# EGFR ring trial II August 2013- results

| | Case A | Case B | Case C | Comments | | Comments by distributor |
|---|---|---|---|---|---|---|
| **definition** | predominant lepidic adenocarcinoma and acinar (MIA), AAH | predominant solid adenocarcinooma and acinar | cell block of pleural effusion with TTF1 positive cells of a pulmonary adenocarcinoma with micropapillary formations | | | digital slides can be viewed www.iapaustria.com user: agpulmo PW: EGFR (case sensitive) |
| **dates** | | | | reception | report | |
| ID01 | | | | 30.07.13 | - | |
| ID02 | | | | 31.07.13 | 06.08.13 | |
| ID04 | | | | 31.07.13 | 06.08.13 | |
| ID05 | | | | - | - | |
| ID06 | | | | - | - | |
| ID07 | | | | - | 15.08.13 | |
| ID08 | | | | 02.08.13 | 23.08.13 | |
| ID09 | | | | 02.08.13 | - | |
| ID10 | | | | 28.07.13 | 02.08.13 | |
| ID11 | | | | 01.08.13 | 05.08.13 | |
| ID12 | | | | 30.07.13 | 02.08.13 | |
| ID13 | | | | 29.07.13 | 31.07.13 | |
| ID14 | | | | 30.07.13 | 05.08.13 | |
| ID15 | | | | 19.08.13 | 29.08.13 | |
| ID16 | | | | 31.07.13 | 01.08.13 | |
| ID 18 | | | | 31.07.13 | 15.08.13 | |
| ID19 | | | | 02.08.13 | 13.08.13 | |
| ID21 | | | | 05.08-13 | 12.08.13 | |
| **percentage of tumor cells within section (as in regular report)** | | | | | | |
| ID01 | 40% | 85% | 10-15% | | | |
| ID02 | 15% | 50% | 80% | | | |
| ID04 | 20% | 50% | 80% | | | |
| ID05 | 50% | 70% | 50% | | | |
| ID06 | 40% | 80% | 90% | | | |
| ID07 | 60% | 100% | 40% | | | |
| ID08 | 30% | 90% | 95% | | | |

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|---|---|---|---|---|---|
| ID09 | 20% | 60% | 60% | | |
| ID10 | 50% of tumor cells in marked area | 70% of tumor cells in marked area | 30% of tumor cells in marked area | | |
| ID11 | 50% | 70% | 60% | | |
| ID12 | 30 | 75 | 40 | | |
| ID13 | Das analysierte Gewebe zeigte 50% Tumorzellen | Das analysierte Gewebe zeigte 80% Tumorzellen | Das analysierte Gewebe zeigte 70% Tumorzellen | | |
| ID14 | 30% in marked area | 70% in marked area | 15% in marked area | | |
| ID15 | 25% | 90% | 50% | | |
| ID16 | 60-70% | 80% | 80% | | |
| ID18 | 10-20% | 70-80% | not to be evaluated, but sufficient to the analysis | In the case C we can not "separate" without IHC the tumor cells from eventual macrophages and mesothelial cells | |
| ID19 | 10% | 50% | 30% | | |
| ID21 | 45-55% | 60-70% | 75-85% | | |
| **how was percentage calculated ?** | | | | | |
| ID01 | - | | | | |
| ID02 | histomorpology | | | | |
| ID04 | Percentage of Tumor cells in the selected area minus stroma and inflammatory cells | | | | |
| ID05 | evaluated by molecular pathologist | | | | |
| ID06 | histological evaluation | | | | |
| ID07 | microscopy | | | | |
| ID08 | estimated by pathologist | | | | |
| ID09 | carcinoma cells in relation to normal cels, one pathologist | | | | |
| ID10 | Percentage of tumor cells in marked area in relation to normal (stroma) cells | | | | |
| ID11 | estimated | | | | |
| ID 12 | ratio of estimated number of tumor cells vs. normal cells | | | | |
| ID13 | amount of tumor cells in marked area | | | | |
| ID14 | amount of tumor cells in marked area | | | | |
| ID15 | percentage of atypical epithelial cells in tumor area | | | | |
| ID16 | estimated | | | | |
| ID18 | semiquantitatively ba agreement of both evaluating pathologists (LP, ZH) | | | | |
| ID19 | histological evaluation | | | | |
| ID21 | Manual counting on HE stained slides on approx 1000 cells | | | | |

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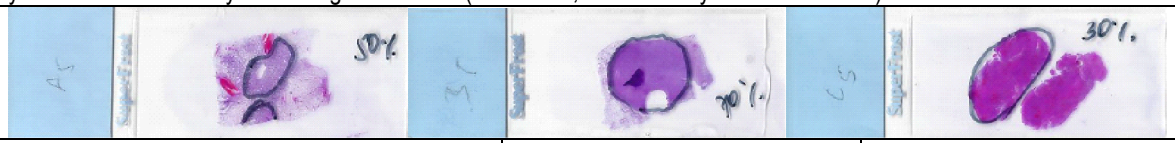
|---|---|---|---|---|---|
