#ECPUPDATES

Iniciativa científica de:

GECP lung cancer research

LUNG CANCER UPDATES

ECP HIGHLIGHTS

7-11 DE SEPTIEMBRE 2019

Con la colaboración de:

Bristol-Myers Squibb

illumina

Lilly

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Biomarcadores en NSCLC. Recomendaciones desde ECP

Federico Rojo

Con la colaboración de:
Bristol-Myers Squibb
illumina
Lilly

Biomarkers in lung cancer: descriptive analysis of a centralised platform in Spain (LungPath)

Javier Martín. Hospital Universitario Puerta de Hierro, Madrid

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Figure 9. Positivity rate for the combination of both **adenocarcinoma and NOS** histology cases:

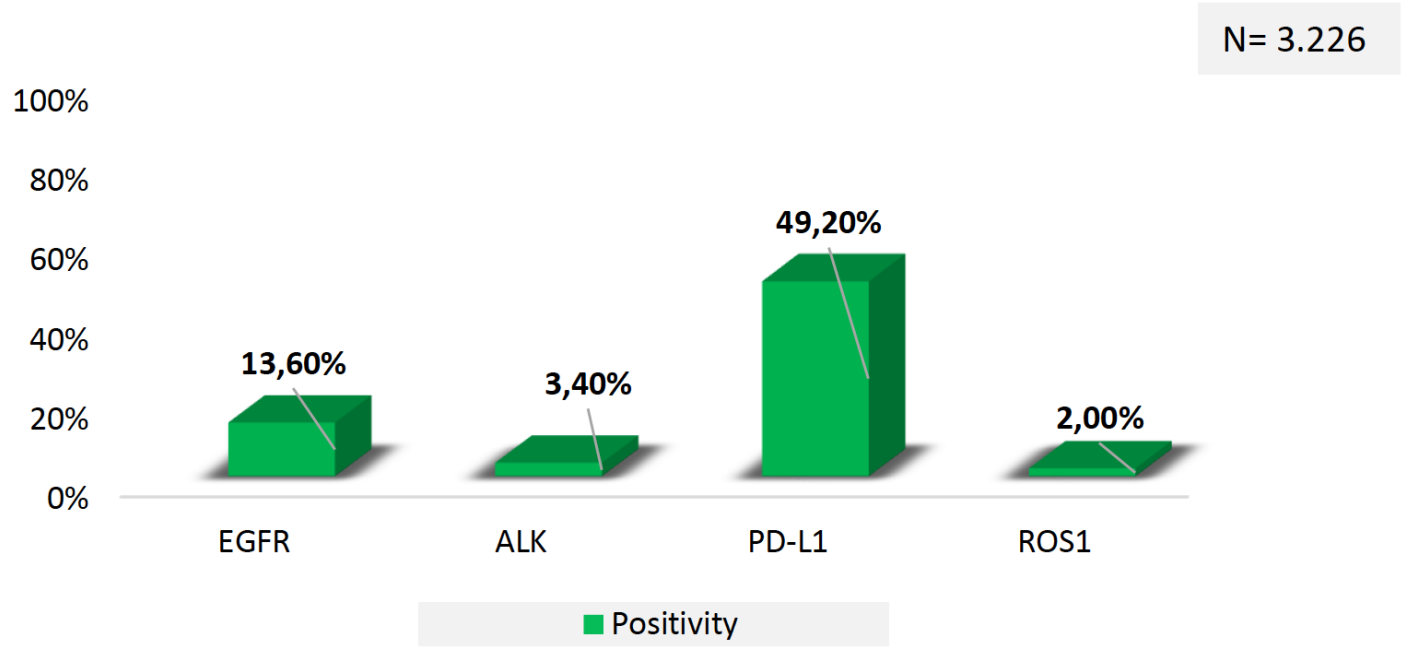
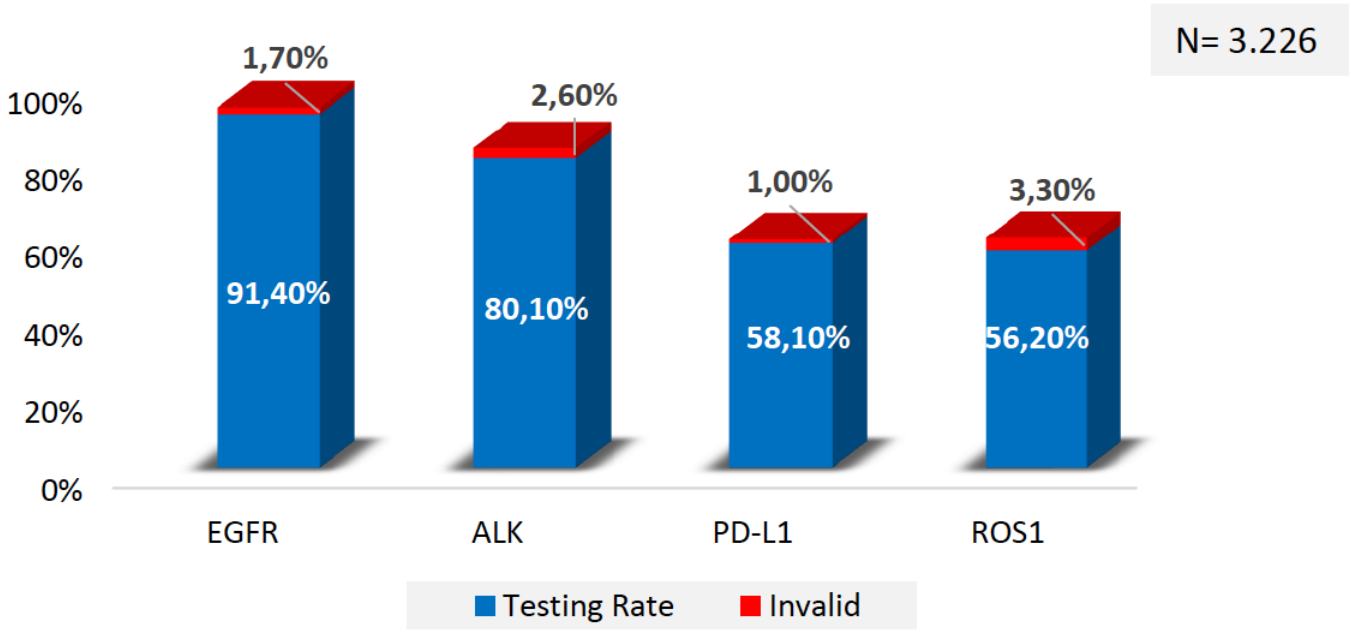


