ISSN 2692-5877
DOI: 10.46998/IJCMCR.2021.10.000240

International Journal of
Clinical Studies & Medical Case Reports

Perspective

Pancreatic Cancer and Liver Cancer Are the Deadliest Cancers; and Still No Effective Chemotherapy. Why?

Leslie C Costello* and Renty B Franklin

Department of Oncology and Diagnostic Sciences, University of Maryland School of Dentistry and the University of Maryland Greenebaum Comprehensive Cancer Center, USA

***Corresponding author:** Adel Ekladious, Department of Oncology and Diagnostic Sciences, University of Maryland School of Dentistry; and the University of Maryland Greenebaum Comprehensive Cancer Center, Baltimore, Md. 21201, USA. Email: lcostello@umaryland.edu.

Received: May 28, 2021 Published: June 14, 2021

Abstract

In 2020, there were about 60,400 cases and 48,200 due to pancreatic cancer; an estimated death rate of 80%. For liver cancer the values are 42,800 new cases and 30,000 deaths; an estimated death rate of 72%. The 5-year survival rate is 9% for pancreatic cancer and 18% for liver cancer. During the recent period of 30 years, there has been no decrease in the incidence of pancreatic cancer deaths or liver deaths; and instead, there has been an increase death. The reason is the continued absence of an efficacious systemic chemotherapy. That is due to the failure of the identification of the important factors that are implicated in the development and progression of those cancers. However, information does exist, which is likely to represent a viable and compelling concept of the manifestation of both cancers; and will provide the basis for a potential effective chemotherapy. The status of zinc is the likely important factor that manifests the development and progression pancreatic and liver cancers and clioquinol zinc ionophore is the treatment.

Purpose and focus of this article

Evidence is presented for treatment of pancreatic and liver cancers.

Keywords: Pancreatic cancer; Liver cancer; Cause; Zinc; Clioquinol; Treatment

Introduction

A PubMed search of "chemotherapy for pancreatic cancer" reveals about 50,000 citations since 1951, and 22,000 citations since 2000. For liver cancer, the results are about 65,000 citations since 1951, and 50,000 citations since 2000. Over a period of about 70 years and about 110,000 reported studies, an effective systemic chemotherapy still does not exist. The reason is that the major factors for the development and progression of pancreatic and liver cancers still have not been established. Instead, the prevailing views are speculative and often mistaken. The medications that are employed (such as 5-fluorouracil, folinic acid, irinotecan, and oxaliplatin) provide the palliative care to extend the survival of the patient while awaiting the impending death, often within 24 months.

Then the question becomes "Why are pancreatic and liver cancers persistently the deadliest of the common cancers? A reason is that the early malignancy most often is not detected. The malignancy is first suspected as a result of the patient's intestinal discomfort, by then localized site of malignancy has spread and metastasized to distant tissues.

The incidence of new cases and deaths of liver and pancreatic cancers.

The incidence for 2020 is expected to be, about 43,000 cases and 30,000 deaths/year exist in the U.S. for liver cancer [1,3]. The 5-year survival rate is 18% (Figure 1); an estimated death rate of 70%. The death rate had been increasing over the past years until 2018, when the death rate began to decline. The population rate of new cases increased from 6% to 12%, including a decline in the recent 3 years (Figure 2) [2]. Figure 1 also shows that liver cancer has the 2nd lowest 5-year survival rate of all common cancers.

The incidence of new cases of pancreatic cancer is 60,400/year and 48,200 deaths/year; an estimated death rate of 80% [4]. The 5-year survival rate continues at 9%; the 1st of all common cancers. The incidence of deaths has not changed over the past 30 years.

Those statistics are revealing and disturbing, and they must be addressed and eliminated. However, they will not change until the correct identification of the major factors involved in the manifestation of both cancers are accurately identified.

The implications of zinc in pancreatic cancer and liver cancer: Liver cancer always exhibits a marked decreased zinc in malignancy compared to the normal acinar epithelial cells [5].

DOI: 10.46998/IJCMCR.2021.10.000240

Fig 1. 5-year cancer survivial rates.

