NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Health Technology Evaluation

Report for Guidance Executive

Review of DG9: EGFR‑TK mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer

This guidance was issued in August 2013.

The review date for this guidance is August 2016.

NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance. Other factors such as the introduction of new technologies relevant to the guidance topic, or newer versions of technologies included in the guidance, will be considered relevant in the review process, but will not in individual cases always be sufficient cause to update existing guidance.

1. Recommendation

Transfer the guidance to the 'static guidance' list

That we should consult on the proposal.

A list of the options for consideration and the consequences of each option is provided in Appendix 1 at the end of this paper.

2. Original objective of guidance

To assess the clinical and cost effectiveness of technologies/methodologies for EGFR-TK mutation testing in adults with chemotherapy naive, locally advanced or metastatic non-small-cell lung cancer (NSCLC) for informing first-line treatment decisions as currently recommended by NICE, in the NHS in England.

3. Current guidance

Adoption recommendations

1.1 The tests and test strategies listed below are recommended as options for detecting epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutations in the tumours of adults with previously untreated, locally advanced or metastatic non-small-cell lung cancer (NSCLC), when used in accredited laboratories participating in an external quality assurance scheme. The

laboratory-developed tests should be designed to detect the mutations that can be detected by one of the CE‑marked tests as a minimum.

- therascreen EGFR RGQ PCR Kit (CE‑marked, Qiagen)
- cobas EGFR Mutation Test (CE‑marked, Roche Molecular Systems)
- Sanger sequencing of samples with more than 30% tumour cells and therascreen EGFR RGQ PCR Kit for samples with lower tumour cell contents
- Sanger sequencing of samples with more than 30% tumour cells and cobas EGFR Mutation Test for samples with lower tumour cell contents
- Sanger sequencing followed by fragment length analysis and polymerase chain reaction (PCR) of negative samples.

1.2 There was insufficient evidence for the committee to make recommendations on the following methods:

- high-resolution melt analysis
- pyrosequencing combined with fragment length analysis
- single-strand conformation polymorphism analysis
- next-generation sequencing
- therascreen EGFR Pyro Kit (CE‑marked, Qiagen).

Research recommendations

7.1 NICE recommends that studies directly comparing different epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation test methods are performed. These studies should include the re-testing of stored NSCLC tumour samples using different EGFR-TK mutation test methods and should link to patient outcomes.

7.2 NICE recommends that a multivariate prediction model is developed with the aim of predicting the response of previously untreated, advanced or metastatic NSCLC to treatment with an EGFR-TK inhibitor.

4. Rationale

Changes in clinical practice, technology costs or evidence that would lead to a change in the recommendations of the original guidance have not been identified. It is therefore proposed that the guidance is placed on the static list.

5. Implications for other guidance producing programmes

No overlaps have been identified.

6. New evidence

The search strategy from the original diagnostics assessment report was re-run on EMBASE, Medline, Medline in-process, Cochrane database, PROSPERO, LILACS, the ISRCTN registry, the WHO ICTRP, BIOSIS Web of Science, Science Citation Index (Web of science), NHS Economic Evaluation Database, the Journal of Clinical Oncology website and the Annals of Oncology website. References from 2012 onwards were reviewed. Additional searches of clinical trials registries were also carried out and relevant guidance from NICE and other professional bodies was reviewed to determine whether there have been any changes to the diagnostic and care pathways. Companies were asked to submit all new literature references relevant to their technology along with updated costs and details of any changes to the technology itself or the CE marked indication for use for their technology. Specialist Committee Members for this guidance topic were also consulted and asked to submit any information regarding changes to the technologies, the evidence base and clinical practice. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies.

6.1 Technologies

6.1.1 cobas EGFR Mutation Test (Roche)

Since the publication of diagnostics guidance 9, a second version of the cobas EGFR Mutation Test has been released (the cobas EGFR Mutation Test v2). The new test identifies 42 mutations in exons 18-21 of the *EGFR* gene, including the 41 mutations of the first version plus an additional mutation. The initial test is unchanged [redacted].

