

# Exploring the Potential for EHR-Derived Real-World Data to Reduce Uncertainty in HTA Decision-Making

## A Case Study of Long-Term Survival Outcomes

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# Research collaboration on the use of EHR-derived RWD for HTA decision-making

## Collaboration objectives:

Conduct **high-quality research** using Flatiron data

Develop and evaluate approaches to **reduce uncertainty in NICE Technology Appraisals** for oncology appraisals

Support NICE in evaluating the ability of RWD to address evidence gaps and **inform HTA decision making**

# Potential sources of uncertainty for HTA decision-making



## Gaps in evidence:

- Existence of evidence
- Lack of relevant comparator
- Immature survival data and amount of follow-up

## Identified 60 NICE TAs as part of aim 1 of the collaboration:

- Selected one of those TAs where immature survival data was the main source of uncertainty

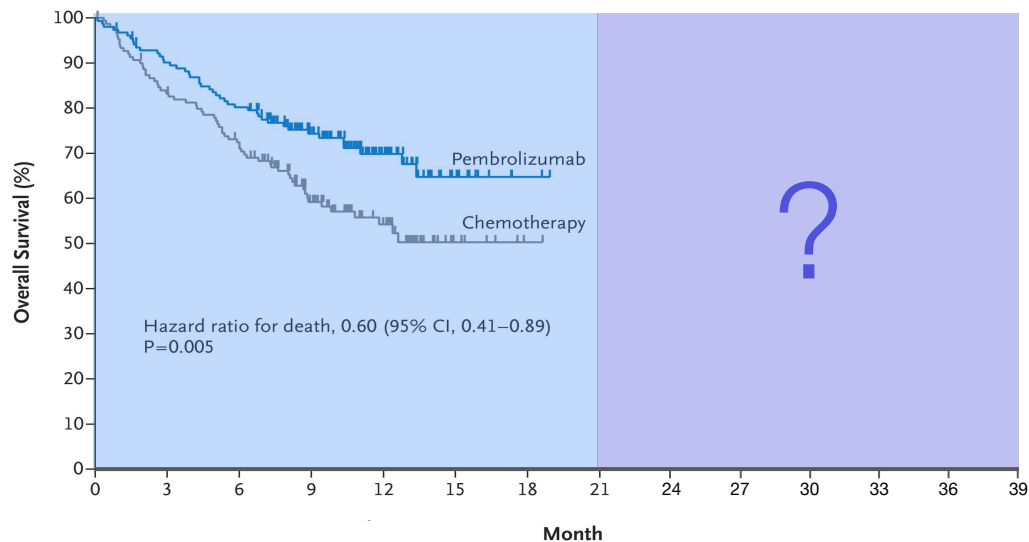
# Long-term outcomes were the main source of uncertainty in NICE TA531

**NICE** National Institute for Health and Care Excellence

**NICE**  
guidance

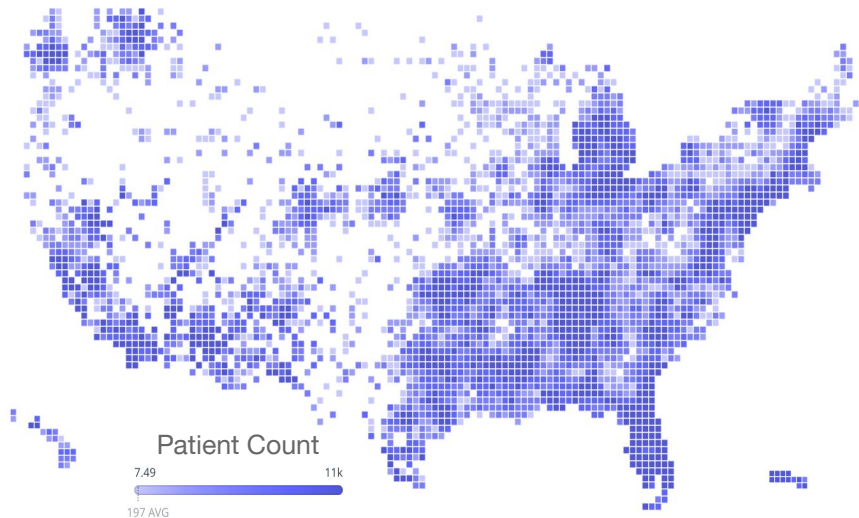
**Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer**

Technology appraisal guidance  
Published: 18 July 2018  
[www.nice.org.uk/guidance/ta531](http://www.nice.org.uk/guidance/ta531)



*“Uncertainty around the overall survival extrapolation even at 2 years is the main source of uncertainty in the cost-effectiveness analyses”*

# EHRs and other sources of real-world data are a promising source of evidence for HTA decision-making



## Data from Flatiron Health

Collected from ~800 sites of care in the U.S.

