THE FUTURE OF CANCER DATA: UNLOCKING INSIGHTS WITH PATHOLOGY REPORTING

Unlocking the Value of Molecular Profiling: The Power of the Integrated Pathology

Matthew Oberley, MD, PhD

OCTOBER 6 | 3:45–4:15 PM CT

COLLEGE of AMERICAN PATHOLOGISTS
Laboratory Quality Solutions

CAP23 | CHICAGO

#PATHDATA

Unlocking the Value of Molecular Profiling:
The Power of the Integrated Pathology Report

Matthew Oberley, MD, PhD

October 6, 2023

Disclaimer

- Decisions on patient care and treatment must be based on the independent medical judgment of the treating physician, taking into consideration all available information concerning the patient's condition, the FDA prescribing information for any therapeutic, and in accordance with the applicable standard of care. Whether or not a particular patient will benefit from a selected therapy is based on many factors and can vary significantly.

- The materials may discuss uses and dosages for therapeutic products that may or may not have not been approved by the United States Food and Drug Administration. A qualified healthcare professional should be consulted before using any therapeutic product discussed.

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- Notable Disclosure(s)
  - Employed by Caris Life Sciences

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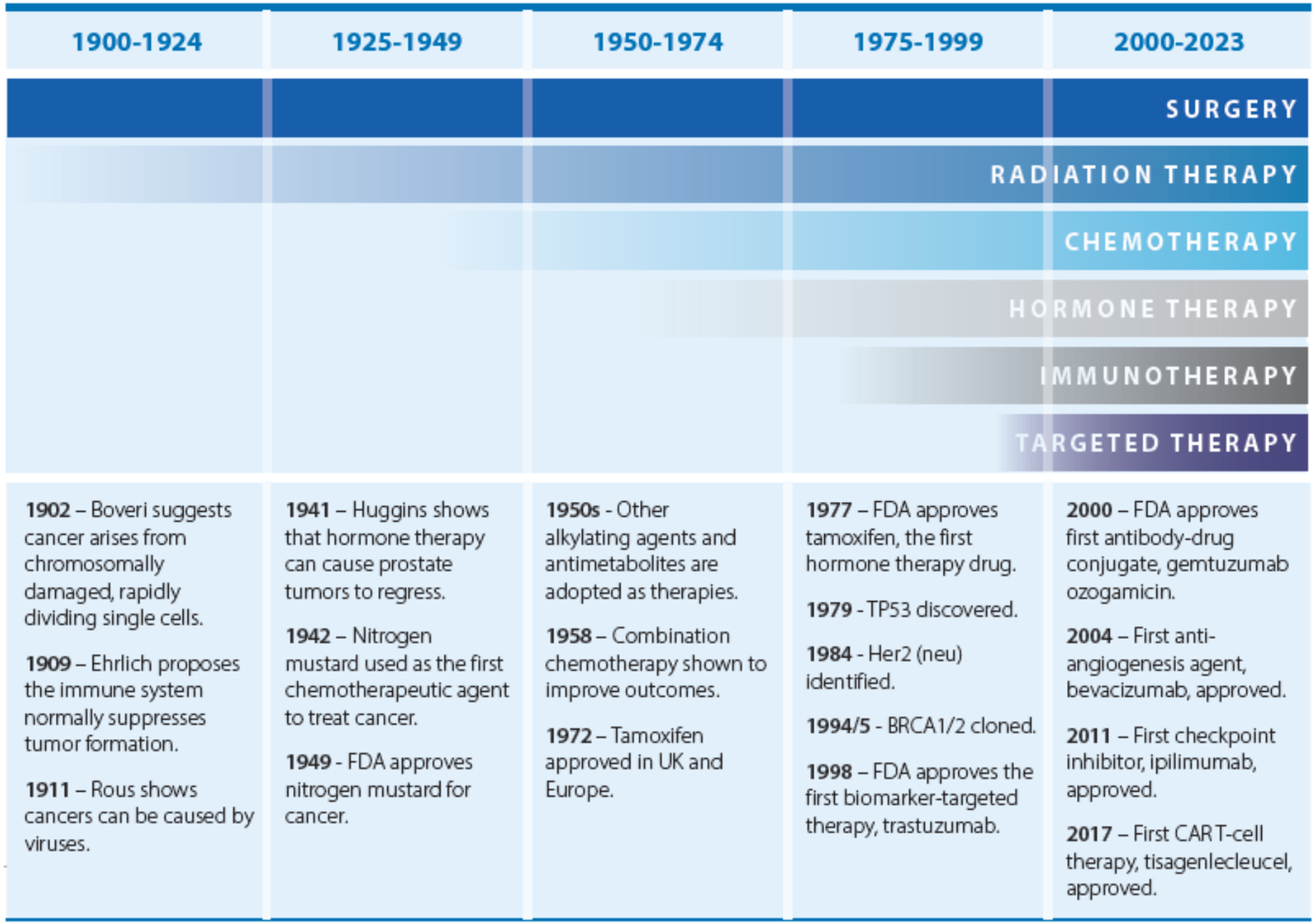
From Scalpels to Genomes

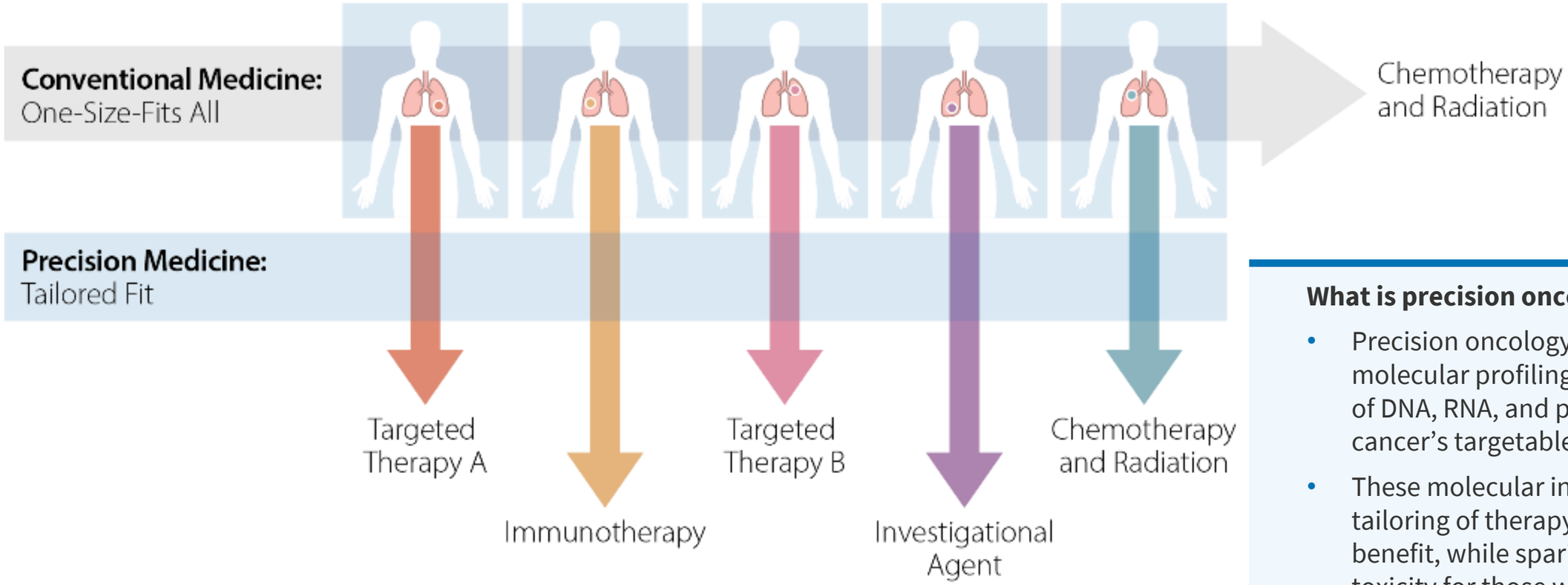
The Changing Landscape of Cancer Care

Oncology is Evolving at an Unprecedented Rate

Milestones in Cancer Therapy (1900–2023)



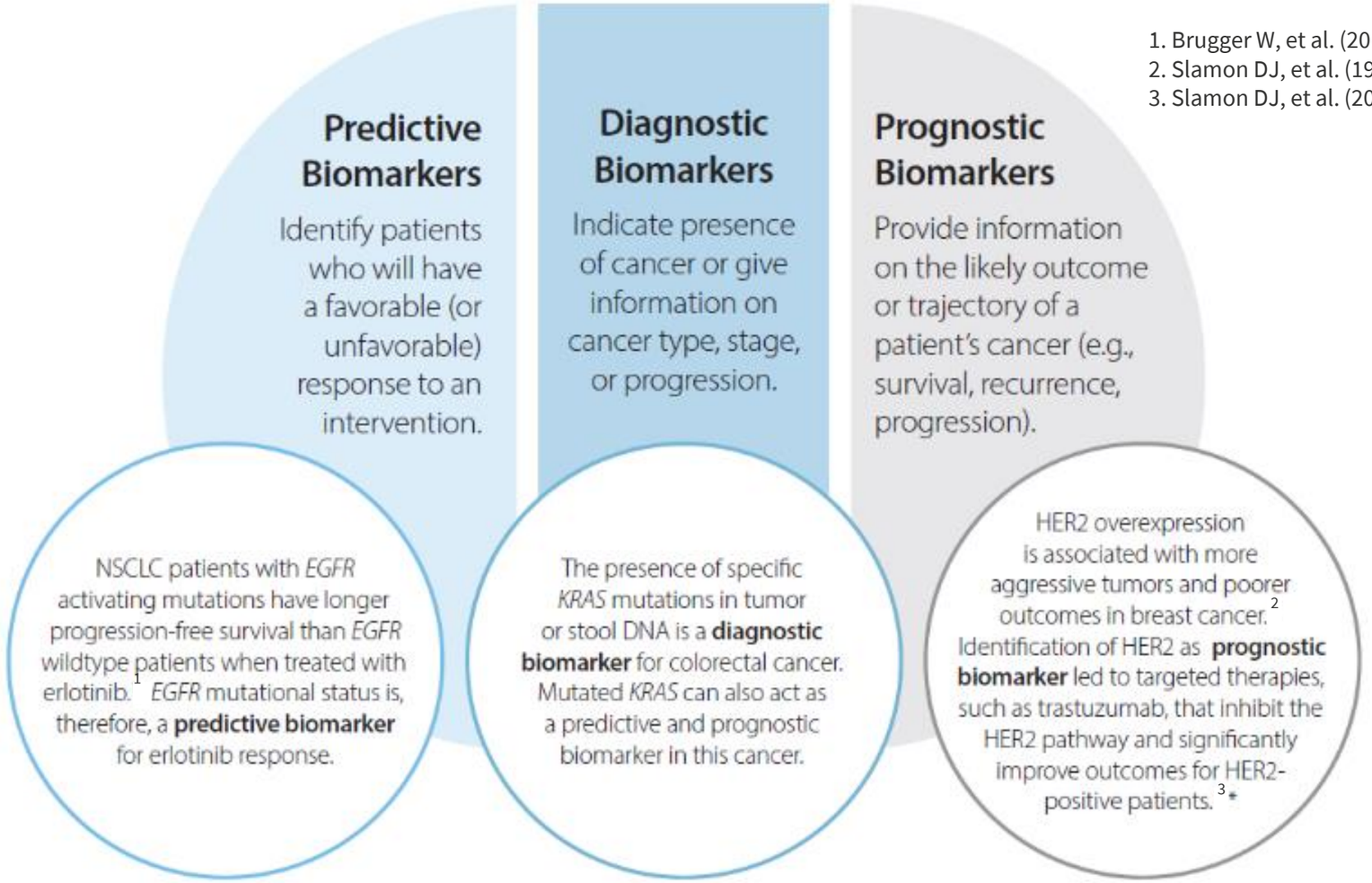
Precision Oncology Tailors Treatment to Each Patient



What is precision oncology?