Both versions of the cobas EGFR Mutation Test are real-time PCR tests for the qualitative detection of defined mutations of the *EGFR* gene in people with non-small cell lung cancer (NSCLC). They both detect mutations in DNA isolated from formalin-fixed paraffin-embedded tumour tissue. In addition, the latest test version can also use circulating-free tumour DNA from plasma (derived from blood samples). A cell free DNA sample preparation kit is available from Roche for extracting DNA from plasma.

No acquisition test costs were available for the cobas EGFR Mutation Test in the original assessment. The charged price used for this test in modelling was £140 (with a standard error of £27.50), based on the results of a survey of laboratories in

England and Wales. Roche has now provided acquisition costs for the cobas EGFR Mutation Test (Table 1).

Table 1 Acquisition cost for the cobas EGFR Mutation Test (Roche)

Product name	Average selling price (GBP) excluding VAT
KIT DNA ISOLATION 24T IVD	[redacted]
KIT COBAS CFDNA SAMP PREP 24T	[redacted]
KIT COBAS EGFR AMP/DET V2 24T IVD	[redacted]

6.1.2 therascreen EGFR RGQ PCR Kit (Qiagen)

No information was received from Qiagen to confirm whether the therascreen EGFR RGQ PCR Kit has been updated, or if costs have changed, since diagnostics guidance 9 was published.

Information from the Qiagen website suggests that an updated version of the therascreen EGFR RGQ PCR kit is now available and that the original version is no longer marketed. It is unclear how the 2 versions differ. The company's website states that therascreen EGFR RGQ PCR Kit version 2 is able to detect 29 mutations in the *EGFR* gene (which are the same mutations detected by the original kit version).

In addition, a therascreen EGFR Plasma RGQ PCR Kit is listed on the Qiagen website. The website states that this kit is an in vitro diagnostic test for the detection of mutations in the *EGFR* gene from circulating-free DNA (cfDNA) extracted from plasma obtained from blood samples.

6.1.3 therascreen EGFR Pyro Kit (Qiagen)

No information was received from the Qiagen to confirm whether the therascreen EGFR Pyro Kit has been updated, or if costs have changed, since diagnostics guidance 9 was published. The kit is listed on the Qiagen website.

6.1.4 Laboratory developed tests

No information was identified on the availability of, or any changes made to, the laboratory-developed tests included in diagnostics guidance 9.

6.1.5 Additional EGFR mutation tests

The field of *EGFR* testing is expanding and a variety of new commercial and laboratory developed tests have become available since the publication of diagnostics guidance 9, including:

- Human EGFR Mutation Qualitative Detection Kit (ACCB Biotech Ltd)

- ADx EGFR Mutations Detection Kit (Amoy Diagnostics)
- PCR invader assay (BML)
- SURVEYOR kit (IDT)
- PNAClampTM EGFR Mutation Detection kit (PANAGENE, Inc.)
- Surplex EGFR Mutation Kit (SurexamBio-Tech)
- Ion Torrent AmpliSeq Custom Panel (Life Technologies).

6.2 Clinical practice

Since diagnostics guidance 9 was published, the Royal College of Pathologists have included the results of *EGFR* mutation testing as a core data item in their guidelines on lung cancer reporting. The EAC commented that *EGFR* testing appears to be becoming more ingrained into standard clinical practice.

A clinical expert commented that since the publication of diagnostics guidance 9, *EGFR* mutation testing using circulating free DNA from plasma samples is now in greater use in the NHS. This testing can be used either when a tumour biopsy sample is inadequate to carry out *EGFR* testing or if it is not possible to carry out a biopsy to obtain a tissue sample.

Since diagnostics guidance 9 published, a further EGFR-TK inhibitor (afatinib) has been recommended by NICE as an option for treating adults with locally advanced or metastatic NSCLC who test positive for EGFR-TK mutations.

A technology appraisal on erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed after prior chemotherapy has also been published since diagnostics guidance 9 published. This guidance is not directly relevant to the scope of diagnostics guidance 9, as the diagnostics guidance specified a 'chemotherapy naïve' population. The technology appraisal recommends erlotinib as a possible treatment for people with locally advanced or metastatic non-small-cell lung cancer that has already been treated with non-targeted chemotherapy because of delayed confirmation of EGFR-TK mutation status, if:

- their cancer tests positive for the EGFR-TK mutation or
- it is not known if the cancer is EGFR-TK mutation-positive because of problems with getting a tissue sample or poor quality DNA, and
    - the cancer is very likely to be EGFR-TK mutation-positive
    - it responds to the first 2 cycles of treatment with erlotinib.