| **Tumor cell enrichment – yes/no : method of enrichment (e.g. macrodissection by needle)** | | | | | |
| ID01 | no | no | no | | |
| ID02 | yes, macrodissection | | | | |
| ID04 | Case B by macrodissection and scrathcing, Case A and C entire section was used | | | | |
| ID05 | macrodissection (by scraping) | | | | |
| ID06 | no | | | | |
| ID07 | no | | | | |
| ID08 | macrodissection by scratching | | | | |
| ID09 | yes | no | no | | |
| ID10 | yes Macrodissection by scratching with needle ( in Case A, B and C only the marked area) | | | | |
| ID10 |  | | | | good and practicable documentation of slide jpg |
| ID11 | macrodissection | macrodissection | macrodissection | | |
| ID 12 | macrodissection by scratching | | | | |
| ID13 | yes, tissue scratching of marked tumor area | | | | |
| ID14 | macrodissection by scratching | | | | |
| ID15 | yes, scratching | | | | |
| ID16 | macrodissection | no | no | | |
| ID18 | no | | | | |
| ID19 | Not done | | | | |
| ID21 | yes, macro dissection by scratching the marked tumor area | | | | |
| **method of DNA extraction** | | | | | |
| ID01 | Maxwell v. Promega | | | | |
| ID02 | MagNA Pure Compact | | | | |
| ID04 | COBAS DNA Sample preparation kit (Roche) | | | | |
| ID05 | High Pure PCR Template Preparation KIT (Roche ) | | | | |
| ID06 | Roche High Pure PCR ZTemplate Kit | | | | |
| ID07 | Quickgene DNA Tissue Kit (Kurabo) | | | | |
| ID08 | High Pure PCR Template Preparation kit Roche | | | | |
| ID09 | DNA FFPE MiniKit (Quiagen) | | | | |
| ID10 | MAXWELL 16 Instrument , Fa.Promega | | | | |
| ID11 | Cobas DNA sample preparation kit | | | | |
| ID12 | EZ 1 AdvancedLS Automat Fa. Qiagen | | | | |
| ID13 | QIAmp DNA FFPE tissue kit Fa Qiagen | | | | |

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|---|---|---|---|---|---|
| ID14 | fullautomatic/ Biorobot EZ1 QUIAGEN investigator kit | | | | |
| ID15 | QIAmp DNA FFPE Tissue Kit (Qiagen) | | | | |
| ID16 | Roche, Extraktionskit | | | | |
| ID18 | cobas DNA Sample Preparation Kit Roche) | | | | |
| ID19 | DNA Sample preparation kit Roche | | | | |
| ID21 | Extraction performed using the kit NucleoSpin FFPE DNA, manufacturer Macherey-Nagel. | | | | |
| **method of measurement of DNA** | | | | | |
| ID01 | Qubit Fluoreszenzmessung (invitrogen) | | | | |
| ID02 | Bio spec nano | | | | |
| ID04 | Bio spec nano | | | | |
| ID05 | NanoDrop ND-1000 spectrophotometer | | | | |
| ID06 | Nanodrop Spectrophotometer | | | | |
| ID07 | GeneQuant Pro Photometer | | | | |
| ID08 | Nanodrop 1000 | | | | |
| ID09 | NanoDrop Peqlab | | | | |
| ID10 | spectralphotometer Nanodrop | | | | |
| ID 11 | Biospec Nano | | | | |
| ID 12 | Nanodrop ND 1000 Fa Peqlab | | | | |
| ID13 | Quant-iT ds DNA BR Assay Kit, Fa Invitrogen(Qubit) | | | | |
| ID14 | photometry Gene Quant 1300 | | | | |
| ID15 | NanoDrop ND 100 Spectrophotometer | | | | |
| ID16 | Bio Spec Nano-Messung | | | | |
| ID18 | Qubit® dsDNA BR Assay Kit and Qubit® 2.0 Fluorometer, Invitrogen (LifeTechnologies) | | | | |
| ID19 | Quan iT ds DNA HS Assay Kit (Invitrogen) | | | | |
| ID21 | UV spectrophotometer evaluation on a Eppendorf BiophotometerPlus and a Hellma TrayCell - Light path 1mm<br>Second measure by fluorimetric method on a Qubit® 2.0 Fluorometer with the Qubit® dsDNA HS Assay Kit | | | | |
| **Amount of DNA extracted (as in regular report)** | | | | | |
| ID01 | 59,85 µg/ml | 50,85 µg/ml | 38,55 µg/ml | | |
| ID02 | 6,76 ng/µL | 10,41 ng/µL | 8,64 ng/µL | | |
| ID04 | 4,2 ng/µl | 4,0 ng/µl | 4,1 ng/µl | | |
