Real-world Response Endpoints in mNSCLC Patients Across Real-World Datasets

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Pilot results presented on behalf of the rw-Response Working Group

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Friends' RWE Portfolio

Broad Goal: Develop and establish methodology for using RWD to inform clinical trial designs, evaluate therapies, and support regulatory decision-making

2017 — 2023

Pilot 1.0

- Established aligned definitions and protocols for capturing rw-endpoints (rwOS, rwTTD, and rwTTNT) in a feasibility study in aNSCLC

Pilot 2.0

- Assessed the performance of rw-endpoints to identify the direction and magnitude of treatment effect
- Evaluated the internal consistency of rw-datasets by applying RCT I/E criteria

rw-Response Pilot

- To establish a framework for evaluating rw-response
- To assess the consistency of the measure across rw-datasets to generate RWE

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Measuring Real-World Response

The Promise

rw-response is a clinical outcome providing valuable details about therapeutic efficacy

- The endpoint has promise in signal-seeking to attribute a real-world outcome to a drug intervention

The Problem

There is no consensus definition or approach for measuring real-world response

- Data are not consistently captured in a structured or systematic way
- No uniform criterion (e.g., RECIST) in the observational setting

The Solution

Establish a unique research partnership:

- To develop an aligned framework for measuring rw-response across datasets
- To initiate a pilot to assess the feasibility and consistency of the measure in an aligned patient population

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rw-Response Pilot Approach

7 Participating Data Partners Contributing 200 Patients Each

Pilot Cohort: Adult patients diagnosed with metastatic NSCLC, treated with a first-line platinum doublet chemotherapy regimen

Pilot Objectives

1. **Assess the availability and frequency of core data components for measuring rw-response including:**
   - Raw images
   - Image reports
   - Clinician assessment
2. **Evaluate the consistency of a composite measure of rw-response across data sources in the aligned patient population**

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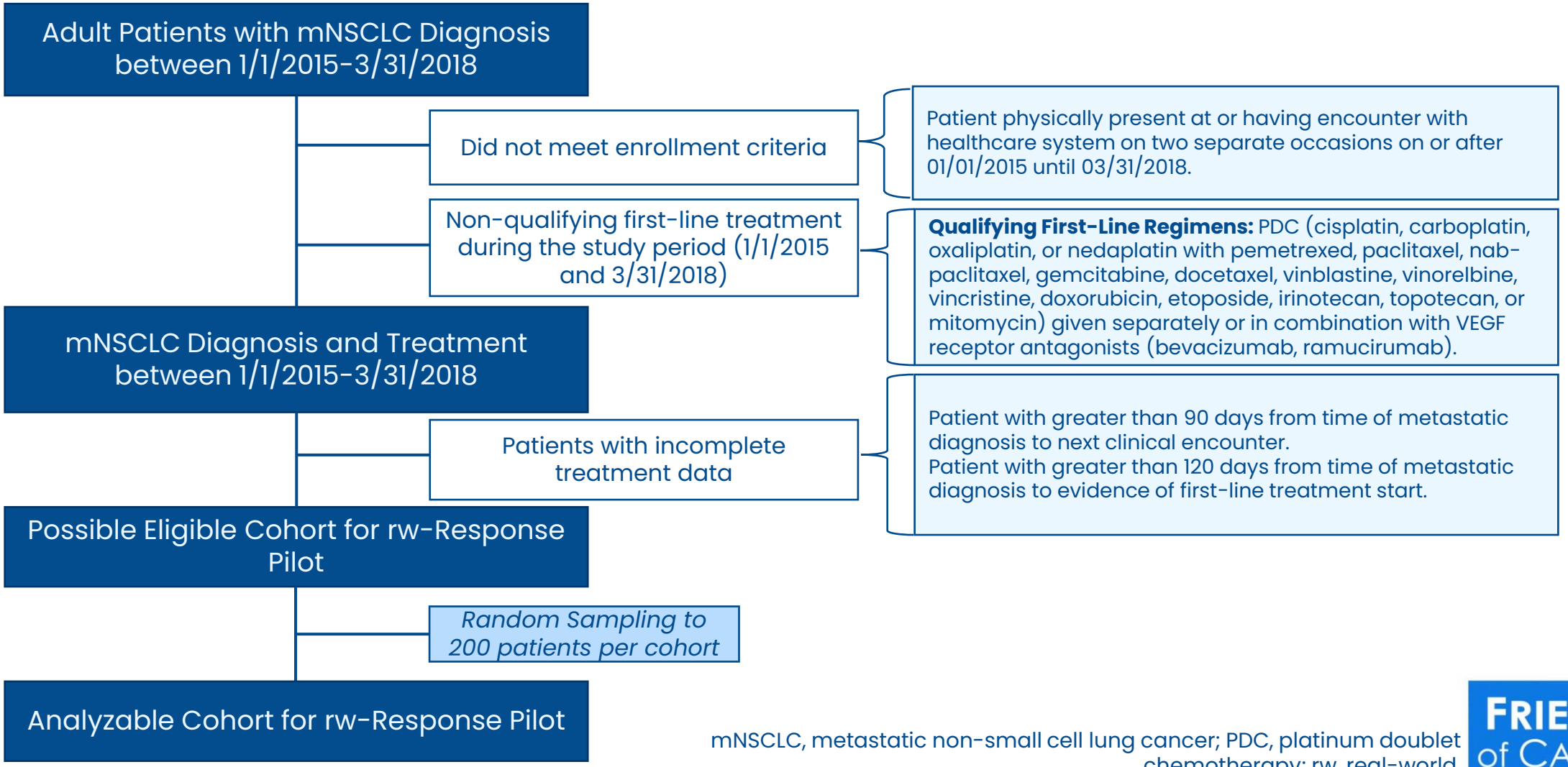
rw-Response Pilot Cohort



