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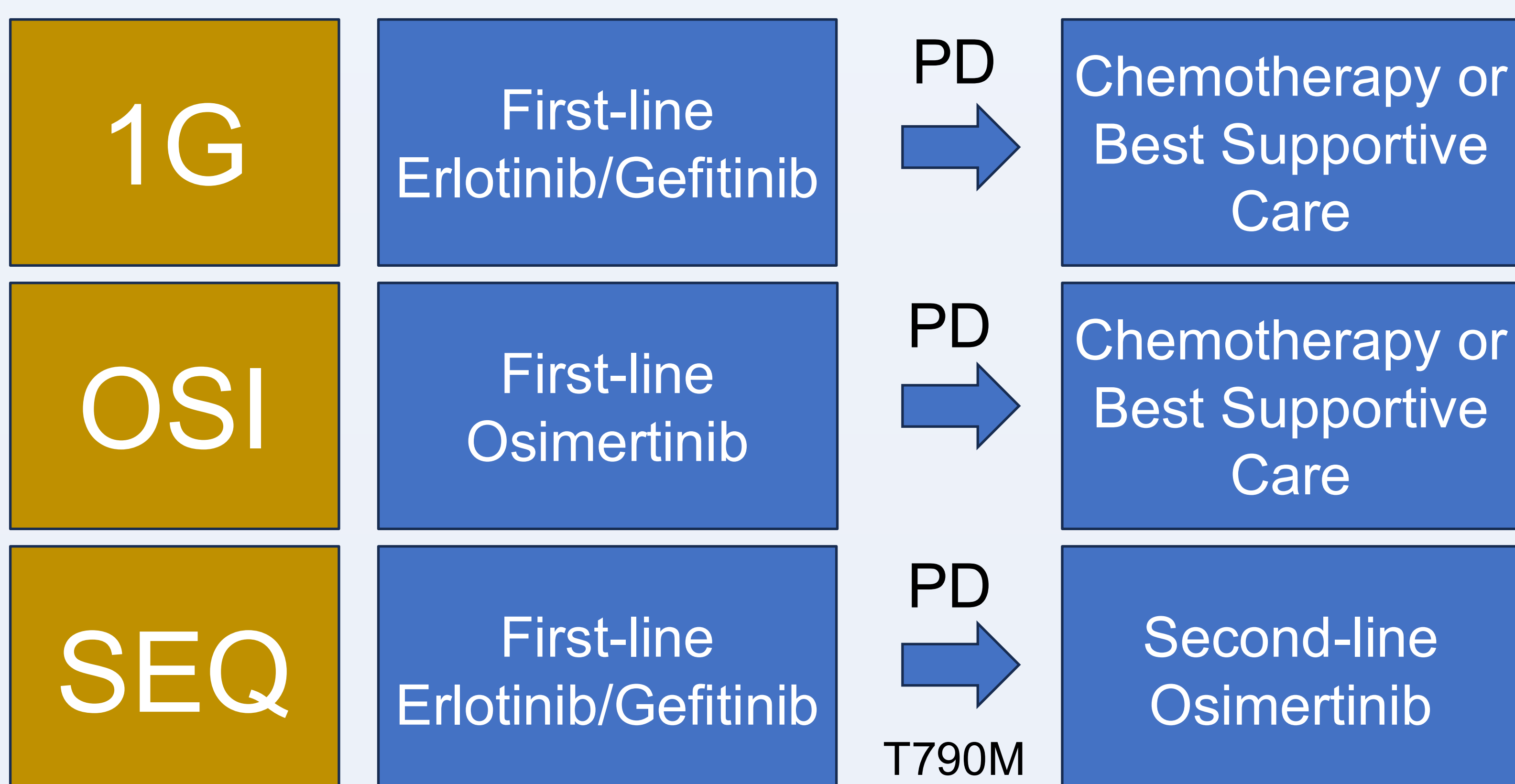
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Introduction

- Frontline osimertinib (OSI) is the current standard of care for patients with EGFR-mutated advanced non–small cell lung cancer (NSCLC), based on improved overall survival (OS) demonstrated in the FLAURA trial compared with first-generation EGFR tyrosine kinase inhibitors (1G TKIs; erlotinib and gefitinib).
- However, survival benefit appeared less pronounced in Asian populations and in patients with EGFR L858R mutations.
- In many countries, OSI remains unreimbursed due to high cost.
- Real-world evidence is therefore needed to inform cost-effectiveness, particularly compared with sequential treatment (SEQ: frontline 1G TKI followed by OSI upon disease progression with acquired EGFR T790M) and 1G TKIs.

