CASE STUDY

Genetic Testing Directs Choice of Targeted Drugs For Lung Cancer Bypassing Generic Chemotherapy

Quick Summary

- Mr. Dhaval Pandya*, a 64-year-old lung cancer (NSCLC) patient was referred to Strand Life Sciences for genetic analysis of his tumor biopsy.
- A specific mutation in the *EGFR* gene- *EGFR*$^{E746\_A750del\ (exon\ 19)}$ – was identified in this case, using the Strand Advantage Tissue Specific Test for Lung Cancer.
- Lack of mutations in other genes associated with NSCLC was also ascertained.
- The analysis allowed for a clear choice of targeted therapies- Afatinib, Gefitinib, and Erlotinib and simultaneously negated the choice of other targeted therapies that were most unlikely to be effective.
- Genetic analysis provided clear decision support evidence for choice of therapies leading to optimal use of patient resources for treatment of cancer.

Introduction

Cancer is a disease wherein the side effects of therapy are quite difficult to deal with. Chemotherapy drugs, are cell destroying drugs that are delivered to the whole body of a cancer patient. Quite often, cancer patients report hair loss and reduced immunity because the chemo drugs have killed other healthy but dividing cells in the body along with cancer cells. Delivery of chemotherapy specifically to cancerous tissues or development of drugs that will be active only in cancer cells have been the objectives of research in cancer biology for a long time.

The development of drugs that can act only in cancer cells, but not in healthy cells has been possible after intensive research in the field of cancer. So, how does one bring these therapies into clinical practice? A genetic analysis of the tumor tissue, that allows for precise identification of specific changes, is necessary in order to choose from a bouquet of approved targeted therapies as well as chemotherapy. A clear choice of therapy was indicated in a case of non-small cell lung cancer (NSCLC) referred recently to Strand Life Sciences.

Patient Profile

Dhaval Pandya was a successful chartered accountant, looking forward to handing over his business to his children and retiring to his farm near Anand, in Gujarat. He had been managing his CA practice for 40 long years and, at the age of 64 years, all he wanted was to retire and pursue his hobbies. For the past year, he had been experiencing pain in his chest and had had some difficulty in breathing. He had ascribed it to his advancing age and had ignored these minor but persistent symptoms. It was only when he started noticing blood in his phlegm that he became worried enough to seek a doctor's opinion. After a preliminary exam, Dhaval's general physician suggested a consultation with a leading oncologist in a prominent hospital in Mumbai. His oncologist suspected the development of cancer and therefore prescribed a lung biopsy for pathological analysis. Additionally, she also suggested that a sample of the biopsy be sent to Strand Life Sciences for genetic analysis.

Name changed to protect patient privacy

Salient Findings of Histopathological Analysis

- Biopsy showed presence of fused acini in a sclerotic stroma.
- Cells have enlarged hyperchromatic nuclei and eosinophilic cytoplasm.
- Cytological markers CK-7, TTF-1 and synaptophysin were expressed in tumor tissue.
- Proteins like CK-20, Pax-8 and Chromogranin A were not expressed in the biopsy sample.

Based on these findings and Mr. Pandya's symptoms, a diagnosis of **Non-Small Cell Lung Cancer - metastatic adenocarcinoma** was determined.

Genetic Analysis of NSCLC Biopsy

The Strand Advantage Tissue Specific Test for Lung Cancer was used to analyze the sample sent to the laboratory in Bangalore. This test includes assays for 6 genes - *BRAF, EGFR, ERBB2, KRAS, MET, PIK3CA* - that are most commonly mutated in lung cancer.

In Mr. Pandya's case, a specific mutation in the *EGFR* gene -*EGFR*$^{E746\_A750del\ (exon\ 19)}$ - was identified in the tumor tissue.

Drug Response

Therapy	Tested Marker(s)	Relevant Marker(s)	Linklihood of Response**
Gefitinib	*EGFR, ERBB2, KRAS, MET*	*EGFR* $^{E746\_A750del\ (exon\ 19)}$	Enhanced
Erlotinib	*EGFR, ERBB2, KRAS, MET*	*EGFR* $^{E746\_A750del\ (exon\ 19)}$	Enhanced
Afatinib	*EGFR, ERBB2, KRAS, MET*	*EGFR* $^{E746\_A750del\ (exon\ 19)}$	Enhanced

Significant Findings

- The identification of a mutation in the *EGFR* gene is an important development that provided decision support for the choice of specific targeted drugs.
- The mutation identified in Mr. Pandya's cancer belongs to a class of well-characterized mutations in this gene that can be categorized as an *EGFR* del19 mutation.
- Tissues bearing this genetic alteration are known to be highly sensitive to three drugs:- Erlotinib, Gefitinib, and Afatinib. These drugs have been developed specifically to kill cells that express the altered gene and NOT cells that express the normal gene.
- These targeted therapies have been shown to increase the progression-free survival and overall survival of patients with metastatic NSCLC, when compared with generic chemotherapy (Barron *et al.* 2016; Hsiue *et al.* 2016).

