

סורה נולית

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סורה נולית | מרכז רפואי אוניברסיטאי
אליהו רabinovitz



צוות המבחן לפטולוגיה

רופא בכיר: ד"ר שמואלי בן ציון

פרטים קליניים:

NGS על ביופסיה מס' 25-19892/1/2 מתאריך 26/10/10.

הערות כלליות:

בדיקות קודמות:

25-19892

אבחנה:

Molecular Pathology Laboratory Test Results

Oncomine™ Comprehensive Assay (OCA) by NGS

The test was performed on DNA extracted from biopsy #25-19892/1/2.

Tumor comprising 80% of the tissue submitted for analysis, as assessed on an H&E slide.

Test results:

- TMB score: 4.7
- MSI: Stable
- Reportable Alterations In Clinically Significant Genes
 - TP53 (Detected): c.401T>G (p.Phe134Cys); See Tier 1 for details
 - FBXW7 (Detected): c.1514G>T (p.Arg505Leu); See Tier 2 for details
 - AKT1 (Not detected)
 - BRAF (Not detected)
 - CCNE1 (Not detected)
 - DPYD (Not detected)
 - ERBB2 (Not detected)
 - MTAP (Not detected)
 - NRG1 (Not detected)
 - NTRK1 (Not detected)
 - NTRK2 (Not detected)
 - NTRK3 (Not detected)
 - POLE (Not detected)
 - PPP2R1A (Not detected)
 - RET (Not detected)

Genomic alterations found in the sample:

OF STRONG CLINICAL SIGNIFICANCE

TP53 | p.Phe134Cys | c.401T>G | NM_000546.6 | VAF: 23.32% | Exon 5 | chr17:7578529 | Pathogenic

TIER II: VARIANTS OF POTENTIAL CLINICAL SIGNIFICANCE

FBXW7 | p.Arg505Leu | c.1514G>T | NM_001349798.2 | VAF: 16.35% | Exon 12 | chr4:153247288 | Likely Pathogenic, Potentially Therapeutic

TIER III: VARIANTS OF UNCERTAIN CLINICAL SIGNIFICANCE

FAT1 | p.Val1010Ala | c.3029T>C | NM_005245.4 | VAF: 54.07% | Exon 2 | chr4:187627953 | VUS

TBX3 | p.Ser320Phe | c.959C>T | NM_005996.4 | VAF: 46.00% | Exon 5 | chr12:115114198 | VUS

TSC2 | p.Glu134Lys | c.400G>A | NM_000548.5 | VAF: 7.40% | Exon 5 | chr16:2104360 | VUS

ENO1 | p.Val350Met | c.1048G>A | NM_001428.5 | VAF: 26.85% | Exon 9 | chr1:8923969 | VUS

COPY NUMBER VARIANTS

Duplication | ETFRF1,KRAS | chr12:25362709-25398388 | 35.68 Kb | Copy number: 6.11 | VUS

Fusions found in the sample:

- No fusions found to report.

These results should be taken into consideration with all clinical information concerning the patient's condition in accordance with the standard of care.

General information:

The Ion Torrent™ Oncomine™ Comprehensive Assay v3 is a targeted, next-generation sequencing (NGS) assay that enables the detection of relevant single-nucleotide variants (SNVs), copy number variations (CNVs), gene fusions, and indels. Oncomine™ Comprehensive Panel is used to construct the library and sequencing is performed using Ion Torrent sequencing system.

This NGS test for identifying alterations in cancer related genes in FFPE tumor tissue was validated by the molecular pathology unit in Soroka University Medical Center and approved by the Israeli Ministry of Health.

Validation showed 100% specificity for each mutation tested and a 1% limit of detection.

The test is aimed to detect hotspot mutations in 165genes, CNV variants in 333 genes, CDS in 227 genes and 51 fusions driver genes linked to cancer, such as:

DNA based alterations: *AKT1, ALK, AR, BRAF, BRCA 1/2, CDK4, CTNNB1, DDR2, EGFR, ERBB2, ERBB3, ERBB4, ESR1, FGFR1-4, GNA11, GNAQ, HRAS, IDH1, IDH2, JAK1-3, KIT, KRAS, MAP2K2, MET, MTOR, NRAS, MAP2K1, MAP2K2, MET, MTOR, NRAS, PDGFRA, PIK3CA, RAF1, RET, ROS1, SMO*.

