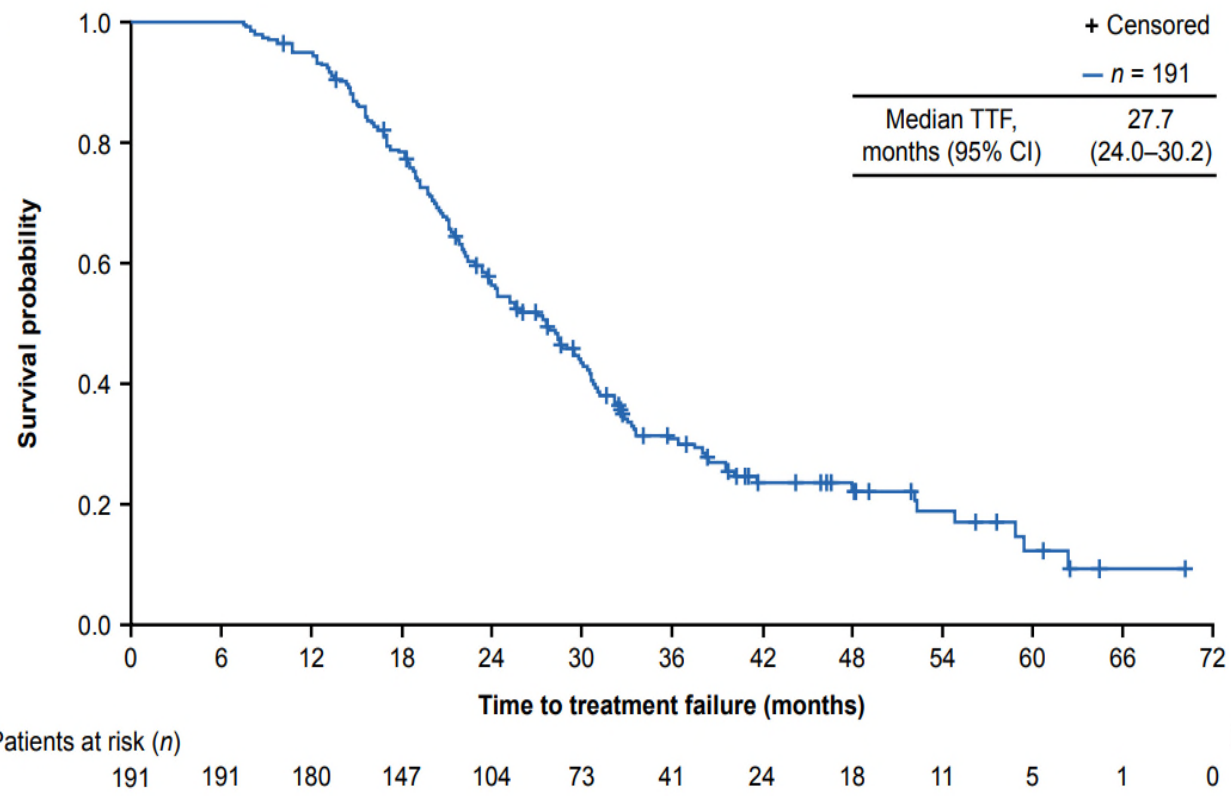
After discontinuation of osimertinib, chemotherapy was the most commonly used treatment