| ID05 | 41,2 ng/µl | 129,7 ng/µl | 47,2 ng/µl | | |
| ID06 | 90,02 ng/µl | 64,46 ng/µl | 55,26 ng/µl | | |
| ID07 | 11 ng/Ml | 13 ng/µl | 10 ng/µl | | |
| ID08 | 104 ng/µl | 154 ng/µl | 72 ng/µl | | |
| ID09 | 88,5 ng/µl | 177,0 ng/µl | 151,6 ng/µl | | |
| ID10 | 117 ng/µl | 153 ng/µl | 91 ng/µl | | |

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|---|---|---|---|---|---|
| ID11 | 89,05 ng/µl | 122,19 ng/µl | 78,94 ng/µl | | |
| ID 12 | 8,0 ng/µl | 20,9 ng/µl | 31,1 ng/µl | | |
| ID13 | 3,86 µg/ml | 1,00µg/ml | 2.19 µg/ml | The amount is documented in a lab-report, not in the patients report | |
| ID14 | 16 ng/µl | 29 ng/µl | 41 ng/µl | | |
| ID15 | 21,08 ng/µl (Vtotal = 50 µl) | 159,61 ng/µl (Vtotal = 50 µl) | 20.35 ng/µl (Vtotal = 50 µl) | | |
| ID16 | 85,56 ng/µl | 156,37 ng/µl | 79,31 ng/µl | | |
| ID18 | 7,38 ng/µl | 8,10 ng/µl | 3,88 ng/µl | | |
| ID19 | 80.1 ng/ml | 80,8 ng/ml | 52,6 ng/ml | | |
| ID21 | 7,6 ng/µl (fluorimetric method) | 11,5 ng/µl (fluorimetric method) | 8 ng/µl (fluorimetric method) | | |
| **qualitiy of DNA** | | | | | |
| ID01 | - | - | - | | |
| ID02 | good | good | good | | |
| ID04 | 1,93 | 2,01 | 2.01 | | |
| ID05 | good | good | good | | |
| ID06 | good | good | good | | |
| ID07 | 1,7 | 1,65 | 1,7 | | |
| ID08 | good | good | good | | |
| ID09 | 1,90 | 1,89 | 1,94 | | |
| ID10 | 1,85 | 1,84 | 1,83 | | |
| ID11 | | | | | |
| ID 12 | 260/280, 2,98 | 260/280, 2,19 | 260/280, 2,06 | | |
| ID13 | good | good | good | | |
| ID14 | ratio 2,3 | ratio 2,2 | ratio 1,4 | | |
| ID15 | A260/280 = 2,23; A260/230 = 0,22 | A260/280 = 2,03; A260/230 = 1,01 | A260/280 = 2,49; A260/230 = 0,21 | | |
| ID16 | - | - | - | | |
| ID18 | optimal | optimal | optimal | | |
| ID19 | not done | not done | not done | | |
| ID21 | 1,91(A260/A280) | 1,91(A260/A280) | 2,10(A260/A280) | | |
| **evaluation of DNA qualitiy** | | | | | |
| ID01 | - | | | | |
| ID02 | internal control of COBAS EGFR mutation test | | | | |
| ID04 | OD 260/280 | | | | |
| ID05 | spectrophotometric analysis | | | | |

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|---|---|---|---|
| ID06 | 260/280 nm ratio, 260/230 nm ratio | | |
| ID07 | - | | |
| ID08 | Nanodrop 1000 (260/280) | | |
| ID09 | control PCR | | |
| ID10 | ratio 260/280 (pure DNA 1,7 – 1,8): | | |
| ID11 | - | | |
| ID12 | Nanodrop ND 10000 Fa Peqlab | | |
| ID13 | Estimation in relation to peak height of the program and in relation to the control DNA | | |
| ID14 | (exon2) control mix (kit) assay + inhibitor control | | |
| ID15 | NanoDrop ND-100 Spectrophotometer measurement + β-globin control PCR | | |
| ID16 | - | | |
| ID18 | convenient | | |
| ID19 | not done | | |
| ID21 | A260/A280 | | |
| **Method of sequencing (as in regular report)** | | | |
| ID01 | Real time cycler cobas 4800 von Roche | | |
| ID02 | - | | |
| ID04 | COBAS 4800 Roche | | |
| ID05 | Sanger sequencing (ABI 3130 Genetic Analyser) | | |
| ID06 | Direct sequencing | | |
| ID07 | quantitative allele specific PCR | | |
| ID08 | Sanger sequencing, next generation sequencing | | |
| ID09 | allele specific PCR | | |
| ID10 | Therascreen EGFR Pyro Kit Ref. 971480, Fa. QIAGEN | | |
| ID11 | COBAS EGFR Mutationsanalyse (Cobas 4800 System) | | |
| ID 12 | Sanger Sequencing ABI 3500xL Dx | | |
| ID13 | Pyrosequencing; Therascreen EGFR Pyro Kit, Fa. Qiagen<br>„Verwendete Methode: DNA-Extraktion mit Qiagen QIAmp® DNamp FFPE Kit,<br>Sequenzierung mit Therascreen® EGFR Pyro Kit (Quiagen, Hilden, Deutschland).“ | | |
| ID14 | (real time PCR) Thera screen EGFR RGQ PCR kit Quiagen | | |