RNA based alterations: *ALK, AXL, BRAF, BRCA1, BRCA2, ERBB2, ERG, ETV1, ETV4, ETV5, FGFR1, FGFR2, FGFR3, MET, NTRK1-3, PDGFRA, PPARG, RAF1, RET, ROS1*.

The test was performed by the molecular laboratory under the direction of Dr. Natalie Aisenberg.



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סורוקה

סורוקה | **המרכז הרפואי האוניברסיטאי סורוקה**
אלעג'יק סורוקה

דוח תוצאות בדיקה פתולוגית מס'

סה"כ 1 דגימות.

תאריך הדפסה:
21:27 16/12/2025

תאריך הפקה:
21:21 16/12/2025

תאריך אישור:
21:21 16/12/2025

ד"ר שמואלי בן ציון
רופא מומחה בפטולוגיה

המסמך המומוחב ערך ו"נסגר" באופן אלקטרוני ומצווה במחשב ע"י הרופא הפטולוג. המסמך מכיל מידע חסוי על פי חוק הגנת הפרטויות וחוק זכויות החולים.

Soroka Medical Center
Pathology Institute
Report date: 16/12/2025

SOROKA
Medical Center
feeling secure

אמה

Female |

Cancer Type: endometrial carcinoma | Tumor Purity: 80.000% | Tumor Cellularity: 0.38 | Tissue Type: FFPE

Summary

Low (4.73 Mut/Mb) TMB	Stable (2.8) MSI	2 Relevant Biomarkers	1 Therapies Available	27 Clinical Trials
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Reportable Alterations In Clinically Significant Genes

Gene	Detected	Finding
AKT1	Not detected	
BRAF	Not detected	
CCNE1	Not detected	
DPYD	Not detected	
ERBB2	Not detected	
FBXW7	Detected	c.1514G>T (p.Arg505Leu);
MTAP	Not detected	
NRG1	Not detected	
NTRK1	Not detected	
NTRK2	Not detected	
NTRK3	Not detected	
POLE	Not detected	
PPP2R1A	Not detected	
RET	Not detected	
TP53	Detected	c.401T>G (p.Phe134Cys);

Strong clinical significance - Tier 1

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דוח תוצאות בדיקה פטולוגית מס'

לתשומת לב הרופא

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שם משפחה:

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Report date: 16/12/2025

TP53 c.401T>G p.Phe134Cys	chr17:7578529-7578529 Transcript: NM_000546.6 Responsive to: None Resistance to: None	23.32% Allelic Frequency
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Potential clinical significance - Tier 2

FBXW7 c.1514G>T p.Arg505Leu	chr4:153247288-153247288 Transcript: NM_001349798.2 Responsive to: None Resistance to: None	16.35% Allelic Frequency
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Unknown clinical significance - Tier 3

FAT1 c.3029T>C p.Vel1010Ala	chr4:187627953-187627953 Transcript: NM_005245.4 Responsive to: None Resistance to: None	54.07% Allelic Frequency
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TBX3 c.959C>T p.Ser320Phe	chr12:115114198-115114198 Transcript: NM_005996.4 Responsive to: None Resistance to: None	46.00% Allelic Frequency
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TSC2 c.400G>A p.Glu134Lys	chr16:2104360-2104360 Transcript: NM_000548.5 Responsive to: None Resistance to: None	7.40% Allelic Frequency
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EN01 c.1048G>A p.Val350Met	chr1.8923969-8923969 Transcript: NM_001428.5 Responsive to: None Resistance to: None	26.85% Allelic Frequency
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DUPLICATION	chr12:25362709-25398388 35.68 Kb ETRF1, KRAS Responsive to: None Resistance to: None	6.11 Copy Number
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MSI **Responsive to:** None
Resistance to: None



אמה

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TMB	Responsive to: None Resistance to: None	4.73 Muts/Mb
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Relevant Therapy

TP53 | p.Phe134Cys

No responsive therapeutic evidence related to this biomarker was found

(A) In this cancer type (B) Based on well-powered studies (C) In other cancer type (D) Based on preclinical studies (-) No evidence

*Showing the most advanced clinical trial phase

FBXW7 | p.Arg505Leu

No responsive therapeutic evidence related to this biomarker was found

(A) In this cancer type (B) Based on well-powered studies (C) In other cancer type (D) Based on preclinical studies (-) No evidence

