

## VHPB Technical meeting

# **Risks and Benefits of Discontinuation of Nucleos(t)ide Analogue Treatment: A Treatment Concept for Patients With HBeAg-Negative Chronic Hepatitis B**

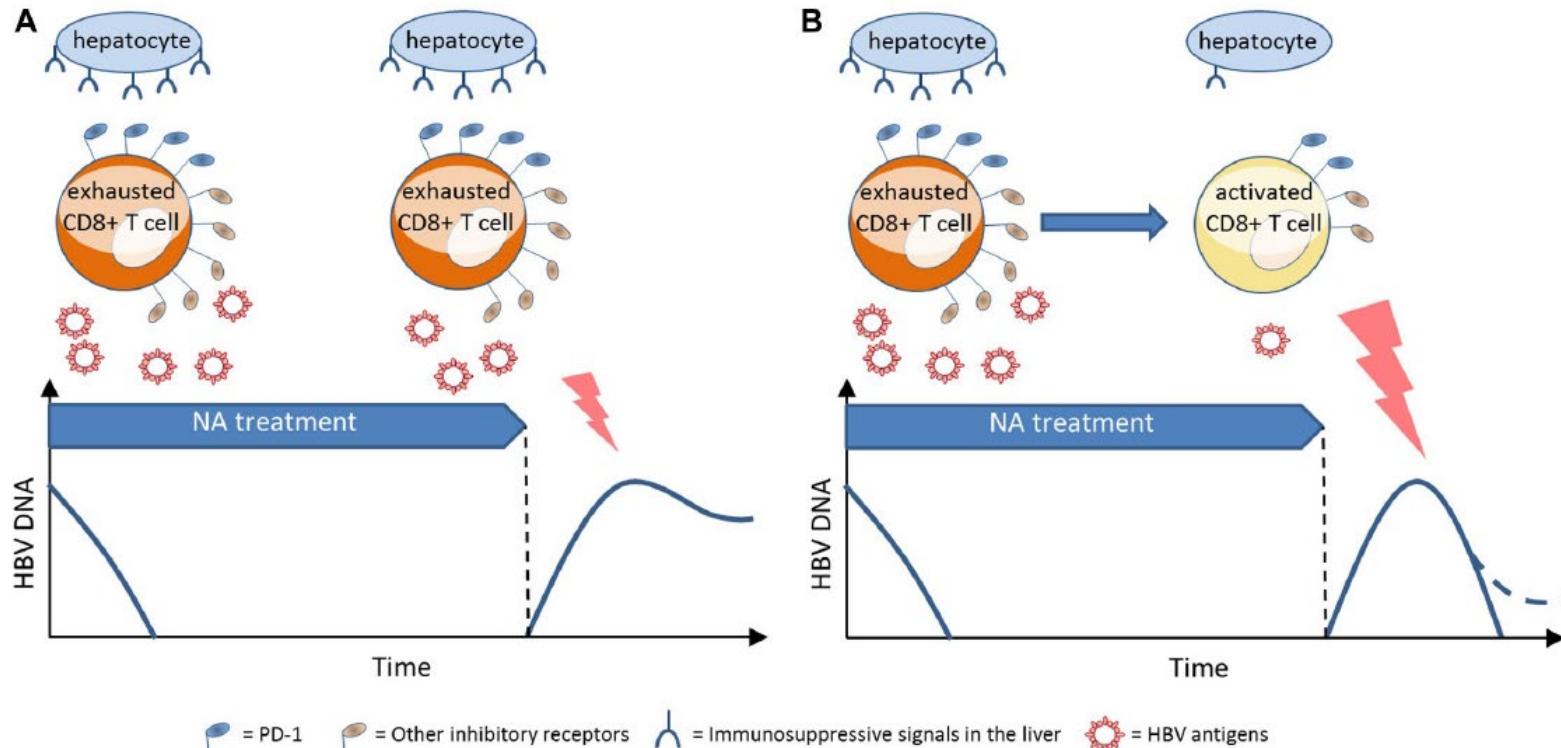
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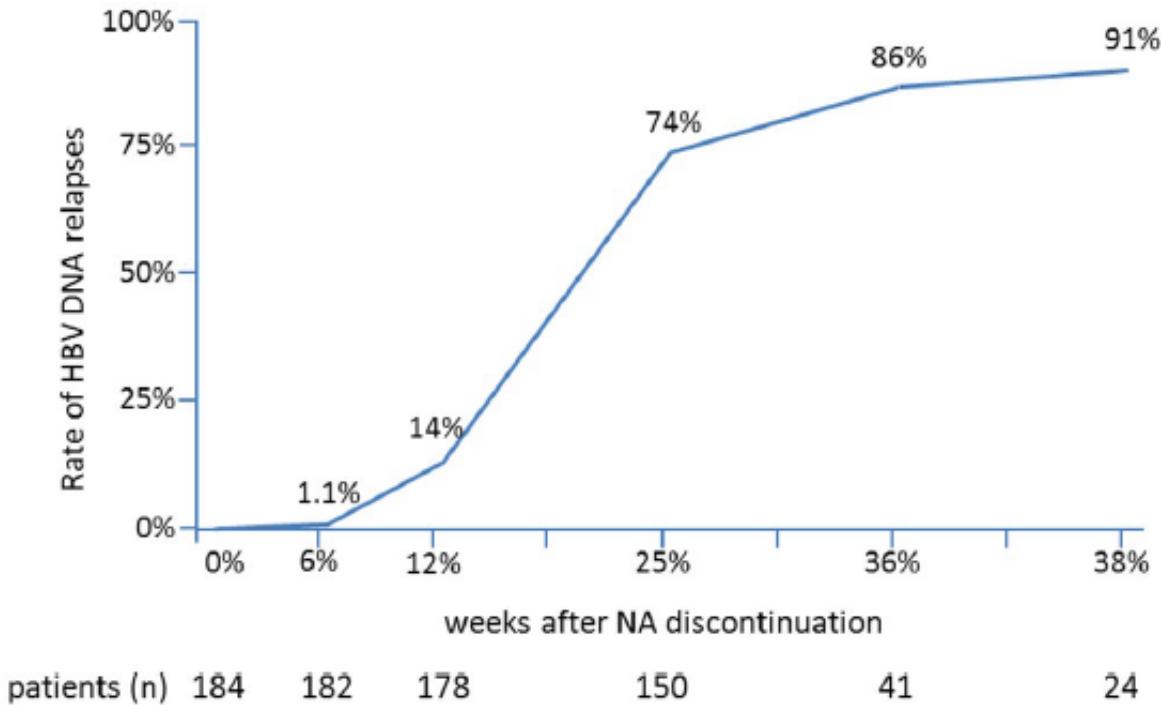
# Risks and Benefits of Discontinuation of Nucleos(t)ide Analogue Treatment: A Treatment Concept for Patients With HBeAg-Negative Chronic Hepatitis B

