

Liquid Biopsy Enabled Monitoring of Bladder Cancer

Quick Summary

- o Ashfaq Mohammed*, a 75-year-old patient, was diagnosed with transitional cell bladder carcinoma in May 2017.
- o Genetic analyses of the solid tumor biopsy has led to the identification of a *KRAS*^{G12D} mutation in the tumor.
- o Trametinib and selumetinib, in addition to other chemotherapeutic drugs, have been suggested as potential targeted therapeutics to treat his *KRAS* mutant cancer.
- o Concordance between the solid tumor biopsy and liquid biopsy has been established, with the identification of the tumor-associated mutation from the patient's blood sample.
- o Tracking the progression of the cancer, evaluating patient response to various therapies administered and obtaining decision support for altering therapy is now possible with the dual genetic analyses of solid tumors and liquid biopsy.



Patient Profile

Ashfaq Mohammed, a 75-year old rubber plantation owner, had been experiencing occasional pain in his abdomen for some months. He put it down to old age and ignored the persistent pain. Eventually, the pain was unbearable, especially when passing urine. The appearance of blood in the urine was the alarm bell that prompted him to consult his physician. Ashfaq's physician referred him to an oncologist since the symptoms were indicative of bladder cancer. Bladder cancer was confirmed by cystoscopy. Histopathological analysis showed that Ashfaq had transitional cell bladder carcinoma.

Treatment Options

Ashfaq's oncologist also advised genetic testing in order to obtain a genetic profile of the cancer. A genetic profile of a cancer often helps to choose from a range of chemotherapy options as well as targeted drugs that can fight cancer while preserving normal tissues.

The StrandAdvantage 48-gene test was prescribed for the genetic analysis of his bladder cancer biopsy.

Results of Genetic Testing

The StrandAdvantage 48-gene test is a pan-cancer test designed to identify mutations in genes that are frequently mutated in most cancers.

*Name changed to protect patient privacy

In Ashfaq's case, a mutation in the KRAS gene was identified.

Therapy	Relevant Markers	Approved Indications	Trials
Trametinib	KRAS ^{G12D}	Melanoma	NCT02703571, NCT01827384
Selumetinib	KRAS ^{G12D}	None	NCT01586624, NCT02583542

Solid tumors bearing the KRAS^{G12D} mutation can be treated with two drugs, Trametinib and Selumetinib.

Cancer-causing mutations in the KRAS gene exert their effects by activating a cell division promoting pathway- the RAS/RAF/MEK/ERK pathway. Drugs like trametinib and selumetinib can inhibit the actions of enzymes that are active in this pathway and thereby, control the rampant growth of cancer cells. Trametinib has been used to treat skin cancer (melanoma) along with another targeted drug, dabrafenib (1,2).

Selumetinib is also another inhibitor of the MEK pathway that is being evaluated for efficacy against solid tumors like non-small-cell lung cancer (NSCLC)(3).

These treatment options were suggested to Ashfaq's oncologist to complement conventional chemotherapy .

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Identification of the KRAS^{G12D} mutation has an added advantage. Tumor cells release their DNA in the bloodstream, much like normal cells do. It is possible to harvest this DNA from a patient's blood sample (also known as cell-free DNA) and thereafter, understand whether DNA from tumor cells is present in it or not. Such liquid biopsy tests can be conducted throughout the course of cancer treatment.

In order to understand whether liquid biopsy can be used in Ashfaq's cancer treatment, a blood sample was also taken from him at the time of the biopsy of the bladder cancer.

Following the identification of the KRAS^{G12D} mutation in the solid biopsy, the presence of the same mutation in cell-free DNA from the liquid biopsy was ascertained.

Sample Collection Date	Test	Sample ID	Gene	Mutation	Result	Copies/ml plasma
22-May-2017	Strand Liquid Biopsy*	RESCH-000001536	KRAS	G12D	Detected	9.35

Results of the liquid biopsy show that the tumor-linked mutation can be detected in cell-free DNA from the patient's blood.

Concordance between the solid biopsy and liquid biopsy has been established. As of August 2017, the patient is undergoing chemotherapy. It is now possible to track the response of the patient to administered therapies, using periodically drawn liquid biopsy samples.

Conclusions

- Ashfaq Mohammed, a 75-year-old patient, was diagnosed with transitional cell bladder carcinoma in May 2017. Genetic analyses of the solid tumor biopsy has led to the identification of a *KRAS*^{G12D} mutation in the tumor.
- Trametinib and selumetinib, in addition to other chemotherapeutic drugs, have been suggested as potential targeted therapeutics to treat his *KRAS* mutant cancer.
- Concordance between the solid tumor biopsy and liquid biopsy has been established, with the identification of the tumor-associated mutation from the patient's blood sample.
- Tracking the progression of the cancer, evaluating patient response to various therapies administered and obtaining decision support for altering therapy is now possible with the dual genetic analyses of solid tumors and liquid biopsy.

References

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