| ID15 | 7500 Real Time PCR System + TaqMan Mutation Detection Assays, Applied Biosystems<br>Dideoxy sequencing (Applied Biosystems, 3100-Avant) | | |
| ID16 | Cobas 4800 EGFR Mutation Test, Roche, Realtime-PCR | | |
| ID18 | cobas® EGFR Mutation Test and cobas z 480 analyser for real-time PCR (Roche) | | |
| ID19 | Real Time PCR – Cobas EGFR Mutation Test | | |
| ID20 | Mutant specific amplification by qPCR with a CE/IVD approved kit (supplier EntroGen- EGFR Mutation Analysis Kit for Real- | | |

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|---|---|---|---|
| | Time PCR, run on a Roche LightCycler 480) | | |
| What types of mutations can be detected by your method? Sensitivity of your method, if known? | | | |
| ID01 | 41 EGFR mutation in exons 18 - 21 | | |
| ID02 | siehe COBAS EGFRmutation test | | |
| ID04 | 41 different mutations in Exon 18,19,20,21 ( 5% of mutated tumor cells in wildtyp background) | | |
| ID05 | All mutations in exons: 18-21 by 10% sensitivity | | |
| ID06 | All types of mutation can be detected. approx 10% mutation | | |
| ID07 | exon, 19, exon 21 | | |
| ID08 | 18 – 21 exon any | | |
| ID09 | 40 mutations detected by the cobas® EGFR Mutation Kit. Sensitivity according to the manufacturer: 1% | | |
| ID10 | Exon 18: Mutations on Codon 719: G719X (X=S, C, A, D)<br>Exon 19: all Deletions within Codon 746-750<br>Exon 20: Mutation Codon 768 (S768I), Insertion Codon 770, 771, 774; Mutation Codon 790 (T790M)<br>Exon 21: Mutation Codon 858 and 861 (L858R, L861Q)<br>5% tumor cells should be tested in minimum to get reliable results | | |
| ID11 | Exon 18: Punktmutationen im Codon 719<br>Exon 19: sämtliche derzeit in Version 1.0/ Oktober 2011 beschriebene Deletionen<br>Exon 20: Punktmutationen Codon 790 (T790M) und 768 (S768I) Insertionen<br>Exon 21: Mutationen Codon 858 (L858R) | | |
| Id 12 | all types (del, ins, sub, dup) | | |
| ID13 | Point mutations codons 719, 768, 790, 858-861; Deletions Exon 19,<br>Sensitivity 5-10% mt in wildtype | | |
| ID14 | 19 deletions in exon 19, T790M,L858R. L861Q, G719X, S763I, 3 insertions in exon 20; sensitivity 1-10% mutated DNA | | |
| ID15 | Exon 18: G719A, G719S, G719C<br>Exon 19: 19 deletions (L747_T751>S, L747_E749del, E746_S752>D, E746_A750del (2235_2249del15), E746_A750del (2236_2250del15), L747_T751del, L747_T752del, E746_S752>A, L747_T751del, L747_P753>S, L747_A750>P, L747_A751>P, E746_S752>V, L747_P753>Q, L747_T751>Q, L747_A750>P, E746_T751>A, E746_T751del and E746_T751>I)<br>Exon 20: T790M, S768I, V769_D770insASV, H773_V774insH and D770_N771insG<br>Exon 21: L858R and L861Q<br>TaqMan Mutation Detection Assays can detect 0,1% mutated DNA in a background of wild type DNA | | |
| ID16 | T790M, Deletionen Exon 19, S768i, L858R, G719X, Insertionen Exon 20 | | |
| ID18 | 41 specific mutations in exons 18, 19, 20 and 21 of the EGFR gene, e.g. deletions (e.g. exon 19 del), insertions (e.g. exon 20 ins) or point mutations (e.g. S768I, L858R, T790M or G719X) can be detected.<br>Sensitivity: >5% mutant copies of FFPE DNA in a background of wild type DNA | | |
| ID19 | by our method 3 point mutations can be detected in exon 18 (G719A, G719C, G719S), 29 deletions and complex mutations in exon 19, 2 point mutations (S768I, T790M) and 5 insertions in exon 20 and L858R in exon 21. overall 41 mutations | | |

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|---|---|---|---|---|---|
