60P

The FIN-EGFR study: A retrospective observational study to investigate the treatment landscape and outcomes of early and advanced stage patients with EGFR mutated non-small cell lung cancer (NSCLC) in Finland

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Key Takeaway

This Finnish retrospective multicenter study provides a comprehensive overview of the characteristics and treatment outcomes of EGFR-mutated NSCLC patients, both in early- and advanced-stage cases. The results highlight mutational- and treatment-specific differences concerning TTNT, particularly in advanced-stage patients. The poor OS in advanced-stage cases underscores the need for improved therapies and earlier diagnostics.

Conclusions

Half of the patients were diagnosed in advanced stage and 19% were previously diagnosed with another cancer. The incidence remained stable throughout the study period, ranging from 7-9%.

Concerning advanced-stage patients the observed 1L TTNT for del19 mutated patients was 18.0 months, for L858R 13.4 and for exon20ins patients 6.6 months. By end of 2023, 33% of the 1L advanced stage patients died before getting 2L treatment, 27% were still on 1L therapy and 37% received 2L treatment, either EGFR TKI (56%) or chemotherapy (34%).

The median OS for the patients diagnosed at advanced stage was 23 months. At 5 years post-diagnosis, 70.3% of early-stage patients and 15.8% of advanced-stage patients were alive.

Acknowledgments

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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

- Multiple activating mutations of the epidermal growth factor receptor (EGFR) of non-small cell lung cancer (NSCLC) patients have been identified, each influencing both the biological behavior of the specific cancer type in questions and the efficacy of targeted therapies.
- Tyrosine kinase inhibitors (TKIs) have revolutionized the treatment of EGFR-mutation positive NSCLC; however, the efficacy and mechanisms of action can vary significantly depending on the specific mutational subtype. The heterogeneity of EGFR mutations also poses challenges regarding the initial treatment response and long-term efficacy.
- The hospital data lakes in Finland enable unique opportunities for real-world evidence (RWE) studies by combining hospital electronic health records (EHRs) with national registers. This study utilizes RWE data to characterize the demographics, clinical characteristics, treatment paths, and outcomes of different EGFR-mutated NSCLC patients in Finland, across both early and advanced disease stages.

Methods

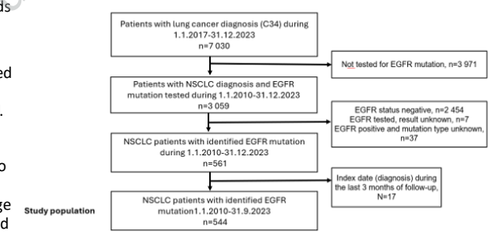
Study design, cohort and timelines

- This retrospective observational study utilized patient level data from hospital medical records and national registers in Finland concerning patients diagnosed with EGFR-mutation positive NSCLC from January 1st, 2017, to September 30th, 2023.
- The study includes all NSCLC patients regardless of disease stage at diagnosis, with any defined EGFR mutation/s in 2 of Finland's university hospitals: Helsinki University Hospital and Turku University Hospital, which together treat approximately 55% of the NSCLC patients in Finland.

Data-analyses and Statistical methods

- Time to next treatment (TTNT) was studied using Kaplan-Meier analysis with a log-rank test to compare outcomes across EGFR mutation sub-groups, and treatment types. TTNT was calculated from the first treatment received for early or advanced-stage disease. Disease stage at diagnosis was determined by treatment type or disease stage. Overall survival was analyzed for the early- and advanced-stage groups separately from the start of respective treatment.

Figure 1: Flowchart of study population inclusion:



Results

Study population and patient characteristics

- A total of 544 EGFR-mutation positive NSCLC-patients were identified. Baseline characteristics of the patients are presented in Table 1.
- The cohort's mean age was 70.6 years; 68% were women. At the first NSCLC diagnosis, 25% had Stage I and 51% Stage IV disease. The most common EGFR mutation was exon 19 deletion (del19, 40%), followed by L858R (33%). EGFR exon 20 insertion (exon20ins) mutations appeared in 6% of patients. Other subgroups included multiple EGFR mutations (multiple, 7%), major uncommon mutations G719X, L861X, S768X (major uncommon, 5%), and other EGFR mutations (other uncommon, 9%) (Table 1). Additionally, 19% had other cancer diagnosis, and 17% had atrial hypertension (Table 1).

