

EGFR-mutation testing and TKI treatment patterns in locally advanced or metastatic NSCLC in Norway – a nationwide cohort study

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BACKGROUND

Since 2013, the national Norwegian guidelines recommend that all non-squamous non-small cell lung carcinomas (NSCLC) are tested for epidermal growth-factor receptor mutations (EGFRm). For EGFRm+ advanced NSCLC patients, 1st line palliative treatment with tyrosine kinase inhibitors (TKI) is recommended. This is the first nationwide study describing real-world EGFR testing and subsequent TKI treatment patterns in Norway.

METHODS

All patients with locally advanced (LA) or metastatic non-squamous NSCLC in Norway during 2010–2017 were included in the study. The patient cohort was identified using the Norwegian Cancer Registry. The patient cohort was linked on individual level to the Norwegian patient registry to obtain information on medical history and to the Norwegian prescription database for TKI use. Follow-up time was obtained by linkage to the Norwegian cause of death registry. The proportion of EGFR tested patients and subsequently treated with TKI was summarized and visualized by Sankey diagrams. Associations between patient characteristics and time to EGFR test and treatment were evaluated by Cox proportional hazards modelling. All estimates were stratified by disease stage.

RESULTS

Baseline characteristics and EGFR testing of non-squamous NSCLC patients by disease stage are presented in Table 1. Of 10,717 patients (mean age 71 years, female 47%), 3782 (35%) were diagnosed with LA NSCLC and 6935 (65%) with metastatic NSCLC. Among LA, 58% were EGFR tested, of which 7% were EGFRm+ For metastatic NSCLC, 53% were EGFR tested and 9% were EGFRm+, as shown in Figure 1.

From the Cox model it was found that for LA patients, younger age (<60 vs. ≥80) was associated with being EGFR tested (HR: 1.5, 95% CI 1.3–1.8), and testing over time (≤2011 vs. ≥2016) increased with 80% (HR: 1.8, 95% CI 1.6–2.0) (Table 1, left half) Similarly for metastatic patients, younger patients were more likely to be tested (HR: 1.6, 95% CI 1.4–1.8), and testing doubled over time (HR: 2.0, 95% CI 1.8–2.2).

For LA EGFRm+ 58% initiated TKI treatment, while the corresponding number was 85% of the metastatic patients (Table 2). Median (IQR) time to treatment initiation was 142 (31–401) for LA EGFRm+ patients and 30 (20–63) days for metastatic EGFRm+ patients respectively. Probability of treatment was not associated with age or study period for any of the disease stages, but for metastatic patients men were less likely to receive TKI-treatment.

Figure 1. Study population flow chart

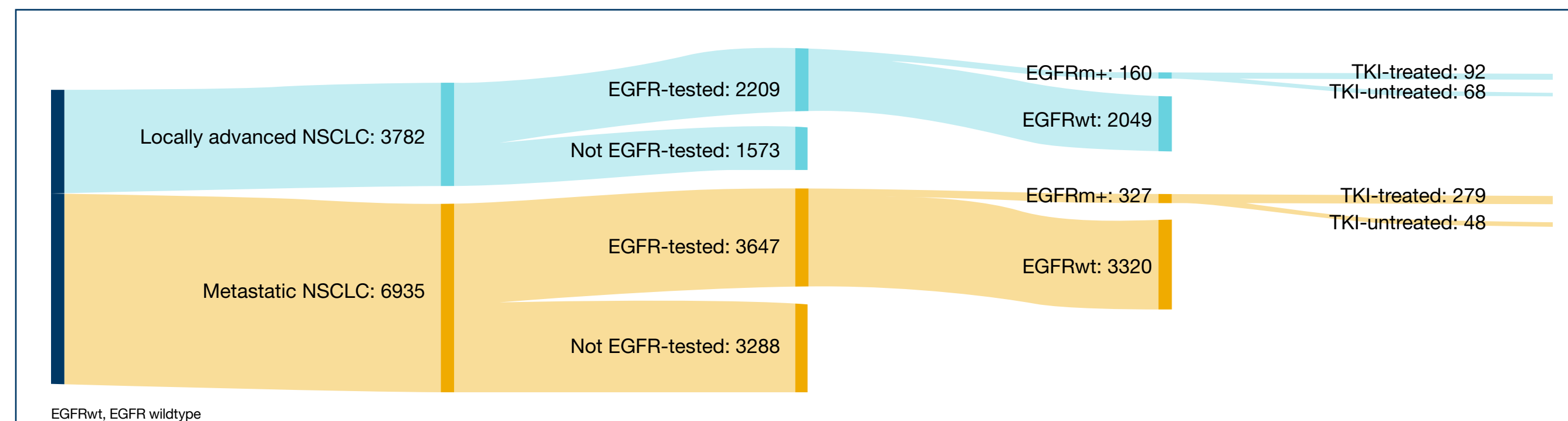


Table 1. Baseline characteristics and EGFR testing of NSCLC patients by disease stage