| ID20 | T790M<br>Exon 19 Deletions - detects 19 deletions, but does not distinguish between them<br>L858R<br>L861Q<br>S768I<br>G719X - detects G719A, G719S and G719C, but does not distinguish between them<br>Exon 20 Insertions - detects 2319-2320 insCAC and 2310-2311 insGGT, but does not distinguish between them<br>Exon 20 Insertion - detects 2307-2308 insGCCAGCGTG (ins9)<br>The limit of detection varies, according to the manufacturer between 0,1-1% diluted in the wild-type genomic DNA. The exqct sensitivity has not been locally validated in order to establish the minimum proportion and number of cancer cells needed for mutation detection as recommended by ACP/IASLC/AMP guidelines. | | | | |
| result as in regular report | | | | | |
| ID01 | pos exon 21 L858R | pos exon 18 G710X | pos exon 19 deletion | | |
| ID02 | Mutation exon 21 (L858R) | Mutation exon 18 (G719X) | Mutation exon 19 (Deletion) | | |
| ID04 | Exon 21 L858R | Exon 18 G719X | Exon 19 Deletion | | |
| ID05 | c.2573T>G p.L858R | c.2126 A>C E709A*, c.2155 G>A G719S | c.2239_2251>C p.L747_T751>P | | |
| ID06 | mutant | mutant | mutant | | |
| ID07 | mutant exon 21 | wt exon 19 and 21 | mutant exon 19 | | |
| ID08 | L858R mutation (10%) | G719S mutation (26%) | del747-751insP (8%) | | |
| ID09 | detectable mutation: p.L858R (c.2573T>G) | detectable mutation p.G719X | detectable Deletion in Exon 19 | | |
| ID10 | using pyrosequencing technology the mutation p.L858R, c.2573T>G in Exon 21 detectable | using pyrosequencing technology the mutation p.G719, c.2155G>A in Exon 18 detectable | using pyrosequencing technology the mutation p.L747_A750>P, c.2239-2248>C (18%) in Exon 19 detectable | | |
| ID11 | Mutation detected in Exon 21 L858R | Mutation detected in Exon 18 G719X | Mutation detected in Exon 19, Deletion | | |
| ID12 | EGFR Exon 18, Exon 19 und Exon 20: keine Mutation<br>EGFR Exon 21: somatische Mutation c.2573T>G, p.L858R | EGFR Exon 19, Exon 20 und Exon 21: keine Mutation<br>EGFR Exon 18: somatische Mutation c.[2126A>C;2155G>A], p.[E709A;G710S] | EGFR Exon 18, Exon 20 und Exon 21: keine Mutation<br>EGFR Exon 19: somatische Mutation c.2239_2248delinsC, p.L747_A750 delinsP | Auf die Angabe von stillen Mutationen und Varianten wurde verzichtet. | |
| ID13 | Molekulargenetische Analyse für EGFR: Mutation p.L858R | Molekulargenetische Analyse für EGFR: Mutation p.G719S | Molekulargenetische Analyse für EGFR: Mutation p.L747_A750>P | | |
| ID14 | L858R | G719X | deletions exon 19 | | |
| ID15 | positieve L858R mutation | positive G719S and E709A mutation | positive 19 del mutation | Mutation Q787Q (silent mutation) was detected in Case A, B and C | |

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|---|---|---|---|---|---|
| ID16 | L858R | G719X | Deletionen Exon 19 | | |
| ID18 | EGFR mutation detected:<br>exon 21 L858R | EGFR mutation detected:<br>exon 18 G719X: | EGFR mutation detected:<br>exon 19 del | | |
| ID19 | activating mutation have been detected in sample Econ21 L858R | activating mutation have been detected in sample Exon 18 G719X | activating mutation have been detected in sample Exon 19 Deletion | | |
| ID21 | Positive for the EGFR c.2573T>G (p.L858R) mutation in the exon 21 | Positive for a mutation in the EGFR c.2155/2156 locus in the exon 18 | Positive for a deletion in the exon 19 of the EGFR gene | | |
| interpretation of result as in regular report | | | | | |
| ID01 | - | - | - | | |
| ID02 | Im vorliegenden Untersuchungsmaterial ist eine aktivierende mutation des EGFR Gens NACHWEISBAR | | | | |
