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Implementing Real-World RECIST-based Tumor Response Assessment in Patients With Metastatic Non-small Cell Lung Cancer

Abstract

Background: To accelerate drug approvals while maintaining scientific rigor in the evaluation of a therapeutic's efficacy and safety, the United States Food and Drug Administration now considers real-world data (RWD) to support New Drug Applications and expanded indications. Response Evaluation Criteria in Solid Tumors (RECIST) are the gold standard in clinical trials, but the derivation of RECIST-based treatment response from RWD is unproven. This study investigated the feasibility of implementing RECIST criteria in RWD by comparing lung cancer response assessments from RECIST-based measurement of lesions on archived radiologic films with results from medical oncologist and radiologist narratives recorded in electronic health records (EHR). **Materials and Methods:** Response to index treatment via different assessment approaches was compared among 30 metastatic non-small cell lung cancer (mNSCLC) patients receiving systemic treatment (index) after progression on a platinum or anti-PD(L)-1-containing regimen. Specifically, responses based on assessments documented in the medical oncologists' narratives were compared to a radiologist's assessments of archived images using RECIST v1.1 criteria. Each patient's best overall response was characterized as complete or partial (CR/PR), stable disease (SD), progressive disease (PD), or not evaluable (NE). **Results:** Similar distributions of best overall response and substantial concordance (77%) between medical oncologist-reported and radiologist re-assessed responses were observed. There were no instances of CR/PR to PD or PD to CR/PR discordance. **Conclusions:** Results suggest that accurate treatment responses, similar to RECIST, may be derived using RWD. Further validation and improvement of real-world response assessment are needed to develop a scalable real-world approach for response assessment.

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Keywords: Electronic health record, NSCLC, Real-world treatment response data, Real-world tumor response assessment, Real-world RECIST

Introduction

To accelerate the drug approval process while maintaining scientific rigor in the evaluation of a therapeutic's efficacy and safety,

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the United States (US) Food and Drug Administration, Health Canada, European Medicines Agency, and Japan's Pharmaceuticals and Medical Devices Agency have considered the use of real-world historical comparators and natural history efficacy benchmarks to support New Drug Applications and expanded indications for approved agents.[1] Although health records are the most commonly used source of real-world data (RWD) in these filings, questions remain regarding how well the clinical assessments in RWD that are not based on the Response Evaluation Criteria in Solid Tumors (RECIST), compare with RECIST-based treatment response, the current gold standard used in the clinical trial setting.[2] This preliminary study investigated the feasibility of implementing RECIST criteria in RWD by comparing lung cancer response assessments obtained with RECIST-based measurement of lesions on archived radiologic films with results obtained from medical oncologist and radiologist narratives recorded in electronic health records (EHR).

Study

This retrospective study evaluated patients with metastatic non-small cell lung cancer (mNSCLC), the most common type of lung cancer,[3] diagnosed between January 2015 and December 2019 in the Syapse Learning Health Network (LHN) of US community health systems. The LHN provides detailed inpatient and outpatient data from various sources including EHR, laboratory and radiology/imaging systems, computerized order entry systems, and hospital-based cancer registries. Structured data feeds were used to identify an "initial cohort" of 153 subjects who were ≥ 18 years old and had no other primary malignancy at the time of their initial, histologically-confirmed, NSCLC diagnosis; received systemic treatment in a line of therapy (index LOT) initiated after a platinum or anti-PD(L)-1-containing line of therapy (pre-index LOT); and had an available baseline computerized tomography, positron emission tomography, or magnetic resonance imaging scan during a baseline that included a 60-day period prior to and up to 14 days following initiation of index LOT (index date). The assessment period for response began ≥ 28 days after the index date, allowing for the index treatment to produce a measurable effect, and extended until the first of: initiation of a subsequent systemic line of treatment (post-index LOT), death, date of last contact, or study end date on December 31, 2020. A random selection computerized algorithm was then used to repeatedly draw samples of 30 patients from this initial cohort of 153, and each patient's eligibility was confirmed by a certified tumor registrar (CTR) until the desired "eligible cohort" of 30 patients was reached. CTRs confirmed that in addition to aforementioned criteria, eligible patients initiated the index LOT before June 2019 and following progression on the pre-index LOT, not only had a qualifying scan during the baseline period, but additionally had a qualifying scan during the assessment period. Ninty-one of the 153 patients were CTR-reviewed until the 30 eligible patients were identified.

Since, in real-world practice, multiple radiologic scans for the same response assessment time point are often ordered and then performed days apart, all qualifying radiologic scans within 14 days of a first qualifying scan formed a scan bundle. All scans within a bundle were evaluated to determine response at a given assessment timepoint. For each assessment timepoint tumor response was determined in three ways: (1) CTR abstraction from the EHR of the response documented in the medical oncologists' narratives using a set of key terms (oncology response, key term examples provided in Supplemental Table 1), (2) using response documented in the radiologists' reports, also abstracted by a CTR (radiology response), and (3) via a radiologist's reassessment of archived images using RECIST v1.1 criteria[2] that the study team adapted for use in RWD (rwRECIST response, Supplemental Table 2). Each approach characterized a patient's response at each timepoint as complete or partial response (CR/PR), stable disease (SD), progressive disease (PD), or not evaluable (NE). All three approaches required a response duration of ≥ 42 days; CR/PR also required confirmation in a subsequent assessment for radiology, oncology, and rwRECIST assessments. The best response across all assessment timepoints denoted the best overall response (OR). The distribution of OR for each approach and the concordance between the approaches were the primary outcomes of this study.

