Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

1. Determine the quantity and quality of evidence available for a technology of interest.
2. Identify any gaps in the evidence/ongoing evidence collection.
3. Inform decisions on topics that warrant fuller assessment by Health Technology Wales.

Topic:	Rapid fully-automated PCR testing (Idylla) to screen for EGFR mutational status in people with lung cancer
Topic exploration report number:	TER191.1

Introduction and aims

The Idylla platform is a PCR machine that allows for a rapid (2 to 3 hour), fully-automated PCR testing for various genetic abnormalities, which can then inform appropriate oncological treatment. At the time of this report there are seven PCR assays available for the Idylla system, and a further one in development.

For this report, Health Technology Wales researchers searched for evidence on rapid, fully-automated PCR testing (such as Idylla) to determine EGFR mutational status in lung cancer. EGFR mutations are found in about 10% of lung cancer cases, and people with this mutational status generally respond well to tyrosine kinase inhibitors.

This report is one of two topic explorations on the Idylla system, exploring two different tests (EGFR test and BRAF test).

Summary of evidence

Guidelines

We identified guidelines that recommend EGFR testing and subsequent treatment regimens from the Health Technology Assessment Group in Ireland, SIGN and the National Institute for Health and Care Excellence (NICE).

NICE diagnostics guidance 9 (2013) includes recommendations for specific testing strategies for EGFR-TK mutations in the tumours of adults with previously untreated, locally advanced or metastatic non-small-cell lung cancer, when used in accredited laboratories participating in an external quality assurance scheme. The recommended tests do not include any fully-automated tests.

Secondary evidence

We did not identify any guidelines or secondary evidence on rapid, fully-automated PCR testing for EGFR status.

Primary evidence

We identified 18 primary studies evaluating the Idylla system for EGFR testing in lung cancer. The majority of studies were retrospective analysis of samples that had previously been analysed with other testing strategies, for examples PCR tests, next generation sequencing or Sanger sequencing. One study reported samples being blinded for analysis. Overall, the studies reported good concordance and diagnostic accuracy of the Idylla system, and that it was able to process samples that were unable to go through next generation sequencing. However, a few studies reported that some EGFR mutations were not identified by the Idylla system.

One study (Thomas De Montpréville et al., 2017) looked at feasibility of implementing Idylla in a pathology laboratory setting and tested prospectively collected samples. The authors reported that there was not a need for complex training and that rapid turnaround allowed mutational status to be defined a few hours after histological diagnosis.

Economic evidence

One study reported economic considerations of implementing Idylla platforms (for multiple assays) compared to next generation sequencing, from a French healthcare perspective (Le Flahec et al. 2017). A second study (Ilie et al. 2017) reported a cost-effectiveness comparison of the Idylla test versus pyrosequencing for EGFR status; the authors concluded that Idylla was cost saving.

Ongoing evidence

We identified one clinical study that had a recent completion date of February 2020. The UK, single centre study aimed to evaluate liquid based cytology specimens as an alternative to formalin-fixed paraffin embedded histology samples. The study planned to enrol 50 participants.

Areas of uncertainty

The evidence identified was for the Idylla rapid fully-automated PCR platform. At this stage it is unknown whether there are similar rapid fully-automated platforms available in the UK.

The samples that were used in the studies varied in lung cancer type (non-small cell lung cancer or its subtypes). In addition, there was some variation in the types of samples (e.g. paraffin fixed). It is not clear whether these variables are generalisable, or whether only evidence using standard testing approaches is relevant.

The topic proposer states that Idylla would be an additional step to support rapid oncological decision making; full next generation sequencing would still be done downstream. It is not clear whether this is the extent of current provision, or whether other PCR testing is currently available as an interim to next generation sequencing from the specialised laboratories.

Conclusions

We identified several primary studies evaluating Idylla EGFR testing for lung cancer; most were retrospective and reported diagnostic accuracy outcomes for Idylla compared to other testing

methods. Initial exploration did not identify any evidence on improved patient outcomes, such as time to treatment, progression-free survival or overall survival. We also identified some economic evidence. A fuller evaluation would be required to ascertain quality and appropriateness of the evidence and outcomes reported.

Brief literature search results

Resource	Results
HTA organisations	
Healthcare Improvement Scotland	We did not identify any relevant evidence from this source.
Health Technology Assessment Group	Lung Chemotherapy Regimens: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/lung/ Does not refer to specific products for EGFR testing but outlines treatment regimen based on EGFR mutational status.
Health Information and Quality Authority	We did not identify any relevant evidence from this source.
UK guidelines and guidance	
SIGN	SIGN137 Management of Lung Cancer https://www.sign.ac.uk/sign-137-management-of-lung-cancer Does not refer to specific products for testing, but states that EGFR testing is "recommended, as proposed in various guidelines, since EGFR tyrosine kinase inhibitors are accepted for restricted use in Scotland."
NICE	NICE Guideline 122 Lung cancer: diagnosis and management. (2019) https://www.nice.org.uk/guidance/ng122 Does not refer to specific products for testing, but outlines treatment regimen based on EGFR status. Diagnostics Guidance DG9. EGFR-TK mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer. (2013) https://www.nice.org.uk/guidance/dg9
Secondary literature and economic evaluations	
ECRI	Not searched.
EUnetHTA	We did not identify any relevant evidence from this source.
Cochrane library	We did not identify any relevant evidence from this source.
Medline (Ovid)	We did not identify any relevant evidence from this source.
Primary studies	
Cochrane library	Marabese M, Broggini M, Reijans M, et al. (2017). Comparison of technologies for EGFR analysis within a subset of a randomized clinical trial. Cancer research. 77(13). doi: 10.1158/1538-7445.AM2017-3739. https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01424056/full
Medline	Al-Turkmani MR, Suriawinata MA, Deharvengt SJ, et al. (2020). Rapid EGFR mutation testing in lung cancer tissue samples using a fully automated system and single-use cartridge. Practical Laboratory Medicine. 20: e00156. doi: https://dx.doi.org/10.1016/j.plabm.2020.e00156 Bocciarelli C, Cohen J, Pelletier R, et al. (2020). Evaluation of the Idylla system to detect the EGFR^{T790M} mutation using extracted DNA. Pathology, Research & Practice. 216(1): 152773. doi: https://dx.doi.org/10.1016/j.prp.2019.152773

