TruSight™ Oncology 500

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Centro AMES
Via Padre Carmine Fico 24 , 80013
Casalnuovo di Napoli (NA)

PATIENT	DOB	DISEASE	MRN	REPORT DATE	REPORT STATUS
[redacted]	[redacted]	[redacted]	TSO500		Final

REPORT SUMMARY

Executive Summary

[Please add your summary for this case.]

Other Biomarkers

BIOMARKER	LEVEL
TMB	High
MSI	Unstable

Genomic Findings

IA	IB	IIC		IID	
No variants reported.	No variants reported.	*BRCA1*	p.K339Rfs*2 c.1016delA	*TET1*	p.K22Rfs*23 c.65delA
		RNF43	p.G659Vfs*41 c.1976delG	*WT1*	p.R369* c.1105C>T
		CSF3R	p.P468Qfs*5 c.1403_1404delCC	*HNF1A*	p.P291Qfs*51 c.864delG
				GLI1	p.G274Afs*6 c.821delG
		MLH1	p.R497Gfs*11 c.1489delC	*NOTCH3*	p.G2035Vfs*50 c.6102delC
		KDR	p.Q472H c.1416A>T	*NOTCH3*	p.A1802Gfs*8 c.5404dupG
		SDHA	p.T308M c.923C>T	*CIC*	p.P1529Lfs c.4586delC
		BCOR	p.K839Sfs*17 c.2514delC	*PTPRS*	p.V1025Sfs*18 c.3072delC
		DNMT3A	p.R729W c.2185C>T	*ASXL1*	p.L815P c.2444T>C
		TET2	p.Q1546* c.4636C>T		

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FLT4	p.G1154R c.3460G>A	*BCORL1*	p.P1681Qfs*20 c.5042delC
FGFR4	p.G388R c.1162G>A	*MED12*	p.Q2115del c.6276_6278delGCA
CARD11	p.R555Gfs*45 c.1663delC	*BRCA1*	p.K1183R c.3548A>G
TP53	p.G244C c.730G>T	*MUTYH*	p.R245H c.734G>A
ERBB2	p.P1170A c.3508C>G	*BCOR*	p.P1621Qfs*53 c.4862delC
27 Clinical Trials		**0** Clinical Trials	

CLINICALLY RELEVANT RESULTS

Tier I - Strong Clinical Significance

No variants were reported for this classification tier.

Tier II - Potential Clinical Significance

VARIANT	CLINICAL IMPACT
BRCA1 p.K339Rfs*2 c.1016delA C NM_007294.3 VAF % 25.1 DEPTH 275	**May benefit from** — Rucaparib or Olaparib *in Hormone refractory prostate cancer or Adenocarcinoma of prostate* — Talazoparib *in Human epidermal growth factor 2 negative carcinoma of breast, Malignant tumor of breast, Infiltrating duct carcinoma of breast, Invasive micropapillary carcinoma of breast, Mixed ductal and lobular carcinoma of breast, Mucinous carcinoma of breast, Inflammatory carcinoma of breast, Infiltrating*

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[redacted]	[redacted]	[redacted]	ONC4		Final

REPORT SUMMARY

Executive Summary

[Please add your summary for this case.]

Other Biomarkers

BIOMARKER	LEVEL
TMB	Medium
MSI	Stable

Genomic Findings

IA	IB		IIC		IID
No variants reported.	***TP53***	p.R213* c.637C>T	***CDK6***	Copy number gain in *CDK6* (3 copies)	No variants reported.
	4 Clinical Trials		***EGFR***	Copy number gain in *EGFR* (3 copies)	
			MET	Copy number gain in *MET* (3 copies)	
			FGFR3	p.F384L c.1150T>C	
			6 Clinical Trials		

CLINICALLY RELEVANT RESULTS

Tier I - Strong Clinical Significance

VARIANT	CLINICAL IMPACT
TP53 p.R213*	**Unfavorable Prognosis in** — Carcinoma of colon

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[redacted]	[redacted]	[redacted]	ONC3		Final

REPORT SUMMARY

Executive Summary

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Other Biomarkers

BIOMARKER	LEVEL
TMB	Low
MSI	Stable

Genomic Findings

IA	IB	IIC		IID
No variants reported.	No variants reported.	***DNMT3A***	p.N552Kfs*99 c.1656delC	No variants reported.

