Welcome to the Sentinel Innovation and Methods Seminar Series

The webinar will begin momentarily

Please visit www.sentinelinitiative.org for recordings of past sessions and details on upcoming webinars.

Note: closed-captioning for today's webinar will be available on the recording posted at the link above.

Sentinel

Imagine a world where real-world caution becomes real-world confidence.

Introducing...


ontada

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Measure what you treasure…

June 2021

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Vice President RWD/RWE
Ontada

Agenda

- Background and introduction to Ontada
- Real World Endpoints and challenges - how to evolve collection
  - Traditional
  - Contemporary
  - Future
- Thoughts for Sentinel

The oncology landscape continues to become more complex

Tailwinds

- Molecularly-guided therapies
- Greater connectivity of oncology ecosystem
- Integration of real-world evidence
- Value-based care

Headwinds

- COVID-19 pandemic
- Awareness of rapidly changing science
- Maintaining workflow given complexity of care
- Keeping the patient in the community

And at the same time, oncology life sciences companies have several key jobs-to-be-done

JOBS

NEEDS

Pre-Clinical Research

Enrich drug pipeline with promising drug candidates

- Biomarker selection & validation
- Drug target identification & lead optimization

Clinical Development

Identify target patient segments
Reduce clinical trial costs
Shorten clinical development timelines

- Data-driven patient cohort mapping & prioritization
- Optimized and adaptive trial design & site selection
- EDC or “smart EMR” (i.e., EMR with EDC capabilities)
- Data-driven rapid trial recruitment
- Patient reported outcomes
- Synthetic control studies

Pre-Launch/ Launch

Optimize and track launch efforts
Educate relevant stakeholders
Remove barriers to access & adherence

- Opportunity sizing & forecasting
- Real-time new patient identification & physician alerts
- Targeted sales & marketing efforts

Growth

Maximize commercial opportunity
Demonstrate differentiated value

- Market intel and clinical insights
- Pragmatic trials & RWE
- Rapid label expansion studies
- Outcomes research / safety studies
- Innovative payer contracting

R&D teams are focused on finding and expediting promising new therapies for FDA approval

Manage **R&D pipeline & product differentiation strategies**

Develop **clinical research protocols**

Identify new **clinico-genomic targets**

Identify & validate potential **companion diagnostics**

Find the **right patient** for the right trial

Understand **efficacy & side effects**

Gather evidence for **regulatory approvals**

Optimize **clinical trial operations**

Commercial teams are focused on maximizing treatment optimization

Understand **market size & segmentation**

Find the **right patients**

Educate relevant stakeholders

Demonstrate **differentiated value**

Identify **barriers to access**

Drive a **positive patient experience**

Expand into **new indications**

Medical & RWE teams are focused on understanding a therapy's effectiveness & safety in a real-world setting

Optimize relationships and educate key **thought leaders & stakeholders**

Ensure timely and relevant **evidence & insights**

Analyze **disease burden & unmet need**

Understand **patterns of therapy & optimal place in therapy**

Generate **evidence of therapy value**

We’re here to help

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Our vision	**Transform the fight against cancer**
How we’ll do it	Partner with life sciences and providers to advance technology and real-world insights across the oncology continuum
Commitment to you	Deliver on the promise of real-world insights to drive innovation across the development lifecycle

It all starts with real-world data you can trust

Today our RWD and expertise are trusted to power key oncology research & decisions

Regulatory decision-making

RWD power numerous regulatory studies & the **first FDA approval** of a first-line therapy in oncology

Life sciences decision-making

RWD support a broad range of retrospective analyses & commercial insights

Provider decision-making

RWD power provider technologies that support evidence-driven decisions at the point-of-need

Published RWE studies

RWD used in **175+ RWE studies** in leading industry publications for 70+ oncology indications

New standards for real-world endpoints

Ontada is helping define & standardize methodologies alongside life sciences & Friends of Cancer Research

We're uniquely positioned to advance cancer care by leveraging our interconnected technology & insights

Our Provider Network

1.2M+ patients
treated annually within
The US Oncology Network

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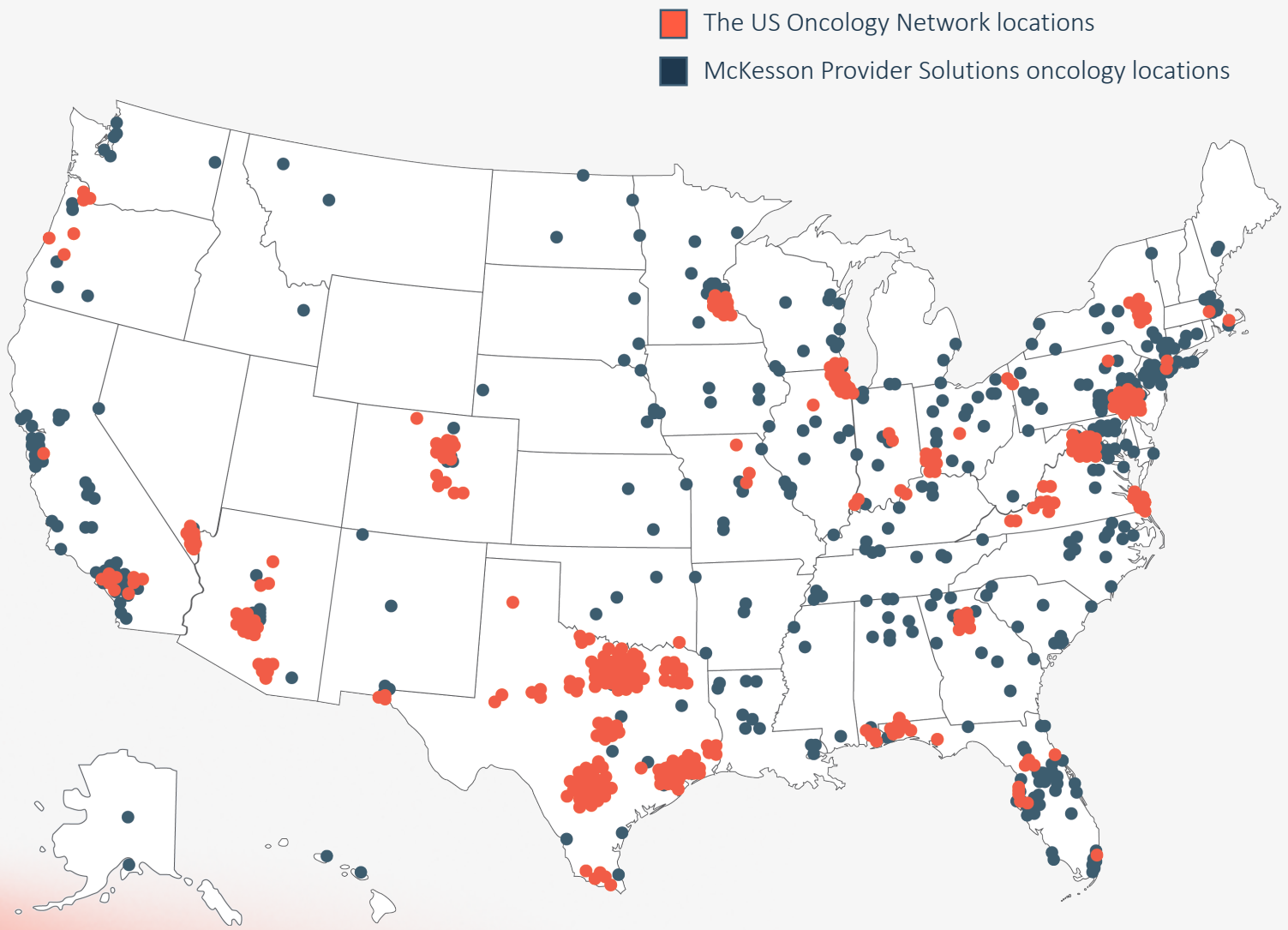
Market-Leading Provider Technology

2,000+ providers
use iKnowMed℠ EHR

Real-World Oncology Data & Insights

2M+ patient records
available for research

Our broad reach creates meaningful opportunities to engage with providers



NOTE: Reach includes oncologists who purchase at least one product or service from Ontada or McKesson

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Traditional Endpoints

Data enhancements on top of our structured clinical and genomic data elements give you the clearest view into the full patient journey

DIAGNOSIS & STAGING | *Biopsy*

- Patient Demographics, Family history
- Diagnosis/Staging
- Treatment plan/scheduling
- Biopsy date
- Comorbidities
- Histology
- Payer information

TREATMENT DECISION | *Biomarker testing* *Regimen selection*

- Current disease state
- Date and location of metastatic disease
- Biomarker type
- Date/type of test ordered (unstructured if pathologist ordered)
- Regimen selection & schedule (stop/start dates)
- Regimen type: chemo, hormonal, supportive care, radiation
- Line of therapy

THERAPY INITIATION

- Patient performance status
- Dosing/duration
- Treatments received
- Supportive care
- Concomitant meds
- Drug reimbursement
- Patient Out of Pocket Costs
- Side effects/adverse events
- PROs

MAINTENANCE / DISEASE PROGRESSION | *Biomarker re-testing*

- Maintenance dosing
- Biomarker results
- Radiologic support
- Disease response or progression
- Reason for discontinuation
- Maintenance dosing or line advancement
- Regimen selection

TREATMENT DECISION / THERAPY INITIATION

- Patient performance status
- Dosing/duration
- Treatments received
- Supportive care
- Concomitant meds
- Drug reimbursement
- Patient Out of Pocket Costs
- Side effects/adverse events
- PROs

