

Supplemental Table 5: Use and performance of the different methods for c.2369C>T p.(Thr790Met) detection between 2013-2018.

Title	Sensitive detection methods are key to identify secondary EGFR c.2369C>T p.(Thr790Met) in non-small cell lung cancer tissue samples.
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Method for c.2369C>T p.(Thr790Met) detection	Scheme years method was used						# tests	% test with correct outcome	% tests with false-negative result	% tests with wrong mutation	% tests with a technical failure
	2013	2014	2015	2016	2017	2018					
Commercial kit	x	x	x	x	x	x	656	85.2	14.3	0.5	2.0
Therascreen EGFR RGQ PCR Kit (Qiagen)*	x	x	x	x	x	x	132	86.8	10.9	2.3	2.3
Cobas EGFR Mutation detection Test v1 (Roche)*	x	x	x	x	x	x	124	76.9	23.1	0.0	2.4
Cobas EGFR Mutation detection Test v2 (Roche)*			x	x	x	x	101	99.0	1.0	0.0	2.0
Therascreen EGFR Pyro Kit (Qiagen)*	x	x	x	x	x	x	90	83.1	16.9	0.0	1.1
EGFR Mutation Analysis Kit (EntroGen)*	x	x	x	x	x	x	63	77.8	22.2	0.0	0.0
Idylla EGFR Mutation Assay (Biocartis)				x	x	x	24	100.0	0.0	0.0	0.0
EGFR StripAssay (ViennaLab)	x	x	x	x			17	56.3	43.8	0.0	5.9
Myriapod Lung Status (Diatech Pharmacogenetics)			x		x	x	16	100.0	0.0	0.0	0.0
EGFR 29 Mutations Detection Kit (AmoyDx)	x		x	x	x	x	13	91.7	8.3	0.0	7.7
EGFR TKI response (Diatech Pharmacogenetics)	x	x					13	46.2	53.8	0.0	0.0
Easy EGFR (Diatech Pharmacogenetics)				x	x	x	12	100.0	0.0	0.0	0.0
Myriapod Cancer Status (Diatech Pharmacogenetics)	x	x	x				8	100.0	0.0	0.0	0.0
PNAclap EGFR Mutation Detection Kit (Panagene)	x	x	x		x		8	62.5	37.5	0.0	0.0
EGFR XL StripAssay (ViennaLab)					x	x	6	100.0	0.0	0.0	0.0
CLART CMA EGFR (Genomica)			x		x	x	5	80.0	20.0	0.0	0.0
EGFR Mutation Analysis Reagents (Applied Biosystems)	x	x					4	100.0	0.0	0.0	25.0
GML Seqfinder EGFR Sequencing Kit		x	x				4	100.0	0.0	0.0	0.0
PentaPanel (Diatech Pharmacogenetics)			x	x	x		4	100.0	0.0	0.0	0.0
Therascreen EGFR29 Mutation Kit (Qiagen DxS)	x	x					4	75.0	25.0	0.0	0.0
Infiniti Plus EGFR Assay (AutoGenomics)		x					3	100.0	0.0	0.0	0.0
Pan cancer panel (Asuragen)						x	2	100.0	0.0	0.0	0.0
Insider EGFR (Evrogen)			x	x			2	100.0	0.0	0.0	0.0