1 Clinical Trial

CLINICALLY RELEVANT RESULTS

Tier I - Strong Clinical Significance

No variants were reported for this classification tier.

Tier II - Potential Clinical Significance

VARIANT	CLINICAL IMPACT
DNMT3A p.N552Kfs*99 c.1656delC C NM_022552.4 VAF % 2.1 DEPTH 292	**Unfavorable Prognosis in** — Myeloproliferative neoplasm or Myelosclerosis with myeloid metaplasia

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PATIENT	DOB	DISEASE	MRN	REPORT DATE	REPORT STATUS
[redacted]	[redacted]	[redacted]	ONC1		Final

REPORT SUMMARY

Executive Summary

[Please add your summary for this case.]

Other Biomarkers

BIOMARKER	LEVEL
TMB	Low
MSI	Stable

Genomic Findings

IA		IB		IIC		IID
KRAS	p.G12D c.35G>A	***FBXW7***	p.R347C c.1039C>T	***FGFR4***	p.G388R c.1162G>A	No variants reported.
14 Clinical Trials		***TP53***	p.Y220C c.659A>G	***SMAD4***	p.R361H c.1082G>A	
		3 Clinical Trials		**2** Clinical Trials		

CLINICALLY RELEVANT RESULTS

Tier I - Strong Clinical Significance

VARIANT	CLINICAL IMPACT
KRAS p.G12D c.35G>A A NM_033360.2 VAF % 4 DEPTH 1,058	**Not likely to benefit from** — Cetuximab or Panitumumab *in Malignant tumor of colon* **Contraindicated** — Oxaliplatin + Panitumumab or Cetuximab + Oxaliplatin *in Malignant tumor of colon*

INTERPRETATION

The KRAS protein has intrinsic GTPase activity and is an important mediator of growth factor receptor signaling resulting in the activation of the PI3K-mTOR and RAS-RAF-MEK pathways (RefSeq, Jul 2008). Cetuximab in combination with oxaliplatin is contraindicated per the EMA (Cetuximab, Revision 28) in metastatic colorectal cancer harboring a RAS mutation. Panitumumab in combination with

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REPORT SUMMARY

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Other Biomarkers

BIOMARKER	LEVEL
TMB	Medium
MSI	Stable

Genomic Findings

IA

KDR	p.Q472H c.1416A>T
KRAS	p.G12V c.35G>T

22 Clinical Trials

IB

TP53	p.R273C c.817C>T

1 Clinical Trial

IIC

ATM	p.S707P c.2119T>C
BRCA2	p.D1420Y c.4258G>T
ETV6	p.L201P c.602T>C
FGF9	Copy number gain in *FGF9* (5 copies)
FGFR2	p.S57L c.170C>T
MET	p.N375S c.1124A>G

IID

BRCA2	Copy number gain in *BRCA2* (4 copies)
CCND3	p.S259A c.775T>G
FANCA	p.S858R c.2574C>G
FGF14	Copy number gain in *FGF14* (4 copies)
LAMP1	Copy number gain in *LAMP1* (5 copies)
TCF7L2	p.? c. 1162-2A>G

1 Clinical Trial

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REPORT SUMMARY

Executive Summary

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Other Biomarkers

BIOMARKER	LEVEL
TMB	High
MSI	Stable

Genomic Findings

IA		IB		IIC		IID	
KDR	p.Q472H c.1416A>T	*TP53*	p.R175H c.524G>A	*RICTOR*	Copy number gain in *RICTOR* (3 copies)	*BRCA2*	Copy number gain in *BRCA2* (3 copies)
0 Clinical Trials		2 Clinical Trials		*LRP1B*	p.P4016L c.12047C>T	*CCND3*	p.S259A c.775T>G
				APC	p.E1397* c.4189G>T	*FGF9*	Copy number gain in *FGF9* (3 copies)
				FGFR2	p.S57L c.170C>T	*LAMP1*	Copy number gain in *LAMP1* (3 copies)
				1 Clinical Trial		0 Clinical Trials	

CLINICALLY RELEVANT RESULTS

Tier I - Strong Clinical Significance

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REPORT SUMMARY

Executive Summary

[Please add your summary for this case.]

