Does Next Generation Sequencing (NGS) Improve Outcomes in Non-Small Cell Lung Cancer (NSCLC)? A Real-World Data (RWD) Example

CO67

Gendy, S.[1]; Kumar, D.[1]; Maskin, J.[1]; Obradovic, T.[1]; Turk, L.[1]; Viaggi, S.[2]

[1]ICON plc, US; [2]ICON plc, EU

Introduction

Assessing the Benefit of Sequencing vs Point Mutation Testing As Well As Timing of Testing in Identifying NSCLC Molecular Aberrations.

In 2018, the Centers for Medicare & Medicaid Services (CMS) established the first national coverage for NGS that have Food & Drug Administration (FDA) approval for recurrent, relapsed, refractory, metastatic or advanced cancers in FDA approved indications and by CLIA approved labs. CMS guidance as well as compendial recommendations for disease treatments have evolved over the years to cover advanced cancers. This analysis sought to understand how these changes in testing practices might impact patient outcomes.

Objectives

This analysis evaluated the impact of using sequencing vs point mutation testing on outcomes in lung cancer as seen in real world data (RWD).

Methods

- ICON's US medical and prescription longitudinal HIPAA compliant claims data was leveraged for this analysis. Each de-identified patient in the data is assigned a longitudinally stable unique identifier, enabling ICON to track de-identified patients longitudinally over time and across locations of care.
- The study analyzed patients 18 years and older with Lung Cancer ICD-10-CM codes [2018-2019 i.e., index period]. A one year look back was implemented to ensure newly diagnosed status. Patients were then tracked forward for 3 years [2019-2022] longitudinally to evaluate lines of therapy and testing patterns. Treatments and secondary codes were evaluated to identify advanced or metastatic NSCLC patients. The patient population was narrowed down to those who had undergone testing that was captured in the data and met the ICON standards for data integrity, longitudinal continuity, and representativeness.

Figure 1. Cohort Selection

–12 months	Y0	Y1	Y2	Y3
June'17–May'18	June'18–May'19	June'19–May'20	June'20–May'21	June'21–May'22
Look back to confirm new diagnosis	Initial Diagnosis for NSCLC	Look forward to assess 1L and 2L 3 years ending May 2022		

- To identify testing targets and techniques, and account for limitations in the claims data, testing codes were categorized broadly into sequencing (targeted or whole genome sequencing) and non-sequencing (mostly IHC and ISH). For unspecified codes, a sensitivity analysis was conducted with validation against known tests and prices, and a price cutoff with the least composite error was selected.

Table 1. Price Cutoff Validation

	Estimated using price to be IHC/ISH	Estimated using price to be Sequencing	Composite error = % missed + % mischaracterized
Known to be IHC/ISH		% mischaracterized (known to be IHC/ISH/total Estimated)	
Known to be Sequencing	% Missed (known to be sequencing/total estimated IHC		

- Because the claims data did not include the results of the tests, the treatment used after a test was performed was used as a proxy to determine the test results. To establish the patients' biomarker status, all treatments observed in their treatment journey were considered. This status was assigned as the patients' lifetime biomarker. Patients were then evaluated for endpoints in 3 groups depending on whether they underwent a sequencing test or not, and, if yes, prior to 1L/adjuvant start or later.
- The study had two endpoints: median progression-free survival on second-line treatment (mPFS2) and hazard ratio (HR) of progression on second-line treatment.
- Statistical analysis involved pairwise comparisons of survival distributions (time to progression) and testing using logrank test statistics.

Results

- A total of 877 patients were included in the study as they met the criteria for inclusion and exclusion, as well as the 3-year longitudinal data integrity criteria. The median age of patients was 66, and half of them were female. 4.3% had evidence of a biomarker aberration estimated through observed targeted treatments.
- 72% of the patients started their 1L/Adjuvant on Immuno-Oncology (IO) based regimens. Current approvals do not require testing before the start of IO-chemo triplet which constitutes the majority (70%) of 1L/Adjuvant IO regimens. For patients who require testing, PD-(L)1 testing is done through IHC even if Sequencing was implemented.
- 18% started on chemo regimens. 9% started on a targeted therapy for clinically relevant molecular aberration.
- 37% of patients had a sequencing test performed either pre 1L/Adjuvant (28%) or in relation to 2L (9%).
- 87% of the patients progressed on 1L/Adjuvant treatment and 40% progressed on 2L treatment within the study time period. mPFS2 was 36.4 months.
- 43% (mPFS2=35.9 mos.) of patients who had a sequencing test performed at any point progressed on 2L compared to 39% (mPFS2=36.6 mos.) amongst those who didn't have a sequencing test (HR=1.15, p=0.3188).

