Poster 1017P

Treatment Patterns and Outcomes of Second- or Third-Line Therapy in Advanced Non-Small Cell Lung Cancer with Actionable Genomic Alterations: A Multicenter Real-World Study in China (RECAP Study)

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Introduction

- Lung cancer remains the leading cause of cancer incidence and mortality worldwide[1]. Non-small-cell lung cancer (NSCLC) constitutes 80% to 85% of all lung cancer diagnoses. Molecular aberrations have led to the integration of actionable genomic alterations (AGA)-directed tyrosine kinase inhibitors (TKIs) as standard first-line (1L) therapies.
- For patients with metastatic NSCLC who experience disease progression following 1L targeted therapy, the choice of subsequent treatment is influenced by tumor molecular profiles, prior therapeutic responses, and patient performance status[2]. Osimertinib is the recommended second-line (2L) agent for patients harboring the EGFR T790M resistance mutation who have not previously received this agent. Emerging real-world data suggest that immune checkpoint inhibitors (ICIs), may offer enhanced clinical benefit in T790M-negative populations. In clinical practice, alternative approaches, including rechallenge with first- or later-generation epidermal growth factor receptor (EGFR) TKIs, ICI monotherapy, chemoimmunotherapy, and anti-angiogenic therapies with or without ICIs, are frequently employed.
- These patterns are particularly variable across China due to disparities in healthcare infrastructure, access to molecular diagnostics, and the availability of targeted agents[3]. As a result, real-world treatment patterns for patients who progress beyond 1L therapy remain heterogeneous, underscoring the need for comprehensive data on biomarker-driven treatment strategies and their associated outcomes in routine clinical settings.

Objective

- The objective of this analysis was to provide real-world insights specific to advanced NSCLC with AGA, to inform personalized treatment strategies and support the refinement of clinical guidelines for managing this specific population.

Methods

Study design :

- The RECAP study is a multicenter, retrospective, real-world study (NCT06617390) conducted at six centers across China. Patients diagnosed with advanced NSCLC on or after January 1, 2018, and who initiated second- or third-line (3L) systemic therapy between September 1, 2019, and December 31, 2022, were eligible for inclusion.
- In the AGA cohort, patients were categorized based on the line of therapy they were receiving at the time of study enrollment into the second-line (2L-enrolled) or third-line (3L-enrolled) groups.

Patient Selection:

- Age of 18 years or older at the time of diagnosis; Histologically or cytologically confirmed stage IV NSCLC; Presence of at least one AGA; and documented initiation of 2L or 3L systemic therapy during the defined study period. Patients with confirmed EGFR, anaplastic lymphoma kinase (ALK), c-ros oncogene 1 receptor tyrosine kinase (ROS1) alterations must have received targeted therapy directed against these mutations in either the 1L or 2L setting.

Variables:

- Regimens were categorized into six groups—targeted monotherapy (T), targeted combination therapies (T+), chemotherapy monotherapy (C+), chemotherapy-based combinations without targeted agents (C+), anti-angiogenic monotherapy (A), and other regimens (O).

Outcomes:

- The primary outcome was the real-world distribution of different treatment options in NSCLC patients with AGA in 2L+ setting. Secondary outcomes included biomarker testing patterns (including timing, proportion, methods, and specimen types associated with biomarker detection) and clinical outcomes (including real-world effectiveness and safety profiles). Real-world effectiveness included real-world progression-free survival (rwPFS), time to treatment discontinuation (rwTTD), time to next treatment or death (rwTTNT), and real-world overall survival (rwOS).

Results

- Between 2018 and 2022, 11194 patients diagnosed with stage IV NSCLC were screened, and 4718 patients receiving 2L or 3L treatment during 2019 and 2022 were identified. Of those, 658 patients with AGAs were included in full analysis set, all of whom were also part of the efficacy analysis set.
- At study enrollment, 602 patients (91.5%) were in the 2L-enrolled group, 56 (8.5%) were in the 3L-enrolled group (Figure 1).
- The mean age of the AGAs cohort at enrollment was 59.3±10.9 years. Of the patients, 57.9% were female, and a history of smoking was reported in 25.2% of the patients.
- Prior tumor surgery and radiotherapy were recorded in 74 (11.3%) and 152 (23.1%) patients, respectively. Regarding EGFR mutation status, 590 (89.7%) patients were EGFR-mutant, while 68 (10.3%) were non-EGFR mutant (Table 1).