Other Biomarkers

BIOMARKER	LEVEL
TMB	Medium
MSI	Stable

Genomic Findings

IA	IB	IIC	IID
KDR p.Q472H c.1416A>T	No variants reported.	***FGFR4*** p.G388R c.1162G>A	***CCND3*** p.S259A c.775T>G
2 Clinical Trials		1 Clinical Trial	0 Clinical Trials

CLINICALLY RELEVANT RESULTS

Tier I - Strong Clinical Significance

VARIANT

KDR

p.Q472H
c.1416A>T

A

NM_002253.2
VAF % 43.5
DEPTH 347

CLINICAL IMPACT

INTERPRETATION

KDR encodes vascular endothelial growth factor receptor (VEGFR-2) which functions as the main mediator of VEGF-induced endothelial proliferation and angiogenesis (RefSeq, May 2009). A missense substitution in KDR, Q472H is identified. Q472H (rs1870377) is a known polymorphism (population frequencies: ExAC = 22%; NHLBI = 19.4%). In literature, KDR Q472H (rs1870377) has been classified as a functional polymorphism and as an activating mutation. KDR Q472H has been demonstrated to be an activating mutation in vitro, resulting in increased phosphorylation of KDR (PMID: 21712447; http://cancerres.aacrjournals.org/content/75/15_Supplement/73). KDR Q472H was associated with proliferation and invasion in vitro; and with the increased microvessel density in non-small cell lung cancer (NSCLC) and melanoma patients (PMID: 21712447; 26631613). KDR Q472H has been reported in colorectal cancer, haemangioblastoma, rhabdomyosarcoma, hematopoietic and lymphoid neoplasms (COSMIC, accessed Oct 2017). A study reported an inverse relationship of

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Other Biomarkers

BIOMARKER	LEVEL
TMB	Low
MSI	Stable

Genomic Findings

IA	IB	IIC		IID	
No variants reported.	No variants reported.	*APC*	p.R283* c.847C>T	*CCND3*	p.S259A c.775T>G
		APC	p.Q1367* c.4099C>T	*CHEK1*	Copy number gain in *CHEK1* (3 copies)
		ATM	p.S49C c.146C>G		
		ERBB2	p.A386D c.1157C>A	*RET*	p.R982C c.2944C>T
		SMARCB1	p.R374Q c.1121G>A	*ZNF217*	p.E914_P915delinsDS c.2742_2743delinsTT
		TP53	p.P278R c.833C>G		
		1 Clinical Trial		0 Clinical Trials	

CLINICALLY RELEVANT RESULTS

Tier I - Strong Clinical Significance

No variants were reported for this classification tier.

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Other Biomarkers

BIOMARKER	LEVEL
TMB	Medium
MSI	Stable

Genomic Findings

IA	IB	IIC	IID
No variants reported.	***PIK3CA*** p.G1049R c.3145G>C	***APC*** p.R876* c.2626C>T	***BRCA2*** Copy number gain in *BRCA2* (3 copies)
	2 Clinical Trials	***ATM*** p.F858L c.2572T>C	
		MUTYH p.Y179C c.536A>G	***CCND3*** p.S259A c.775T>G
		NOTCH1 p.R621H c.1862G>A	***LAMP1*** Copy number gain in *LAMP1* (3 copies)
		ZRSR2 p.S447_R448dup c.1338_1343dup6	**0** Clinical Trials
		ABL1 p.(=) c.3324A>G	

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Other Biomarkers

BIOMARKER	LEVEL
TMB	Medium
MSI	Stable

Genomic Findings

IA		IB		IIC		IID	
KDR	p.Q472H c.1416A>T	*TP53*	p.? c.559+1G>T	*APC*	p.E536* c.1606G>T	*CCND3*	p.S259A c.775T>G
KRAS	p.G12V c.35G>T	0 Clinical Trials		*APC*	p.L1489Yfs*18 c.4466delT	*FANCA*	p.S858R c.2574C>G
3 Clinical Trials				*ATM*	p.R1618* c.4852C>T	*MDC1*	p.P1177S c.3528_3529delinsAT
				FGFR4	p.G388R c.1162G>A	0 Clinical Trials	
				MYC	p.N26S c.77A>G		
				PIK3R1	p.W583del c.1748_1750delGGT		
				ABL1	p.(=) c.3324A>G		