Real-world response endpoints in patients with mNSCLC treated with chemotherapy across real-world datasets

Brittany Avin McKelvey[1*], Elizabeth Garrett-Mayer[2], Andrew J. Belli[3], Thomas D. Brown[4], Jessica Dow[5], Janet L. Espirito[6], Paul Kluetz[7], Xinran Ma[8], Andrea McCracken[9], Pallavi Shruti Mishra-Kalyani[10], Yanina Natanzon[11], Danielle Potter[12], Donna Rivera[7], Hillary Stires[1], Mark Stewart[1], Jeff Allen[1]

1 Friends of Cancer Research; 2 American Society of Clinical Oncology; 3 COTA Inc; 4 Syapse; 5 Tempus Labs, Inc.; 6 Ontada; 7 Oncology Center of Excellence, U.S. Food and Drug Administration; 8 Flatiron Health; 9 Guardian Research Network; 10 US Food and Drug Administration; 11 ConcertAI; 12 IQVIA.
*Corresponding author (bmckelvey@focr.org)

@cancerresrch

Abstract # 6595

Background

- Response is an important outcome for measuring therapeutic benefit in oncology clinical trials. However, measurement of response in clinical trials differs from the real-world setting.
  - Response Evaluation Criteria in Solid Tumors (RECIST)-based measures of response rely on imaging data at specific timepoints for uniform assessment.
  - There is no consensus approach to measure real-world response (rw-response) from routine clinical practice data.
- Friends of Cancer Research formed a multi-stakeholder partnership to evaluate access to available data elements for measuring rw-response across real world data (RWD) sources to inform development of a consistent method for response assessment.

Methods

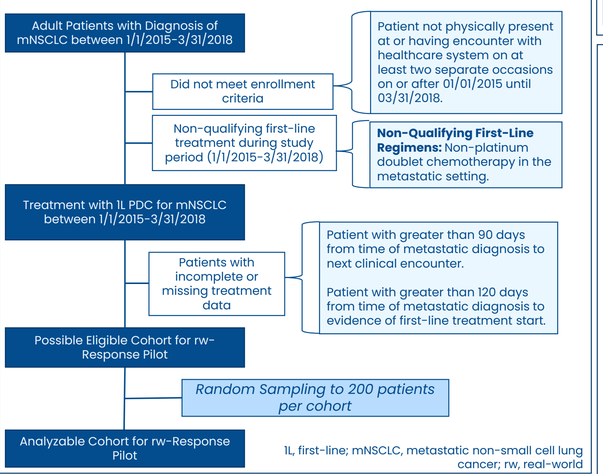
- A multi-stakeholder partnership developed the common protocol and statistical analysis plan to achieve the following objectives:

Assess the Availability and Frequency of Core Data Components for Measuring rw-Response
- Images
- Image reports
- Clinician response assessments

Evaluate the Consistency of a Measure of rw-Response Across Data Sources in an Aligned Population
- rw-response rate (rwRR)
- rw-duration of response (rwDOR)
- Association between rw-response and time-to-event endpoints

- Seven RWD EHR-focused partners (ConcertAI, COTA, Flatiron Health, Guardian Research Network/IQVIA, Ontada, Syapse, Tempus) who identified and analyzed a cohort of 200 patients with mNSCLC each defined by the criteria specified below in the CONSORT diagram.

CONSORT Diagram



Key Definitions
- **Baseline**: All imaging and image reports from unique imaging modalities, between the metastatic diagnosis and index date.
- **Post-Baseline**: All image reports within first-line treatment, after the index date, and up to the earliest of the start of new 2L treatment, 30 days post-first-line treatment, death, or data cutoff.
- **Index**: Date of the earliest drug episode (e.g., first administration) of the first-line therapy for metastatic disease.
- **Follow-up time**: Time from the index date to the earliest of last confirmed activity date, date of death, or data cutoff.