COMPLICATIONS / ADVERSE EVENTS | *Hospitalization* *Hospice*

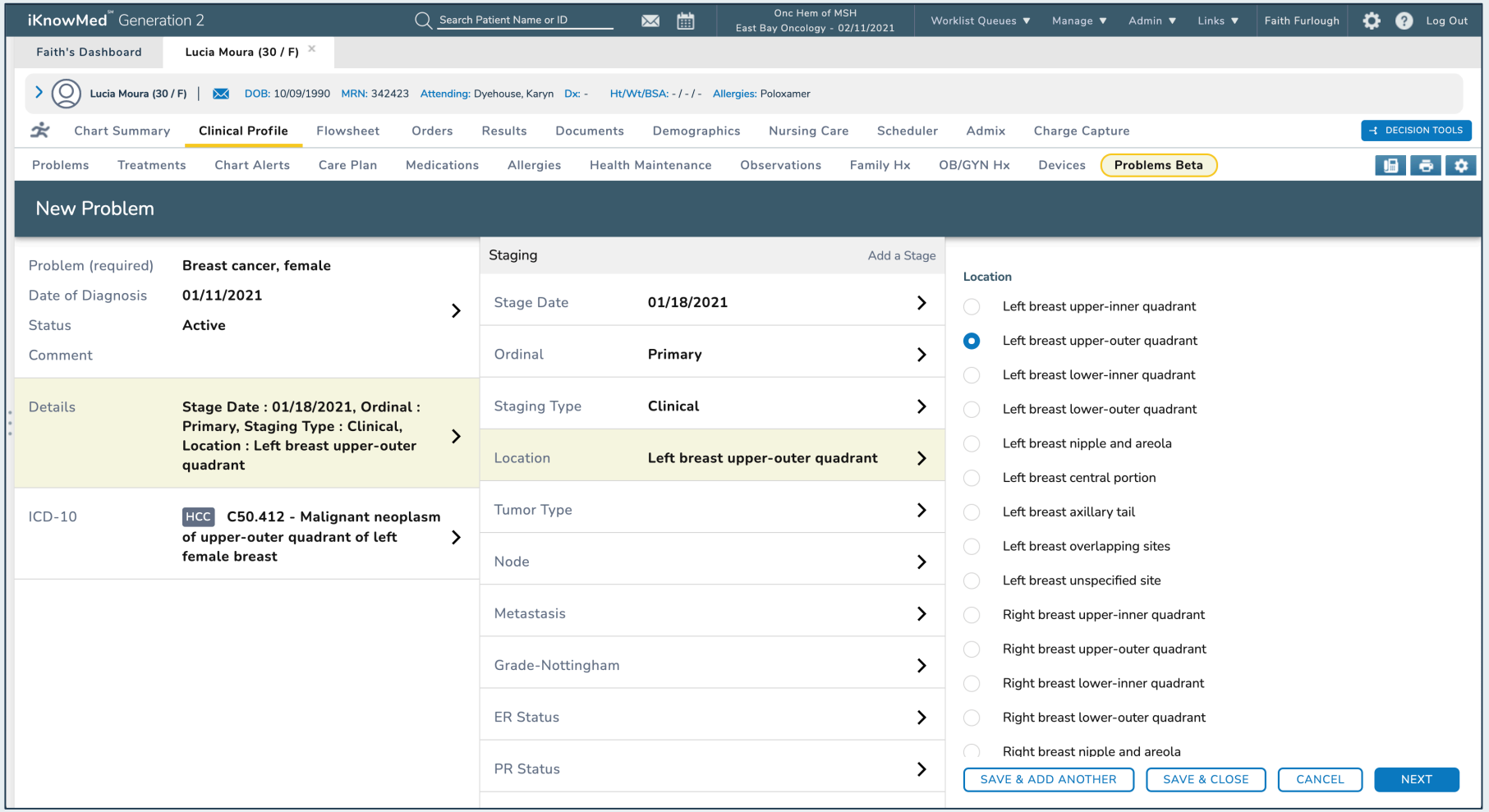
- Date of hospitalization
- Cost of care
- Reimbursement / Claims

SURVIVORSHIP

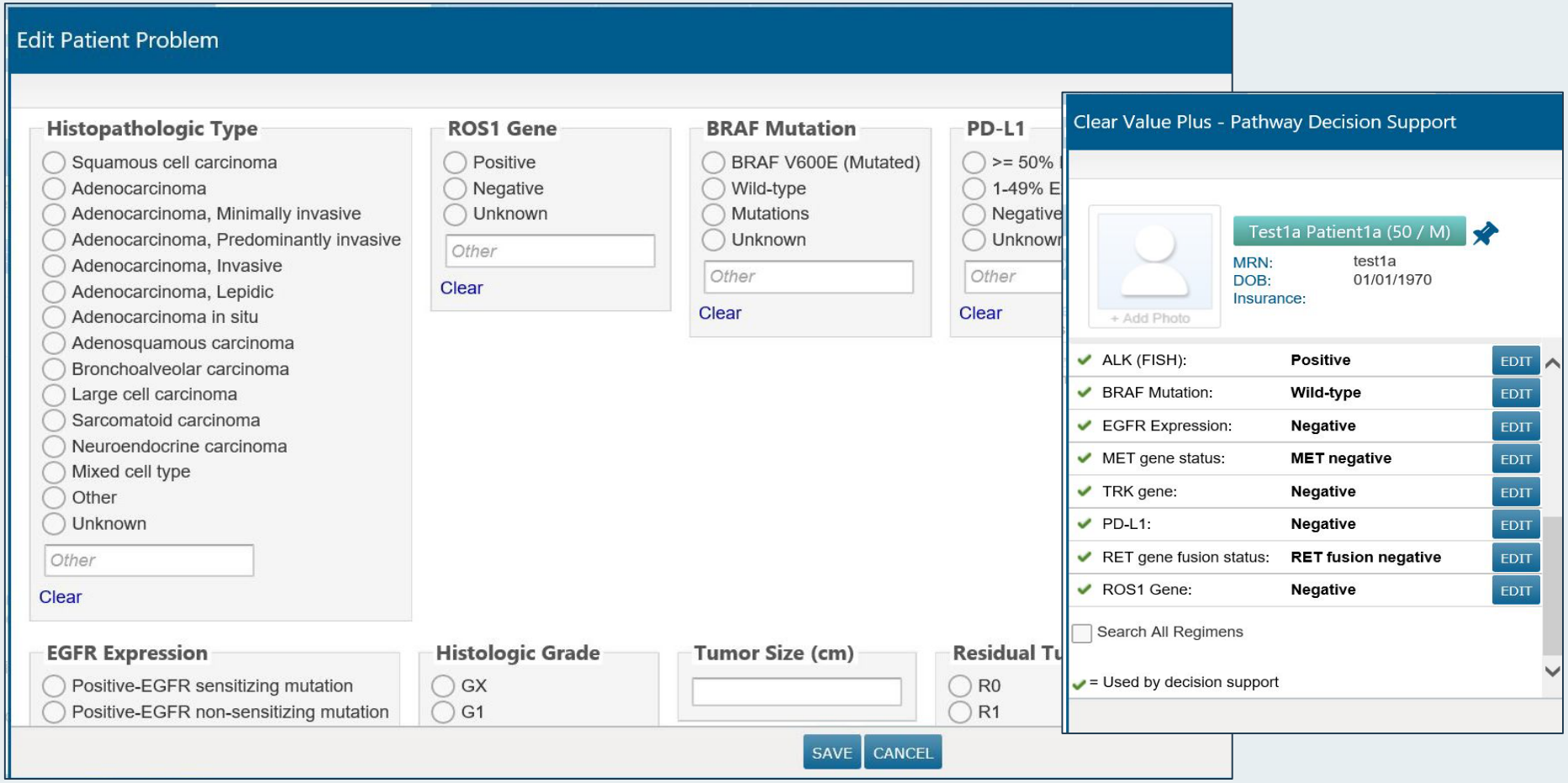
- Date of death
- Date of death

Structured EHR data	Unstructured EHR data	Claims data	**External data**

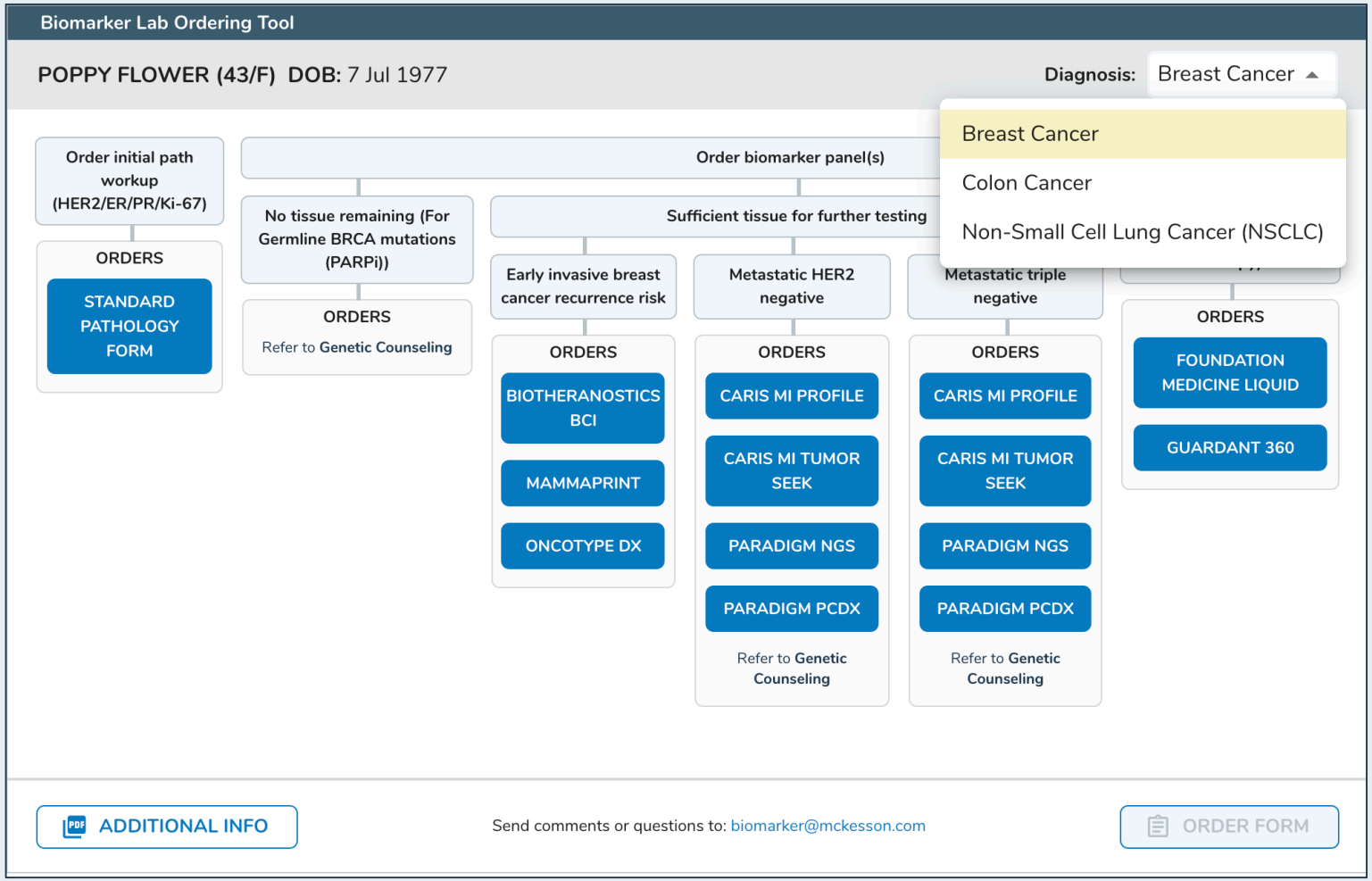
Our EHR supports providers in delivering the leading evidence-based care, while also capturing structured clinical data at the point-of-care



