LiquidHALLMARK®

Physician Brochure

LUCENCE

Detect What Others May Miss

LiquidHALLMARK®

Designed to detect guideline-recommended cancer biomarkers — including RNA fusions — often missed by ctDNA-only liquid biopsy tests.

15.6% more

guideline-recommended lung cancer biomarkers detected versus an FDA-approved liquid biopsy test[1*]

36% more

fusions detected with the inclusion of RNA testing[2,3*]

Median 7

business days to results*

93-100%

concordance with tissue NGS for 9 NCCN-recommended biomarkers*

*Refer to inside spread for more information.

References: [1] Samol J, et al. JCO Precis. Oncol. 2025; 9: e2500181. [2] Heeke et al. JTO Clin Res Rep. 2025: 100795. [3] Chan, D. Paper presented at: ASCO Annual Meeting; June 2, 2025; Chicago, IL.

120,000 Cancer Patients

Annually in the US Have Actionable Fusions[1,2]

In a study of 1007 plasma samples from real-world combined ctDNA + ctRNA testing across the USA and Asia for over 30 cancer types,

- ctDNA alone was only able to detect **65%** (52/80) of all gene fusions.[3]
- Addition of ctRNA to ctDNA detected **36.7%** (11/30) more actionable fusions.[3]

In another study (NCT03707938), retrospective analysis of 86 plasma samples from 33 NSCLC patients showed that combining ctDNA and ctRNA in LiquidHALLMARK® detected 19 *ALK* fusions, compared to 14 *ALK* fusions detected by ctDNA alone.[4]

This means that

36% more

patients with *ALK* fusions were detected and have the potential for treatment.

ALK fusions detected by ctDNA

ALK fusions only detected by combining with ctRNA with ctDNA

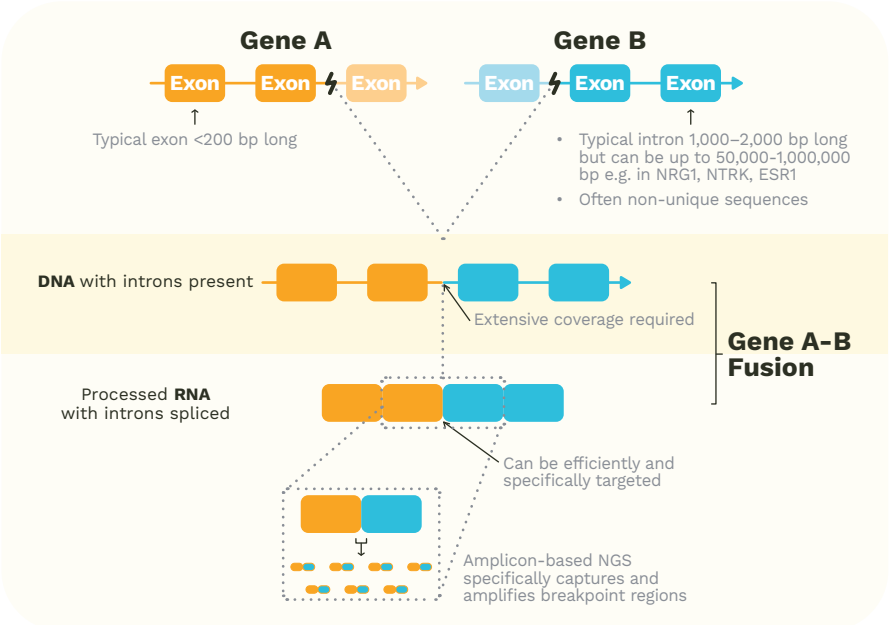
References: Calculated from [1] Gao, Q. et al. Cell Reports 2018; 23(1): 227-238.E3. [2] National Cancer Institute. Cancer Statistics. Accessed August 15 2025. https://www.cancer.gov/about-cancer/understanding/statistics [3] Chan, D. Paper presented at: ASCO Annual Meeting; June 2, 2025; Chicago, IL. [4] Heeke et al. JTO Clin Res Rep. 2025: 100795.