mNSCLC, metastatic non-small cell lung cancer; PDC, platinum doublet chemotherapy; rw, real-world.

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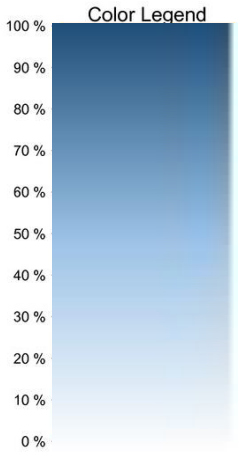
Demographic and Clinical Characteristics

		A	B	C	D	E	F	G
Age at Index	≤49	S	S	S	7	6	S	S
	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	S	S	23	S	S	S	S
	Non-Hispanic	81	86	68	75	82	85	92
	Unknown/Missing	16	15	9	22	14	11	S
Practice Site	Non-Academic Institution	90	67	69	S	100	100	100
	Academic Institution	10	34	31	S	S	S	S
	Unknown	S	S	S	100	S	S	S
Status at Diagnosis	Progressed/Recurred	14	S	S	8	S	S	S
	Metastatic at Dx	85	93	97	86	95	96	89
Histology	Non-squamous cell carcinoma	69	59	78	73	70	68	70
	Squamous cell carcinoma	26	20	15	20	18	23	26
	Other/Missing	S	22	8	7	12	10	S
Smoking Status	History of Smoking	92	90	87	92	39	80	91
	No History of Smoking	8	10	13	8	S	14	7
	Unknown/Not Documented	S	S	S	S	58	6	S

Percent of Patients in Each Cohort



S= Suppressed data, if ≤5%

Demographic and clinical characteristics are similar across cohorts, with some variability by practice site, largely non-academic institutions

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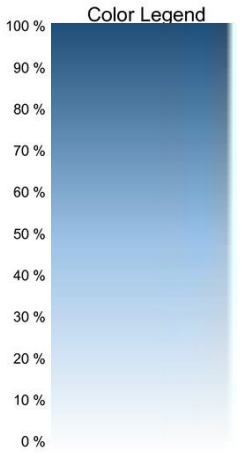
Clinical Characteristics