Erlotinib is not recommended for treating locally advanced or metastatic non-small-cell lung cancer that doesn't test positive for the EGFR-TK mutation. Gefitinib is not recommended for treating NSCLC that has progressed after chemotherapy.

6.3 New studies

The EAC identified 12 studies relevant to this review. Five studies reported test accuracy and 8 studies reported clinical outcomes related to use of the tests. One abstract also reported on the technical performance of a kit. Summaries of data from identified studies are presented below, categorised by the test used.

Several ongoing studies relating to EGFR tests were identified, however many of these studies relate to the use of *EGFR* mutation testing to monitor treatment or disease progression, or to compare testing of tissue from tumours with testing using circulating-free tumour DNA (ctDNA). Identified ongoing studies are listed in appendix 2.

6.3.1 therascreen EGFR RGQ PCR kit (Qiagen)

Four studies investigated clinical outcomes based on *EGFR* testing using the therascreen EGFR RGQ PCR kit using tissue samples.

Douillard et al. (2014b) reported on the efficacy of gefitinib in people who were *EGFR* mutation positive (determined by the therascreen EGFR RGQ PCR kit), with all included patients receiving gefitinib. After a median follow-up of 13.0 months objective response rate was 69.8%, disease control rate was 90.6%, median progression free survival (PFS) was 9.7 months and median overall survival was 19.2 months.

Sequist et al. (2013) randomised advanced NSCLC patients who were *EGFR* mutation positive (as determined by the therascreen EGFR RGQ PCR Kit) to either receive afatinib or chemotherapy. PFS was prolonged for people receiving afatinib compared with chemotherapy; median PFS values were 11.1 months and 6.9 months respectively (HR 0.58; 95% CI 0.43 to 0.78). Median PFS among those with exon 19 deletions and L858R *EGFR* mutations was 13.6 months for people receiving afatinib and 6.9 months for people receiving chemotherapy (HR, 0.47; 95% CI, 0.34 to 0.65).

Yang et al. (2014) used the therascreen EGFR RCQ PCR Kit to test people with locally advanced or metastatic non-squamous NSCLC after randomisation for different treatments: initial pemetrexed-cisplatin chemotherapy followed by maintenance gefitinib; or gefitinib monotherapy. In the *EGFR* mutation positive subgroup, the PFS difference between arms was not significant (HR 0.83, p = 0.585). The pemetrexed-cisplatin chemotherapy followed by maintenance gefitinib treatment arm had longer PFS compared with the gefitinib monotherapy arm for the *EGFR* mutation negative subgroup (HR 0.18, p = 0.001).

Hung et al. (2016) evaluated the response to first-line erlotinib, gefitinib or afatinib based on the amount of mutant *EGFR* in lung cancer tissue (for people with exon 19 deletions and L858R mutations, determined by the therascreen EGFR RGQ PCR

kit). The authors reported increased PFS in patients categorised as having a high percentage of mutant DNA (above 4.77%); 26.3 versus 12.3 months.

A conference abstract reported that the therascreen EGFR RGQ PCR test required 40 minutes for DNA extraction and 2 hours for the PCR to run (Denis et al. 2014).

6.3.2 therascreen EGFR RGQ PCR Kit (Qiagen) - plasma testing

Two studies compared the accuracy of the therascreen EGFR RGQ PCR kit used on DNA derived from tumour samples and circulating-free tumour DNA (ctDNA) derived from either serum or plasma samples.

Douillard et al. (2014a) investigated the accuracy of this technology to detect exon 19 deletions, L858R point mutations, and T790M point mutations in circulating-free tumour DNA obtained from plasma samples from patients with locally advanced or metastatic NSCLC. Concordance between tests results using DNA from tumour tissue samples and from plasma-derived ctDNA samples was 94.3%. When test results derived from tumour tissue samples were considered a reference standard, ctDNA based testing had a sensitivity of 65.7%, a specificity of 99.8%, a positive-predictive value of 98.6% and a negative-predictive value of 93.8%.

