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Long-Term Survival Outcome After First-line Osimertinib Monotherapy in Advanced/Metastatic NSCLC in Japanese Population: Results from LC-SCRUM-Asia

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Key Takeaway

Real-world outcomes of first-line osimertinib in a Japanese cohort revealed shorter overall survival compared to clinical trial data, underscoring the need for improved 1L treatment strategies in advanced cEGFRm NSCLC.

Conclusions

In this "trial-eligible" real-world Japanese cohort, 1L osimertinib resulted in a median OS that was approximately 3.4 months shorter than that reported in the FLAURA trial.

Majority of patients (86%) had at least one risk factor associated with poor survival, including aged 75 years or older, presence of EGFR L858R mutations, or metastases to the brain, bone, or liver.

A substantial proportion of patients (26%) did not receive 2L therapy after discontinuing 1L osimertinib.

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Poster

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Disclosures
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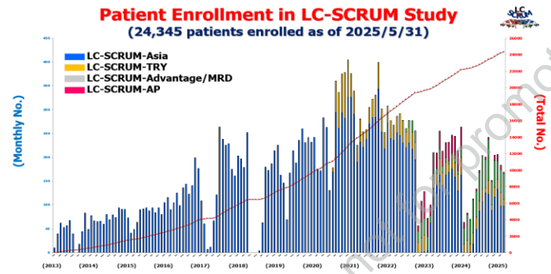
Introduction

- The long-term survival rate remains poor for advanced/metastatic common EGFR-mutated (a/m cEGFRm) NSCLC patients
- Osimertinib was approved in Japan in 2018 for patients with cEGFRm. FLAURA trial reported a median overall survival (OS) of 38.6 months[1]. The survival rate at 2- and 3-year was 74% and 54%, respectively[1]
- However, real-world evidence on long-term outcomes with 1L osimertinib in Japan remains limited. Existing real-world studies in Japan are often limited by small sample sizes and short follow-up durations[2-5]
- This study aims to assess real-world overall survival (rwOS) following 1L osimertinib among Japanese patients using LC-SCRUM-Asia

Methods

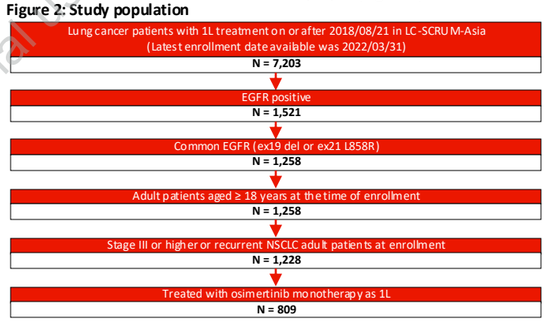
- Data were obtained from LC-SCRUM-Asia, a nationwide, multicenter genomic registry to advance personalized medicine in lung cancer. The registry enrolled NSCLC patients with stage II or higher, ECOG<2, with adequate organ functions, without serious complications, and have >3 months life expectancy
- Index date was defined as the initiation date of 1L osimertinib on or after approval date in Japan (2018/08/21)
- The latest enrollment date available was 2022/03/31. Patients were followed-up until death, loss to follow up, or data cut-off (2024/12/31), whichever comes first

Figure 1: Patient enrollment by year from 2013 to May 2025 in LC-SCRUM



- Our study included adult patients with a/m cEGFRm NSCLC patients who initiated 1L osimertinib on or after 2018/08/21 (**Figure 2**)

Figure 2: Study population



Results

Study population and baseline characteristics

- A total of 809 patients with 1L osimertinib were included **(Table 1)**
- At enrollment, the median age was 71 years (IQR: 63, 77), 65% were female and 59% having never smoked
- ECOG performance status was 0 in 42% of patients, 95% were stage IV, and 52% had exon19 deletions. Baseline metastases were noted in 31% of patients for brain, 11% for liver, and 40% for bone
- The median follow up duration from index date was 37.5 months (95%CI: 12.6, 62.0) in 333 censored cases

Table 1: Baseline demographic and clinical characteristics of patients with cEGFRm NSCLC who were treated with 1L osimertinib monotherapy

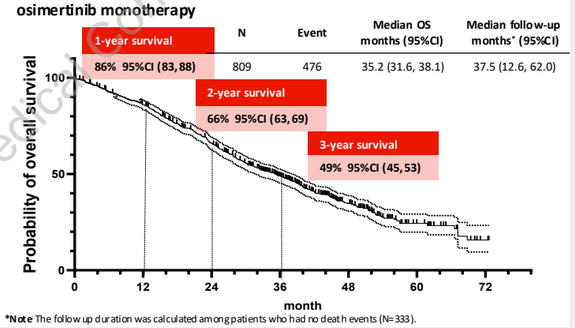
Characteristics	Study population (N=809)
Age, median (range)	71 (63, 77)
Female (%)	526 (65%)
Stage at enrollment (%)	
Stage III	39 (5%)
Stage IV	770 (95%)
Smoking status (%)	
Current smoker	276 (34%)
Past smoker	49 (6%)
Never smoker	480 (59%)
ECOG (%)	
0	338 (42%)
1	471 (58%)
EGFR mutation type (%)	
Ex19del	420 (52%)
L858R	389 (48%)
Metastatic sites (%)	
Brain	247 (31%)
Liver	91 (11%)
Bone	323 (40%)