Results (cont'd)

- 42% (mPFS2=35.9 mos.) of patients who had sequencing test performed pre 1L/Adjuvant progressed on 2L compared to 45% (mPFS2=35.8 mos.) amongst those who had a sequencing test in relation to 2L (HR=0.881, P=0.6285)

Figure 2. Kaplan Meier Curve for Sequencing (1L or 2L) vs Non-Sequencing Tests

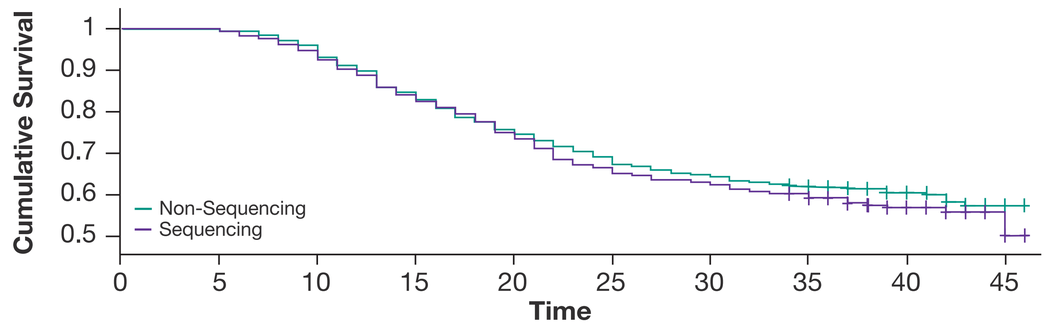

Figure 3. Kaplan Meier Curve for Sequencing Associated With 1L vs 2L

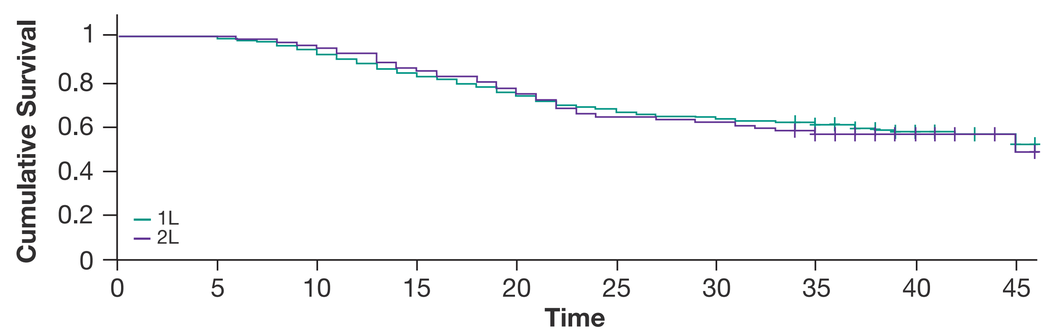

Table 2. Results – Sequencing vs No Sequencing

Lifetime Observed CDx Treatment	Patient Count	% Progressed on 1L	Median Estimated PFS1 (mos)	% Progressed on 2L	HR (p value)	Median Estimated PFS2 (mos)
Clinically relevant molecular aberration observed	**113**	**97%**	**13.9**	**42%**		**36.7**
1L or 2L Sequencing	60	97%	14.5	38%	0.7511	36.6
No Sequencing captured	53	98%	12.8	45%	(p=0.4549)	36.8
None observed	**764**	**85%**	**10.3**	**40%**		**36.2**
1L or 2L Sequencing	267	88%	9.6	43%	1.2307	35.7
No Sequencing captured	497	83%	10.5	38%	(p=0.1779)	36.6
Total	**877**	**87%**	**10.5**	**40%**		**36.4**
1L or 2L Sequencing	327	90%	10.5	43%	1.152	35.9
No Sequencing captured	550	85%	10.5	39%	(p=0.3188)	36.6

Table 3. Results – 1L vs 2L Sequencing

Lifetime Observed CDx Treatment	Patient Count	% Progressed on 2L	HR (p value)	%Median Estimated PFS2 (mos)
Clinically relevant molecular aberration observed	**60**	**38%**		**36.6**
1L Sequencing	37	38%	0.7511	36.7
2L Sequencing	23	39%	(p=0.4549)	35.2
None observed	**267**	**43%**		**35.7**
1L Sequencing	212	42%	1.2307	35.6
2L Sequencing	55	47%	(p=0.1779)	36.0
Total	**327**	**43%**		**35.9**
1L Sequencing	249	42%	0.8812	35.9
2L Sequencing	78	45%	(p=0.6285)	35.8

Limitations

- The study utilizes broad claims data, but lacks details on tumor stage, histopathology, and testing specifics. Despite using validated intelligence and ensuring data integrity, inherent errors and coverage gaps may affect interpretation. Outcomes of patients with missed/unidentified aberrations due to non-sequencing tests couldn't be assessed.
- Interpretation should consider correlation vs causation, inherent prognosis differences, and testing preferences. Identifying biomarker status without pathology reports may affect sensitivity and specificity. Test choice, insurance factors, and specimen quality should also be considered. Small samples for some aberrations require further investigation using other data sources.

Conclusions

- The analysis did not show significant difference in HR or PFS2 amongst patients who underwent sequencing and those who had non-sequencing tests. However, there is an apparent albeit non statistically significant trend that sequencing benefits patients who require targeted therapy and that performing a sequencing test earlier is more beneficial.
- Upon investigating the patterns in clinically relevant molecular aberration that have a targeted therapy with a companion diagnostic, Sequencing arm showed apparent benefit (HR=0.751, p=0.4549) and longer PFS after first treatment (14.5 mos. vs 12.8 mos.) albeit not significant. Similarly, mPFS2 showed apparent benefit in performing Sequencing tests earlier (36.7 mos.) rather than later (35.2 mos.) in the treatment journey.

References

1. CMS.gov Medicare coverage database. https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=372&ncdver=2.

Disclosure and Acknowledgements

All authors are employed by ICON plc. Research and presentation of the matter herein were conducted under this affiliation. The authors have no conflicts of interest to disclose.

Special thanks to DeMonde, K; Kunz, K; Tu, X.; ICON Data Science Team for their contributions in data methodology and review.

Presented at ISPOR Europe, November 15-19, 2023, Copenhagen, Denmark