Brief Report
Volume 9:4, 2023

Archives of Surgical Oncology

ISSN: 2471-2671 Open Access

Cabozantinib's Therapeutic Potential in Scirrhous Gastric Cancer

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Introduction

Gastric cancer remains a significant global health challenge, with scirrhous gastric cancer representing one of its aggressive and challenging subtypes. This variant is associated with a high propensity for peritoneal carcinomatosis and ascites formation, contributing to its poor prognosis. Among the various factors influencing its progression, Hepatocyte Growth Factor (HGF) emerges as a key player in stimulating the proliferation of scirrhous cancer cells. Scirrhous gastric cancer is a histological subtype characterized by the abundant fibrous stroma that engulfs malignant cells, leading to dense and diffuse tumor growth within the stomach wall. This unique microenvironment poses challenges in terms of diagnosis, treatment and prognosis. One of the most devastating complications associated with scirrhous gastric cancer is peritoneal carcinomatosis, where cancer cells spread to the peritoneum, the membrane lining the abdominal cavity.

Description

This process often leads to the accumulation of ascites, an abnormal fluid buildup, exacerbating patient discomfort and deteriorating overall health. HGF, a potent cytokine produced by various cells in the body, plays a crucial role in tissue repair, cell migration and angiogenesis. In the context of cancer, HGF has gained attention for its role in promoting tumor growth, invasion and metastasis. In scirrhous gastric cancer, HGF's impact is particularly notable. It serves as a growth factor for cancer cells, stimulating their proliferation and rendering them more invasive. HGF does this by binding to its receptor, the Met proto-oncogene receptor (MET), triggering a cascade of events that enhance cancer cell survival and metastatic potential [1].

The relationship between HGF and ascites formation in scirrhous gastric cancer involves several interconnected mechanisms. As scirrhous gastric cancer cells infiltrate the peritoneum, they trigger an inflammatory response that contributes to increased vascular permeability. This, coupled with the tumor cells' pro-angiogenic properties, leads to the formation of new blood vessels, a process known as angiogenesis. HGF's ability to stimulate angiogenesis further exacerbates ascites accumulation, as the increased vessel density facilitates fluid leakage into the peritoneal cavity. Given HGF's pivotal role in promoting scirrhous gastric cancer progression, therapeutic interventions targeting the HGF-MET pathway have gained attention [2].

Cabozantinib, a dual inhibitor of both MET and VEGFR2 (a receptor for vascular endothelial growth factor or VEGF), has shown promise in preclinical studies. By inhibiting these pathways, cabozantinib suppresses HGF-induced proliferation of scirrhous cancer cells and VEGF-driven angiogenesis. Notably, cabozantinib's effectiveness extends to reducing ascites formation and extending survival in murine models of scirrhous gastric cancer. Scirrhous gastric cancer's association with peritoneal carcinomatosis and ascites poses substantial challenges for patients and clinicians alike. The role of Hepatocyte Growth Factor (HGF) in stimulating cancer cell proliferation and angiogenesis within the peritoneum highlights its potential as a therapeutic target [3].

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Received: 29 July, 2023, Manuscript No. aso-23-110993; **Editor assigned:** 01 August, 2023, PreQC No. P-110993; **Reviewed:** 17 August, 2023, QC No. Q-110993; **Revised:** 22 August, 2023, Manuscript No. R-110993; **Published:** 29 August, 2023, DOI: 10.37421/2471-2671.2023.9.60

The emergence of agents like cabozantinib, which inhibit HGF-related pathways and mitigate the development of peritoneal carcinomatosis and ascites, offers a glimmer of hope for improving outcomes in patients with this aggressive form of gastric cancer. Further research into HGF's intricate interactions and the therapeutic potential of targeted agents is crucial to advancing our understanding and management of scirrhous gastric cancer. The field of cancer therapeutics is continuously evolving, with researchers and clinicians exploring innovative approaches to combat the complexities of tumor progression. One such advancement is the emergence of cabozantinib, a remarkable dual inhibitor targeting the MET and VEGFR2 signaling pathways. With its potential to hinder not only cancer cell proliferation but also pathological processes like angiogenesis and ascites formation, cabozantinib is proving to be a potent weapon in the battle against cancer [4].

Cabozantinib, a multi-targeted tyrosine kinase inhibitor, is specifically designed to simultaneously block the activity of two crucial signaling pathways: the MET receptor tyrosine kinase and Vascular Endothelial Growth Factor Receptor 2 (VEGFR2). The MET pathway is known to play a vital role in cancer progression by promoting cell survival, proliferation and invasion. On the other hand, VEGFR2 is a key player in angiogenesis, the process by which new blood vessels form to nourish growing tumors. In addition to targeting the MET and VEGFR2 pathways, cabozantinib exhibits a fascinating ability to counteract the effects of Hepatocyte Growth Factor (HGF) and Vascular Endothelial Growth Factor (VEGF) on cellular proliferation. Specifically, cabozantinib demonstrates the potential to inhibit HGF- and VEGF-enhanced proliferation of Human Umbilical Vein Endothelial Cells (HUVECs). By doing so, cabozantinib interferes with the intricate molecular signals that sustain cancer cell growth and angiogenesis, offering a unique therapeutic edge.

One of the most challenging consequences of advanced cancer is the development of ascites – the accumulation of fluid in the abdominal cavity. This fluid buildup not only leads to discomfort and reduced quality of life but also fuels tumor progression by fostering a conducive microenvironment for cancer cells. In a groundbreaking discovery, cabozantinib has demonstrated its ability to inhibit ascites formation. By targeting the MET and VEGFR2 pathways, cabozantinib intervenes in the intricate network of signals that trigger fluid accumulation, offering hope to patients grappling with this distressing condition. The effectiveness of a therapeutic agent is often assessed in preclinical models before it enters clinical trials. In this context, cabozantinib's potential has been highlighted in mouse models injected with NUGC4, a gastric cancer cell line.

Notably, cabozantinib's administration led to prolonged survival in these mice. This outcome underscores the compound's ability to impact tumor growth and metastasis, suggesting its promise as a potential therapy for cancer patients. The remarkable attributes of cabozantinib, including its dual inhibition of the MET and VEGFR2 pathways, inhibition of HGF- and VEGF-enhanced proliferation and suppression of ascites formation, offer a tantalizing glimpse into the future of cancer therapy. As researchers delve deeper into the intricate mechanisms underlying these effects, there is growing optimism about cabozantinib's potential as a game-changing treatment option [5].

Conclusion

Clinical trials and ongoing studies will likely shed more light on its safety and efficacy across various cancer types, paving the way for a new era in personalized and targeted cancer treatment. Cabozantinib's unique ability to simultaneously inhibit the MET and VEGFR2 signaling pathways, coupled with its capacity to counteract the proliferation-enhancing effects of HGF and VEGF, has positioned it as a beacon of hope in cancer therapy. Its potential to thwart ascites formation and extend survival in experimental models further accentuates its significance. As researchers continue to explore and harness its capabilities, cabozantinib holds the promise of transforming the landscape of cancer treatment, offering renewed optimism for patients and clinicians alike.

Acknowledgement

None.

Conflict of Interest

None.

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How to cite this article: Blanco, Gerardo. "Cabozantinib's Therapeutic Potential in Scirrhous Gastric Cancer." *Arch Surg Oncol* 9 (2023): 60.