*Showing the most advanced clinical trial phase

Relevant Clinical Trials

Details	Status	ID	Phase	Biomarkers
Phase I Study of Autologous CDB+ and CD4+ Engineered T Cell Receptor T Cells in Subjects With Advanced or Metastatic Solid Tumor	Recruiting	NCT6105021 https://clinicaltrials.gov/ct2/show/NCT06105021	1 2	DUPLICATION
A First-in-Human (FIH), Open-Label, Phase Ia/b Dose Escalation and Expansion Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of SON-DP in Participants With Relapsed/Metastatic Solid Tumors	Recruiting	NCT5989724 https://clinicaltrials.gov/ct2/show/NCT05989724	1	TP53 p.Phe134Cys
A Phase 1, Open-label Study of Oral BDTX-4933 in Patients With KRAS, BRAF and Other Select RAS/MAPK Mutation Positive Neoplasms	Recruiting	NCT5786924 https://clinicaltrials.gov/ct2/show/NCT05786924	1	DUPLICATION
Trial of Maintenance With Niraparib in Patients With Stage III, Stage IV or Platinum-sensitive Recurrent Uterine Serous Carcinoma	Recruiting	NCT4080284 https://clinicaltrials.gov/ct2/show/NCT04080284	2	TP53 p.Phe134Cys



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Phase I/II Safety and Pharmacodynamic Study of Neoadjuvant (NACT) Paclitaxel and Carboplatin With Ipatasertib as Initial Therapy of Ovarian Cancer PTMA 100805	Recruiting	NCT5276973 https://clinicaltrials.gov/ct2/show/NCT05276973	1 3	TP53 p.Phe134Cys
Efficacy and Safety of Camrelizumab Plus Albumin-bound Paclitaxel/Carboplatin Followed by Camrelizumab With or Without Fluzoparib Maintenance Therapy for TP-53 Mutated Recurrent or Metastatic Endometrial Cancer: A Phase II Trial	Recruiting	NCT6413992 https://clinicaltrials.gov/ct2/show/NCT06413992	2 2	TP53 p.Phe134Cys
An Open-Label Phase 1 Study of ASP4396 in Participants With Locally Advanced (Unresectable) or Metastatic Solid Tumor Malignancies With KRAS G12D Mutation	Recruiting	NCT6364696 https://clinicaltrials.gov/ct2/show/NCT06364696	1 6	DUPLICATION
A Phase I/II Dose Escalation Study to Evaluating the Tolerability, Safety, Efficacy and Pharmacokinetics of ZG2001 Tosilate Tablets in Participants With KRAS Mutated Advanced Solid Tumours	Recruiting	NCT6237413 https://clinicaltrials.gov/ct2/show/NCT06237413	1 2 3	DUPLICATION
A Phase 1 Study of the SHP2 Inhibitor BBP-398 (Formerly Known as IACS-15509) in Combination With the Programmed Death Receptor-1 Blocking Antibody Nivolumab in Patients With Advanced Non-Small Cell Lung Cancer With a KRAS Mutation	Recruiting	NCT5375084 https://clinicaltrials.gov/ct2/show/NCT05375084	1 4	DUPLICATION
Refining Adjuvant Treatment IN Endometrial Cancer Based On Molecular Features: the p53abn-RED Trial, the MMRd-GREEN Trial, the NSMP-ORANGE Trial and the POLEMut-BLUE Trial	Recruiting	NCT5255653 https://clinicaltrials.gov/ct2/show/NCT05255653	3 2 3	TP53 p.Phe134Cys
A Phase 3, Randomized, Placebo-Controlled, Double-Blind, Multicenter Trial of Selinexor in Maintenance Therapy After Systemic Therapy for Patients With p53 Wild-Type, Advanced or Recurrent Endometrial Carcinoma	Recruiting	NCT5611931 https://clinicaltrials.gov/ct2/show/NCT05611931	3 1	TP53 p.Phe134Cys