Figure 1. Patient flowchart

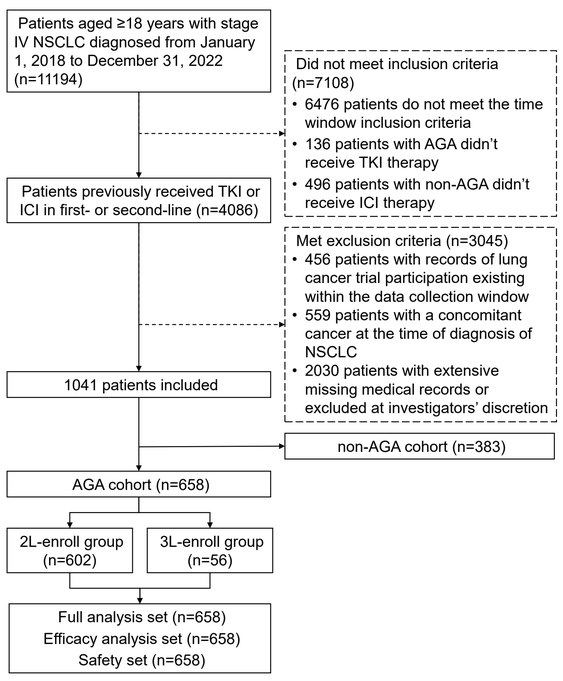

Table 1. Characteristics of patients with AGA

Variable	All (N = 658)
Age (years), Mean±SD	59.3±10.9
Sex, *n* (%)	
Male	277 (42.1)
Female	381 (57.9)
Smoking history, *n* (%)	
Yes	166 (25.2)
No	458 (69.6)
Unknown	34 (5.2)
ECOG performance status, *n* (%)	
0	88 (13.4)
1	195 (29.6)
2	39 (5.9)
3	11 (1.7)
4	6 (0.9)
Not assessed	319 (48.5)
Presence of comorbidities, *n* (%)	432 (65.7)
Histological type, *n* (%)	
Squamous cell carcinoma	13 (2.0)
Adenocarcinoma	632 (96.1)
Adenosquamous carcinoma	8 (1.2)
Other	3 (0.5)
Unknown	2 (0.3)
History of intracranial metastases, *n* (%)	301 (45.7)
History of other distant metastatic sites, *n* (%)	643 (97.7)
Prior tumor surgery, *n* (%)	74 (11.3)
Prior tumor radiotherapy, *n* (%)	152 (23.1)
Newly developed brain metastases at enrollment, *n* (%)	48 (7.3)
EGFR mutation status, *n* (%)	
EGFR-mutant	590 (89.7)
Non-EGFR mutant	68 (10.3)

Results

- All patients underwent molecular profiling. EGFR was detected in 90.9% of patients (598 of 658), and 89.7% of patients (590 of 658) had the EGFR mutation. For ALK alterations, records were available for 100 patients (15.2%), with 44 patients (6.7%) testing positive.

Table 2. Biomarker testing pattern

Variable, *n* (%)	All (N = 658)
EGFR alteration record	598 (90.9)
Positive	590 (89.7)
Negative	8 (1.2)
ALK alteration record	100 (15.2)
Positive	44 (6.7)
Negative	56 (8.5)
ROS1 alteration record	58 (8.8)
Positive	13 (2.0)
Negative	45 (6.8)
NTRK alteration record	10 (1.5)
Positive	0
Negative	10 (1.5)
BRAF alteration record	35 (5.3)
Positive	13 (2.0)
Negative	22 (3.3)
RET alteration recor	21 (3.2)
Positive	7 (1.1)
Negative	14 (2.1)
MET alteration record	45 (6.8)
Positive	28 (4.3)
Negative	17 (2.6)

Figure 2. The real-world distribution of different treatment options for NSCLC patients.

- Among patients in the 2L-enrolled group (n=602), T therapy (75.3%, 453/602) was the most frequently administered in 1L treatment, with similar patterns observed among EGFR-mutated patients (74.5%, 404/542) (Figure 2A).
- For patients enrolled into 3L-enrolled group (n=56), T (85.7%, 48/56) therapy was predominant during prior 2L treatment. Among patients with EGFR mutations (n=48), the usage rate of T therapy was 12.5% in the 3L setting (Figure 2B).