| ID04 | Im vorliegenden Untersuchungsmaterial ist eine aktivierende Mutation des EGFR Gens nachweisbar (Punktmutation Exon 21 L858R) | Im vorliegenden Untersuchungs-material ist eine aktivierende Mutation des EGFR Gens nachweisbar (Exon 19 G719X) | Im vorliegenden Untersuchungs-material ist eine aktivierende Mutation des EGFR Gens nachweisbar (Exon 18 Deletion) | | |
| ID05 | classical exon 21 point mutation | double exon 20 mutation: G719S classical activating, E709A: not present in outside database, biological significance unknown | classical exon 19 deletion | | |
| ID06 | Mutation of exon 21: CTG>CGG p.L858R – 12,8% | Mutation of exon 18 GGC>AGC G719S – 21 % | Mutation Exon 19: 2239-2248>C L747-A750>P 16,2% | | |
| ID07 | activating EGFR mutation detected (L858R, C.2573T>G), 35% | activating EGFR mutation not detected | activating EGFR mutation detected (174Edel A750P, c.2239-2248delins), 20% | | |
| ID08 | EGFR activating mutation in exon 21 | EGFR **resistance mutation** in exon 18 | EGFR activating mutation in exon 19 | | |
| ID09 | confers sensitivity to EGFR TKIs | confers sensitivity to EGFR TKIs | confers sensitivity to EGFR TKIs | | |
| ID10 | activating mutation | activating mutation | activating mutation | | |
| ID11 | Im vorliegenden Untersuchungsmaterial zeigt sich eine aktivierende Mutation im Exon 21, L858R | Im vorliegenden Untersuchungs-material zeigt sich eine aktivierende Mutation im Exon 18, G719X L858R | Im vorliegenden Untersuchungs-material zeigt sich eine aktivierende Mutation im Exon 19, Deletion | | |
| ID 12 | Derzeit **keine** unterstützte Datenlage für den Einsatz von IRESSA | | Derzeit keine unterstützte Datenlage für den Einsatz von IRESSA | | |
| ID13 | substitution missens Exon 21 | Substitution missense Exon 18 | Complex deleition Exon 19 | | |
| ID14 | - | - | - | | |

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|---|---|---|---|---|---|
| ID15 | Sample is positive for activating L858R mutation. | Sample is positive for activating G719S and E709A mutations. | Sample is positive for activating 19 del mutation | | |
| ID16 | - | - | - | | |
| ID18 | This mutation is considered to represent an activating EGFR mutation sensitive to TKIs | This mutation is considered to represent an activating EGFR mutation sensitive to TKIs | This mutation is considered to represent an activating EGFR mutation sensitive to TKIs | | |
| ID19 | EGFR positive result confers TKI sensitivity | EGFR positive result confers TKI sensitivity | EGFR positive result confers TKI sensitivity | | |
| ID21 | Presence of the c.2573T>G p.L858R mutation in the exon 21 of the EGFR gene | Presence of the G719X mutation in exon 18 of the EGFR gene without the possibility to differentiate between :<br>c.2156G>C (p.G719A)<br>c.2155G>A (p.G719S)<br>c.2155G>T (p.G719C). | Presence of a deletion in the exon 19 of the EGFR gene without the possibility to differentiate between :<br>2235-2249 del 15<br>2235-2252>AAT del 18<br>2236-2253 del 18<br>2237-2251 del 15<br>2237-2254 del 18<br>2237-2255>T del 19<br>2236-2250 del 15<br>2238-2255 del 18<br>2238-2248>GC del 11<br>2238-2252>GCA del 15<br>2239-2247 del 9<br>2239-2253 del 15<br>2239-2256 del 18<br>2239-2248>C del 10<br>2239-2258>CA del 20<br>2240-2251 del 12<br>2240-2257 del 18<br>2240-2254 del 15<br>2239-2251>C del 13 | | |
| Additional comments to oncology department or recommendations | | | | | |
| ID01 | - | | | | |
| ID02 | In diesem Fall ist ein Ansprechen auf eine Therapie mit einem Tyrosin-Kinase-Inhibitor zu erwarten. | | | | |
| ID04 | - | - | - | | |
| ID05 | the patient is eligible for EGFR TKi therapy | the patient is eligible for EGFR TKI therapy (Iressa registered in this setting) | the patient is eligible for EGFR TKi treatment | | |

