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# FIN-EGFR/CNS: Real World Survival and patient characteristics of Epidermal Growth Factor Receptor (EGFR) mutated Non-Small Cell Lung Cancer (NSCLC) Patients with central nervous system (CNS) Metastases in Finland

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## Key Takeaway

EGFR mutated NSCLC patients with CNS metastases exhibit poor OS, regardless of the specific EGFR mutation. This underscores the need for earlier diagnosis and improved treatments to prevent and manage CNS metastases in EGFR-mutant NSCLC.

## Conclusions

40% of the advanced EGFR-mutated NSCLC patients had CNS metastases at diagnosis and they were younger compared to those without CNS metastases at diagnosis.

The median OS for patients with CNS metastases at diagnosis (Early-CNS) was poor (5.0 vs 22.9 months in the Non-CNS group). There were no significant OS differences among Early-CNS patients across Del19 (9.7 months), L858R (4.0 months), and other EGFR (2.5 months) mutation groups.

Among EGFR-mutated NSCLC patients, bone metastases were most common at diagnosis (31%), followed by CNS (21%) and liver (17%). In patients who developed metastases later, OS declined notably after 1 year for liver, 2 years for CNS, and 3 years for bone metastases (Late groups), compared to their respective non-metastatic groups (Non groups).

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**Disclosures**

Aija Knuuttila and Maria Silvoniemi has nothing to disclose. Lalli Nurmi and Eija Heikkilä received consulting fees paid to their employer by Johnson & Johnson company. Monica Ekblom and Anna Bonin are employees of Johnson & Johnson company.

## Introduction

- Approximately 30%-50% of the EGFR-mutation positive patients develop CNS metastases within 5 years of diagnosis. However, real-world studies on these patients, their characteristics, and treatment outcomes remain scarce.
- The third-generation EGFR TKI, osimertinib, has improved CNS penetrance compared to first- and second-generation TKIs. It has demonstrated superior efficacy against CNS metastases in EGFR-mutated NSCLC compared to platinum-pemetrexed treatment. Osimertinib received reimbursement status for first-line treatment of advanced EGFR-mutated NSCLC in Finland in October 2020.
- In addition to brain metastases, liver and bone metastases are common in lung cancer and are associated with shorter survival. Understanding metastatic patterns is therefore essential for improving patient management.
- Finland's hospital data lakes enable unique real-world evidence (RWE) studies by linking electronic health records (EHRs) with national registers. This study used such data to examine the proportion of metastasis, patient characteristics, and treatment patterns of EGFR-positive NSCLC patients with CNS metastases. Overall survival (OS) was also analyzed separately for patients with liver and bone metastases.

## Methods

### Study design, cohort and timelines

- This retrospective observational study used individual-level data from hospital data-lakes and national registers in Finland. It included NSCLC patients with defined EGFR mutations diagnosed between January 2017 and September 2023 at the two university hospitals—Helsinki (HUS) and Turku (TYKS)—covering about 55% of all NSCLC cases in the country.
- Advanced NSCLC was identified by stage IIIb or IV records or by receiving advanced treatments such as chemotherapy (CT) or tyrosine kinase inhibitors (TKIs). CNS, liver, and bone metastases were identified from doctors' notes.
- Metastases were categorized as Early (within ±3 months of diagnosis) or Late (after 3 months from diagnosis), resulting in groups: Early-/Late-CNS, Early-/Late-Liver, and Early-/Late-Bone. The reference groups without the respective metastases were referred to as Non-CNS, Non-Liver, and Non-Bone.

### Data-analyses and Statistical methods

- Overall survival was analyzed from the initiation of first line (1L) treatment. Early and Late metastatic groups were compared to reference advanced NSCLC groups without respective metastasis (Non groups) using Kaplan-Meier analysis and log rank test.

## Results

### Study population and proportion of patients with CNS metastasis

- A total of 544 EGFR mutation-positive NSCLC patients were included in the study. Of these, 286 (53%) were diagnosed with advanced-stage disease (aNSCLC), of which 242 (85%) had stage IV disease at initial diagnosis.
- During the follow-up, 21% of the total population (115 among 544) and 40% of advanced-stage patients (115 among 286) developed CNS metastases at any time-point of their disease. Among advanced-stage patients, 24% (n=70) had CNS metastases at diagnosis (±3 months; Early-CNS group), while 12% (n=33) developed CNS metastases later during treatment (Late-CNS group).
- Approximately 5% of patients diagnosed in early-stage developed CNS metastases later during their disease (Recurrent-CNS group, not included in this analysis).

