Radiotherapy after Neoadjuvant Chemotherapy

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Question 1: Do You Recommend Locoregional Radiotherapy to Patients after Neoadjuvant Therapy According to the Tumor Stage and Clinical Situation before Neoadjuvant Therapy or after Neoadjuvant Therapy?

Haffty: Yes, according to tumor stage and clinical situation we recommend locoregional radiotherapy to patients receiving neoadjuvant therapy.

Sedlmayer: Up to now, and in absence of prospective trials, indications for radiotherapy should follow the respective recommendations for the adjuvant settings. This is valid for any possible target (sub)volume: breast/thoracic wall/regional lymph nodes, as elaborated in various recent DEGRO practical guidelines.

Wenz: We recommend locoregional radiotherapy to patients based on the staging before neoadjuvant therapy.

Question 2: If Patients Have a Pathologic Complete Remission in the Breast and in the Axillary Lymph Nodes (ypT0 (is) ypN0) Do You Recommend Additional Radiotherapy to the Thoracic Wall (in Case of Mastectomy) and to the Regional Lymph Node Areas?

Haffty: Yes, in case of pathologic complete remission (pCR) we recommend additional radiotherapy to the regional lymph nodes. In patients with mastectomy we recommend additional radiotherapy to the thoracic wall.

Sedlmayer: Again, indication for radiotherapy of these target volumes should follow pre-treatment staging information, irrespective of response to primary systemic treatment. The necessity for whole-breast radiotherapy in case of breast conserving surgery is unquestioned. After mastectomy, the best available evidence on the value of postmastectomy radiotherapy (PMRT) in case of pCR is derived from 2 retrospective studies, comprising about 780 patients with more the advanced stages II and III, receiving PMRT vs. no irradiation. Although biased in terms of more advanced stages in the irradiated cohorts, there was a clear benefit in locoregional control, distant metastases-free and overall survival.

Wenz: Until data from the RTOG and Alliance studies are available, we recommend additional radiotherapy depending on the situation before primary systemic treatment in selected patients.

Question 3: If Patients Convert from Histologically Axillary Lymph Node Positive (Proved by Biopsy or by Fine Needle Aspiration or Sentinel Node Biopsy before Neoadjuvant Therapy) to Histologically Proven Axillary Lymph Node Negative Status (by Sentinel Node Biopsy and/or by Axillary Lymph Node Dissection) Do You Recommend Additional Thoracic Wall Irradiation (in Case of Mastectomy) and Locoregional Radiotherapy (Thoracic Wall and/or Lymphatic Areas) after Neoadjuvant Therapy?

Haffty: Yes, if patients convert from node positive to node negative we do recommend additional radiotherapy.

Sedlmayer: For patients with pathologically negative nodes after primary systemic treatment, who had initially presented with clinical lymphadenopathy, the decision for regional lymph node irradiation (RNI) should comply to the pretreatment stage, irrespective of the response to chemotherapy. This is based on analogy to adjuvant situations, where, in case of positive nodes, additional RNI resulted in higher cancer-specific survival rates in mature follow-up.

Wenz: Yes, there are no prospective data available identifying patients who will not benefit from radiotherapy in this situation. Regarding overall survival, most likely these patients receive the strongest benefit from additional radiotherapy.

Question 4: Is There a Place for Intraoperative Radiotherapy after Neoadjuvant Therapy with Breast Conserving Surgery to Replace Postoperative Radiation Boost to the Breast?

Haffty: No, I do not see room for that, not off protocol.

Sedlmayer: Apart from an own series of 83 patients with locally advanced breast cancer, there is no literature on this topic up to now. In our cohort, however, intraoperative radiotherapy with electrons (IOERT) as precedent boost technique during breast conserving surgery followed by whole breast irradiation achieves excellent results on local control. This seems to be superior in comparison to standard treatment after retrospective long-term analyses, warranting further prospective investigation.

Wenz: All available clinical data indicate that the choice of boost technique has no strong influence on tumor control as long as the method is used properly. There may be some differences regarding toxicity and patient convenience.

Question 5: Is There a Place for Hypofractionation (with or without Boost) for Patients Who Have Received Neoadjuvant Therapy and Had Breast Conserving Surgery?

Haffty: Yes, I think hypofractionation is an option for patients with BCS after neoadjuvant treatment, although data is slim.

Sedlmayer: This has not yet been explicitly investigated. So far, experience on normal tissue tolerances for hypofractionation schedules has been derived from studies where patients received either no adjuvant chemotherapy, or were treated without taxanes or targeted therapies. These composites of primary systemic therapy might have different sensitizing potential in hypofractionation if administered in a different sequence and currently should not be considered outside prospective trials.

Wenz: There is only limited published experience (especially with multiagent chemotherapy +/- targeted therapy). Therefore patients should best be treated within the framework of clinical studies specifically addressing this question.

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