Boureille A, Ferraro-Peyret C, Pontarollo G, et al. (2020). Rapid detection of EGFR mutations in decalcified lung cancer bone metastasis. Journal of Bone Oncology. 21: 100277. doi: https://dx.doi.org/10.1016/j.jbo.2020.100277

Colling R, Bancroft H, Langman G, et al. (2019). Fully automated real-time PCR for EGFR testing in non-small cell lung carcinoma. Virchows Archiv. 474(2): 187-92. doi: https://dx.doi.org/10.1007/s00428-018-2486-y

De Luca C, Conticelli F, Leone A, et al. (2019). Is the Idylla EGFR Mutation Assay feasible on archival stained cytological smears? A pilot study. Journal of Clinical Pathology. 72(9): 609-14. doi: https://dx.doi.org/10.1136/jclinpath-2019-205863

De Luca C, Gragnano G, Pisapia P, et al. (2017). EGFR mutation detection on lung cancer cytological specimens by the novel fully automated PCR-based Idylla EGFR Mutation Assay. Journal of Clinical Pathology. 70(4): 295-300. doi: https://dx.doi.org/10.1136/jclinpath-2016-203989

De Luca C, Rappa AG, Gragnano G, et al. (2018). Idylla assay and next generation sequencing: an integrated EGFR mutational testing algorithm. Journal of Clinical Pathology. 71(8): 745-50. doi: https://dx.doi.org/10.1136/jclinpath-2018-205197

Evrard SM, Taranchon-Clermont E, Rouquette I, et al. (2019). Multicenter Evaluation of the Fully Automated PCR-Based Idylla EGFR Mutation Assay on Formalin-Fixed, Paraffin-Embedded Tissue of Human Lung Cancer. Journal of Molecular Diagnostics. 21(6): 1010-24. doi: https://dx.doi.org/10.1016/j.jmoldx.2019.06.010

Heeke S, Hofman P. (2019). EGFR Mutation Analysis in Non-small Cell Lung Carcinoma from Tissue Samples Using the Fully Automated Idylla TM qPCR System. Methods in Molecular Biology. 2054: 147-55. doi: https://dx.doi.org/10.1007/978-1-4939-9769-5_10

Huang H, Springborn S, Haug K, et al. (2019). Evaluation, Validation, and Implementation of the Idylla System as Rapid Molecular Testing for Precision Medicine. Journal of Molecular Diagnostics. 21(5): 862-72. doi: https://dx.doi.org/10.1016/j.jmoldx.2019.05.007

Ilie M, Butori C, Lassalle S, et al. (2017). 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. 8(61): 103055-62. doi: https://dx.doi.org/10.18632/oncotarget.21476

Kaanane H, El Attar H, Louahabi A, et al. (2019). Targeted methods for molecular characterization of EGFR mutational profile in lung cancer Moroccan cohort. Gene. 705: 36-43. doi: https://dx.doi.org/10.1016/j.gene.2019.04.044

	Lambros L, Caumont C, Guibourg B, et al. (2017). 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. Journal of Clinical Pathology. 70(6): 544-9. doi: https://dx.doi.org/10.1136/jclinpath-2016-204202 Thomas De Montpreville V, Ghigna MR, Lacroix L, et al. (2017). EGFR and KRAS molecular genotyping for pulmonary carcinomas: Feasibility of a simple and rapid technique implementable in any department of pathology. Pathology, Research & Practice. 213(7): 793-8. doi: https://dx.doi.org/10.1016/j.prp.2017.03.011
Ongoing primary or secondary research	
PROSPERO database	We did not identify any relevant evidence from this source.
Clinicaltrials.gov	NCT04086680. Use of the Idylla Platform for the Detection of EGFR Mutations in Liquid- Based Cytology Specimens of Lung Adenocarcinoma. https://clinicaltrials.gov/ct2/show/NCT04086680
Other	
Additional evidence identified from topic submission	Le Flahec G, Guibourg B, Marcorelles P, et al. (2017). Financial implications of Idylla testing in colorectal cancer, lung cancer and melanoma: a French laboratory point of view. Journal of Clinical Pathology. 70(10): 906. doi: http://dx.doi.org/10.1136/jclinpath-2017-204579 Van Haele M, Vander Borght S, Ceulemans A, et al. (2020). Rapid clinical mutational testing of KRAS, BRAF and EGFR: a prospective comparative analysis of the Idylla technique with high-throughput next-generation sequencing. Journal of Clinical Pathology. 73(1): 35. doi: http://dx.doi.org/10.1136/jclinpath-2019-205970 Brohawn DG, Mu X, Tong Z, Rao E, Wang Y, et al. (2018) Biocartis Idylla proves Fast and Accurate in Detecting Oncogenic KRAS and EGFR Mutations in Paraffin Embedded Tumor Samples. J Diagn Tech Biomed Anal 7:2. doi: http://dx.doi.org/10.4172/2469-5653.1000134

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Concepts used:	Idylla, rapid PCR test, automated PCR test, EGFR or epidermal growth factor receptor, lung cancer