NCCN Guidelines Recommend

Combined DNA and RNA Testing to Maximize Detection of Actionable Fusions in NSCLC Patients[5]

- *METex14*: "RNA-based NGS may have **improved detection**." (NSCL-H, 5 of 8)[5]
- *RET*: "**RNA-based NGS is preferable** to DNA-based NGS for fusion detection" (NSCL-H, 5 of 8)[5]
- *NTRK1/2/3*: "DNA-based NGS may not detect some *NTRK1* and *NTRK3* fusions; **RNA-based NGS may be considered**." (MS-21)[5]
- *ROS1*: "False-negative results may occur with [...] DNA-based NGS. **RNA-based NGS may be considered**." (MS-22)[5]

RNA-based NGS is particularly well-suited for gene fusions with long intronic regions like *NTRK* and *NRG1*.[6]



References: [5] National Comprehensive Cancer Network. Non-Small Cell Lung Cancer (Version 3.2025). Accessed March 18 2025. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf.
[6] Benayed et al. Clin Cancer Res. 2019 August 01; 25(15): 4712–4722.

LIQUIK-01 Prospective Study

Demonstrates Utility of Combined ctDNA and ctRNA[1]

Study Design

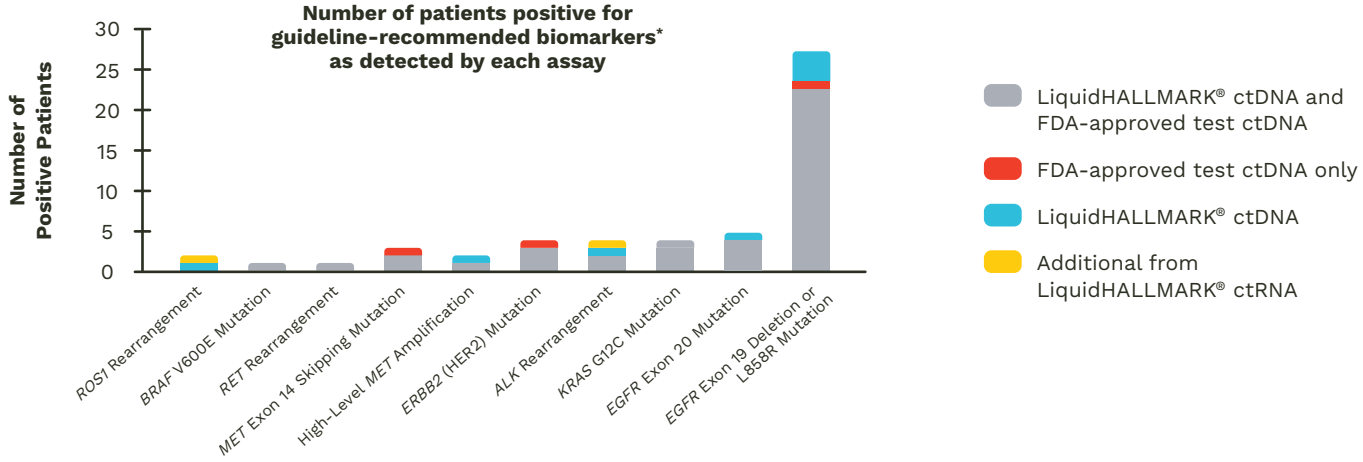
151
Newly Diagnosed NSCLC patients
prospectively recruited between April 2021 and December 2022

9
NCCN Guideline-Recommended Biomarkers*
tested with 3 different assays:
- **tissue NGS**
- **LiquidHALLMARK® ctDNA + ctRNA**
- **FDA-approved ctDNA only liquid NGS**

10
International Centers
across Singapore and the United States (including University of Miami, University of Maryland, and Kaiser Permanente Hawaii)[2]

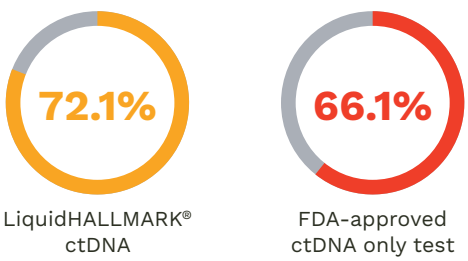
Results

LiquidHALLMARK® ctDNA + ctRNA detected **15.6% (52 vs 45)** more tissue-confirmed, guideline-recommended biomarkers* than the ctDNA only FDA-approved test, with **93-100% concordance** with tissue NGS for 9 guideline-recommended biomarkers.[1]



