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ASO AUTHOR REFLECTIONS

ASO Author Reflections: Complete Pathological Response after Neoadjuvant Treatment for Pancreatic Ductal Adenocarcinomas—Curative Surgery in Cured Patients?

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PAST

Surgery followed by adjuvant chemotherapy has represented the standard treatment for a long time for resectable and borderline pancreatic adenocarcinomas. The introduction of neoadjuvant chemotherapy (FOLFIRINOX) and chemoradiotherapy regimens has modified the therapeutic sequence for pancreatic cancer. Neoadjuvant treatment can select the best candidates for surgery by excluding those with rapidly progressive disease and/or with precarious/poor performance status ("futile surgery").[1,2] The benefits of this strategy have been reported by several retrospective studies and few prospective studies.[3–6] With the increasing adoption of induction treatments, we have seen an increased rate of complete pathologic response (CRP) not reported previously.[7,8] How this complete pathologic response affects the overall survival of patients remains to be determined.

PRESENT

In 2024, 13 years after the evidence of the survival benefits of the FOLFIRNOX regimens,[9] two large retrospective studies including the current TONO study,[8,10] showed that CPR is associated with considerable survival benefits exceeding 60% at 5-years. CPR, however, does not mean cure, and one third of patients recur even long after surgery. These recurrences appear more frequent and associated with lower survival in patients receiving preoperative radiochemotherapy, indicating that local control likely does not mean systemic control. Unfortunately, some of these patients did not really benefit from CPR because of postoperative mortality, which persists after pancreatic resection. Other patients received adjuvant chemotherapy with an impact on survival and recurrence that could not be accurately evaluated. Finally, the evolution of a CPR without surgery remains unknown.

FUTURE

The combination of chemotherapy and surgery treat pancreatic cancers. Since CPR is associated with proven long-term survival, cure efforts should be made to: (1) identify preoperatively predictive factors of response to FOLFIRINOX, (2) recognize biological and radiological characteristics of responders, and (3) to develop noninvasive tests to precisely identify patients with "active" pancreatic cancers. In 2024, pancreatic surgery seems to reach its maximal development by reducing mortality, developing extended pancreatic surgery and reducing the invasiveness by minimally invasive surgery.[11,12] In the immediate next future research could help to best select optimal candidate for surgery.

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