EP12.07: Real-World Treatment Patterns and Outcomes After Osimertinib Progression in *EGFR*-Mutant NSCLC: A Multi-Center Taiwan Study

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INTRODUCTION

- The expanding therapeutic landscape for *EGFR*-mutated non-small cell lung cancer (NSCLC)[1] highlights the need for real-world evidence to evaluate outcomes and address unmet needs beyond osimertinib
- Taiwan presents a distinct context, as first-line osimertinib only became fully reimbursed in 2024.[1,2] Previously, National Health Insurance coverage was restricted to patients with del-19 and brain metastases,[2,3] leading many treatment-naive patients to receive first- or second-generation EGFR tyrosine kinase inhibitors (TKIs), followed by osimertinib upon acquisition of the T790M resistance mutation.[3] Of note, novel regimens preferred by NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[4] are currently not reimbursed in Taiwan: Category 1 lazertinib plus amivantamab-vmjw as a first-line therapy, and amivantamab-vmjw plus chemotherapy after progression on osimertinib
- This study investigates **the real-world effectiveness and treatment patterns of therapies after osimertinib progression in NSCLC patients** across two major medical centers in Taiwan, aiming to provide valuable insights into real-world clinical practice

METHODS

Design

- Retrospective database analysis using records from the National Taiwan University Hospital Integrated Medical Database and the Chang Gung Memorial Hospital Research Database in Taiwan
- Patients who initiated second-line (2L) or third-line (3L) systemic anti-cancer therapy (SACT) after progressing from osimertinib between 1 January 2017 and 31 December 2021 were included

Primary endpoints

- **Treatment patterns**
- **Real-world progression-free survival (rwPFS)**
- **Real-world time to next therapy (rwTTNT)**
- **Real-world overall survival (rwOS)**

RESULTS

Patient disposition

- A total of 304 patients were enrolled, comprising **58 and 246 patients who received 2L and 3L SACT**, respectively (Figure 1)

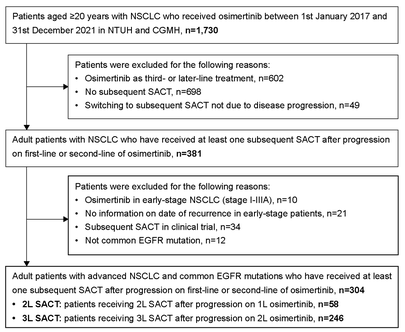


Figure 1. Study population flow diagram

1L, first-line; 2L, second-line; 3L, third-line; EGFR, epidermal growth factor receptor; CGMH, Chang Gung Memorial Hospital; NSCLC, non-small cell lung cancer; NTUH, National Taiwan University Hospital; SACT, systemic anti-cancer therapy

RESULTS

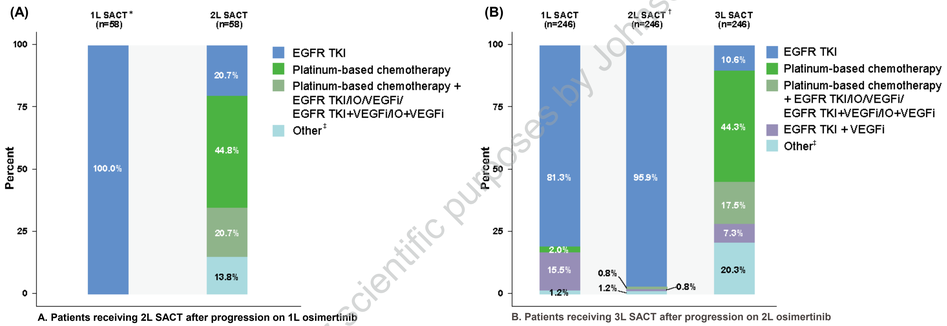
Table 1. Baseline patient and clinical characteristics

Variables	2L SACT (n=58) n	2L SACT (n=58) (%)	3L SACT (n=246) n	3L SACT (n=246) (%)
Age (years)				
Mean (SD)	64.8 (16.8)		62.0 (28.1)	
<65 years	29	(50.0)	149	(60.6)
≥65 years	29	(50.0)	97	(39.4)
Sex				
Male	21	(36.2)	85	(34.6)
Female	37	(63.8)	161	(65.4)
Smoking status				
Never smoker	38	(74.5)	190	(80.2)
Current / ever smoker	13	(25.5)	47	(19.8)
Missing	7		9	
TNM staging at initial diagnosis				
I	2	(3.4)	3	(1.3)
II	1	(1.7)	5	(2.1)
IIIA	1	(1.7)	6	(2.6)
IIIB	0	(0.0)	6	(2.6)
IV	54	(93.1)	215	(91.5)
Missing	0		11	
ECOG performance status group				
Grade 0/1	47	(92.2)	219	(93.2)
Grade 2+	4	(7.8)	16	(6.8)
Missing	7		11	