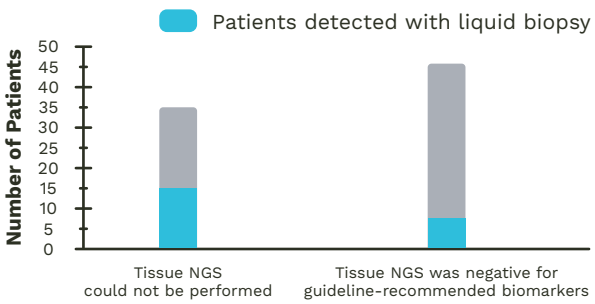
LiquidHALLMARK® ctDNA demonstrated **non-inferiority** compared to the FDA-approved ctDNA only test in detecting tissue-confirmed guideline-recommended biomarkers. [1]

% patients detected with tissue-confirmed, guideline-recommended biomarkers



When tissue NGS was negative for guideline-recommended biomarkers (46/151), liquid biopsy detected **7** patients with actionable biomarkers. When tissue NGS could not be performed (e.g. quantity not sufficient) (31/151), liquid biopsy detected actionable biomarkers in **48.4%** of patients (15/31).[1]

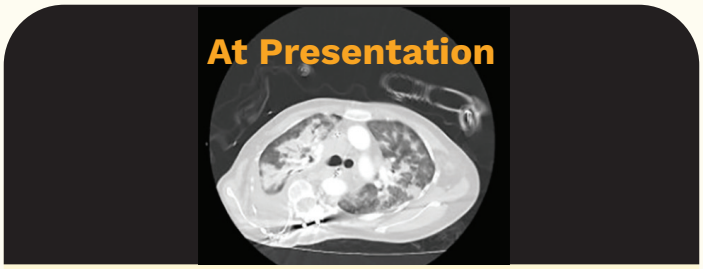
Number of patients with actionable biomarkers detected by liquid biopsy when tissue NGS could not be performed or was negative



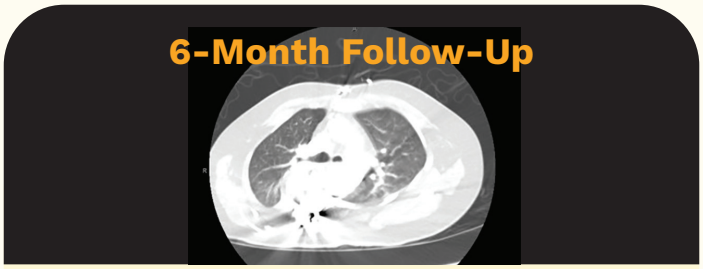
**EGFR, ALK, RET, ROS1, BRAF, KRAS, MET, ERBB2,* and *NTRK1/2/3.* References: [1] Samol J, et al. JCO Precis. Oncol. 2025; 9: e2500181. [2] ClinicalTrials.gov. LIQUIK: LIQUId Biopsy for Detection of Actionable Genomic BiomarKers in Patients With Advanced Non-small Cell Lung Cancer (NSCLC) (LIQUIK). Accessed August 21 2025. https://www.clinicaltrials.gov/study/NCT04703153

Case Studies:

When ctDNA Alone Misses Targets in Lung Cancer – Additional ctRNA Identifies[3]



