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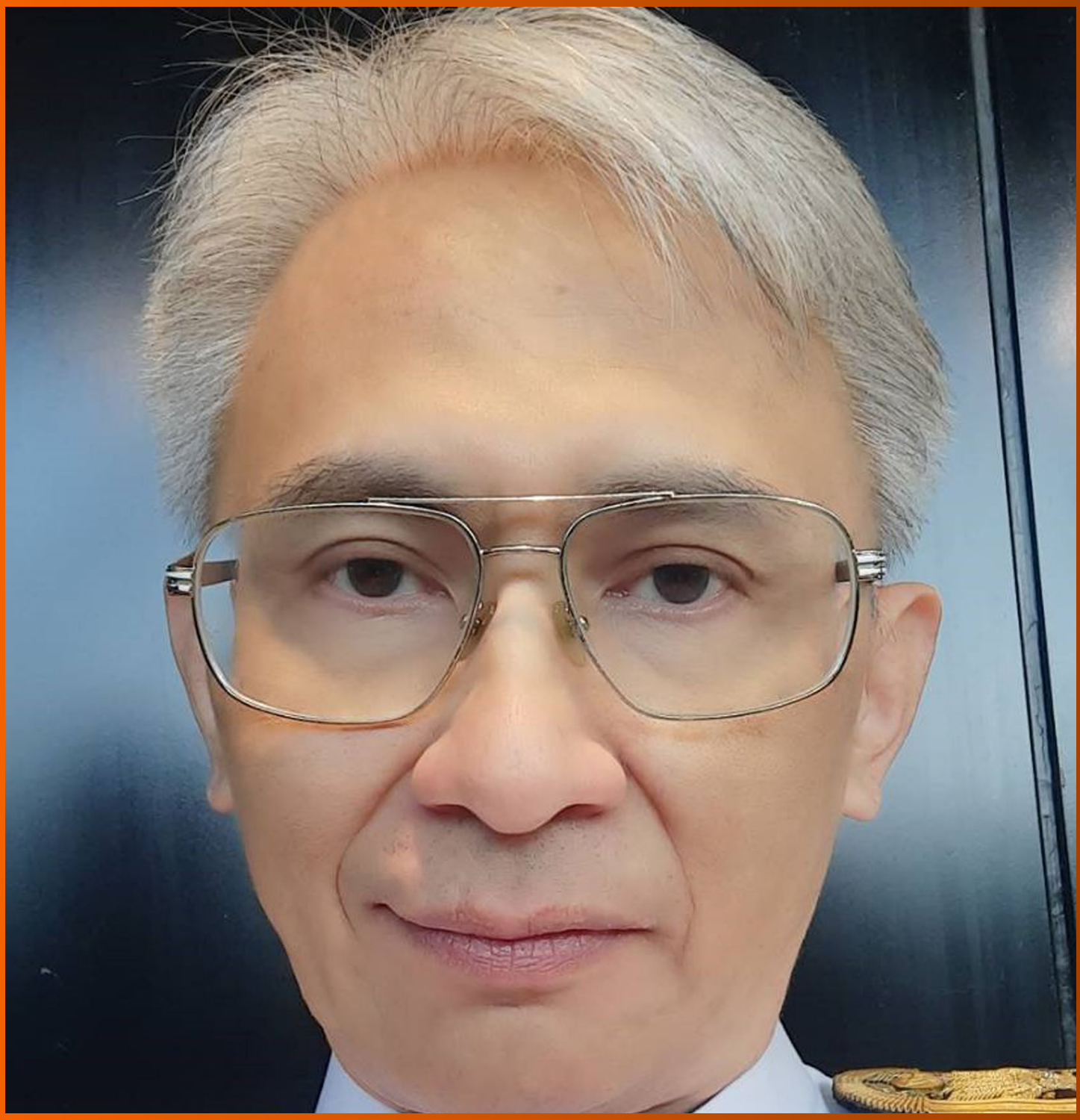

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EDITORIAL

Erdafitinib and checkpoint inhibitors for first-line and second-line immunotherapy of hepatic, gastrointestinal, and urinary bladder carcinomas: Recent concept

Mohamed Wishahi

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Abstract

Cancer immunotherapy is administered for first-line, second-line, neoadjuvant, or adjuvant treatment of advanced, metastatic, and recurrent cancer in the liver, gastrointestinal tract, and genitourinary tract, and other solid tumors. Erdafitinib is a fibroblast growth factor receptor (FGFR) inhibitor, and it is an adenosine triphosphate competitive inhibitor of FGFR1, FGFR2, FGFR3, and FGFR4. Immune checkpoint inhibitors are monoclonal antibodies that block programmed cell death protein 1 (PD-1) and its ligand that exert intrinsic antitumor mechanisms. The promising results of first-line treatment of advanced and metastatic urothelial carcinoma with PD-1 blockades with single or combined agents, indicate a new concept in the treatment of advanced, metastatic, and recurrent hepatic and gastrointestinal carcinomas. Cancer immunotherapy as first-line treatment will improve overall survival and provide better quality of life. Debate is arising as to whether to apply the cancer immunotherapy as first-line treatment in invasive carcinomas, or as second-line treatment in recurrent or metastatic carcinoma following the standard chemotherapy. The literature in the field is not definite, and so far, there has been no consensus on the best approach in this situation. At present, as it is described in this editorial, the decision is applied on a case-by-case basis.