Method

We conducted a retrospective cohort study of patients with advanced EGFR-mutated NSCLC treated at Siriraj Hospital, Bangkok, Thailand. PFS and OS were estimated using the Kaplan–Meier method and compared using log-rank tests. Hazard ratios (HRs) were derived from Cox proportional hazards models.



Results

- Between 2019 and 2025, a total of 883 patients were included (1G TKI: n=508; OSI: n=218; SEQ: n=157).
- OSI significantly improved PFS and OS compared with 1G TKIs in the overall population (OS HR 0.65, $P<0.001$), with consistent benefit across all subgroups, including EGFR exon 19 deletion, EGFR L858R mutation, and patients with or without baseline CNS metastasis.
- SEQ also demonstrated superior OS compared with 1G TKIs in overall population (OS HR 0.57, $P<0.001$), with consistent benefit in most subgroups, including patients with EGFR exon 19 deletion, EGFR L858R mutation, and patients without baseline CNS metastasis.
- No significant differences in OS were observed between OSI and SEQ in overall population (OS HR 1.15, $P=0.29$), and across all subgroups, including EGFR exon 19 deletion (OS HR 1.06, $P=0.76$), EGFR L858R mutation (OS HR 1.06, $P=0.77$), patients with baseline CNS metastasis (OS HR 1.12, $P=0.70$), and without baseline CNS metastasis (OS HR 1.10, $P=0.55$).

Table 1. Baseline characteristics of the patients

Variable	1G (n=508)	OSI (n=218)	SEQ (n=157)	p-value
Female – n (%)	331 (65.2)	142 (65.1)	104 (66.2)	0.975
Age (years) ± mean (SD)	67.2 ± 10.9	66.6 ± 11.7	65.8 ± 10.7	0.352
Smoking – n (%)	95 (20.4)	21 (11.7)	17 (12.5)	0.009
Brain metastasis – n (%)	160 (31.5)	92 (42.2)	51 (32.5)	0.019
ECOG – n (%)				0.039
0	34 (6.8)	22 (10.2)	17 (10.9)	
1	407 (80.9)	182 (84.2)	128 (82.1)	
2	55 (10.9)	9 (4.2)	10 (6.4)	
EGFR mutation – n (%)				0.072
Exon 19 deletion	268 (53.1)	111 (51.1)	93 (59.2)	
L858R	222 (43.9)	93 (42.9)	61 (38.9)	

