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Introduction

Hepatocellular carcinoma is the h most common cancer in men and eighth in women worldwide, resulting in at least 500,000 deaths per year. e burden of HepatoCellular Carcinoma (HCC) has been increasing in Egypt with a doubling in the incidence rate in the past 10 years. is has been attributed to several biologi

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the rst to show signi cant impact on survival and disease progression, and is widely accepted as a standard rst-line systemic therapy [4].

Due to nancial cost of sorafenib, and need to improve response and survival, the need to search for other non-hepatotoxic regimens of systemic therapy for HCC is investigated. Results obtained in phase II studies with di erent regimens using new cytotoxic drugs have not been very impressive. us, systemic chemotherapy cannot be considered as the standard of care for HCC patients. is situation could be related to a combination of poor e cacy and increased toxicity. Obviously the underlying liver cirrhosis increases the risk of severe adverse events as many chemotherapeutic drugs are metabolized or eliminated via the liver. Moreover severe complications are certainly more likely if a cytotoxicity-related side e ect occurs on a cirrhotic liver. Certain causes of the underlying cirrhosis, e.g. hepatitis B virus infection, may be reactivated a er chemotherapy-induced immunodepression, producing an additive toxic e ect [5].

Systemic chemotherapy likely lacks e cacy because of the frequently observed multidrug tumor resistance (P-glycoprotein overexpression, p53 gene mutations) [6,7].

Patients and Methods

Patients were eligible if they had:

1- Advanced stage HCC not amenable to curative treatment;

(ORR), de ned as the sum of complete and partial responses based on the RECIST system. Tumor responses were assessed by means of helic CT every 2 months (a er 4 cycles), or earlier in patients with suspected disease progression. Complete responses (CR) were de ned as complet disappearance of all assessable disease. Partial responses (PR) we de ned by a decrease of >30% in the sum of the largest dimensions of target lesions. Stable disease (SD) was de ned as a decrease of <30% an increase of <20% in measurable lesions. Progressive disease (PD was de ned as an increase of at least 20% in measurable lesions or th appearance of new malignant lesions. A second CT scan was performed

patients was 1.1, 5.0, and 7.3 months respectively, whereas duration of SD ranged from 2.2 to 20.5 months (median: 5.4 months). In the intention-to-treat group (N=50), the tumour control rate (PR and SD)

HCC patients given the ECF/ECC regimen obtained objective response rate 22%, with a disease control rate (objective response plus stable disease) of 52%. e median time to progression was 6 months, in addition, despite the fact that most tumors were huge, the reduction in tumor size was su cient to allow surgical resection in 2 patients having only one huge tumor. Toxicity was mild and most side e ects were manageable; one patient died suddenly between two courses. ese two regimens (ECF and ECC) are very similar in terms of response and toxicity since capecitabine is the oral form of 5FU [5]. Response rate is close to that obtained from gemcitabine/Carboplatin in this study.

In conclusion, Gemcitabine and Carboplatin is a safe and e ective combination in management of advanced hepatocellular carcinoma not candidate for surgical resection or other interventional measures with fair control rate and accepted toxicity pro le.

References

1. Anwar WA, Khaled HM, Amra HA, El-Nezami H, Loffredo CA (2008) Changing pattern of hepatocellular carcinoma (HCC) and its risk factors in Egypt: Possibilities for prevention. Mutat Res 659: 176-184.

2. El-Zayadi AR, Badran HM, Barakat EM, Attia Mel-D, Shawky S, et al. (2005) Hepatocellular carcinoma in Egypt: a single center study over a decade. World J Gastroenterol 11: 5193-5198.

3. Jelic S, Sotiropoulos GC; ESMO Guidelines Working Group (2010) Hepatocellular carcinoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 21: v59-v64.

4. Llovet JM, Ricci S, Mazzaferro V, Hilgard P, Gane E, et al. (2007) Randomized phase III trial of sorafenib vs placebo in patients with advanced hepatocellular carcinoma. J Proc Am Soc Clin Oncol 25: 1384-1390.

5. Edeline J, Raoul JL, Vauleon E, Guillygomac'h A, Boudjema K, et al. (2009) Systemic chemotherapy for hepatocellular carcinoma in non-cirrhotic liver: A retrospective study. World J Gastroenterol 15: 713-716.

6. Chan KT, Lung ML (2004) Mutant p53 expression enhances drug resistance in a hepatocellular carcinoma cell line. Cancer Chemother Pharmacol 53: 519-526.

7. Endo T, Yoshikawa M, Ebara M, Kato K, Sunaga M, et al. (2004) Immunohistochemical metallothionein expression in hepatocellular carcinoma: relation to tumor progression and chemoresistance to platinum agents. J Gastroenterol 39: 1196-1201.

8. Fleming TR (1982) One-sample multiple testing procedure for phase II clinical trials. Biometrics 38: 143-151.

9. Kim SJ, Seo HY, Choi JG, Sul HR, Sung HJ, et al. (2006) Phase II study with a combination of epirubicin, cisplatin, UFT, and leucovorin in advanced hepatocellular carcinoma. Cancer Chemother Pharmacol 57: 436-442.

10. Yeo W, Mok TS, Zee B, Leung TW, Lai PB, et al. (2005) A randomized phase III study of doxorubicin versus cisplatin/interferon alpha-2b/doxorubicin/ À X R U R X U D F L O 3 , $) F R P E L Q D W L R Q F K H P R W K H U D S \ carcinoma. J Natl Cancer Inst 97: 1532-1538.

11. Park SH, Lee Y, Han SH, Kwon SY, Kwon OS, et al. (2006) Systemic chemotherapy with doxorubicin, cisplatin and capecitabine for metastatic hepatocellular carcinoma. BMC Cancer 6: 3.

12. Boige V, Raoul JL, Pignon JP, Bouché O, Blanc JF, et al. (2007) Multicentre phase II trial of capecitabine plus oxaliplatin (XELOX) in patients with advanced hepatocellular carcinoma: FFCD 03-03 trial. Br J Cancer 97: 862-867.

13. Lombardi G, Zustovich F, Farinati F, Cillo U, Vitale A, et al. (2011) Pegylated liposomal doxorubicin and gemcitabine in patients with advanced hepatocellular carcinoma: results of a phase 2 study. Cancer 117: 125-133.