**Table 1: Patient characteristics of EGFR-mutated advanced NSCLC patients with CNS metastases identified within ±3 months of diagnosis (Early-CNS) or without CNS metastases during follow-up (Non-CNS)**

| Characteristic | Non-CNS | Early-CNS | Total |
|---|---|---|---|
| N (%) | 183 (72%) | 70 (28%) | 253 (100% |
| Female, n (%) | 121 (66%) | 44 (63%) | 165 (65%) |
| Age, years median (IQR) | 73.2 (67-80) | 69.2 (62-74) | 72.05 (65-78) |
| Age group, n (%): | | | |
| Age <65 | 38 (21%) | 23 (33%) | 61 (24%) |
| Age 65-75 | 69 (38%) | 34 (49%) | 103 (41%) |
| Age >75 | 76 (42%) | 13 (19%) | 89 (35%) |
| BMI, mean (sd) | 25.7 (5) | 24.79 (4) | 25.4 (5) |
| BMI missing, n (%) | 68 (37%) | 13 (19%) | 81 (32%) |
| Stage, n (%) | | | |
| Stage IIIb | ~10%* | <5* | 21 (8%) |
| Stage IV | 154 (84%) | 66 (94%) | 220 (87%) |
| Stage unknown | ~6%* | <5* | 12 (5%) |
| EGFR mutation, n (%) | | | |
| Del19 | 76 (42%) | 28 (40%) | 104 (41%) |
| L858R | 61 (33%) | 23 (33%) | 84 (33%) |
| Other EGFR mutation | 46 (25%) | 19 (27%) | 65 (26%) |

*Results based on fewer than five patients (<5) cannot be shown. Additionally, any values in the table that could be used to infer results for groups smaller than five are not reported as exact numbers but are instead presented as approximate proportions (~%).

### Patient characteristics for patients with or without CNS metastasis

- The Early-CNS group had a lower median age (69.2 years) and lower proportion of patients over 75-years of age (19%) compared to the patients diagnosed with advanced NSCLC without CNS-metastasis (Non-CNS group) (73.2 years and 42% over 75 years of age).
- 23% of the Early-CNS patients were treated with third generation TKI, 24% with second generation TKI and 9% with first generation TKI. 25% received only palliative radiotherapy without systematic treatments and 9% got no active lung cancer treatment.

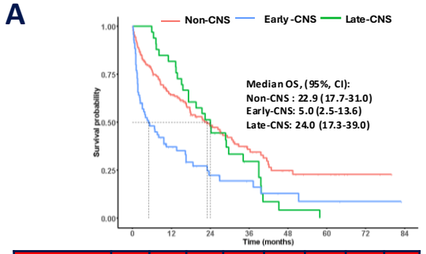
### Proportion of patients with liver and bone metastasis

- During the follow-up, 17% developed liver and 31% developed bone metastasis from the total study population

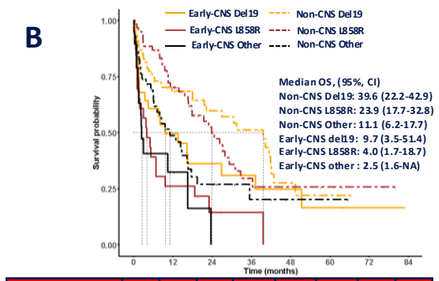
### OS analysis for CNS metastasis by CNS metastasis groups and EGFR mutational groups

- The median OS was significantly shorter for the Early-CNS group (5.0 months, 95% CI: 2.5–13.6) compared to the Non-CNS group (22.9 months, 95% CI: 17.7–31.0, p<0.001). There was no significant difference between the Late-CNS group (24 months, 95% CI: 17.3–39.0) and the Non-CNS group (22.9 months, p=0.363). However, OS for the Late-CNS group began to decline more compared to the Non-CNS group after two years from the initiation of 1L treatment (Figure 1A).
- The median OS did not differ significantly between different mutational groups for Early-CNS patients (Figure 1B).