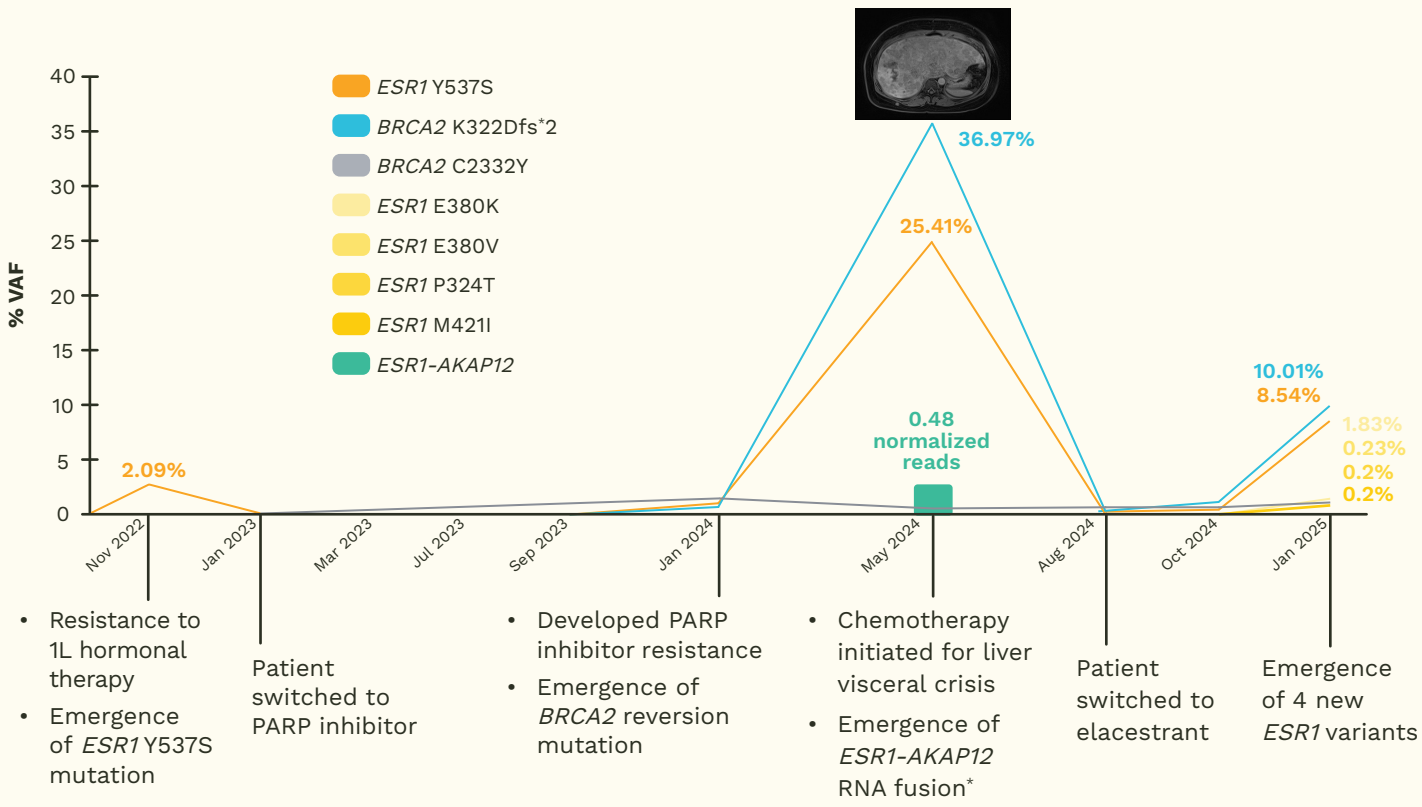
- A 50 year old woman with lung cancer was mechanically ventilated in a Florida ICU.
- Cervical lymph node biopsy had **inadequate tissue**.
- An FDA-approved plasma ctDNA-only test showed **no treatment targets**.



- LiquidHALLMARK® detected an **actionable *ALK* fusion in the ctRNA in 7 days**.
- The patient was treated with an *ALK*-targeting TKI.
- The patient was weaned off ventilator and discharged well.
- 1-year follow-up showed no disease progression.

Emergence of Multiple *ESR1* Targets in gBRCA+ Metastatic Breast Cancer

A 40+ year-old female with **ER+**, **PR+**, **HER2- metastatic breast cancer** is treated with **hormonal therapy** in January 2022. Testing confirms germline *BRCA2* mutation C311Vfs*13, Exon 10 Frameshift indel.



Disclaimer: The case studies above are based on a real patient cases. Individual results may vary. Product is not indicated or intended as a companion diagnostic or to supplant physician medical judgement. *Fusion detected is not a target
Reference: [3] Chan, D. Paper presented at: ASCO Annual Meeting; June 2, 2025; Chicago, IL.

