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Sorafenib and radiotherapy in hepatocellular carcinoma

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Σοραφενίμπη και ακτινοθεραπεία στο ηπατοκυτταρικό καρκίνωμα

Περίληψη στο τέλος του άρθρου

Key words: HCC, Hepatocellular carcinoma, Radiotherapy, Sorafenib

Liver cancer is the sixth most common cancer worldwide and ranks third in cancer-related deaths. The most common type of liver cancer is hepatocellular carcinoma (HCC). Liver transplantation is the first choice for HCC treatment, whereas chemotherapy and radiotherapy (RT) are among the other options. Sorafenib is the first drug to be approved by the Food and Drug Administration (FDA) for use in the treatment of HCC, showing signs of improved survival; sorafenib can prolong the life of the patient up to 6 months, after which resistance to the treatment occurs.[1–3]

Sorafenib (BAY 43-9006, Nexavar) is an oral multikinase inhibitor. Sorafenib exerts its effect by inhibiting multiple intracellular and cell surface kinases that are involved in tumor cell communication, angiogenesis and apoptosis.[1,2] While first-line treatment with sorafenib is considered the standard treatment for patients with advanced HCC, the results are still disappointing, because of the development of drug resistance.[3–5] In view of the fact that sorafenib causes serious side effects and does not alleviate the course of symptoms for some groups of patients, search has been made for additional supportive treatment, especially for patients with advanced cirrhosis. Other tyrosine kinase inhibitors that may offer hope are being investigated, but Phase III studies of these tyrosine kinase inhibitors failed to show an improvement in survival over sorafenib.[1–3] Given the early encouraging results of liver-assisted RT for patients with advanced HCC, there has been interest in its combination with sorafenib to improve survival by maximizing both local and remote disease control, but the reported results are contradictory.[4–9] Sorin and colleagues analyzed the efficacy particle RT as an alternative treatment in different stages of HCC. The patients were divided into three groups, with early, intermediate-stage and advanced-stage HCC. The median radiation dose was 72.6 GyE for proton beam and 45.0 GyE for carbon ray. Local control rates of 6 months, 1 year and 2 years of the target tumor were 91.9%, 86.3% and 84.8%, respectively. Overall survival rates of 1, 2 and 3 years were 83.0%, 65.6% and 55.1%, respectively. These results show that the local control rates after particle RT were high compared with sorafenib.[5] Brade and colleagues planned a Phase 1 study to determine the maximum tolerated dose of sorafenib given prior to, during and after stereotactic body radiation therapy (SBRT) with locally advanced HCC Child-Pugh class A, performance status 0–1, which is not suitable for standard local regional treatments. In this study, significant toxicity was observed in high-effective irradiated liver volume, and it was recommended that SBRT should not be applied with sorafenib.[4] Moore and colleagues reported that the combination of sorafenib and SBRT increased overall survival in advanced stage HCC.[7] Yoon and colleagues studied a group of patients with HCC receiving RT. The average follow-up was 48 months, and the median survival time was longer in the RT group combination. They suggested RT as a combined treatment modality in patients with HCC limited to liver, but not resectable.[9] In the meta-analysis of Wang and colleagues of patients with locally advanced HCC, those treated with selective internal radiotherapy showed similar efficacy, but less toxicity than those treated with sorafenib.[3]

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Sorafenib, as an oral multikinase inhibitor, is the first drug to be used in the treatment of HCC. Sorafenib can prolong the life of the patient up to 6 months, after which resistance to treatment is observed. Early results are encouraging of SBRT in combination with a sorafenib to improve survival, as both local and remote disease control are maximized.

In conclusion, the use of SBRT with sorafenib for the treatment of HCC is promising, but further randomized clinical trials are needed to better define the efficacy.

ΠΕΡΙΛΗΨΗ

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Η σοραφενίμπη (sorafenib), ως αναστολέας πολυκινάσης από του στόματος, είναι το πρώτο φάρμακο που χρησιμοποιείται στη θεραπεία του ηπατοκυτταρικού καρκινώματος (HCC). Το φάρμακο μπορεί να παρατείνει τη ζωή του ασθενούς έως 6 μήνες, λόγω αντίστασης στην περαιτέρω θεραπεία. Δεδομένων των πρώτων αποτελεσμάτων, η ενθάρρυνση του συνδυασμού στερεοτακτικής σωματικής ακτινοθεραπείας (SBRT) με σοραφενίμπη για τη βελτίωση της επιβίωσης μεγιστοποιεί τον έλεγχο της νόσου. Η χρήση της SBRT σε συνδυασμό με τη σοραφενίμπη για τη θεραπεία της HCC υπόσχεται πολλά, αλλά απαιτούνται πολλές τυχαιοποιημένες κλινικές δοκιμές για τον καλύτερο προσδιορισμό της αποτελεσματικότητας της θεραπείας.

Λέξεις ευρετηρίου: Ακτινοθεραπεία, HCC, Ηπατοκυττραικό καρκίνωμα, Σοραφενίμπη

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