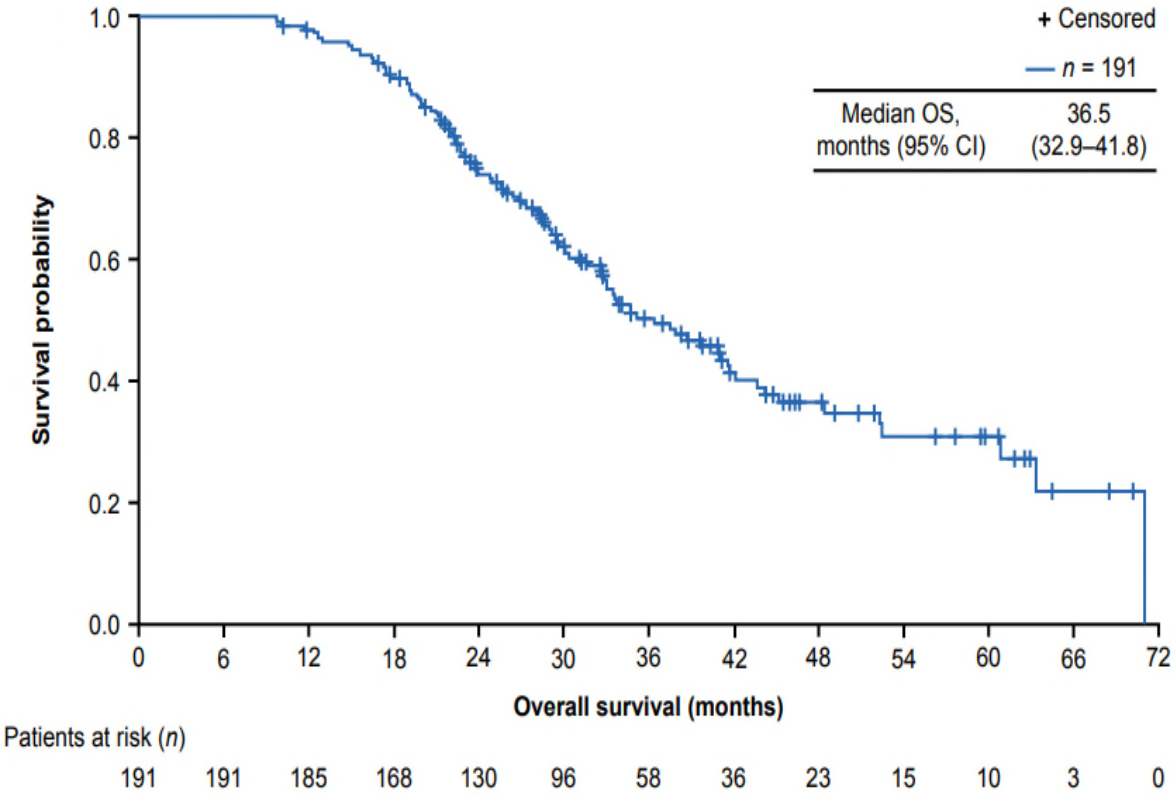
Results

Median TTF and OS were ~2 and 3 years respectively

Median TTF was > 2 years



Median OS was > 3 years



CI, confidence interval

Results (continued)

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

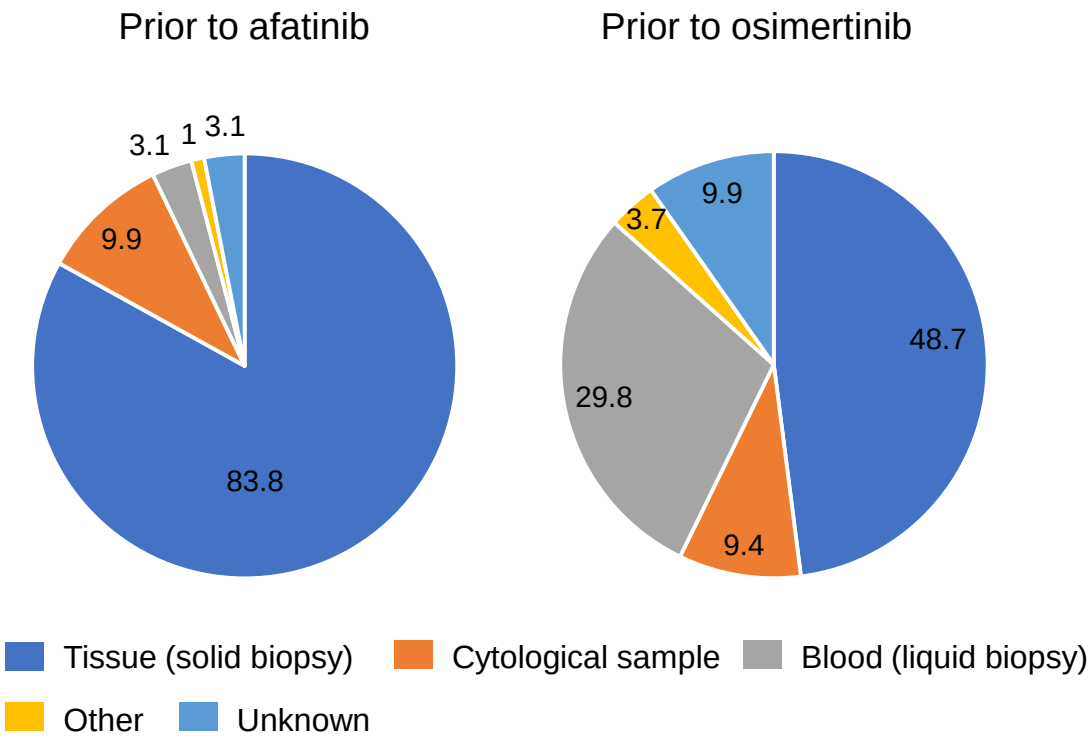
	Median TTF, months (95% CI)	Median OS, months (95% CI)	ORR, %	
			Afatinib	Osimertinib
All patients	27.7 (24.0–30.2)	36.5 (32.9–41.8)	73.6	45.2
Mutation type				
Del19	28.6 (24.5–31.2)	38.0 (33.1–44.4)	74.0	47.1
L858R	22.1 (19.8–30.4)	33.1 (24.9–41.8)	72.7	40.4
Ethnicity				
Asian	28.8 (22.4–31.2)	42.3 (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 reported