Florian van Bömmel  and Thomas Berg

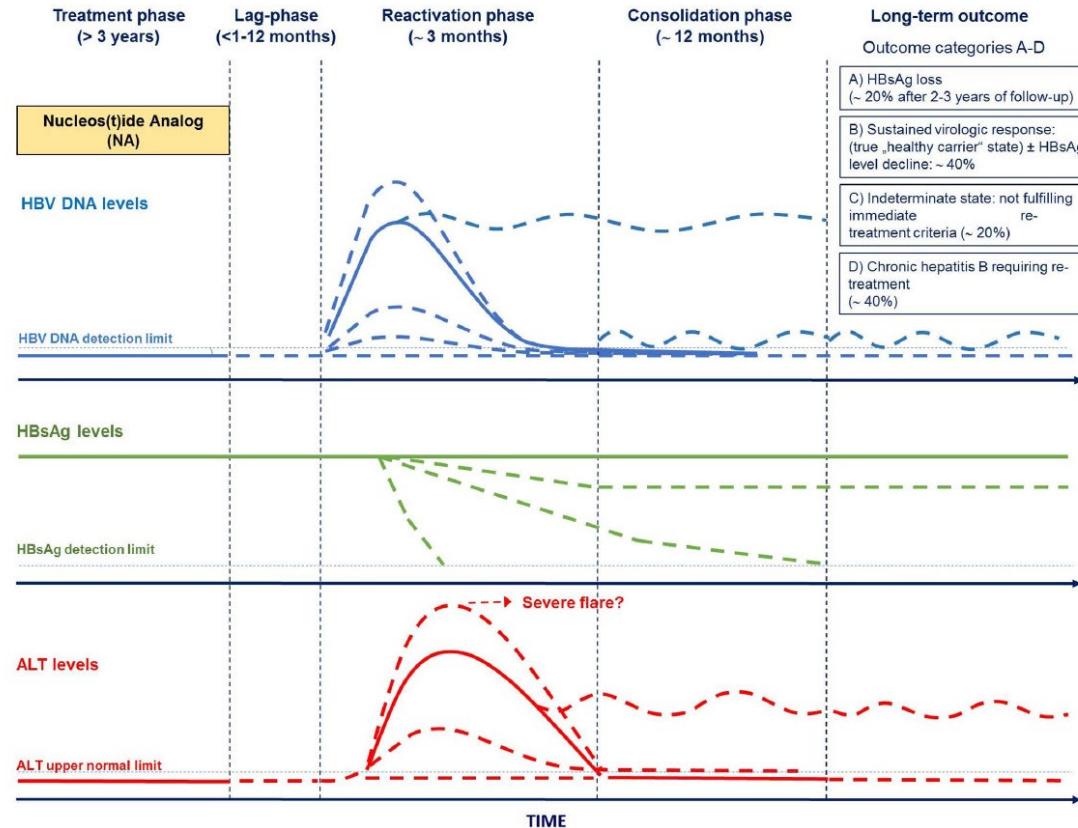
# The Concept of NA Withdrawal as an Approach to Achieve a Functional Cure