Our integrated clinical decision support tool helps providers to deliver on the promise of precision medicine

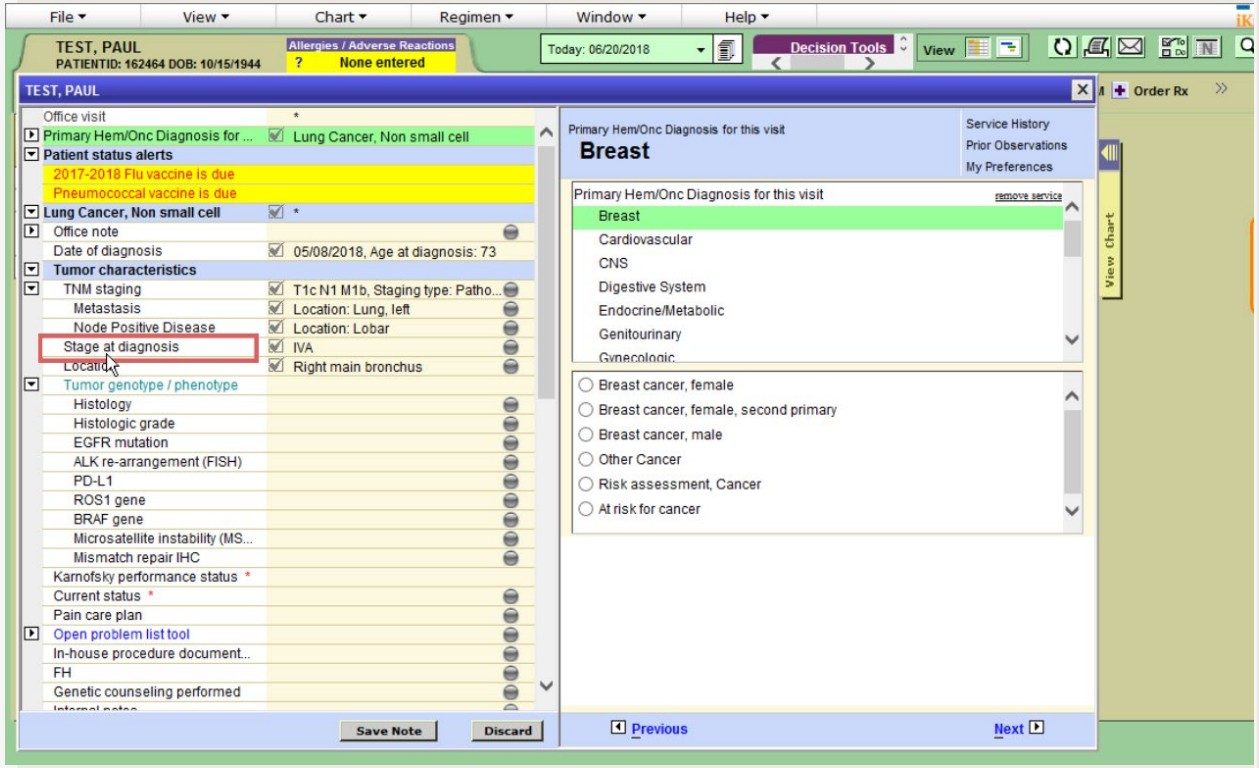


New enhancements make it even easier for providers to select and order the right testing, supporting our growing precision medicine data set