Figure 8. Testing rate and invalid samples in **adenocarcinoma and NOS** histology cases:



Solving PD-L1 test dilemmas once and for all

Marius Ilié, Université Côte d'Azur

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- EQA requires continuous participation to:
  - Monitor staining and interpretative methods
  - Provide individual feedback to laboratories to improve staining methodologies
- EQA for PD-L1 can highlight whether or not an assay is performing in line with expectations and highlight any potential issues with staining that may lead to false-positive or false-negative results
- Ring studies can be used to compare the reproducibility of results between laboratories.

The rate of adherence for pathologists remains relatively low !!!

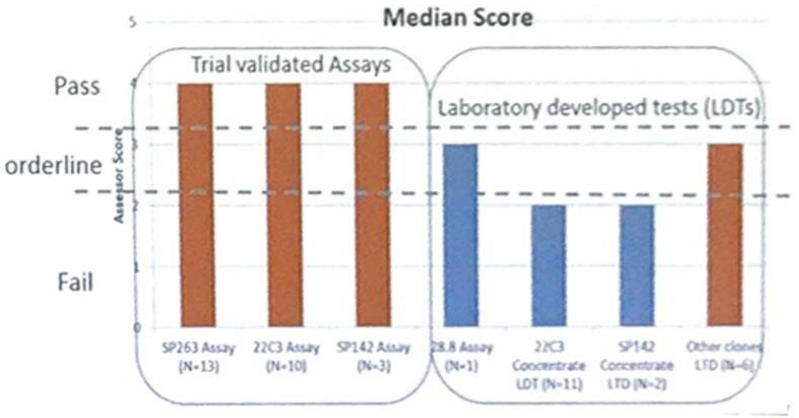
EQA data show there are issues with LDTs