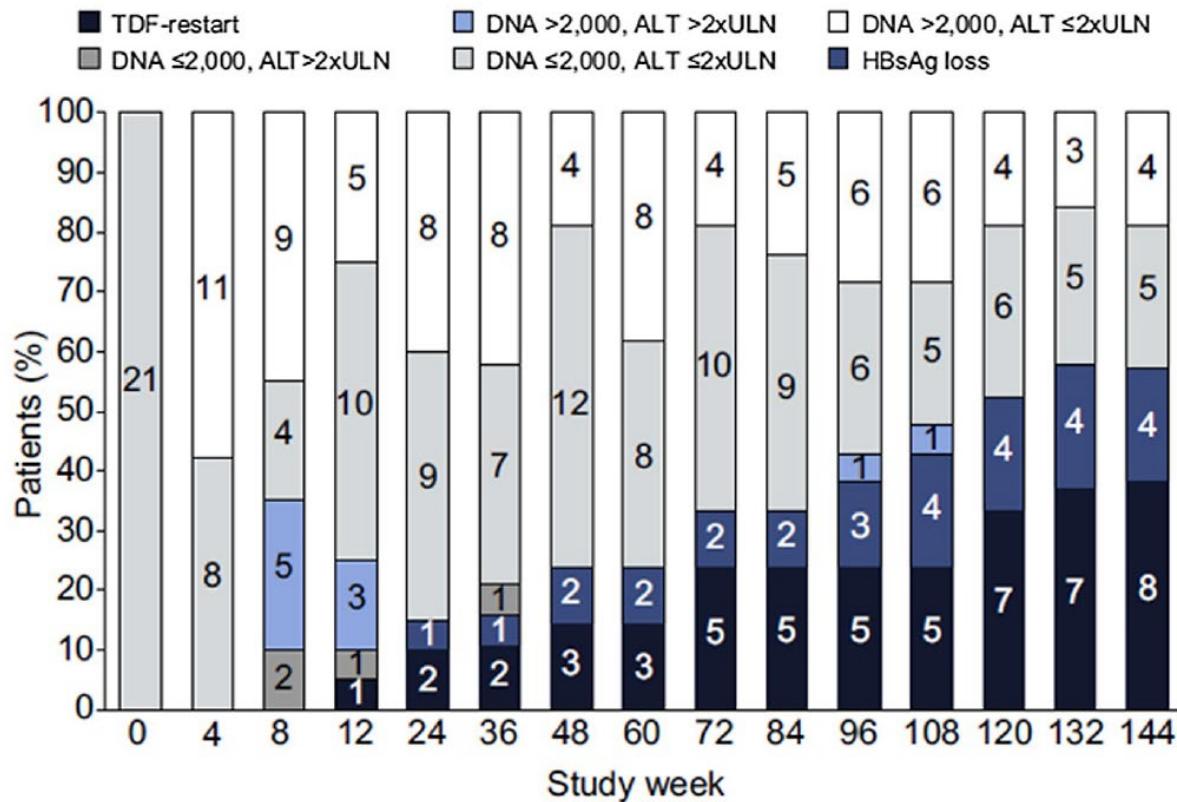
# Frequency of HBV DNA relapses



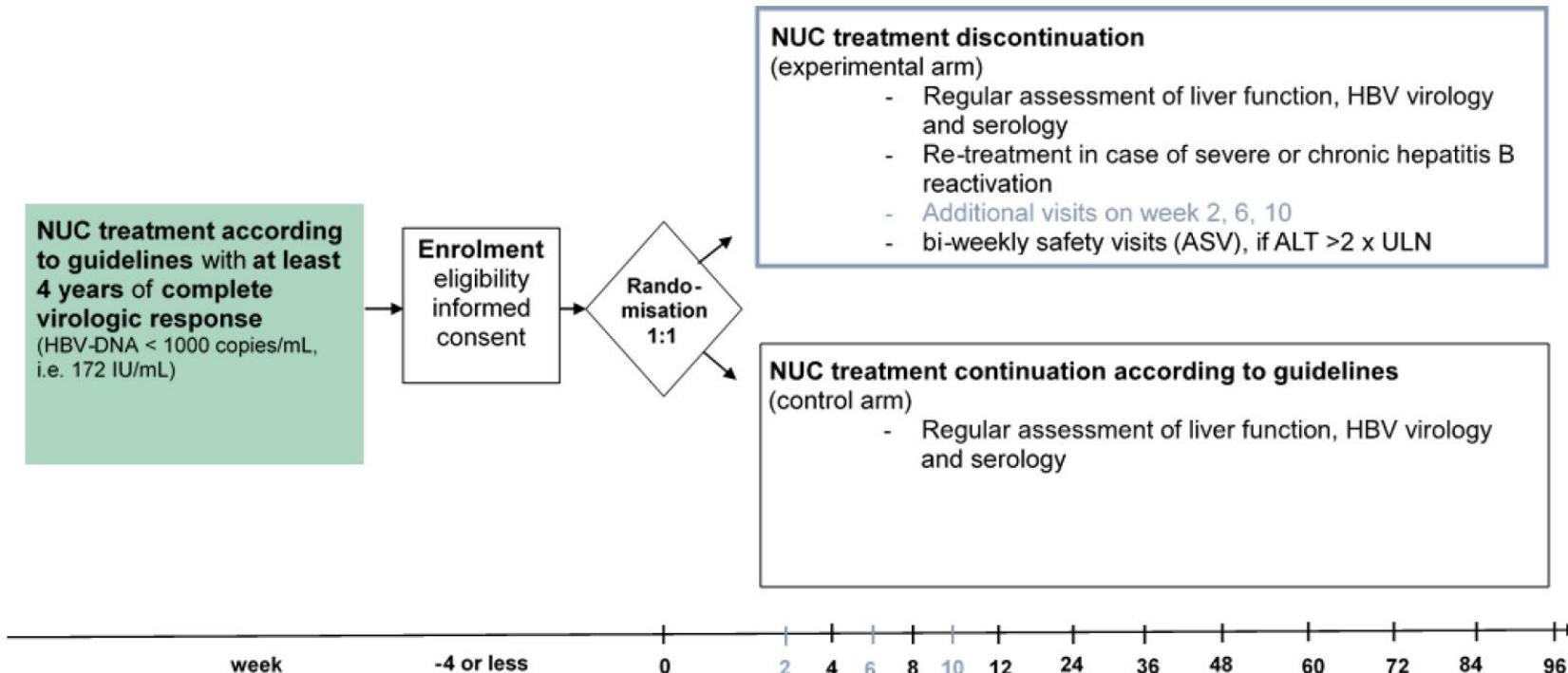
# Response to NA Discontinuation Runs Through Different Phases