		A	B	C	D	E	F	G
Metastatic Site	Brain Only	10	9	10	14	7	11	14
	Bone Only	12	14	10	11	8	14	12
	Brain and Bone Only	S	S	S	S	S	S	S
	Brain and Other Visceral Mets	8	6	11	7	S	S	S
	Bone and Other Visceral Mets	17	22	24	12	11	12	18
	Brain and Bone and Other Visceral Mets	S	6	6	S	6	S	S
	Brain Mets with Unknown Other	S	S	S	S	S	S	S
	Bone Mets with Unknown Other	S	S	S	S	7	S	S
	Other Visceral Only	30	27	34	42	30	31	33
	Unknown/Not Documented	9	17	S	8	22	23	12
VEGF Receptor Antagonists	VEGF Receptor Antagonists	30	15	22	19	22	19	16
	None	71	85	78	81	78	78	84
Other Treatment Modalities	Surgical Intervention	S	S	S	S	S	S	S
	Radiation Therapy	28	28	S	12	14	36	27
	Other	S	S	S	S	S	S	S
	None	14	S	S	S	86	55	S
	Not Documented	57	73	95	87	S	S	73

Percent of Patients in Each Cohort



S= Suppressed data, if ≤5%

The site of metastasis and other treatment modalities documented during first line treatment varied across cohorts

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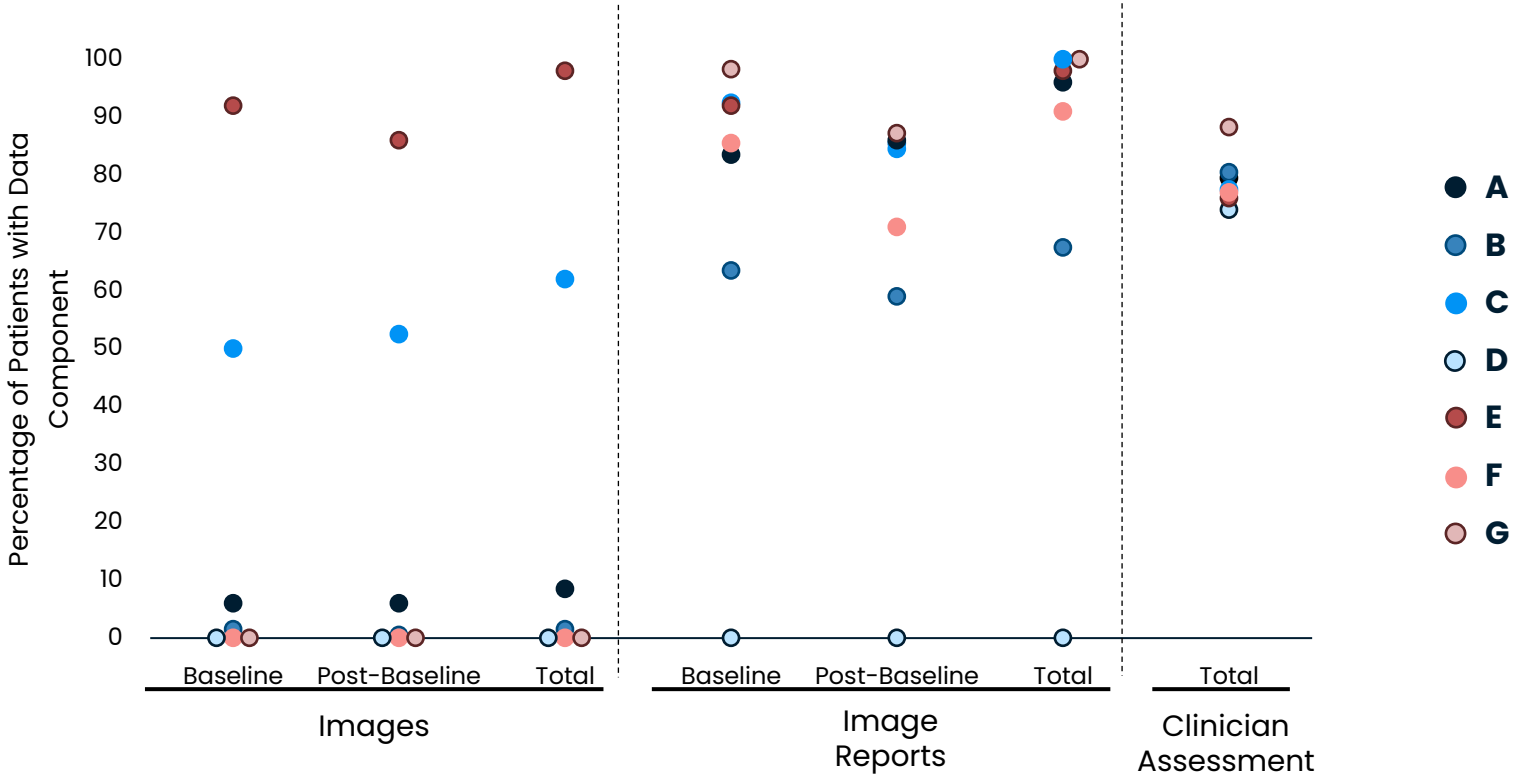
Data Components for Measuring rw-Response

