RUOLO RETE ONCOLOGICA ACCESSO, APPROPRIATEZZA

COORDINATORE AREA OSPEDALIERA RETE ONCOLOGICA DEL PIEMONTE E DELLA VALLE D'AOSTA

Coordinatore MTB Regionale

CRITICITA’ BIOLOGIA MOLECOLARE

- **MANCANZA PSDTA UNICO PER PATOLOGIA**
- **MANCANZA DI LINEE GUIDA DI RETE PER OTTIMIZZARE IMMAGINI RADIOLOGICHE E BIOPSIE VALIDE PER VALUTAZIONI BIOMOLECOLARI**
- **MANCANZA DI ELENCO DI RETE PER I TEST DA CONSIDERARE STANDARD NELLE DIVERSE PATOLOGIE**

CRITICITA' BIOLOGIA MOLECOLARE

* **NON IDENTIFICATI I LABORATORI CERTIFICATI IN GRADO DI PROCESSARE IL MATERIALE PER I TEST CON LE RELATIVE TEMPISTICHE**

* **NECESSITA' DI IMPLEMENTARE LA GENETICA IN ONCOLOGIA**

* **NON INDICAZIONI SUI TEST AGNOSTICI**

ATTIVITA' DI RETE

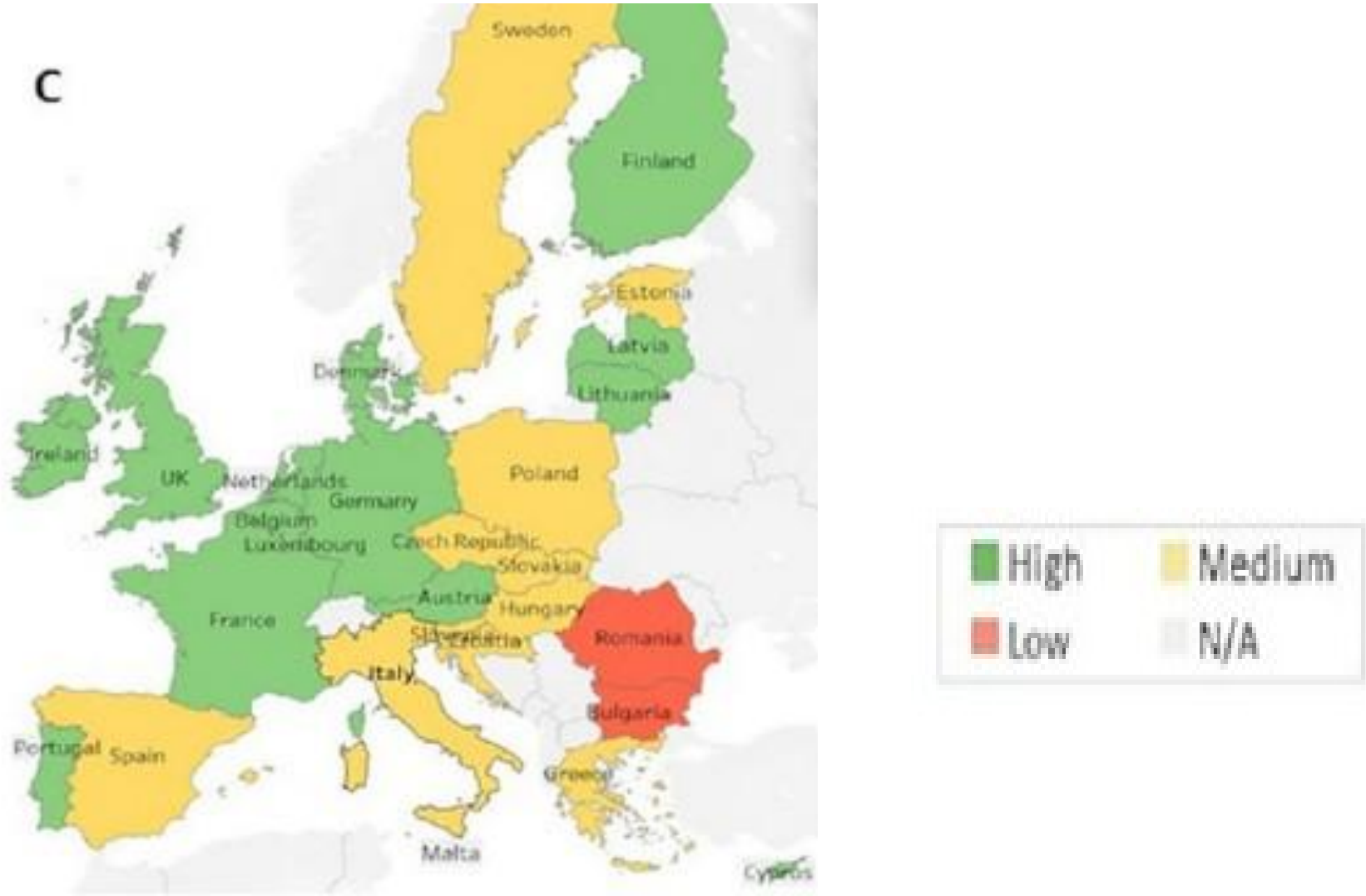
UNIFICATI 36 PSDTA DI PATOLOGIA

INDICATE MODALITA' DI BIOPSIA E GESTIONE DEL MATERIALE

INDIVIDUATI DAI GRUPPI DI STUDIO I TEST BIOMOLECOLARI FONDAMENTALI PER LA GESTIONE DELLE PATOLOGIE ONCOLOGICHE

ISTITUZIONE MTB UNICO REGIONALE (23.7.21)

NGS Laboratories Quality (ISO 15189)



LABORATORI NGS PIEMONTE

5 OPERATORI (1 Direttore, 2 biologi dirigenti, 2 tecnici)

Refertazione NGS con doppio operatore

ISO 15189 da ACCREDIA

IVDR (2024) solo laboratori ISO 15189 potranno utilizzare «laboratory developed tests»
Tutti gli altri laboratori dovranno utilizzare Kit marchiato IVDR

- AOU Città della Salute e della Scienza di Torino

  - Esecuzione test diagnostici in Oncoematologia
    AOU Città della Salute e della Scienza di Torino
  - Esecuzione test diagnostici in NGS per neoplasie solide (esclusi sarcomi):
    AOU Città della Salute e della Scienza di Torino
  - Esecuzione test diagnostici in NGS per sarcomi:
    AOU Città della Salute e della Scienza di Torino - Presidi ospedalieri 0.I.R.M. - S. Anna, Centro Trapianti cellule staminali

- ASL Città di Torino

- ASL di Biella

- AOU Maggiore della Carità di Novara

  - Esecuzione test diagnostici in Oncoematologia

- AO Santa Croce e Carle Cuneo
- AO SS. Antonio e Biagio e Cesare Arrigo di Alessandria
- AOU San Luigi Gonzaga di Orbassano

