

CASE STUDY

Identification of Mutations in Endometrial Cancer Leads to Selection of Suitable Targeted Therapies

Quick Summary

- o Sunetra Deshmukh, a 65-year old lawyer, was diagnosed with endometrial cancer and a biopsy of the cancer was sent to Strand Life Sciences for genetic analysis.
- o The Strand Advantage 48-Gene Cancer Test indicated the presence of mutations in three genes – *PIK3CA*, *PTEN* and *KRAS*.
- o Targeted therapies that are known to act against cancers with these mutations are available and were suggested to her oncologist in Strand's report.
- o Genetic Analysis of her tumor helped to circumvent trial and error with chemotherapy options by providing suitable targeted therapy options.



Patient Profile

Sunetra Deshmukh*, a 65-year old lawyer (name and profession changed to protect patient privacy), had been experiencing post-menopausal vaginal bleeding, increased vaginal discharge and stomach cramps for a few months. She had been losing weight as well despite the lack of special efforts to do so. Her symptoms led her to seek a consultation with a prominent oncologist in Mumbai. Pathological investigations led to the diagnosis of endometrial cancer.

In addition to standard diagnostic procedures, her oncologist also advised her to obtain a genetic analysis of her tumor biopsy. Endometrial cancer can be treated with hysterectomy (if the cancer has not spread to other organs from the uterus), radiotherapy and adjuvant chemotherapy. Targeted drugs like Everolimus are also being tried out for treatment of endometrial cancer (Slomovitz et al. 2015; Husseinzadeh & Husseinzadeh 2014). A mutation profile of the tumor is essential in order to determine whether drugs like Everolimus would be effective for the treatment of Sunetra's cancer or not.

Genetic Analysis of Sunetra's Endometrial Cancer

The Strand Advantage 48- Gene Cancer Test was used to identify mutations from the endometrial cancer biopsy provided by the patient.

Therapy	Relevant Markers	Approved Indications	Trials
Trametinib	<i>KRAS</i> ^{G12C}	Melanoma	NCT01827384
Everolimus	<i>PIK3CA</i> ^{Q546R} , <i>PTEN</i> ^{Y177*}	Pancreatic Neuroendocrine Tumor, Gastrointestinal Neuroendocrine Tumor, Lung Neuroendocrine Tumor, Kidney Cancer, Astrocytoma, Hormone receptor-positive HER2-negative Breast Cancer	NCT02188550, NCT02397083
Olaparib	<i>PTEN</i> ^{Y177*}	Ovarian Cancer	NCT02576444

*Name changed to protect patient privacy

Key Interpretations

- Mutations in three genes- *KRAS* (*KRAS*^{G12C}), *PIK3CA* (*PIK3CA*^{Q546R}) and *PTEN* (*PTEN*^{Y177*}) were identified in the endometrial cancer biopsy obtained from Sunetra Deshmukh.
- Tumors bearing the *KRAS*^{G12C} mutation can be treated by a new targeted, drug called Trametinib (Grimaldi et al. 2017; Li et al. 2017).
- The presence of the *PIK3 CAQ546R* and *PTEN*^{Y177*} mutations in the tumor also indicates that growth of the tumor cells can possibly be stopped by using Everolimus. Both these genes are engaged in regulating a pathway involved in the growth of cells. Everolimus inhibits this biochemical pathway by targeting another protein in it.
- Cancers wherein the *PTEN* gene is inactivated may respond to another class of drugs that inhibit an enzyme called poly-ADP ribose polymerase (PARP). PARP inhibitors have not been extensively used for treatment of endometrial cancer. Evidence from preliminary studies suggest that PARP inhibitors can control the growth of endometrial as well as other solid tumors which have mutations in the *PTEN* gene (Miyasaka et al. 2014; Forster et al. 2011; McEllinet al. 2010).

Conclusions

- A genetic profile of Sunetra's endometrial cancer was established using the StrandAdvantage 48-gene test.
- Mutations in three genes- *KRAS*, *PIK3CA* and *PTEN*- were identified in the tumor biopsy
- The genetic profile indicated three targeted therapies that are currently being evaluated for treatment of other solid tumors.
- Sunetra's oncologist now has a choice of selecting three different targeted therapies- Trametinib, Everolimus and PARP inhibitors in addition to surgery, radiotherapy and adjuvant chemotherapy for her treatment.
- Genetic testing increased the range of therapeutic options for the treatment of endometrial cancer.

StrandAdvantage 48-Gene Test

StrandAdvantage 48-Gene Test is a pan-cancer test designed to identify mutations in genes involved in most common cancers. In addition to providing on-label drug recommendations, this test can also provide off-label recommendations where the drugs are undergoing trials for therapeutic efficacy in other solid tumors (besides the approved ones).



References

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