Images	Images present in the EMR containing evidence of tumor burden, relevant to the evaluation of mNSCLC
Image Reports	Radiology report present in the EMR containing evidence of tumor burden, relevant to the evaluation of mNSCLC
Clinician Assessment	Assessment of tumor response, noted in the clinician's notes, relevant to the evaluation of mNSCLC

Availability of Response Assessment Data



Imaging reports and clinician assessments were available for most patients across cohorts, while images were not as common

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Timing of Response Assessment Data

	Median Time Between, in weeks (Range)		
	Baseline to Index	Baseline to Post-Baseline	1st to 2nd Post-Baseline
Images	2.95 (2.4-5)	13.2 (7.3-18)	6 (3.29-7)
Image Reports	3.63 (2.3-4)	9.62 (7.5-18)	5 (3.7-6.3)
		Index to Assessment	1st to 2nd Assessment
Clinician Assessment		7.9 (6.9-8)	7.9 (6-9)

Timing of clinician assessments was relatively consistent across cohorts

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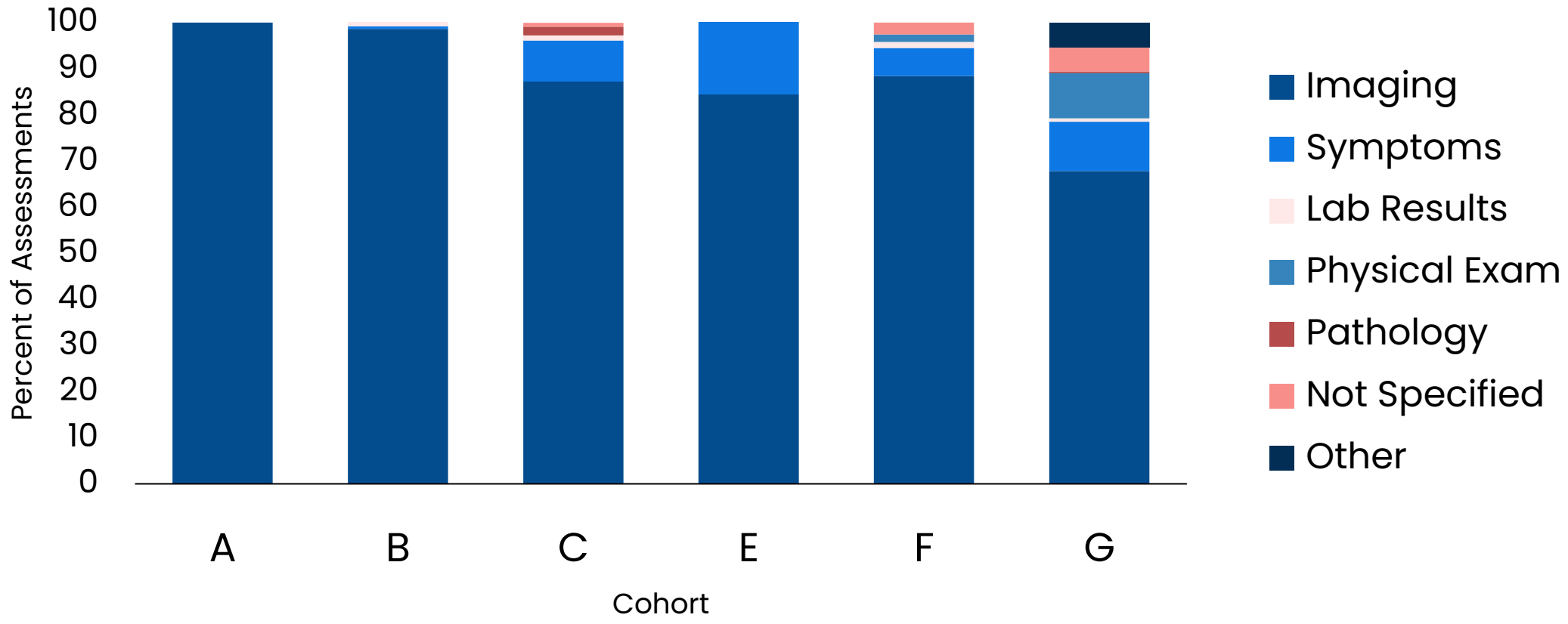
Source of Clinician Response Assessments