Contains structured, unstructured and derived elements like demographics, biomarker status, lines of therapy

Non-Small Lung Cancer  
Enhanced Datamart (EDM)

# Retrospective study



**Treatment:** Pembrolizumab



**Time Horizon:** Jun 2016 - Dec 2020



**Study Population:** Patients with previously untreated, metastatic non-small cell lung cancer and PD-L1 positive biomarker status

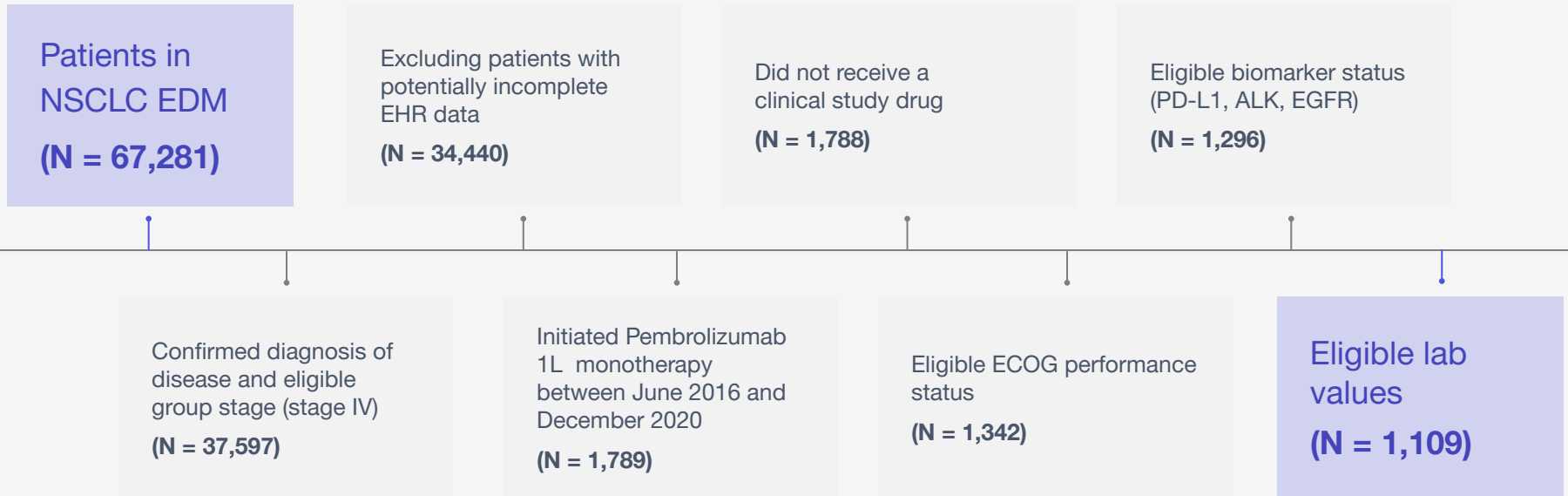


**Methods:** Kaplan Meier analysis



**Research Objective:** Highlight the additional evidence on overall survival offered by EHR data

# Cohort selection based on structured and unstructured data elements

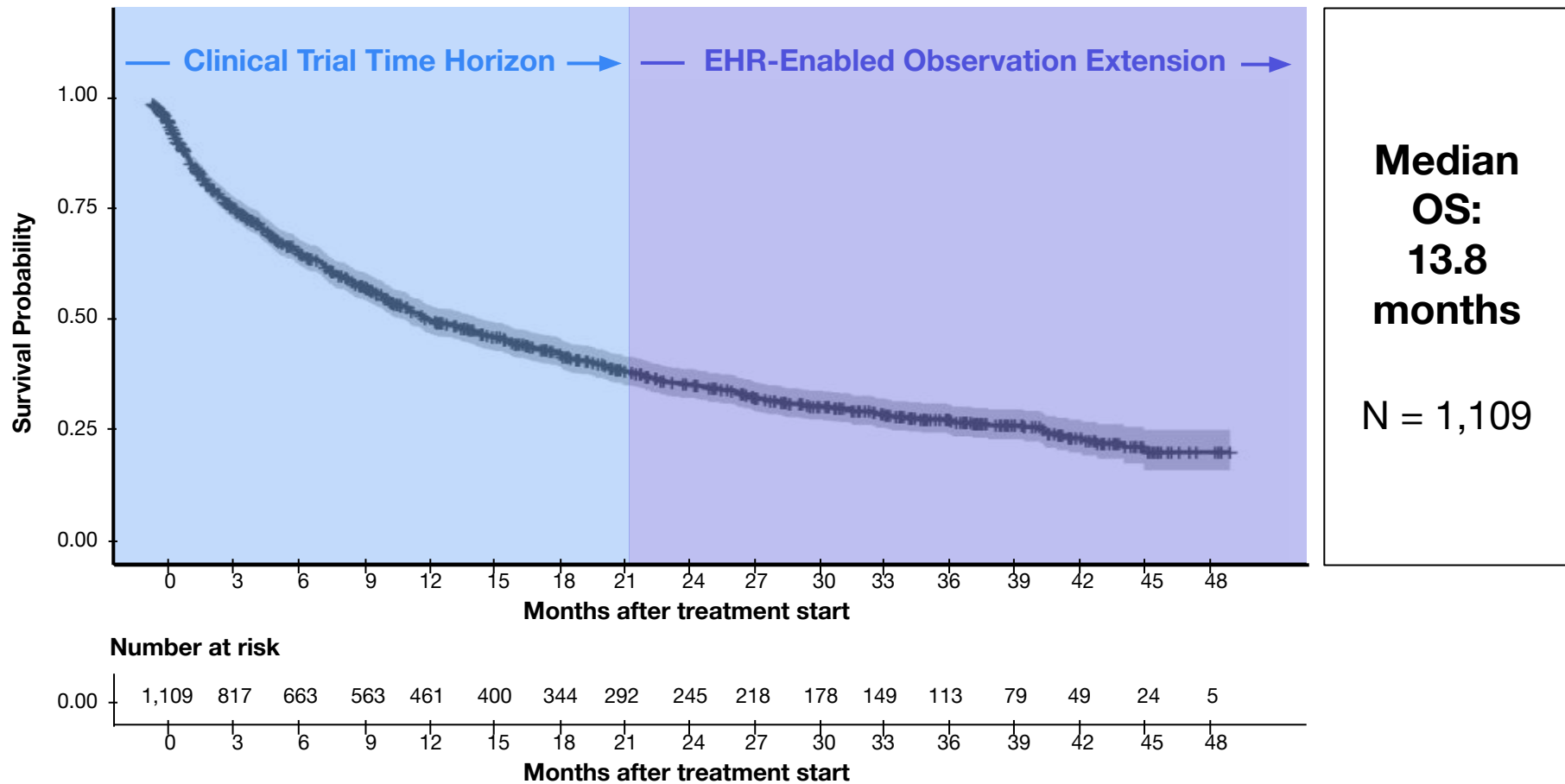


# Clinical depth of EHR data indicated a heterogeneous study population

Baseline characteristics

Highlighted baseline characteristic	EHR-derived cohort (N = 1,109)
PD-L1 Biomarker Test Results	
Yes	993 (90%)
Unknown	116 (10%)
No	Excluded
Lab Results	
Bilirubin, units mean(sd)	0.46 (0.43)
Bilirubin unknown/not documented n(%)	200 (18%)
Performance Status, n(%)	
ECOG of 0	492 (44%)
ECOG of 1	313 (28%)
ECOG unknown/not documented	304 (27%)
Histology abstracted from chart, n(%)	
Non-squamous cell carcinoma	808 (73%)
Squamous cell carcinoma	251 (23%)
NSCLC histology not otherwise specified	50 (5%)







Original Investigation | Oncology

## Association Between First-Line Immune Checkpoint Inhibition and Survival for Medicare-Insured Patients With Advanced Non-Small Cell Lung Cancer

Kenneth L. Kehl, MD, MPH; Scott Greenwald, PhD; Nassib G. Chamoun, MS; Paul J. Marberg, PhD; Deborah Schrag, MD

### Abstract

**IMPORTANCE** Immunotherapy is now a cornerstone of treatment for advanced non-small cell lung cancer (NSCLC), but its uptake and effectiveness among older patients outside clinical trials remain poorly understood.

