Protocol

Topic

Comparison of two regimens of antiviral prophylaxis of hepatitis B for cancer patients with chemotherapy.

Scientific title

A prospective single-center, open-label, randomized study to compare the effectiveness of extended 6 versus 12 months tenofovir or entecarvir therapy between HBV patients with cancer after completion of immunosuppressive anticancer therapy

Study hypothesis

There might be difference of the effectiveness of extended 6 versus 12 months tenofovir or entecavir therapy between HBV patients with cancer after completion of immunosuppressive anticancer therapy

Background and study aims

Reactivation of hepatitis B virus, characterized by the reappearance or increase in serum HBV DNA and ALT level, is now a well-recognized complication in HBsAg-positive patients receiving chemotherapy or immunosuppressive therapy. The guidelines recommend that prophylaxis against HBV is recommended in the current guidelines as early as possible before the onset of immunosuppressive therapy in HBsAg-positive candidates. Entecavir (ETV) was approved in 2008 for treatment of chronic hepatitis B. It offers the potent antiviral efficacy and a higher resistance barrier. Tenofovir (TDF) also has a high anti-HBV suppressive effect, rendering 67% of HBeAg-positive and 90% of HBeAg-negative patients to have undetectable HBV DNA after one year of therapy. To date, there is no clinical trial using TDF or ETV in the prophylaxis and treatment of HBV reactivation for patients who undergo cytotoxic chemotherapy. Therefore, we aim to conduct a prospective single-center, open-label, randomized study to compare the effectiveness of extended 6 versus 12 months tenofovir or entecavir therapy between HBV patients with cancer after completion of immunosuppressive anticancer therapy.

Study design

A prospective single-center, open-label, randomized controlled study

Participants

Eligible patients over 20 years old were enrolled if they met the following criteria: (1)

Hepatitis B surface antigen (HBsAg) seropositive for > 6 months (2) cancer patients receiving chemotherapy. Exclusion criteria were as follows: (1) co-infection with hepatitis C virus (HCV), hepatitis D virus and/or human immunodeficiency virus (2) autoimmune or metabolic liver disease (3) alcohol dependence or drug abuse (4) use of any antiretroviral, and interferon within 1 year prior to the initiation of study.

Intervention

After screening, all qualified patients will be recruited and randomized to one of the following treatment groups in a 1:1 ratio. The randomization will be stratified by two strata, (1) baseline HBV DNA low (< 2000 IU/ml) or high (≥ 2000 IU/ml) before chemotherapy; (2) extended 6 or 12 months after completing chemotherapy. Patients received TDF 300mg or ETV 0.5mg once daily orally one week before chemotherapy and the duration of chemotherapy was assigned according to the randomization table. There were 4 treatment groups. They were (A) Patients with baseline HBV DNA < 2000 IU/ml who received consolidation of TDF or ETV for 6 months after completing chemotherapy; (B) patients with baseline HBV DNA < 2000 IU/ml who extended consolidation TDF or ETV to 12 months after completing chemotherapy; (C) patients with baseline HBV DNA ≥ 2000 IU/ml received consolidation of TDF or ETV for 6 months after completing chemotherapy; and (D) patients with baseline HBV DNA ≥ 2000 IU/ml received extended TDF or ETV to 12 months after completing chemotherapy.

Statistical plan and power Calculation

Demographic data and the events of primary and secondary end points were compared between groups. Continuous variables with normal distribution were compared using independent Student's *t* test. Continuous variables without normal distribution were compared using. Categorical variables were compared using chi-square or Fisher's exact test. Kaplan-Meier estimation was used to exam the time to occurrence of HBV relapse in patients after cessation of NA therapy. Log rank test and Holm-Sidak method were used to analyze the difference of relapse rate between the patients with different treatment groups. Univariate and multi-variate analysis using Cox regression model. Data was analyzed using the SPSS software (SPSS Inc., Chicago, IL, USA). All statistical tests were two-sided, and *P*-values <0.05 were consider significance.

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Possible benefits and risks of participating

Participants may benefit from the prolonged treatment after the completion of

chemotherapy.

Study period

January 2013 to December 2016

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Ethics approval

Ethics Committee of Chang Gung Memorial Hospital, 12/11/2012, (IRB No 101-2130A3)

ISRCTN registry

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