Is One Year of Adjuvant Herceptin for Early Stage Breast Cancer Really Optimal?

Since the FDA approval of Herceptin in the adjuvant setting for HER2-positive, early stage breast cancer, one year of Herceptin has been the standard length of therapy. This was based on the design of multiple, large, randomized trials that were published in 2005. Many people, however, argued that the choice of one year was not based on scientific data, and that is was somewhat arbitrary. Two studies presented at the 2012 Congress of the European Society for Medical Oncology (ESMO) in Vienna this past week, however, supported the belief that one year of therapy is optimal. In the two studies presented at ESMO, investigators evaluated both shorter and longer durations of Herceptin treatment.

The PHARE Trial

Although one year of Herceptin was felt to be the optimal length of therapy, valid concerns were raised about the risk of cardiac toxicity as well as the inconvenience and significant financial cost of such lengthy therapy. Furthermore, a very small study conducted in Finland found that nine weeks of Herceptin reduced the risk of recurrence and that the reduction appeared to be approximately as large as that seen with one year of treatment in the larger studies. These concerns led to the need to address the important question of whether shorter therapy could be as beneficial as one year.

The PHARE trial (Pivot & colleagues, ESMO 2012, Abstract #LBA5) was a randomized study conducted by the French National Cancer Institute (INCa) comparing six months of Herceptin to one year in over 3,000 patients with HER2-positive early breast cancer. After a median follow-up of 3.5 years, the trial results were inconclusive. There was however a trend towards fewer recurrences and deaths for the women who received a year of Herceptin. The investigators plan to look at various subsets of patients to see if there is a group for whom 6 months of Herceptin may be sufficient. There are also other studies of shorter treatment being conducted in other European countries, including Great Britain and Italy. But for now, the results of the PHARE trial support the current standard of one year.

The HERA Trial

So, if a shorter length of Herceptin is not as beneficial, what about longer therapy? The HERA trial (Goldhirsch & colleagues, ESMO 2012, Abstract #LBA6) was an international, multi-center, phase III randomized study. After finishing primary therapy with surgery, chemotherapy, and radiation, more than 5000 women with HER2-positive early breast cancer were randomized to observation or to receive Herceptin every three weeks for one year or two years.

Results presented at ESMO show that receiving Herceptin for two years does not significantly
improve outcomes compared to one year. Both disease-free survival (DFS) and overall survival (OS) were comparable in the two groups. Furthermore, after eight years of median follow-up, the significant benefit in DFS and OS of one year of Herceptin compared to no Herceptin remained stable. One year of Herceptin reduced the risk of both recurrence and death by 24%.

In conclusion, one year of Herceptin therapy remains the standard for HER2-positive early stage breast cancer.