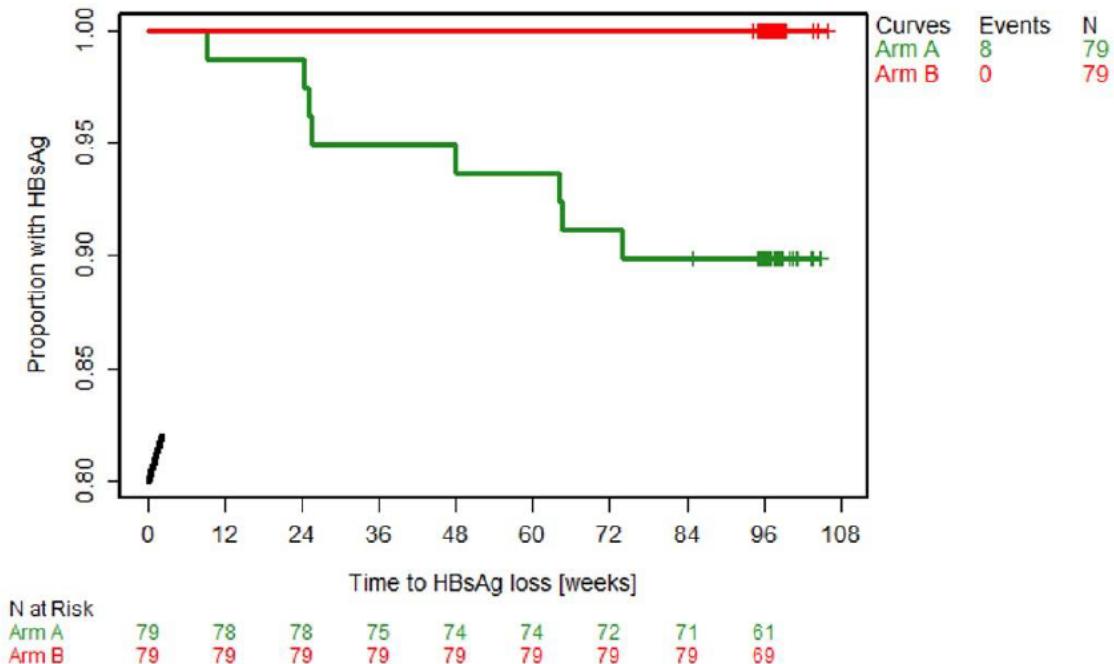
# FINITE-study: endpoints



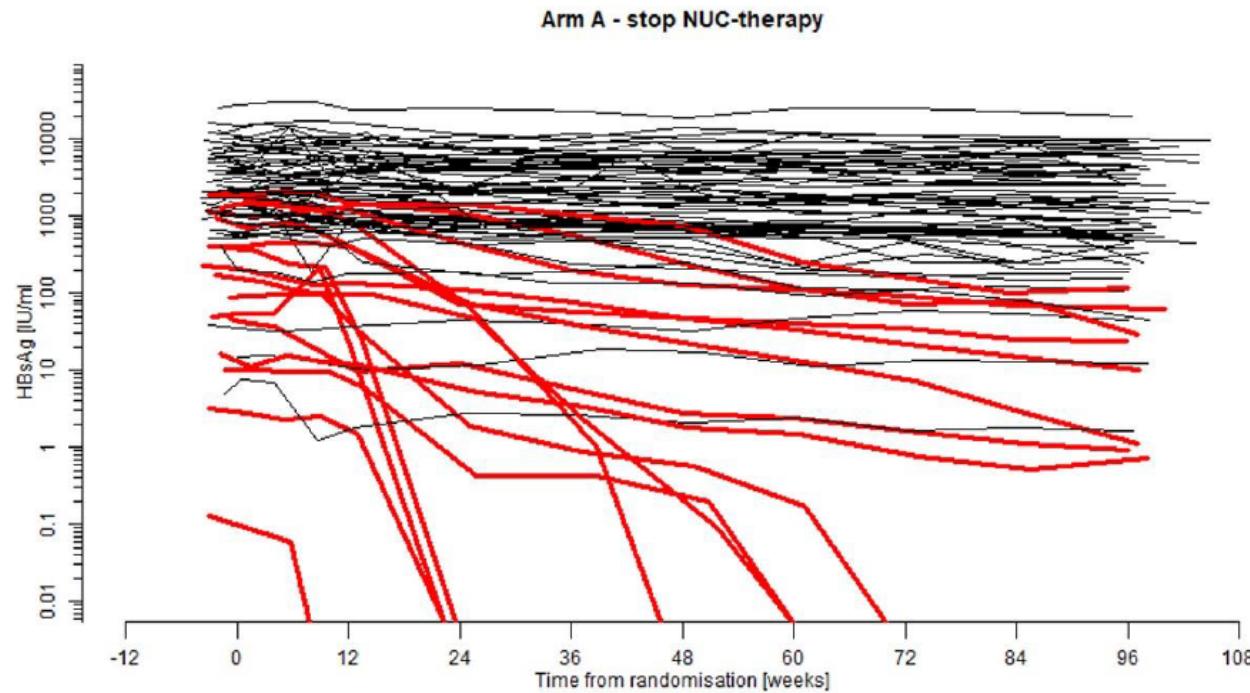
# STOP-NUC: Cessation of nucleos(t)ide treatment in HBeAg-negative chronic hepatitis B: A randomized controlled trial