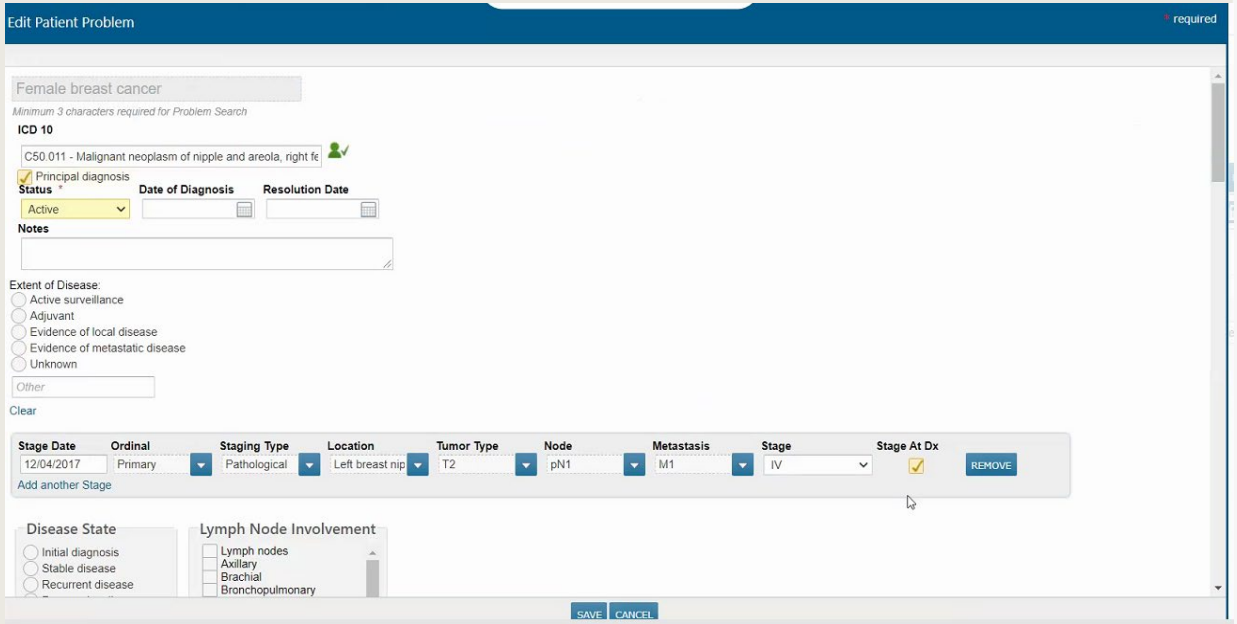


iKnowMed Data Points – Stage at Diagnosis

Stage at Diagnosis G1

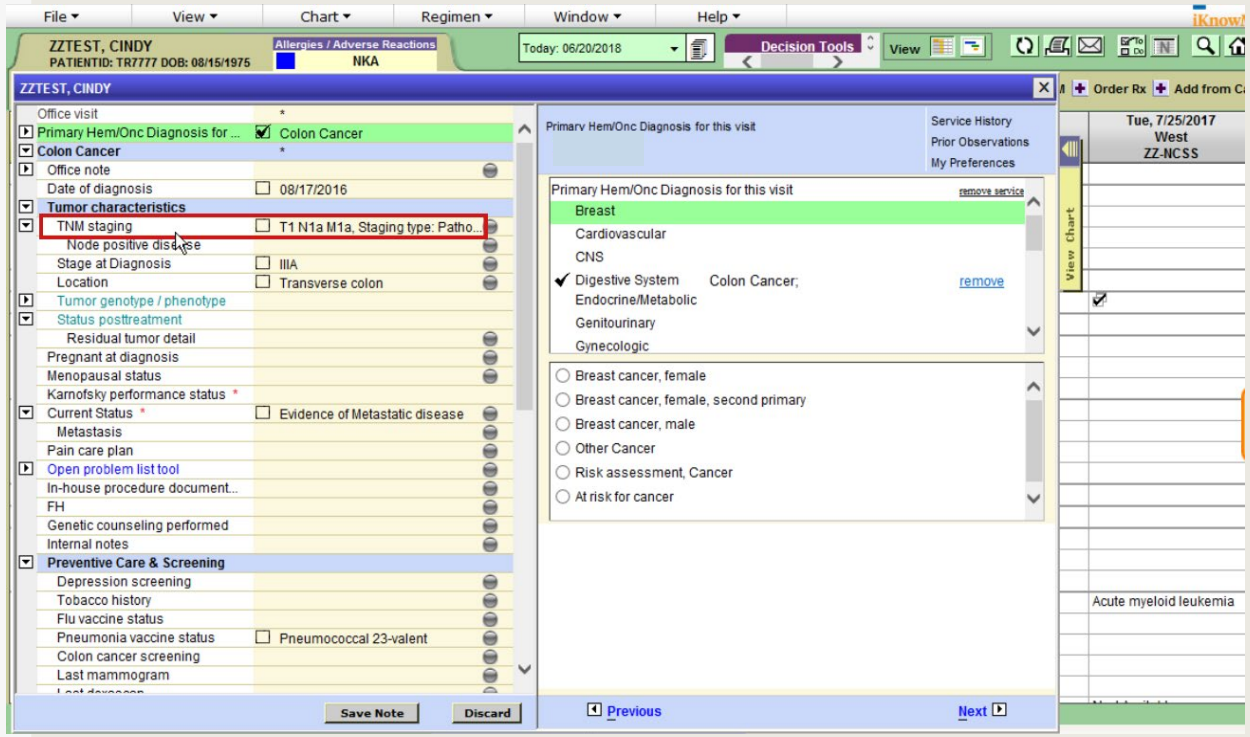


Stage at Diagnosis G2

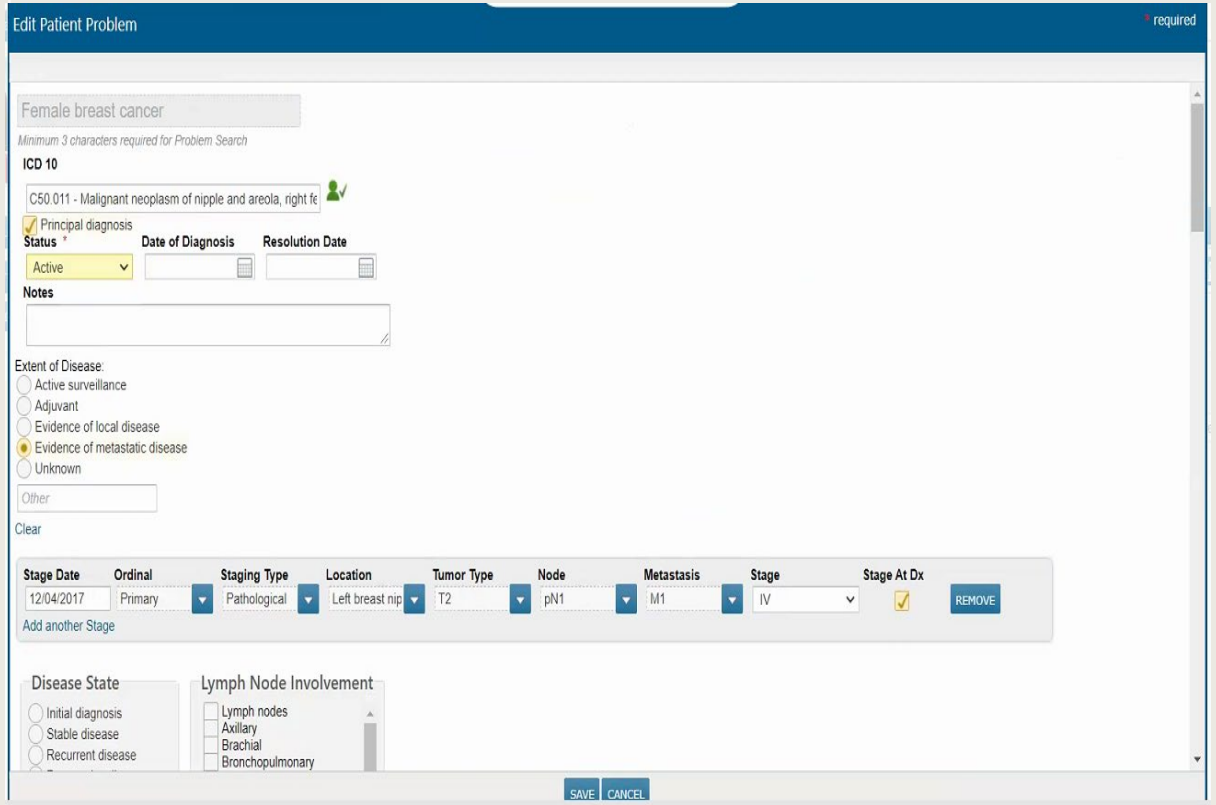


iKM Data Points- Disease Status

Current Disease Status G1

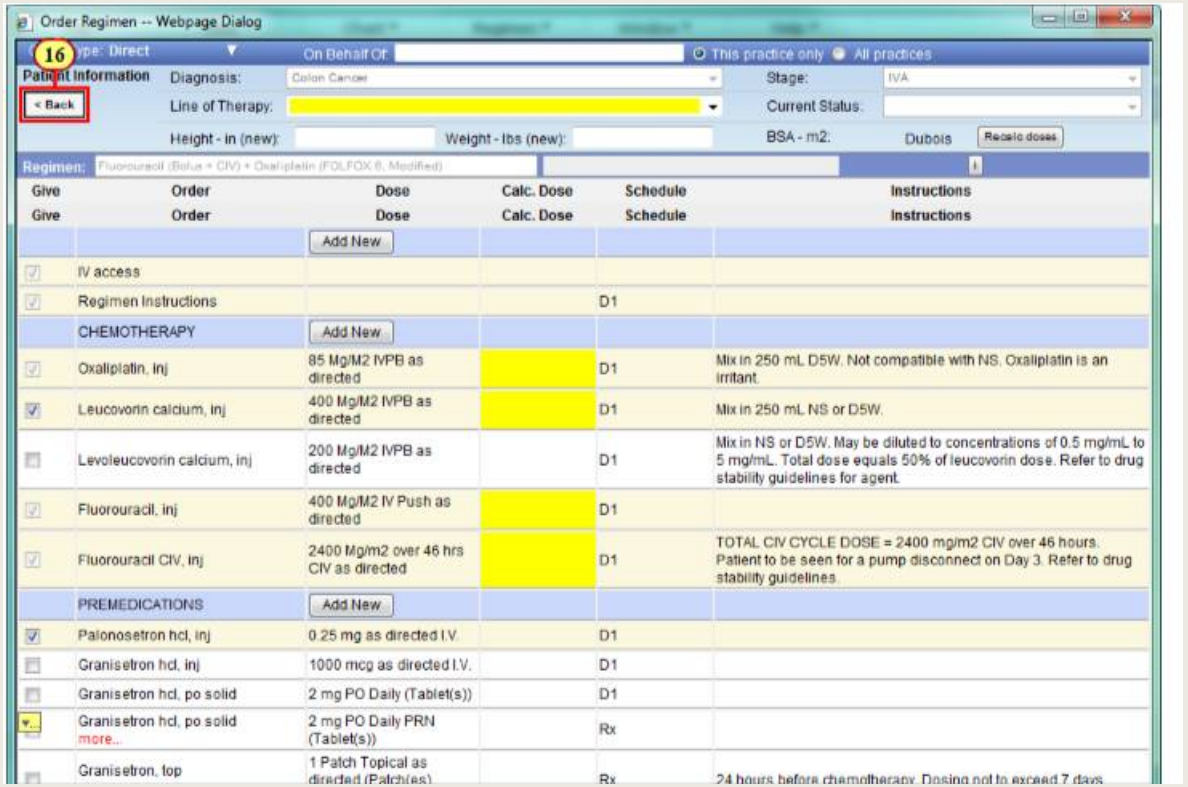


Current Disease Status G2

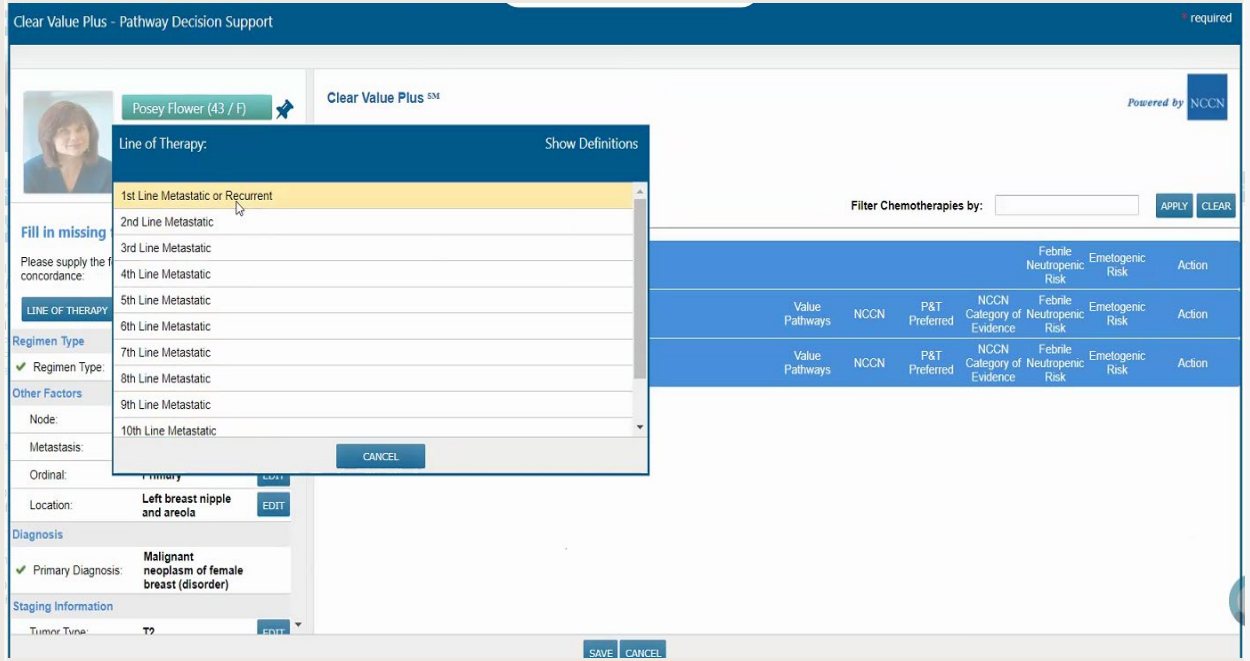


iKM Data Points – Line of Therapy

Line of Therapy G1



Line of Therapy G2



Challenges

- Date of death concordance
  - Presentation in March from Flatiron Health perfectly describes
  - We evaluated 102911 patients using structured data and a subset of 826 patients were using unstructured data[1].
    - Among patients with death dates reported by either structured data or DMF (n=36,941), 93.3% were captured by structured data, with DMF providing dates for an additional 6.7%.
    - Among patients with dates reported by both structured data and DMF (14.9%), concordance was 88.0%.
    - Among subset of patients with unstructured data (n=358), 99.4% of death dates were captured from structured and unstructured data, with DMF providing dates for an additional 0.6%. Death dates were reported by all three sources for 16.2% with concordance of 94.8%.
  - Work to do:
    - Loss to follow up
    - Condolence cards
    - Survivorship programs

