# Pertuzumab MMAE: A Novel ADC to Treat Drug-Resistant Breast Cancer Patients

Patel, Shaurya (School: Adani International School)

Cancer patients have access to advanced drugs like biosimilars of trastuzumab, pertuzumab, and trastuzumab emtansine (T-DM1). However, continuous devleopment of new drugs is required to treat patients who have become resistant to existing therapeutics. New drug development is both costly and time consuming, therefore ideas on betterment of existing therapies are required. This work involves testing the hypothesis as to whether Pertuzumab could be converted into an antibody-drug conjugate just like trastuzumab was converted into T-DM1, thereby making a novel drug that could be prescribed to T-DM1-resistant patients. The monoclonal antibody, Pertuzumab, was chemically conjugated with MMAE, a payload toxin different from DM-1, to make a novel ADC - pertuzumab conjugated to MMAE (P-MMAE). P-MMAE was compared with T-DM1 in a pair of human breast cancer cell lines that were either resistant or non-resistant to T-DM1. It was observed that P-MMAE could kill both cancer cell types efficiently, thereby providing a potential new cure for HER2-positive breast cancer patients in India after they have become resistant to T-DM1. Based on the results of the study in breast cancer cell lines, the candidate P-MMAE drug was also be evaluated in other cancer cell lines. Protein Atlas database was used to short-list cancers in which the target is expressed and cell lines were identified as a potential model for testing the P-MMAE candidate. P-MMAE demonstrated a dose-dependent cytotoxicyt in the gastric cancer cell line NCI-N87. The data demonstrates the utility of P-MMAE as a candidate drug for the treatment of cancers in a time and cost-effective way.

**Awards Won:**