Table 1: Patient characteristics

Characteristics	del19	L858R	exon20ins	Multiple	Major uncommon	Other uncommon	All
Patients, n (%)	220 (100%)	180 (100%)	30 (100%)	37 (100%)	28 (100%)	49 (100%)	544 (100%)
Share by mutation group (%)	40%	33%	6%	7%	5%	9%	100%
Female, n (%)	151 (69%)	129 (72%)	20 (67%)	30 (81%)	18 (64%)	23 (47%)	371 (68%)
Mean age, years (SD)	69.9 (11.8)	71.3 (8.7)	71.0 (8.9)	69.4 (8.8)	74.1 (9.7)	71.3 (8.1)	70.6 (10.1)
Histology, n (%) Adenocarcinoma Other	194 (88%) 26 (12%)	164 (91%) 16 (9%)	25 (83%) 5 (13%)	~90% ~10%	~90% ~10%	30 (61%) 19(39%)	472 (87%) 72 (13%)
BMI Mean (SD) Missing, n (%)	26.3 (5.3) 45 (20%)	25.4 (5.3) 33 (18%)	27.0 (4.6) 8 (27%)	24.4 (4.8) 8 (22%)	25.6 (5.7) 6 (21%)	25.5 (3.9) 8 (16%)	25.8 (5.2) 108 (20%)
Smoking status, n (%) Never Current smoker Ex-smoker Missing	69 (31%) 9 (4%) 15 (7%) 127 (58%)	54 (30%) 9 (5%) 17 (9%) 100 (56%)	12 (40%) <5 <5 14 (47%)	9 (24%) 0 5 (14%) 23 (62%)	6 (21%) <5 <5 16 (57%)	7 (14%) <5 10 (20%) 29 (59%)	157 (29%) 27(5%) 51(9%) 309 (57%)
Stage, n (%) Stage I Stage II Stage III Stage IV Missing	64 (29%) 11 (5%) 16 (7%) 110 (50%) 19 (9%)	45 (25%) 15 (8%) 12 (7%) 91 (51%) 17 (9%)	<5 <5 <5 19 (63%) <5	11 (30%) 0 (0%) <5 18 (49%) #	8 (29%) <5 <5 15 (54%) <5	# <5 7 (14%) 25 (51%) 7 (14%)	138 (25%) 36 (7%) 41 (8%) 278 (51%) 51 (9%)
Charlson Comorbidity Index, mean (SD)	0.30 (0.76)	0.20 (0.48)	0.40 (0.86)	0.30 (0.52)	0.39 (0.57)	0.76 (0.88)	0.32 (0.69)

The results based on less than five patients cannot be shown, also any numbers in the table that could be used to calculate results based on fewer than five patients are not shown and are marked as #.

Incidence

- The incidence of EGFR mutations in NSCLC was 8% across all stages and histology types, and remained stable, ranging between 7% and 9%, during the study period. The highest incidence was observed with the del19 mutation (3%), followed by L858R (2%).

Treatment patterns

- First diagnosis early-stage: More than half (58%) underwent surgery. Among those who received their first treatment for early-stage NSCLC, 51% finished the first treatment without having received a second treatment during the study period. Of the 38% who did receive a second treatment, more than half got treatment for advanced-stage (Figure 2A).
- First diagnosis advanced stage: Third-generation TKI (3rd-gen TKI) was the most common first-line (1L) treatment during the study period (34%), followed by first-generation (21%) and second-generation TKI (20%). 33% died during or after 1L treatment without receiving 2L therapy, while 27% still were receiving 1L therapy at follow-up. Overall, 37% received 2L treatment, of which 56% got EGFR TKI and 34% chemotherapy (CT) (Figure 2B)

Figure 2: Treatment progression for A) patients diagnosed at early-stage and B) advanced-stage

