Duration of endocrine therapy and its impact on the results of adjuvant trials in premenopausal breast cancer patients

Gnant et al. presented the final results of the Austrian Breast and Colorectal Cancer Study Group Trial 12 (ABCSG-12) trial after a median follow-up of 94.4 months [1]. Although there was no disease free survival (DFS) difference between patients who received ovarian function suppression (OFS) plus either tamoxifen or anastrozole, patients treated with anastrozole + OFS had a significantly worse overall survival (OS) compared with patients treated with tamoxifen + OFS (hazard ratio = 1.63; 95% confidence interval 1.05–1.45; P = 0.030). These results contradict the results of the combined analysis of SOFT/TEXT trials which showed that 5 years of an aromatase inhibitor (AI) + OFS was associated with a superior DFS when compared with 5 years of tamoxifen + OFS and similar OS. Moreover, these results also contradict the results of numerous trials in the postmenopausal setting that have consistently shown a clear superiority of AI over tamoxifen in DFS and in some trials even an OS benefit [2].

This raises a relevant question regarding the design of the Austrian study and the importance of the duration of adjuvant endocrine therapy, which was only 3 years in the ABCSG-12 trial. Although the authors referred to discrepancies in post-relapse therapy as a possible confounding factor to the poorer OS in the anastrozole arm, they did not address whether some patients were offered further adjuvant therapy ‘off study’ beyond the initial 3 years. Unless the study protocol controlled treatment beyond 3 years and in light of its open-label design, it is plausible that many patients in the control arm (tamoxifen + OFS) would have been offered by their treating physician additional tamoxifen to complete the classic 5-year therapy [3]. In contrast, a continuation of adjuvant therapy beyond 3 years would less likely occur in the investigational arm (anastrozole + OFS) where extension of endocrine therapy is not supported by evidence in the premenopausal setting.

This would make it difficult to interpret the hazard rate potentially be confounded by heterogeneity in the duration of the adjuvant endocrine therapy between study arms.

These challenges are not unique to the current study, but would be less of an issue in interpreting the initial results of the SOFT/TEXT trials (median follow-up 5.6 years) where treatment is given for the standard 5 years. This may however confound longer follow-up results as extended tamoxifen beyond 5 years becomes more widely adopted.

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References


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Sunitinib 2 weeks on, 1 off: strengths and weaknesses

We read with great interest the article by Kalra et al. in this journal, where authors reviewed the available data on alternate sunitinib schedules for treatment of metastatic renal cell carcinoma (mRCC) [1]. Mainly, we focused on the use of the 2 weeks on, 1 off schedule, which has received large consensus among oncologists treating mRCC in recent years due to (i) the reduction of adverse events compared with the standard schedule of 4 weeks on, 2 off and (ii) the promising data in the overall disease control and outcome.

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