Different outcomes for positive, negative pancreatic cancer patients receiving chemoradiation and systemic therapy

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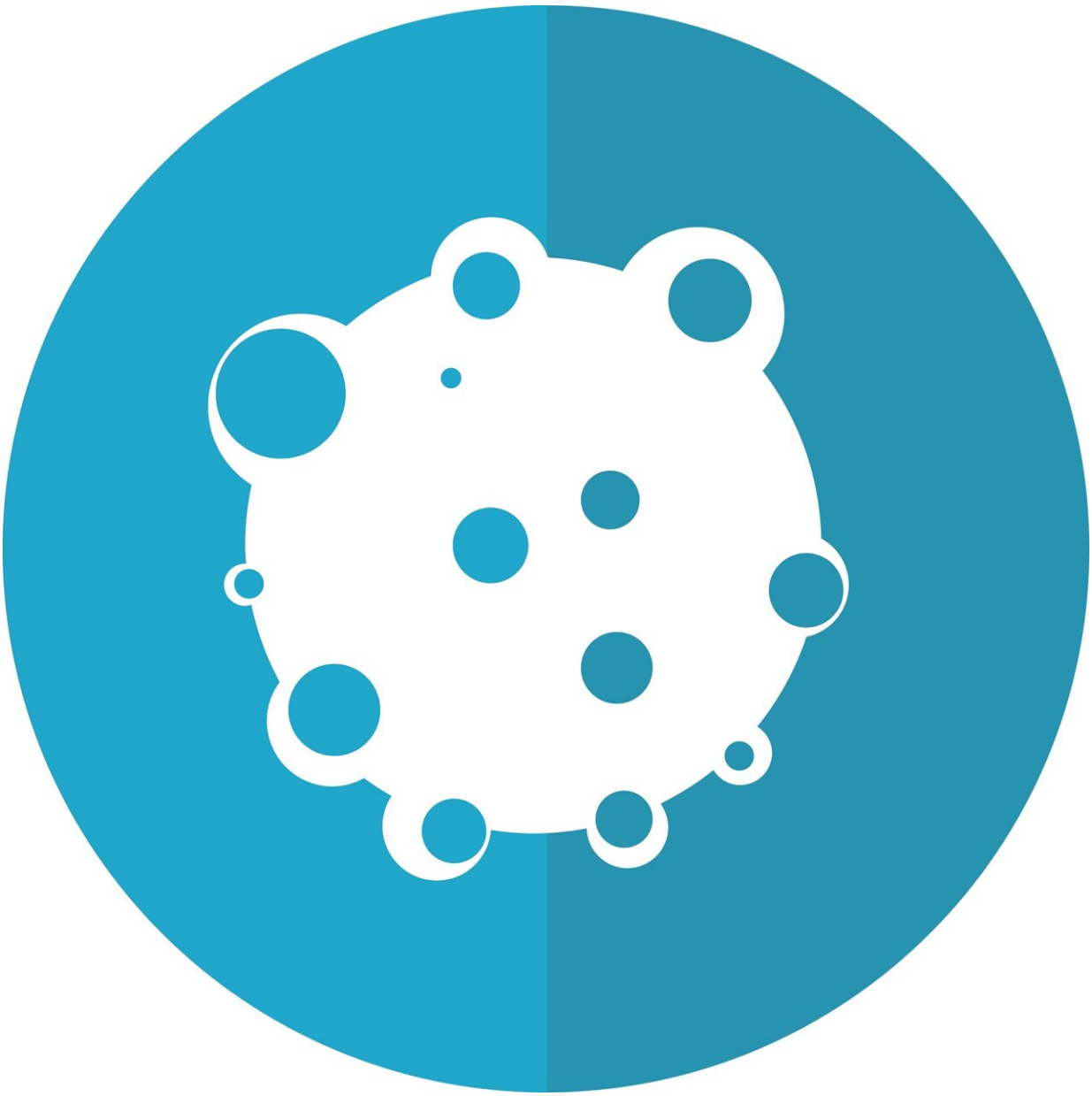

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NRG Oncology recently reported the results from the radiotherapy randomization, which was the second step of their NRG-RTOG 0848 clinical study comparing adjuvant chemotherapy with or without chemoradiation for patients with resected periampullary pancreatic adenocarcinoma.

The trial data did not show that the addition of radiation and chemotherapy to adjuvant systemic therapy improved overall survival (OS) for all patients in the study. However, OS was improved among node-negative patients. OS was essentially the same between treatment arms for node positive patients. The trial data also showed that disease-free survival (DFS) was improved with the addition of radiation and chemotherapy to adjuvant systemic therapy, driven by the DFS improvement in node negative patients. The addition of chemoradiation did not increase grade 4 or 5 adverse events.

These results were presented at the American Society of Clinical Oncology (ASCO) 2024 Annual Meeting in Chicago, Illinois, and were distinguished as a "Best of ASCO" abstract.

"This trial was initially designed to address the need for a more effective and tolerable adjuvant systemic therapy for pancreatic cancer. When this study was developed, gemcitabine was the only effective treatment available, and this treatment commonly corresponds with distant and local failures for this patient population. Therefore, we designed NRG-RTOG 0848 to evaluate the role of adjuvant radiation with 5-fluorouracil (5-FU) or capecitabine following surgical resection and

adjuvant systemic treatment to see if this additional treatment would further improve survival outcomes for patients," stated Ross A. Abrams, MD, the Principal Investigator of the NRG-RTOG 0848 study.

NRG-RTOG 0848 treatment started with 5 cycles of systemic treatment, initially randomizing patients at step 1 to either Arm 1 to receive gemcitabine alone, or Arm 2 to receive gemcitabine with erlotinib. Following the results of the LAP07 trial (Hammel, 2013), the erlotinib randomization was stopped and all patients were registered at step 1 to receive gemcitabine alone. Two years later, the trial was amended to allow oxali-based combination chemotherapy regimens.

Following step one, patients were evaluated to confirm there was no disease progression. Non-progressing patients were stratified by nodal status, CA19-9, surgical margins, and adjuvant systemic therapy. Following stratification, patients were then randomly assigned to receive radiotherapy for one month on either Arm 3 (Chemo), including gemcitabine or combination chemotherapy, or Arm 4 (Chemo+CRT), receiving gemcitabine or combination chemotherapy followed by chemoradiation with either capecitabine or 5-FU.

There were 354 patients included in the step 2 randomization of the NRG-RTOG 0848 study and median follow-up was 2.2 years for all patients (0.02-12.8) and 7.4 years for living patients (0.02-12.8). The primary endpoint for the trial was OS, which was only improved for patients with node-negative disease (5-year OS 48.1% for patients on the Chemo+CRT arm versus 28.6% on the Chemo arm). Node-positive patients in the study did not experience an improvement in OS.

DFS was improved for all patients, driven by the node-negative patients (5-year DFS 21.4% for patients on the chemo+CRT arm versus 15.2% on the Chemo arm. Patterns of failure will be examined. Grade 4 and 5 adverse events reported were similar on both treatment arms (5% on the

Chemo arm and 6% on the Chemo+CRT arm).

"The results of NRG-RTOG 0848 suggests that, with the appropriate planning and considerations, chemoradiation could be utilized in further testing for future adjuvant and neoadjuvant trials," Dr. Abrams added.

Future research is needed to assess an alternative way to improve DFS and OS for node-positive patients that are at a high-risk of disease progression. Additionally, it would be worthwhile to investigate if adjuvant could derive more of a benefit in these patient populations if combined with a more effective systemic therapy.

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