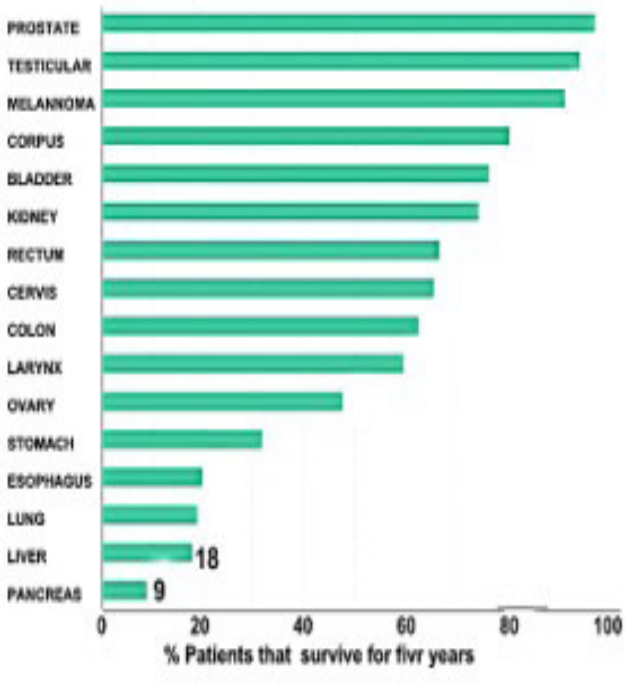

Fig 2. The new cases and deaths of pancreatic and liver cancers since 2018

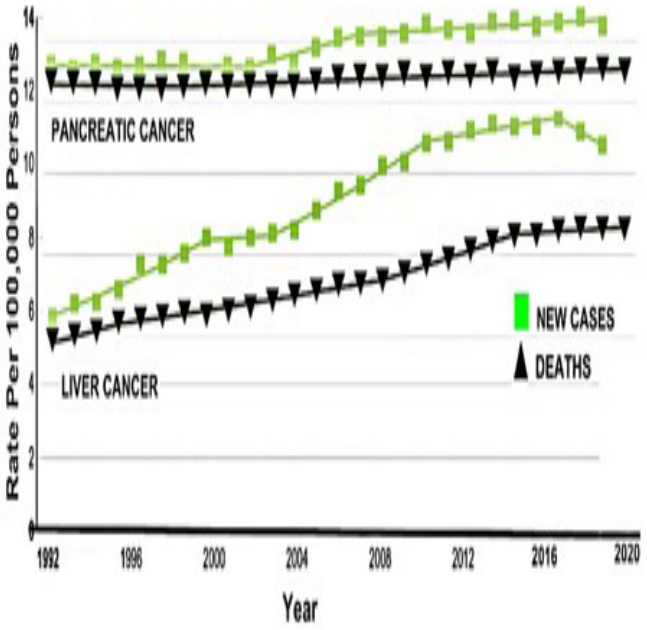

Fig 3, The zinc and ZIP14 zinc transporter levels in normal and malignant liver tissue sections. Zinc dithizone stain shows the marked decrease in malignancy. ZIP immunohistochemistry shows the membrane stain in normal cell and its absence in malignancy.

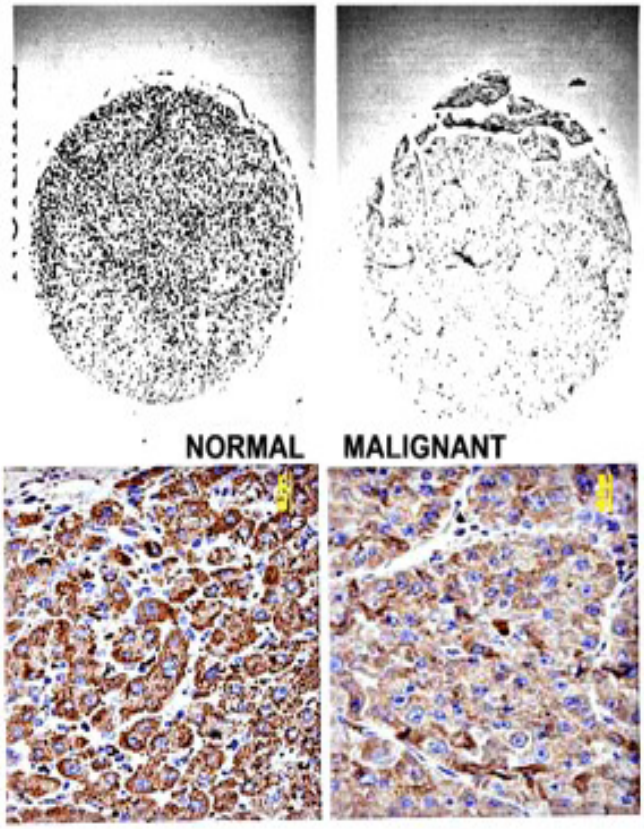

Fig 4. Zinc concentration in liver tissue from HCC and normal subjects. "NORMAL" is liver tissue from non-cancerous patients. "Non-Cirr" is normal tissue adjacent to the HCC malignant tissue. "Cirr" is cirrhotic tissue adjacent to the HCC malignant tissue. "Malig" is the HCC tumor tissue region. *P < 0.001 for "Malig" vs. other groups

