4.31: Neoadjuvant Radiation Therapy in Pancreatic Adenocarcinoma with Dr. William Hall

Season	4
Type	Plenary Session

We Discuss:

Plenary Session 4.31 Show Notes

Overview

Conversation with Dr. William Hall

- **Introduction [0:47]**
  - Dr. Hall is an Associate Professor of Radiation Oncology and Surgery at Medical College of Wisconsin

        - He earned his MD from Loyola University Chicago Stritch School of Medicine
            - He finish his radiation oncology training at Emory University

- **Neoadjuvant Radiation Therapy [2:05]**
    - Value of Neoadjuvant Radiation Therapy in the Management of Pancreatic Adenocarcinoma
        - William Hall et al., JCO
    - November is Pancreatic Cancer Awareness Month
        - Therefore this paper is very timely for a variety of reasons:
            1. As an oncologic profession we must pay close attention to pancreatic adenocarcinoma
            2. What are the weaknesses in existing data?
                a. People are too quick to draw conclusions from bite clip interpretations of the literature
    - A randomized trial of chemoradiotherapy and chemotherapy after resection of pancreatic cancer
        - Neoptolemos et al., NEJM, 2004
            - In reference from Hall et al., JCO

> 💡 *"Up-front surgical resection for resectable pancreatic cancer remains a standard that has been debated for over a decade. When patients undergo surgery first, the rate of positive margins range from 30% to 50% and local recurrence events range from 20% to 50%. 10 These event rates are five times higher than other types of adenocarcinoma treated with up-front surgical resection.11,12 Although improving OS outcomes have been reported for patients who have successfully completed up-front surgical resection and adjuvant chemotherapy,13 these OS data are at least partially driven by intense biological selection. Specifically, these outcomes are enriched by the inclusion of patients who withstood the challenges associated with surgical resection, recovery, postoperative restaging, and enrollment into a clinical trial. This timing of enrollment selects for patients without early disease progression on postoperative imaging. Biological selection, driven by surgery first (in sharp contrast to systemic therapy first), is not a strategy to meaningfully improve the OS of all patients with localized pancreatic cancer." - Hall et al.*

- **Adjuvant vs Neoadjuvant [10:00]**
  - Is there a role for adjuvant therapy? And should that therapy be given to neoadjuvantly?
    - Adjuvant radiation may or may not be beneficial in the postoperative setting

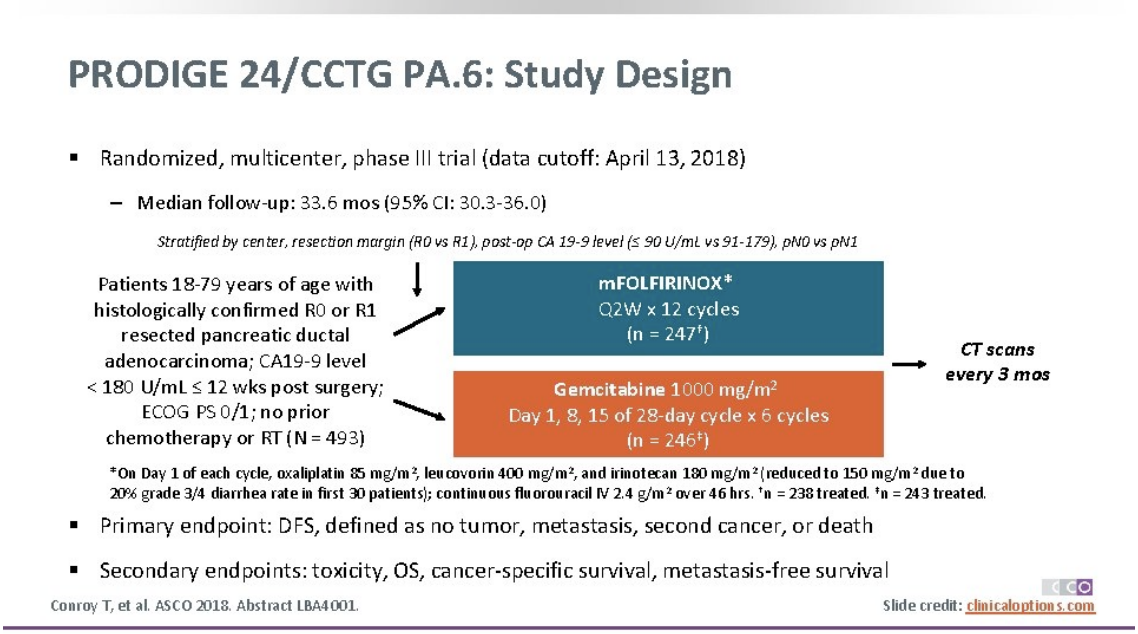
> 📘 *"Neoadjuvant therapy is delivered before surgery with the goal of shrinking a tumor or stopping the spread of cancer to make surgery less invasive and more effective. Adjuvant therapy is administered after surgery to kill any remaining cancer cells with the goal of reducing the chances of recurrence." - Source*