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A Phase II Study of Tailored Adjuvant Therapy in POLE-Mutated and p53-Wildtype/NSMP Early Stage Endometrial Cancer (RAINBO BLUE & TAPER)	Recruiting	NCT5640999 https://clinicaltrials.gov/ct2/show/NCT05640999	9	TP53 p.Phe134Cys
A Phase 1, Open-Label Dose Escalation of HBI-2376 in Patients With Advanced Malignant Solid Tumors Harboring KRAS or EGFR Mutations	Recruiting	NCT5163028 https://clinicaltrials.gov/ct2/show/NCT05163028	0	DUPLICATION
A Phase 1/2a, Multicenter, Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Preliminary Evidence of Antitumor Activity of JAB-3312 Based Combination Therapies in Adult Patients With Advanced Solid Tumors	Recruiting	NCT4720976 https://clinicaltrials.gov/ct2/show/NCT04720976	6	DUPLICATION
An Open-label, Phase 1, Multicenter Study to Evaluate the Safety and Preliminary Antitumor Activity of NT-112 in Human Leukocyte Antigen-C*08:02 Positive Adult Subjects With Unresectable, Advanced, and/or Metastatic Solid Tumors That Are Positive for the KRAS G12D Mutation	Recruiting	NCT6218914 https://clinicaltrials.gov/ct2/show/NCT06218914	4	DUPLICATION
A Phase I Clinical Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Preliminary Efficacy of QLC1101 Monotherapy in the Treatment of Patients With Advanced Solid Tumors Harboring a KRAS G12D Mutation	Recruiting	NCT6403735 https://clinicaltrials.gov/ct2/show/NCT06403735	5	DUPLICATION
Canadian Multi-arm Multi-stage Randomized Controlled Trial Assessing Front Line and Maintenance Treatment in Serous or p53 Mutant Endometrial Cancer	Recruiting	NCT4159155 https://clinicaltrials.gov/ct2/show/NCT04159155	5	TP53 p.Phe134Cys
A Phase 1/2 Open-label Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Efficacy of PC14586 in Patients With Locally Advanced or Metastatic Solid Tumors Harboring a TP53 Y220C Mutation (PYNNACLE)	Recruiting	NCT4585750 https://clinicaltrials.gov/ct2/show/NCT04585750	0	TP53 p.Phe134Cys

דוח תוצאות בדיקה פתולוגית מס'

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A Phase 1/2 Multiple Expansion Cohort Trial of MRTX1133 in Patients With Advanced Solid Tumors Harboring a KRAS G12D Mutation	Recruiting	NCT5737706 https://clinicaltrials.gov/ct2/show/NCT0573770	1 2	DUPLICATION
Phase I Study of NEROFE and Doxorubicin in KRAS-mutated ST2-positive Solid Tumors	Recruiting	NCT5661201 https://clinicaltrials.gov/ct2/show/NCT0566120	1	DUPLICATION
A Phase 1 Study of ASP3082 in Participants With Previously Treated Locally Advanced or Metastatic Solid Tumor Malignancies With KRAS G12D Mutation	Recruiting	NCT5382559 https://clinicaltrials.gov/ct2/show/NCT0538255	1	DUPLICATION
A Phase 1/2, Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of TNG260 as Single Agent and in Combination With an Anti-PD-1 Antibody in Patients With STK11 Mutated Advanced Solid Tumors	Recruiting	NCT5887492 https://clinicaltrials.gov/ct2/show/NCT0588749	1 2	DUPLICATION
A First-in-Human, Phase 1a/1b, Open Label, Dose-Escalation and Expansion Study to Investigate the Safety, Pharmacokinetics, and Antitumor Activity of the RAF Dimer Inhibitor BGB-3245 in Patients With Advanced or Refractory Tumors	Recruiting	NCT4249843 https://clinicaltrials.gov/ct2/show/NCT0424984	1	DUPLICATION
A Phase 1/2 Multiple Expansion Cohort Trial of the SOS1 Inhibitor MRTX0902 in Patients With Advanced Solid Tumors Harboring Mutations in the KRAS MAPK Pathway	Recruiting	NCT5578092 https://clinicaltrials.gov/ct2/show/NCT0557809	1 2	DUPLICATION
Sotorasib in Advanced KRASG12C-mutated Non-small Cell Lung Cancer Patients With Comorbidities	Recruiting	NCT5311709 https://clinicaltrials.gov/ct2/show/NCT0531170	2	DUPLICATION
A Phase 1, Open Label, Dose Escalation of HBI-2438 in Patients With Advanced Malignant Solid Tumors Harboring KRAS G12C Mutation	Recruiting	NCT5485974 https://clinicaltrials.gov/ct2/show/NCT0548597	1	DUPLICATION
A Phase 1b/II, Open-label Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of D-1553 Combined With IN10018 in Subjects With Locally Advanced or Metastatic Solid Tumors With KRAS G12C Mutation	Recruiting	NCT6166836 https://clinicaltrials.gov/ct2/show/NCT0616683	1 2	DUPLICATION