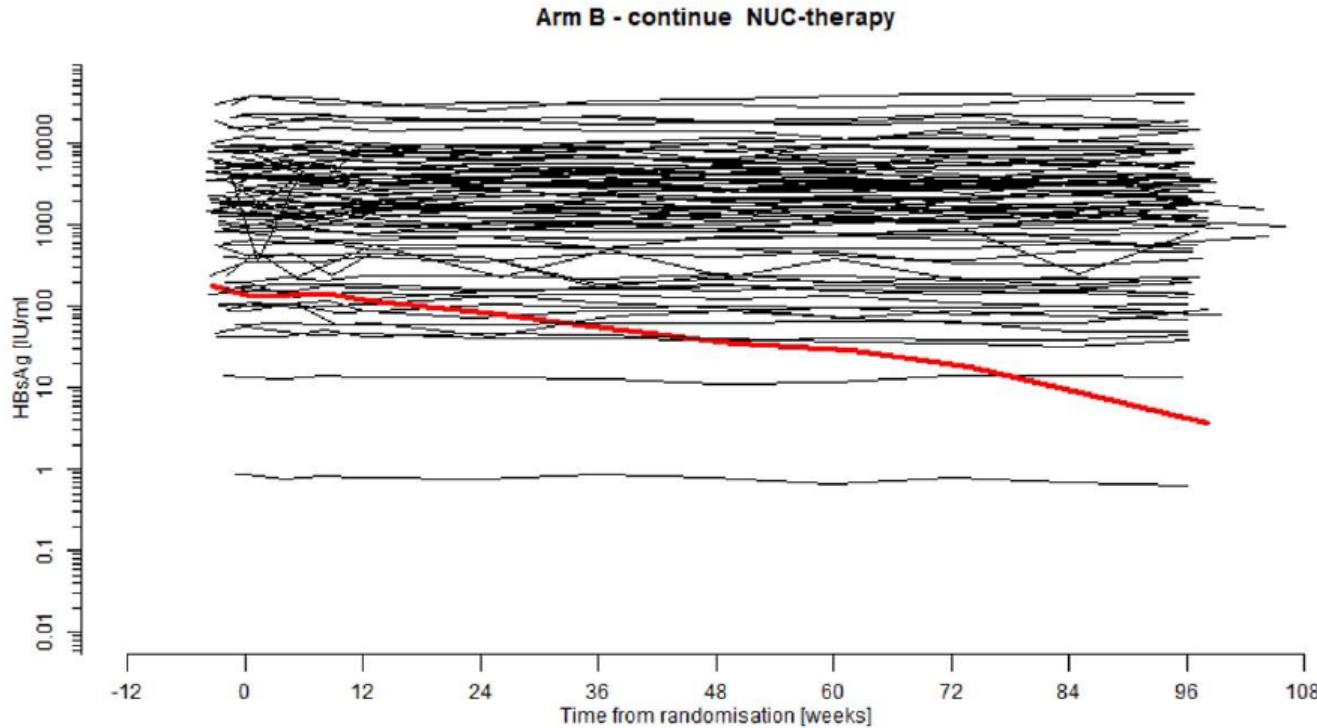
# STOP-NUC: End point HBsAg loss

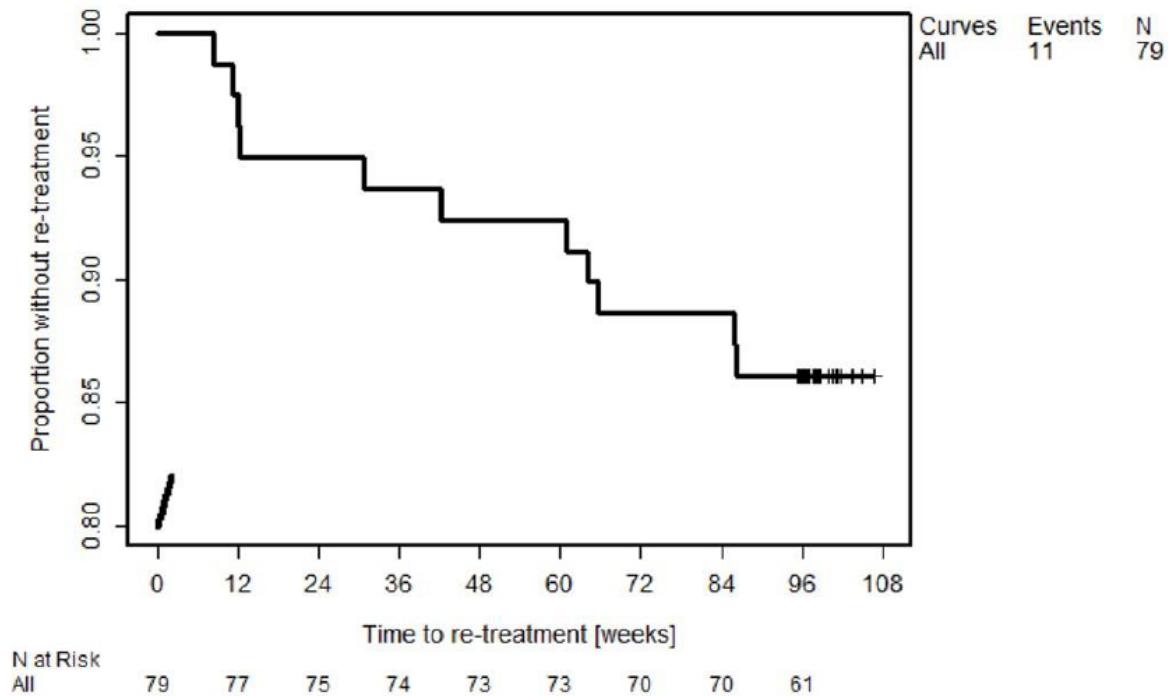


# STOP-NUC: HBsAg levels after stopping NA



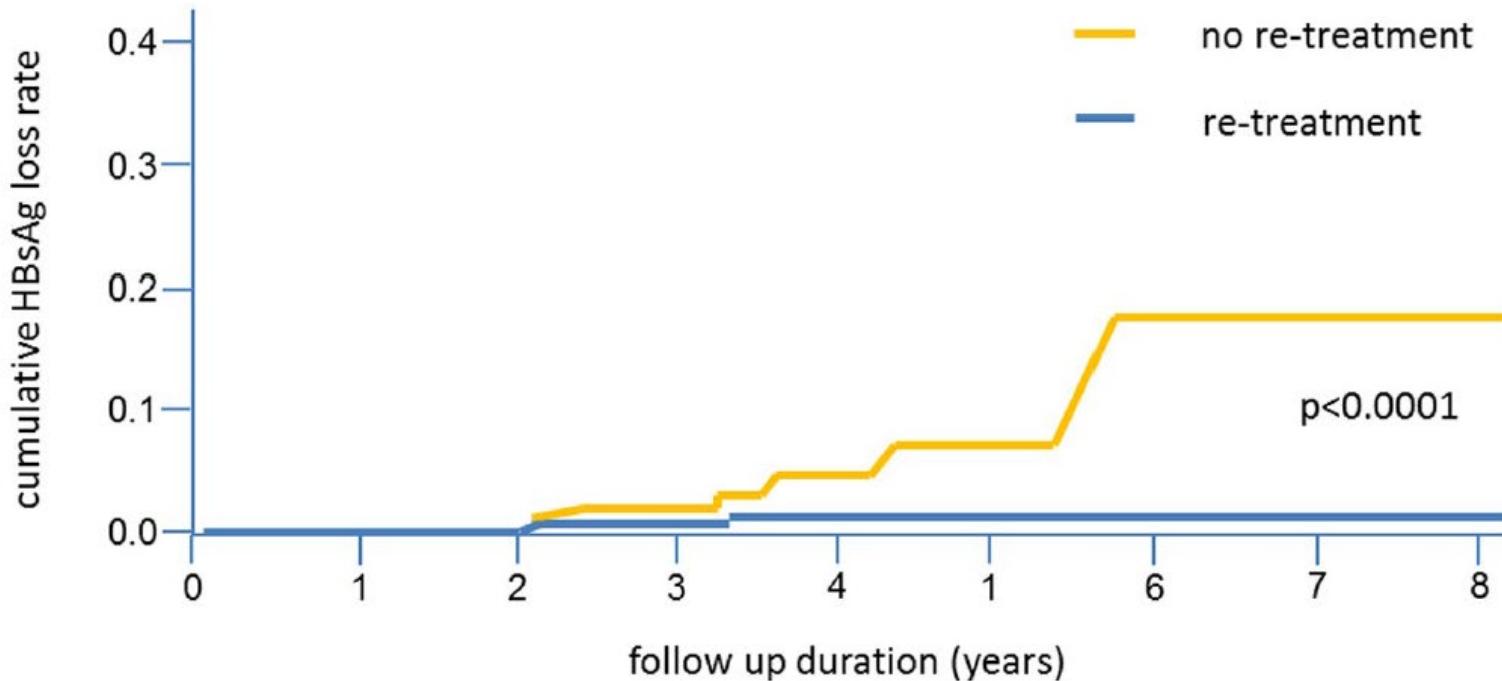
# STOP-NUC: HBsAg levels in control arm





# Negative effect of early on HBsAg losses

Cumulative HBsAg