Poster 1152P

Real-world outcomes in resected stage IB-IIIA EGFR-mutated NSCLC in Canada: analysis from the POTENT study

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Study Overview

- The POTENT study evaluated the prevalence/frequency of the epidermal growth factor mutation (EGFRm), clinical outcomes, treatment, and testing patterns among patients with early-stage resected non-small-cell lung cancer (NSCLC) living in Canada.

Objectives

- Primary:
  - To estimate the prevalence/frequency of EGFR-sensitizing mutations (common and uncommon)
  - To describe treatment patterns
  - To assess overall survival (OS)
- Secondary:
  - To describe demographic and clinical characteristics, recurrence outcomes, and testing methods
- Exploratory:
  - To assess disease-free survival (DFS)

Conclusions

- Real-world data provide critical context to clinical trials and inform treatment and reimbursement decisions.
- The current study found that patients with resected IB-IIIA EGFRm NSCLC had suboptimal outcomes despite adjuvant chemotherapy. DFS at 2 years was consistent with 2-year DFS results in the placebo arm of the ADAURA trial (stage IB, 71%; stage II, 56%, and stage IIIA, 32%).[1]
- These results highlight the need for improved therapeutic options for early-stage patients with resected NSCLC.

Plain language summary

Why did we perform this research?
In Canada, recent real-world outcomes data for patients with NSCLC who are EGFRm are limited to advanced and metastatic patient populations.[2,3] It is important to understand the characteristics, treatment, and outcomes of patients with resected, early-stage EGFRm NSCLC given the recent results of the ADAURA trial of adjuvant osimertinib[1] and upcoming results for adjuvant immunotherapy[4].

How did we perform this research?
The study was a retrospective, longitudinal, observational study that involved three Canadian cancer centres and data derived from the pan-Canadian Lung Cancer Observational Study (PALEOS) registry. Data were collected for EGFRm status, treatment, survival outcomes, and site of relapse.

What were the findings of this research and what are the implications?
The study found EGFRm frequency to be 22%. Among these patients, survival outcomes were similar to historical reports of 5-year OS rates.[4] At the time of first disease recurrence, almost 90% of tumours involved distant sites. These findings suggest that new adjuvant treatment options are needed for resected early-stage EGFRm NSCLC. These data may inform the treatment decisions of clinicians as well as the reimbursement decisions of payers.

Where can I access more information?
Additional information on this study can be obtained from the corresponding and lead author, Dr. M.S. Kuruvilla (Sara.Kuruvilla@lhsc.on.ca).

This POTENT study was funded by AstraZeneca Canada. The PALEOS observational study is academically led and sponsors (including AstraZeneca Canada & Pulse Infoframe Inc.) have supported this registry that is focused on real world data collection.

Poster presented at ESMO Congress 2021 (September 16-21, 2021).

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Background

- Most patients with advanced NSCLC who have EGFR driver mutations benefit from EGFR-targeted tyrosine kinase inhibitor (EGFR-TKI) therapy.[5]
- In the ADAURA trial of patients with resected early-stage (IB-IIIA) EGFRm NSCLC, adjuvant treatment with the EGFR-TKI osimertinib was associated with significant improvement of DFS compared with placebo (hazard ratio: 0.20; 99.12% CI: 0.14, 0.30; $P < 0.001$).[1]
- Despite current standard of care, the risk of disease recurrence after surgery and adjuvant chemotherapy remains high across disease stages. There is a paucity of literature examining the heterogeneous early-stage resected patient population in terms of their treatment, outcomes, and variations related to biomarker status.

Methods

- A retrospective, longitudinal, observational study was conducted at three Canadian cancer centres. Each centre had routine reflex testing during study time period. Reflex testing is a policy that does not require physicians to order the required test for individual patients; the pathologist orders and provides samples for molecular testing.
- Included patients were adults diagnosed with stage IB to IIIA (AJCC 7th edition) NSCLC between January 2016 and December 2019 (study time period) who had undergone resection; patients who had received neo-adjuvant treatment were excluded.
- Data were collected on EGFRm status, treatment, and clinical outcomes. The clinical outcomes included DFS and OS (stratified by age at diagnosis) and site of relapse categorized as local-regional or distant metastatic disease.
- Data were derived from the pan-Canadian Lung Cancer Observational Study (PALEOS) registry.
- Ethics approval was obtained from each of the three participating cancer centres.

