International Proficiency Test EGFR Exon 20 Insertions (2021)

Lead Institute:
Prof. Dr. rer. nat. S. Merkelbach-Bruse, University Hospital Cologne

Panel Institutes:
Prof. Dr. med. F. Haller, University Hospital Erlangen
Dr. med. A. Streubel, Helios Klinikum E. v. Behring Berlin
Dr. rer. nat. U. Siebolts, University Hospital Halle (Saale)

These instructions are preliminary! Please refer to the final instructions enclosed with the proficiency test samples or available for download online at www.quip.eu during the test period.

Against the backdrop of the development of therapeutic options for patients with EGFR exon 20 insertions, QuIP is now offering a proficiency test on this topic. Various clinical studies have also been conducted, where patients with insertions in exon 20 of the *EGFR* gene were targeted (insertions of known significance in the region between amino acids D761 to C775; Vyse & Huang, Signal Transduction and Targeted Therapy, 2019). The testing for EGFR mutation insertions is therefore the goal of this QuIP proficiency test.

The QuIP proficiency test specifically supports diagnostics using liquid biopsy. Since the analysis of EGFR exon 20 insertions by means of liquid biopsy is not yet established in all institutes, the liquid biopsy part of this proficiency test is to be understood as voluntary. The proficiency test is only available as a package with both liquid biopsy and tissue analysed but assessed independently. Participants who do not/cannot analyse the liquid biopsy samples will not be at a disadvantage.

Instructions

Material:

Artificial tissue (section 1): A total of five samples of artificial FFPE tissue must be tested. You will receive a 10-µm section in a screw-cap tube. Please centrifuge the tube before opening it to avoid losing any material.

Liquid Biopsy (section 2): A total of five samples must be tested. You will receive, per sample, a 5-ml screw-cap tube with 2 ml human plasma to which 60 ng wild-type or mutated fragmented DNA in various allele frequencies above or equal to 1% have been added. In addition, each sample contains wt-DNA for internal extraction control.

The reference samples for this proficiency test are produced by SensID. **If necessary, replacement material can be ordered by e-mail** (office@quip.eu) at an additional cost charged to the participant.

Shipping: The samples will be sent between **20.-24.09.2021.** If the samples do not arrive in perfect condition, please inform us immediately. Do pay particular attention to whether the box is damaged when unpacking.

Analysis: The test should be performed according to the established methods of analysis (i.e. NGS, PCR, Sanger sequencing). The analysis of the *EGFR* gene must be carried out in the participating pathology facility in its entire scope of services and performed under the responsibility of a medical specialist. This will be confirmed through the authorized submission of the test results. The choice of test method is free and at the discretion of the participants. **Please note though that not all analysis methods may be adequate for this proficiency test as they have only a limited mutation spectrum to be detected.** The aim of the analysis is to differentiate between wild-type and mutated EGFR sequences in exon 20 in the region between amino acids D761 to C775. The samples will therefore contain different insertions.
The proficiency testing, including complete result submission, must be performed within 20 working days.

Evaluation: Each section (tissue and liquid biopsy) is assessed separately with a maximum of 10 points each. Two points are awarded for each correct determination of the *EGFR* mutation status of the test sample (`Is there an insertion in EGFR exon 20?: yes / no`). In addition, the name of the insertion is requested, but has no influence on whether the proficiency test is passed. If a sample cannot be analysed due to technical

reasons, a replacement sample can be ordered at an additional cost. The passing score for each section (tissue or liquid biopsy) is 10 points.

In addition, data on the method used is requested in the form of a drop-down menu, but this has no influence on the success of the proficiency test. We do however ask that you provide precise information, especially on the assays used, in order to be able to draw conclusions as to which assays are more suitable for this detection in comparison to others and to cover the broadest possible spectrum of mutations.

Evaluation period: The test results must be submitted online via the relevant survey. To access the survey, log on to qualityinpathology.com - under Enrolments & Invoices, choose the EGFR Ex. 20 Ins. trial and click on Survey. Please submit your results online between **27.09.2021 and 22.10.2021.** All results must be submitted within the evaluation period as the survey is only accessible during this period!

Certificate: Participants will receive a certificate stating "successful participation" when they meet the proficiency test requirements stated above. A confirmation of participation will be provided otherwise.

Subcontracts: The control testing is subcontracted to the above lead panel institute, while the test set production is subcontracted to Sens ID GmbH, Rostock, Germany.