loss rate in 519 patients with clinical relapse and retreatment (blue line; n = 269) or patients with clinical relapse but no retreatment (yellow line; n = 150)



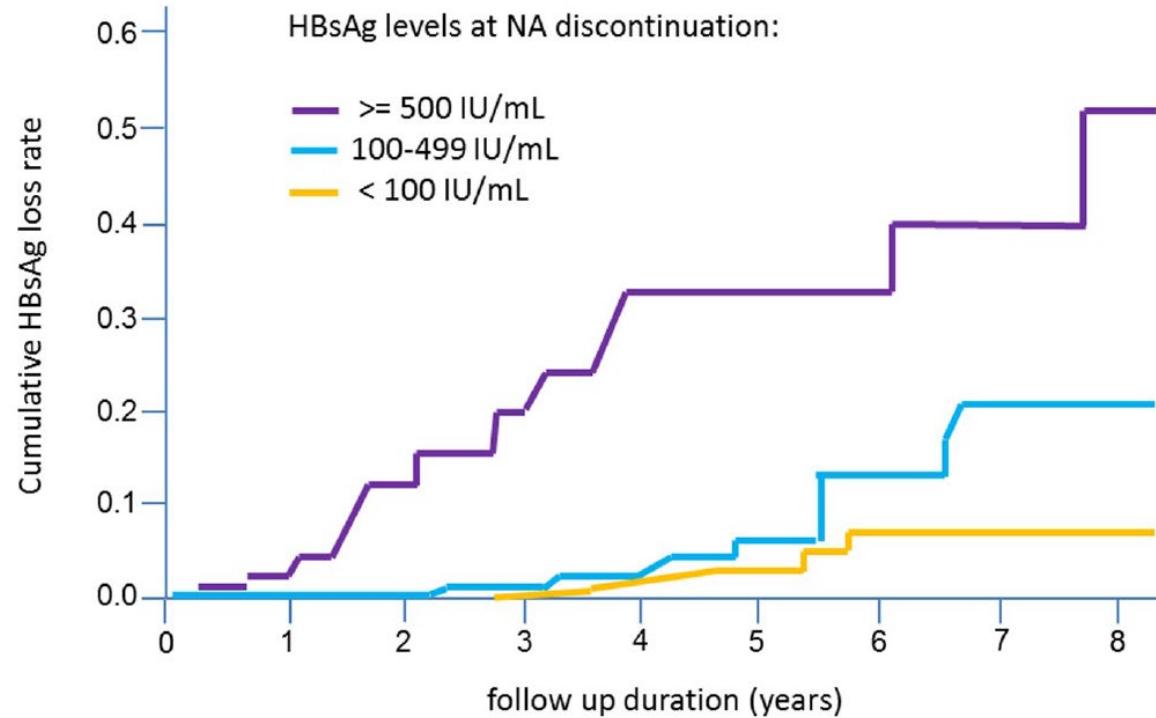
## TABLE 3. PROPOSED RETREATMENT CRITERIA FOR HBeAg-NEGATIVE PATIENTS AFTER NA DISCONTINUATION<sup>(62)</sup>