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דו"ח תוצאות בדיקה פתולוגית מס'

ת.א.:

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Interpretation

Strong clinical significance - Tier 1

TP53 | p.Phe134Cys

p.Phe134Cys | c.401T>G | NM_000546.6 | CHR17: 7578529 None | VAF: 23.32% | Coverage: 1998 | COSMIC ID: COSV52722353 | rs780442292 | ClinVar ID: RCV000656580, RCV000214547, RCV005600832

GENE SUMMARY

Tumor protein p53 (TP53), is a tumor suppressor and oncogene transcription factor involved in cell cycle arrest, DNA repair, and apoptosis, and is the most frequently mutated gene in cancer. TP53 somatic missense mutations are highly frequent in most cancer types. TP53 germline mutations are common in Li-Fraumeni syndrome, a cancer predisposition syndrome. TP53-NTRK1 fusion is observed in Spitz nevus and TP53-PPRAD, TP53-VAV1, TP53-EMR1, TP53-DDX39B, and TP53-SAT2 fusions are observed in osteosarcoma.

VARIANT INTERPRETATION

p.Phe134Cys, a non synonymous variant in the TP53, an oncogene and a tumor suppressor gene. The variant resides within the P53 domain. The variant was reported in COSMIC (COSV52722353,COSM4169324) and ClinVar (230477). The variant was classified as a Tier 3 using the ASCO/CAP/AMP Guidelines and as Pathogenic according to the ACMG Guidelines.

ATHERAPEUTIC EVIDENCE

Below is list of therapies for which evidence was found associated with the tumor profile

Responsive

No responsive therapeutic evidence related to this biomarker was found

Resistance

No resistant therapeutic evidence related to this biomarker was found

DIAGNOSTIC EVIDENCE

Below is list of evidences pertain to tumor profile's diagnostic attributes

Diagnostic Positive

PMID: N/A

The WHO committee on CNS tumors now recommends subclassification of medulloblastomas into four distinct groups: i) WNT-activated; ii) Sonic hedgehog (SHH)-activated and TP53-mutant; iii) SHH-activated and TP53-wild type; and iv) non-WNT/non-SHH. None of the molecular markers associated with each medulloblastoma subtype is specific to medulloblastoma; the diagnosis of medulloblastoma is still made on the basis of light microscopy (category 2A).

PROGNOSTIC EVIDENCE

Below is list of evidences pertain to tumor profile's prognostic attributes

Prognostic Poor Outcome

PMID: N/A

The authors analyzed 328 patients with CLL, of which 28 were identified to have TP53 mutations. Patients with TP53 mutations were found to have significantly shorter progression-free (HR = 3.8; P < 0.001) and overall survival (HR = 7.2; P < 0.001).

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Prognostic ↓ Poor Outcome		PMID: N/A
In a study of 126 patients with long-term follow-up, TP53 mutations were significantly associated with shorter median survival in patients ($P = 0.002$) from time of diagnosis. The median survival from the time of first observation of a TP53 mutation was much more pronounced ($P < 0.001$). These findings were statistically independent of 17p deletions.		
Prognostic ↓ Poor Outcome		PMID: N/A
In a multivariate analysis of 774 CLL patients, TP53 aberrations were significantly correlated with shorter time to first treatment (HR=2.081; 95% CI=1.431-3.021). This finding was independent of IGHV mutation status.		
Prognostic ↓ Poor Outcome		PMID: N/A
In the CLL4 trial assessing first line treatment with chlorambucil or fludarabine with or without cyclophosphamide, patients with TP53 mutations experienced poorer overall response rates (27% vs 83%), shorter progression free survival (5 year PFS 5% vs 17%), and overall survival (20% vs 59%) compared to patients without TP53 mutations.		
Prognostic ↓ Poor Outcome		PMID: N/A
In a cohort of 406 patients with CLL, those patients with clonal or sub-clonal mutations in TP53 had significantly shorter overall survival (HR: 1.71; 95% CI: 1.28-2.26, $P = .0001$).		
Prognostic ↓ Poor Outcome		PMID: N/A
Among SHH-activated medulloblastomas, detection of TP53 mutations is associated with more aggressive behavior, often in the setting of germline TP53 mutations, wildtype SHH-activated medulloblastomas have a variable course, and are uncommon in adults (category 2A).		
Prognostic ↓ Poor Outcome		PMID: N/A
TP53 mutation has been associated with poor prognosis in patients with mantle cell lymphoma (MCL) treated with conventional therapy, including transplant (category 2A). TP53 sequencing would be useful to identify patients with typical MCL with an expected aggressive clinical course, particularly if upfront HCT is anticipated.		
Prognostic ↓ Poor Outcome		PMID: N/A
TP53 mutation is associated with poor prognosis in patients treated with conventional therapy, including hematopoietic cell transplantation (HCT). In an analysis that evaluated the prognostic effect of the most common genomic alterations in 183 patients with MCL treated in clinical trials, TP53 mutations were significantly associated with Ki-67 >30%, blastoid morphology, and inferior responses to both induction chemotherapy and high-dose chemotherapy.		