- Precision oncology is the use of molecular profiling – including analysis of DNA, RNA, and protein – to identify a cancer's targetable alterations.
- These molecular insights enable the tailoring of therapy to patients likely to benefit, while sparing exposure and toxicity for those who will not.
- The goal of precision oncology is to deliver the right therapy to the right patient at the right dose and time.

Biomarkers Guide the Way to Targeted Therapies



*HER2 is also a predictive biomarker for trastuzumab response.

1. Brugger W, et al. (2011) *J Clin Oncol.*
2. Slamon DJ, et al. (1987) *Science*.
3. Slamon DJ, et al. (2001) *N Engl J Med*.

DIRECT BIOMARKER

A molecular **target** acted upon by the associated drug.

$KRAS^{G12C}$ is a biomarker and target for sotorasib (AMG 510) in non-small cell lung cancer (NSCLC).

INDIRECT BIOMARKER

A **phenotype** that is more likely to respond to the associated drug.

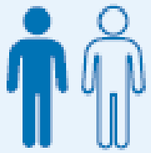
High tumor mutational burden (TMB) is a biomarker for response to immune checkpoint inhibitors.

PATHWAY BIOMARKER

A **component** of a pathway complementary to that of the target.

Mutations in homologous recombination DNA repair pathway genes, such as *BRCA1*, are biomarkers for response to PARP inhibitors.

Biomarker Testing and Matched Therapies Improve Outcomes



~1 in 2 cancer patients has a detectable actionable mutation.[1]

Patients who receive a biomarker-matched therapy have significantly better outcomes than those with non-matched treatments.[2]

28

biomarker-targeted drugs were approved by the FDA in 2020.[3]

9 in 10 new breast cancer drugs approved by the FDA in 2009-2018 were biomarker-targeted.[4]

Comprehensive genomic profiling reduces the likelihood of missing targeted therapy options compared to smaller tests.[5]

Broad profiling of multiple biomarkers is guideline-recommended standard of care in many cancers.[6]

1. Nono Djotsa A, et al. (2023) Journal of Clin Oncol.
2. Tsimberidou AM, et al. (2012) Clin Cancer Res.
3. Chakravarty D, et al. (2022) Journal of Clin Oncol.
4. Leo CP, et al. (2020) Nat Rev Drug Discov.
5. Paz-Ares L, et al. (2022) Lung Cancer.
6. Palmero R, et al. (2021) JCO Prec Oncol.

ASCO special articles

Somatic Genomic Testing in Patients With Metastatic or Advanced Cancer: ASCO Provisional Clinical Opinion

Debyani Chakravarty, PhD[1]; Amber Johnson, PhD[2]; Jeffrey Sklar, MD, PhD[3]; Neal I. Lindeman, MD[4]; Kathleen Moore, MD[5]; Shridar Ganesan, MD, PhD[6]; Christine M. Lovly, MD, PhD[7]; Jane Perlmutter, PhD[8]; Stacy W. Gray, MA, MD[9]; Jimmy Hwang, MD[10]; Christopher Lieu, MD[11]; Fabrice André, MD, PhD[12]; Nilofer Azad, MD[13]; Mitesh Borad, MD[14]; Laura Tafe, MD[15]; Hans Messersmith, MPH[16]; Mark Robson, MD[1]; and Funda Meric-Bernstam, MD[2]

"Patients with metastatic or advanced cancer should undergo genomic sequencing in a certified laboratory if the presence of one or more specific genomic alterations has regulatory approval as biomarkers to guide the use of or exclusion from certain treatments for their disease. Multigene panel–based assays should be used if more than one biomarker-linked therapy is approved for the patient's disease. Site-agnostic approvals for any cancer with a high tumor mutation burden, mismatch repair deficiency, or neurotrophic tyrosine receptor kinase (*NTRK*) fusions **provide a rationale for genomic testing for all solid tumors**."

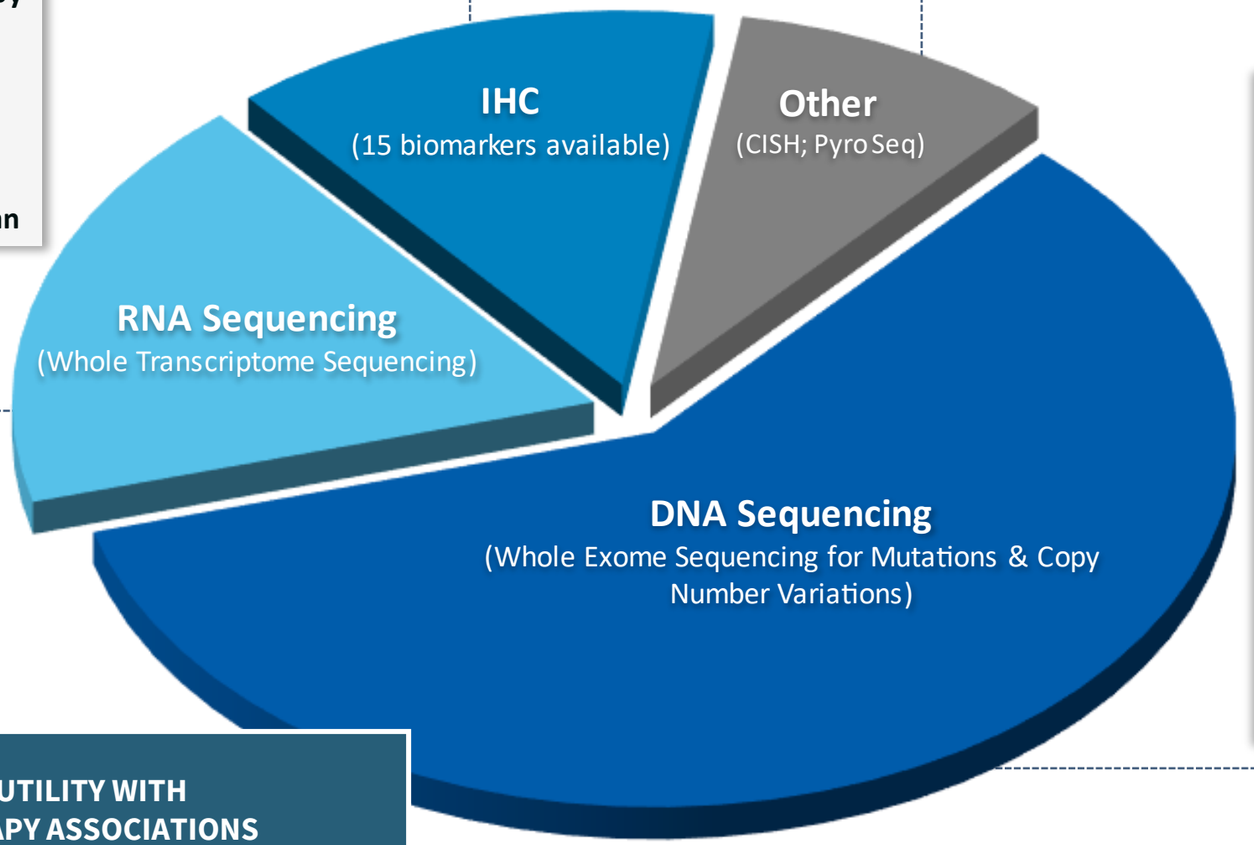
Chakravarty et al., *JCO*. (2022)
Available as open-access at: https://ascopubs.org/doi/full/10.1200/JCO.21.02767

CARIS LIFE SCIENCES

Comprehensive Molecular Profiling

Providing Value Across the Patient Journey

Adherence to Guidelines Requires a Multi-Technology Approach



alectinib
atezolizumab
bicalutamide
brigatinib
CDK4/6 inhibitors
ceritinib
crizotinib
endocrine therapy
entrectinib
enzalutamide
everolimus
HER2-targeted therapy
leuprolide
lorlatinib
nivolumab
ipilimumab
pembrolizumab
sacituzumab-govitecan

HER2-targeted therapy
sacituzumab-govitecan
temozolomide

alectinib
brigatinib
ceritinib
crizotinib
cabozantinib
capmatinib
entrectinib
erdafitinib
larotrectinib
lorlatinib
pemigatinib
pralsetinib
selpercatinib
tepotinib

afatinib
alpelisib
amivantamab
avapritinib
binimetinib
capmatinib
carboplatin
cetuximab
cisplatin
crizotinib
dabrafenib
cobimetinib
encorafenib
erlotinib
gefitinib
imatinib
ivosedinib
mobocertinib
niraparib
imatinib
olaparib
osimertinib
oxaliplatin
panitumumab
pembrolizumab
regorafenib
rucaparib
sotorasib
sunitinib
T-DM1
temozolomide
trametinib
vemurafenib

MAXIMIZING CLINICAL UTILITY WITH 100+ FDA-APPROVED THERAPY ASSOCIATIONS

For illustrative purposes. For a complete list of therapies assessed, please view the profile menu.

Comprehensive Molecular Profiling (CMP): The Most In-depth Insights into a Patient's Cancer

What Is CMP?