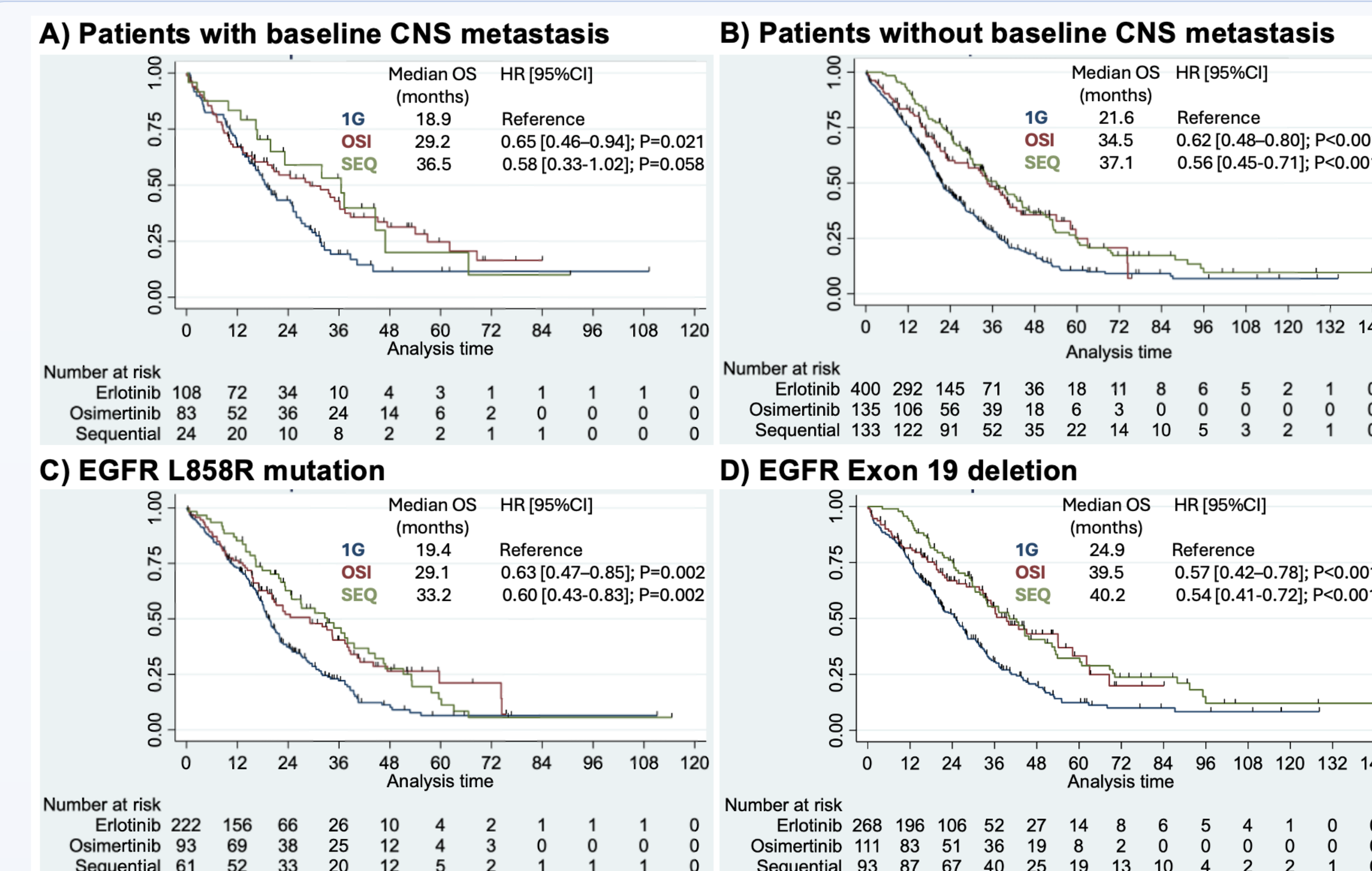


Figure 1. OS of subgroups of advanced NSCLC patients who received different EGFR TKI treatment strategies

Table 2. Median PFS and OS of patients who received different EGFR TKI strategies

	Median PFS – months (number of cases)			Median OS – months (number of cases)		
Treatment	1G TKI	OSI	SEQ	1G TKI	OSI	SEQ
Overall population	12.6 (508)	22.6 (218)	11.4 (157)	21.1 (508)	33.9 (218)	37.1 (157)
Baseline CNS metastasis	11.5 (108)	16.2 (83)	8.5 (24)	18.9 (108)	29.2 (83)	36.5 (24)
No baseline CNS metastasis	13.2 (400)	26.6 (135)	12.5 (133)	21.6 (400)	34.5 (135)	37.1 (133)
EGFR Exon 19 deletion	12.3 (268)	32.0 (111)	12.0 (93)	24.9 (268)	39.5 (111)	40.2 (93)
EGFR L858R mutation	12.8 (222)	17.1 (93)	10.8 (61)	19.4 (222)	29.1 (93)	33.2 (61)

Conclusion

- In this real-world cohort, frontline OSI was associated with improved survival compared with 1G TKIs across all clinically relevant subgroups, including L858R mutation.
- Sequential therapy achieved comparable outcomes to upfront OSI, suggesting it remains a viable strategy in resource-limited settings.
- These findings support further pharmacoeconomic evaluation to guide reimbursement policies.

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