93

AASLD Foundation Abstract Award recipient

Lipophilic Statins and Risk of Hepatocellular Carcinoma and Mortality: A Prospective, Nationwide Population with Chronic Viral Hepatitis

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Abstract Text

Background:

In the U.S. and Europe, the incidence of hepatocellular carcinoma (HCC) has tripled over the past thirty years, and rates of HCC mortality are rising more rapidly than for any other cancer. A body of epidemiological evidence now suggests that for patients with chronic hepatitis B virus (HBV) or hepatitis C virus (HCV), statins may improve clinical outcomes and reduce HCC risk. Recent experimental data further suggests that lipophilic statins (i.e. atorvastatin, simvastatin, fluvastatin and lovastatin) may prevent hepatocarcinogenesis more potently than hydrophilic statins (i.e. pravastatin, rosuvastatin). However, in humans, prospective data regarding the optimal statin type and dose for effective HCC prevention are limited.

Methods:

We conducted a nationwide, propensity score-matched cohort study of 16,668 patients with confirmed chronic HBV (n=3,906) or HCV (n=12,762) living in Sweden between 2005-2015, using prospectively-collected and updated data from validated, nationwide Swedish Registers. Using the Prescribed Drug Register, we defined lipophilic statin use or hydrophilic statin use as a filled prescription for ≥30 cumulative defined daily doses (cDDD) of the relevant statin type, and data were updated monthly over the study follow-up. All HCC cases and deaths were confirmed. Using Cox proportional hazard modeling with time-varying exposures and covariates, we estimated multivariable-adjusted subdistribution hazard ratios (aHRs) for HCC and all-cause mortality, accounting for competing risks.

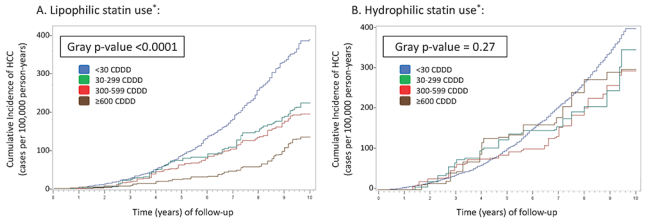
Results:

Over a median follow-up of 96 months, we identified 606 cases of incident HCC and 1,664 deaths. Significantly lower HCC risk was observed with lipophilic statin use, compared to non-use (aHR 0.56, 95% CI 0.33-0.80; number-needed-to-treat=23). This benefit appeared dose-related: compared to non-users, the aHRs for HCC were 0.78 (95% CI 0.51-1.09) for 30-299 cDDD, 0.57 (95% CI 0.50-0.65) for 300-599 cDDD, and 0.48 (95% CI 0.34-0.62) for ≥600 cDDD ($P_{trend\ among\ users}$ <0.0001). Lipophilic statin use was also associated with significantly lower risk of death (aHR 0.73, 95%CI 0.72-0.75), in a dose-dependent manner ($P_{trend\ among\ users}$<0.0001). In contrast, hydrophilic statin use was not associated with HCC risk reduction (aHR 1.01, 95%CI 0.81-1.88), or with a dose-dependent reduction in mortality ($P_{trend\ among\ users}$=0.52). Similarly, no significant association was found with incident HCC risk, when non-statin lipid-lowering medication users and non-users were compared (aHR 1.06, 95% CI 0.86-1.29).

Conclusion:

In this nationwide population with chronic viral hepatitis, use of lipophilic but not hydrophilic statins was associated with dose-dependent reductions in risk for incident HCC and all-cause mortality. Our findings support the potential incorporation of lipophilic statins into HCC primary prevention strategies.

Figure 1. Cumulative incidence of HCC according to cumulative defined daily dose (CDDD) of lipophilic statins (A) and hydrophilic statins (B) in the propensity score matched cohort (n=16,668), accounting for competing risk[1]



Abbreviations: HCC, hepatocellular carcinoma; cDDD, cumulative defined daily dose; Ref., Reference
*Statin use defined as a filled prescription for ≥ 30 cDDD of statin medications, over study observation period. Lipophilic statins included use of atorvastatin and/or simvastatin. Hydrophilic statins included use of rosuvastatin and/or pravastatin.
[1]Competing risks for HCC included death and liver transplantation

Disclosures

Soo Aleman – AbbVie: Speaking and Teaching; Gilead: Speaking and Teaching; MSD: Speaking and Teaching; BMS: Speaking and Teaching; AbbVie: Grant/Research Support; GIlead: Grant/Research Support

The following people have nothing to disclose: Tracey G Simon, Ann-Sofi Duberg, Hannes Hagström

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