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Prognostic ↓ Poor Outcome		PMID: N/A
<p>Patients with TP53 mutations are group with poor prognosis, and should be considered for enrollment in clinical trials. TP53 mutations have been reported in approximately 12-13% of AML cases, and are associated with unfavorable risk and poor outcomes. TP53 mutations are also most common in AML with complex karyotype. However, in therapy related AML, TP53 mutations are more frequently associated with monosomal karyotype, and with abnormalities in chromosomes 5 and 7. Interestingly, compared to TP53 deletions, TP53 mutations negatively impacted survival in AML (36 months vs. 9 months, respectively; P<0.001), suggesting the importance of evaluating both TP53 mutation and deletion status. Both NCCN and the ELN classify non APL AML patients with wild type NPM1 and FLT3-ITDhigh, mutated TP53, mutated RUNX1, or mutated ASXL1 as having poor risk. TP53 mutations are significantly associated with AML with complex and monosomal karyotype. Prognostic impact of a marker is treatment dependant and may change with new therapies. Several gene mutations are associated with prognoses in a subset of patients (category 2A) and may guide treatment decisions (category 2B). Presently c-KIT, FLT3-ITD, FLT3-TKD, NPM1, CEBPA (biallelic), IDH1, IDH2, RUNX1, ASXL1, TP53, BCR-ABL and PML-RAR alpha are included in this group.</p>		
Prognostic ↓ Poor Outcome		PMID: N/A
<p>"In a study of 97 patients with AML treated with HSCT, 40 had TP53 mutations comprising a total of 44 mutations. Patients with a TP53 mutation had a reduced three year probability of overall survival and event-free survival compared to patients with the wild-type TP53."</p>		
Prognostic ↓ Poor Outcome		PMID: N/A
<p>Nonsense or frameshift mutations in TP53 are independently associated with a poor prognosis in patients with myelodysplastic syndromes (MDS) (category 2A).</p>		
Prognostic ↓ Poor Outcome		PMID: N/A
<p>The presence of at least one of the "adverse variants/mutations" (SH2B3/IDH2/U2AF1/SRSF2/SF3B1/EZH2/TP53/RUNX1) is associated with inferior overall survival (compared to other sequence variants/mutations) in patients with essential thrombocythemia (ET), independent of age and karyotype. TP53 mutations in patients with essential thrombocythemia (ET) are associated with inferior leukemia-free survival in multivariate analysis (category 2A).</p>		
Prognostic ↓ Poor Outcome		PMID: N/A
<p>In patients with primary myelofibrosis (PMF), TP53 mutations are associated with leukemic transformation (category 2A).</p>		
Prognostic ↓ Poor Outcome		PMID: N/A
<p>"TP53 mutation was shown to be associated with shorter overall survival in patients with adrenocortical tumors (log-rank test; P=0.098). Of 20 patients studied, 5 had coding mutation in TP53. Four of the 5 patients with a TP53 mutation had metastases at diagnosis or detected soon thereafter, and 3 of 4 died of disease within 12 months of surgical resection."</p>		
Prognostic ↓ Poor Outcome		PMID: N/A
<p>In a retrospective study of patients with esophageal carcinoma, those with mutations in TP53 had worse overall survival.</p>		

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Prognostic ↓ Poor Outcome

PMID: N/A

"In children with bone marrow relapsed B-cell precursor acute lymphoblastic leukemia, in multivariate analysis those with mutations in TP53 had worse event-free survival than patients without mutations."