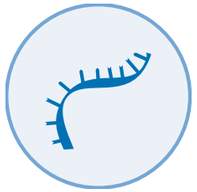
Comprehensive molecular profiling (CMP) analyzes DNA (by whole exome sequencing), RNA (by whole transcriptome sequencing), and protein (using immunohistochemistry) to generate the most in-depth picture of a patient's cancer.

- CMP is standard of care for advanced stage cancer to **predict** the most appropriate therapy.
- Molecular testing is also an integral part of the **diagnostic** workup of many cancer types.
- As molecular profiling becomes more comprehensive, there is increasing **overlap** between predictive and diagnostic testing.

Best-in-Class Profiling Reveals a More Comprehensive Molecular Blueprint

Analyzing DNA, RNA, and proteins to reveal a more complete molecular blueprint to guide precise and individualized treatment decisions.

Transcription & Gene Regulation



Translation

DNA

Whole Exome Sequencing

SNVs, Indels, CNAs, Karyotyping, Viruses

RNA

Whole Transcriptome Sequencing

Gene Fusions & Variant Transcripts

Protein

Immunohistochemistry

*Tumor-Relevant Protein Biomarkers**

Standard of Care + Clinical Trial Biomarkers

Immunotherapy	Targeted Therapy	Chemotherapy/Hormonal Therapies	Clinical Trials

Next-Generation Sequencing — DNA —

Illumina NovaSeq System

- ✓ 23,000+ full gene coverage (whole exome coverage)
- ✓ 1,500x for clinical genes
- ✓ SNVs, Indels, CNAs, Karyotyping*, Viruses*
- ✓ ~250,000 exonic/intronic/intergenic SNPs – gLOH, gene loss or amplification
- ✓ Genomic signatures: gLOH, HRD*, TMB and MSI
- ✓ HLA genotype*

Next-Generation Sequencing — RNA —

Illumina NovaSeq System

- ✓ 23,000+ full gene coverage (whole transcriptome coverage); 61,000 transcripts
- ✓ 17 million read count
- ✓ Gene fusions and variant transcripts
- ✓ Novel translocation detection independent of intronic breakpoint

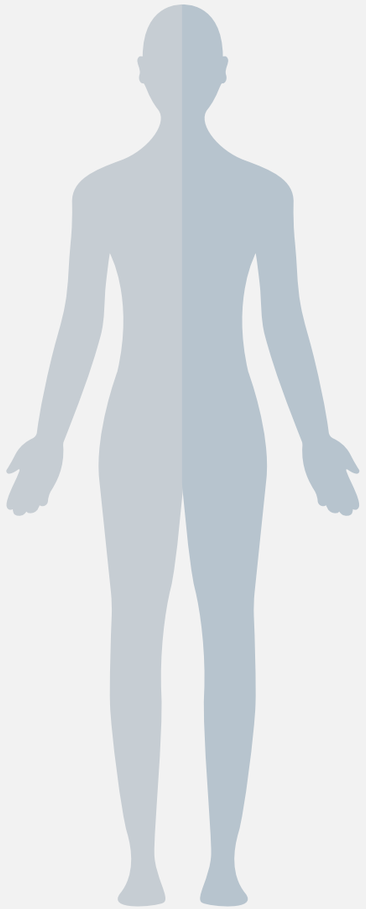
Immunohistochemistry — Protein —

Ventana & Dako IHC

- ✓ 15+ clinically relevant IHCs (optimized across 25 tumor types)
- ✓ Additional 50+ antibodies for RUO
- ✓ Multiple FDA approved CDx PD-L1 tests for different disease types (per label)
- ✓ Controls on every IHC
- ✓ 4 µm cuts to preserve tissue

*Certain tests or features are not available in all locations. See website for details.

The Power of DNA and RNA Across 23,000+ Genes, Proteins + AI



DNA — CARIS MI EXOME

RNA — CARIS MI TRANSCRIPTOME

Protein — 15+ IHCs

CARIS MOLECULAR AI — CARIS GPSai — CARIS FOLFIRSTai

CARIS TRIAL SOLUTIONS — Biomarker Driven Clinical Trials

Whole Exome and Whole Transcriptome, plus Proteins …

…and the first AI-driven set of proprietary molecular signatures

Caris Company Footprint

4 PRECISION MEDICINE FACILITIES
(Phoenix and Dallas) Totaling 360K+ Sq. Ft.

Blood / Solid Clinical Lab (Dallas, TX)
Clinical Tissue and Blood Lab
138K sq. ft.
(under construction)

Blood Lab (Phoenix, AZ)
Clinical Blood Lab
35K sq. ft.

Clinical Lab (Phoenix, AZ)
Clinical Tissue Lab
130K sq. ft.

R&D Lab (Phoenix, AZ)
Drug Target Discovery Lab
59K sq. ft.

FOOTPRINT OF 50 NOVASEQS

Over 1 trillion "reads" every day
Enhanced depth of coverage in **NGS DNA**

Pioneer in Molecular Science – Robust Data to Inform Precision Medicine

525,000+

Molecular Database

of Comprehensive Tumor Profiles

417,000+

Growing Database

With Matched Molecular Data and Clinical Outcomes

- Exploiting the power of deep molecular data to improve patient outcomes through machine learning
- Facilitating new product development

CARIS LIFE SCIENCES

Synoptic Reporting

Streamlining the Collection of Biomarker Data for Optimal Patient Care

Synoptic Reporting is Vital in Precision Oncology

What is synoptic reporting?

- Synoptic reporting is the systematic and structured recording of patient medical information.
- Instead of freeform text, synoptic reporting employs predefined templates or checklists with specific fields.
- The aim is to improve care by ensuring consistency, accuracy, and completeness in medical records.
- In oncology, synoptic reporting is used to standardize reporting of diagnoses, pathology, and surgeries.
- Synoptic reporting ensures each patient gets the appropriate workup, with all relevant data in one place.

Benefits of Synoptic Reporting

Pathologists Improves completeness, accuracy, and ease of creating reports.

Clinicians Makes data extraction from reports quicker and more accurate.

Researchers Enables creation of structured data sets to facilitate research.

CAP is at the Forefront of Structured Data Capture

- CAP develops cancer biomarker synoptic reports to capture structured data for inclusion in surgical pathology reports.
- There are currently >100 CAP Cancer Biopsy, Resection and Biomarker Protocols and electronic Cancer Protocols (eCP).

CAP Cancer Protocols are a resource developed by pathologists for pathologists to help deliver the synoptic information necessary for quality patient care and data aggregation.

Based on timely data from standard-setting organizations:

WHO Blue Books	AJCC (8th edition/9th version chapters)	FIGO	CAP/ASCO Center Guidelines

CAP Cancer Protocols

- Incorporate latest standards to help pathologists and labs keep up with reporting advances and updates.
- Provide guidelines for collecting essential data elements for complete reporting and optimal patient care.
- Allow directed flow of biomarker data from the reference testing lab in a concise, beneficial manner for the pathologist, oncologist, and patient.
- Offer explanatory notes, references, and case summaries with standard question and answer sets.

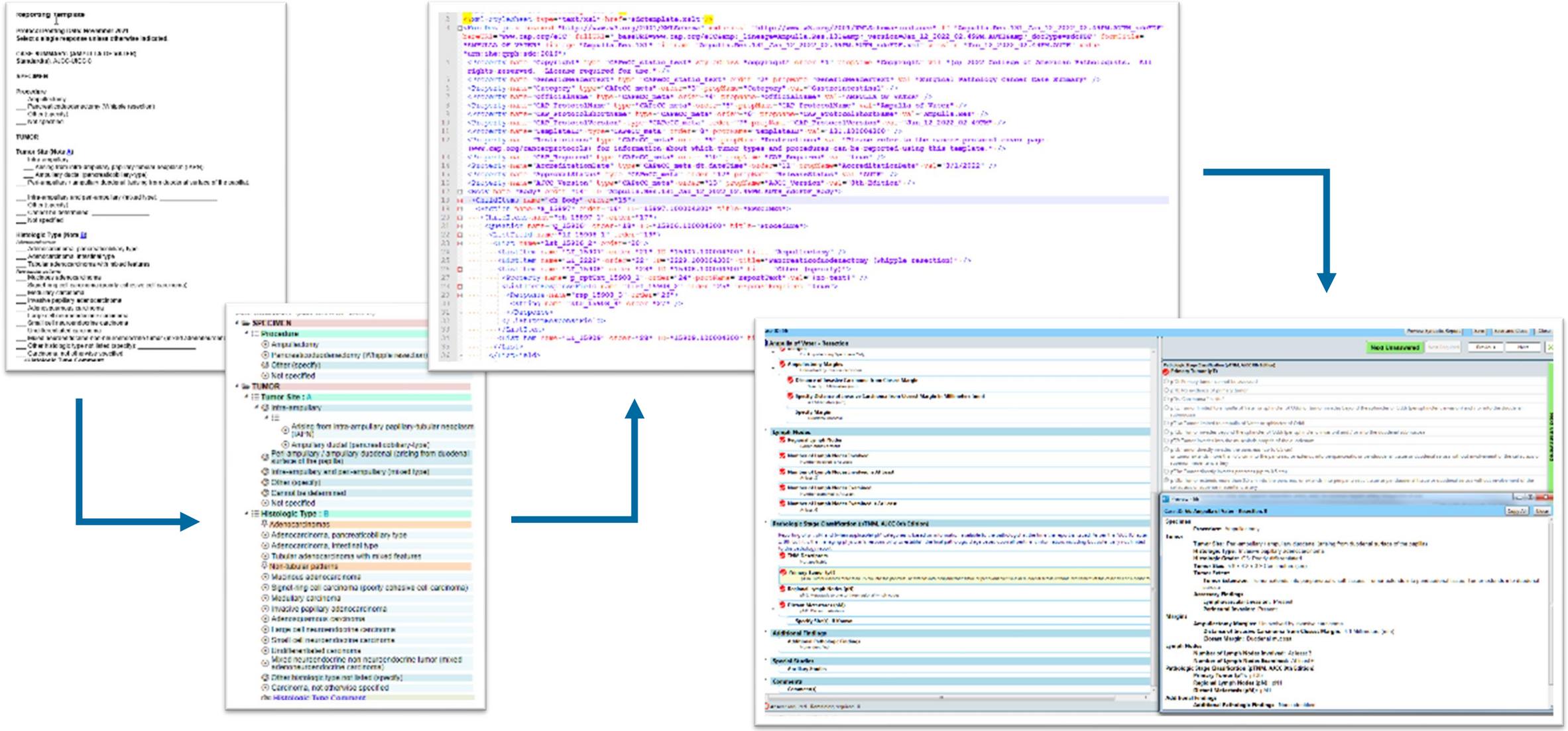
CAP Electronic Cancer Protocols (eCP)

- Provide core data elements mandated for accreditation by ACoS-CoC & CAP LAP.