Imaging is the source of the majority of clinician assessments for most cohorts

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Measuring rw-Response

- Aligned on a framework for measuring rw-response derived from the clinician's assessment of tumor burden
- Each data partner abstracted a response measurement from the clinician's notes. Examples of clinical notes:

rw-Complete Response (rwCR)	rw-Partial Response (rwPR)
• Complete response, Full/Complete resolution • Remission, Complete remission • All lesions have disappeared, All lesions resolved • No evidence of disease, NED • No disease present, No sites of disease	• Improved disease • Responding disease • Partial response, Partial remission, PR • Positive, significant, marked, good, meaningful, substantial, vast, excellent, near complete

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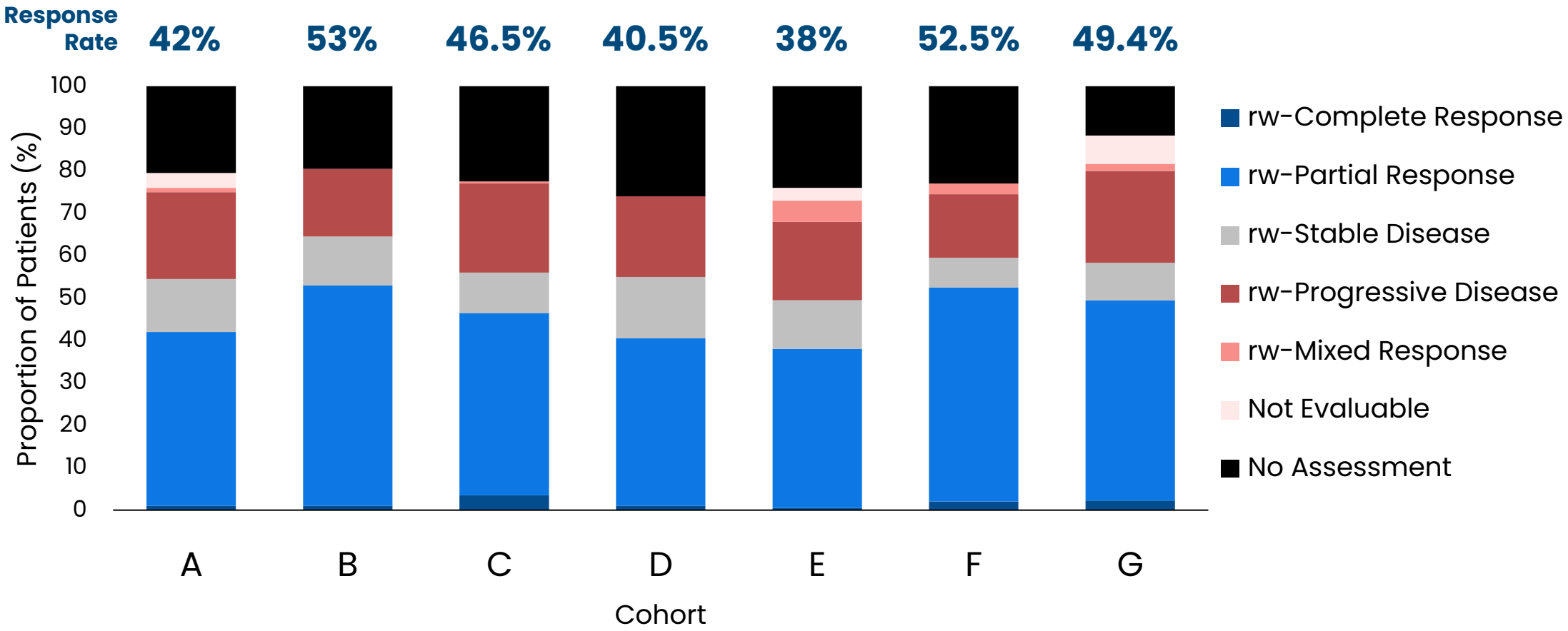
Estimation of rw-Response Parameters