Results

Baseline Characteristics

- Among 440 patients with stage IB-IIIA NSCLC whose tumours had EGFR reflex testing, 95 (22%) were EGFRm (Table 1).
- Among the patients with EGFRm tumours, the mean age was 65 years and 66% were female; of those with known ethnicity, 23% were Asian (Table 1).
- Across all patients, 12.5% with stage IB disease, 75.0% with stage II, and 82.4% with stage IIIA received adjuvant therapy (Table 1).

22% of patients were EGFRm

Table 1. Baseline characteristics of EGFRm patients*

Variable	n (%), N = 93*
Cancer Centre	
Princess Margaret	41 (44.1)
London	31 (33.3)
William Osler	21 (22.6)
Sex, female	61 (65.6)
Age at Diagnosis, mean (SD)	65 (7.5)
Race	
East or South-East Asian	14 (15.1)
Caucasian	11 (11.8)
Central Asian	4 (4.3)
Asian (NOS)	2 (2.2)
North American	1 (1.1)
South Asian	1 (1.1)
Other	3 (3.2)
Unknown	57 (61.2)
Stage at Diagnosis	
Stage IB	48 (51.6)
Stage II	28 (30.1)
Stage IIIA	17 (18.3)

Variable	No. of Patients (%), N = 93*
Mutation	
Common**	57 (61.3)
Uncommon	36 (38.7)
Result of Surgery	
R0	91 (97.8)
R1	1 (1.1)
R2	1 (1.1)
Recurrence	
Locoregional	5 (5.3)
Metastatic	30 (32.3)
No recurrence	58 (62.4)
CNS at First Recurrence/Patients with Metastatic Recurrence	5/30 (16.7)
IB	3/9 (33.3)
II	1/11 (9.0)
IIIA	1/10 (10.0)

Adjuvant Type(s)	Stage IB (n = 48)	Stage II (n = 28)	Stage IIIA (n = 17)	Total (N = 93)
Chemotherapy and RT	1 (2.1)	0 (0.0)	4 (23.5)	5 (5.4)
Chemotherapy and no RT	5 (10.4)	21 (75.0)	10 (58.8)	36 (38.7)
No chemotherapy or RT	42 (87.5)	7 (25.0)	3 (17.6)	52 (55.9)

Abbreviations: CNS = central nervous system; EGFRm = epidermal growth factor mutation positive; NOS = not otherwise specified; RT = radiotherapy; SD = standard deviation.
* Two patients were excluded due to insufficient data; ** Common mutations: exon 19 deletion, L858R.

Clinical Outcomes

- Median follow-up was 29 months.
- The number of DFS events at 2 years, median DFS, and the probability of being alive at 2 years are summarized in Table 2.
- At 2 years, DFS was 84.6%, 53.9%, and 35.9% for patients with stage IB, II, and IIIA disease, respectively (Figure 1D).
- Patients who did not receive adjuvant chemotherapy had longer DFS than those who did receive such therapy (Table 2). Adjuvant chemotherapy was more commonly used among patients diagnosed at later disease stages.
- Patients diagnosed with stage IB disease had higher OS and DFS rates at both 2 and 4 years than those diagnosed with stage II and IIIA disease (Figures 1C and 1D) and combined stage II/IIIa patients (Table 2).
- At the time of first recurrence, 85.7% of tumours involved distant sites; among these distant first recurrences, central nervous system metastasis occurred in 33% of stage IB, 9% of stage II, and 10% of stage IIIA patients.