Challenges

- Line of Therapy
  - Concordance of Clinical Vs. Algorithm Based Line of Therapy Determination in Lung Cancer[2]
    - 150 patients with SCLC, 148 initiated 1L by both structured and unstructured data (98.6% percentage-agreement); all reported the same regimen (100% percentage-agreement).
    - By algorithm and clinical inputs, 33 patients initiated 2L having identical regimens (kappa-statistic: 0.81, 95%CI: 0.69-0.92). There were 11 discordant patients for 2L: 1 and 10 patients by unstructured and structured data, respectively.
    - Of the 150 patients with NSCLC, 147 initiated 1L by both structured and unstructured data (98% percentage-agreement); 135/147 reported the same regimen (91.8% percentage-agreement).
    - By algorithm and clinical inputs, 29 patients initiated 2L having identical regimens (kappa-statistic: 0.56, 95%CI: 0.42-0.70). There were 27 discordant patients for 2L: 4 and 23 patients by unstructured and structured data, respectively.
  - Work to do:
    - Data source matters
    - Doctors are people too

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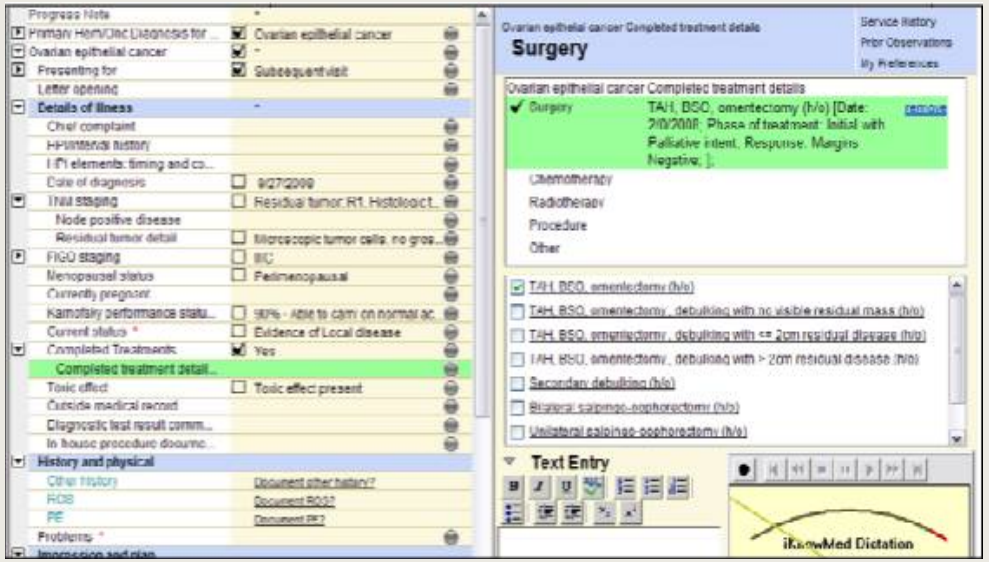
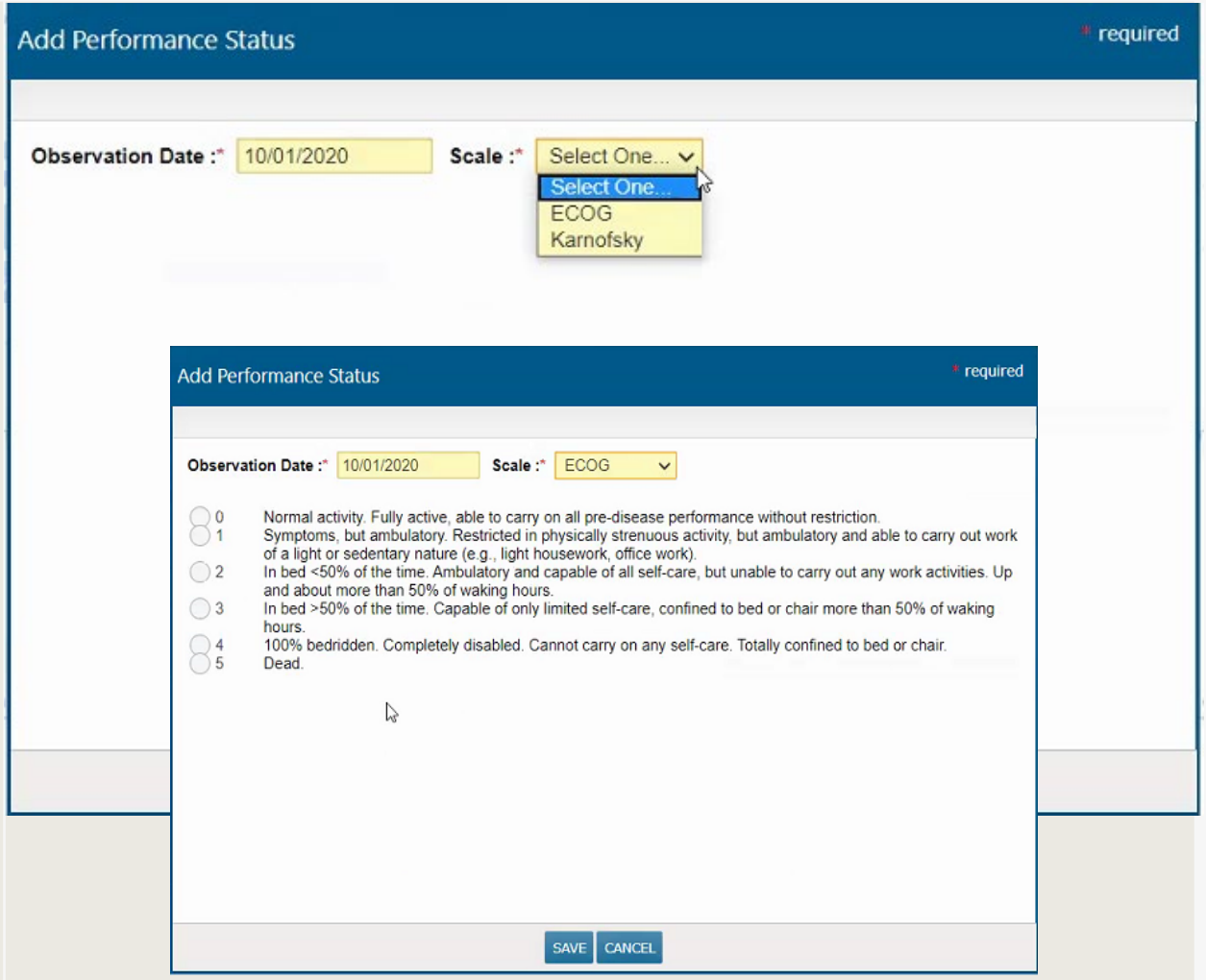
Contemporary Endpoints