There is relative consistency across cohorts in best overall response and response rate

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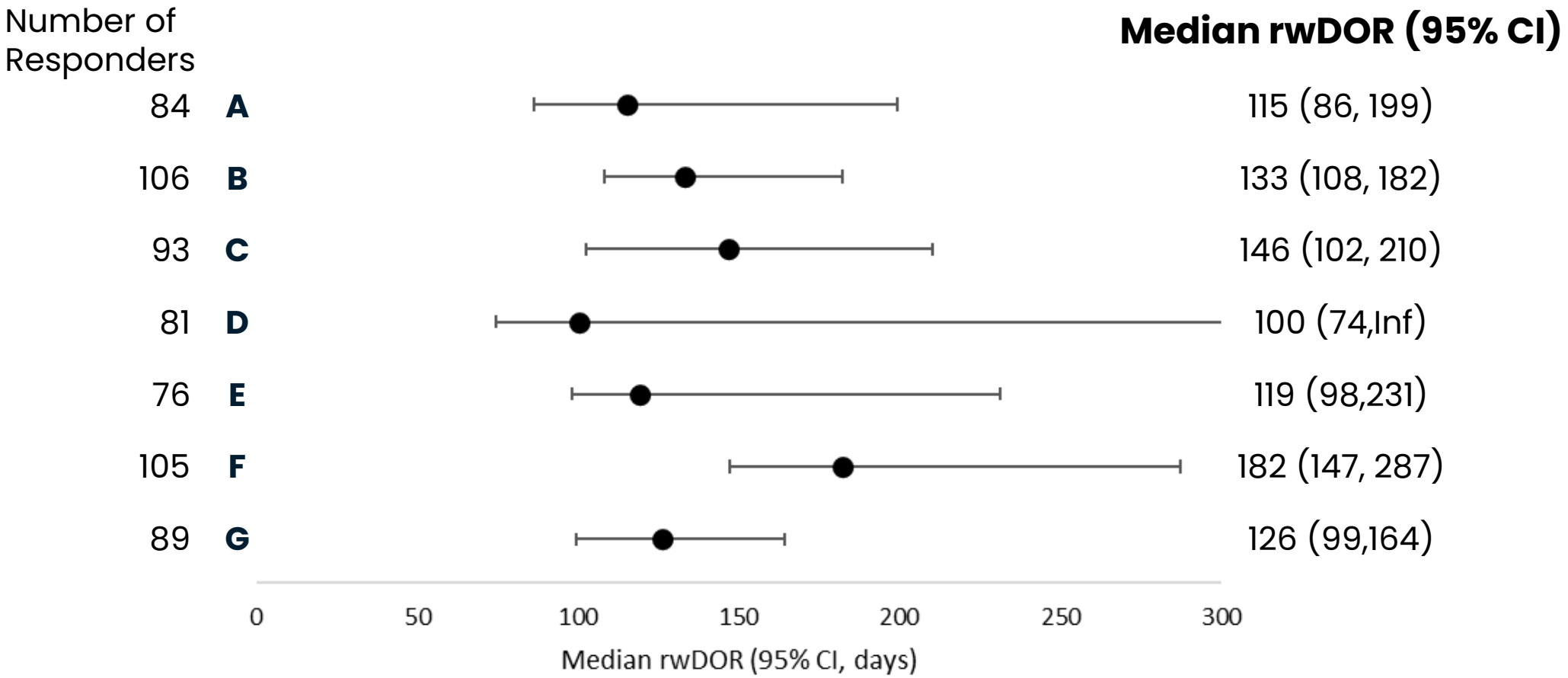
rw-Duration of Response



rw-duration of response (rwDOR) is variable across cohorts, likely due to variability in timing and reporting of assessment