Prognostic ↓ Poor Outcome

PMID: N/A

In relapsed B-ALL patients, TP53 mutations were associated with morphologic nonresponse to therapy (>5% blasts in the bone marrow after 9 weeks of treatment) as well as reduced event free and overall survival when compared to TP53 wildtype patients.

Prognostic ↓ Poor Outcome

PMID: 12509970

Oral squamous cell carcinoma patients with TP53 mutations in the DNA binding domain (L2, L3 and the LSH motif) have significantly reduced cumulative survival when compared to patients with TP53 mutations outside of this DNA binding domain. These mutations were also significantly associated with locoregional failure, cervical lymph node metastasis and distant metastasis, likely contributing to this finding.

Prognostic ↓ Poor Outcome

PMID: 11595686

In a study of invasive ovarian carcinoma patients who had undergone surgery, the p53 alteration variant was defined as p53 mutation or p53 overexpression by immunostain (>10% positive). Patients with p53 alterations showed increase in poor tumor cell differentiation ($p<0.001$) and increase in tumor cellular S-phase fraction ($p<0.001$). Out of 178 patients, p53 alteration ($n=132$) was associated with decreased overall survival in comparison to normal p53 ($n=46$), $p=0.007$.

Prognostic ↓ Poor Outcome

PMID: 11595686

Patients with conserved domain p53 mutation ($n=61$) were compared with those with wild type or non-conserved domain p53 mutation ($n=117$) in a cohort of 178 invasive ovarian carcinoma patients who had undergone surgery. Overall survival was decreased in the cohort with conserved domain mutation ($p=0.005$). Conserved domain mutation was an independent factor in univariate (but not multivariate) analysis of overall survival with relative risk 1.70 (1.17-2.47, $p<0.007$).

Prognostic ↓ Poor Outcome

PMID: N/A

In a retrospective study of patients with esophageal carcinoma, those with mutations in TP53 had worse overall survival.

Prognostic ↓ Poor Outcome

PMID: N/A

"Tumors from 114 patients with head and neck squamous cell carcinoma were analyzed for TP53 mutations. Of the 93 patients treated with radiotherapy, patients with mutations in TP53 had lower rates of loco-regional control and shorter disease-free, disease-specific, and overall survival."

Prognostic ↓ Poor Outcome

PMID: N/A

"In a study of 74 patients with head and neck squamous cell carcinoma, those with disruptive mutations in TP53 had shorter overall survival and a higher rate of locoregional recurrence than those without mutations or with nondisruptive mutations."

דוח תוצאות בדיקה פטולוגית מס'

לתשומת לב הרופא

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שם פרטי:

שם משפחה:

אפריל

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Prognostic		Poor Outcome	PMID: N/A
"In patients with myelodysplastic syndrome, in a multivariate analysis those with mutations in TP53 had shorter overall survival than wild-type patients."			
Prognostic		Poor Outcome	PMID: N/A
A study of 53 patients with B-CLL found a significant resistance to chemotherapy and corresponding poor clinical outcomes among the 7 treated patients with p53 mutations compared to the 29 treated patients without.			
Prognostic		Poor Outcome	PMID: N/A
"In patients with myeloma, those with mutations in TP53 had worse overall survival than those without."			
Prognostic		Poor Outcome	PMID: N/A
Acute and lymphoma subtypes were associated with higher frequencies of TP53 and IRF4 mutations as well as programmed death ligand 1 (PD-L1) amplifications and CDKN2A deletions compared with chronic and smoldering subtypes.			
Prognostic		Poor Outcome	PMID: N/A
Genetic alterations in MYC, NRAS and TP53 are seen only in monomorphic post-transplant lymphoproliferative disease (PTLD) and BCL6 mutations (present in 43% of the polymorphic PTLD) have been associated with shorter survival and poor response to therapy.			

Potential clinical significance - Tier 2

FBXW7 | p.Arg505Leu

p.Arg505Leu | c.1514G>T | NM_001349798.2 | CHR4: 153247288 None | VAF: 16.35% | Coverage: 2000 | COSMIC ID: COSV55908371 | rs10527519896

GENE SUMMARY
F-box WD repeat-containing protein 7 (**FBXW7**), encodes an F-box protein subunit involved in recognition and targeting of c-MYC and/or mTOR proteins, which are involved in cell division and cell growth, for degradation. **FBXW7** mutations have been associated with cholangiocarcinoma, acute lymphocytic leukemia, colorectal cancer, gastric cancer, and endometrial cancer.

