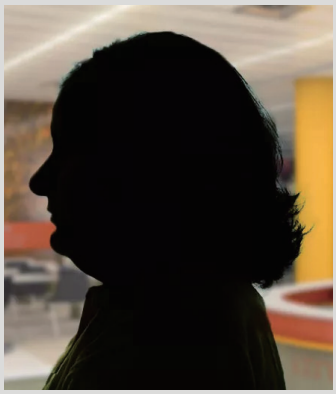
CASE STUDY

Selection of Targeted Chemotherapy Regimens Enabled by Genetic Analysis

Quick Summary



- Rashmi Eashwar*, a 68-year-old retired MNC executive, was diagnosed with breast cancer.
- Genetic analysis of her breast cancer biopsy established the fact that she had ER-ve, PR-ve but HER2+ve breast cancer.
- Identification of molecular markers allowed for bifurcation of therapies that were most likely to be effective from those that were not, resulting in considerable savings of time and treatment cost for the patient.

Patient Profile

Rashmi Eashwar, 68 years, had retired from the post of COO of a large MNC in 2016 and was thoroughly enjoying her days of solitude. She was a grandmother of two tiny tots and was looking forward to meeting another one in the next six months. She lived in an upscale Kolkata neighbourhood and was content with her hobbies and social life. A stabbing sensation of pain in the breasts had been nagging her for three months. Not a person to make a fuss about small issues, she had ignored it to begin with but the persistent and worsening pain made her realise that she MUST have it looked at.

Rashmi consulted a doctor at a hospital in Kolkata. The doctor suspected the incidence of breast cancer after preliminary investigations and asked her to undergo a biopsy to confirm the incidence of cancer. In addition to histopathological analysis, he also advised her to send a biopsy sample to Strand Life Sciences for genetic analysis.

Results of Genetic Analysis

Rashmi's biopsy sample was examined for the presence of estrogen receptor (ER), progesterone receptor, and another cell surface receptor known as HER2.

Her tumor tissue did not express ER and PR but immunohistochemistry staining (IHC) revealed that her tumor tissue expressed the HER2 protein.

Based on this analysis, the following recommendations were provided to the doctor:

*Name changed to protect patient privacy

Clinical Indications

Breast carcinoma (ER-ve/PR-ve/HER2+ve)

Summary for Standard Drugs

Drugs NOT INDICATED Based on FDA Mandated/ Guideline Recommended Markers

Therapy	Tested Marker(s)	Relevant Marker(s)
Everolimus	*ER, HER2*	None
Palbociclib	*ER, HER2*	None
Tamoxifen	*ER*	None

Drug Response

Therapy	Tested Marker(s)	Relevant Marker(s)	Likelihood of Response
Pertuzumab	*EGFR, HER2, ERBB2 PIK3CA, PTEN*	*$HER2^{IHC+}$*	*Enhanced*
Lapatinib	*HER2, ERBB2, PIK3CA*	*$HER2^{IHC+}$*	*Enhanced*
Trastuzumab	*EGFR, HER2, ERBB2 PIK3CA, PTEN*	*$HER2^{IHC+}$*	*Enhanced*
Fluorouracil	*SMAD4*	*None*	*Standard*

Drugs like Everolimus (acting against mutant *PIK3CA,* Palbociclib (ER +ve and HER2-ve breast cancer and Tamoxifen (acting against ER+ve breast cancer cells) were ruled out because the cellular target proteins were not expressed in Rashmi's cancer tissue.

In contrast, the positive expression of the HER2 protein indicated that drugs like Pertuzumab, Trastuzumab and Lapatinib were most likely to act against Rashmi's cancer cells.

Pertuzumab is a humanized antibody that blocks cell signaling via the HER2 receptor. It has been shown to be effective against solid tumors with only minor skin conditions and diarrhea as side effects. In fact, a combination of Pertuzumab and Trastuzumab has been shown to be more effective in controlling cancer, than Trastuzumab alone (Zhu et al. 2017; Beitsch et al. 2017).

Likewise, Lapatinib is a synthetic inhibitor of tyrosine kinase activity of the HER2 receptor and is effective against tumors expressing this marker (Nielsen et al. 2013; Burstein et al. 2008).

In addition, a non-targeted, conventional chemotherapy drug, fluorouracil was also predicted to produce a standard inhibitory response against the cancer.

Conclusions

- Rashmi, a 68-year-old retired MNC executive, was diagnosed with breast cancer.
- Genetic analysis of her breast cancer biopsy established the fact that she had ER-ve, PR-ve but HER2+ve breast cancer.
- Based on the expression pattern of these receptors, drugs like Pertuzumab, Trastuzumab and Lapatinib were recommended for her treatment. These were expected to act against the HER2 receptor in multiple ways to stop the growth of cancer cells.
- *A priori,* drugs like Everolimus, Palbociclib and Tamoxifen were ruled out, thereby saving the patient time and expenses that a trial-and-error method of treatment would have entailed.

References

Beitsch, P. *et al.,* 2017. Pertuzumab/Trastuzumab/CT Versus Trastuzumab/CT Therapy for HER2+ Breast Cancer: Results from the Prospective Neoadjuvant Breast Registry Symphony Trial (NBRST). *Annals of Surgical Oncology*. Available at: http://www.ncbi.nlm.nih.gov/pubmed/28447218 [Accessed June 5, 2017].

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