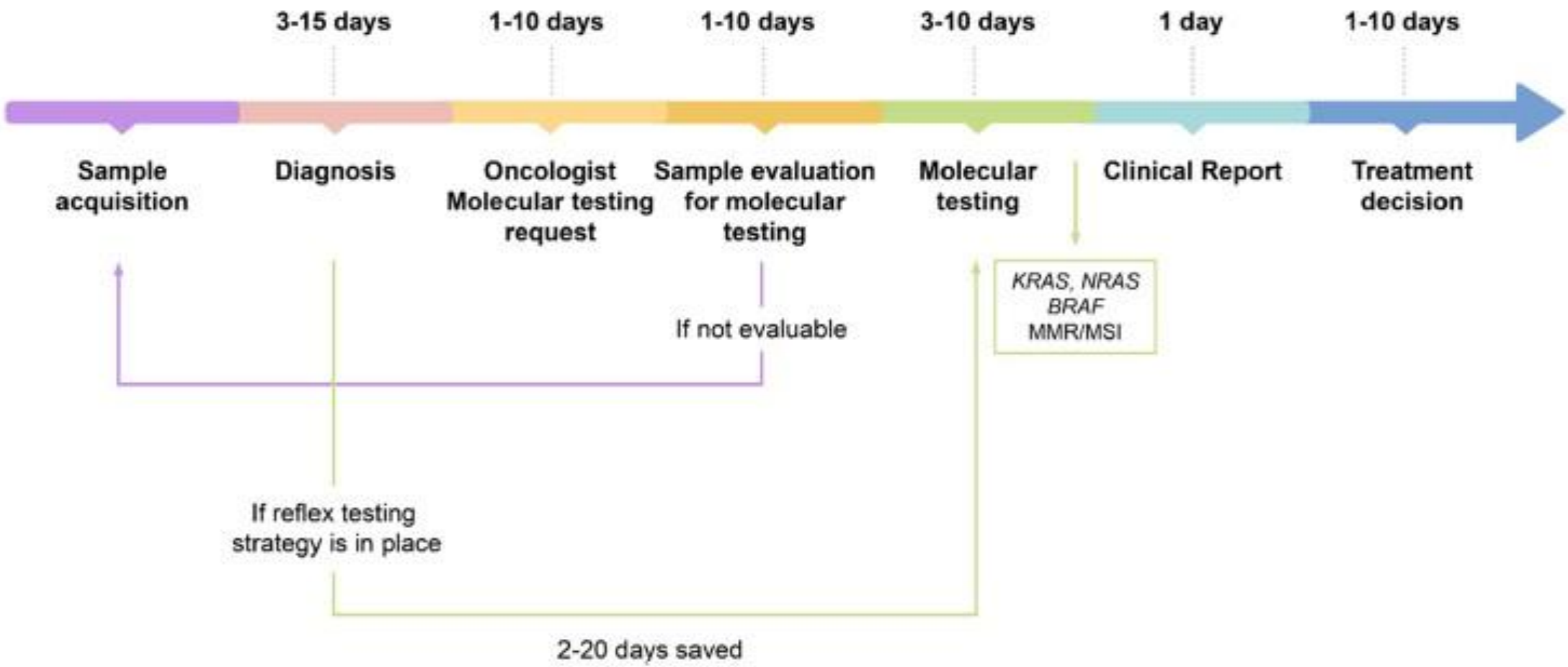
  - Esecuzione test diagnostici in NGS per neoplasie solide (esclusi sarcomi)

- Istituto di Candiolo – IRCCS

  - Esecuzione test diagnostici in Oncoematologia
  - Esecuzione test diagnostici in NGS per neoplasie solide (esclusi sarcomi)

TEST NGS PIEMONTE

- **8 laboratori NGS POLMONE (DGR del 22.12.22)**
- **3 laboratori NGS COLANGIOCARCINOMA (DGR del 9.10.23)**
- **1 laboratorio per HRD**
- **1 laboratorio per PANNELLO MTB**


3-15 days
1-10 days
1-10 days
3-10 days
1 day
1-10 days
Sample acquisition
Diagnosis
Oncologist Molecular testing request
Sample evaluation for molecular testing
Molecular testing
Clinical Report
Treatment decision
KRAS, NRAS
BRAF
MMR/MSI
If not evaluable
If reflex testing strategy is in place
2-20 days saved

TIMING (MAX)

- **LUNG CANCER : 15 DAYS**
- **COLANGIOCARCINOMA: 21 DAYS**
- **HRD : 15-21 DAYS**

- **MTB : 15 DAYS**

TARIFFE NGS PIEMONTE

REAGENTI

MATERIALE LABORATORIO

AMMORTAMENTO STRUMENTI

CONTRATTI ASSISTENZA TECNICA E

MANUTENZIONE (15% VALORE STRUMENTO /ANNO)

MANTENIMENTO CERTIFICAZIONI QUALITA’