Characteristics	Locally advanced NSCLC (N=3782)					Metastatic NSCLC (N=6935)				
		Testing prevalence		p-value	Time to EGFR testing		Testing prevalence		Time to EGFR testing	
	EGFR Tested N (%)	Not tested N (%)	HR (95% CI)		p-value	EGFR Tested (%)	Not tested N (%)	p-value	HR (95% CI)	p-value
Age at diagnosis	Below 60	392 (17.7)	193 (12.3)	<0.01	1.48 (1.25 - 1.76)*	<0.01	743 (20.4)	379 (11.5)	<0.01	1.59 (1.41 - 1.79)*
	60 - 69	830 (37.6)	397 (25.2)		1.45 (1.25 - 1.70)*		1347 (36.9)	858 (26.1)		1.53 (1.37 - 1.71)*
	70 - 79	781 (35.4)	481 (30.6)		1.39 (1.19 - 1.62)*		1126 (30.9)	1052 (32.0)		1.33 (1.19 - 1.49)*
	80+	206 (9.3)	502 (31.9)		1.00 (ref)		431 (11.8)	999 (30.4)		1.00 (ref)
Sex	Female	1040 (47.1)	712 (45.3)	0.27	1.00 (ref)	0.51	1783 (48.9)	1506 (45.8)	0.01	1.00 (ref)
	Male	1169 (52.9)	861 (54.7)		1.03 (0.95 - 1.12)		1864 (51.1)	1782 (54.2)		0.97 (0.91 - 1.04)
Year of diagnosis	2010 - 2011	425 (19.2)	478 (30.4)	<0.01	1.00 (ref)	<0.01	737 (20.2)	1076 (32.7)	<0.01	1.00 (ref)
	2012 - 2013	556 (25.2)	424 (27.0)		1.39 (1.22 - 1.57)*		867 (23.8)	850 (25.9)		1.34 (1.22 - 1.48)*
	2014 - 2015	584 (26.4)	342 (21.7)		1.60 (1.41 - 1.82)*		957 (26.2)	761 (23.1)		1.57 (1.43 - 1.73)*
	2016 - 2017	644 (29.2)	329 (20.9)		1.80 (1.59 - 2.04)*		1086 (29.8)	601 (18.3)		1.98 (1.80 - 2.18)*
Morphological groups	Adenocarcinoma	1794 (81.2)	615 (39.1)	<0.01	1.00 (ref)	<0.01	2976 (81.6)	1514 (46.0)	<0.01	1.00 (ref)
	Other	390 (17.7)	482 (30.6)		0.48 (0.43 - 0.54)*		643 (17.6)	868 (26.4)		0.56 (0.51 - 0.61)*
	Not classified	25 (1.1)	476 (30.3)		0.05 (0.04 - 0.08)*		28 (0.8)	906 (27.6)		0.04 (0.03 - 0.06)*
Time to first EGFR-test	Median (IQR)	0 (0 - 15)	NR			0 (0 - 12)	NR			

* denotes p-value ≤0.05 in comparison with the corresponding reference level. The overall p-value for each variable is conducted by the likelihood ratio test.

Table 2. Treatment patterns of EGFRm+ NSCLC patients by disease stage

Characteristics	Locally advanced NSCLC (N=160)					Metastatic NSCLC (N=327)				
		TKI treatment prevalence		p-value	Time to TKI treatment		TKI treatment prevalence		Time to TKI treatment	
	Treated N (%)	Not treated (%)	HR (95% CI)		p-value	Treated N (%)	Not treated N (%)	p-value	HR (95% CI)	p-value
Age at diagnosis	Below 60	28 (30.4)	14 (20.6)	0.08	0.89 (0.41 - 1.93)	0.47	78 (28.0)	12 (25.0)	0.41	1.03 (0.71 - 1.50)
	60 - 69	24 (26.1)	11 (16.2)		1.10 (0.51 - 2.38)		76 (27.2)	10 (20.8)		0.85 (0.58 - 1.25)
	70 - 79	30 (32.6)	35 (51.5)		0.70 (0.34 - 1.48)		77 (27.6)	13 (27.1)		0.89 (0.62 - 1.29)
	80+	10 (10.9)	8 (11.8)		1 (ref)		48 (17.2)	13 (27.1)		1.00 (ref)
Sex	Female	53 (57.6)	47 (69.1)	0.14	1 (ref)	0.24	201 (72.0)	25 (52.1)	<0.01	1.00 (ref)
	Male	39 (42.4)	21 (30.9)		1.31 (0.83 - 2.07)		78 (28.0)	23 (47.9)		0.68 (0.52 - 0.88)*
Year of diagnosis	2010 - 2011	24 (26.1)	13 (19.1)	0.23	1.00 (ref)	0.66	67 (24.0)	15 (31.3)	0.34	1.00 (ref)
	2012 - 2013	29 (31.5)	16 (23.5)		0.83 (0.45 - 1.54)		62 (22.2)	9 (18.8)		1.24 (0.87 - 1.77)
	2014 - 2015	22 (23.9)	18 (26.5)		0.75 (0.38 - 1.50)		62 (22.2)	6 (12.5)		1.47 (1.02 - 2.12)*
	2016 - 2017	17 (18.5)	21 (30.9)		0.65 (0.33 - 1.29)		88 (31.5)	18 (37.5)		1.44 (1.02 - 2.05)*
Time to first EGFR-test	Median (IQR)	2.5 (0 - 26.8)	0 (0 - 16.5)	0.08			0 (0 - 14)	1 (0 - 16)	0.184	
Time to first TKI-treatment	Median (IQR)	141.5 (31 - 400)	NR				30 (20 - 63)	NR		

* denotes p-value ≤0.05 in comparison with the corresponding reference level. The overall p-value for each variable is conducted by the likelihood ratio test.

CONCLUSIONS

- Increases in EGFR testing were observed over time, which may reflect improvement in routine diagnostics according to guidelines.
- Initiation of TKI treatment in metastatic EGFRm+ NSCLC was substantial and independent of patient characteristics.
- Time to TKI treatment initiation in LA EGFRm+ NSCLC showed a greater variation than for the patients with metastatic disease, which may reflect different treatment options in accordance with the guidelines.