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|---|---|---|---|---|---|
| ID06 | The L858R activating mutation is known to be associated with sensitivity to drugs targeting EGFR | The G719S activating mutation is known to be associated with sensitivity to drugs targeting EGFR | The exon 19 deletion is an activating mutation to be associated with sensitivity to drugs targeting EGFR | | |
| ID07 | exons required for drug prescription tested | exons required for drug prescription tested | exons required for drug prescription tested | | |
| ID08 | response to therapy with TKI to be expected | **response to therapy with TKI not expected** | response to therapy with TKI to be expected | | |
| ID09 | EGFR mutation and EML4-ALK alterations aec considered mutually exclusive | EGFR mutation and EML4-ALK alterations aec considered mutually exclusive | EGFR mutation and EML4-ALK alterations aec considered mutually exclusive | | |
| ID10 | - | - | - | | |
| ID11 | - | - | - | | |
| ID 12 | Datenlage **unterstützt** den Einsatz von IRESSA | Derzeit **eingeschränkte-Datenlage** bezügl. des einsatzes von IRESSA betreffend **G719S**, betr. **E709A** liegt keine geischerte Datenlage vor | Datenlage **unterstützt** den Einsatz von IRESSA | | |
| ID13 | partial response | clinical partial response with Gefitinib | partial response | | |
| ID14 | - | | | | |
| ID15 | Presence of the activating L858R mutation is associated with EGFR TKI sensitivity: EGFR TKI therapy is recommended.<br>Reference:<br>Travis W. D. et al. Proc Am Thorac Soc. 2011 Sep;8(5):381-5 | Presence of the activating G719S and E709A mutations is associated with EGFR TKI sensitivity: EGFR TKI therapy is recommended.<br>Reference:<br>Travis W. D. et al. Proc Am Thorac Soc. 2011 Sep;8(5):381-5. | Presence of the activating 19 del mutation is associated with EGFR TKI sensitivity: EGFR TKI therapy is recommended.<br>Reference:<br>Travis W. D. et al. Proc Am Thorac Soc. 2011 Sep;8(5):381-5 | | |
| ID16 | - | - | - | | |
| ID18 | Analyses of other genes genes (e.g. ALK, etc.) seem to be unnecessary | Analyses of other genes genes (e.g. ALK, etc.) seem to be unnecessary | Analyses of other genes genes (e.g. ALK, etc.) seem to be unnecessary | | |
| ID19 | - | order mucin stain and/or IHC | cell block (pleural fluid?) clinical information and radiology neede, order IHC (TTF1) | | |
| ID21 | Presence of the L858R mutation of the EGFR | Presence of the G719X mutation | Presence of the exon 19 Deletions | | |

| | | | | | |
|---|---|---|---|---|---|
| | gene confers sensitivity to the EGFR tyrosine-kinase inhibitors. | of the EGFR gene confers sensitivity to the EGFR tyrosine-kinase inhibitors. | mutation of the EGFR gene confers sensitivity to the EGFR tyrosine-kinase inhibitors | | |
| Diagnosis of case as done in regular reports | | | | | |
| ID01 | seröses in situ Adenocarcinom G2 ohne invas. anteil | gering diff. solid balenförmigesa Adenocarcinom G3 | gering diff. Adenoca G3 | | |
| ID02 | MIA (minimally invasive adenocarcinoma) | Adenocarcinoma | Adenocarcinoma | | |
| ID04 | Adenokarzinom mit lepidischem Wachstumsmuster | Adenokarzinom mit überwiegend mikropapillärem Wachstumsmuster (80% mikropapillär, 20% solid) | Adenokarzinom mit überwiegend solidem Wachstumsmuster (95% solid, 5% azinär) | | |
| ID05 | Lung MIA with classical activating exon 21 point mutation of EGFR | Lung adenocarcinoma with activating exon 20 mutation | Pleural effusion of lung adenocarcinoma with classical activating mutation in exon 19 of EGFR | | |