NA treatment should be immediately re-installed if one of the following criteria is met:

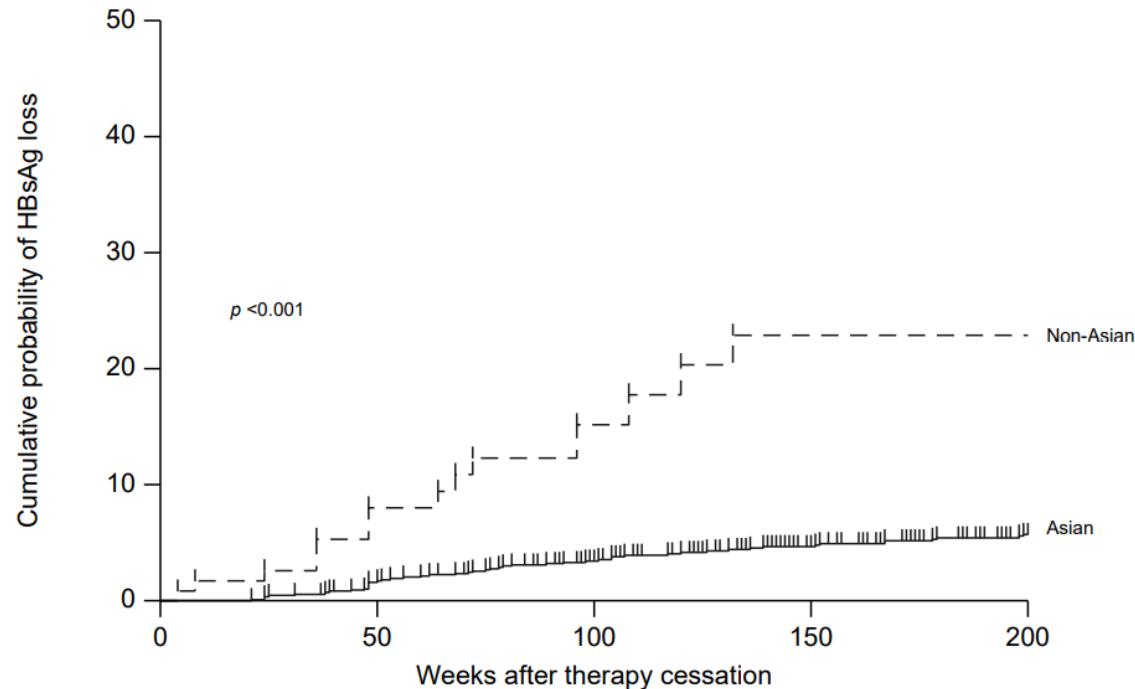
1. Confirmed (i.e., two consecutive central laboratory results) increase in direct bilirubin from baseline and ALT ULN at the confirmatory test
2. Confirmed sustained increase in prothrombin time  $\geq 2.0$  seconds from baseline with appropriate vitamin K levels and elevated ALT
3. Confirmed elevated ALT  $10\times$  ULN with or without associated symptoms
4. ALT  $2\times$  ULN and  $\leq 5\times$  ULN persisting for  $\geq 84$  days (12 weeks) as well as an HBV-DNA relapse  $\geq 20,000$  copies/mL
5. ALT  $5\times$  ULN and  $\leq 10\times$  ULN persisting for  $\geq 28$  days (4 weeks)

# Influence of qHBsAg at NA cessation

Cumulative HBsAg loss rates according to different HBsAg levels at the time point of NA treatment discontinuation  
(log-rank test,  $P < 0.0001$ )