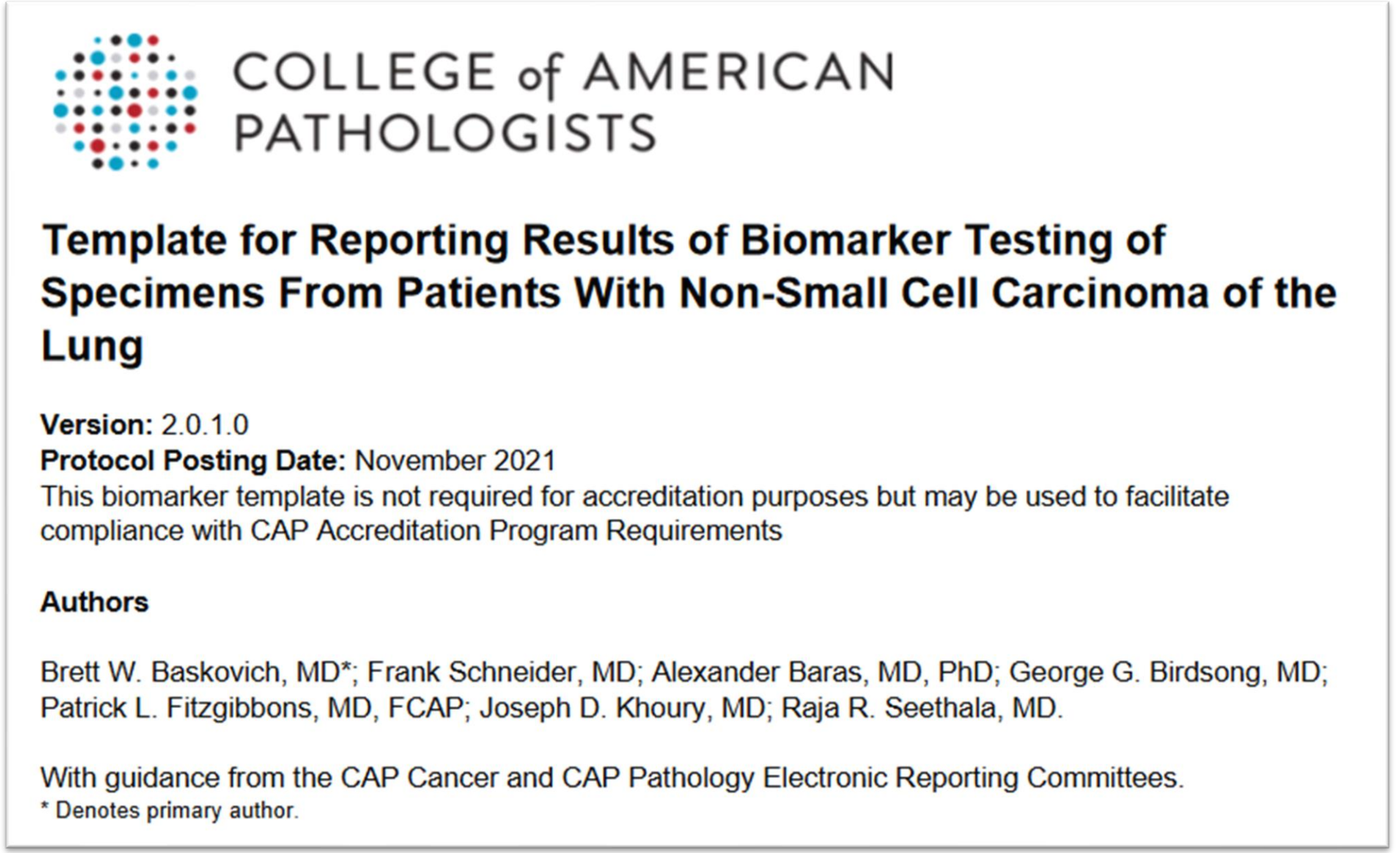
CAP Biomarker Reporting Protocols

- Currently cover 10 organ systems and 150+ biomarkers.
- Available in electronic and paper formats.

Process Overview: Paper Protocol to eCP



CAP Biomarker Templates Provide Guidance on Testing



COLLEGE of AMERICAN PATHOLOGISTS

Template for Reporting Results of Biomarker Testing of Specimens From Patients With Non-Small Cell Carcinoma of the Lung

Version: 2.0.1.0
Protocol Posting Date: November 2021
This biomarker template is not required for accreditation purposes but may be used to facilitate compliance with CAP Accreditation Program Requirements

Authors

Brett W. Baskovich, MD*; Frank Schneider, MD; Alexander Baras, MD, PhD; George G. Birdsong, MD; Patrick L. Fitzgibbons, MD, FCAP; Joseph D. Khoury, MD; Raja R. Seethala, MD.

With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.
* Denotes primary author.

CAP Biomarker Reporting Template: Lung

CAP
Approved

Lung.Bmk_2.0.1.0.REL_CAPCP

Reporting Template

Protocol Posting Date: November 2021
Select a single response unless otherwise indicated.

CASE SUMMARY: (Lung Biomarker Reporting Template)

Completion of the template is the responsibility of the laboratory performing the biomarker testing and / or providing the interpretation. When both testing and interpretation are performed elsewhere (e.g., a reference laboratory), synoptic reporting of the results by the laboratory submitting the tissue for testing is also encouraged to ensure that all information is included in the patient's medical record and thus readily available to the treating clinical team.
Gene names should follow recommendations of The Human Genome Organisation (HUGO) Nomenclature Committee (www.genenames.org; accessed February 10, 2015).
All reported gene sequence variations should be identified following the recommendations of the Human Genome Variation Society (www.hgvs.org/mutnomen/; accessed February 10, 2015).

SPECIMEN

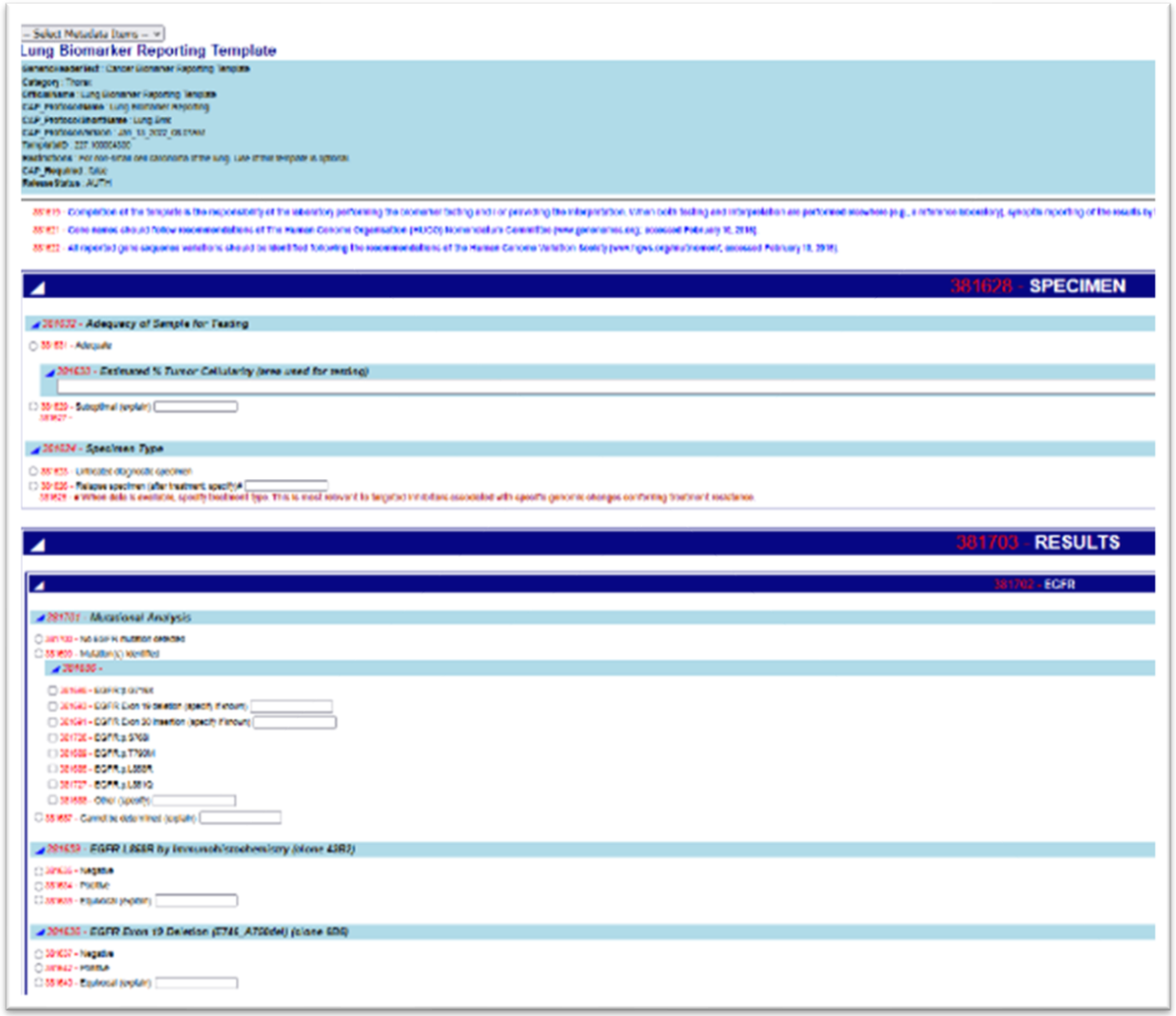
+Adequacy of Sample for Testing
___ Adequate
+Estimated % Tumor Cellularity (area used for testing): _____ %
___ Suboptimal (explain): _____

+Specimen Type
___ Untreated diagnostic specimen
___ Relapse specimen (after treatment; specify)#: _____
 # When data is available, specify treatment type. This is most relevant to targeted inhibitors associated with specific genomic changes conferring treatment resistance.