iKM Data Points – Performance Status

Performance Status G1

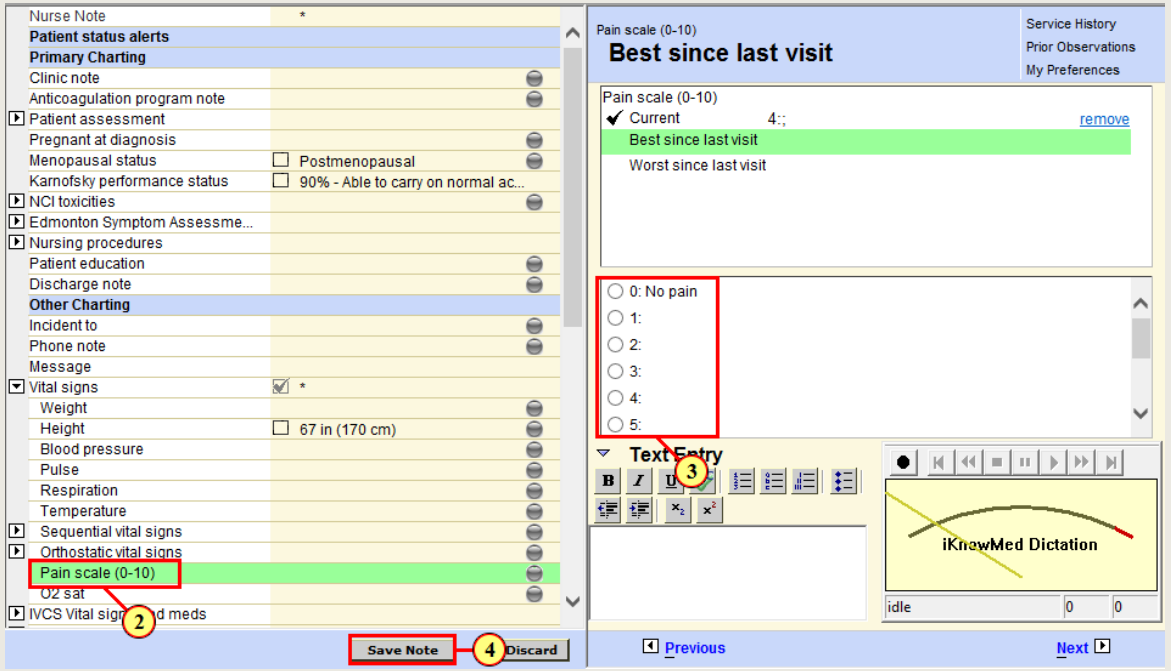


Performance Status G2

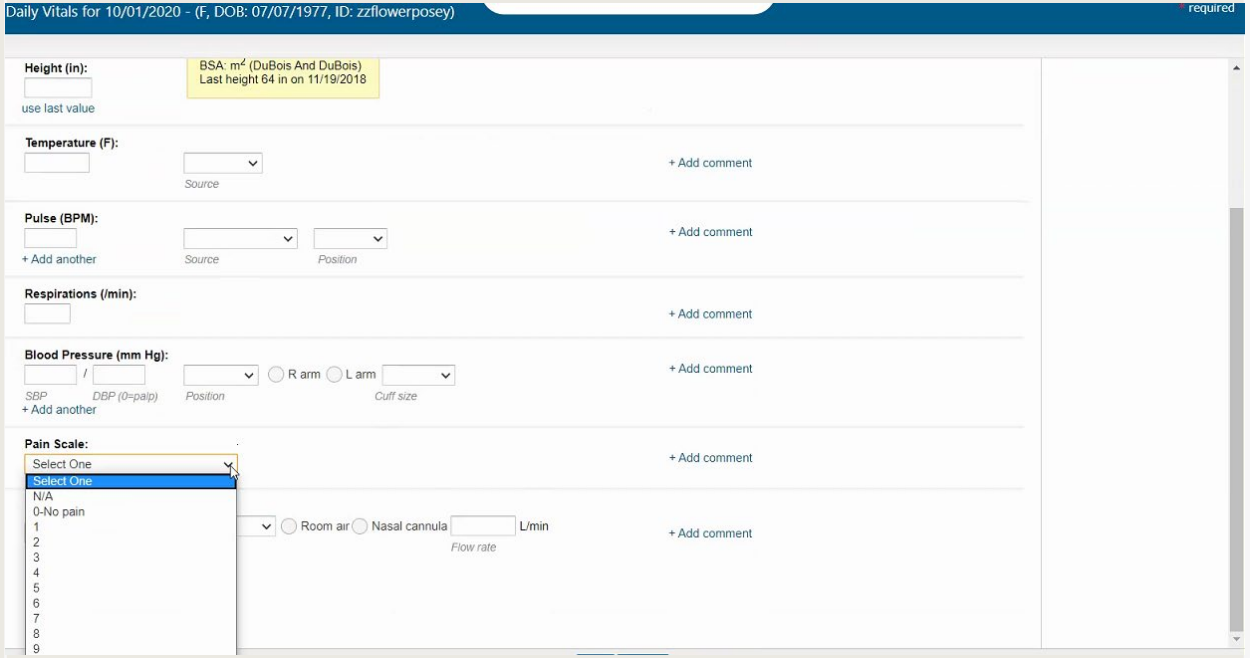


iKM Data Points - Pain

Pain G1

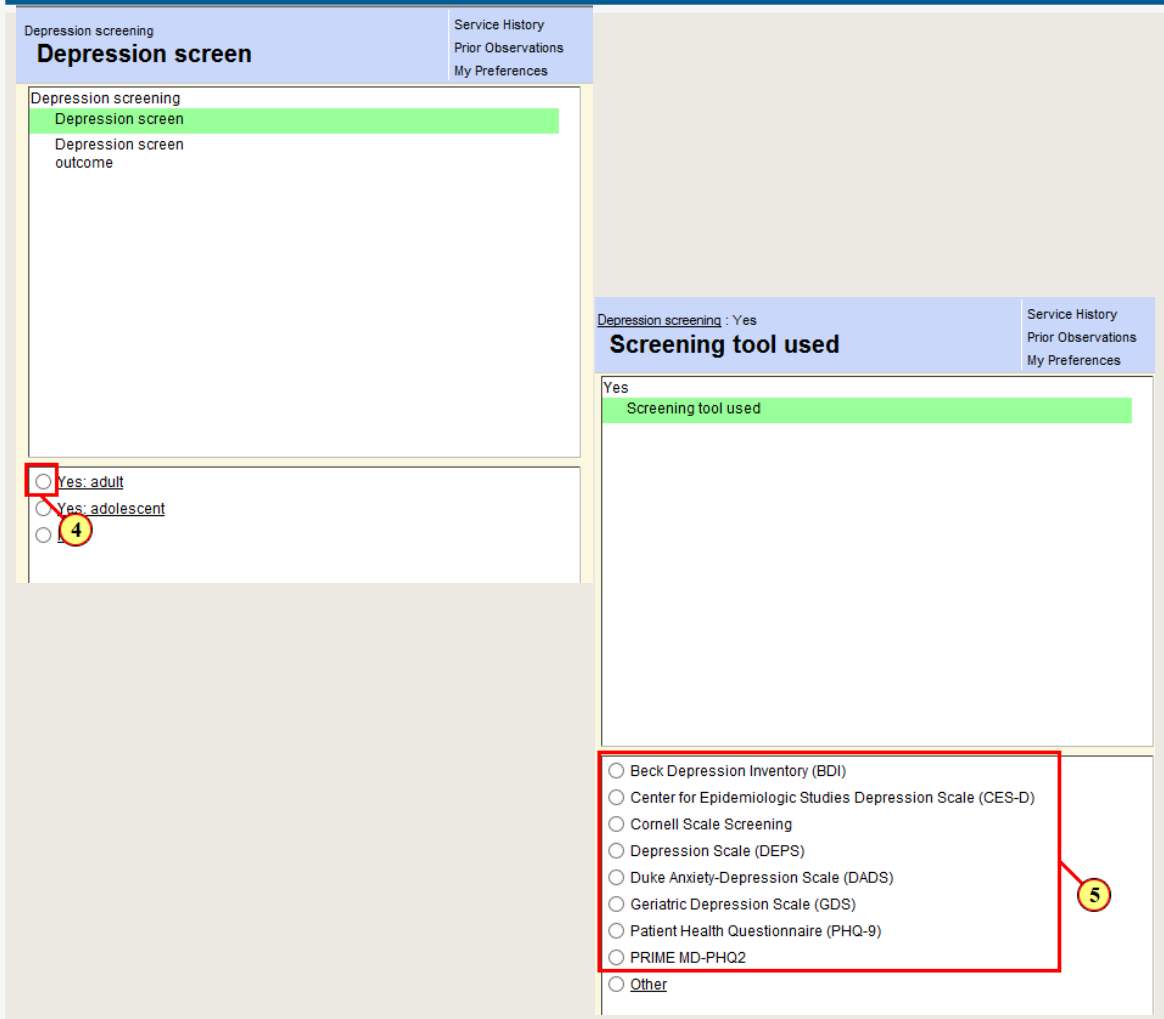


Pain G2

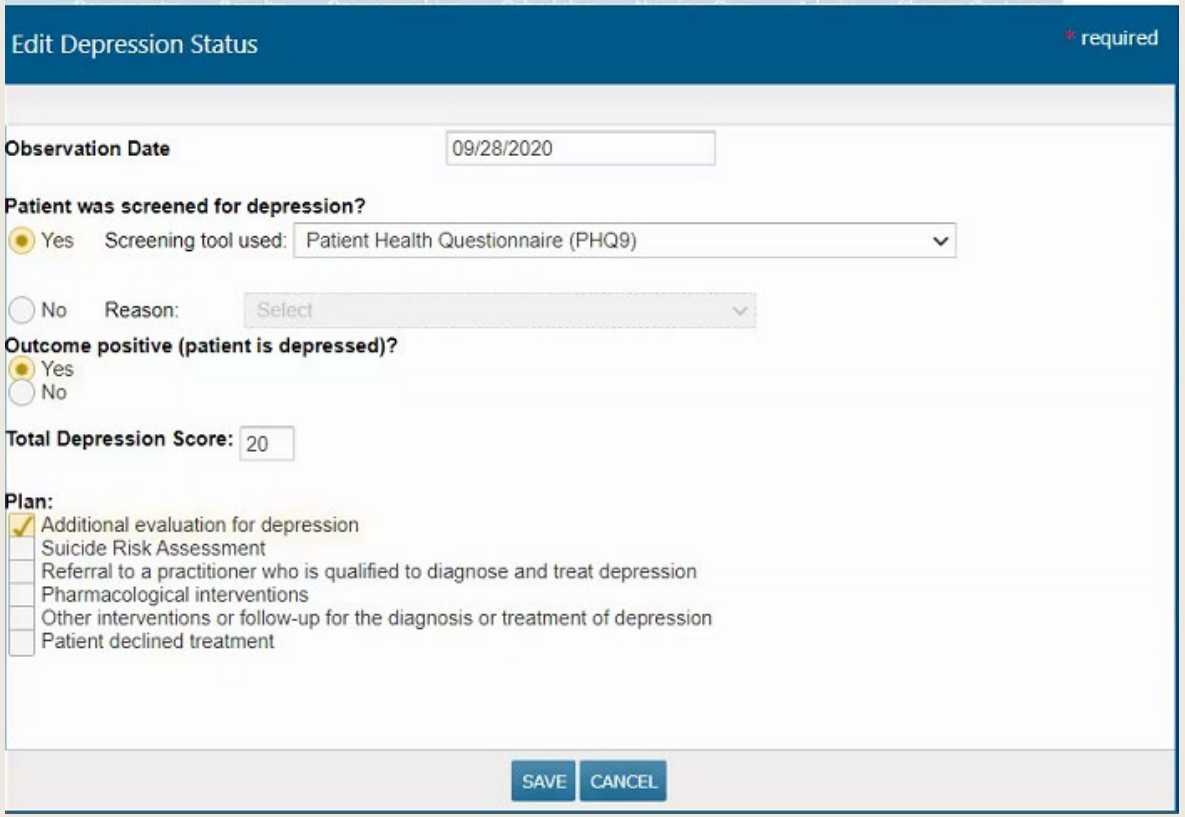


iKM Data Points - Depression

Depression G1

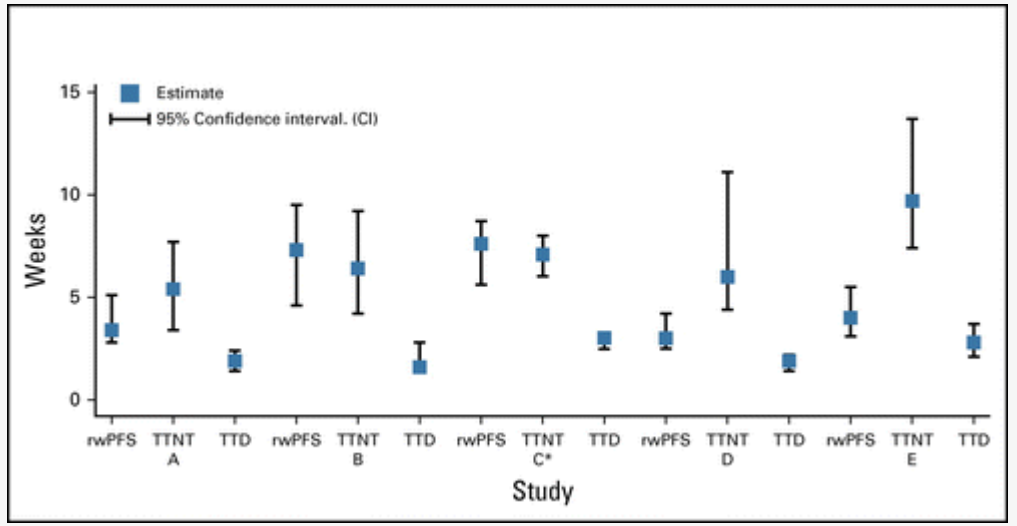


Depression G2



Challenges

- Progression
  - Comparisons of Real-World Time-to-Event End Points in Oncology Research[3-5]
    - Across all studies, median TTD durations were shorter than median rwPFS and TTNT durations, with 95% CIs overlapping just once among the measures.
    - The 95% CIs for TTNT and rwPFS overlapped for three of the five studies, but the 95% CIs for TTNT were greater than rwPFS in the remaining two studies.
    - When expressed as point estimate ratios between surrogate measures and rwPFS, TTD or rwPFS ranged from 0.22 to 0.70 while TTNT or rwPFS ranged from 0.88 to 2.43. Additionally, the available samples to analyze TTD and TTNT were larger than for rwPFS.
  - Work to do:
    - Data source matters
    - Doctors are people too, again
    - RECIST in practice is not practical



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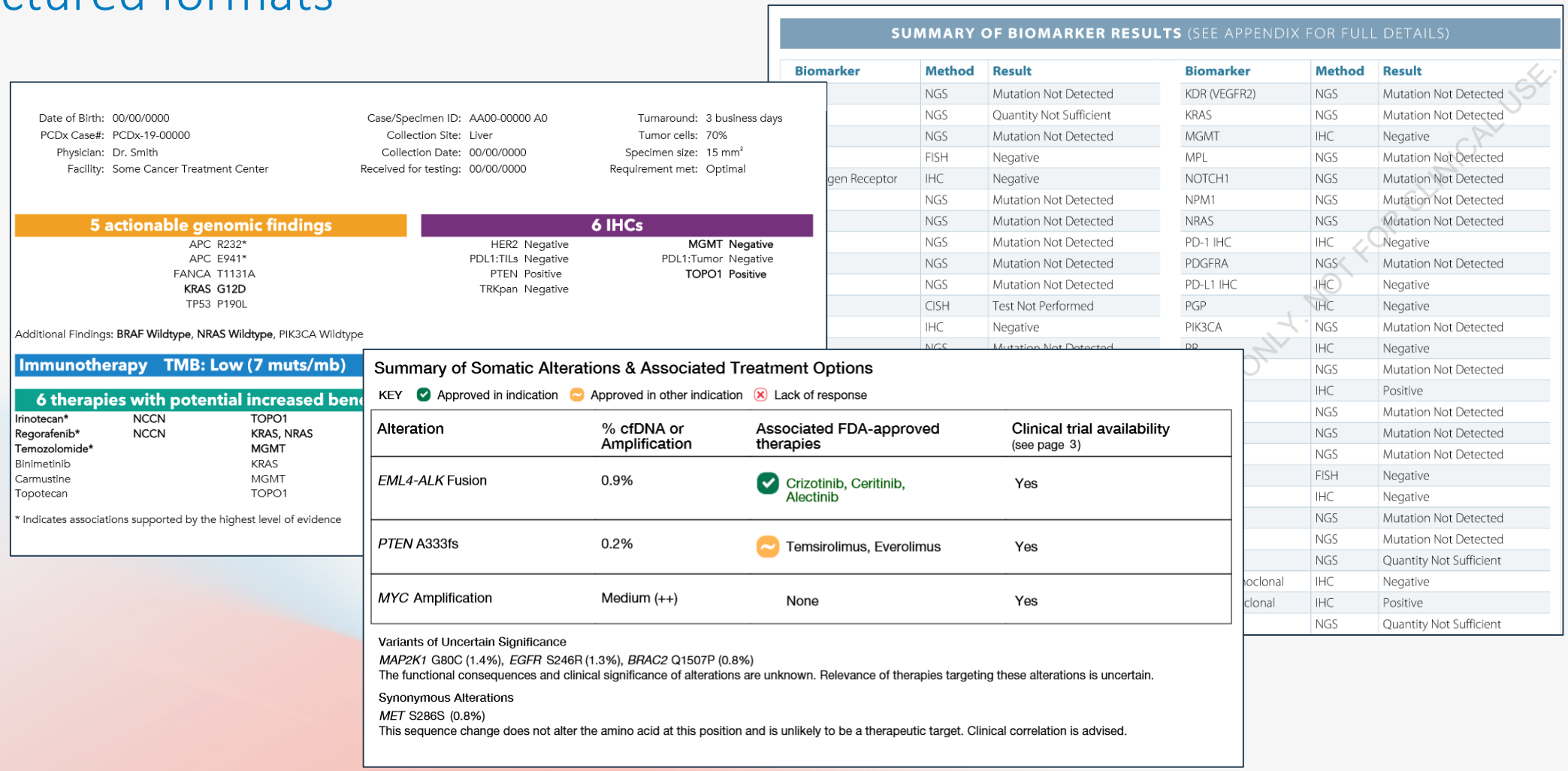
Future Endpoints

We have access to lab and genomic test results in both structured and unstructured formats



Date of Birth: 00/00/0000
PCDx Case#: PCDx-19-00000
Physician: Dr. Smith
Facility: Some Cancer Treatment Center

Case/Specimen ID: AA00-00000 A0
Collection Site: Liver
Collection Date: 00/00/0000
Received for testing: 00/00/0000

Turnaround: 3 business days
Tumor cells: 70%
Specimen size: 15 mm²
Requirement met: Optimal

5 actionable genomic findings

APC R232*
APC E941*
FANCA T1131A
KRAS G12D
TP53 P190L

6 IHCs

HER2 Negative
PDL1:TILs Negative
PTEN Positive
TRKpan Negative
MGMT Negative
PDL1:Tumor Negative