# Influence of ethnicity on HBsAg loss



N° at risk\*

Non-Asian

115

64

33

30

30

Asian

1,101

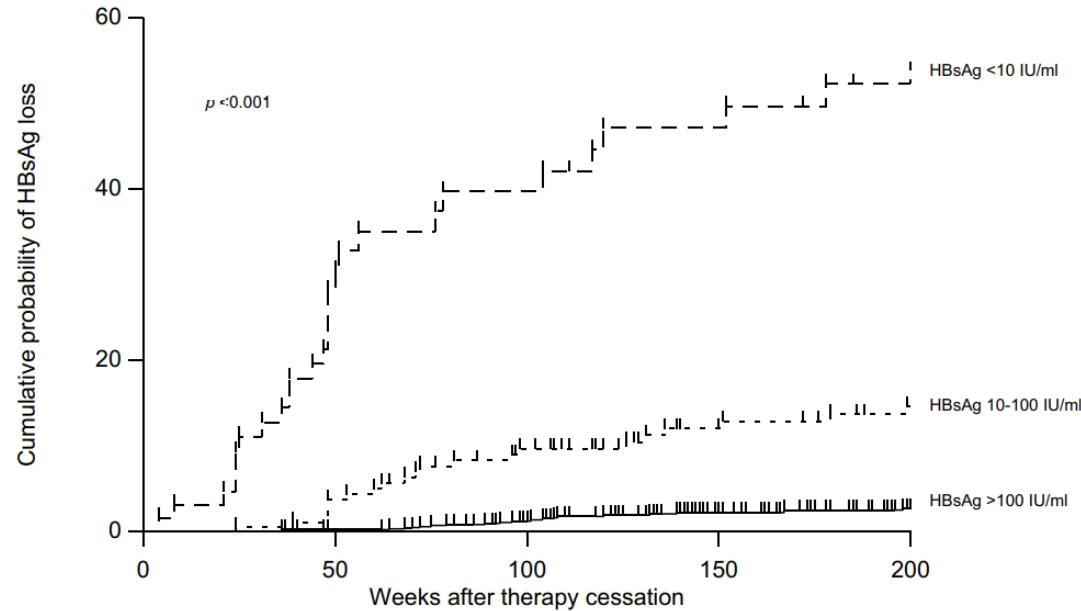
925

809

744

684

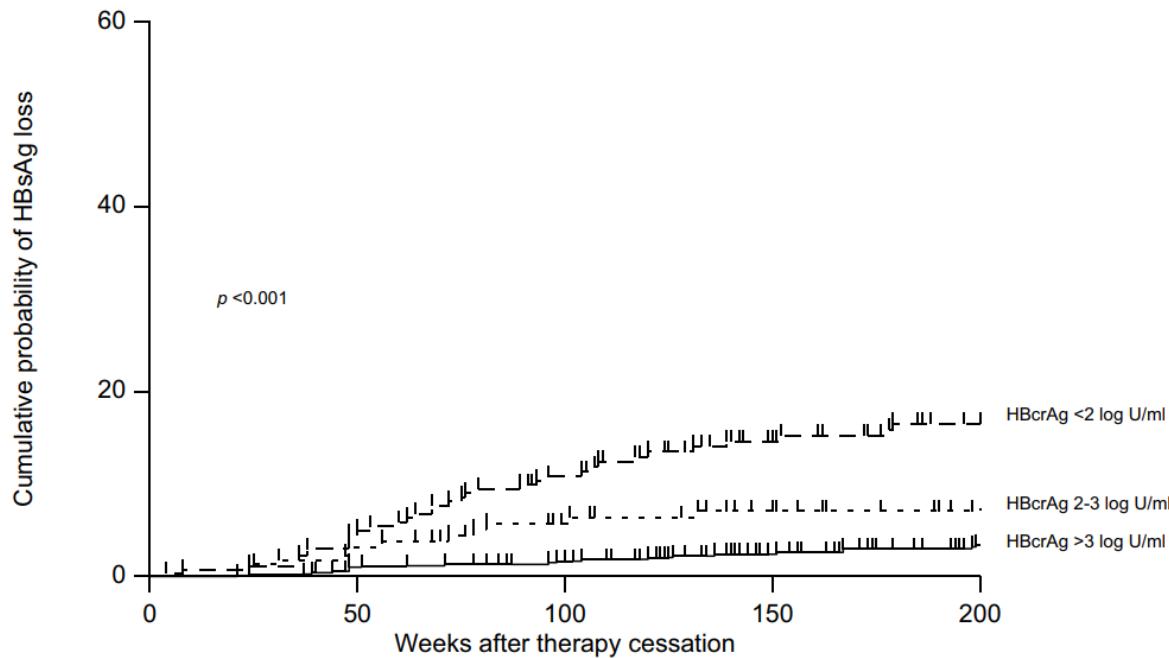
# Influence of HBsAg levels on HBsAg loss



N° at risk\*

|              |     |     |     |     |     |
|--------------|-----|-----|-----|-----|-----|
| HBsAg <10    | 64  | 31  | 25  | 21  | 16  |
| HBsAg 10-100 | 192 | 150 | 126 | 108 | 96  |
| HBsAg >100   | 960 | 808 | 691 | 645 | 602 |

# Influence of HBcrAg levels on HBsAg loss



N° at risk\*

| HBcrAg <2 log  | 272 | 214 | 167 | 143 | 123 |
|----------------|-----|-----|-----|-----|-----|
| HBcrAg 2-3 log | 234 | 156 | 135 | 124 | 114 |
| HBcrAg >3 log  | 710 | 619 | 540 | 507 | 477 |

**TABLE 2. RELAPSES, HEPATIC DECOMPENSATION, AND FATAL OUTCOMES IN HBeAg-NEGATIVE PATIENTS AFTER NA DISCONTINUATION (SELECTED STUDIES)**

| Study   | Number of Patients<br>With Cirrhosis, n | HBV-DNA<br>Relapse, n (%) | ALT Relapse,<br>n (%)   | Hepatic Decompensation,<br>n (% Cirrhosis) | Death,<br>n (% Cirrhosis) |
|---|---|---------------------------|-------------------------|--|---------------------------|
| Lim et al. <sup>(82)</sup> (two case reports) | 2                                       | 2 (100)                   | 2 (100)                 | 2 (100)                                    | 1 (100)                   |
| Jeng et al. <sup>(65)</sup>                   | 691 (308)                               | 547 (79.2)*               | 419 (60.6) <sup>†</sup> | 9 (100)                                    | 3 (100)                   |
| Kuo et al. <sup>(66)</sup>                    | 22                                      | N/A                       | 82 (68.4)               | 1 (100)                                    | 1 (100)                   |

\*Increase of HBV DNA > 2,000 IU/mL.

<sup>†</sup>Increase of ALT > 2× ULN.

- ⌚ Cessation of NA treatment is a potent tool to induce functional cure in HBeAg negative patients
- ⌚ HBsAg levels < 1000 IU/mL are a strong positive predictor of HBsag loss
  - Role of other bio markers is unclear
- ⌚ Cessation of NA is safe in non-cirrhotic patients
  - patients with liver cirrhosis NA should not be stopped
- ⌚ The long term development of immune control after NA cessation is unclear

# Thank you for your attention!