RESULTS
EGFR
+Mutational Analysis
___ No EGFR mutation detected
___ Mutation(s) identified
___ EGFR:p.G719X
___ EGFR Exon 19 deletion (specify if known): _____
___ EGFR Exon 20 insertion (specify if known): _____
___ EGFR:p.S768I
___ EGFR:p.T790M
___ EGFR:p.L858R
___ EGFR:p.L861Q
___ Other (specify): _____
___ Cannot be determined (explain): _____

+EGFR L858R by Immunohistochemistry (clone 43B2)
___ Negative
___ Positive
___ Equivocal (explain): _____

+EGFR Exon 19 Deletion (E746_A750del) (clone 6B6)
___ Negative
___ Positive



Where Does Biomarker Testing Data Come From?

Most cancer biomarker testing is carried out at **third party reference laboratories.**

Results are typically provided to the clinical laboratory in **PDF format.**

PDF reports require **further manipulation** to get data into a synoptic report for pathologist sign-off and oncologist use.

These manipulations are **usually manual**, and thus unscalable, error-prone, and time-consuming, plus often not remunerated.

Auto-population would help reduce the need for direct data entry and opportunities for errors.

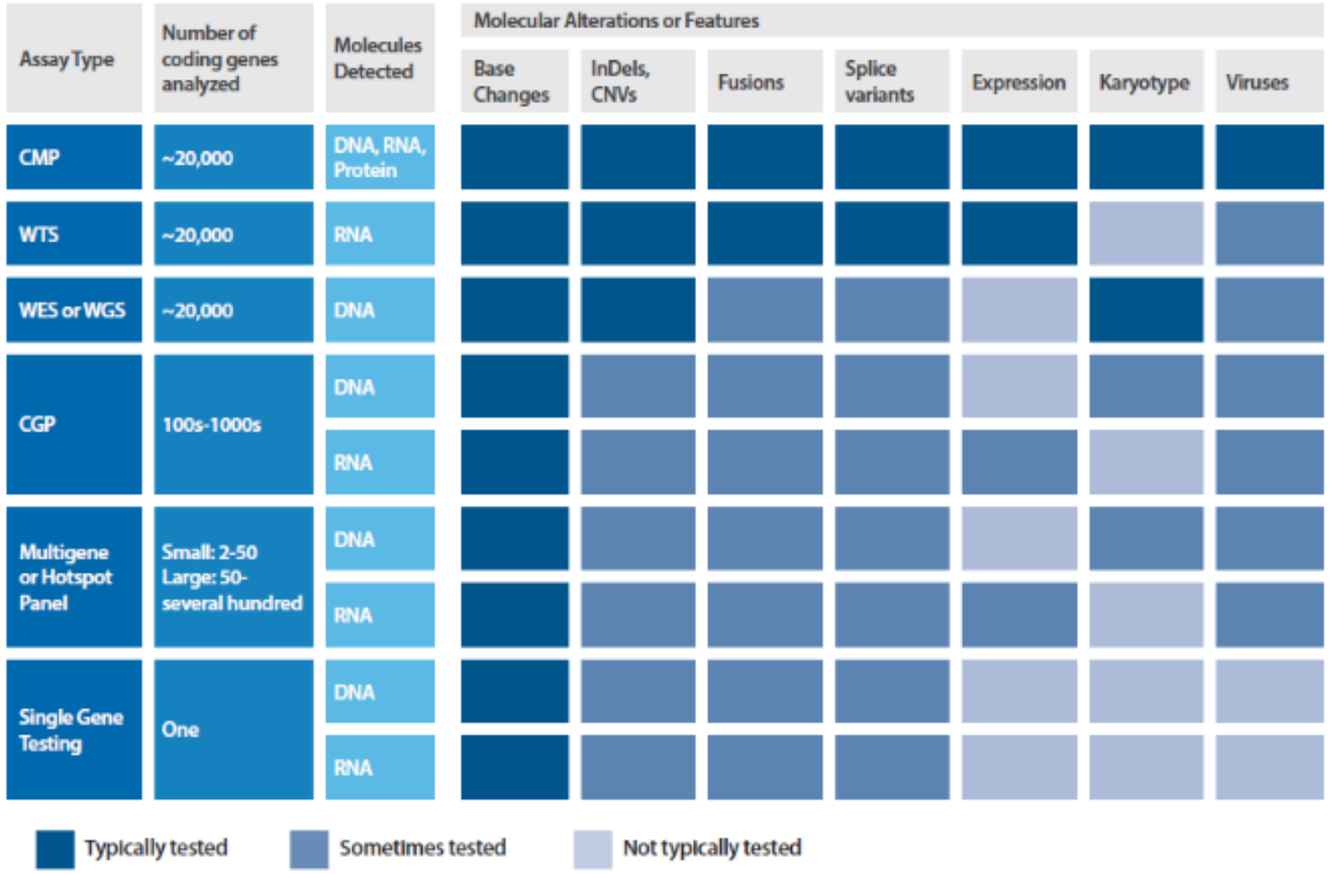
Biomarker Testing is Growing Rapidly

Dramatic recent increases in:

- **Utilization** of biomarker testing.
- **Comprehensiveness** of profiling.
- **Overlap** between diagnostic and predictive biomarker profiling.

Potential to help pathologists **gather all relevant data to inform patient care.**

However, to take full advantage there must be **more efficient transfer** of biomarker data into reports.

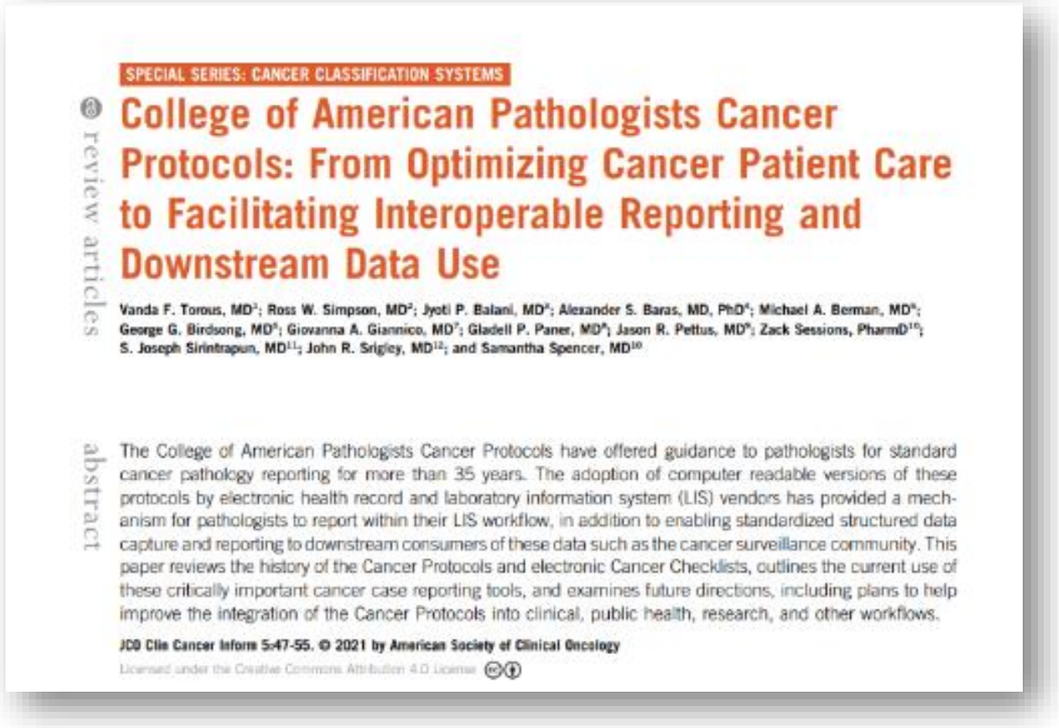


How Can We Improve Transfer of Biomarker Data into Reports?

Rapid growth in biomarker testing demands a **scalable, efficient, and accurate** data transfer solution.

Mapping logic would be required for **seamless electronic auto-population** of reference lab results into a structured data capture format.

This auto-population would **support timely diagnosis, enhance patient care,** and **reduce pathologist data entry.**



SPECIAL SERIES: CANCER CLASSIFICATION SYSTEMS

review articles

College of American Pathologists Cancer Protocols: From Optimizing Cancer Patient Care to Facilitating Interoperable Reporting and Downstream Data Use

Vanda F. Torous, MD[1]; Ross W. Simpson, MD[2]; Jyoti P. Balani, MD[3]; Alexander S. Baras, MD, PhD[4]; Michael A. Berman, MD[5]; George G. Birdsong, MD[6]; Giovanna A. Giannico, MD[7]; Gladell P. Paner, MD[8]; Jason R. Pettus, MD[9]; Zack Sessions, PharmD[10]; S. Joseph Sirintrapun, MD[11]; John R. Srigley, MD[12]; and Samantha Spencer, MD[10]

abstract

The College of American Pathologists Cancer Protocols have offered guidance to pathologists for standard cancer pathology reporting for more than 35 years. The adoption of computer readable versions of these protocols by electronic health record and laboratory information system (LIS) vendors has provided a mechanism for pathologists to report within their LIS workflow, in addition to enabling standardized structured data capture and reporting to downstream consumers of these data such as the cancer surveillance community. This paper reviews the history of the Cancer Protocols and electronic Cancer Checklists, outlines the current use of these critically important cancer case reporting tools, and examines future directions, including plans to help improve the integration of the Cancer Protocols into clinical, public health, research, and other workflows.

JCO Clin Cancer Inform 5:47-55. © 2021 by American Society of Clinical Oncology

Initiative to Directly Integrate Molecular Results

Objective

Assess how CAP eCPs can provide a targeted evidence-based **framework for direct mapping of molecular biomarker data** from reference labs into corresponding CAP cancer biomarker synoptic report data elements.