Nishio et al. (2016) compared the therascreen EGFR RGQ PCR kit used on serum samples from chemotherapy-naïve, advanced NSCLC patients with the same assay using tumour derived samples. When compared with tumour sample analysis, the detection rate of ctDNA serum analysis (for the detection of exon 19 deletions or L858R point mutations) was 26.3% overall, with a detection rate of 35.6% for exon 19 deletions and 18.0% for L858R mutations. The agreement rate between tumour and serum sample testing was 96.2% when serum status was detected.

6.3.3 therascreen EGFR Pyro Kit (Qiagen)

Khode et al. (2013) compared the accuracy of the Qiagen EGFR Pyro Kit and the Qiagen EGFR RGQ PCR Kit in patients with matched cytology and formalin-fixed, paraffin-embedded (FFPE) tissue samples. Concordance between the tests was 84% for FFPE samples and 85% for cytology samples. When the EGFR Pyro Kit was considered as the reference standard, sensitivity and specificity of the RGQ kit were 56.25% and 97.05% for FFPE samples and 44.44% and 92.59% for cytology samples.

6.3.4 cobas EGFR Mutation Testing Kit (Roche)

Benlloch et al. (2014) retrospectively compared the cobas EGFR mutation test with laboratory-developed tests and Sanger sequencing. Samples were from stage IIIB or stage IV NSCLC patients with no history of chemotherapy for metastatic disease from the EURTAC trial. When laboratory developed tests were considered as the reference standard, the cobas EGFR mutation test had a sensitivity of 94.2%,

specificity of 97.5% and overall agreement of 96.3%. Of the discordant results, the cobas EGFR mutation test result was confirmed (by massively parallel pyrosequencing) in 68.8% of cases. When Sanger sequencing was considered as the reference standard, the cobas EGFR mutation test had a sensitivity of 96.6%, specificity of 88.3% and overall agreement of 90.6%. Of the discordant results, massively parallel pyrosequencing confirmed the cobas EGFR mutation test result in 78.9% of cases.

This study also reported on clinical outcomes based on the result of cobas EGFR mutation testing. For people with a positive test result, those treated with erlotinib had a significantly longer PFS compared with those treated with chemotherapy; with median PFS values of 10.4 months and 5.4 months respectively (HR 0.34; 95% CI: 0.21 to 0.54). Similar results were seen for people who had a positive test result with laboratory developed tests; people receiving erlotinib had a median PFS of 9.7 months compared with a median PFS of 5.2 months in people treated with chemotherapy. No significant difference in overall survival between the treatment arms was observed.

A further study (Winther Larsen et al. 2014) reported that among people with NSCLC with somatic *EGFR* mutations (as identified by the cobas EGFR mutation test) treated with erlotibinb, a lower number of cytosine-adenosine repeats in intron 1 of the *EGFR* gene is associated with longer PFS and overall survival.

Oh et al. (2013; abstract only) investigated the agreement between 3 *EGFR* mutation tests in people with recurrent NSCLC treated with EGFR-TKIs after surgery: the cobas EGFR mutation test, the PNA Clamp EGFR mutation test (Panagene) and direct sequencing. The agreement of the cobas test and PNA Clamp test was 93.7% (k=0.864, p<0.001), that of the cobas test and sequencing was 84.7% (k=0.653, p<0.001), and that of PNA Clamp test and sequencing was 78.4% (k=0.528, p<0.001).

6.3.5 Further test strategies

One RCT (Khozin et al. 2014) investigated the effect of *EGFR* exon 19 deletions and L858R point mutations on the response to first-line erlotinib and standard chemotherapy. *EGFR* mutations were identified by laboratory-developed tests, specifically, Sanger sequencing followed by length analysis of fluorescently labelled PCR for exon 19 deletions and TaqMan-based PCR (Applied Biosystems) for L858R mutations. People identified as having *EGFR* mutations using these tests were subsequently tested with the cobas EGFR Mutation Test; with mutations confirmed in 87% of cases. People with NSCLC and *EGFR* mutations (identified by laboratory developed tests) were randomly allocated to receive either erlotinib or chemotherapy. Progression free survival was significantly improved in the erlotinib arm (median 10.4 months in the erlotinib arm and 5.2 months in the chemotherapy arm; HR 0.27 95% CI: 0.17, 0.43). No significant difference in overall survival was

observed (median 22.9 and 19.5 months for the erlotinib and chemotherapy arms, respectively; HR 0.93; 95% CI: 0.64, 1.35).