NORDIC QC

- 37 laboratories using IVDs
- 28-8 pharmDx, 22C3 PharmDx, SP263
  - ☑ 69% – 92% pass rate
- 29 laboratoires using LDTs
  - ☑ 30% pass rate

UK NEQAS

- ☑ Trial validated IVDs – 100% pass rate
- ☑ LDTs – 47% pass rate



Strategies for addressing the intrinsic source of error associated with PD-L1 scoring and interpretation

Bharat Jasani, Targos

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Systematic Approach to All Biopsies

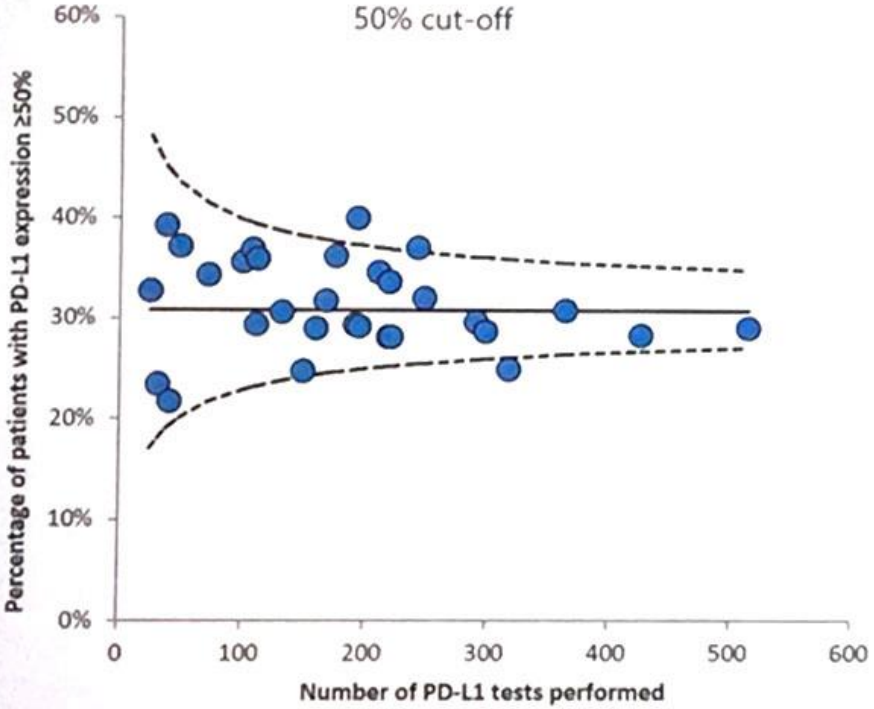
Targos Advance
Training & Consulting

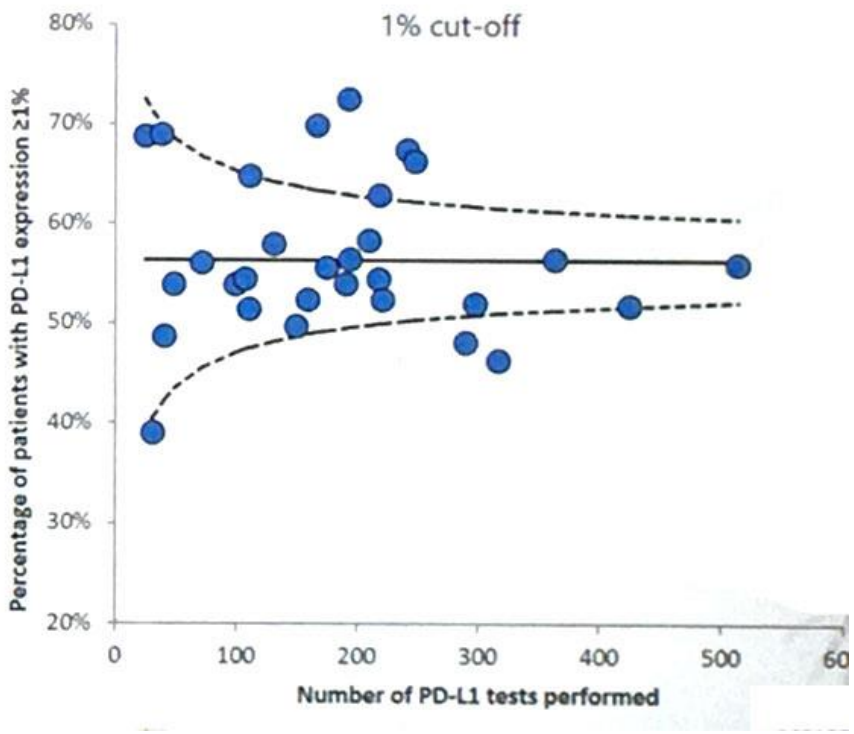
1. Include for analysis all elements of the biopsy present on the slide or in the digital image
2. Identify all areas of viable tumour cell presence
3. Do a total count of these cells in case of a small biopsy; or
4. Estimate average number of viable tumour cells/x20 mag field in case of a large biopsy
5. Identify and count all viable tumour cells showing discernible membranous staining, however weak or partial, in each x20 mag counting frame
6. Exclude tumour cells showing only cytoplasmic or pseudomembranous staining
7. Exclude staining associated with dying or necrotic tumour cells, or reactive tissue elements

Interlaboratory variation in PD-L1 positivity in histological and cytological material of non-small cell lung cancer patients