Reimbursement Simplified

We Process the Patient's Sample

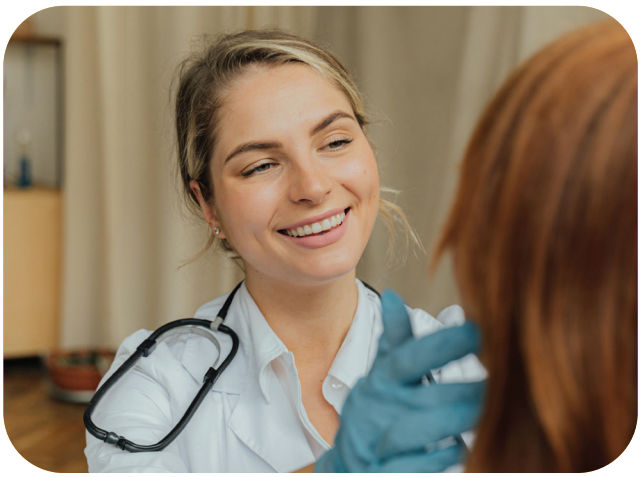
We will proceed with testing consistent with the doctor's order, regardless of insurance plan. We will provide claims support to save you and your team time. Please help ensure that the patient provides the required information in the test order form to facilitate this. Note that missing insurance information or prior authorization may cause a slight delay in processing. Patients will be responsible for any cost-sharing amounts required by their insurance plan, and for the cost of testing if their insurance plan denies coverage.

We Bill the Patient's Insurance

We will bill the patient's insurance and support with the appeals process. Once the claim is processed, we will bill the patient for any required cost-sharing amounts. If the claim is denied or the patient is a self-paying patient, we will issue an invoice at our self-pay rate.

We Make Paying Easy

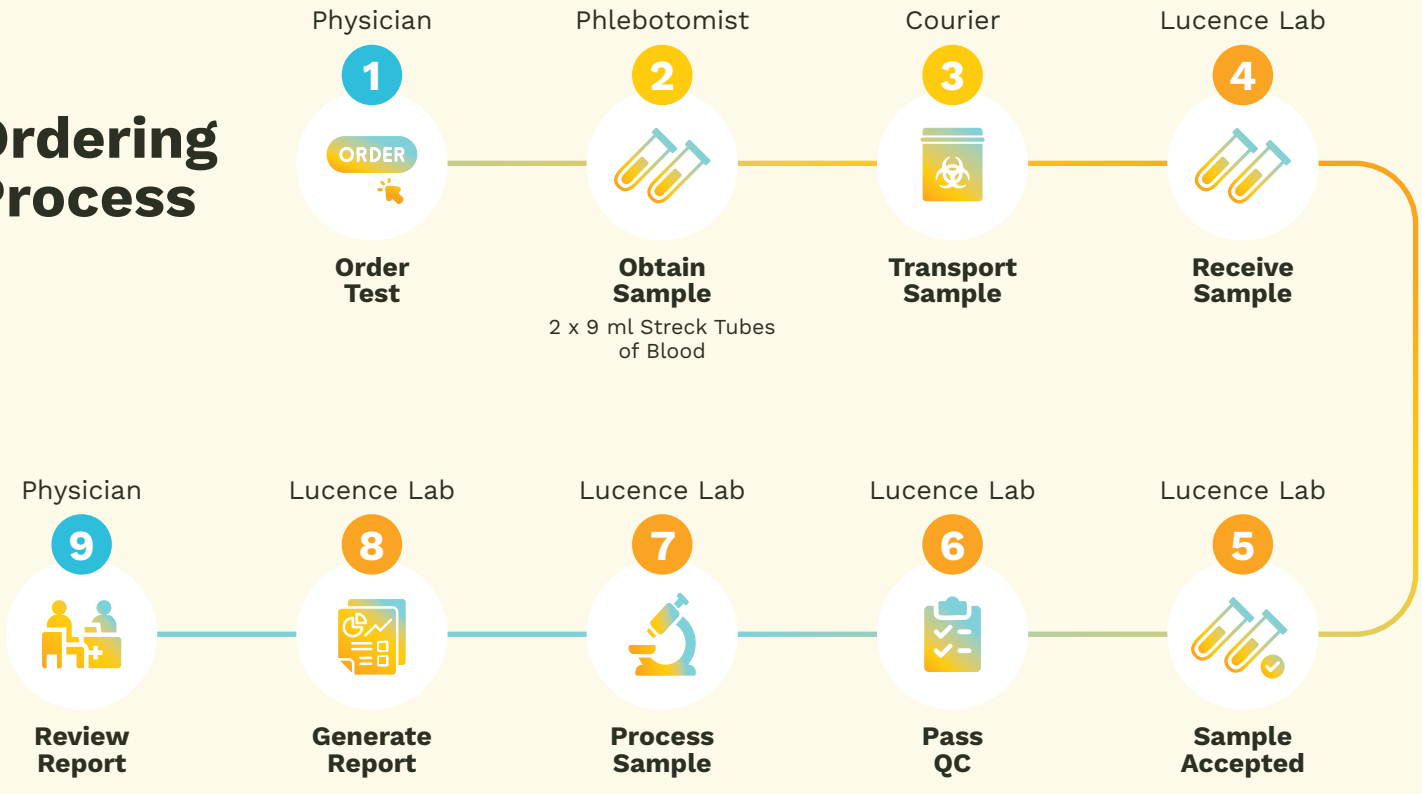
For uninsured patients, we will require their contact information upon sample receipt to email a bill for their review and payment while the sample is being processed.