6.3.6 Economic evidence

One study was identified (Towse et al. 2013) which reported that the cobas EGFR Mutation Test had an incremental cost per QALY gained of £18,394 compared to Sanger sequencing. The model was constructed from the perspective of a UK payer, and included input parameters describing mutation testing accuracy, treatment response (EGFR inhibitor, standard chemotherapy or best supportive care) and adverse events arising from treatment. However, further details of model structure and inputs were not available as this study was presented only as an abstract.

7. Summary of new evidence and implications for review

As in the original assessment, new studies on clinical outcomes indicate that progression free survival is statistically significantly better in people with *EGFR* mutations treated with tyrosine kinase inhibitors compared with people with *EGFR* mutations treated with chemotherapy. Similarly, studies in the original review and the new studies identified both show no statistically significant difference in overall survival between people with *EGFR* mutations having EGFR-TK inhibitors and people with *EGFR* mutations having standard chemotherapy.

In the original assessment, data on the accuracy of *EGFR* mutation testing for predicting the response to treatment with EGFR-TK inhibitors was only available for Sanger sequencing methods and the therascreen EGFR RGQ PCR Kit, using objective response as a reference standard. The therascreen EGFR RGQ PCR kit was suggested to have the best overall performance; with sensitivity of 99% and specificity of 69%. In the economic model, test accuracy for the cobas EGFR Mutation test was assumed to be equal to the test accuracy for the therascreen EGFR RGQ PCR test. A new study suggests similar sensitivity value for the cobas EGFR mutation test (96.6%) and a higher specificity value (88.3%), with Sanger sequencing as reference standard. Given that new accuracy data are comparable to those used in the original model, they would be unlikely to have an effect on the existing guidance recommendations.

In the original assessment, the therascreen EGFR Pyro Kit was not included in cost effectiveness analysis because of a lack of data, and no recommendations were made on this test. In this review, 1 study was identified that reported on the test accuracy of this kit compared test with the therascreen EGFR RGQ PCR kit. However, no studies were identified that reported on the clinical effectiveness of treating people based on therascreen EGFR Pyro Kit testing. Diagnostics guidance 9 only recommended tests that had some clinical outcome data (therascreen EGFR RGQ PCR Kit, cobas EGFR Mutation Kit and Sanger sequencing based methods) and did not recommend tests that only had analytical validity data (high-resolution

melt analysis, pyrosequencing combined with fragment length analysis and single-strand conformation polymorphism analysis). Therefore, the new data on the accuracy of the therascreen EGFR Pyro Kit would be unlikely to have an effect on the existing recommendations.

New versions of the cobas EGFR Mutation Test and the therascreen EGFR RGQ PCR Kit have been released since diagnostics guidance 9 published. The therascreen EGFR RGQ PCR Kit version 2 appears to detect the same set of mutations as the original version of the kit. The cobas EGFR Mutation Test version 2 detects 1 more mutation than the first version of this test. Both of these tests were recommended for use and it is unlikely that the minor changes made will adversely affect the test performance.

Since the diagnostics guidance was published, the use of circulating free DNA from plasma samples for *EGFR* mutation testing is in greater use in the NHS. Published studies and ongoing trials relating to this modality of testing were identified in this review. *EGFR* mutation testing on plasma samples is indicated for use when tumour tissue samples are unobtainable or inadequate for *EGFR* testing. However, this population is outside the scope for diagnostics guidance 9, which specified a population of "*adults with previously untreated, locally advanced or metastatic (stage III or IV) NSCLC of any histological subtype, with either a biopsy sample or a cytology sample available for EGFR-TK mutation testing*" (underlining added).