    - Surgery first
        - Patients who are receiving surgical treatment for pancreatic cancer are typically our fittest patients, given that their cancer are resectable
            - If you look at the available studies that have brought people to surgery first, the results are very poor
                - The rates of positive margins in this disease are north of 60%

> "I would challenge anyone to think of any solid tumor from head to toe in which you would recommend surgery first [in reference to nodal positivity]" - Dr. Hall

    - The whipple
        - You frequently find in papers on pancreatic cancer that surgery is the sole curative modality, which may or may not be accurate
            - There may be more to this story
                - There's a lot of evidence that when individuals arrive with clinical presentation of pancreatic adenocarcinoma → a high proportion of those instances have microscopic metastatic disease
                    - Unfortunately, a huge number of these patients develop these metastasis

- **Cohorts [19:31]**
    - PRODIGE-24-ACCORD trial



Source

- Dr. Hall's takeaway
  - The argument is well made in that, in order to enroll in a randomized control study comparing FOLFIRINOX to Gemicitabine, the investigator must feel that the patient, if allocated to the FOLFIRINOX arm, can tolerate FOLFIRINOX
    - Not only that, but these patients tolerated these therapies after surgery and recovery, which may not translate to other patient populations

> "There's a dramatic, dramatic paucity of randomised trials evaluating different types of neoadjuvant therapy in this disease" - Dr. Hall

- **Phase III trial [37:54]**
  - It is possible that in regard to pancreatic surgery, you're going to take a big number of patients for a very large procedure that will most likely provide them with no benefit
    - In other words, they will undergo major operation that confers them little to no benefit when they develop early recurrence or distant metastases

> "Anytime you look at the results of a randomized adjuvant trial post surgery in which there was no chemoradiotherapy adjuvantly given, it's just a sliver of the question on one side of the scale, not the whole sort of picture on the other side of the scale." - Vinay Prasad

- Neoadjuvant care [46:33]
  - The only way we're going to meaningfully improve the outcomes for these patients is to do robust, randomized trial

> "The goal is really not to say that radiation should be blindly done or that chemotherapy should be blindly done in the neoadjuvant setting, but to say that, we don't know the best way to treat these patients." - William Hall

- **Summary:**
  - Resectable pancreas adenocarcinoma
    1. We often resect it and then provide adjuvant treatment
    2. There has long been discussion in the oncology space concerning the role of adjuvant radiation
    3. The discussion has now shifted to the role of adjuvant or neoadjuvant treatment, chemotherapy, radiation, or radiotherapy
    4. This paper goes through some of the evidence and discuss what kinds of research we need to see
    5. We need to take all of these patients and put them into into robust studies that evaluate different types of neoadjuvant therapy
    6. The author drives hope the point that maybe in the future, we'll really have some agreement on how radiation may be provided to increase overall survival for these patients
- **Other literature mentioned:**

- RTOG-0848
- ESPAC4
- The CONKO-001 Randomized Trial
- SWOG S1505
- Oncological benefits of neoadjuvant chemoradiation with gemcitabine versus upfront surgery in patients with borderline resectable pancreatic cancer
  - Jang et al., Ann Surg
- PREOPANC trial
  - Van Eijck et al., JCO
- Alliance A021501
  - Katz et al., JCO, 2021

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