**OBJECTIVE** To understand treatment patterns and evaluate the overall survival associated with checkpoint inhibitor immunotherapy, cytotoxic chemotherapy, and combined chemioimmunotherapy for older patients who have advanced NSCLC and Medicare coverage.

**DESIGN, SETTING, AND PARTICIPANTS** This retrospective cohort study included Medicare-insured patients in the US aged 66 to 89 years who initiated first palliative-intent systemic therapy for lung cancer between January 1, 2016, and December 31, 2018. Survival follow-up continued through March 31, 2020. A total of 19 529 patients who had advanced lung cancer and were insured by a Medicare fee-for-service plan were included in the analysis.

**EXPOSURES** Regimens included pembrolizumab monotherapy (n = 3079), combined platinum-based drug (ie, cisplatin or carboplatin [hereinafter, platinum]) and pemetredez disodium (n = 5159), combined platinum and a taxane (ie, paclitaxel, nab-paclitaxel, or docetaxel) (n = 9866), and combined platinum, pemetredez, and pembrolizumab (n = 1425), as ascertained using Medicare claims from the Centers for Medicare & Medicaid Services.

**MAIN OUTCOMES AND MEASURES** The primary outcome was overall survival, which was measured using the restricted mean survival time (RMST) with propensity score adjustment for clinical and sociodemographic characteristics. Median survival was also reported for comparison with outcomes from registrational trials.

**RESULTS** A total of 19 529 patients (54% male, 46% female; median age, 73.8 [interquartile range, 69.9–78.4] years) were identified for analysis. The uptake of pembrolizumab-containing regimens in the Medicare population was rapid, increasing from 0.7% of first-line treatments in the second quarter of 2016 to 42.4% in the third quarter of 2018. Patients who were older (≥70 years, 2484 [89%]), were female (577 [51%]), and/or had higher Risk Stratification Index scores (highest quintile, 322 [30%]) were more likely to receive single-agent pembrolizumab than chemotherapy. After propensity score adjustment, pembrolizumab was associated with survival similar to platinum/pemetredez (RMST difference, -0.2 [95% CI, -0.5 to 0.2] months) or platinum/taxane (RMST difference, -0.7 [95% CI, -1.0 to -0.4] months). Patients receiving platinum/pemetredez/pembrolizumab chemioimmunotherapy also had adjusted survival similar to those receiving platinum/pemetredez chemotherapy (RMST difference, 0.5 [95% CI, 0.1–0.9] months). The unadjusted median survival was 11.4 (95% CI, 10.5–12.3) months among patients receiving single-agent pembrolizumab, approximately 15 months shorter than observed among pembrolizumab-treated participants in the KEYNOTE-024 trial. The unadjusted median survival was 12.9 (95% CI,

(continued)

### Key Points

**Question** Has the incorporation of checkpoint inhibitor immunotherapy into initial treatment of older Medicare-insured patients with advanced non-small cell lung cancer been associated with meaningful improvements in overall survival?

**Findings** This cohort study included 19 529 patients with Medicare coverage who initiated first systemic therapy for advanced lung cancer using 1 of 4 regimens of checkpoint inhibitor immunotherapy, cytotoxic chemotherapy, and combined chemioimmunotherapy. The median overall survival was 11.4 months among patients receiving pembrolizumab monotherapy and 12.9 months among patients receiving platinum/pemetredez/pembrolizumab chemioimmunotherapy, both substantially shorter than observed in registrational trials, with an adjusted restricted mean survival time through 18 months of follow-up of 11 to 12 months for all 4 treatment groups.

**Meaning** In this study, immunotherapy among older Medicare-insured patients with advanced non-small cell lung cancer was associated with shorter overall survival than observed in key clinical trials, providing patients and physicians with estimates of outcomes for older patients who have lung cancer and are being treated with immunotherapy.

### Supplemental content

Author affiliations and article information are listed at the end of this article.

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Findings of 13.8 months median overall survival is consistent with Kehl et al. analysis of CMS claims of 11.4 months overall survival

A long train of colorful shipping containers in a yard at sunset. The containers are in various colors including red, orange, yellow, green, and blue. The sky is a mix of orange, yellow, and blue, suggesting a sunset or sunrise. The train is on tracks that curve into the distance.

Differences between countries may limit the transportability of evidence

# Enabling managed access agreements stands to **benefit all key stakeholders**



**Patients**



**HTA Bodies**



**Manufacturers**