Antibody-Drug Conjugate T-DM1 Offers New Mechanism and Significant Benefit in HER2-Positive Breast Cancer

Right at the top of the list of the most exciting news from the 2012 American Society of Clinical Oncology (ASCO) meeting in Chicago this week involved using T-DM1 to treat metastatic, HER2-positive breast cancer. T-DM1 is an “antibody-drug conjugate” (ADC).

ADCs combine a tumor-specific antibody with a chemotherapy drug. They are therefore specifically designed to be able to deliver chemotherapy drugs directly to tumor cells (like a “smart bomb”), potentially increasing efficacy and decreasing damage to normal cells. T-DM1 combines the anti-HER2 antibody Herceptin (trastuzumab), a stable linker and a chemotherapy agent, DM1, also known as emtansine.

Befitting its importance, the EMILIA trial was presented at the high profile Plenary Session. In this study almost 1000 patients with metastatic, HER2-positive breast cancer whose disease had progressed after treatment with a taxane and Herceptin were randomized to receive Xeloda (capecitabine) plus Tykerb (HER2-inhibiting tyrosine kinase inhibitor lapatinib) or T-DM1. Xeloda and Tykerb are oral drugs; the T-DM1 was given intravenously every 3 weeks. There was no “cross-over”, meaning that patients whose disease progressed on Xeloda and Tykerb did not have access to T-DM1.

T-DM1 was much better than Xeloda and Tykerb in numerous comparisons. More patients had their disease respond to T-DM1 (43.6%) than to Xeloda and Tykerb (30.8%). Also, the median progression-free survival or PFS (length of time before the breast cancer progresses again) was significantly longer for the patients receiving T-DM1 (9.6 months) compared to those receiving Xeloda and Tykerb (6.4 months). Perhaps most importantly, the patients receiving T-DM1 lived longer than those receiving Xeloda and Tykerb. Approximately 65% of the patients receiving T-DM1 were alive after 2 years compared to 48% of those receiving Xeloda and Tykerb.

T-DM1 was also better tolerated and controlled symptoms longer than Xeloda and Tykerb. Decreases in heart function were rare on both therapies and neither therapy causes significant
hair loss. The most common severe side effects for T-DM1 were low platelet counts and elevated liver enzymes while the most common severe side effects for xeloda and tykerb were diarrhea, hand-foot syndrome and vomiting.

These data are very exciting and will likely lead in the near future to a new option to treat HER2-positive, metastatic breast cancer. On a broader note, the success of T-DM1 may hopefully lead to the successful development of other ADCs with better efficacy and less toxicity than our current, standard treatments.