Rapid EGFR Mutation Testing in Lung Cancer Samples: The Idylla™ System

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Introduction

Test for possible mutations in **EGFR exons 18, 19, 20, and 21** is the current standard of care in advanced non-small cell lung cancer.[1] Moreover, EGFR gene mutations should be obtained **quickly** given the rapid tumor progression and availability of effective targeted therapy. However, lack of time or tissue for molecular testing are among the main reasons why patients are often deprived of quick access to the proper targeted therapies.

Methodology

Idylla™ is a fully integrated and automated molecular diagnostics platform that combines **speed** and **ease-of-use** with high sensitivity and high multiplexing capabilities. Moreover, it overcomes the current problem of lack of tissue, and the time-consuming step of processing FFPE tissue samples.
After insertion of a **single FFPE** slice into the cartridge, the complete process of sample liquefaction, nucleic acid preparation, real-time PCR, data analysis and reporting is fully automated. The Idylla™ EGFR Mutation Test allows the sensitive detection of 51 mutations including insertions and deletions in exons 18, 19, 20 and 21, in one single test. The complete process takes less than 2.5 hours and has a LOD of ≤5% for all most prevalent EGFR mutations.[2]

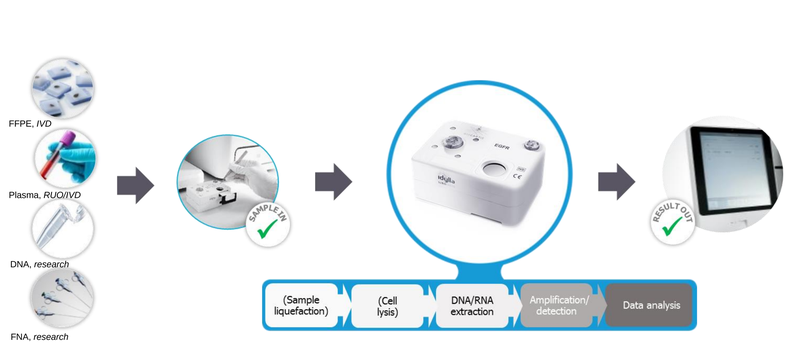


Figure 1: general presentation of the workflow of the Idylla™ assays

EGFR as part of a complete testing algorithm

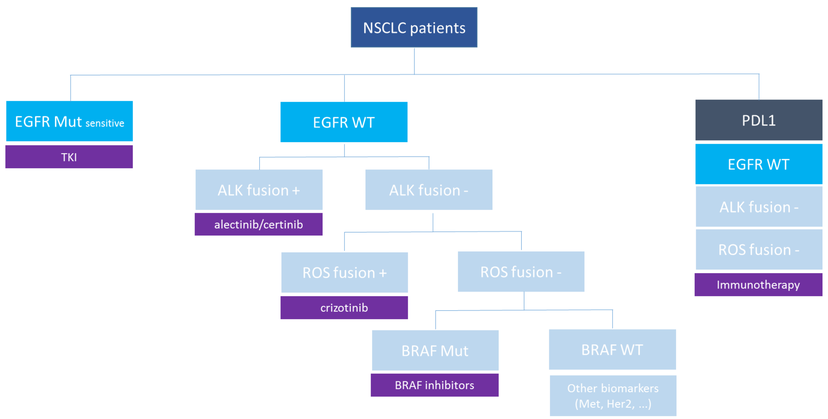


Figure 2: presentation of a testing algorithm for NSCLC patients at baseline, including the guideline recommendations.

The Idylla™ EGFR Mutation Test

PERFORMANCE

Comparison study *versus* Therascreen, Qiagen [2]
- Overall concordance with Therascreen was 97.5%
- Inter-laboratory reproducibility (3 sites, 5 days, 2 operators, 2 instruments): 100% on 600 samples, 120 replicates per sample
- Inter-lot reproducibility (3 lots, 2 instruments, 5 days, 1 operator): 100% on 300 samples, 60 replicates per sample
- No tissue-size related correlation with valid and concordant results observed on 179 metastatic NSCLC samples, with a tissue area ranging from 1 to 567 mm²

Also, in literature high concordance rates between Idylla™ and reference technologies (NGS, Pyrosequening, ...) have been shown.[5,6,7]

LOW INVALID RATE

- Invalid rate for Idylla™ was 7% (13/179) whereas for Therascreen 30% (54/179) [2]
- 80% (20/25) of the samples that resulted in an invalid test result with NGS (25/68; 37%) could be 'rescued' by the Idylla™ test.[5]

