New findings on optimal duration of trastuzumab therapy for women with HER2+ early breast cancer

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New studies that advance understanding of the optimal duration of therapy with the targeted cancer drug trastuzumab were released today at the ESMO 2012 Congress of the European Society for Medical Oncology in Vienna.

"These long awaited results constitute a further milestone in the treatment of patients with early breast cancer over-expressing HER2/neu, corresponding to a population of about 12-15% of all cases of breast cancer," commented Prof Christoph Zielinski, Chairman of the Clinical Division of Oncology, at Medical University Vienna, Austria, who was not involved in the studies.

Landmark results from HERA trial—extending trastuzumab for 2 years does not significantly improve outcomes versus 1 year

One year of treatment with the targeted drug trastuzumab is as good as two years of treatment, for women with HER2-positive early breast cancer who have already received initial treatment with surgery, chemotherapy and radiotherapy as needed, researchers have found.

The HERA trial, which has been run by the Breast International Group (BIG) since 2001, is an international, multi-center, phase III randomized

study involving 5102 women with early HER2-positive breast cancer. After finishing primary therapy with surgery, chemotherapy and radiotherapy as indicated, they were randomly assigned to trastuzumab therapy every 3 weeks for 1 year, 2 years or observation.

As of 12 April 2012, the unadjusted hazard ratio for a woman experiencing disease relapse in the 2-year treatment arm versus the 1-year arm was 0.99 (95% CI and P-value), Prof Richard Gelber of Harvard Medical School and Dana-Farber Cancer Institute, Boston, MA, USA, said. The overall survival rate in the two arms was comparable [HR=1.05 (95% CI 0.86-1.28; P=0.6333)].

"The key message for 2012 is that 1 year of treatment with trastuzumab remains the standard of care for HER2 positive early breast cancer patients," Prof Gelber said.

The researchers found that the durable benefit in disease-free survival and overall survival of 1-year trastuzumab compared to no trastuzumab that had been reported previously remained stable at 8 years of median follow-up.

"This prolonged benefit in disease-free survival and overall survival of 1-year trastuzumab over no trastuzumab is remarkably impressive and reassuring to patients," Prof Gelber said. "These results show that the benefit of adjuvant trastuzumab remains over time and it is not lost after some years. Patients can be reassured that 1 year trastuzumab is a very effective treatment, reducing the risk of disease recurrence and death by one-quarter compared to not using trastuzumab."

"While extending the duration of trastuzumab administration to 2 years did not significantly improve outcome compared with 1 year trastuzumab, ongoing trials are testing whether combining trastuzumab with other anti-HER2 agents (for example pertuzumab or lapatinib)

might further benefit patients with HER2-positive early breast cancer," Prof Gelber noted.

Commenting on the data, Prof Zielinski noted: "Progress in the treatment of patients with early breast cancer over-expressing HER2/neu was extremely impressive and particularly successful by the introduction of trastuzumab as adjuvant treatment. This was administered in the first trials for one year and resulted in a highly significant prolongation of progression-free and overall survival. However, the question lingered whether a prolongation of treatment to two years would result in even better data than the ones obtained before."

"The present trial shows that this is not the case, which strongly supports the correctness of adjuvant treatment duration delivered to patients with HER2/neu over-expressing early breast cancer. Moreover, it teaches us about the biology of the disease in that the therapeutic interference with growth factor signaling for a period of one year cannot be improved by a longer duration of such treatment," said Prof Zielinski.

"Thus, we can be assured that patients are being treated in the best possible and most cost-effective way, by weighing benefit versus costs for the healthcare system. The latter aspect is quite important, as the recurrence of disease in a patient leads not only to suffering and death, but also to an immensely increased burden for the society. The current data thus add to the evidence how the latter aspects can be avoided by the delivery of an optimal duration of treatment for a selected patient population."

PHARE trial results comparing 6 to 12 months of trastuzumab in adjuvant early breast cancer

An academic randomized, non-inferiority trial instituted by the French

National Cancer Institute (INCa) has compared a shorter trastuzumab exposure of 6 months versus the standard 12 months.

The Phare trial addressed the question of the trastuzumab duration in HER-positive early breast cancer adjuvant treatment. More than 150 cancer care centers all over France participated, recruiting more than 3380 patients representative of the French population. The trial's primary objective was to compare 6 months versus 12 months trastuzumab therapy in terms of disease free-survival according to a non-inferiority schema.

"The trial results are inconclusive for this non-inferiority hypothesis," said Prof Xavier Pivot, of the Université de Franche Comté, France. "Nevertheless, there is a trend in favor of 12 months treatment for the overall population. Analysis of subgroups will be presented in December."

The median follow-up in the trial was 42.5 months and at the time of the analysis 395 disease-free survival events were reported. "According to the design of this trial, which allowed for a non-inferiority hazard ratio margin of 1.15, the 6-month trastuzumab arm (arm B) was not demonstrated to be significantly inferior to 12-month trastuzumab (arm A), since the confidence interval contains the 1.15 non inferiority margin (HR=1.28 (95%CI: 1.04 – 1.56, p=0.29). However despite the inconclusive result in terms of non-inferiority, the HR of 1.28 suggests a trend favoring 12 months," Prof Pivot said.

"Further exploration of the data, especially in selected subgroups is ongoing; further results will be presented in a couple of months. The results probably won't give a black and white answer, and the researchers will probably need to look at subsets of patients to see who benefits from six months of treatment and who should get a full year," Prof Pivot said.

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