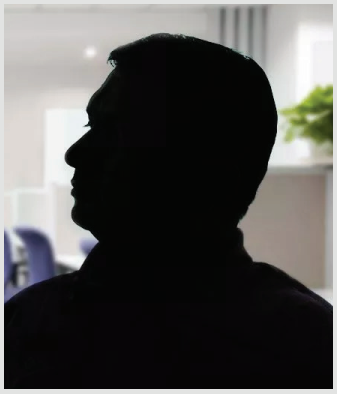
CASE STUDY

Liquid Biopsy – A Convenient Solution To Monitor Cancer Recurrence

Quick Summary

- Suneet Varma*, a 55-year-old colorectal cancer patient was advised to take Strand's pan-cancer StrandAdvantage 152-gene Cancer Test.
- The StrandAdvantage 152-gene cancer test was used to identify a *KRAS*^{G13D} mutation from the solid tumor biopsy as well as from a liquid biopsy (a blood sample from the patient) at the time of initiation of cancer treatment.
- Liquid biopsy tests performed at 4-month and 8-month intervals helped to establish the absence of residual cancer in the patient.
- Strand's highly sensitive liquid biopsy tests have provided accurate snapshots of cancer progression to the patient.
- Liquid biopsy based follow-up tests may be performed at desired time intervals to monitor progression of cancer, in every patient. These tests can circumvent limitations of PET-CT scans such as exposure to radiation and access to scan facilities.



Introduction

A diagnosis of cancer is not easy to live with. Cancer treatment is a long, drawn-out, expensive and emotionally taxing journey. Quite often, the waiting period between treatment and confirmatory tests like a PET-CT scan is the most anxious period for a patient. Radioactive tests like PET-CTs cannot be performed too often as well. In such cases, a blood based test for ascertaining the presence or absence of residual tumor tissue would be a highly suitable alternative to understand a person's cancer status. Recent research has shown that liquid biopsy tests can be used effectively to track the presence or absence of cancer DNA and can be used to predict the prognosis of the patient, even before cancer is detected on PET-CT scans (Tie et al. 2016; Zheng et al. 2016; Ai et al. 2016; Pécuchet et al. 2016).

Patient Profile

Suneet Varma, a 55-year-old bank employee, was diagnosed with colorectal cancer in August 2016. He was an avid badminton player, a bike enthusiast and a father of two young kids, aged 7 and 11 years. The diagnosis of cancer had turned his life completely upside down.

Treatment Options

Suneet's tumor showed signs of invading tissues adjacent to the wall of the colon and surgical removal of the tumor was advised by a prominent oncologist in Hyderabad.

In addition to surgery, genetic profiling of the solid tumor as well as follow-up liquid biopsy tests were also advised to Suneet. Tumor cells as well as normal cells release their DNA into the bloodstream when they die as part of the natural turnover of cells in various tissues. This DNA, called cell-free DNA (cfDNA) can be harvested from blood and can be checked for presence or absence of genetic mutations that have been identified from the solid tumor as well. The process is akin to assigning a barcode to an item and using that tag to track it.

A biopsy of the solid colorectal tumor as well as a 20ml blood sample (essentially a 'liquid' biopsy) from Suneet were sent to Strand Life Sciences for genetic analyses in August 2016.

Name changed to protect patient privacy

Results of Genetic Testing

Strand offers a pan-cancer test – the StrandAdvantage 152-Gene Cancer Test- that can assay for genes that are frequently mutated in all cancers. This broad-ranging cancer test is useful in identifying genetic mutations that can support choice of therapeutic options in the form of chemotherapy as well as targeted therapeutics.

In Suneet's case, this pan-cancer test helped to identify the presence of the *KRAS*^{G13D} mutation in the solid tumor biopsy.

StrandAdvantage 152 gene test

Sample Collection Date	Test	Gene	Mutation	Result	Details
Solid Tumor Result (DNA Source: FFPE)					**Supporting Reads**
11-Aug-2016	StrandAdvantage 152 Gene Cancer Test	*KRAS*	G13D	Detected	31.0%

The same mutation was also detected in cell-free DNA (cfDNA) obtained from the blood sample provided by him at the same time.

Liquid Biopsy Test 1 (DNA Source: cfDNA from blood)

Sample Collection Date	Test	Gene	Mutation	Result	Details
11-Aug-2016	Strand Liquid Biopsy	*KRAS*	G13D	Detected	1100

These initial results established the fact that tumor DNA from the colorectal cancer (marked by the identified mutation) was present in Suneet's blood.

Suneet was advised adjuvant chemotherapy, following the surgery, to target residual cancer, if any.

Keeping Tabs on the Cancer with Liquid Biopsy

Four months after the surgery, Suneet sent another blood sample to Strand Life Sciences for a follow-up liquid biopsy test.

In December 2016, cell-free DNA from his blood was analyzed again and the *KRAS*^{G13D} mutation was NOT identified.