VARIANT INTERPRETATION

VARIANT INTERPRETATION
p.Arg505Leu, a non synonymous variant in the FBXW7, a tumor suppressor gene. The variant resides within the PQQ_2, WD40 domains. The variant was reported in COSMIC (COSVS55908371, COSM1732672) and ClinVar (376424). The variant was classified as a Tier 2 using the ASCO/CAP/AMP Guidelines and as Likely Pathogenic according to the ACMG Guidelines.

THERAPEUTIC EVIDENCE

THERAPEUTIC EVIDENCE
Below is list of therapies for which evidence was found associated with the tumor profile

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 Responsive

No responsive therapeutic evidence related to this biomarker was found

 Resistance

No resistant therapeutic evidence related to this biomarker was found

DIAGNOSTIC EVIDENCE

Below is list of evidences pertain to tumor profile's diagnostic attributes

No diagnostic evidence related to this biomarker was found

PROGNOSTIC EVIDENCE

Below is list of evidences pertain to tumor profile's prognostic attributes

No prognostic evidence related to this biomarker was found

General Information

The Ion Torrent™ Oncomine™ Comprehensive Assay v3 is a targeted, next-generation sequencing (NGS) assay that enables the detection of relevant single-nucleotide variants (SNVs), copy number variations (CNVs), gene fusions, and indels. Oncomine™ Comprehensive Panel is used to construct the library and sequencing is performed using Ion Torrent Sequencing System.

This Next Generation Sequencing (NGS) test for identifying alterations in cancer related genes in FFPE tumor tissue was validated by the molecular pathology unit in Soroka University Medical Center and approved by Israeli Ministry of Health. Validation showed 100% specificity for each mutation tested and 1% limit of detection.

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ת.ז. :

שם פרטי :

שם משפחה :

Soroka Medical Center
Pathology Institute
Report date: 16/12/2025



אמה

Female |

Cancer Type: | Tumor Purity: 80.000% | Tumor Cellularity: 0.38 | Tissue Type: FFPE

SUMMARY

Relevant Biomarkers	Therapies Available	Clinical Trials	TMB	MSI
2	1	27	Low 4.73 Mut/Mb	Stable 2.8

Reportable Alterations In Clinically Significant Genes

AKT1 (Not detected)
 BRAF (Not detected)
 CCNE1 (Not detected)
 DPYD (Not detected)
 ERBB2 (Not detected)
 FBXW7 (Detected): c.1514G>T (p.Arg505Leu);
 MTAP (Not detected)
 NRG1 (Not detected)
 NTRK1 (Not detected)
 NTRK2 (Not detected)
 NTRK3 (Not detected)
 POLE (Not detected)
 PPP2R1A (Not detected)
 RET (Not detected)
 TP53 (Detected): c.401T>G (p.Phe134Cys);

TIER I: VARIANTS OF STRONG CLINICAL SIGNIFICANCE

TP53 | p.Phe134Cys | c.401T>G | NM_000546.6 | VAF: 23.32% | Exon 5 | chr17:7578529 | Pathogenic

TIER II: VARIANTS OF POTENTIAL CLINICAL SIGNIFICANCE

FBXW7 | p.Arg505Leu | c.1514G>T | NM_001349798.2 | VAF: 16.35% | Exon 12 | chr4:153247288 | Likely Pathogenic

TIER III: VARIANTS OF UNCERTAIN CLINICAL SIGNIFICANCE

FAT1 | p.Val1010Ala | c.3029T>C | NM_005245.4 | VAF: 54.07% | Exon 2 | chr4:187627953 | VUS

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TBX3 | p.Ser320Phe | c.859C>T | NM_005006.4 | VAF: 40.00% | Exon 5 | chr12:115114198 | VUS

TSC2 | p.Glu134Lys | c.400G>A | NM_000548.5 | VAF: 7.40% | Exon 5 | chr16:2104360 | VUS

ENO1 | p.Val350Met | c.1048G>A | NM_001428.5 | VAF: 26.85% | Exon 9 | chr1:8923969 | VUS

Duplication | ETFRF1,KRAS | chr12:25362709-25398388 | 35.68 Kb | Copy number: 6.11 | VUS

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