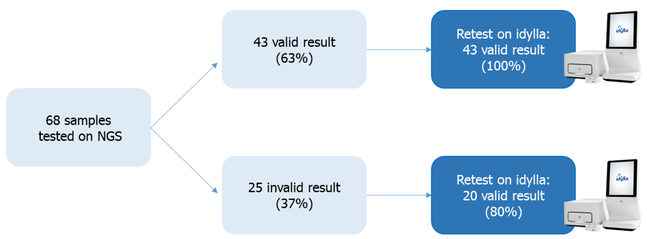


Figure 3: 80% of the samples with an invalid test result by NGS could be rescued by the Idylla test [5]

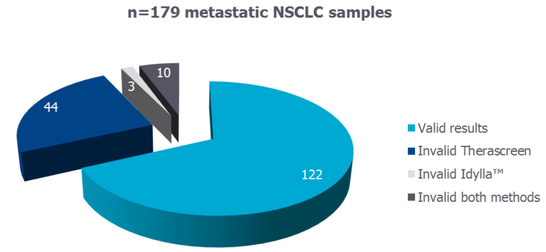
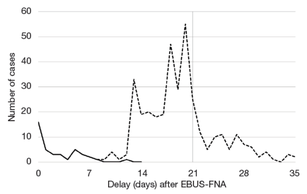


Figure 4: The invalid rate of the performance study of the Idylla™ EGFR Mutaton Test [2]

TURN AROUND TIME

- EGFR and KRAS testing with rapid systems could **spare time**, statistically in about 45% of cases.[8]
- Compared to pyrosequencing, it has been shown that idylla™ had a substantial **shorter turn around time** (3 hours *versus* 12 hours).[6]
- It has been shown that testing on a local on-site system (cfr. Idylla™) versus external biopathological platform is much quicker, <1 week *versus* <3 weeks.[4]



Dotted line: External platform
Full line: Idylla

Figure 5: Comparison of the delay for EGFR/KRAS mutational status by the on-site rapid system and the external biopathological platform [2]

SAMPLE TYPE

- The Idylla™ EGFR Mutation Test has been validated for FFPE use. A single 5µm FFPE tissue section can be used.
- A liquid biospy test, ctEGFR Mutation Assay, will be available soon. 2mL plasma can be used.
- Several researchers have conducted feasibility studies to show the suitability of other sample types:
  - Extracted DNA of cytological samples and cytological smears [3]
  - Extracted DNA of FFPE samples [5]
  - EBUS-FNA samples [4] and Touch prep fresh lung tissue [9]

REFERENCES
1. Novello S. et al. Metastatic non-small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 2016 / **2.** Instructions for use, the Idylla™ EGFR Mutation Test / **3**. De Luca C *et al*. EGFR mutation detection on lung cancer cytological specimens by the novel fully automated PCR-based Idylla EGFR Mutation Assay. J Clin Pathol. 2017 Apr;70(4):295-300 / **4** .Ghigna M *et al*. Endobronchial ultrasound-guided fine-needle aspiration for pulmonary carcinomas genotyping: experience with 398 cases including rapid EGFR/KRAS analysis in 43 cases. J Thorac Dis. 2018 Jul;10(7):4653-4658 / **5**. De Luca C *et al.* The Idylla assay and Next Generation Sequencing: an integrated EGFR mutational testing algorithm J Clin Pathol. 2018 Aug;71(8):745-750. / **6.** Ilie M *et al*. Optimization of *EGFR* mutation detection by the fully-automated qPCR-based Idylla system on tumor tissue from patients with non-small cell lung cancer. Oncotarget. 2017 Oct 4;8(61) / **7.** Lambros L *et al.* Evaluation of a fast and fully automated platform to diagnose EGFR and KRAS mutations in formalin-fixed and paraffin-embedded non-small cell lung cancer samples in less than one day. J Clin Pathol. 2017 Jun;70(6):544-549 / **8.** De Montpréville TV *et al.* EGFR and KRAS molecular genotyping for pulmonary carcinomas: Feasibility of a simple and rapid technique implementable in any department of pathology. Pathol Res Pract. 2017 Jul;213(7):793-798. / **9.** Rabie Al-Turkmani M. *et al*. Stat EGFR Mutation Detection in Fresh Lung Cancer Tissue Specimens Using Touch Preparation and the Idylla™ System. Abstract AMP 2018: TT060