"Newly diagnosed Hepatocellular Carcinoma in patients with advanced hepatitis C treated with DAAs: a prospective population study".

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Abstract

BACKGROUND & AIMS:

Direct-acting antiviral agents (DAAs) are safe and effective in patients with hepatitis C. Conflicting data were reported on the risk of Hepatocellular carcinoma (HCC) during/after therapy with DAAs. Aim of this study was to evaluate incidence of newly diagnosed hepatocellular carcinoma and associated risk factors in patients with advanced hepatitis C treated with DAAs.

METHODS:

The study is based on the NAVIGATORE platform, a prospectively recording database of all patients with hepatitis C receiving DAAs in Veneto region (Italy).

INCLUSION CRITERIA:

fibrosis stage ≥ F3.

EXCLUSION CRITERIA:

Child-Pugh C, liver transplantation before DAAs, history or presence of HCC, follow-up <4 weeks after starting DAAs RESULTS: 3917 of 4234 consecutive patients were included, with a mean follow-up of 536.2±197.6 days. Overall, HCC was diagnosed in 55 patients. During the first year, HCC incidence was 0.46% (95% CI: 0.12-1.17) in F3, 1.49% (1.03-2.08) in Child-Pugh-A and 3.61% (1.86-6.31) in Child-Pugh-B cirrhotics. In the second year HCC incidences were: 0%, 0.2%, and 0.69%, respectively. By multivariate analysis, HCC was significantly associated with an APRI≥2.5 (HR: 2.03, 95% CI: 1.14-3.61; p=0.016) and HBV (HR: 3.99, 1.24- 12.91; p=0.021). Failure to achieve SVR was strongly associated with development of HCC (HR: 9.09, 5.2-16.1; p=0.0001). 29% of the patients with HCC had an aggressive tumor, often seen in the early phase of treatment.

CONCLUSIONS:

These data, obtained in a large, prospective, population-based study, indicate that in patients with advanced hepatitis C receiving DAAs, the risk of "de novo" hepatocarcinoma during the first year is

not higher, and might be lower, than that of untreated patients, and further declines thereafter. Early hepatocarcinoma appearance may reflect pre-existing, microscopic, undetectable tumors.

LAY SUMMARY:

Hepatocellular carcinoma is one of the complications of Hepatitis C related cirrhosis. Therapy of patients with advanced hepatitis C with the new interferon-free direct-acting antiviral agents has been associated with improvement in liver function and survival, while more conflicting data have been reported regarding the risk of hepatocellular carcinoma. We report the results of a prospective population study on the incidence of newly diagnosed hepatocellular carcinoma in patients with advanced hepatitis C treated with direct-acting antiviral agents, clearly indicating that the residual HCC risk is reduced and decline progressively with time after a sustained virological response. Development of a liver tumor during/after therapy was associated with known risk cofactors and with virological failure.