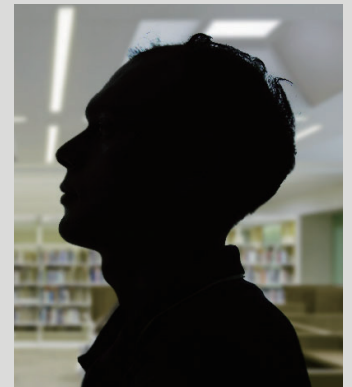


## CASE STUDY

# Genetic Analysis for Precise Treatment of Nasopharyngeal Carcinoma

## Quick Summary

- o Prateek Saini\*, age 35 years, was diagnosed with nasopharyngeal carcinoma.
- o Genetic analysis of the tumor was advised in order to gain decision support for choice of targeted drugs.
- o Genetic analysis of Prateek's nasopharyngeal carcinoma revealed the presence of cancer-causing mutations in three different genes: *FGFR3*, *KIT* and *PTEN*.
- o Targeted therapies for mutations in the *FGFR3*, *KIT* and *PTEN* genes, currently being evaluated for their therapeutic use in head and neck cancers in clinical trials, were suggested for Prateek's treatment.
- o Tumor heterogeneity was established by genetic analysis. This knowledge can be leveraged to choose appropriate combinations of drugs.



## Introduction

In India, cancers of the head and neck are prevalent with about 30% of total cancer cases in men and 13% of total cancers in women being head and neck cancers (Sanghvi et al. 1989). A review of global statistics shows that the burden of head and neck cases is shifting to the developing world. In India, tobacco-related head and neck cancers are the most abundant head and neck cancers with nasopharyngeal cancer taking up the second spot. Infection with the Epstein-Barr virus is considered to be one of the causative factors of nasopharyngeal carcinoma (Zhang et al. 2017; Stevens et al. 2006).

## Patient Profile

Prateek Saini\*, a 35-year-old fashion photographer was hale and hearty except for some occasional bouts of nasal congestion. The frequency of these bouts had increased and he often suffered from headaches. When he started noticing fresh blood in his spit, he consulted a physician who referred him to an oncologist at a leading hospital in Ahmedabad.

The oncologist noted a growing lump in the nasopharyngeal region and advised a tissue biopsy. When the tissue was examined under a microscope, the oncologist's suspicions of a nasopharyngeal carcinoma were confirmed.

## Treatment Options

Nasopharyngeal cancers are treated with a combination of chemotherapy and radiotherapy (Chen et al. 2017; Chan 2011). In order to explore the possibility of using targeted therapies for Prateek, his oncologist advised genetic testing in order to identify mutations that may possibly indicate the root cause of Prateek's nasopharyngeal cancer as well as provide some therapeutic indications.

\*Name changed to protect patient privacy

## Results of Genetic Testing

The StrandAdvantage 48-gene test was prescribed for Prateek. This test is designed to ascertain the presence of mutations in genes associated with most sporadic (somatic) cancers.

Summary of Test Results					
Gene	Variation	FDA Approved Therapy (for tumor type)	FDA Approved Therapy (for other tumor type)	Relevant Drugs/ Clinical Trials	
<i>FGFR3</i> NM_000142	chr4:g.1807889A>G c.1948A>G p.Lys650Glu	None	None	pan FGFR Kinase Inhibitor BGJ398 NCT02160041	
<i>KIT</i> NM_000222	chr4:g.55592208A>T c.1532A>T p.Asn511Ile	None	Possible response to sunitinib	NCT01309633	
<i>PTEN</i> NM_000314	chr10:g.89712011C>T c.629C>T p.Thr210Ile	None	Possible response to everolimus and temsirolimus	NCT01111058 NCT01256385	

In Prateek's case, mutations in three genes - *FGFR3*, *KIT* and *PTEN* - were identified in the tumor biopsy.

## Clinical Significance of Identified Mutations

- FGFR3*:** A mutation in exon 14, which results in an activated version of this protein was found in Prateek's nasopharyngeal tumor. Tumors bearing this mutation can be treated using two inhibitors- Pazopanib and BGJ398. The same gene has been considered as a potential target to stop cell division, in head and neck squamous cell carcinoma (von Mässenhausen et al. 2016). The anti-cancer activity of BGJ398 against solid tumors bearing *FGFR3* mutations has been demonstrated in a Phase 1 trial as well (Nogova et al. 2017).
- KIT*:** A novel mutation in the *KIT* gene was found in Prateek's nasopharyngeal tumor. The role of this mutation in the progression of this kind of cancer is not clearly understood, although mutations in *KIT* in nasopharyngeal carcinomas have been documented (Zhang et al. 2014). Sunitinib is a targeted therapy drug that has been shown to have modest effects against nasopharyngeal cancer and is being evaluated in current clinical trials [NCT01309633].
- PTEN*:** The *PTEN* mutation identified in this case is a loss-of-function mutation, which compromises the role of this enzyme in stopping cell divisions. Mutations in this gene have been reported in nasopharyngeal cancers (Squarize et al. 2013). Drugs like Everolimus and Temsirolimus are effective in solid tumors bearing *PTEN* mutations and are being evaluated for therapeutic use in head and neck cancers, in clinical trials [NCT01256385 and NCT01111058].

## Targeted Therapeutic Options For Nasopharyngeal Carcinoma

No.	Mutant Gene	Potential Drug	Reference
1	<i>FGFR3</i>	Pan <i>FGFR</i> kinase inhibitor BGJ398	(Nogova <i>et al.</i> 2017)
2	<i>KIT</i>	Sunitinib	NCT01309633
3	<i>PTEN</i>	Everolimus	NCT01111058
4	<i>PTEN</i>	Temsirolimus	NCT01256385

## Conclusions

- Genetic analysis of Prateek's nasopharyngeal carcinoma revealed the presence of cancer-causing mutations in three different genes: *FGFR3*, *KIT* and *PTEN*.
- Targeted therapies for mutations in the *FGFR3*, *KIT* and *PTEN* genes were being evaluated for their therapeutic use in head and neck cancers, at the time of this analysis.
- The genetic analysis showed tumor heterogeneity in this case, based on the prevalence of each mutation in the biopsy tissue. Identification of the genetic profile of this nasopharyngeal carcinoma has helped to choose a set of three drugs that could possibly be used to treat Prateek, either simultaneously or sequentially.
- Mutations identified in this solid tumor can also be tracked using liquid biopsy assays, thereby facilitating continuous tumor monitoring. This is expected to provide decision support for altering Prateek's treatment at different stages of the cancer.

## StrandAdvantage 48-gene Test

StrandAdvantage 48-gene test is a pan-cancer test that is designed to identify mutations in genes that are most frequently mutated in almost all solid tumors. This test is a laboratory-developed test and has been used to identify actionable mutations in multiple solid cancers. An expanded version of this test is available as the StrandAdvantage 152-gene test.

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