VERIFICHE ESTERNE (controlli europei EMQN)

Codici e rimborsi NGS Lombardia

Descrizione	tariffa_euro
ANALISI DI SEQUENZA GENICHE MEDIANTE NEXT GENERATION SEQUENCING (NGS) e tecniche assimilabili per analisi mutazionale di malattia, incluso ove previsto test di conferma delle varianti refertate che necessita di un solo gene per la diagnosi	518,00
ANALISI DI SEQUENZA GENICHE MEDIANTE NEXT GENERATION SEQUENCING (NGS) e tecniche assimilabili per l'analisi mutazionale di malattia, incluso ove previsto il test di conferma delle varianti refertate che necessita da 2 a fino al massimo 10 geni refertati per la diagnosi.	1.036,00
ANALISI DI SEQUENZA GENICHE MEDIANTE NEXT GENERATION SEQUENCING (NGS) e tecniche assimilabili per l'analisi mutazionale di malattia, incluso ove previsto il test di conferma delle varianti refertate che necessita da 11 a fino al massimo 50 geni refertati per la diagnosi.	1.554,00
ANALISI DI SEQUENZA GENICHE MEDIANTE NEXT GENERATION SEQUENCING (NGS) e tecniche assimilabili per l'analisi mutazionale di malattia, incluso ove previsto test di conferma delle varianti refertate, che necessita di un numero superiore a 50 geni refertati per la diagnosi.	2.072,00

REFERTO

- **NECESSITA' DI REFERTAZIONE OMOGENEA SUL TERRITORIO**
- **LEGGIBILITA' CLINICA DEL REFERTO**
- **SEGNALAZIONE DI EVENTUALI ULTERIORI APPROFONDIMENTI**
- **INDICAZIONE DEI LIMITI DELLA ATTENDIBILITA' DEI DATI**
- **SEGNALAZIONE DI BIAS INTERPRETATVI (MUTAZIONI CHE INDICANO UNA SENSIBILITA' AL TARGET UNITAMENTE A MUTAZIONI DI RESISTENZA)**

FUTURO NGS

- **UN LABORATORIO OGNI 600.000 – 1 MILIONE ABITANTI**
- **E’ UN ATTIVITA’ DI LABORATORIO (REFERTO) O UN ATTIVITA’ CLINICA INTEGRATA ?**
- **I PATOLOGI / BIOLOGI MOLECOLARI DEVONO CONTAMINARE ONCOLOGI**
- **CREARE UN TEAM UNICO CON PATOLOGI DI DIVERSA COMPETENZA NEI DIVERSI CONTESTI CLINICI / BIOMOLECOLARI ?**

rete
oncologica
Piemonte | Valle d'Aosta

Molecular Tumor Board

CONSUNTIVO ATTIVITA’

- **PRIMA SEDUTA : 14.12.23**
- **NUMERO SEDUTE : 55**
- **CASI PRESENTATI DAI GIC AL MTB : 165**
- **CASI DISCUSSI MTB : 153 (93%)**
- **CASI TESTATI = 118/153 (77%)**
- **CASI DRUGGABLE = 85/118 (72%)**

NGS (118 TEST)

- **SOMATICO** **110**
- **BIOPSIA LIQUIDA** **8**

- **FondationOne CDx** **106**
- **FondationOne HEME** **4**

- **TURNAROUND TIME** **13 gg (median) (12-17)**

CONSUNTIVO DRUGGABLE

- **N. CASI : 85**
- **SESSO : 53 F (62%) / 32 M (38%)**
- **ETA’ : mediana 55 (23-80)**
- **PS: 0 = 30 (35 %), 1 = 47 (56 %) , 2 = 8 (9 %)**
- **MEDIANA TERAPIE MEDICHE = 2 (0-9)**