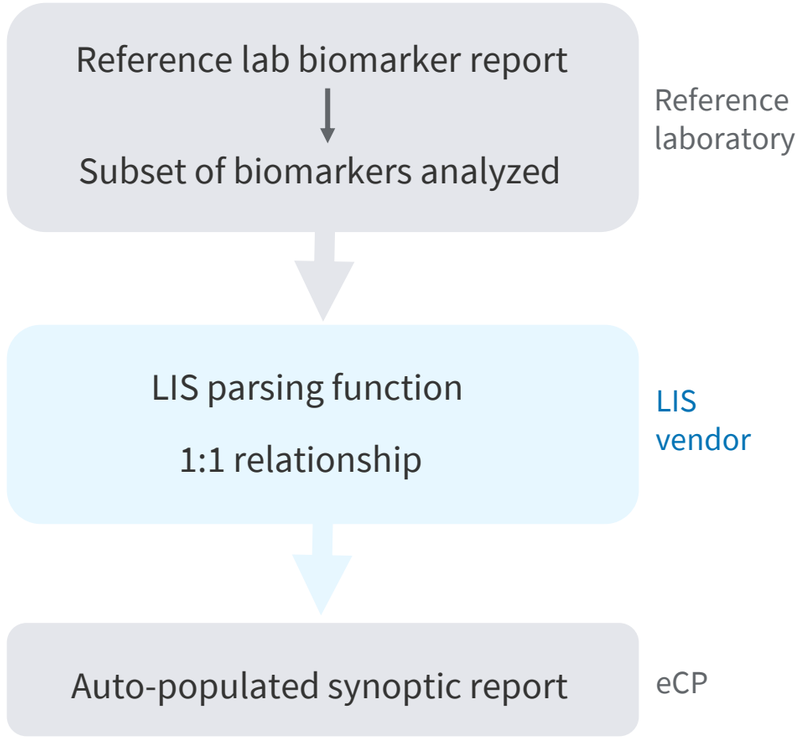
Method

- **Biomarker testing**
  - Caris' comprehensive profiling provides maximum insights in one test, including diagnostic and predictive biomarkers, thereby reducing duplicative testing.
- **Data processing**
  - Each data element within a CAP cancer biomarker template has an assigned unique identifier (Ckey).
  - Ckeys can be leveraged by reference labs to direct the mapping of results into a CAP eCP residing on an institution's LIS/EHR server.
  - This direct result-to-protocol transfer solution would be available to all reference labs/EHR/LIS vendors.

Proof of Concept

The current development work with Caris and mTuitive is a first step in proof of concept.

Conceptual Workflow



Developing a Data Transfer Solution for Auto-population of CAP Synoptic Reports

A Collaboration of CAP with Caris Life Sciences and mTuitive Inc.

Developing a Synoptic Report Auto-population Solution

Conception

CAP provided eCP synoptic report **format**.

CAP also shared a list of pertinent **biomarkers** from the Biomarker Working Group.

Caris tests for **97%** of these specified biomarkers.

Planning

mTuitive developed a parsing script using Caris' JSON schema.

This script extracts relevant biomarkers from Caris Tumor Seek Hybrid™ + IHC report.

Prototyping

Structured extraction of genomic data points.

Mapping to correct fields in the NSCLC synoptic report.

Program looks for specific genes in the Caris report.

Validation

Caris provided 25 deidentified real-world NSCLC cases in JSON format.

Cases run through process to validate parsing and mapping.

Best-in-Class Profiling Reveals a More Comprehensive Molecular Blueprint

Analyzing DNA, RNA, and proteins to reveal a more complete molecular blueprint to guide precise and individualized treatment decisions.

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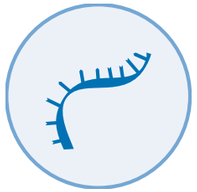

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- ✓ 4 µm cuts to preserve tissue

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Easy-to-Interpret Results – Caris Report

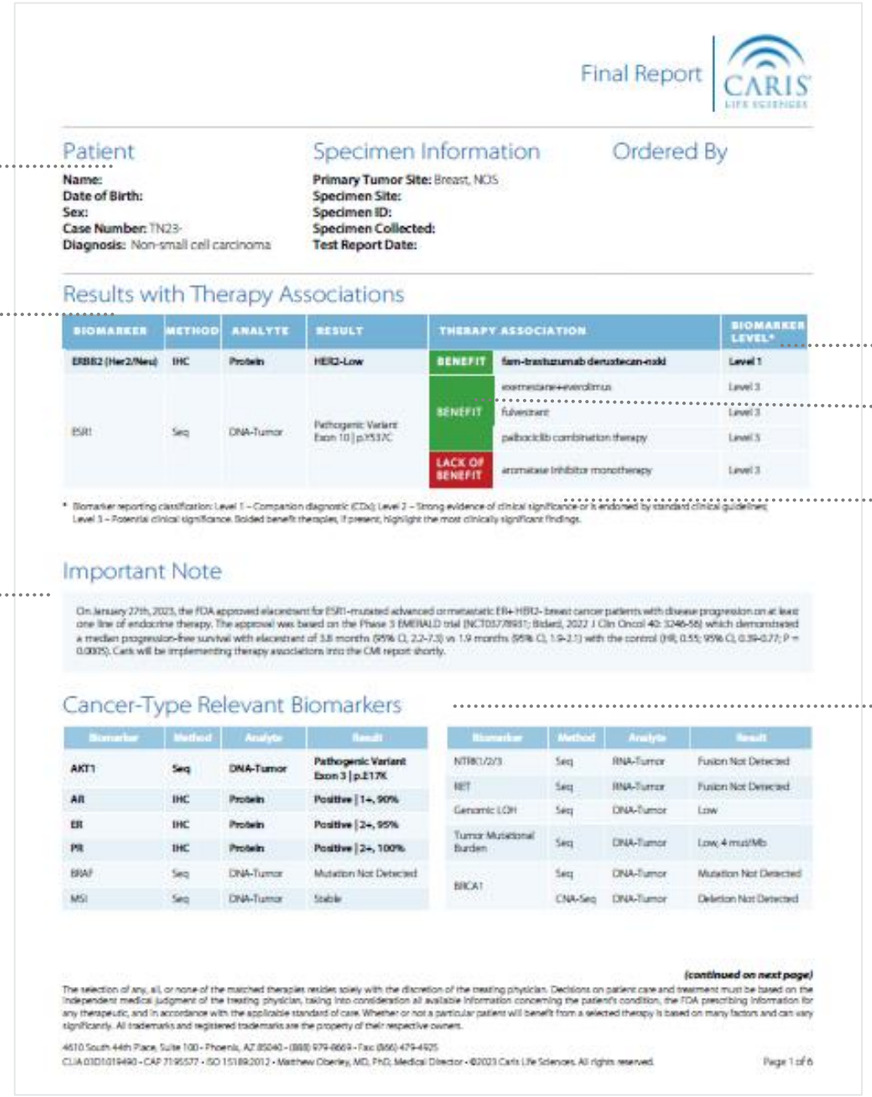
Patient and Specimen Information

Results with Therapy Associations
Contains drug associations ranked by level of evidence:
Level 1 = Biomarker test noted in FDA indication
Level 2 = Endorsed by clinical guidelines
Level 3 = Evidence exists in patient's tumor type

Important Note
Contains significant information about drug/biomarker associations and comments from Caris pathologists and/or molecular geneticists, if applicable.

Therapeutic associations are constantly updated based on:

- FDA approvals
- Industry guidelines
- Literature
- **Physician** feedback



Final Report

Patient
Name:
Date of Birth:
Sex:
Case Number: TN23-
Diagnosis: Non-small cell carcinoma

Specimen Information
Primary Tumor Site: Breast, NOS
Specimen Site:
Specimen ID:
Specimen Collected:
Test Report Date:

Ordered By

Results with Therapy Associations

BIOMARKER	METHOD	ANALYTE	RESULT	THERAPY ASSOCIATION		BIOMARKER LEVEL*
ERBB2 (Her2/Neu)	IHC	Protein	HER2-Low	BENEFIT	fam-trastuzumab deruxtecan-nxki	Level 1
ESR1	Seq	DNA-Tumor	Pathogenic Variant Exon 10 | p.Y537C	BENEFIT	exemestane+everolimus	Level 3
					fulvestrant	Level 3
					palbociclib combination therapy	Level 3
				LACK OF BENEFIT	aromatase inhibitor monotherapy	Level 3

* Biomarker reporting classification: Level 1 – Companion diagnostic (CDx); Level 2 – Strong evidence of clinical significance or is endorsed by standard clinical guidelines; Level 3 – Potential clinical significance. Bolded benefit therapies, if present, highlight the most clinically significant findings.

Important Note

On January 27th, 2023, the FDA approved elacestrant for ESR1-mutated advanced or metastatic ER+/HER2- breast cancer patients with disease progression on at least one line of endocrine therapy. The approval was based on the Phase 3 EMERALD trial (NCT03778931; Bidard, 2022 J Clin Oncol 40: 3246-56) which demonstrated a median progression-free survival with elacestrant of 3.8 months (95% CI, 2.2–7.3) vs 1.9 months (95% CI, 1.9–2.1) with the control (HR, 0.55; 95% CI, 0.39–0.77; P = 0.0035). Caris will be implementing therapy associations into the CMI report shortly.

Cancer-Type Relevant Biomarkers

Biomarker	Method	Analyte	Result
AKT1	Seq	DNA-Tumor	Pathogenic Variant Exon 3 | p.E17K
AR	IHC	Protein	Positive | 1+, 90%
ER	IHC	Protein	Positive | 2+, 95%
PR	IHC	Protein	Positive | 2+, 100%
BRAF	Seq	DNA-Tumor	Mutation Not Detected
MSI	Seq	DNA-Tumor	Stable

Biomarker	Method	Analyte	Result
NTRK1/2/3	Seq	RNA-Tumor	Fusion Not Detected
RET	Seq	RNA-Tumor	Fusion Not Detected
Genomic LOH	Seq	DNA-Tumor	Low
Tumor Mutational Burden	Seq	DNA-Tumor	Low, 4 mut/Mb
BRCA1	Seq	DNA-Tumor	Mutation Not Detected
	CNA-Seq	DNA-Tumor	Deletion Not Detected

(continued on next page)

The selection of any, all, or none of the matched therapies resides solely with the discretion of the treating physician. Decisions on patient care and treatment must be based on the independent medical judgment of the treating physician, taking into consideration all available information concerning the patient's condition, the FDA prescribing information for any therapeutic, and in accordance with the applicable standard of care. Whether or not a particular patient will benefit from a selected therapy is based on many factors and can vary significantly. All trademarks and registered trademarks are the property of their respective owners.

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Biomarker Levels
Indicates the strength of evidence and testing (e.g., Level 1 is a FDA CDx).