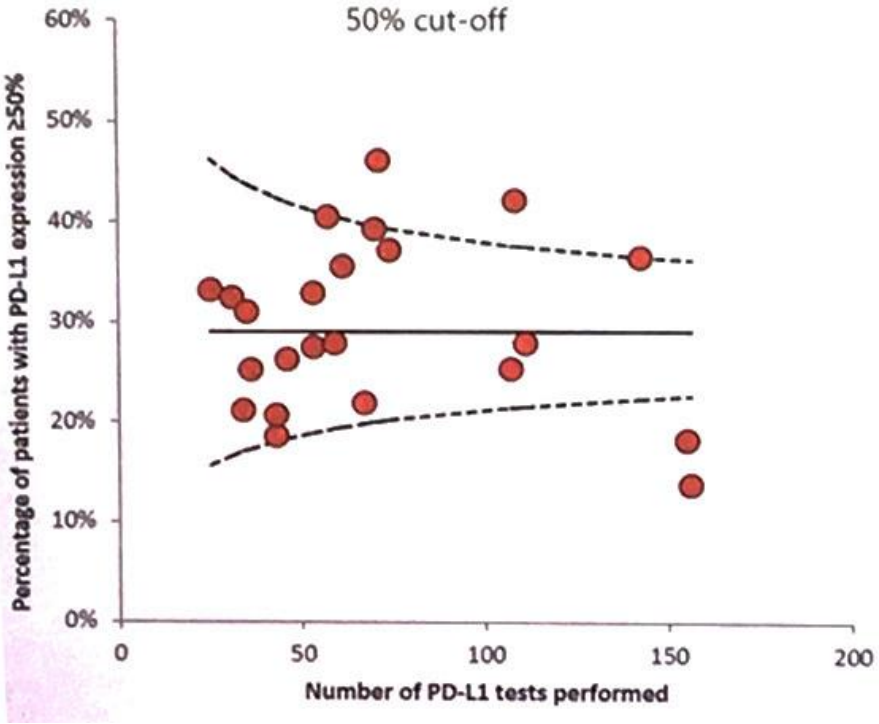
Bregie Koomen, UMC Utrecht

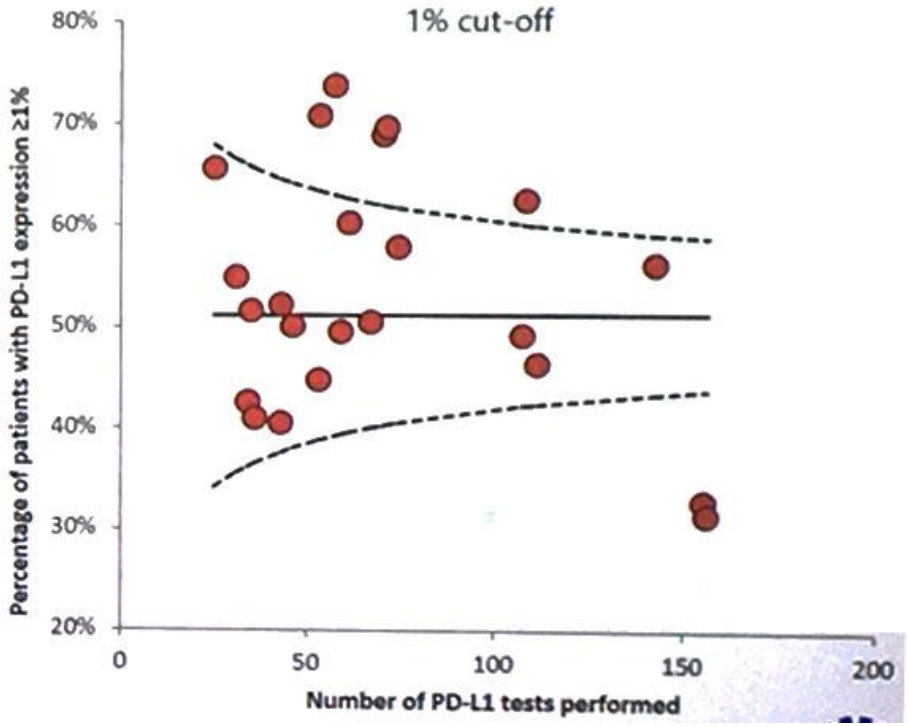
Results Histology: 5634 patients, 30 labs





Results Cytology: 1637 patients, 23 labs





Utility of cytologic specimens and preanalytical procedures for PD-L1 testing in NSCLC cytopathology

Birgit Guldhammer Skov. Rigshospitalet, Copenhague

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Lung cancer

- Patients in advanced stage >72% (UK) and 57% (US)

50-70%
cytology

30-50%
histology

www.cancerresearchuk.org, www.cancer.org

Studies addressing concordance between histology and cytology specimens (CB mainly)

Publication	N	Assay	Platform	Concordance TPS ≥ 50%
Skov BG	86	22C3pharmDX 28-8pharmDX	ASL48 (DAKO)	94% 90%
Ilie M	70	22C3 LDTs	ASL48 (DAKO) BM U (Ventana)	96%
Hernandez A	52	22C3pharmDX	ASL48 (DAKO)	67% (61% – 86%)
Russel-Goldman E	46	E1L3N LDT	ASL48 (DAKO)	84%
Noll B	38	22C3pharmDX	ASL48 (DAKO)	81%*
Wang	27	22C3pharmDX	ASL48 (DAKO)	TPS scores (r= 0.925, P 0.001)**

High overall concordance of PD-L1 expression between cell blocks and histology samples in the majority of the studies across different PD-L1 IHC assays

Quality assurance issues for biomarker testing in practice

Michael Hummel, Institute of Pathology Charité - Universitätsmedizin Berlin

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Example 2: ring trial for *EGFR* T790M testing – liquid biopsy

Reporting results for 10 FFPE and 10 blood samples		
Turnaround time: 14 days		
T790M mutated: yes or no		
ctDNA extraction method		
Analysis method for FFPE and blood tests		
cDNA change, amino acid change, and allele frequency		
Scoring scheme RRT phase 1 and 2		
Material	10 FFPE samples	10 blood samples
Maximum score	20 points	20 points
Successful pass	19 of 20 points	18 of 20 points
Correct call: T790M-wt or T790M-mut	2 points	2 points
Exclusion of 1 blood sample		20−2x−2
Technical problem with 1 sample	1-point penalty	1-point penalty

cDNA, copy DNA; ctDNA, circulating tumor DNA; EGFR, epidermal growth factor receptor; FFPE, formalin-fixed paraffin-embedded; RRT, round robin trial.