CONSUNTIVO DRUGGABLE : SEDI

- **FOCUS IGNOTO = 10**
- **PANCREAS = 9**
- **MAMMELLA = 11**
- **GH. SALIVARI = 7**
- **SARCOMI = 4**
- **OVAIO = 6**
- **ANO = 3**
- **FEGATO = 3**
- **TESTA COLLO = 6**
- **PLEURA/POLMONE = 3**
- **ENDOMETRIO = 2**
- **PROSTATA = 2**
- **ALTRO = 16**

COLON = 2

UTERO =1

MUTAZIONI DRUGGABLE (85 casi)

- **PI3KCA/PTEN = 17 (20 %) (4 GH SALIVARI)**
- **HTMB = 14 (19 %) (3 FOCUS IGNOTO)**
- **BRCA 1-2 + HRD = 15 (14 %) (5 MAMMELLA germ neg)**
  ATM BAP 1 PAP 1
- **CDKN2A/2B+CDK4= 19 (22 %) (4 PANCREAS)**
- **KRAS/BRAF/ = 6 (7%)**
  NF1/HRAS

*** FGFR = 2 (2,3%)**

PAZ IN TERAPIA

- **PI3K = 11/17 (PI3K / mTOR INIB)**
- **HTMB = 12/14 (ANTI PD1)**
- **BRCA 1-2/ HRD + = 11/15 (PARP INIBITORI)**

- **CDKN2A = 10/19 (INIBITORI CICLINE)**
- **MEK INIBITORI = 5 /6 (MEK INIBITORI)**

SOFT TISSUE FIBROMATOSIS: Nirogacestat

FOUNDATIONONE® CDx

PATIENT
03-2024-00104923, IT

TUMOR TYPE
Soft tissue fibromatosis

COUNTRY CODE
IT

REPORT DATE
14 Mar 2024

ORDERED TEST #
ORD-1830469-01

ABOUT THE TEST FoundationOne®CDx is a next-generation sequencing (NGS) based assay that identifies genomic findings within hundreds of cancer-related genes.

PATIENT
- **DISEASE** Soft tissue fibromatosis
- **NAME** 03-2024-00104923, IT
- **DATE OF BIRTH** 05 April 1986
- **SEX** Male
- **MEDICAL RECORD #** MTB-004

PHYSICIAN
- **ORDERING PHYSICIAN** AIROLDI, MARIO
- **MEDICAL FACILITY** OSPEDALE S G BATTISTA MOLINETTE - REPARTO ONCOLOGIA MEDICA 2
- **ADDITIONAL RECIPIENT** None
- **MEDICAL FACILITY ID** 333537
- **PATHOLOGIST** Not Provided

SPECIMEN
- **SPECIMEN SITE** Abdominal wall
- **SPECIMEN ID** I 3058 2023 A2
- **SPECIMEN TYPE** Block
- **DATE OF COLLECTION** 06 March 2023
- **SPECIMEN RECEIVED** 01 March 2024

Genomic Signatures

Microsatellite status - MS-Stable

Tumor Mutational Burden - 1 Muts/Mb

Gene Alterations

For a complete list of the genes assayed, please refer to the Appendix.

APC **E422fs*32, D610fs*14, E1464fs*8**

Report Highlights

- Variants with **diagnostic implications** that may indicate a specific cancer type: ***APC*** **D610fs*14, E1464fs*8, E422fs*32** (p. 3)
- Evidence-matched **clinical trial options** based on this patient's genomic findings: (p. 4)

CARCINOMA TIMICO

PATHOLOGIST COMMENTS

Douglas A. Mata, MD, MPH 11-Nov-2024

A KIT exon 11 V560del mutation was detected. This particular mutation has been recurrently identified in thymic carcinomas, gastrointestinal stromal tumors, and mucosal melanomas, and less commonly has been reported in non-small-cell lung carcinomas. Clinicopathologic correlation is advised.