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Method for c.2369C>T p.(Thr790Met) detection (continued)	Scheme years method was used						# tests	% test with correct outcome	% tests with false-negative result	% tests with wrong mutation	% tests with a technical failure
	2013	2014	2015	2016	2017	2018					
MAD-EGFR mut (Master Diagnostica S. L.)	x						1	0.0	0.0	0.0	100.0
Next-generation sequencing	x	x	x	x	x	x	239	97.0	2.6	0.4	1.7
Ion Ampliseq Custom panel - regions selected by the laboratory (Life technologies)*		x	x	x	x	x	35	100.0	0.0	0.0	0.0
Ion AmpliSeq Colon and Lung Cancer Panel (Life technologies)*			x	x	x	x	33	93.8	6.3	0.0	3.0
TruSight Tumor OncoPanel / TruSight Tumor 15 (Illumina)*				x	x	x	32	96.9	3.1	0.0	0.0
Oncomine Solid Tumour DNA kit (Life Technologies)			x	x	x	x	16	100.0	0.0	0.0	6.3
Custom panel (unspecified)	x	x	x	x		x	15	86.7	13.3	0.0	0.0
Actionable Mutations panel (Qiagen)			x		x	x	14	100.0	0.0	0.0	0.0
TruSeq Amplicon Cancer Panel (Illumina)			x		x	x	12	100.0	0.0	0.0	0.0
In-house primers		x	x	x	x	x	12	91.7	0.0	8.3	0.0
Tumor Hotspot MASTR Plus (Multiplicom)			x		x	x	11	100.0	0.0	0.0	0.0
Ion AmpliSeq Colon and Lung Cancer Panel v2 (Life technologies)				x	x		5	100.0	0.0	0.0	0.0
Ion Ampliseq Lung Cancer Panel (Life Technologies)		x		x			5	100.0	0.0	0.0	0.0
Oncomine Focus Assay (Life Technologies)					x	x	5	100.0	0.0	0.0	0.0
SeqCap EZ Choice (KAPA Hyperplus Workflow) (Nimblegen)					x	x	4	100.0	0.0	0.0	0.0
Ion Ampliseq Cancer Hotspot Panel v2 (Life Technologies)			x			x	4	100.0	0.0	0.0	0.0
MassArray OncoCarta panel (Sequenom)	x	x		x			4	100.0	0.0	0.0	25.0
TruSight Tumor 26 (Illumina)				x		x	4	100.0	0.0	0.0	0.0
MassArray custom panel (Sequenom)		x	x				4	100.0	0.0	0.0	0.0
TruSeq Custom Amplicon (Illumina)				x	x		4	100.0	0.0	0.0	0.0
Massarray 4 analyser (Sequenom)	x			x	x		3	100.0	0.0	0.0	33.3
Accel-Amplicon™ Plus EGFR Pathway Panel						x	2	100.0	0.0	0.0	0.0
Comprehensive Thyroid and Lung (CTL) Kit (Archer)						x	2	100.0	0.0	0.0	0.0
GeneRead QIAact Lung DNA UMI Panel (Qiagen)						x	2	100.0	0.0	0.0	0.0

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Method for c.2369C>T p.(Thr790Met) detection (continued)	Scheme years method was used						# tests	% test with correct outcome	% tests with false-negative result	% tests with wrong mutation	% tests with a technical failure
	2013	2014	2015	2016	2017	2018					
SiReTM (Genedin)						x	2	100.0	0.0	0.0	0.0
TruSight Tumor Cancer panel (Illumina)			x				2	100.0	0.0	0.0	0.0
Custom Panel (Qiagen)						x	2	100.0	0.0	0.0	0.0
Access Array System (Fluidigm)				x			1	100.0	0.0	0.0	0.0
Life technologies (Unspecified)	x						1	0.0	100.0	0.0	0.0
Sentosa®SQ NSCLC Panel (Vela Diagnostics)				x			1	100.0	0.0	0.0	0.0
GeneRead DNaseq Custom Panel v2 (Qiagen)				x			1	100.0	0.0	0.0	0.0
Ion Ampliseq Custom panel v2 - regions selected by the laboratory (Life technologies)				x			1	100.0	0.0	0.0	0.0
Non-commercial method	x	x	x	x	x	x	293	81.1	18.6	0.4	2.7
Dideoxy sequencing*	x	x	x	x	x	x	138	73.1	26.9	0.0	2.9
High-resolution melting*	x	x	x	x	x	x	64	93.5	6.5	0.0	3.1
TaqMan-based sequencing (ARMS/LNA/PNA/CAST-PCRs)*	x	x	x	x	x		32	75.0	21.9	3.1	0.0
Pyrosequencing	x	x	x	x	x		19	82.4	17.6	0.0	10.5
Sanger sequencing		x		x	x	x	16	100.0	0.0	0.0	0.0
Fragment analysis	x	x				x	15	80.0	20.0	0.0	0.0
SNaPshot	x	x		x			5	100.0	0.0	0.0	0.0
RT-PCR		x	x				4	100.0	0.0	0.0	0.0
Missing data	x						2	100.0	0.0	0.0	50.0
Grand Total	x	x	x	x	x	x	1190	86.6	13.0	0.4	2.2

Technical failures are represented with respect to the total number of tests. Correct results, false-negatives and wrong mutations are calculated in relation to the total number of analyzable tests (total tests minus technical failures). A combination of all scheme years (2013-2018) is represented. Missing data: no method information was available. *A breakdown of the performance during each scheme year for the most widely used methods per technique type is given in **Supplemental Table 4**. Abbreviations: #: number.