Fassunke J, et al. Virchows Arch. 2017;471:509-20.

Example 2: ring trial for *EGFR* T790M testing – results phase 2

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Test center No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36*	37	38	39	40	41	42
Case No. /Sequencing system	1	2, 3	0	4	3	1, 3	2	4	4	4	2	1	4	4	3	1	5	4	3	6	4	4	3, 1	1	3	2	1	4	4	1	2	4	3	4	1	0	2, 1	1	3	1	7, 2	8
1 (T790M)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	0	2	2	2	2	0	2
2 (wild-type)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	2	0	2	2	2	2	2	2
3 (EGFRm)	2	1	1	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	0	2
4 (T790M)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	0	2	2	2	2	0	2
5 (EGFRm)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	2	2
6 (EGFRm)	2	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	2	0	2	2	2	2	2	2
7 (wild-type)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	2	2
8 (T790M)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	2	2
9 (T790M)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	2	2
10 (wild-type)	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	**	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	2	2
	20	19	19	20	20	20	20	19	20	20	20	19	20	20	20	20	20	20	20	18/18	20	20	20	20	20	20	20	20	20	16	16	20	20	20	20	0	20	20	20	20	14	20

Test center No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36*	37	38	39	40	41	42
ctDNA extraction	B	A	0	A	A	C	D	A	B	A	A	B	A	A	A	B	D	D	A	B	B	A	B	A	A	D	C	B	D	B	A	A	A	A	D	0	A	D	A	B	B	A
Samples /Sequencing system	1	1, 3	0	4	3	1, 3	2	4	4	1,4	3	1	4	3, 4	3	1	5	3	3	6	4	4, 1	1	4	3, 1	3	1	4, 1	3	1	1	1	3	4	1	0	1	1	3	1	7, 2	8
T790M/ 96 ng	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	0	2
T790M/ 10 ng	2	0	2	1	1	2	0	2	0	0	0	0	2	2	2	2	0	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	0	2	2	2	2	2	2
T790M/ 22 ng	2	0	2	2	2	2	0	2	2	2	0	0	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	0	2
T790M/ 45 ng	2	1	2	2	2	2	2	2	2	0	2	0	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	0	2
wild type	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	2	2
T790M/ 45 ng	2	0	2	2	2	2	2	2	2	2	0	0	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	0	2
T790M/ 10 ng	2	0	2	1	2	2	2	2	2	2	2	0	0	2	2	2	2	2	2	2	2	0	2	2	2	2	2	1	2	2	2	2	2	2	2	0	2	2	2	2	0	2
T790M/ 96 ng	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	0	2
T790M/ 22 ng	2	1	2	2	2	2	0	2	2	2	2	0	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	0	2
wild type	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	0	2
	20	10	20	18	19	20	14	20	18	16	14	4	18	20	20	20	18	20	20	20	20	18	20	20	20	20	20	18	20	20	20	20	20	20	20	0	20	20	20	20	4	20

Sequencing system: 0, not stated; 1, allele-specific PCR; 2, Sanger sequencing; 3, massive parallel sequencing; 4, pyrosequencing; 5, PCR and reverse hybridization; 6, MALDI-TOF analysis; 7, melting point determination; 8, ddPCR.
Platform: A, manual, QIAGEN; B, manual, others; C, automated, QIAGEN; D, automated Maxwell.
*No result notification. **Case number 10 did not contain enough tumor cells and was excluded from the result's calculation.
ddPCR, digital droplet polymerase chain reaction; MALDI-TOF, matrix assisted laser desorption/ionization time-of-flight; PCR, polymerase chain reaction.

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