GENOMIC SIGNATURES	THERAPY AND CLINICAL TRIAL IMPLICATIONS
HRD signature - HRDsig Negative	**No therapies or clinical trials.** See Genomic Signatures section
Microsatellite status - MS-Stable	**No therapies or clinical trials.** See Genomic Signatures section
Tumor Mutational Burden - 2 Muts/Mb	**No therapies or clinical trials.** See Genomic Signatures section

GENE ALTERATIONS	THERAPIES WITH CLINICAL RELEVANCE (IN PATIENT'S TUMOR TYPE)	THERAPIES WITH CLINICAL RELEVANCE (IN OTHER TUMOR TYPE)
KIT - exon 11 deletion (V560del)	none	Dasatinib
		Imatinib
		Nilotinib
		Ponatinib
		Sorafenib
		Sunitinib

10 Trials see p. 9

CA ADENOIDEO CISTICO

GENOMIC SIGNATURES	THERAPY AND CLINICAL TRIAL IMPLICATIONS
HRD signature - HRDsig Negative	**No therapies or clinical trials.** See Genomic Signatures section
Microsatellite status - MS-Stable	**No therapies or clinical trials.** See Genomic Signatures section
Tumor Mutational Burden - 1 Muts/Mb	**No therapies or clinical trials.** See Genomic Signatures section

GENE ALTERATIONS		VAF%	THERAPIES WITH CLINICAL RELEVANCE (IN PATIENT'S TUMOR TYPE)	THERAPIES WITH CLINICAL RELEVANCE (IN OTHER TUMOR TYPE)
KIT -	amplification	-	none	Imatinib
				Nilotinib
				Sorafenib
				Sunitinib
10 Trials see p. 10				
PDGFRA -	amplification	-	none	Imatinib
1 Trial see p. 13				

MESOTELIOMA PERITONEALE

GENOMIC SIGNATURES	THERAPIES WITH CLINICAL RELEVANCE (IN PATIENT'S TUMOR TYPE)	THERAPIES WITH CLINICAL RELEVANCE (IN OTHER TUMOR TYPE)
HRD signature - HRDsig Positive	none	Niraparib
		Olaparib
		Rucaparib
10 Trials see p. 10		Talazoparib
Microsatellite status - MS-Stable	No therapies or clinical trials. See Genomic Signatures section	
Tumor Mutational Burden - 5 Muts/Mb	No therapies or clinical trials. See Genomic Signatures section	

GENE ALTERATIONS	THERAPIES WITH CLINICAL RELEVANCE (IN PATIENT'S TUMOR TYPE)	THERAPIES WITH CLINICAL RELEVANCE (IN OTHER TUMOR TYPE)
CDKN2A - loss	none	none
10 Trials see p. 12		
MTAP - loss	none	none
6 Trials see p. 14		
NF2 - splice site 448-2A>T	none	none
3 Trials see p. 15		

CORDOMA

FOUNDATIONONE®CDx

PATIENT	TUMOR TYPE	REPORT DATE
03-2026-00145170, IT	Bone chordoma	26 Jan 2026
	COUNTRY CODE	ORDERED TEST #
	IT	ORD-2264782-01

GENOMIC SIGNATURES

Tumor Mutational Burden - 12 Muts/Mb

10 Trials see p. 14

THERAPIES WITH CLINICAL RELEVANCE (IN PATIENT'S TUMOR TYPE)	THERAPIES WITH CLINICAL RELEVANCE (IN OTHER TUMOR TYPE)
none	Nivolumab + Ipilimumab 2A
	Pembrolizumab 2A
	Atezolizumab
	Avelumab
	Cemiplimab
	Dostarlimab
	Durvalumab
	Nivolumab
	Retifanlimab
	Serplulimab
	Sugemalimab
	Tislelizumab
	Toripalimab

CA PANCREAS : MEK INIBITORE

GENOMIC SIGNATURES	THERAPY AND CLINICAL TRIAL IMPLICATIONS
HRD signature - HRDsig Negative	No therapies or clinical trials. See Genomic Signatures section
Microsatellite status - MS-Stable	No therapies or clinical trials. See Genomic Signatures section
Tumor Mutational Burden - 0 Muts/Mb	No therapies or clinical trials. See Genomic Signatures section

