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Opinion

Pancreatic Cancer Treatment- Search for the Elusive Silver Bullet

Christopher S Gondi*

Department of Internal Medicine, University of Illinois College of Medicine at Peoria, Peoria, IL, USA

***Corresponding Author:** Christopher S Gondi, Department of Internal Medicine, University of Illinois College of Medicine at Peoria, Peoria, IL, USA.

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Pancreatic Ductal Adeno Carcinoma (PDAC) is the fourth most common cause of cancer deaths in the United States and is gaining importance worldwide as the survival rates are very poor for all four stages combined. The combined 1-year survival is only about 25% and the 5-year survival is less than 8%. It has been often observed that PDAC tumors reoccur after surgery and chemotherapy. These new tumors tend to be chemo-resistant, leading to poor survival rates, which have not changed in the last 40 years. A major hallmark of pancreatic cancer is extensive local tumor invasion, early systemic dissemination, and extremely poor response to chemotherapy. The basis for these adverse characteristics is not well understood. Identifying the mechanisms involved in chemo-resistance and tumor recurrence will enable the development of better strategies to combat this disease.

One of the main reasons why pancreatic cancer is so deadly is that by the time it is diagnosed it usually is too late. Unlike other cancers such as lung and colon, which present numerous symptoms, pancreatic cancer at an early stage shows almost no symptoms. Symptoms can be as common as abdominal pain, weight loss, and loss of appetite; because the symptoms are so common it is very difficult to determine whether a person has pancreatic cancer or something else. Constant persistent symptoms accompanied by more severe indications such as jaundice is usually when a patient realizes that something is wrong.

Challenges and strategies

Anti-Angiogenic therapy: Tumors need nutrients to grow, and for this growth, they attract blood vessels towards themselves. Successful suppression of these tumor induced blood vessels can 'starve' tumor growth. This form of treatment is called anti-angiogenic therapy. Numerous attempts have been made to suppress tumor growth using this method but have failed to achieve clinically significant outcomes.

Anti-cancer stem cell therapy: Studies suggest that the capacity of tumors to recur is dependent on a subset of cells within the tumors called cancer stem cells (CSC) or cancer initiating cells. Studies also show that these CSC are able to form tumors that are indistinguishable from parental tumors. Further these CSC contribute to chemo resistance and are responsible for tumor relapse. Understanding the mechanisms of chemo-resistance and developing ways to overcome this will enable the development of new treatment strategies aimed at increasing the survival rates of PDAC patients specifically by targeting cancer stem cells.

Individualized Combination Therapies: Failure of one form of therapy usually warrants alternative approaches. Newer therapies are now being developed which use tumor genetic profiles and tailor specific therapeutic combinations to address the genetic variants of a particular patient. This method of treatment is developing fast with favorable outcomes.

Future of PDAC Therapy: Cancer therapy as such will move into the realm of disease management rather than a cure. There will of course be "cures" as such where no evidence of cancer can be detected but there will still be an issue of disease management where constant monitoring will need to be done.

Overall, promising therapies are emerging and the future for pancreatic ductal adenocarcinoma treatment appears to be individualized combination therapy.

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