

Limited Sustained Remission After Nucleos(t)ide Analog Withdrawal: Results From a Large, Global, Multiethnic Cohort of Patients With Chronic Hepatitis B (RETRACT-B Study)

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Abstract

Introduction: Complete viral suppression with nucleos(t)ide analogs (NAs) has led to a profound reduction in hepatocellular carcinoma and mortality among patients with chronic hepatitis B. Finite therapy yields higher rates of functional cure; however, initial hepatitis B virus (HBV) DNA and alanine aminotransferase (ALT) elevations are almost certain after treatment interruption. We aimed to analyze off-treatment outcomes beyond 12 months after NA cessation.

Methods: Patients with well-suppressed chronic hepatitis B who were hepatitis B e antigen-negative at NA cessation and remained off treatment without hepatitis B surface antigen (HBsAg) loss at 12 months were included (n = 945). HBV DNA and ALT fluctuations were allowed within the first 12 months. We used Kaplan-Meier methods to analyze outcomes beyond 12 months. Sustained remission was defined as HBV DNA <2,000 IU/mL and ALT <2× upper limit of normal (ULN) and an ALT flare as ALT ≥5× ULN.

Results: Cumulative probability of sustained remission was 29.7%, virological relapse was 65.2% with a mean peak HBV DNA of 5.0 ± 1.5 log₁₀ IU/mL, an ALT flare was 15.6% with a median peak ALT × ULN of 8.3 (5.7–11.3), HBsAg loss was 9.9% and retreatment was 34.9% at 48 months after NA cessation. A single occurrence of virological relapse or an ALT flare within the first 12 months off-treatment were associated with significantly lower rates of sustained remission beyond 12 months.

Discussion: Despite allowing for HBV DNA and ALT fluctuations within the first 12 months off-treatment, most patients without HBsAg loss did not maintain a sustained response thereafter. The best candidates for NA withdrawal are patients with low HBsAg levels at NA cessation, and those without profound or recurrent virological and biochemical relapses in the first off-treatment year.

Σχόλιο: Πρόκειται για μία παγκόσμιας κατανομής πολυκεντρική μελέτη, σε 945 ασθενείς με αντιγόνο Ε αρνητική χρόνια ηπατίτιδα Β, στους οποίους διεκόπη η αντιική αγωγή. Στην πορεία της παρακολούθησης καταγράφηκαν μικρές διακυμάνσεις HBV DNA <2,000 IU/mL και ALT <2× ΑΦΤ. Ιολογική υποτροπή σημειώθηκε στο 65.2% των ασθενών, ενώ απώλεια του HBsAg στο 9.9% και επαναθεραπεία στο 34.9% στους 48 μήνες από την διακοπή του αντιικού παράγοντα.

Η μελέτη υποστηρίζει ότι οι καλύτεροι υποψήφιοι για διακοπή της αγωγής είναι οι ασθενείς με χαμηλά επίπεδα HBsAg κατά την φάση αυτή, καθώς και όσοι δεν εκδηλώνουν σημαντικές διακυμάνσεις σε ιολογικό και βιοχημικό επίπεδο κατά το πρώτο έτος χωρίς θεραπεία.

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