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RAPID COMMUNICATION

Controversial Opinion of "All pCRs are the Same" in St. Gallen International Consensus Guidelines 2021

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Abstract: The opinion of "all pCRs are the same" in St. Gallen International Consensus Guidelines 2021 attracted the attention from clinical doctors. But this opinion is not consistent with the current clinical practice guidelines. The evidence-based medical evidence supported that the survival benefit of pCR was associated with treatment regimes, initial staging, and tumor biomarkers. To compare with the different status, the survival prognosis of pCRs is not the same. Furthermore, the pretreatment clinical stage, pathological stage, tissue grade, and subtype still influence on the survival prognosis of pCR. The pCR should be stratified according to histological factors and to guide the identification of individualized treatment after neoadjuvant therapy. In the future, a de-escalation treatment might be detected by the clinical trials of neoadjuvant therapy which would approach "all pCRs are the same".

Keywords: breast cancer, neoadjuvant therapy, prognosis, pathologic complete response, St. Gallen International Consensus Guidelines

The St. Gallen International Breast Cancer Consensus Conference (SG-BCC) 2021 panelists strongly believed that "all pathologic complete responses (pCRs) are the same", that is, the prognosis of pCR in one tumor type was similar whatever treatment was used to achieve that end.[1] But this opinion is not conformed to the clinical practice guideline and the clinical trial data. The current evidence-based medical evidence supported that the survival benefit of pCR was associated with treatment regimes, initial staging, and tumor biomarkers.

In the subtype of Human epidermal growth factor receptor 2 (HER2) positive with pCR after neoadjuvant therapy, the 5-year event-free survival rate was 87% (95% CI: 82–90%) in patients with trastuzumab (H) neoadjuvant therapy followed H adjuvant therapy (n = 236), 92% (95% CI: 87–95%) in patients with H and pertuzumab (P) neoadjuvant therapy followed H adjuvant therapy (n = 185), and 95% (95% CI: 90–97%) in patients with H and P neoadjuvant therapy followed H and P adjuvant therapy (n = 352).[2] Although pCR was approached after neoadjuvant target therapy combined with chemotherapy, the different regimes have different prognosis and not all the same. The dual target therapy provided more benefit of survival which is compared to the single target therapy.

In the triple-negative breast cancer (TNBC), combination with immune therapy could significantly improve pCR and survival compared to chemotherapy alone. The three-year invasive disease-free survival (iDFS) of pCR was 95.5% (95% CI: 83.0–98.8%) in the immune therapy group and 86.1% (95% CI: 69.8–94%) in the placebo group (Hazard ratio [HR]=0.22, 95% CI: 0.05–1.06, p = 0.038). The distant disease-free survival (DDFS) was 100% (95% CI: 100–100%) in the immune therapy group and 86.1% (95% CI: 69.8–94%) in the placebo group (HR = 0, 95% CI: 0.00-, p = 0.005). The OS was 100% (95% CI: 100–100%) in the immune therapy group and 88.9% (95% CI: 73.1–95.7%) in the placebo group (HR = 0.00, 95% CI: 0.00-, p = 0.024).[3] If patients with TNBC receive immune therapy combined with chemotherapy, pCR would be enhanced and survival would be improved.

The initial clinical stage and tumor biomarkers, as well as pathological stage after neoadjuvant therapy, are also associated with disease-specific survival (DSS), and these factors were incorporated in the neo-bioscore systems to assess the prognosis after neoadjuvant therapy. This system shows that the neo-bioscore point of clinical stage I–IIA is 0 but the point of clinical

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Table 1 The Prognosis of pCR Group After Neoadjuvant Therapy with Different Subtype

Clinical Stage	Grade	Subtype	Pathological Stage	Neo-Bioscore, 5 Year-DSS
IIIC	3	Triple negative	pCR	Score=5, 71%
IIIC	3	ER-, HER2+	pCR	Score=4, 86%
IIIC	3	ER+, HER2+	pCR	Score=3, 93%
IIB	3	Triple negative	pCR	Score=4, 86%
IIB	2	Triple negative	pCR	Score=3, 93%
IIB	2	ER-, HER2+	pCR	Score=2, 97%

stage IIIB-IIIC is 2. Therefore, patients with different initial clinical stage, grade, hormone receptor and HER2 status will have different prognosis in the pCR group after neoadjuvant therapy (Table 1). Furthermore, in patient with pCR, clinical stage III, grade III, the neo-bioscore is 5 and the DSS is 71% in triple negative breast cancer, the neo-bioscore is 3 and the DSS is 93% in estrogen receptor (ER) positive HER2 positive breast cancer. Even if the pre-treatment clinical stage is the same with pCR after neoadjuvant therapy, different subtypes would have different prognosis. Therefore, there is still a need to optimize systemic treatment after neoadjuvant therapy based on the recurrence risk factors.

A number of clinical trials have been designed to explore a precise treatment for patients receiving neoadjuvant therapy. The aim of CompassHER2-pCR study is to evaluate the de-escalation of chemotherapy for HER2 positive breast cancer after neoadjuvant chemotherapy and targeted therapy.[4] The PHERGain study will assess the effects of neoadjuvant treatment with dual target therapy (± endocrine therapy according to hormone receptor status) in patients with HER2 positive breast cancer through a FDG-PET response-adapted strategy.[5] These studies will find that patient with pCR after neoadjuvant therapy following a short course chemotherapy or chemotherapy-free regime would acquire a satisfactory survival.

In conclusion, the survival prognosis of pCRs are not the same. The pretreatment clinical stage, pathological stage, tissue grade, subtype, and regimens still influence on the survival prognosis of pCR. The pCR should be stratified according to histological factors, and to guide the identification of individualized treatment after neoadjuvant therapy. In the future, a de-escalation treatment might be detected by the clinical trials of neoadjuvant therapy which would approach "all pCRs are the same".

Disclosure

The authors report no conflicts of interest in this work.

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