Variables	2L SACT (n=58) n	2L SACT (n=58) (%)	3L SACT (n=246) n	3L SACT (n=246) (%)
Histological classification				
Adenocarcinoma	51	(87.9)	239	(97.2)
Adenosquamous	2	(3.4)	6	(2.4)
Pleomorphic	1	(1.7)	0	(0.0)
Sarcomatoid	2	(3.4)	0	(0.0)
Other	2	(3.4)	1	(0.4)
EGFR mutations				
Exon 19 deletion	42	(72.4)	129	(52.4)
Exon 21 L858R substitution	13	(22.4)	120	(48.8)
Exon 20 T790M	8	(13.8)	135	(54.9)
Exon 18 G719X mutation	1	(1.7)	0	(0.0)
Exon 20 S768I mutation	0	(0.0)	1	(0.4)
Exon 20 insertion	0	(0.0)	17	(6.9)
Exon 19 L747P mutation	0	(0.0)	1	(0.4)
Exon 20 C797S mutation	0	(0.0)	4	(1.6)
Brain metastasis at the initial dose of post-progression SACT line	17	(29.3)	111	(45.1)
Prior local therapies				
Surgery	7	(12.1)	43	(17.5)
Radiotherapy	16	(27.6)	90	(36.6)

Percentages are derived from non-missing observations only (n).
2L, second-line; 3L, third-line; ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; SACT, systemic anti-cancer therapy; TNM, tumor, node, metastasis

Figure 2. Treatment pathways



A. Patients receiving 2L SACT after progression on 1L osimertinib

B. Patients receiving 3L SACT after progression on 2L osimertinib

*All patients receiving first-line osimertinib therapy were treated with osimertinib monotherapy (100%). †All patients classified as receiving EGFR TKI therapy as 2L SACT were treated exclusively with osimertinib monotherapy. Other classifications of osimertinib as 2L SACT involved combination with additional SACT; ‡Other treatment includes non–platinum-based chemotherapy; IO monotherapy; non–EGFR TKI regimens; osimertinib + non–EGFR TKI; osimertinib + non–platinum-based chemotherapy.
1L, first-line; 2L, second-line; 3L, third-line; EGFR TKI, epidermal growth factor receptor tyrosine kinase inhibitor; IO, immuno-oncology; SACT, systemic anti-cancer therapy; VEGFi, vascular endothelial growth factor inhibitor

Table 2. SACT regimens of post-progression SACT

Variables	2L SACT (n=58) n	2L SACT (n=58) (%)	3L SACT (n=246) n	3L SACT (n=246) (%)
SACT regimens				
EGFR TKI	12	(20.7)	26	(10.6)
EGFR TKI + VEGFi	0	(0.0)	18	(7.3)
Platinum-based chemotherapy	26	(44.8)	109	(44.3)
Platinum-based chemotherapy + EGFR TKI / IO / VEGFi / EGFR TKI + VEGFi / IO + VEGFi	12	(20.7)	43	(17.5)
Other*	8	(13.8)	50	(20.3)

*Other treatment includes non–platinum-based chemotherapy; IO monotherapy; non–EGFR TKI regimens; osimertinib + non–EGFR TKI; osimertinib + non–platinum-based chemotherapy.
2L, second-line; 3L, third-line; CI, confidence interval; EGFR TKI, epidermal growth factor receptor tyrosine kinase inhibitor; IO, immuno-oncology; SACT, systemic anti-cancer therapy; VEGFi, vascular endothelial growth factor inhibitor

- Among patients who received 2L SACT (n=58), median duration on 1L osimertinib monotherapy was 7.2 months (95% CI: 3.3 to 11.2); patients who received 3L SACT (n=246) had a median duration of 2L osimertinib monotherapy of 7.4 months (95% CI: 5.85 to 8.96)
- Across 2L and 3L SACT, platinum-based chemotherapy was the most common regimen (135 patients), followed by platinum-based chemotherapy with other medications (55 patients), EGFR TKIs alone (38 patients), and EGFR TKIs plus anti-angiogenic agents (18 patients) (Table 2, Figure 2A and 2B)