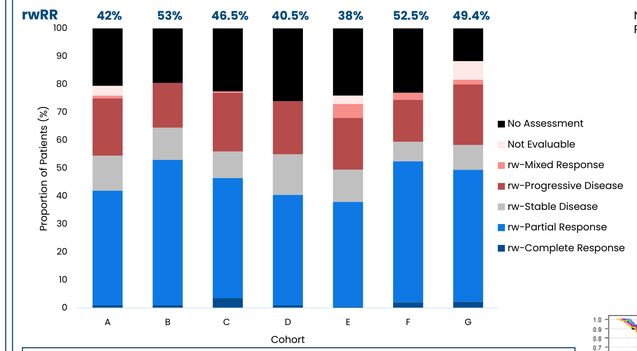
Cohort Characteristics

		A	B	C	D	E	F	G
Age at Index	≤49	5	5	5	7	6	5	5
	50–64	31	46	35	42	40	29	38
	65–74	44	37	34	37	35	40	41
	≥75	22	14	26	14	20	28	19
Gender	Female	47	42	44	44	42	53	44
	Male	54	58	56	56	57	47	56
Race	White	66	77	84	70	65	77	83
	Black or African American	13	14	6	15	19	10	11
	Other/Missing	21	10	11	15	17	14	6
Ethnicity	Hispanic	5	5	23	5	5	5	5
	Non-Hispanic	81	86	68	75	82	85	92
	Unknown/Missing	16	15	9	22	14	11	5
Practice Site	Non-Academic Institution	90	87	69	5	100	100	100
	Academic Institution	10	14	31	5	5	5	5
	Unknown	5	5	5	100	5	5	5
Year of Initial Diagnosis	Prior to 2015	5	5	5	7	5	5	5
	2015	38	38	39	30	32	34	23
	2016	32	38	34	35	36	35	41
	2017	23	21	22	23	28	27	29
	2018	5	5	5	5	5	5	5
Year of Index Date	2015	33	35	36	31	30	31	23
	2016	36	38	35	37	34	32	39
	2017	24	23	25	23	28	32	31
	2018	8	5	5	9	9	5	7
Status at Diagnosis	Progressed/Recurred	14	5	5	8	5	5	5
	Metastatic at Dx	86	93	97	86	95	95	89
Histology	Non-squamous cell carcinoma	89	89	78	73	70	68	70
	Squamous cell carcinoma	26	20	15	20	18	23	26
	Other/Missing	5	22	8	7	12	10	5
Smoking Status	History of Smoking	92	90	87	92	39	80	91
	No History of Smoking	8	10	13	8	5	14	7
	Unknown/Not Documented	5	5	5	5	58	6	5
Performance Status (ECOG)	0	22	24	24	6	12	66	12
	1	40	37	34	15	34		15
	2+	18	19	21	7	10	18	5
	Unknown	21	21	21	72	44	17	73
Metastatic Site	Brain Only	10	9	10	14	7	11	14
	Bone Only	12	14	10	11	8	14	12
	Brain and Bone Only	5	5	5	5	5	5	5
	Brain and Other Visceral Mets	8	7	11	7	5	5	5
	Bone and Other Visceral Mets	17	17	22	24	12	11	18
	Brain and Bone and Other Visceral Mets	5	6	6	5	6	5	5
	Brain Mets with Unknown Other	5	5	5	5	5	5	5
	Bone Mets with Unknown Other	5	5	5	5	7	5	5
	Other Visceral Only	30	27	34	42	30	31	33
	Unknown/Not Documented	9	17	5	8	22	23	12
VEGF Receptor Antagonists	VEGF Receptor Antagonists	30	15	22	19	22	19	16
	None	71	86	78	81	78	78	84
Other Treatment Modalities	Surgical Intervention	5	5	5	5	5	5	5
	Radiation Therapy	28	28	5	12	14	36	27
	Other	5	5	5	5	5	5	5
	None	14	5	5	86	55	5	
	Not Documented	67	73	69	87	5	5	73

Demographic and clinical characteristics of cohorts. Characteristics are largely similar across cohorts (A-G) with more variability in practice type, race/ethnicity, ECOG status, and site of metastasis. Numbers indicate the proportion of patients in each category. Shading denotes the proportion of patients from white (0%) to dark blue (100%). Data are suppressed (S, in grey) if ≤5%.

Results: rw-Response Estimates and Endpoints

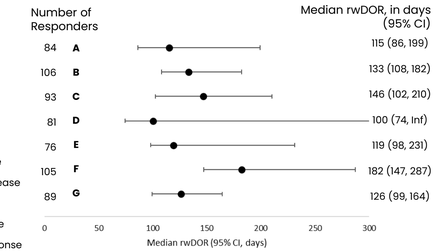
Clinician-Stated rw-Response Rate (rwRR)



rw-response rates were consistent using clinician stated response across cohorts, with a median of 46.5%. rw-RR was calculated as the number of patients with a rw-best overall response of rw-complete response or rw-partial response by clinician assessment out of all patients (including those without a response assessment). Cohorts A-F n=200, G n=180 patients.