Therapies NOT Recommended For Mr. Pandya

In addition to indicating suitable therapies, Strand's cancer tests can also help to identify drugs that are NOT likely to be effective for a patient. In Mr. Pandya's case, results of the Strand Tissue Specific Test suggest that the following drugs can be eliminated from his therapy regimen:

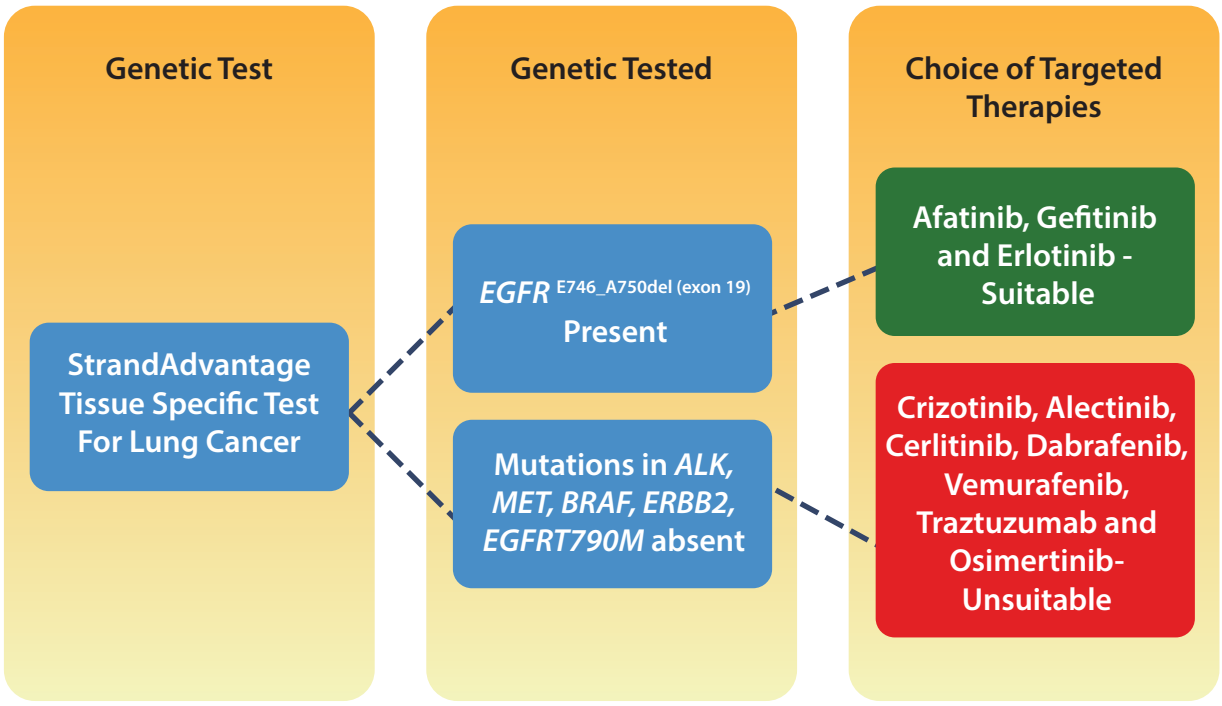
Drugs NOT INDICATED Based on FDA Mandated/ Guideline Recommended Markers

Therapy	Tested Marker(s)	Relevant Marker(s)
Alectinib	*ALK*	None
Ceritinib	*ALK*	None
Crizotinib	*ALK, MET*	None
Dabrafenib	*BRAF*	None
Vemurafenib	*BRAF*	None
Osimertinib	*EGFR*	None
Trastuzumab	*ERBB2*	None

In Mr. Pandya's case, mutations in genes such as *ALK, MET, BRAF, ERBB2* and a specific *EGFR* mutation relevant to a drug- Osimertinib were not present in the tumor tissue.

Therefore, drugs like Alectinib, Ceritinib, Crizotinib, Dabrafenib, Vemurafenib, Osimertinib and Trastuzumab were unlikely to be effective in eliminating his cancer cells.

A clear indication of avoidance of these drugs helped his oncologist in the choice of the right drug for his cancer therapy .



Conclusions

- Genetic testing of Mr. Pandya's NSCLC biopsy led to the identification of a specific mutation in his tumor.
- Targeted therapeutics designed to act against cells expressing the mutant gene were advised to him.
- A set of drugs that were most unlikely to work against his tumor were identified, based on the presence or absence of mutations in other normal genes linked to other targeted therapies.
- Clear decision support evidence was provided by genetic analysis of the patient's tumor.
- The genetic profile of the tumor is expected to allow the patient to direct financial and other personal resources towards therapies with optimal chances of success against NSCLC.

References

Barron, F. et al., 2016. The safety of afatinib for the treatment of non-small cell lung cancer. Expert Opinion on Drug Safety, 15(11), pp.1563–1572. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27633264 [Accessed June 19, 2017].

Hsiue, E.H.-C. et al., 2016. Safety of gefitinib in non-small cell lung cancer treatment. Expert Opinion on Drug Safety, 15(7), pp.993–1000. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27212579 [Accessed June 19, 2017].

Strand Life Sciences Pvt. Ltd.
5th Floor, Kirloskar Business Park, Bellary Road, Hebbal, Bangalore - 560 024
Phone: 1800-1022-695, support.strandx@strandls.com, www.strandls.com

#StayAheadOfCancer

Strand Patient ID: SC462812062017