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Response to the consultation of the second draft WHO discussion paper

World Hepatitis Alliance welcomes the inclusion of hepatitis B immunization as a "best buy" for preventing liver cancer. In addition, we would also call for hepatitis B and C treatment to be included in this important document.

The evidence of the link of both chronic hepatitis B and C infection to liver cancer is well established:

- Hepatitis B and hepatitis C are the most common causes of liver cirrhosis and cancer. Together they are responsible for more than 70% of liver cancer cases and are recognised as cancer-preventable risk factors in Europe's Beating Cancer Plan and by the WHO[1,2,3].
- Chronic hepatitis B infection can be treated with effective and low-cost medicines, including oral antiviral agents. Treatment can slow the progression of cirrhosis, reduce the incidence of liver cancer and improve long-term survival.
- Hepatitis C can be cured through effective treatment. Without being linked to care, chronic hepatitis infection can lead to liver cirrhosis and an increased risk of developing liver cancer[4].
- According to the European Centre for Disease Prevention and Control (ECDC), "deaths attributed to hepatitis B virus (HBV) and hepatitis C virus (HCV) are estimated to account for around 55% of liver cancer deaths and 45% of all deaths due to cirrhosis and other chronic liver disease"[5].
- Models suggest that the elimination of viral hepatitis C alone would reduce the burden of liver cancer by more than 65%[6].

In addition to hepatitis B vaccination, hepatitis B and C treatment have been proven to be a cost-effective method to decrease liver cancer:

- Hepatitis C testing and treatment is a cost-saving method for preventing liver cancer[7].
- A meta-analysis of 5 studies including 1,267 chronic hepatitis B patients treated with Lamivudine compared with 1,022 untreated patients demonstrates that hepatocellular carcinoma (HCC) incidence is reduced by 78% (2.5% vs 11.7%, RR = 0.22; $P < 0.001$)[8,9].
- In an Asian study, entecavir-treated patients (with chronic hepatitis B) have a 63% reduction in the incidence of HCC at 5 years compared to those not treated (3.7% vs 13.7%; $P < 0.001$)[10].
- In 2018, an American study[11] showed that direct-acting antiviral agents (DAAs) therapy was associated with a lower risk of HCC as compared to untreated patients (HR = 0.84) and to interferon (IFN) based treatment (HR = 0.69). During the same year, another study found that sustained virologic response (SVR) after DAA treatment led to a lower incidence rate of HCC in patients with HCV-related cirrhosis over a follow-up of 14 months[12].
- Recently, a French prospective cohort study on 9,895 HCV-infected patients with a long-term follow-up (mean 33.4 mo) reported that after adjusting for several variables (including non-modifiable risk factors as age, sex, geographical origin, HCV genotype and modifiable ones as FIB score, alcohol consumption, diabetes, arterial hypertension, and model for end-stage liver disease score in patients with cirrhosis), DAAs exposure decreased all-cause mortality (adjusted HR = 0.48) and the risk of HCC development (adjusted HR = 0.66)[13].

In light of this strong and direct evidence, we call for hepatitis B and C treatment to be included in this important document.

Many thanks for your consideration.

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CEO

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