Patient Assistance Program

If the patient meets certain household income and other eligibility criteria, the patient may qualify for our Patient Assistance Program, which limits their out-of-pocket cost to $95. Patients can apply for the program at the same payment link included in their bill. After patients submit their income documentation, our reimbursement advisors will determine their eligibility within 3-5 business days after initial submission.

Ordering Process



LiquidHALLMARK®

Targets List

Genes* (SNVs and Indels)

ABL1	*CDK6*#	*FLT3*	*KIT*#	*NRAS*#	*RHOA*
AKT1	*CDKN2A*#	*GATA3*	*KRAS*#	*NTRK1*	*RIT1*
ALK#	*CREBBP*	*GNA11*	*MAP2K1* (MEK1)	*NTRK3*	*ROS1*
APC	*CTNNB1*	*GNAQ*	*MAP2K2* (MEK2)	*PDGFRA*#	*SF3B1*
AR#	*EGFR*#‖	*GNAS*	*MED12* (ERK2)	*PIK3CA*#	*SMAD4*#§
ARAF	*ERBB2*# (HER2)	*HNF1A*	*MED12*	*PIK3R1*	*SMO*
ATM#	*ERCC2*	*HRAS*	*MET*#	*PPP2R1A*	*SPOP*
BRAF	*ESR1*#	*IDH1*	*MLH1*	*PTEN*#	*STK11*
BRCA1#‡	*EZH2*	*IDH2*	*MTOR*	*PTPN11*	*TERT* Promotor
BRCA2#†	*FBXW7*#	*JAK1*	*MYC*#	*RAF1*	*TP53*#§
CCND1#	*FGFR1*	*JAK2*	*NF1*	*RB1*	*U2AF1*
CCND2#	*FGFR2*	*JAK3*	*NFE2L2*	*RET*	*VHL*
CDH1	*FGFR3*	*KEAP1*‡	*NOTCH1*	*RHEB*	

DNA Fusions	*ALK*	*FGFR2*	*NTRK1*	*NTRK3*	*ROS1*
	CD274 (PD-L1)	*FGFR3*	*NTRK2*	*RET*	*TMPRSS2*
RNA Fusions	*ALK*	*FGFR3*	*NTRK1*	*NTRK3*	*ROS1*
	FGFR2	*MET* (Includes exon 14 skipping)	*NTRK2*	*RET*	*TMPRSS2*
MSI Regions	*FBXW7*#	*JAK1*	*MYC*#	*RAF1*	*TP53*#§
	FGFR1	*JAK2*	*NF1*	*RB1*	*U2AF1*

*Targeted regions selected to maximize detection of known hotspot mutations, in all clinically relevant exons of tested genes ‖Includes sequencing of *EGFR* kinase and extracellular domain mutations #Includes detection of copy number alterations †> 98.4% coverage of coding exons ‡> 99% coverage §Full coverage

LiquidHALLMARK®

Specifications[7-10]

	Limit of Detection	Sensitivity	Specificity
Single Nucleotide Variants (SNVs)	0.1% VAF	> 91%	> 99%
Insertions / Deletions (Indels)	0.1% VAF	> 90%	> 99%
ctDNA Fusions	0.5% VAF	> 91%	> 99%
ctRNA Fusions	10 copies	> 99%	> 99%

References: [7] Poh J. et al. 2022. PLoS ONE 17(4): e0267389. [8] Choudhury, Y. et al. Ann. Oncol., 29, 2018 (suppl_9; mdy441.010). [9] Choudhury, Y. et al. J Clin Oncol 36: 2018 (suppl; abstr e24107). [10] Choudhury, Y. et al. AACR; Clin Cancer Res 2020; 26(11_Suppl): Abstract nrA41.

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