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Clinical Trial: Hepatitis B Virus Genotype and a Combination of End-of-Treatment Biomarkers Predict Severe Flares After Nucleos(t)ide Analogue Cessation

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Abstract

Background: Nucleos(t)ide analogue (NUC) cessation can induce a functional cure in chronic hepatitis B virus (HBV) infections, but severe post-cessation virologic relapses (SVRel) and severe biochemical flares (SBF) frequently occur.

Aims: To identify predictive biomarkers for patients at highest risk for SVRel and SBF.

Methods: In the multicentre prospective COIN-B trial, start-of-treatment HBeAg-negative, long-term virologically suppressed patients without advanced fibrosis are followed up for 72 weeks after NUC cessation. We performed a predefined exploratory analysis of the associations between HBV genotype, or end-of-treatment (EOT) biomarkers (HBcrAg, HBV RNA, HBsAg, and anti-HBc IgG) and SVRel (HBV DNA > 5 log IU/mL) or SBF (ALT > 10× ULN) within 48 weeks post-cessation.

Results: Of 91 recruited patients, 85 completed 48 weeks of follow-up. SVRel and SBF occurred in 36 (42.4%) and 21 (24.7%) patients, respectively. Genotypes C, D, and E were associated with higher relapse and flare rates, whereas none of the 18 genotype A patients developed SBF. In multivariate analysis, SVRel was independently associated with detectable HBcrAg (aOR 3.93, p = 0.01), and SBF with non-A genotype (aOR 19.03, p = 0.018), detectable HBV RNA (aOR 7.84, p = 0.005), and lower anti-HBc IgG levels (aOR 0.31, p = 0.016). A risk stratification tool, the COBRA score, was developed incorporating HBcrAg, HBV RNA, and anti-HBc IgG. A score ≥ 2 identified patients at increased risk, with 80.0% sensitivity and 90.7% NPV for SBF.

Conclusions: HBV genotype and EOT biomarkers, including HBcrAg, HBV RNA, and anti-HBc IgG predict SVRel and SBF following NUC cessation. The COBRA score enables pragmatic, individualised risk stratification.

Trial registration: ClinicalTrials.gov identifier: NCT04779970, EudraCT: 2021-001003-32.

Keywords: antiviral agents; flares; hepatitis B virus; nucleosides; withholding treatment.

Related information

GEO Profiles
MedGen
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Full Text Sources

Ovid Technologies, Inc.

Medical

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Miscellaneous

NCI CPTAC Assay Portal