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HIGHLIGHT ARTICLE

New Developments in the Management of Borderline Resectable Pancreatic Cancers

Highlights from the "2013 ASCO Annual Meeting". Chicago, IL, USA; May 30 - June 4, 2013

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Summary

There remains great variability in the treatment for patients with borderline resectable pancreatic head cancers. Whether surgery should be attempted or neoadjuvant therapy consisting of chemoradiation or chemotherapy alone is at some debate. Each neoadjuvant regimen does show efficacy but there is no clear consensus which would be most beneficial. We will discuss three abstracts (#4043, #4057, #e15082) that were presented in the 2013 ASCO Annual Meeting that will discuss neoadjuvant therapies and how they are related to getting an R0 resection.

What Did We Know Before the 2013 American Society of Clinical Oncology (ASCO) Annual Meeting?

Pancreatic cancer is the fourth projected cause of cancer related mortality in 2012. Patients rarely present early and at time of diagnosis usually have advanced disease. Only 20% of patients present with resectable tumors. There are 45,220 new cases of pancreatic cancer with a projected mortality of 37,390 patients based on recent cancer statistics [1].

The only known curative treatment for pancreatic cancer is surgical resection with negative margins (R0). A borderline resectable pancreatic head tumor includes locally advanced disease with surrounding structures involved including the superior mesenteric vessels and portal vein. Some have also included patients with involved lymph nodes of the resection area because of the very poor 5-year survival. These locally advanced tumors have a very high likelihood of having positive margins which portends a very poor prognosis. The survival of patients with positive margins is similar as if the patient never underwent resection. The role of neoadjuvant therapy in borderline tumors is an active area of investigation where several chemotherapy regimens alone or with radiotherapy were are used in an attempt to achieve R0 resection. Many different regimens improve disease survival and improve overall survival [2, 3, 4, 5, 6, 7]. We are presenting a summary of three abstracts from the recent ASCO Annual Meeting in 2013 which discuss the trials of the past year addressing this issue.

Keywords Neoadjuvant Therapy; Pancreatic Neoplasms; Radiosurgery

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What Did We Learn at the 2013 American Society of Clinical Oncology (ASCO) Annual Meeting?

Gemcitabine Plus Docetaxel as Neoadjuvant Chemotherapy in Borderline Resectable Pancreatic Cancer (Abstract #4043 [8])

Rose *et al*. evaluated the use of an extended regimen for 24 weeks of gemcitabine and docetaxel without radiation. They had 64 patients undergo the treatment with 53 (83%) patients completing the regimen with either some response of stable disease. Fifty of the 53 patients underwent local treatment either as surgery or fluoropyrimidine-based chemoradiotherapy. Forty patients went to the operating room for an attempted R0 resection. Thirty (75%) had a successful R0 resection. The median overall survival for patients receiving the extended regimen of gemcitabine and docetaxel plus chemoradiotherapy was 17 months; in patients that underwent R0 resection it was greater than 20 months. They concluded that the extended neoadjuvant treatment was feasible with good efficacy. They also felt that the extended treatment was superior compared to the literature in both the resected and non-resected patients.

Association Between Successful Resection and Improved Tumor-Vessel Relationship (Abstract #4057 [9])

Dholakia *et al*. performed a retrospective study looking at prognostic factors of neoadjuvant chemoradiation for borderline pancreatic cancers. Fifty patients with borderline tumors underwent neoadjuvant therapy with 29 undergoing resection and 21 remained inoperable. Patients selected for surgery had a small tumor volume and the lack of major vessel encasement, superior mesenteric artery involvement, or ascites. However, despite treatment, the tumor volume or the amount of vessel involvement did not change on the pre- and post-neoadjuvant therapy scans (P>0.05). The median overall survival was 22.9 months in the resected patients and 13.0 months in the unresected patients (P<0.001). Out of patients that underwent resection, 93% were R0 with 12% having a pathologic complete response and 27% showing only less than 10% viable tumor. They concluded that, despite minimal changes in radiographic imaging pre- and post-neoadjuvant therapy, R0 resection rates are high with low lymph node involvement. The outcomes were similar if deemed resectable from time of initial diagnosis. The lack of improvement on post neoadjuvant imaging should not be the sole determination if surgery is warranted.

Association of Decline in Serum CA19-9 After Neoadjuvant Therapy with Improved Survival Among Borderline Resectable Pancreatic Cancer Patients (Abstract #e15082 [10])

Tsai *et al*. looked at the role of CA 19-9 as a prognostic indicator for borderline pancreatic tumors treated neoadjuvant chemoradiation. Seventy-three patients had a CA 19-9 level obtained prior to treatment (baseline), after induction chemotherapy, and after radiation therapy. Prior to treatment, 20 patients had normal CA 19-9 and were excluded. The mean CA 19-9 levels at baseline, after chemotherapy, and after radiation were 956, 164, and 139 U/mL, respectively. Of the remaining 53 patients, 49 (92%) were considered for surgery with 38 (72%) patients having a resection. Patients that had no change or increase in their CA 19-9 level from baseline to completion of neoadjuvant therapy had a much worse outcome than patients with a decrease in the level. The median survival was 11.5 months with no change and 30.1 months if there was a decrease (P=0.0002). They concluded that a decline in the CA 19-9 level after neoadjuvant therapy is associated with higher resection rate and overall survival. An increase in the CA 19-9 level during and after neoadjuvant therapy is a poor prognostic indictor.

Discussion

Currently, R0 resection is the only potentially curative treatment for pancreatic cancers. The goal of any neoadjuvant therapy for borderline pancreatic head cancers is to be able to have the patient undergo surgery for an R0 resection. This is why neoadjuvant therapy for borderline tumors is an active area of investigation. We have summarized three abstracts presented at ASCO Annual Meeting in 2013. Two have evaluated prognostic indictors of the neoadjuvant therapy and one presented a novel treatment option.

Prognostic indicators are an important part of any treatment regimen. The abstracts discussed have used pre- and post-therapy CA 19-9 and imaging studies to evaluate the appropriateness of surgical intervention in getting an R0 resection. As each of these abstracts has shown, you cannot use a single variable to determine surgical resection. Dholakia *et al*. has shown that the lack of radiologic response of a borderline tumor to neoadjuvant therapy could be misleading [9]. Tsai *et al*. has shown that if CA 19-9 at baseline does not change or increase with therapy, then surgery might not be the next step [10].

Neoadjuvant therapy for borderline tumors is very promising; however, we have a lot of work to do to determine the best therapy. Rose *et al*. has given us another perspective on giving extended treatment of two chemotherapy agents with some improvement in overall survival [8]. As with any of these promising studies, we need to investigate in a larger clinical trial.

Conflicts of interest The authors have no potential conflicts of interest

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