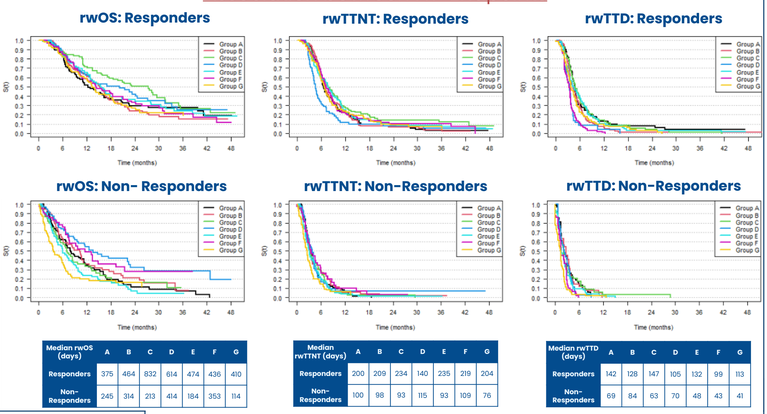
Real-world response was relatively consistent across data sources in an aligned patient population using clinician-stated response.

rw-Duration of Response



rw-duration of response (rwDOR) is variable across cohorts, likely due to variability in timing and reporting of assessment. rw-duration of response was calculated without interval censoring for patients with complete or partial response (responders) across cohorts. Graphs show the median rwDOR with 95% confidence intervals (CI).

Association between rw-Endpoints



Median rwOS (days)	A	B	C	D	E	F	G
Responders	375	464	832	614	474	436	410
Non-Responders	245	314	213	414	184	353	114

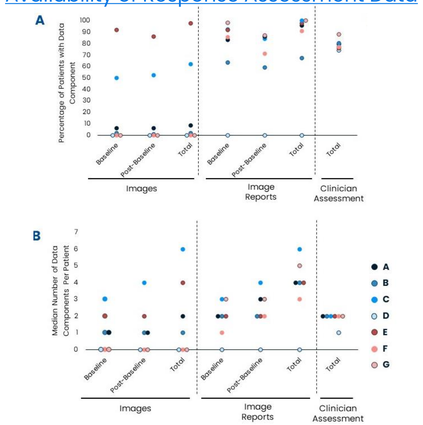
Median rwTTNT (days)	A	B	C	D	E	F	G
Responders	200	209	234	140	235	219	204
Non-Responders	100	98	93	115	93	109	76

Median rwTTD (days)	A	B	C	D	E	F	G
Responders	142	128	147	105	132	99	113
Non-Responders	69	84	63	70	48	43	41

Relative consistency in the medians and directionality of the time-to-event endpoints: rw-overall survival (rwOS), rw-time to next treatment (rwTTNT), and rw-time to treatment discontinuation (rwTTD) across datasets for responders vs. non responders. Consistency in Kaplan-Meier curves for responders and non-responders across cohorts increases confidence in the measurement of response.

Results: Availability of Response Data Components

Availability of Response Assessment Data



Timing of Response Assessment Data

		Baseline to Index	Baseline to 1st Post-Baseline	1st to 2nd Post-Baseline
Images	Median Percentage of Patients with Data (Range)	28% (1.5–92%)	22% (0.5–79.5%)	29% (0.5–86%)
	Median Time between in weeks (Range)	2.95 (2.4–5)	13.2 (7.3–18)	6 (3.29–7)
Image Reports	Median Percentage of Patients with Data (Range)	88.8% (63.5–98.3%)	75% (55–85.6%)	85% (59–87.2%)
	Median Time between in weeks (Range)	3.63 (2.3–4)	9.62 (7.5–18)	5 (3.7–6.3)
			Index to Assessment	**1st to 2nd Assessment**
Clinician Assessment	Median Percentage of Patients with Data (Range)	N/A	77.5% (74–88.3%)	44.5% (32–61%)
	Median Time between in weeks (Range)	N/A	7.9 (6.9–8)	7.9 (6–9)

Variability in the availability and timing of response assessment data within and across cohorts. Availability of images in EHRs is limited, indicating the need to rely on other data elements to assess response. Image reports and clinician assessments were available across most cohorts for most patients. The timing of clinician assessments was relatively consistent across cohorts and somewhat mimics clinical trials (6-8 weeks). The median number of data components is calculated only for patients with at least one data component in the record (patients with 0 assessments are not included).

Conclusions

This unique partnership allowed us to assess the availability of data attributes to assess rw-response and evaluate the consistency of the measure across RWD sources.

- Imaging reports and clinician assessments of response were available for most patients across cohorts, unlike images, with greatest consistency in the timing of assessments for the clinician assessment.
- The rwRR among patients with mNSCLC, using the clinician assessment, was relatively consistent across all RWD sources, with consistent trends in time-to-event endpoints.
- The demonstrated feasibility of response endpoints based on clinician assessment suggests rw-response is clinically relevant and further exploration may inform drug effectiveness evaluation w/ RWD sources.

Aligning methodologies for aggregating and analyzing RWD will help ensure RWD is a reliable and consistent source of real-world evidence to support oncology drug development and regulatory decision-making.