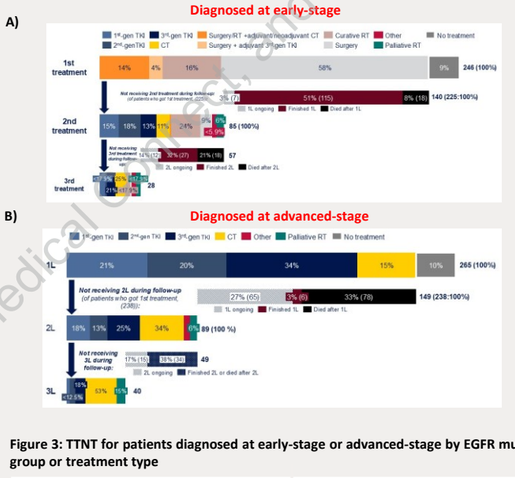
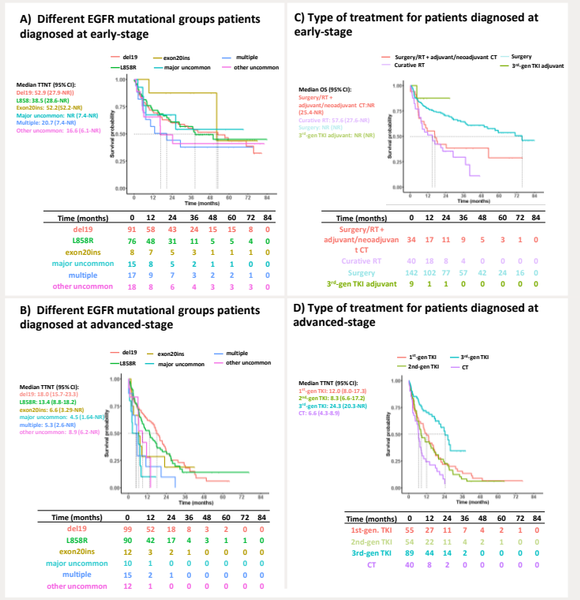


Figure 3: TTNT for patients diagnosed at early-stage or advanced-stage by EGFR mutational group or treatment type



TTNT (Figure 3A-D)

- First diagnosis early-stage: There were no significant differences in TTNT between EGFR mutational sub-groups (Figure 3A). Among treatment types, patients who underwent surgery had the longest median TTNT (75.5 months), while those receiving curative RT had the shortest (15.0 months, p<0.001) (Figure 3B).
- First diagnosis advanced stage: Median TTNT was longest for patients with del19 mutation (18 months) and shortest for major uncommon (4.5 months, p=0.0026) (Figure 3C). The median TTNT for L858R patients was 13.4 months and for exon20ins patients 6.6 months. Patients receiving 3rd-gen TKI had a significantly longer median TTNT (24.3 months) compared to patients receiving 1st-genTKI (12.0 months, p=0.0025), 2nd-gen TKI (8.3 months, p<0.001) or CT (6.6 months, p<0.001)) (Figure 3D).

OS (Figure 4, Table 2)

- First diagnosis early-stage: The median OS was not reached. The probability of survival at 5 years is 70.3%.
- First diagnosis advanced stage: The median OS was 23.0 months (95% CI: 18.0–29.0). The probability of survival at 5 years is 15.8%.

Figure 4: OS for patients diagnosed at early-stage and advanced-stage

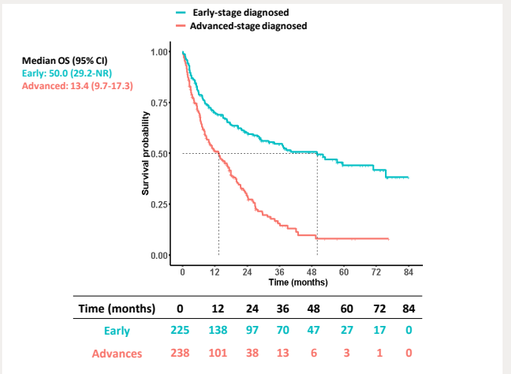


Table 2: Survival rate for patients diagnosed at early-stage and advanced stage

	Survival rate, %				
	1-year	2-year	3-year	4-year	5-year
Early-stage	92.2%	85.5%	82.2%	77.8%	70.3%
Advanced-stage	69%	48.2%	35.1%	20%	15.8%

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