Liquid Biopsy Test 2 (DNA Source: cfDNA from blood)

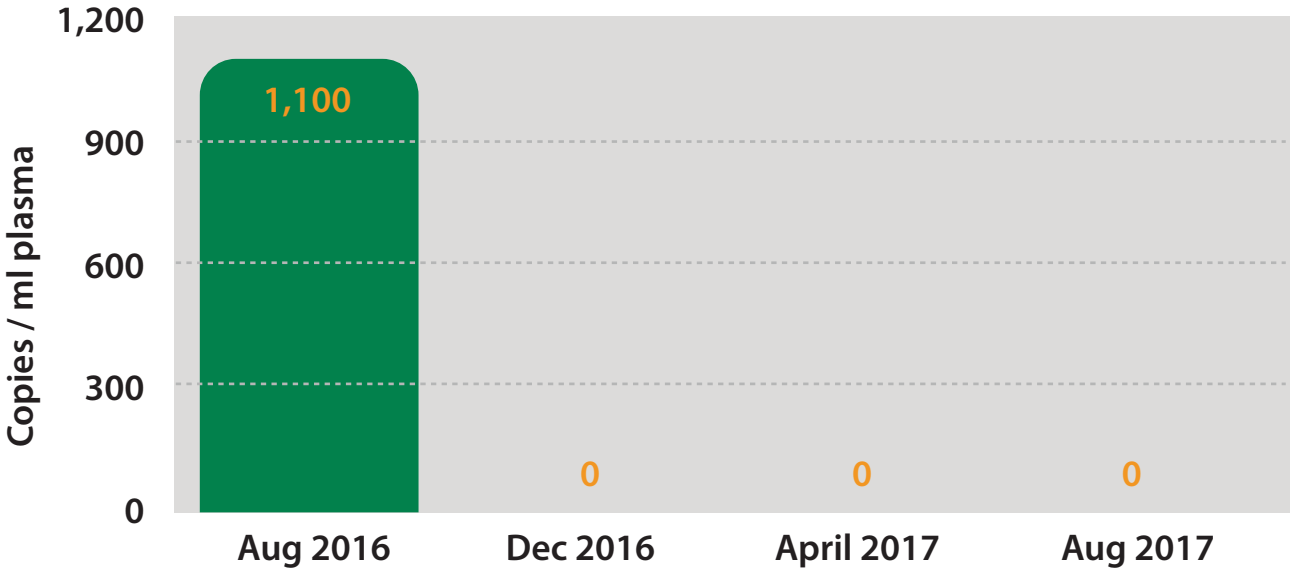
Sample Collection Date	Test	Gene	Mutation	Result	Details
23-Dec-2016	Strand Liquid Biopsy	*KRAS*	G13D	Not detected	N/A

This follow-up liquid biopsy test is performed at a high sensitivity of detection. The test can detect the presence of the mutation even if it is present at a concentration of 1 mutant DNA / 1000 normal DNA molecules. Therefore, absence of the mutation in cell-free DNA suggests that tumor DNA (from residual colorectal cancer) is not present in Suneet's blood. Hence it is safe to conclude that Suneet's colorectal tumor was removed completely and the chemotherapy has been effective in killing remnant tumor cells.

In cancer parlance, we refer to people as 'survivors' or 'people living with cancer' instead of 'people cured of cancer' and with good reason. One has to make allowances for the fact that a cancer may start growing again, if some cancer cells escape all the given treatment.

In order to understand whether Suneet is still free of cancer, another blood sample was sent to Strand in April 2017 and August 2017.

Detection of cfDNA from Liquid Biopsies-Suneet Varma



Liquid Biopsy Test 3 (DNA Source: cfDNA from blood)

Sample Collection Date	Test	Gene	Mutation	Result	Details
18-Apr-2017	Strand Liquid Biopsy	*KRAS*	G13D	Not detected	N/A

The marker mutation $KRAS^{G13D}$ was not detected in cell-free DNA from blood samples provided in April 2017 and August 2017. The absence of this mutation in cell-free DNA indicates that Suneet has remained free of cancer for12 months, post-surgery.

An additional advantage is that the results of the follow-up liquid biopsy tests were obtained within 5 working days.

We have shared these results with Suneet's oncologist who has been highly appreciative of the accurate results provided by these tests. The ease with which the progression of cancer has been monitored in this case is a significant improvement in cancer care.

Conclusions

- Genetic analysis of a solid colorectal cancer biopsy and a concurrent liquid biopsy sample allowed for identification of a characteristic mutation- $KRAS^{G13D}$- in Suneet Varma, a 55-year-old bank employee.
- Liquid biopsy samples provided by the patient at 4-month intervals were analyzed for the presence of the genetic signature of the tumor.
- The characteristic genetic marker was NOT identified in cell-free DNA isolated from the patient, in three follow-up LB tests, despite using highly-sensitive DNA detection techniques (1:1000 sensitivity), indicating the absence of recurrent cancer. Suneet has been relieved to know that his cancer has been controlled and that it can be detected early, if the cancer recurs.
- Liquid biopsy based personalized genetic analyses of cancer have provided significant emotional relief to a cancer survivor. These tests can be availed of at a desired frequency (monthly, bi-monthly or quarterly) and are free of limitations like exposure to radiation and accessibility to PET-CT scan facilities.

Strand Liquid Biopsy Tests For Tumor Monitoring

Strand Life Sciences offers a combination of their Strand Advantage 48-Gene and 152-Gene Cancer Tests and 58 liquid biopsy based tests as personalized cancer monitoring tests. Another 56-Gene test for analysis of solid and liquid biopsies has been recently included in the test portfolio. Solid tumor biopsies as well as liquid biopsies (blood samples) from cancer patients are analyzed to identify a set of mutations present in cancer at the time of diagnosis / initiation of treatment.

These unique, personalized genetic profiles of cancer can then be used in a patient-specific manner to track the progression of cancer in every patient, at the desired time intervals.

References

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