TOPO1 Positive

Additional Findings: **BRAF Wildtype**, **NRAS Wildtype**, PIK3CA Wildtype

Immunotherapy TMB: Low (7 muts/mb)

6 therapies with potential increased ben

Irinotecan*	NCCN	TOPO1
Regorafenib*	NCCN	KRAS, NRAS
Temozolomide*		MGMT
Binimetinib		KRAS
Carmustine		MGMT
Topotecan		TOPO1

* Indicates associations supported by the highest level of evidence

SUMMARY OF BIOMARKER RESULTS (SEE APPENDIX FOR FULL DETAILS)

Biomarker	Method	Result	Biomarker	Method	Result
	NGS	Mutation Not Detected	KDR (VEGFR2)	NGS	Mutation Not Detected
	NGS	Quantity Not Sufficient	KRAS	NGS	Mutation Not Detected
	NGS	Mutation Not Detected	MGMT	IHC	Negative
	FISH	Negative	MPL	NGS	Mutation Not Detected
gen Receptor	IHC	Negative	NOTCH1	NGS	Mutation Not Detected
	NGS	Mutation Not Detected	NPM1	NGS	Mutation Not Detected
	NGS	Mutation Not Detected	NRAS	NGS	Mutation Not Detected
	NGS	Mutation Not Detected	PD-1 IHC	IHC	Negative
	NGS	Mutation Not Detected	PDGFRA	NGS	Mutation Not Detected
	NGS	Mutation Not Detected	PD-L1 IHC	IHC	Negative
	CISH	Test Not Performed	PGP	IHC	Negative
	IHC	Negative	PIK3CA	NGS	Mutation Not Detected
				IHC	Negative
				NGS	Mutation Not Detected
				IHC	Positive
				NGS	Mutation Not Detected
				NGS	Mutation Not Detected
				NGS	Mutation Not Detected
				FISH	Negative
				IHC	Negative
				NGS	Mutation Not Detected
				NGS	Mutation Not Detected
				NGS	Quantity Not Sufficient
oclonal				IHC	Negative
clonal				IHC	Positive
				NGS	Quantity Not Sufficient

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Summary of Somatic Alterations & Associated Treatment Options

KEY ✓ Approved in indication ~ Approved in other indication ✗ Lack of response

Alteration	% cfDNA or Amplification	Associated FDA-approved therapies	Clinical trial availability (see page 3)
EML4-ALK Fusion	0.9%	✓ Crizotinib, Ceritinib, Alectinib	Yes
PTEN A333fs	0.2%	~ Temsirolimus, Everolimus	Yes
MYC Amplification	Medium (++)	None	Yes