**Figure 1: OS for patients in the A) Non-CNS, Early-CNS and Late-CNS groups and B) Non-CNS and Early-CNS stratified by del19, L858R and all other EGFR mutations combined.**




| Time (months) | 0 | 12 | 24 | 36 | 48 | 60 | 72 | 84 |
|---|---|---|---|---|---|---|---|---|
| Non-CNS | 183 | 98 | 50 | 25 | 13 | 8 | 2 | 0 |
| Early-CNS | 70 | 20 | 9 | 6 | 3 | 2 | 1 | 0 |
| Late-CNS | 33 | 27 | 14 | 7 | 1 | 0 | 0 | 0 |

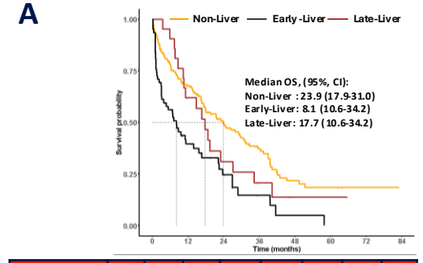



| Time (months) | 0 | 12 | 24 | 36 | 48 | 60 | 72 | 84 |
|---|---|---|---|---|---|---|---|---|
| Early-CNS del19 | 28 | 11 | 7 | 5 | 3 | 2 | 1 | 0 |
| Early-CNS L858R | 23 | 6 | 2 | 1 | 0 | 0 | 0 | 0 |
| Early-CNS other | 19 | 3 | 0 | 0 | 0 | 0 | 0 | 0 |
| Non-CNS del19 | 76 | 44 | 23 | 14 | 6 | 3 | 0 | 0 |
| Non-CNS L858R | 61 | 37 | 19 | 8 | 6 | 4 | 2 | 0 |
| Non-CNS other | 46 | 17 | 8 | 3 | 1 | 1 | 0 | 0 |

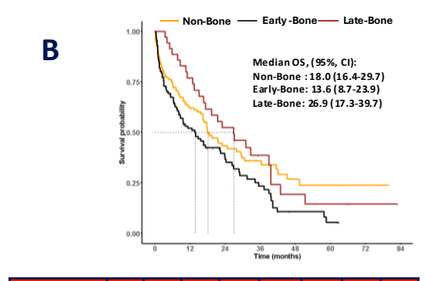
### OS analysis for liver and bone metastasis

- The median OS was significantly shorter for the Early-Liver group (8.1 months, 95% CI: 10.6–34.2) compared to the Non-Liver group (23.9 months, 95% CI: 17.9–31.0, p<0.001). No significant difference was observed between the Late-Liver group (17.7 months, 95% CI: 10.6–34.2) and the Non-Liver group (p=0.371), nor between the Early- and Late-Liver groups (p=0.094). OS for the Late-Liver group began to decline more noticeably than the Non-Liver group after one year from first line treatment initiation (Figure 2A). There was a significant difference in OS between Early-Liver Del19 mutation (22.5 months; 95% CI: 4.6–NA; n=18) and L858R mutation (5.0 months; 95% CI: 2.9–NA; n=27, p=0.026) groups.
- The median OS was significantly shorter for the Early-Bone group (13.6 months, 95% CI: 8.7–23.9) compared to both the Non-Bone group (18.0 months, 95% CI: 16.4–29.7, p=0.039) and the Late-Bone group (26.9 months, 95% CI: 17.3–39.7, p=0.039). OS for the Late-Bone group declined more noticeably than the Non-Bone group after three years from 1L treatment initiation (Figure 2B).

**Figure 2: OS for patients in the A) Non-Liver, Early-Liver and Late-Liver groups and B) Non-Bone, Early-Bone and Late-Bone groups**




| Time (months) | 0 | 12 | 24 | 36 | 48 | 60 | 72 | 84 |
|---|---|---|---|---|---|---|---|---|
| Non-Liver | 198 | 112 | 56 | 31 | 15 | 9 | 3 | 0 |
| Early-Liver | 62 | 19 | 9 | 3 | 1 | 0 | 0 | 0 |
| Late-Liver | 21 | 12 | 6 | 3 | 1 | 1 | 0 | 0 |




| Group | 0 | 12 | 24 | 36 | 48 | 60 | 72 | 84 |
|---|---|---|---|---|---|---|---|---|
| Non-Bone | 135 | 69 | 33 | 18 | 10 | 5 | 2 | 0 |
| Early-Bone | 135 | 52 | 24 | 13 | 4 | 2 | 0 | 0 |
| Late-Bone | 35 | 25 | 17 | 8 | 4 | 3 | 1 | 0 |

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