Results (continued)

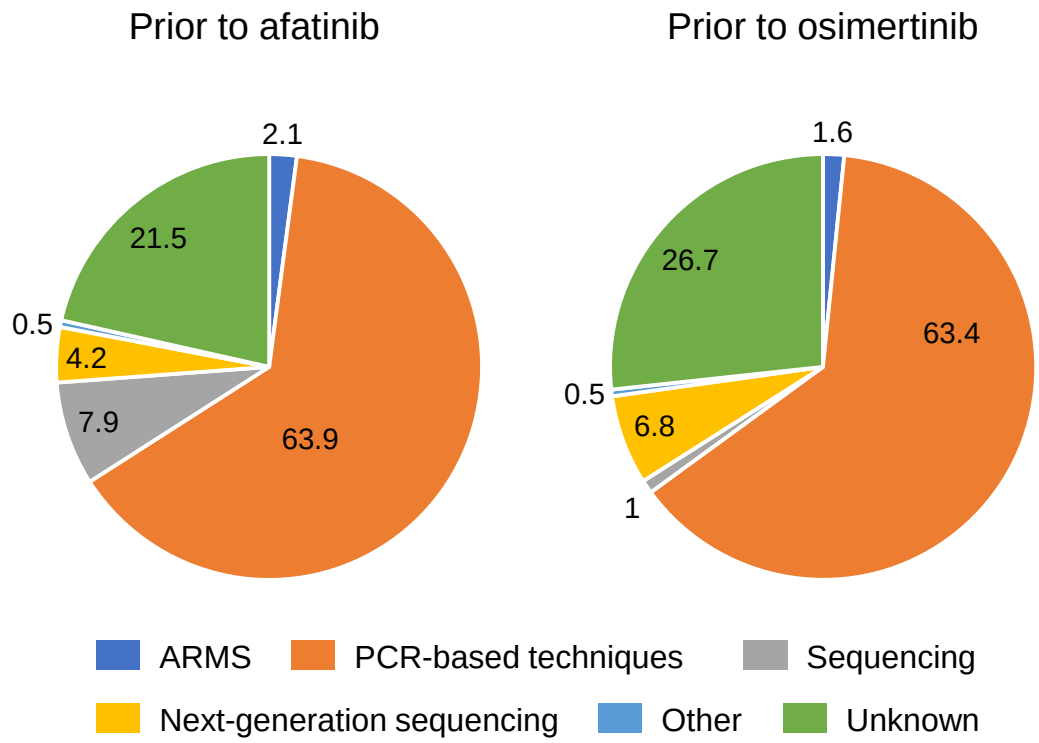
Most patients underwent tissue biopsy; liquid biopsies were uncommon

Biological 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

Key findings and conclusions

- Promising activity with sequential afatinib and osimertinib in patients with *EGFRm+* NSCLC
- Consistent outcomes across patient subgroups, including those with ECOG PS ≥2 and brain metastases
- Promising OS in Asian patients (42.3 months). These data are of special interest because osimertinib did not improve OS versus first-generation TKIs in FLAURA (37.1 vs 35.8 months)[5]
- The data substantiate previous studies, including GioTag (NCT03370770)
- The use of NGS and liquid biopsies is still low in real-world clinical practice
- Greater implementation of these technologies could increase the number of patients who might benefit from targeted therapies
- Sequential afatinib and osimertinib could be considered in everyday clinical practice, especially in Asia

5. Nogami et al. The 60th Annual meeting of the Japanese Society for Lung Cancer 2019. NGS, next-generation sequencing

Presented at the World Conference on Lung Cancer (WCLC)
September 8–14, 2021

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This study was funded by Boehringer Ingelheim. The authors were fully responsible for all content and editorial decisions, were involved at all stages of poster development, and have approved the final version.

Medical writing support for the development of this poster, under the direction of the authors, was provided by Becky O'Connor of Ashfield MedComms, an Ashfield Health company, and funded by Boehringer Ingelheim.