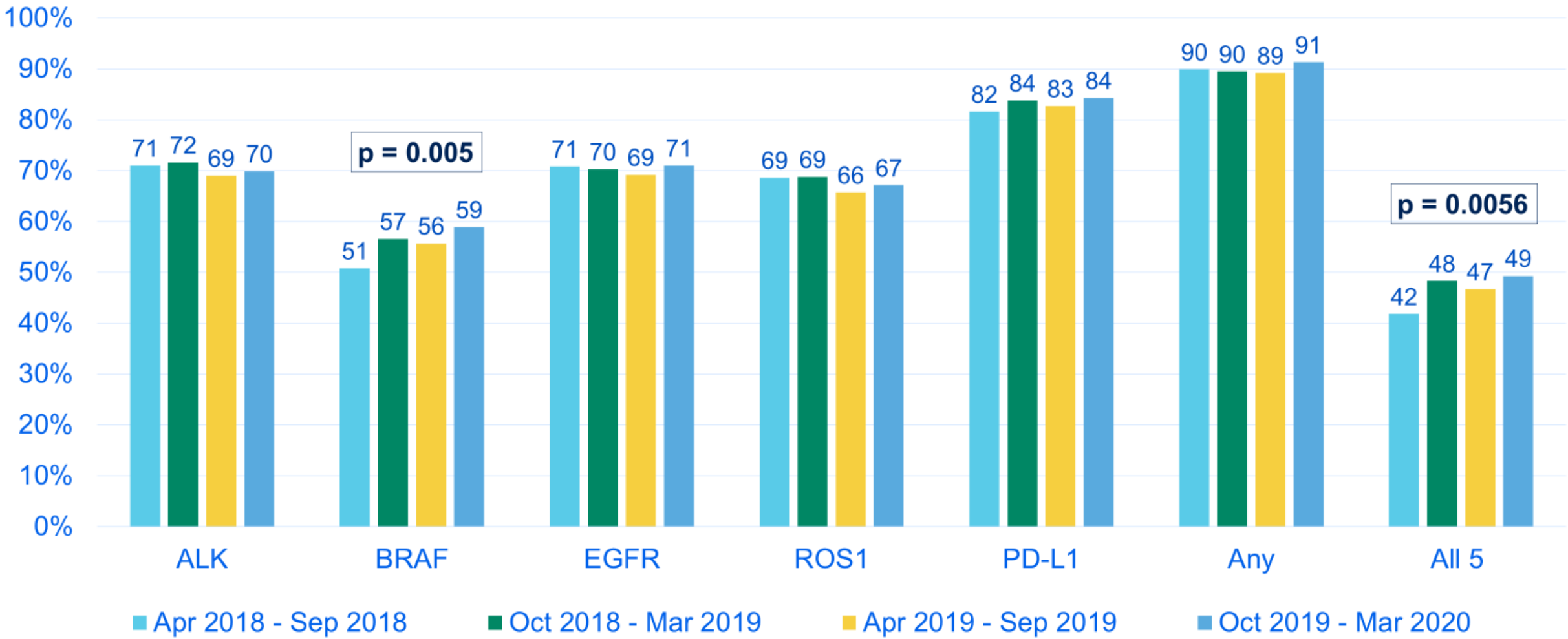
Variants of Uncertain Significance

MAP2K1 G80C (1.4%), *EGFR* S246R (1.3%), *BRAC2* Q1507P (0.8%)
The functional consequences and clinical significance of alterations are unknown. Relevance of therapies targeting these alterations is uncertain.

Synonymous Alterations

MET S286S (0.8%)
This sequence change does not alter the amino acid at this position and is unlikely to be a therapeutic target. Clinical correlation is advised.

Biomarker testing rates over time



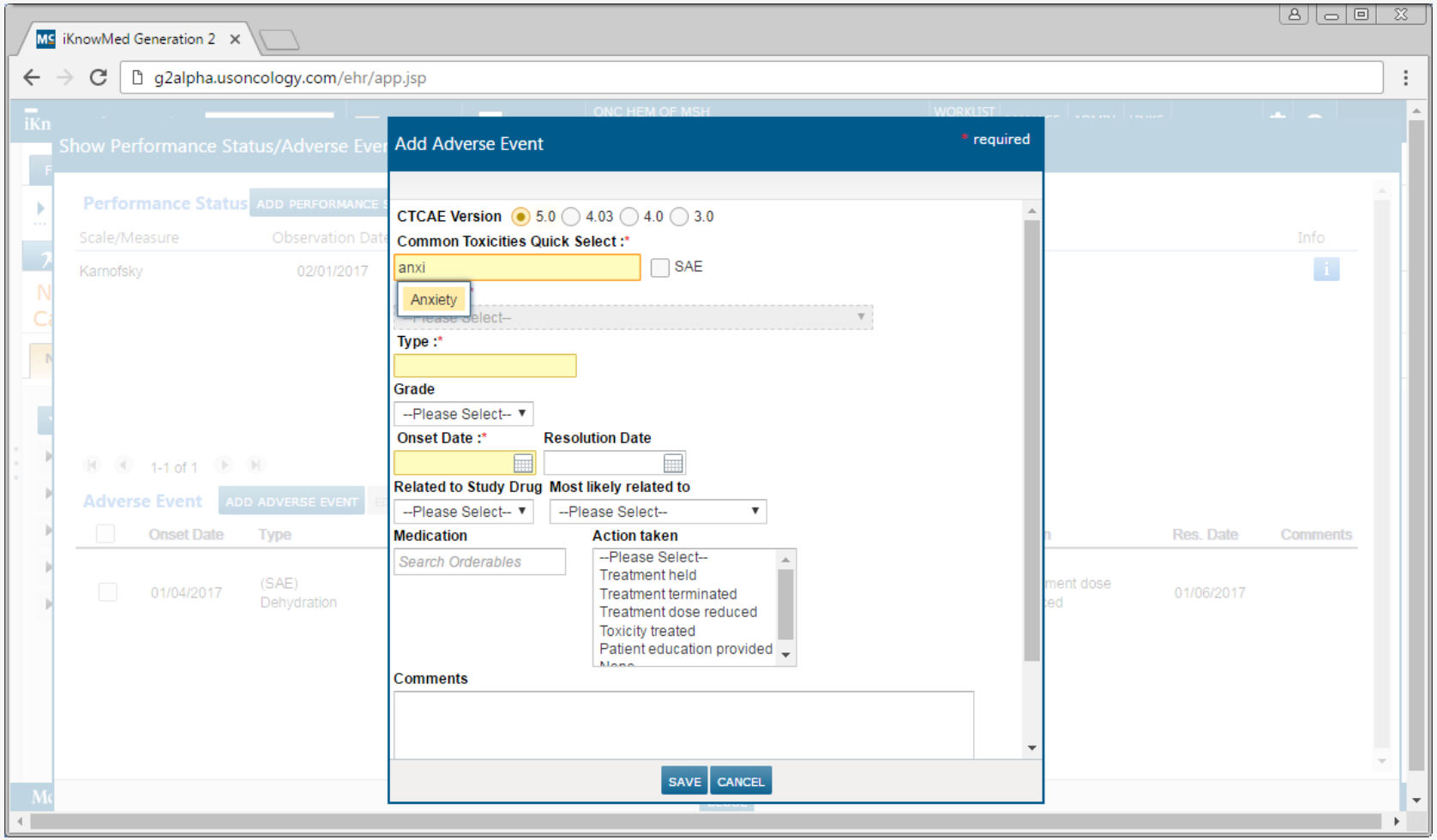
iKM Data Points – Genomic data

This real-world study showed that most patients received at least one biomarker test prior to 1L; however, <50% of patients received all 5 tests

- NGS testing increased over time, suggesting that comprehensive testing is increasing
- Median time from diagnosis to 1L therapy was about 5 weeks and turn around time from testing orders to results about 2 weeks.
- Results were similar for the overall study population and for patients with nonsquamous histology

Data from this phase will be compared to the next phase of the MYLUNG study, which will evaluate contemporary ordering practices and turnaround times prospectively.

iKM Data Points – Adverse Events



Measure what you treasure

You can't measure or analyze what was never collected

- People (doctors, patients, etc,) are responsible for the entry of these data

Do we need to rethink our most often used endpoints

- Patient-centric views
- What really matters

Broader industry adoption of methods and measurements

- Friends of Cancer
- ISPOR/ISPE

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Thoughts for Sentinel

A few more thoughts

Data collection in the hands of the patient

- Real time symptom monitoring
- New patient reported outcomes (even better if patterned after those collected in trials)

Training

- Adverse events aren't what they used to be
- I/O therapy
- Cell and gene therapy

Thank You!

References

1. Boyd M, Fulcher N, Annavarapu S. Concordance of death date assessments between the Social Security Death Master File and electronic health records in a US community oncology setting. International Society of Pharmacoeconomics and Outcomes Research Annual Meeting; May 16-20, 2020; virtual.
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6. Walker B, Frytak J, Hayes J, Neubauer M, Robert N, Wilfong L. Evaluation of practice patterns among oncologists participating in the Oncology Care Model. JAMA Netw Open 2020 May 1;3(5):e205165. doi: 10.1001/jamanetworkopen.2020.5165.
7. ERivera DR, Lasiter L, Christian J, Enewold L, Espirito JL, Hansen E, Henk HJ, Kushi LH, Lane D, Natanzon Y, Benito RP, Rasmusssen E, Robert NJ, Stewart M, Sweetnam C, Tymejczyk I, Valice E, Wagner J, Zander A, Allen J. Overall survival (OS) in advanced non-small cell lung cancer (aNSCLC) patients treated with frontline chemotherapy or immunotherapy by comorbidity: A real-world data (RWD) collaboration. American Society of Clinical Oncology 2020 Virtual Scientific Program; May 29-June 2, 2020.

Illustrative Example

NSCLC
EGFR-Positive