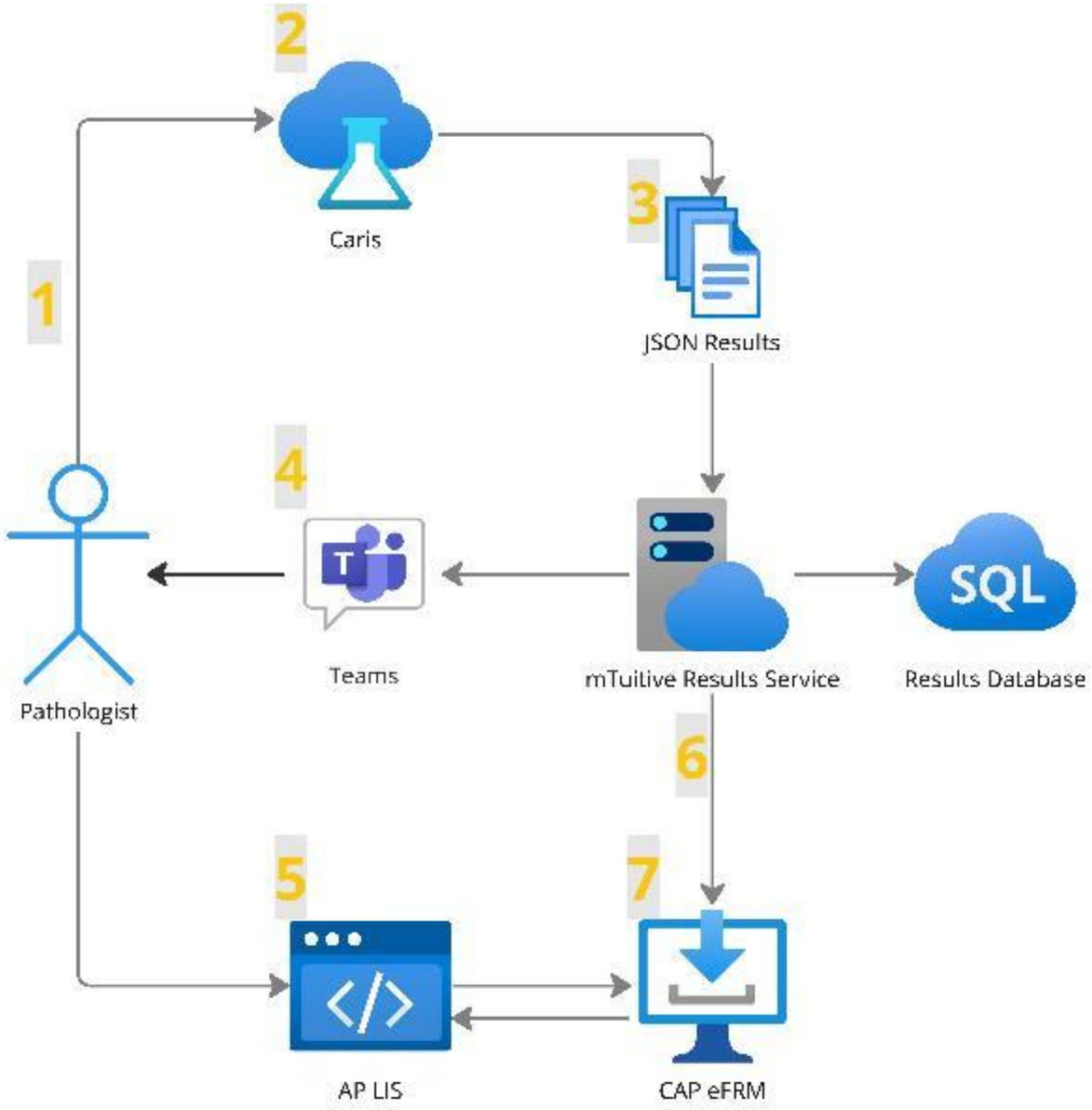
Therapies with potential Benefit
are noted in **green**.

Therapies with potential Lack of Benefit
are noted in **red**.

Cancer-Type Relevant Biomarkers
Pre-defined biomarkers whose results will show regardless of presence or absence of an alteration.

Clinical Trials
Clinical trial information, including Right-In-Time Clinical Trials, can be found later in the report.

Caris Biomarker Results Auto-populate CAP eCP in mTuitive eFRM



1. Pathologist or other provider orders test from Caris via normal channels.
2. Caris performs lung biomarker test suite.
3. Caris sends JSON results to mTuitive Results Web Service.
4. mTuitive Results Web Service notifies pathologists that results are available using Microsoft Teams or another messaging medium.
5. The pathologist opens the AP LIS to the specified case and begins a synoptic report using the Lung Biomarkers eCP.
6. eFRM looks up results and populates the CAP protocol with test results, avoiding onerous, redundant, error-prone data entry.
7. The pathologist continues to augment the report with additional interpretation, and submits.

Pertinent Information is Automatically Extracted From the Caris Report to CAP Synoptic Report

Results with Therapy Associations

BIOMARKER	METHOD	ANALYTE	RESULT	THERAPY
PD-L1 (22c3)	IHC	Protein	Positive, TPS: 80%	BENEFIT
PD-L1 (28-8)	IHC	Protein	Positive | 1+, 70%	BENEFIT
RET	Seq	RNA-Tumor	Fusion Detected	BENEFIT
ALK	Seq	RNA-Tumor	Fusion Not Detected	LACK OF BENEFIT
BRAF	Seq	DNA-Tumor	Mutation Not Detected	LACK OF BENEFIT
EGFR	Seq	DNA-Tumor	Mutation Not Detected	LACK OF BENEFIT
KRAS	Seq	DNA-Tumor	Mutation Not Detected	LACK OF BENEFIT
ROS1	Seq	RNA-Tumor	Fusion Not Detected	LACK OF BENEFIT
MET	CNA-Seq	DNA-Tumor	Amplification Not Detected	LACK OF BENEFIT
	Seq	DNA-Tumor	Mutation Not Detected	

• Biomarker reporting classification: Level 1 – Companion diagnostic (CDx); Level 2 – Strong evidence of cl
Level 3 – Potential clinical significance. Bolded benefit therapies, if present, highlight the most clinically s

PD-L1 → Positive

RET → Fusion Detected

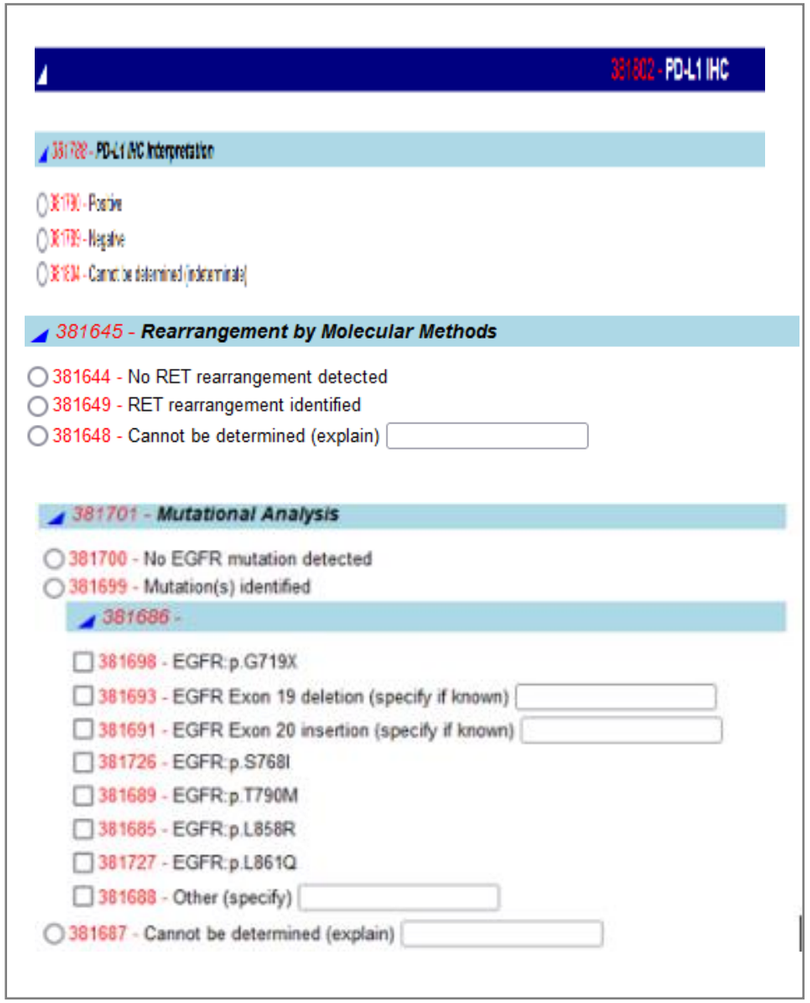
ALK → Wildtype

BRAFV600 → Not Detected

EGFR → Wildtype

• • •

Extract Lung Biomarker Reporting Template

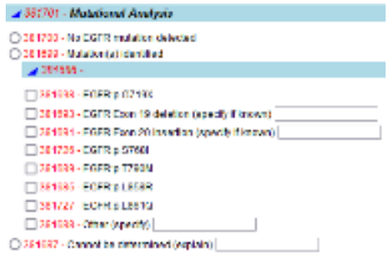


Caris Data is Delivered to mTuitive in JSON Format

Pathogenic Mutations


```
  {
    "genomicAlteration" : {
      "resultCount" : "8",
      "biomarkerName" : "EGFR",
      "result" : "Pathogenic Variant",
      "gene" : "EGFR",
      "hgvsCodingChange" : "c.2311_2312insGGG",
      "hgvsProteinChange" : "p.N771delinsRD",
      "chromosome" : "chr7",
      "genomeBuild" : "GRCh38/hg38",
      "exon" : "20",
      "transcriptID" : "NM_005228.4",
      "alleleFrequency" : "45",
      "molecularConsequence" : "CODON_CHANGE_PLUS_CODON_INSERTION",
      "readDepth" : "1288"
    }
```