The distribution of baseline characteristics were similar among the initial and eligible cohorts (Table 1). In the eligible cohort, the median age at mNSCLC diagnosis was 62 years. Most (73%) patients were male, 28 (93%) were White, and 2 (7%) were Black (Table 1). Twenty-one of the 22 patients with a documented Eastern Cooperative Oncology Group performance status (ECOG PS), had a status of 0 or 1; the remaining patient had an ECOG PS of 2. The majority (63%) of patients were alive at the end of study, and the median follow-up was 8 months.

The distributions of the oncology and rwRECIST best overall responses were similar (Supplemental Table 3): approximately 20% of patients experienced CR/PR, half experienced stable disease, and one-third experienced PD. Additionally, substantial concordance (23/30 [77%]) was observed between medical oncology and rwRECIST responses (Table 2). Causes of discordance were lack of CR/PR confirmation in the oncology narratives, absence of such narratives, or presence of clinical symptoms or signs suggesting progression not matched by measurable disease progression. There were no instances of CR/PR to PD, and PD to CR/PR discordance. rwRECIST responses and those reported in the original radiology reports were also similarly distributed (Table 2) with reasonable concordance (22/30 [73%]), and no instances of CR/PR to PD, and PD to CR/PR discordance (Supplemental Table 4).

Discussion

In contrast to a 2019 study which concluded that it was not feasible to use a RECIST-based approach to ascertain response with information obtained from EHR,[4] this study demonstrates both the feasibility of assessing tumor response from archived images and preliminarily a high concordance of this approach with response sourced from oncologists' documentation in lieu of image reassessment. Other prior studies have also evaluated EHR-derived real-world response in NSCLC patients,[5,6,7] including a recent study in which participating physician abstractors estimated a real-world RECIST response measure based on lesion measurements from available imaging reports, or from the images themselves where avaiable.[7]

Table 1 Characteristics of the Initial and Eligible Cohorts

	Initial Identified N = 153	Eligible Cohort N = 30
Age at mNSCLC diagnosis, Median (minimum, maximum)	63 (33, 88)	61.5 (42, 85)
Sex, N (%)		
Female	70 (46)	8 (27)
Male	83 (54)	22 (73)
Missing	0 (0)	0 (0)
Race/ethnicity, N (%)		
White	138 (90)	28 (93)
Black or African American	14 (9)	2 (7)
Other	1 (1)	0 (0)
Missing	0 (0)	0 (0)
ECOG, N (%)		
0-1	98 (64)	21 (70)
≥2	9 (6)	1 (3)
Missing	46 (30)	8 (27)

ECOG = Eastern Cooperative Oncology Group Performance Status; mNSCLC = metastatic non-small cell lung cancer; N = number

Table 2 Concordance Between Oncology and Real-world RECIST Measures of Best Overall Response, n (%)

Real-World RECIST response	Medical Oncologist-reported Response			
		CR/PR	SD	PD
	CR/PR	4 (67)	2 (33)	0
	SD	1 (7)	11 (79)	2 (14)
	PD	0	2 (20)	8 (80)

CR/PR = complete/partial remission; PD = progressive disease; RECIST = Response Evaluation Criteria in Solid Tumors; SD = stable disease.

Conclusion

To our knowledge, this is the first study to directly assess concordance between oncologist-documented responses and those obtained when a radiologist re-assessed archived images. These results demonstrate the feasibility of obtaining accurate and reliable treatment response from data captured in EHR. Future studies are needed to further demonstrate the value of RWD to regulatory agencies by validating these findings in larger samples, exploring the use of Natural Language Processing for evaluating response from EHRs at scale, and potentially improving concordance by the use of additional data elements.

Disclosures

Monika A. Izano, Liz Toland, Danny Idryo, Matthew Rioth, Chris Sommers, and Thomas Brown are employees of Syapse and hold Syapse stock. In addition, Thomas Brown has received honoraria, served on the Scientific Advisory Board, and holds stock from GenomiCare Biotechnology, and has also served on the Advisory Board and holds stock for Sygnomics. Ryan Hilbelink has received consulting fees from Syapse. Ngyuet Tran, Alan Fu, and Hil Hsu are employees of Amgen, Inc and hold Amgen stock. Huakang Tu was formerly employed by Amgen, Inc and holds Amgen stock.

Amgen, Inc. provided financial support for data collection, curation, and analysis by Syapse. Sponsor staff were involved in study design and data interpretation. All authors participated in the conceptualization and design of this study, as well as the review and editing of the manuscript. Monika A. Izano, Ryan Hilbelink, Liz Toland, and Danny Idryo conducted data collection, curation, and analysis. Monika A. Izano led the writing of the original manuscript draft.

Prior Presentations

Select results from this study were presented at the 2021 annual meeting of the American Society of Clinical Oncology (ASCO). Tran N, Fu A, Izano MA, et al. Feasibility of RECIST-based real-world tumor response assessment in metastatic non-small cell lung cancer patients. DOI:10.1200/JCO.2021.39.15_suppl.e21121 Journal of Clinical Oncology 39, no. 15_suppl

Data Availability

Data used for this study reside in the proprietary Syapse LHN database.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cllc.2022.01.002.

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