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WORD COUNT 1038
TIME SUBMITTED 13-MAR-2024 09:34AM
PAPER ID 107523047

Name of Journal: *World Journal of Hepatology*
Manuscript NO: 90058
Manuscript Type: EDITORIAL

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

Wishahi M. Erdafitinib and PD-L1, PD-L2 blockades

Mohamed Wishahi

Abstract

Cancer immunotherapy is administered for first-line treatment, second-line treatment, neoadjuvant, or adjuvant for treatment of treatment of advanced, metastatic, and recurrent cancer in the liver, gastrointestinal tract, genitourinary tract, and solid tumors. Erdafitinib is a fibroblast growth factor receptor (FGFR) inhibitor, it is an adenosine Tri-4 phosphate competitive inhibitor of FGFR1, FGFR2, FGFR3, 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 carcinomas, and gastrointestinal carcinomas. Cancer immunotherapy as first- line treatment will improve overall survival and better quality of life. Debate is arising whether to apply the cancer immunotherapy as first- line treatment in invasive carcinomas, or to be used as second-line in recurrent or metastatic carcinoma following the standard chemotherapy. The literature in the field is not definite, so far, there is no consensus on the best approach in this situation. At present, as it is described in this editorial, the decision is applied case-by-case.

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

Wishahi M. Erdafitinib, and checkpoint inhibitors for first-line and second-line immunotherapy for hepatic, gastrointestinal, and urinary bladder carcinomas: Recent concept. *World J Hepatol* 2024; In press

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 carcinomas, and gastrointestinal carcinomas. Cancer immunotherapy as a first-line treatment will improve overall survival and quality of life. As for applying the cancer immunotherapy as first- line treatment in invasive carcinomas, or as second-line in recurrent or metastatic carcinoma following the standard chemotherapy is applied case-by-case.

INTRODUCTION

Recently, critical studies were published on cancer immunotherapy, 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 treatment, second-line treatment, neoadjuvant, or adjuvant for treatment of advanced, recurrent, or metastatic carcinoma in the liver, oesophagus, small bowel, colon, urinary bladder, and solid tumors[1-6]. This research addressed the recently approved two immunotherapeutic drugs for treatment of advanced, metastatic, and recurrent solid tumors.

ERDAFITINIB

Erdafitinib is a fibroblast growth factor receptor (FGFR) inhibitor, it is an adenosine Tri-4 phosphate (ATP)-competitive inhibitor of FGFR1, FGFR2, FGFR3, FGFR4. Food and drug administration (FDA) approval erdafitinib for advanced and metastatic urothelial carcinoma in patient's 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 is 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 that results in decreasing the downstream signaling. Normally FGFR1-4 binds to the fibroblast growth factors to initiate the regulatory effects of tyrosine kinase, which plays a crucial role in angiogenesis and damage repair processes[7,8]. was administered in recurrent HCC therapy which resulted in increased overall survival (OS)[1]. Erdafitinib targets anticancer therapy in cholangiocarcinomas and urothelial carcinomas, it is recommended for 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[12]. These ICIs are at present the therapeutic option for different cancers and are becoming the standard anticancer therapy for several types of solid malignancies[3,7,8,11]. Recent advances in treatment with ICIs includes treatment of naive patients with locally advanced, or metastatic urothelial carcinoma of the bladder, special indication is 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. OS in patients with advanced HCC treated with pembrolizumab had improved OS compared to 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 initially the FDA approval for metastatic melanoma, metastatic non-small cell lung cancer, advanced renal cell carcinoma, locally advanced or metastatic urothelial carcinoma. Nivolumab has the FDA approved for use in the adjuvant therapy for patients with urothelial tumors treated with radical surgery who are at considerable risk of recurrence after surgery[6].

Nivolumab is a human anti-PD-1 IgG4 monoclonal antibody, it enhances the native immune defenses. ICIs can restore T-cell activity, which is the sole element for competing cancer cells. T-cell has an important role in 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 better quality of life. quality of life 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.

Do we follow-up the patients with cancer to develop metastasis or recurrence, and then we treat him with cancer immunotherapy, or, to 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 the standard chemotherapy.

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