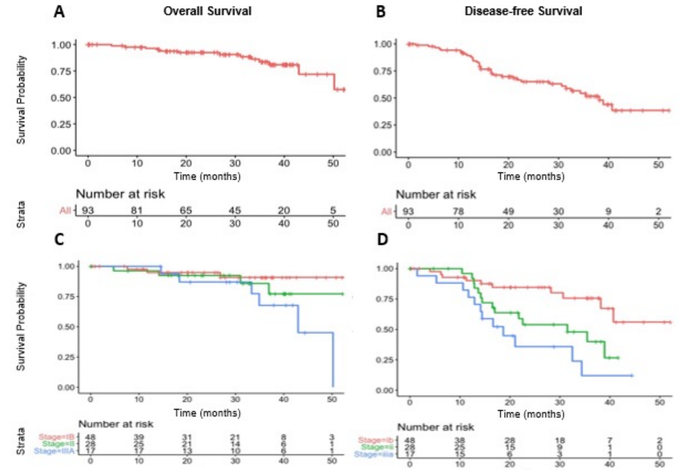
At 2 years, DFS was 84.6% for stage IB, 53.9% for stage II, and 35% for stage IIIA patients

Table 2. Survival outcomes*

Variable	No. of Patients (No. of DFS Events at 2 Years)	Median DFS in Months (95% CI)	Probability of Being Alive at 2 Years (95% CI)
Stage			
IB	48 (10)	NR (38.2-NE)	0.95 (0.88-1.00)
II	28 (14)	31.5 (17.0-NE)	0.92 (0.83-1.00)
IIIA	17 (12)	18.7 (14.1-NE)	0.87 (0.72-1.00)
II and IIIA combined	45 (26)	22.6 (16.6-38.9)	0.90 (0.82-1.00)
Mutation Type			
Common mutation**	57 (22)	38.2 (32.5-NE)	0.94 (0.88-1.00)
Uncommon mutation	36 (14)	38.9 (21.0-NE)	0.88 (0.78-1.00)
Surgical Resection			
R0	91 (35)	38.2 (31.5-NE)	0.92 (0.87-0.98)
R1	1 (1)	17 (NE-NE)	NA
R2	1 (0)	NR (NE-NE)	NA
Adjuvant Chemotherapy			
Did not receive	51 (14)	40.7 (38.2-NE)	0.90 (0.82-1.00)
Received	42 (22)	31.5 (18.7-NE)	0.95 (0.93-1.00)

Abbreviations: CI = confidence interval; DFS = disease-free survival; NA = not available; NE = not evaluable (due to insufficient events); NR = not reported.
* Two patients were excluded due to insufficient data.
** Common mutations: exon 19 deletion, L858R.

Figure 1. OS and DFS among all EGFRm patients (A, B) and stratified by disease stage (C, D)



Abbreviations: EGFR = epidermal growth factor receptor mutation positive; DFS = disease-free survival; OS = overall survival.

References

1. Wu Y-L et al. Osimertinib in resected *EGFR*-mutated non-small-cell lung cancer. NEJM. 2020; 383:1711.
2. Seung S.J et al. Real-world treatment patterns and survival in stage IV non-small-cell lung cancer in Canada. Curr Oncol. 2020; 17(4):e361.
3. Seung S.J et al. Retrospective cohort study of unresectable stage III non-small-cell lung cancer in Canada. Curr Oncol. 2020; 27(4):e354.
4. Deslypere G. et al. Immunotherapy in non-metastatic non-small cell lung cancer: can the benefits of stage IV therapy be translated into earlier stages? Ther Adv Med Oncol. 2018; 10;1.
5. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer. Version 5.2021. Fort Washington, PA. NCCN. 2021.

Acknowledgements

The authors wish to acknowledge Dr. Geoffrey Liu of Princess Margaret Hospital, University Health Network, Toronto, Ontario, Canada and Dr. Richard Malthaner, Thoracic Surgery Department at Western University, London, Ontario, Canada for their collaboration and extended support.

Disclosures

Lead author disclosures: advisory boards/honorarium from AstraZeneca, Bristol Myers Squibb, and Merck.