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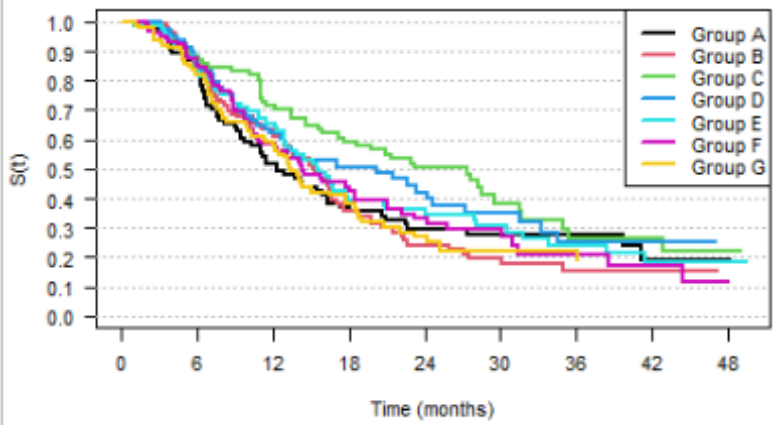
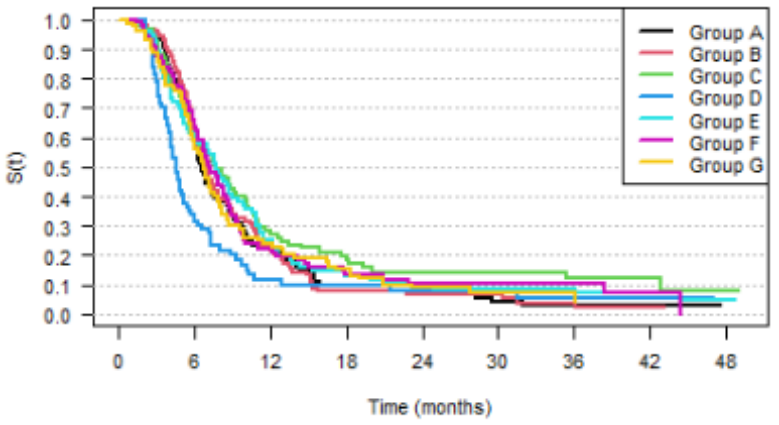
Time to Event Endpoints by rw-Response