Real-world outcomes

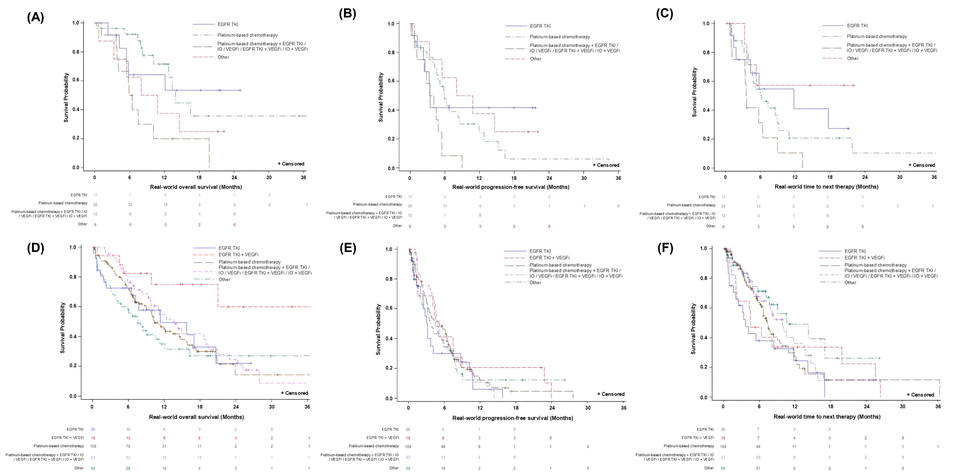
- For 2L and 3L cohorts receiving platinum-based chemotherapy, median rwPFS was 5.9 and 5.2 months, respectively; median rwTTNT was 6.2 and 7.3 months; and median rwOS was 13.9 and 10.4 months, respectively (Table 3, Figure 3A–3F)

Table 3. Real-world outcomes of post-progression SACT, median time in months (95% CI)

Post-progression SACT regimen	2L SACT (n=58) n	2L SACT (n=58) rwOS	2L SACT (n=58) rwPFS	2L SACT (n=58) rwTTNT	3L SACT (n=246) n	3L SACT (n=246) rwOS	3L SACT (n=246) rwPFS	3L SACT (n=246) rwTTNT
EGFR TKI	12	N.R.	3.4 (1.2 to N.R.)	11.8 (1.4 to N.R.)	26	11.3 (6.5 to 20.7)	3.2 (2.0 to 4.1)	3.7 (1.6 to 11.8)
EGFR TKI + VEGFi	0	–	–	–	18	N.R.	4.5 (1.3 to 9.0)	4.5 (2.0 to 19.9)
Platinum-based chemotherapy	26	13.9 (10.2 to N.R.)	5.9 (4.2 to 8.5)	6.2 (4.1 to 9.2)	109	10.4 (9.0 to 14.8)	5.2 (3.3 to 6.4)	7.3 (6.4 to 9.4)
Platinum-based chemotherapy + EGFR TKI / IO / VEGFi / EGFR TKI + VEGFi / IO + VEGFi	12	6.2 (3.7 to 10.1)	3.7 (0.7 to 5.5)	3.6 (1.0 to 6.4)	43	13.6 (9.3 to 19.4)	4.8 (4.1 to 5.8)	9.9 (6.2 to 13.5)
Other*	8	9.4 (0.7 to N.R.)	9.4 (0.7 to N.R.)	N.R.	50	7.6 (4.1 to 11.2)	3.7 (2.1 to 6.0)	10.6 (4.1 to N.R.)

*Other treatment includes non–platinum-based chemotherapy; IO monotherapy; non–EGFR TKI regimens; osimertinib + non–EGFR TKI; osimertinib + non–platinum-based chemotherapy.
CI, confidence interval; 2L, second-line; 3L, third-line; EGFR TKI, epidermal growth factor receptor tyrosine kinase inhibitor; IO, immuno-oncology; N.R., not reached; rwOS, real-world overall survival; rwPFS, real-world progression-free survival; rwTTNT, real-world time to next therapy; SACT, systemic anti-cancer therapy; VEGFi, vascular endothelial growth factor inhibitor

Figure 3. Real-world outcomes of post-progression SACT



(A) Real-world overall survival; (B) Real-world progression-free survival; (C) Real-world time to next therapy; (D) Real-world overall survival; (E) Real-world progression-free survival; (F) Real-world time to next therapy
(A)–(C) represent real-world outcomes for patients receiving 2L SACT following progression on 1L osimertinib. (D)–(F) represent real-world outcomes for patients receiving 3L SACT following progression on 2L osimertinib.
2L, second-line; 3L, third-line; EGFR TKI, epidermal growth factor receptor tyrosine kinase inhibitor; IO, immuno-oncology; SACT, systemic anti-cancer therapy; VEGFi, vascular endothelial growth factor inhibitor

DISCUSSION AND CONCLUSION

- In real-world setting, platinum-based chemotherapy was the predominant subsequent treatment after first- or second-line osimertinib
- The effectiveness of real-world subsequent treatments following osimertinib remains suboptimal, highlighting the need for novel therapies for the treatment of this patient population
- The findings support future strategies to improve first-line treatment outcomes and to manage patients after progression on osimertinib

REFERENCES, ACKNOWLEDGEMENTS & DISCLOSURES

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