GENE ALTERATIONS	THERAPIES WITH CLINICAL RELEVANCE (IN PATIENT'S TUMOR TYPE)	THERAPIES WITH CLINICAL RELEVANCE (IN OTHER TUMOR TYPE)
CDKN2A - p16INK4a D84G	none	none
8 Trials see p. 9		
KRAS - G12D	none	none
10 Trials see p. 11		

CA MAMMELLA lum B : BIOPSIA LIQUIDA (PALB 2: VAF 5,3%)

GENOMIC SIGNATURES	THERAPIES WITH CLINICAL RELEVANCE (IN PATIENT'S TUMOR TYPE)	THERAPIES WITH CLINICAL RELEVANCE (IN OTHER TUMOR TYPE)
HRD signature - HRDsig Positive	Olaparib	Niraparib
10 Trials see p. 10	Talazoparib	Rucaparib
Microsatellite status - MS-Stable	No therapies or clinical trials. See Genomic Signatures section	
Tumor Mutational Burden - 4 Muts/Mb	No therapies or clinical trials. See Genomic Signatures section	

GENE ALTERATIONS		VAF%	THERAPIES WITH CLINICAL RELEVANCE (IN PATIENT'S TUMOR TYPE)	THERAPIES WITH CLINICAL RELEVANCE (IN OTHER TUMOR TYPE)
PALB2 -	R175fs*2 - subclonal	5.3%	Olaparib 2A	Niraparib
10 Trials see p. 12			Talazoparib	Rucaparib

☐ *NCCN category for genomic findings in patient's tumor type*

CA POLMONE KRAS G12 C : BIOPSIA LIQUIDA

GENOMIC SIGNATURES	THERAPIES WITH CLINICAL RELEVANCE (IN PATIENT'S TUMOR TYPE)	THERAPIES WITH CLINICAL RELEVANCE (IN OTHER TUMOR TYPE)
Blood Tumor Mutational Burden - 11 Muts/Mb	Atezolizumab	Avelumab
	Cemiplimab	Dostarlimab
	Durvalumab	Retifanlimab
	Nivolumab	Serplulimab
	Pembrolizumab	Toripalimab
	Sugemalimab	
	Tislelizumab	
10 Trials see p. 22		
ctDNA Tumor Fraction - High (3.5%)	**High ctDNA Tumor Fraction defined as ≥ 1.0% based on concordance for defined short variants and fusions. See Genomic Signatures Finding Summary.**	

GENE ALTERATIONS		VAF%	THERAPIES WITH CLINICAL RELEVANCE (IN PATIENT'S TUMOR TYPE)	THERAPIES WITH CLINICAL RELEVANCE (IN OTHER TUMOR TYPE)
KRAS -	G12C	3.5%	Adagrasib 2A	None
			Sotorasib 2A	
10 Trials see p. 26				
ATM -	Y2954C	0.37%	None	None
	Q1825*	0.12%		
10 Trials see p. 24				
PALB2 -	Q856*	0.12%	None	None
10 Trials see p. 28				
STK11 -	E57*	2.3%	None	None

CA UROTELIO : BIOPSIA LIQUIDA

Genomic Signatures

Tumor Mutational Burden - 14 Muts/Mb
HRD signature - Cannot Be Determined
Microsatellite status - MS-Stable

Gene Alterations

For a complete list of the genes assayed, please refer to the Appendix.

ERBB2 **amplification**
ARAF **amplification**
BRCA2 **splice site 9649-1G>C**
CDKN2A **loss, p16INK4a rearrangement exon 1 and p14ARF rearrangement intron 1**
CDKN2B **loss**
FGFR3 **amplification**
MTAP **loss**
CIC **A319fs*87**
KDM6A **A1115fs*7 - subclonal†**
KMT2D (MLL2) **Q3877*, Q2004* - subclonal, L1883fs*32, deletion exons 20-24†**
TP53 **K319***