In conclusion, the evidence base and clinical environment has not changed to an extent that is likely to have a material effect on the adoption recommendations in the existing guidance; it is therefore suggested that the guidance is transferred to the static list.

8. Implementation

No relevant Implementation data were found.

9. Equality issues

It was noted that people with locally advanced or metastatic non-small-cell lung cancer (NSCLC) would fall within the provisions of the Equality Act 2010 from the point at which a diagnosis of cancer has been made. In addition, it was noted that the frequency of EGFR-TK mutations is highest in Asian women who have never smoked and have tumours with adenocarcinoma histology.

No new equality issues have been identified since the publication of the guidance.

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Appendix 1 – explanation of options

If the published diagnostics guidance needs updating NICE must select one of the options in the table below:

Options	**Consequence**	**Selected – 'Yes/No'**
Standard update of the guidance	A standard update of the diagnostics guidance will be planned into NICE's work programme.	No
Accelerated update of the guidance	An accelerated update of the diagnostics guidance will be planned into NICE's work programme. Accelerated updates are only undertaken in circumstances where the new evidence is likely to result in minimal changes to the decision problem, and the subsequent assessment will require less time to complete than a standard update or assessment.	No
Update of the guidance within another piece of NICE guidance	The guidance is updated according to the processes and timetable of that programme.	No

If the published diagnostics guidance does not need updating NICE must select one of the options in the table below:

Options	**Consequences**	**Selected – 'Yes/No'**
Transfer the guidance to the 'static guidance list'	The guidance remains valid and is designated as static guidance. Literature searches are carried out every 5 years to check whether any of the diagnostics guidance on the static list should be flagged for review.	Yes
Produce a technical supplement	A technical supplement describing newer versions of the technologies is planned into NICE's work programme.	No
Defer the decision to review the guidance to [specify date or trial].	NICE will reconsider whether a review is necessary at the specified date.	No
Withdraw the guidance	The Diagnostics Guidance is no longer valid and is withdrawn.	No

Appendix 2 – supporting information

Relevant NICE work

Published

- Suspected cancer: recognition and referral (2015) NICE guideline NG12
- erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed after prior chemotherapy (2015) NICE technology appraisal guidance TA374
- afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-cell lung cancer (2014) NICE technology appraisal guidance TA310
- EGFR-TK mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer (2013) NICE diagnostics guidance DG9
- erlotinib for the first-line treatment of locally advanced or metastatic EGFR-TK mutation-positive non-small-cell lung cancer (2012) NICE technology appraisal guidance TA258
- erlotinib monotherapy for maintenance treatment of non-small-cell lung cancer (2011) NICE technology appraisal guidance TA227
- Lung cancer: diagnosis and management. (2011) NICE guideline CG121
- gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer (2010) NICE technology appraisal guidance TA192
- Metastatic malignant disease of unknown origin in adults: diagnosis and management (2010) NICE guideline CG104
- Pemetrexed for the first-line treatment of non-small-cell lung cancer (2009) NICE technology appraisal guidance TA181

In progress

- Lung cancer: diagnosis and management. NICE guideline. Publication expected: TBC
- Lung cancer (non-small cell) - afatinib [ID357] NICE technology appraisal guidance. Publication expected: TBC NICE technology appraisal guidance. Publication expected: TBC
- Lung cancer (non-small-cell, advanced or metastatic second line) - erlotinib (in combination with bevacizumab) [ID43] NICE technology appraisal guidance. Publication expected: TBC

- Lung cancer (non-small-cell, advanced or metastatic maintenance treatment) - erlotinib (in combination with bevacizumab) [ID44] NICE technology appraisal guidance. Publication expected: TBC
- Diagnostic services. NICE guideline. Publication expected: November 2017

Referred - QSs and CGs

None identified

Suspended/terminated

None identified

Details of new technologies

See section 6.1.4.

Registered and unpublished trials

Trial name and registration number	Details
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
Study Comparing Bevacizumab + Erlotinib vs Erlotinib Alone as First Line Treatment of Patients With EGFR Mutated Advanced Non Squamous Non Small Cell Lung Cancer NCT02633189	[redacted] Estimated study completion date: December 2017
[redacted]	[redacted]

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