Long-term Survivors with EGFR Positive Non-Small Cell Lung Cancer Treated with Tyrosine Kinase Inhibitors: A Combined Canadian Cohort

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BACKGROUND

- TKIs, used to treat EGFRmut+ NSCLC yield better overall survival than traditional platin-based chemotherapy.[1]
  - However, there is known heterogeneity in outcome.[2]
- This may be due to differences in patient characteristics.
  - Asian ancestry improves prognostic outcome in EGFRmut+ populations when treated with 1st/2nd generation TKI.[3-4]
- However, most studies were conducted in largely Asian populations, instead of ethnically heterogenous populations.

OBJECTIVE

To identify clinical characteristics associated with long term survival (LTS) in patients with de novo advanced NSCLC with EGFRmut+ treated with first-line TKIs in a more heterogeneous, Canadian population.

METHODS

Entire Cohort

De novo advanced EGFRmut+ NSCLC patients receiving a 1st/2nd generation EGFR-TKI as first line treatment between 2004 and 2016 extracted from:

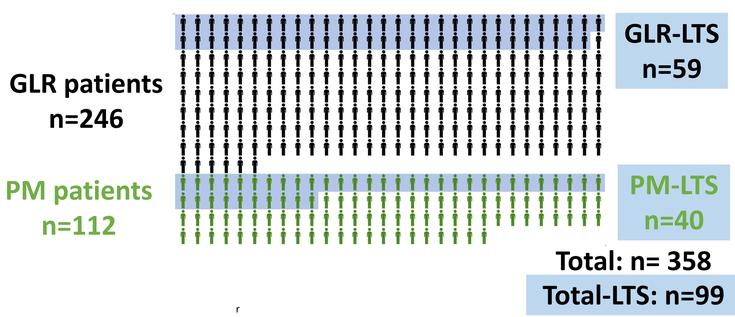
- Glans-Look Lung Cancer Research Base of Alberta
- Ontario's Princess Margaret Cancer Centre, Canada

Long Term Survivors

A subset of these patients who additionally lived longer than the upper quartile time (38.8 months)

Average Term Survivors

The remainder of patients who did not meet the criteria for long term survivors



RESULTS AND DISCUSSION

Table 1. Demographics and outcomes of the combined and divided cohorts, based upon survivorship and patient treatment location.

Demographics	Entire cohort	LTS	ATS	p-value	PM	GLR	p-value
N	358	99	259		112	246	
Age at diagnosis *(median, years)*	64	64	67	P=0.49	62.95	65	P=0.56
Gender *(male: female)*	123:226	33:66	90:160	P=0.80	34:78	89:157	P=0.28
Ethnicity *(Asian:Non-Asian)*	119:239	42:57	77:182	P=0.02	54:58	65:181	P<0.000
EGFR mutation *(19del:1858r)*	223:135	66:33	157:102	P=0.29	76:36	147:99	P=0.14
Smoking status (Never:Ever)	220:137	64:35	156:102	P=0.47	77:35	143:102	P=0.061
LTS:ATS	111:259				40:72	59:187	P=0.02
Overall survival from start of TKI *(median, months)*	23.2	56	17.5		34.1	23.4	Logrank p=0.001

- Median overall survival was 23.2 months. LTS median survival was 56 months from initiation of TKI, whereas ATS was 17.5 months.
- The LTS cohort did not significantly differ from ATS in the majority of clinical and pathologic characteristics.
  - However, LTS patients were significantly more likely to be Asians than non-Asians (38% vs 31%, p= 0.024) and from PM LTS (PM: 386, GLR: 29%, p=0.02).
- Further, PM patients were more likely to be Asian (PM: 48%, GLR: 36%, p<0.001), and had longer median survival outcomes (PM: 34.1 months, GLR: 23.4 months, log-rank p=0.001)

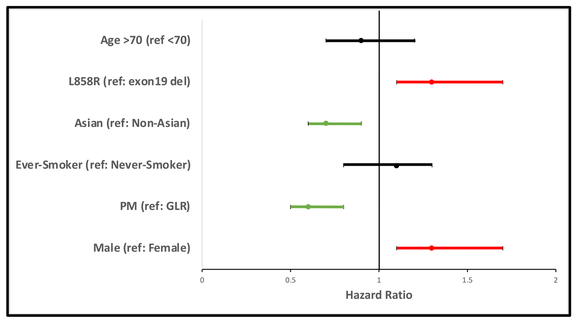


Figure 1. Forest plot comparing demographics and survival after TKI initiation.

- In multivariate analysis both PM (HR: 0.6, p<0.001) and Asian ethnicity (HR: 0.73, p=0.017) were independent prognostic factors of longer survival times (Figure 1).
- Males (HR: 1.3, p=0.27), and L858R mutation (HR 1.3, p=0.016) were found to be independent prognosticators of shorter overall survival.

LIMITATIONS

- The retrospective nature of the study increases the likelihood that observed differences between long term survivors and average term survivors could be caused by unmeasured confounders.

CONCLUSION

- This multicentre study confirmed previously known prognosticators including Asian ancestry (suggestive of improved outcome), and males and L858R mutation(suggestive of poorer outcome) within a real world, multicentre Canadian cohort.
- When comparing centres within this cohort, PM had significantly more patients with Asian ancestry compared to GLR, which may explain the significant difference in overall survival between these two cohorts.
- Future work to better understand biologic reasons for ethnicity resulting in different prognosis and the impact of socio-economic factors are needed to better guide management.

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The authors have no relevant conflicts of interests to declare.