A




```
    },
    {
      "genomicAlteration" : {
        "resultCount" : "13",
        "biomarkerName" : "KRAS",
        "result" : "Pathogenic Variant",
        "gene" : "KRAS",
        "hgvsCodingChange" : "c.34G>T",
        "hgvsProteinChange" : "p.G12C",
        "chromosome" : "chr12",
        "genomeBuild" : "GRCh38/hg38",
        "exon" : "2",
        "transcriptID" : "NM_004985.4",
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        "molecularConsequence" : "Missense",
        "readDepth" : "3216"
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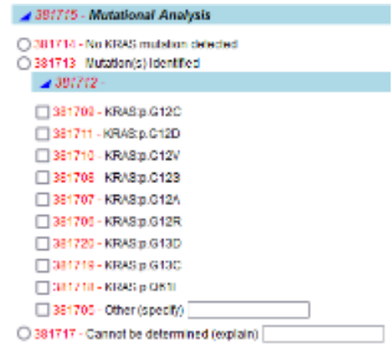
A

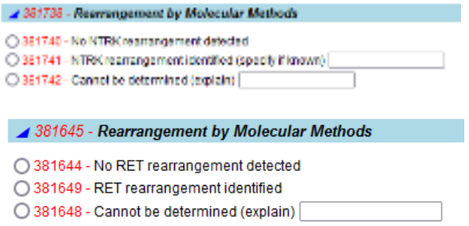


A = mTuitive Parsing Function

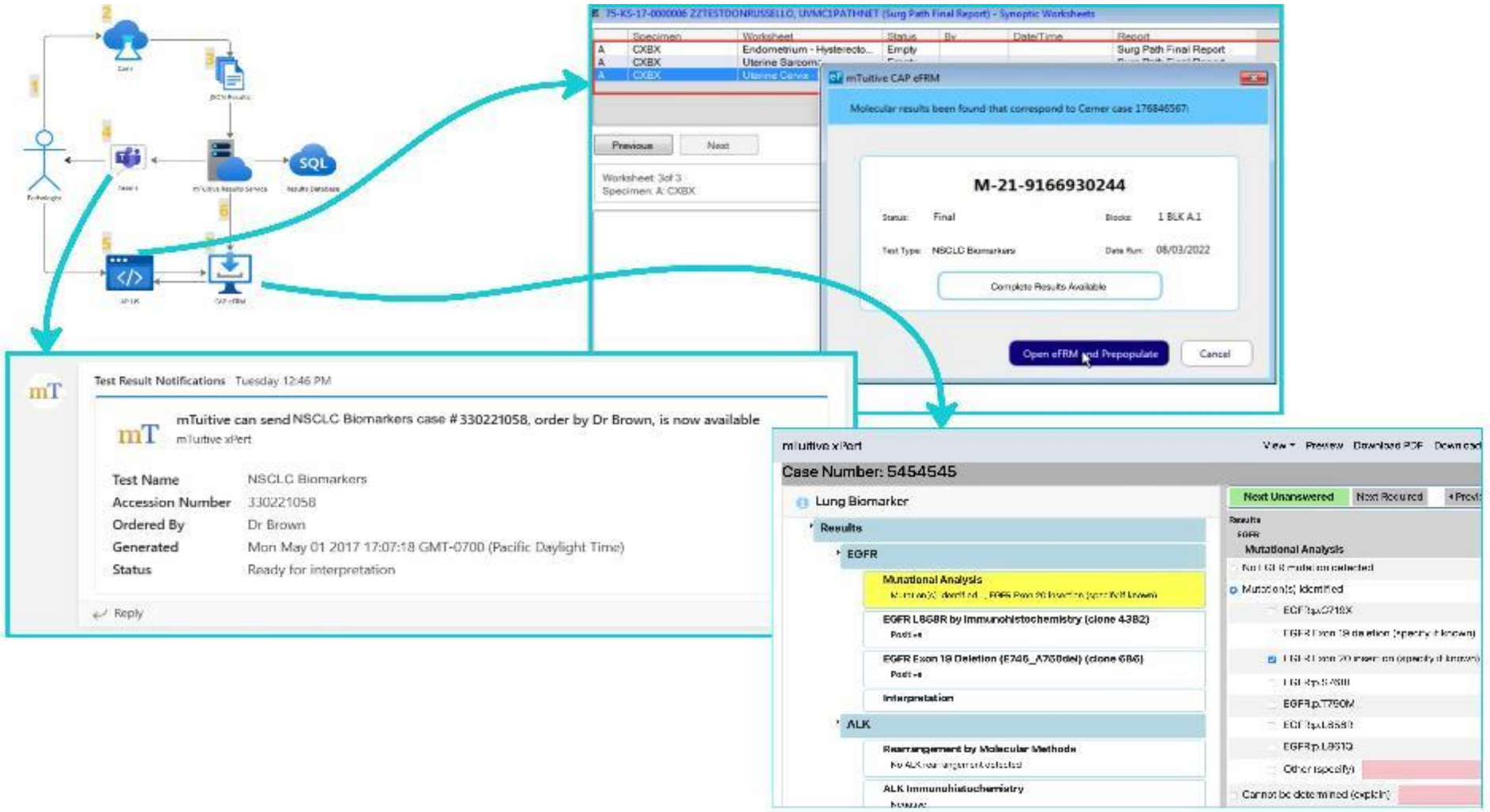
Wildtype or Biomarkers Not Detected


```
  {
    "translocation" : {
      "resultCount" : "5",
      "gene" : "NTRK1",
      "biomarkerName" : "NTRK1",
      "result" : "Fusion Not Detected"
    }
  },
  {
    "translocation" : {
      "resultCount" : "6",
      "gene" : "NTRK2",
      "biomarkerName" : "NTRK2",
      "result" : "Fusion Not Detected"
    }
  },
  {
    "translocation" : {
      "resultCount" : "7",
      "gene" : "NTRK3",
      "biomarkerName" : "NTRK3",
      "result" : "Fusion Not Detected"
    }
  },
  {
    "translocation" : {
      "resultCount" : "8",
      "gene" : "RET",
      "biomarkerName" : "RET",
      "result" : "Fusion Not Detected"
    }
```

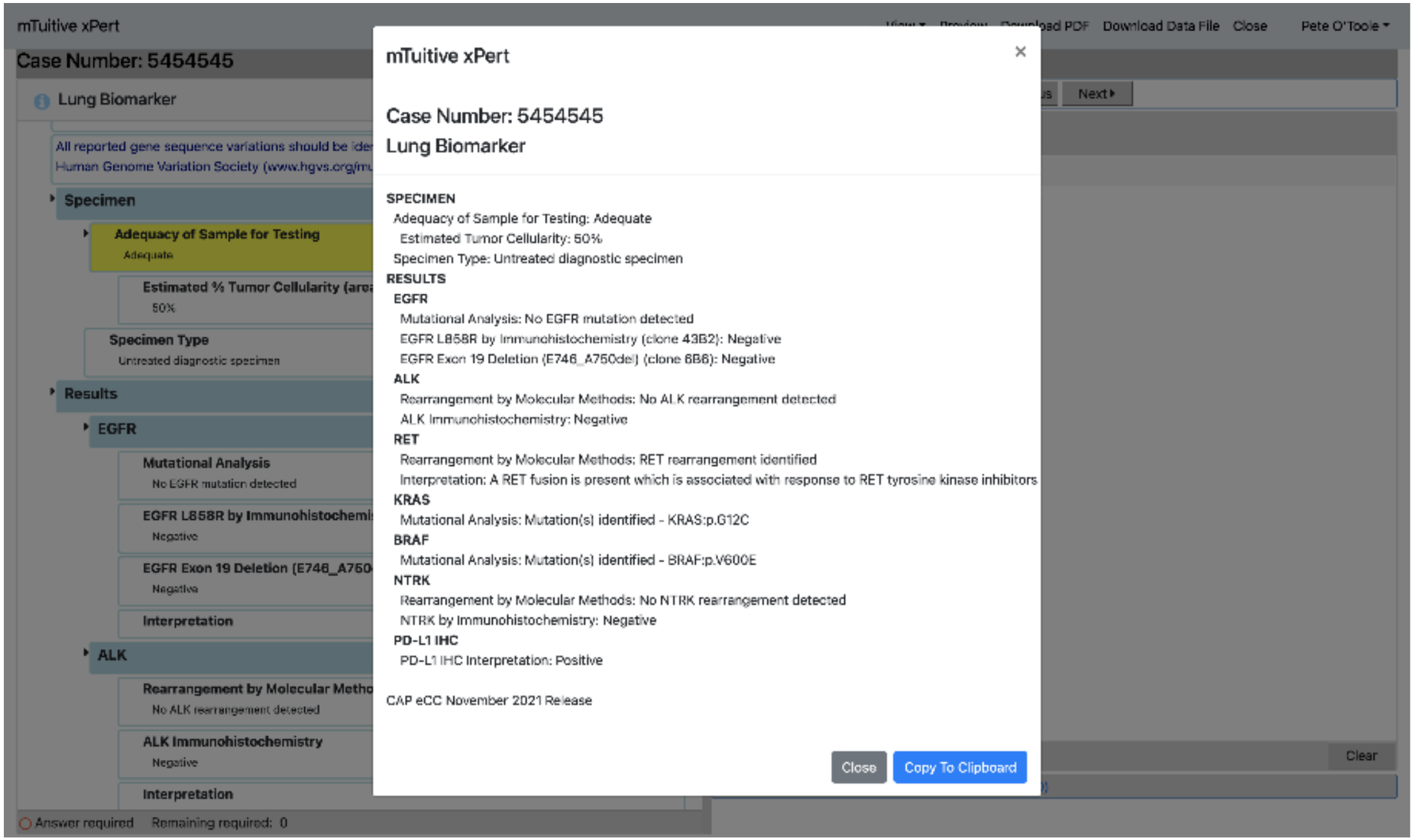

A



Caris Biomarker Results Auto-populate CAP eCP in mTuitive eFRM



Caris Biomarker Results Auto-populate CAP eCP in mTuitive eFRM



Summary

- **Precision oncology** improves patient outcomes.
- Molecular profiling of **biomarkers** is central to precision oncology.
- **Comprehensive molecular profiling** offers the most in-depth molecular insights, enabling pathologists to gather all relevant information in one go without the need for duplicative testing.

- **Rapid growth** in biomarkers and biomarker testing is driving innovation in reporting.
- **Synoptic reporting** ensures patients get the correct workup and all data is gathered appropriately.
- **Auto-populating** the eCP with reference lab results and integrating the local LIS with the eCP can simplify workload, enabling pathologists to report within their workflow.

- Caris is collaborating with CAP to develop a method for **automatic population** of synoptic report fields with comprehensive molecular profiling results.
- CAP has begun discussions with two possible **test sites** (Banner University Health Phoenix, AZ, and Georgetown University School of Medicine, Washington, DC).
- **Further refinement** of and/or parsing to the CAP Biomarker Reporting Protocols may be necessary to capture relevant results.

Collaborators

Caris Life Sciences

- Matthew Oberley, MD, PhD, Senior Vice President, Executive Medical Director
- Jared Cotta, MPH, Head of Precision Oncology Programs

mTuitive, Inc

- Peter O'Toole, President & Chief Software Architect
- Colin Murphy, Chief Executive Officer

CAP Cancer Protocols and Data Standards Staff

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- Keren Hulkower, PhD: Senior Clinical Release Manager
- Ted Carithers: Director, Cancer Protocols and Data Standards

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