| ID06 | adenocarcinoma of lung with EGFR activating mutation | adenocarcinoma of lung with EGFR activating mutation | adenocarcinoma of lung with EGFR activating mutation | | |
| ID07 | EGFR /exon 21) activating mutation detectable | EGFR( exon 19 and 21) activating mutation is not detected | EGFR (exon19) activating mutation detectable | | |
| ID08 | pulmonary adenocarcinoma lepidic pattern | pulmonary adenocarcinoma solid and glandular | anaplastic carcinoma | | |
| ID09 | dominant lepidic adenocarcinoma (90%), acinar (10%) ,area of AAH | dominant solid adenocarcinoma (80%) and acinar (20%) with vascular invasion | adenocarcinoma cells incl micropapillary and signet ring cells | | |
| ID10 | Adenocarcinoma in situ, well differentiated with 50% tumor cells in the marked area. Using pyrosequencing technology the mutation L858R ind Exon 21 detectable | Solid adenocarcinoma, low differentiated with 70% tumor cells in the marked area. Using pyrosequencing technology the mutation G719S in Exon 18 detectable | Moderate an low differentiated adenocarcinoma with signet ring cells . With 30% tumor cells in the marked area.Using pyrosequencing technology the mutation L747_A759>P, 2239_2248>C in Exon 19 detecrtable | | |
| ID11 | Adenokarzinom, lepidisches Wachstum (G1) | Wenig differenziertes Adenokarzinom (G3) | Adenocarzinom, teilweise mikropapillär (G2) | | |
| ID 12 | - | - | - | | |
| ID13 | Adenocarcinoma in situ serös | mixed type G3 (solid > 90% acinar >10% | Adenocda (Mikro-)papillär G3 | | |
| ID14 | lepidic (100%) | pred. solid (80%), acinar (20%) | in case of lung ca: micropapillary | | |

| | | | | | |
|---|---|---|---|---|---|
| | | | 100% | | |
| ID15 | Minimal invasive adenocarcinoma | Adenocarcinoma, predominantly solid (solid 85%, acinar 15%) | Adenocarcinoma, necrotic, predominantly solid (solid 80%, micropapillary 20%) | | |
| ID16 | hoch diff. Adenoca, predominant papillär, partiell lepidischer Typ | gering diff. Adenoca, präd. solid, part. acinär | gering diff. adenoca (Zytoblock??) | | |
| ID18 | If it is an invasive adenocarcinoma, then it represents a predominantly lepidic adenoCa. The lesion is smal (less than 3 cm)l, we did not observe a clear-cut invasive patterns (no vascular and or pleural invasion, susp. microinvasive stromal pattern is to be recognized).<br>Theres is a "confusing" presence of (previous ?) inflammatory proceses (septal fibrosis, lymphocytes, granulomatous reaction , organisation of hyaline membranes ?) –see the commentary | Invasive predominantly acinary adenocarcinoma with a predominance of solid-alveolar growth, without IHC analysis (e.g. p40, p63, CK5/6) we can not exclude definitivelly a co-presence of a squamous cell component | Morphology of a NSCLC proliferation (fluidothorax ?), predominance of micropapillary structure, presence of pseudoacinary structure,<br>in this case we would like to see the IHC (e.g. CK7, TTF12, calretinin, WT1, CD68 and Ki-67) | In the case A we have had doubts, whether it is really an invasive adenoCa, or possibly AIS and would like to know the anamnesis of the patient because of the presence of unusual v.s. inflammamory changes | |
| ID19 | Adneocarcinoma in situ, nonmujcinous type (100% lepidic pattern, no invasion) | Adenocarcinoma G3, predominant solid type (solid 90%, acinar 10%) | - | | |
| ID21 | nonmucinous adenocarcinoma with lepidic pattern | adenocarcinoma with solid and acinar pattern | tumor cells of an adenocarcinoma with acinar and papillary features | | |