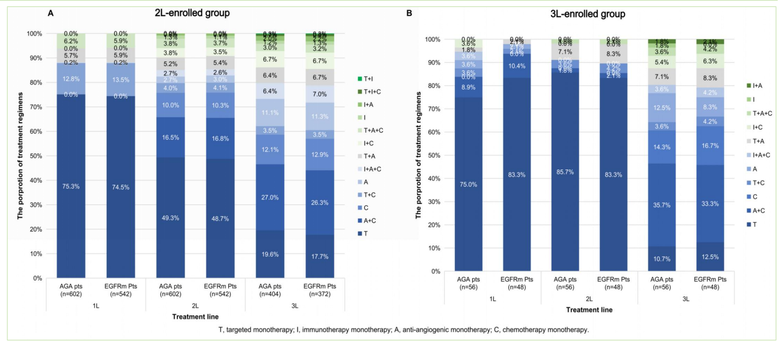

Figure 3. Sankey diagrams of treatment sequences in EGFRm 2L-enrolled patients.

- Among 542 patients harbored EGFR mutations in the 2L-enrolled group, 136 received third-generation TKIs, while 404 were treated with first- or second-generation TKIs in the 1L setting.
- For patients initially treated with third-generation TKIs, 47.8%, 24.3% and 15.4% transitioned to C+, T+, and C regimens, respectively, during 2L therapy (Figure 3A).

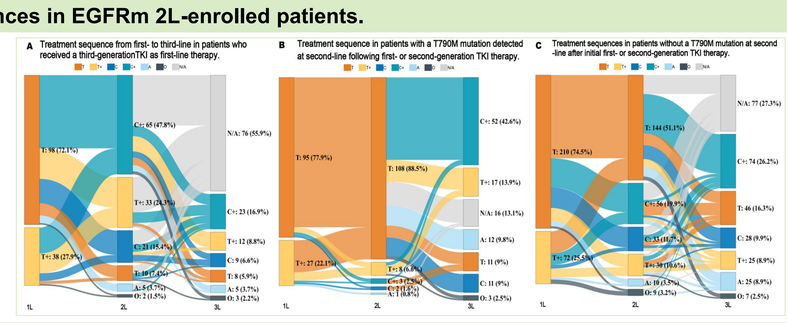

Figure 4. rwPFS at 2L and 3L treatment in 2L-enrolled patients.

- With a median follow up of 10.1 months (range, 0.03-38.2), the median rwPFS for the 2L-enrolled group was 7.4 months (95% CI, 6.5-8.0) in 2L treatment (Figure 4A). In the EGFR-mutated subgroup, patients initially received third generation TKIs followed by T+ in 2L treatment achieved a median rwPFS of 14.0 months (95% CI, 8.3-not estimable [NE]) (Figure 4B).
- The median rwPFS was 5.4 months (95% CI, 4.6-6.2) in 3L treatment (Figure 4D). EGFR-mutated patients who initially received third generation TKIs followed by T+ in 3L treatment achieved a median rwPFS of 11.3 months (95% CI, 3.6-NE) (Figure 4E).

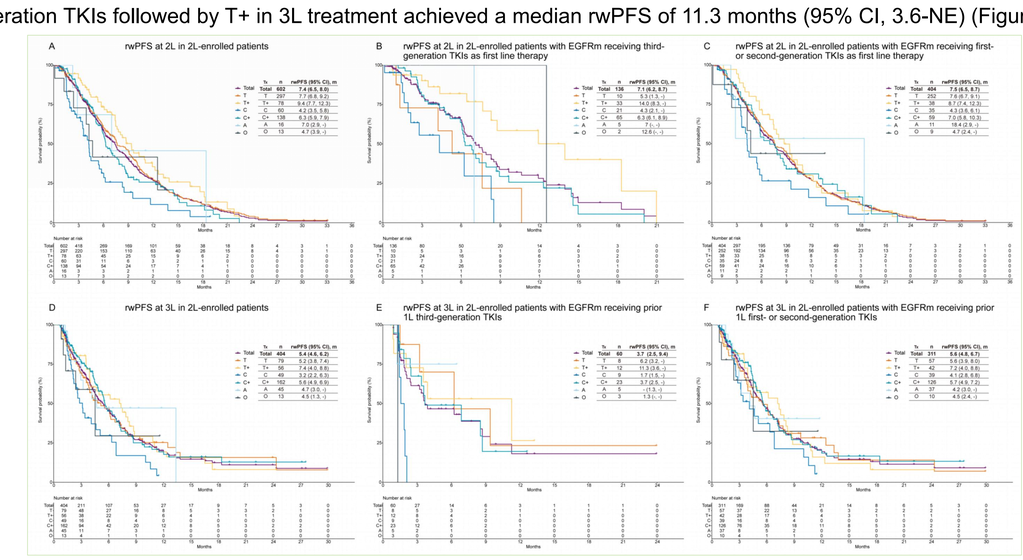

Figure 5. rwPFS in 3L-enrolled patients.