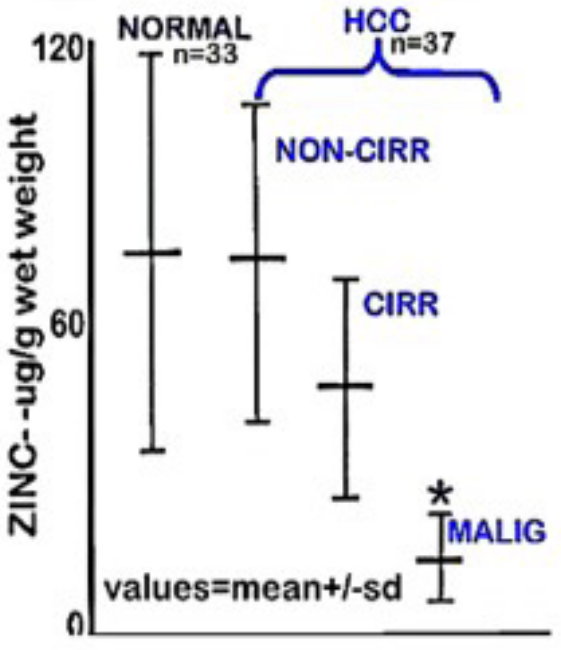

Figure 3 shows the marked decreased zinc in malignancy. That is consistent with the report of Kew [6], who showed (Figure 4) that malignancy always exhibits significantly decreased zinc compared to normal tissue, cirrhotic, and non-cirrhotic tissue. The reason is the zinc is that decreased is that the zinc level that exists in the normal cell is cytotoxic in the malignant cell. Pancreatic cancer malignancy also exhibits a marked decreased zinc (Figure 5). Our study [7] included 47 cancer patients and 10 normal patients. All cancer cases exhibited decreased zinc malignancy.

ZIP-family zinc-uptake transporter: the major factor for the zinc effects: The above relationship leads to the issue of the cause of the decrease in zinc in pancreatic and liver cancers. The zinc in blood plasma is not capable of permeating the cell membrane. Therefore, all mammalian cells exhibit a ZIP-family zinc-uptake transporter that facilitates the uptake of zinc. ZIP14 is the transporter for liver cells (Figure 5) [5]; and ZIP3 is the transporter for pancreatic cells [7]. In malignant cells, the transporters are downregulated. Therefore, the major factor for the development and progression of advanced liver cancer and pancreatic cancer is that they are "ZIP-deficient/decreased zinc" malignancies

Clioquinol zinc ionophore: The effective systemic chemotherapy for both cancers: An effective systemic chemotherapy that will induce cytotoxicity in the pancreatic cancer malignant cells and/or the liver cancer malignant cell is presently not available. The current medications that are employed (such as gemcitabine, oxaliplatin, cisplatin, doxorubicin, 5-fluorouracil, capecitabine, mitoxantrone, novantrone) are not cytotoxic for the malignant cells. They are employed for the palliative care of the terminal cancer patients. The intent is to suppress the progression of malignancy, and to extend the survival time of the patient.

The identification of pancreatic cancer and liver cancer as "ZIP-deficient/decreased zinc" malignancies make it likely that the zinc ionophore, clioquinol, will be an effective chemotherapy. systemic. It was employed (3% Clioquinol Cream) in the successful treatment of a patient who presented with untreatable terminal testosterone-dependent prostate cancer [8]. That cancer is also a "ZIP-deficient/decreased zinc" malignancy. In the absence of a better alternative, gastroenterologists and oncologist should be employ the Clioquinol Cream for their pancreatic cancer and liver cancer patients.

Presently, it is employed as an FDA-approved "off-label" or "right to try" treatment for patients with terminal medical conditions for which an FDA-approved medication is not available. If corroborating successful cases are reported, the FDA should proceed with clinical trials that will lead to its specific approval of 3% Clioquinol Cream for both cancers. Then, for the first time, we could be on the verge of eliminating most patient deaths due to advanced pancreatic cancer and advanced liver cancer.

Acknowledgement

The LCC and RBF cited reports were funded, in part, by NIH grant CA79903.

References

1. Cancer Connect.
2. American Cancer Society.
3. NCI: Cancer Stat Facts: Liver and Intrahepatic Bile Duct Cancer.
4. NCI: Cancer Stat Facts: Pancreatic Cancer.
5. Costello LC, Franklin RB. The status of zinc in the development of hepatocellular cancer: an important, but neglected, clinically established relationship, Cancer Biol Ther, 2014; 4(15): pp.353-360.
6. Kew MC, Mallett RC. Hepatic zinc concentrations in primary cancer of the liver, Br J Cancer, 1974; 29(1): pp 80-83.
7. Costello LC, Levy BA, Desouki MM, Zou J, Bagasra O, Johnson LA, et al. Decreased zinc and downregulation of ZIP3 zinc uptake transporter in the development of pancreatic adenocarcinoma, Cancer biology & therapy, 2011; 12(4): pp 297–303.
8. Costello LC, Franklin RB, Yu GW. A Novel Patient Case Report to Show the Successful Termination of Untreatable Androgen-independent Prostate Cancer: Treatment with Cabergoline (Dopamine agonist), Mathews J Case Rep, 2019; 4(42): pp1-4.