

Review Summary

NTP Executive Committee Working Group for the Report on Carcinogens (RG2)

Nomination: Hepatitis C Virus (HCV)

Date: July 22, 2002

Major issues discussed

Application of criteria

Exposure: Approximately 3 to 4 million individuals are infected with hepatitis C virus (HCV) in the United States. The major risk factor for HCV infection is illegal intravenous drug use.

Human studies: IARC classified HCV as a *known human carcinogen* in 1994 based on sufficient evidence in humans. Numerous cohort and case-control studies conducted in different geographical populations have demonstrated a causal relationship between HCV infection and hepatocellular carcinoma. A meta-analysis of 32 studies reported an ORs of 11.5 (95% CI=9.9 to 13.3). These studies show that the association between HCV and hepatocellular is independent of hepatitis B virus (HBV) and is unaltered after adjustment for nonviral risks factors for hepatocellular carcinoma. The meta-analysis also suggested a synergistic interaction between HBV and HCV coinfection on the risk of hepatocellular carcinoma. There is some evidence that HCV may increase the risk of B cell lymphoma but more studies are needed to confirm these findings.

Experimental animal studies: HCV has a limited host range and the chimpanzee and tree shrews are the only animals that are susceptible to HCV infection. Hepatocellular carcinoma has been reported in one chimpanzee infected with HCV for seven years but not in HCV-infected tree shrews. Hepatocellular carcinoma has also developed in some strains of transgenic mice expressing the HCV core protein or the complete HCV polyprotein.

Genotoxicity and mechanistic concerns: The mechanisms of carcinogenicity are unknown. HCV may cause cancer indirectly as a result of hepatic inflammation and regeneration association with chronic hepatitis or directly. There is some evidence that the HCV core protein participates in the carcinogenesis process.

Recommendation

Motion:

Recommend that HCV be listed as *known to be a human carcinogen*, based on overwhelming evidence from human studies that demonstrate a causal relationship between chronic HCV infection and hepatocellular carcinoma in humans.

Vote on the motion: 8 yes votes to 0 no votes.