- The overall median rwPFS was 7.2 months (95% CI, 4.2-9.1) in 3L treatment. Among all regimen, T+ showed the longest median rwPFS at 12.0 months (95% CI, 5.9 - NE) in 3L treatment (Figure 5A).
- The overall median rwPFS in the EGFRm subgroup was 7.1 months (95% CI, 4.1-9.1) (Figure 5B).

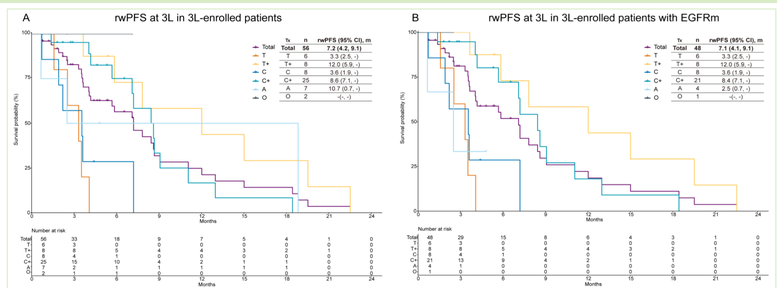

Table 3. Summary of adverse events (AEs).

- Among the 658 patients, 97 (14.7%) experienced at least one AE. Grade 3 and grade 4 AEs occurred in 2.4% (16 patients) and 1.5% (10 patients), respectively.
- The most frequently reported AE was myelosuppression (7.4%).
- It is important to note that the incidence of AEs was likely underreported due to incomplete documentation by clinicians.

Variables, *n* (%)	All (N = 658)
Patients with any AE	97 (14.7)
Grade	
1	22 (3.3)
2	25 (3.8)
3	16 (2.4)
4	10 (1.5)
Unknown	54 (8.2)
Impact on treatment	
No impact	71 (10.8)
Treatment discontinued	18 (2.7)
Treatment interrupted	8 (1.2)
Dose adjusted	3 (0.5)
Medication switched	2 (0.3)
Unknown	1 (0.2)

Variables, *n* (%)	All (N = 658)
Common AEs	
Myelosuppression	49 (7.4)
Gastrointestinal reactions	29 (4.4)
Dermatologic/mucosal abnormalities	17 (2.6)
Fatigue	10 (1.5)
Anemia	6 (0.9)
Infection	4 (0.6)
Cardiac dysfunction	4 (0.6)
Hepatic dysfunction	4 (0.6)
Pain	3 (0.5)

Conclusion

- The RECAP study highlights the therapeutic heterogeneity and evolving treatment paradigms among Chinese patients with advanced NSCLC harboring AGAs.
- This study demonstrates that targeted therapies remain the cornerstone of 2L and 3L treatment for advanced NSCLC, exhibiting favorable clinical effectiveness. Furthermore, rechallenge with targeted agents following disease progression is frequently observed in practice.

Abbreviations:

1L, first-line; 2L, second-line; 3L, third-line; AE, adverse event; AGA, actionable genomic alterations; ALK, anaplastic lymphoma kinase; BRAF, v-raf murine sarcoma viral oncogene homolog B1; ECOG, eastern cooperative oncology group; EGFR, epidermal growth factor receptor; ICI, immune checkpoint inhibitor; MET, MET proto-oncogene, receptor tyrosine kinase; NE, not estimable; NSCLC, non-small-cell lung cancer; NTRK, neurotrophic receptor tyrosine kinase; RET, ret proto-oncogene; ROS1, c-ros oncogene 1 receptor tyrosine kinase; rwOS, real-world overall survival; rwPFS, real-world progression-free survival; rwTTD, time to treatment discontinuation; rwTTNT, time to next treatment or death; TKIs, tyrosine kinase inhibitors.

Disclosures:

All authors declare no competing interests. Leilei Ma is employed by Daiichisankyo (China) Holdings Co., Ltd.

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