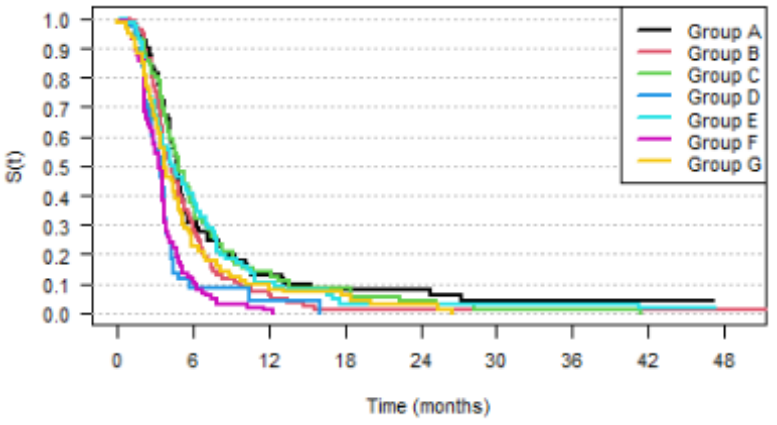
rwOS: Responders



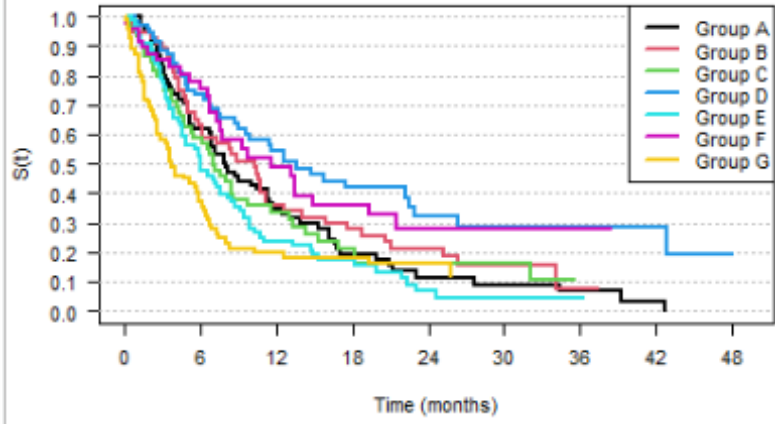
rwTTNT: Responders



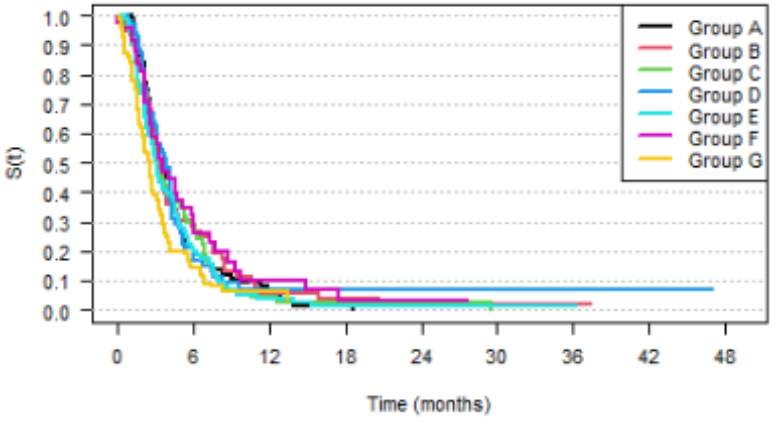
rwTTD: Responders



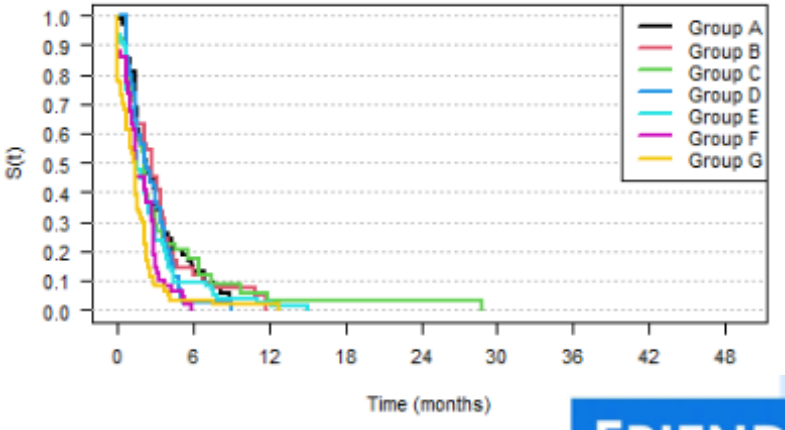
rwOS: Non- Responders



rwTTNT: Non-Responders



rwTTD: Non-Responders



Relative consistency in the medians and directionality of rwOS, rwTTNT, and rwTTD across datasets for responders vs. non responders

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Conclusions

- Our collaborative partnership allowed us to:
  - Assess the availability of data components to assess rw-response
  - Evaluate the consistency of the measure across RWD sources
- Clinician assessments of response were available for most patients across all cohorts, with consistency in the timing of assessments.
- rwRR 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.

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rw-Response Pilot Project Partners

- ConcertAI
- COTA
- Flatiron Health
- Guardian Research Network
- IQVIA
- Ontada
- Syapse
- Tempus Labs
- American Society of Clinical Oncology (ASCO)
- U.S. Food and Drug Administration (FDA)

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