Abbreviations: ECOG: Eastern Cooperative Oncology Group; EGFR: Epidermal Growth Factor Receptor

Overall survival

- The median rwOS following 1L osimertinib was 35.2 months (95% CI: 31.6, 38.1, **Figure 3**)
- In this patient cohort, the real-world survival rate was 86% at 1 year, 66% at 2 years, and 49% at 3-year of follow up, respectively
- The 2-year and 3-year real-world survival rate was 8% and 5% lower than those reported in the FLAURA trial

Figure 3: OS in patients with cEGFRm NSCLC who were treated with 1L osimertinib monotherapy



***Note** The follow up duration was calculated among patients who had no death events (N=333).

Multivariate analysis for survival

- Risk of death was evaluated using a multivariate Cox model adjusted for age at the index date, brain, liver and bone metastasis status, presence of L858R substitutions. The attrition rate was assessed with 95% CI
- Patients with older age (≥75 years), brain metastases, liver metastases, bone metastases and L858R were associated with a statistically significantly increased risk of death compared with patients without these clinical features (**Table 2**)

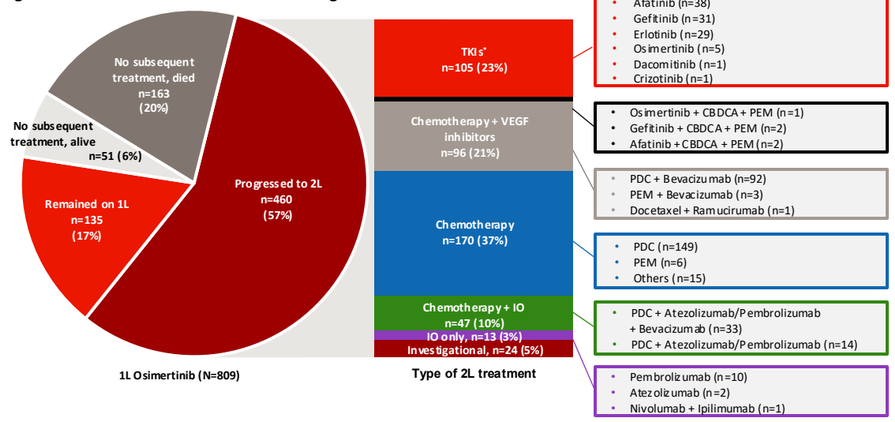
Table 2: Multivariate analysis for survival

Risk factors	Prevalence (%)	Hazard Ratio (95% CI)	P-value*
≥75 years of age	33%	1.53 (1.26, 1.85)	<0.001
Brain metastases	31%	1.38 (1.14, 1.68)	<0.001
Liver metastases	11%	1.72 (1.33, 2.24)	<0.001
Bone metastases	40%	1.54 (1.28, 1.87)	<0.001
EGFR exon 21 L858R	48%	1.37 (1.14, 1.65)	<0.001

Abbreviations: CI: confidence interval
***Note**: P-values were obtained from the Cox regression analysis.

Second-line (2L) treatments post 1L osimertinib monotherapy

Figure 4: Distribution of 2L treatments following 1L osimeritinib



- Among all patients, 26% ((163+51)/809) did not receive 2L therapy following 1L osimertinib (**Figure 4**)
- Among 57% patients who received 2L therapy, the most common treatments were:
  - Chemotherapy (37%)
  - Tyrosine kinase inhibitor (23%)
  - Chemotherapy plus VEGFi (21%)

* Among 105 patients with TKIs as 2L treatment, 16 were combined with VEGF inhibitors

Abbreviations: 1L, first-line; 2L, second-line; CBDCA, carboplatin; IO, immunotherapy; PDC, platinum-doublet chemotherapy; PEM, pemetrexed; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor

Real-world Best Overall Response (rwBOR)

- The real-world BOR of 1L osimertinib is 65%

Note: Calculated among patients who had an evaluable tumor response

Limitations

- The population eligible for the registry may not fully represent those outside the registry enrollment criteria
- The study was a real-world observational study. Given the retrospective and observational nature, the study may be subject to considerations such as missing document of information, variability in the quality of the information recorded and difference in clinical practices across Japan

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