Key Words: Programmed cell death protein-ligand 1; Erdafitinib; Liver cancer; Fibroblast growth factor receptor inhibitors; Checkpoint inhibitors; Bladder cancer; Metastases

Core Tip: The promising results of first-line treatment of advanced and metastatic urothelial carcinoma with programmed cell death protein 1 blockades with single or combined agents, indicate a new concept in the treatment of advanced, metastatic, and recurrent hepatic and gastrointestinal carcinomas. Cancer immunotherapy as a first-line treatment will improve overall survival and quality of life. At present, cancer immunotherapy as first-line treatment in invasive carcinomas or as second-line treatment in recurrent or metastatic carcinoma following the standard chemotherapy is applied on a case-by-case basis.

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INTRODUCTION

Recently, critical studies were published on cancer immunotherapy, and these publications addressed recurrent hepatocellular carcinoma (HCC)[1], esophageal squamous cell carcinoma[2], small bowel adenocarcinoma[3], cholangiocarcinomas[4], urothelial carcinomas[4-6], gastric carcinoma[7], colorectal cancer[8], and other solid tumors[5]. Cancer immunotherapy is administered for first-line, second-line, neoadjuvant, or adjuvant treatment of advanced, recurrent, or metastatic carcinoma in the liver, oesophagus, small bowel, colon, and urinary bladder, and other solid tumors[1-6]. This article will address the recently approved two immunotherapeutic drugs for the treatment of advanced, metastatic, and recurrent solid tumors.

ERDAFITINIB

Erdafitinib is a fibroblast growth factor receptor (FGFR) inhibitor, and it is an adenosine triphosphate (ATP) competitive inhibitor of FGFR1, FGFR2, FGFR3, and FGFR4. The United States Food and Drug Administration (FDA) has approved erdafitinib for the treatment of advanced and metastatic urothelial carcinoma in patients ineligible for standard chemotherapy, or refractory to platinum-containing chemotherapy. Erdafitinib has satisfactory clinical activity for metastatic urothelial carcinoma and other solid tumors. Erdafitinib toxicity is acceptable and it has been approved for initial treatment of advanced and metastatic urothelial carcinoma[4-6]. Erdafitinib administration resulted in prolonged progression-free survival. Approved FGFR inhibitors include erdafitinib, pemigatinib, and futibatinib[9]. Erdafitinib is an ATP competitive inhibitor of FGFR1-4. It inhibits FGFR kinase autophosphorylation, thus decreasing the downstream signaling. Normally, FGFR1-4 are bound by fibroblast growth factors to initiate the regulatory effects, which play a crucial role in angiogenesis and damage repair processes[7,8]. When erdafitinib was administered in recurrent HCC therapy, it resulted in increased overall survival (OS)[10]. Erdafitinib has been used in anticancer therapy for cholangiocarcinomas and urothelial carcinomas, and it is also recommended for the treatment of esophageal squamous cell carcinoma and small bowel adenocarcinoma[1-3].

IMMUNE CHECKPOINT INHIBITORS

Immune checkpoint inhibitors (ICIs) are monoclonal antibodies that block programmed cell death protein 1 (PD-1) and its ligand that exert intrinsic antitumor mechanisms[11]. These ICIs are at present the therapeutic option for different cancers and are becoming the standard anticancer therapy for several types of solid malignancies[3,7,8,12]. Recent advances in treatment with ICIs includes treatment of naive patients with locally advanced, or metastatic urothelial carcinoma of the bladder, especially for patients who are ineligible for standard chemotherapy, or refractory to platinum-containing chemotherapy.

Pembrolizumab and nivolumab are both monoclonal antibodies that target the PD-1 receptor on T cells and have been approved for the treatment of advanced HCC. Pembrolizumab has demonstrated consistent efficacy compared with nivolumab. Patients with advanced HCC treated with pembrolizumab had improved OS compared to those treated with placebo. The median OS was 14.6 months in the pembrolizumab group compared to 13.0 months in the placebo group [13].

Nivolumab is one of the ICIs that has shown efficacy in urothelial carcinoma treatment. Nivolumab was initially approved by the FDA for the treatment of metastatic melanoma, metastatic non-small cell lung cancer, advanced renal cell carcinoma, and locally advanced or metastatic urothelial carcinoma. Nivolumab was also approved by the FDA for use in the adjuvant therapy of patients with urothelial tumors who had been treated with radical surgery but are at considerable risk of recurrence after surgery[6].

Nivolumab is a human anti-PD-1 IgG4 monoclonal antibody, and it enhances the native immune defenses. ICIs can restore T-cell activity, which is the sole element for fighting against cancer cells. T cells have an important role in mediating the effects of various immune-related cytokines that assist CD8+ T cells in the elimination of cancer cells[11,12].

CONCLUSION

The promising results of first-line treatment of urothelial carcinoma with cancer immunotherapy indicate a new concept in the treatment of advanced, metastatic, and recurrent cancer in the hepatic, gastrointestinal tract, and genitourinary tract. Cancer immunotherapy as first-line treatment will improve overall survival and provide better quality of life. This will pave the way to consider first-line treatment of gastrointestinal and hepatic cancer with immunotherapy rather than to be applied in metastatic and recurrent disease.

Should we follow the patients with cancer to develop metastasis or recurrence and treat them with cancer immunotherapy, or, start the treatment as a first-line treatment?

The literature in the field is not definite. There is evidence that first-line immunotherapy has a promising result, but it has its side effects and toxicity. Besides, the costs of cancer immunotherapy are much higher compared to those of the standard chemotherapy.

FOOTNOTES

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