COMMENTARY

The one-dose schedule opens the door to rapid scale-up of HPV vaccination

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In 2020, the World Health Organization launched a global strategy to accelerate the elimination of cervical cancer as a public health concern, with achieving 90% coverage of human papillomavirus (HPV) vaccination among girls as one of the core measures [1]. However, challenges related to the high vaccine procurement and delivery costs, logistical barriers, and supply constraints have led to ongoing slow uptake and low accessibility to HPV vaccines, particularly in low- and middle-income countries (LMICs) with a high burden of cervical cancer. The COVID-19 pandemic has further exacerbated financial, logistics, and supply constraints, resulting in only 12% HPV vaccine coverage for adolescent girls (9−14 years) in 2021 worldwide [2]. Accumulating evidence has indicated that one-dose vaccination schedules might provide comparable protection against persistent HPV infection as two-dose schedules [3–5]. The potential lower costs and simplified administration of the one-dose schedule have positioned it as a promising means to improve HPV vaccine uptake in populations with healthcare access. Clarifying the potential health and economic impacts of reduced-dose HPV vaccination optimal strategy for expanding HPV vaccination.

Main text

In *BMC Medicine*, Prem and colleagues compared the long-term health benefits and cost-effectiveness of one-dose versus two-dose HPV vaccination in 188 countries, under scenarios in which the one-dose schedule provides either a shorter duration of protection or lower vaccine efficacy compared to two doses [6]. Prem et al.'s study revealed that if a single HPV vaccine dose confers ≥ 30 years of protection or lifelong protection but at 80% efficacy, the difference in population benefits of the one-dose versus two-dose vaccination schedule would be minimal [6]. Importantly, the study underscored that, in contrast to high-income countries (HICs), the one-dose schedule in LMICs would avert a greater number of cervical cancer cases and necessitate the vaccination of fewer girls per prevented case [6]. This highlights the value of the one-dose program for cervical cancer prevention in LMICs.

Inequality in the allocation of HPV vaccines persists globally, impeding the expansion of HPV vaccination initiatives. In recent years, ongoing shortages in vaccine supplies have disproportionately affected LMICs, leading to delays in their vaccination rollout [7]. In countries where HPV vaccination programs have been imple-

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Conclusions

The one-dose schedule emerges as a prospective strategy for scaling up HPV vaccination, particularly in LMICs. As data continue to emerge, continued exploration of potential differences in the effectiveness of one and two doses, as well as strategies to gradually expand HPV vaccination coverage within budgetary constraints, remains of paramount importance.

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INVITED EDITORIAL

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Editorial: Negative impact of diabetes mellitus and obesity on the prognosis of patients with chronic liver disease

There is a strong association between diabetes mellitus (DM) and chronic liver disease (CLD).[1] The incidence of DM is higher in patients with CLD.[1] The presence of DM is independently associated with the development of fibrosis and poor clinical outcomes in patients with CLD, including reduced survival and development of major complications such as hepatocellular carcinoma, refractory ascites and hepatic encephalopathy.[1-4] The main driver of all these complications is portal hypertension; non-selective beta blockers (NSBB) can prevent cirrhotic complications in patients with portal hypertension. Reduction in hepatic venous pressure gradient (HVPG) of more than 20% from baseline, or to below 12 mmHg, reduces the risk of variceal bleeding and decompensation.[5]

Several factors influence the HVPG response to NSBB such as the degree of liver failure, dose, portosystemic collaterals and varices or 2-adrenoceptor gene polymorphisms.[5,6] A preliminary study by the same authors suggested that in patients with metabolic dysfunction-associated steatohepatitis, the presence of DM (aOR:0.16, $p=0.038$) was independently associated with NSBB response.[7]

This retrospective study included 93 patients with compen-

Child–Pugh B and DM. The effect of DM in hepatic decompensation was also observed after adjusting for HVPG response.

These findings are very interesting and suggest that both DM and obesity should be taken into account when monitoring NSBB response. In addition, DM seems to have an impact on the prognosis of patients with advanced CLD. However, further randomised studies are needed to confirm these findings, considering not only patients with HVPG>12 mmHg (as in this study), but also patients with clinically significant portal hypertension (HVPG ≥10 mmHg). It would also be of great interest to see whether there is a difference in response in patients with DM and obesity using propranolol or carvedilol.

Finally, NSBB appear to have several beneficial effects independent of their haemodynamic effects.[5] Furthermore, the use of carvedilol in patients with DM has been shown to improve some components of the metabolic syndrome, such as a reduction in insulin resistance and an improvement in total cholesterol.[10]

AUTHOR CONTRIBUTIONS

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Review

Safety considerations for withdrawal of nucleos(t)ide analogues in patients with chronic hepatitis B: First, do no harm

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Nucleos(t)ide analogues (NA) are widely used to treat hepatitis B virus (HBV) infection, but they cannot eradicate the virus and treatment duration can be lifelong if the endpoint is set at seroclearance of the hepatitis B surface antigen (HBsAg). As an alternative strategy, finite NA therapy without the prerequisite of HBsAg seroclearance has been proposed to allow treatment cessation in patients with sustained undetectable HBV viremia for two to three years. However, reactivation of viral replication almost always follows NA withdrawal. Whereas HBV reactivation might facilitate HBsAg seroclearance in some, it could lead to serious acute flare-ups in a certain proportion of patients. Occurrence and consequences of NA withdrawal flares are complicated with various factors involving the virus, host, and treatment. Accurate risk prediction for severe flares following NA cessation is essential to ensure patient safety. The risks of life-threatening flares in patients who discontinued NA according to the stopping rules of current guidelines or local reimbursement policies have recently been quantitatively estimated in large-scale studies, which also provided empirical evidence to help identify vulnerable patients at risk of devastating outcomes. Moreover, risk predictors were further explored and validated to hopefully aid in patient selection and management. In this narrative review with a focus on patient safety, we summarize and discuss current literature on the incidence of severe flares following NA cessation, risk stratification for candidate selection, rules of posttreatment monitoring, and indications for treatment resumption. We also share our thoughts on the limitations of existing knowledge and suggestions for future research. **(Clin Mol Hepatol 2023;29:869-890)**

Keywords: Hepatitis B virus infection; Antiviral agents; Hepatitis B surface antigens; Patient safety

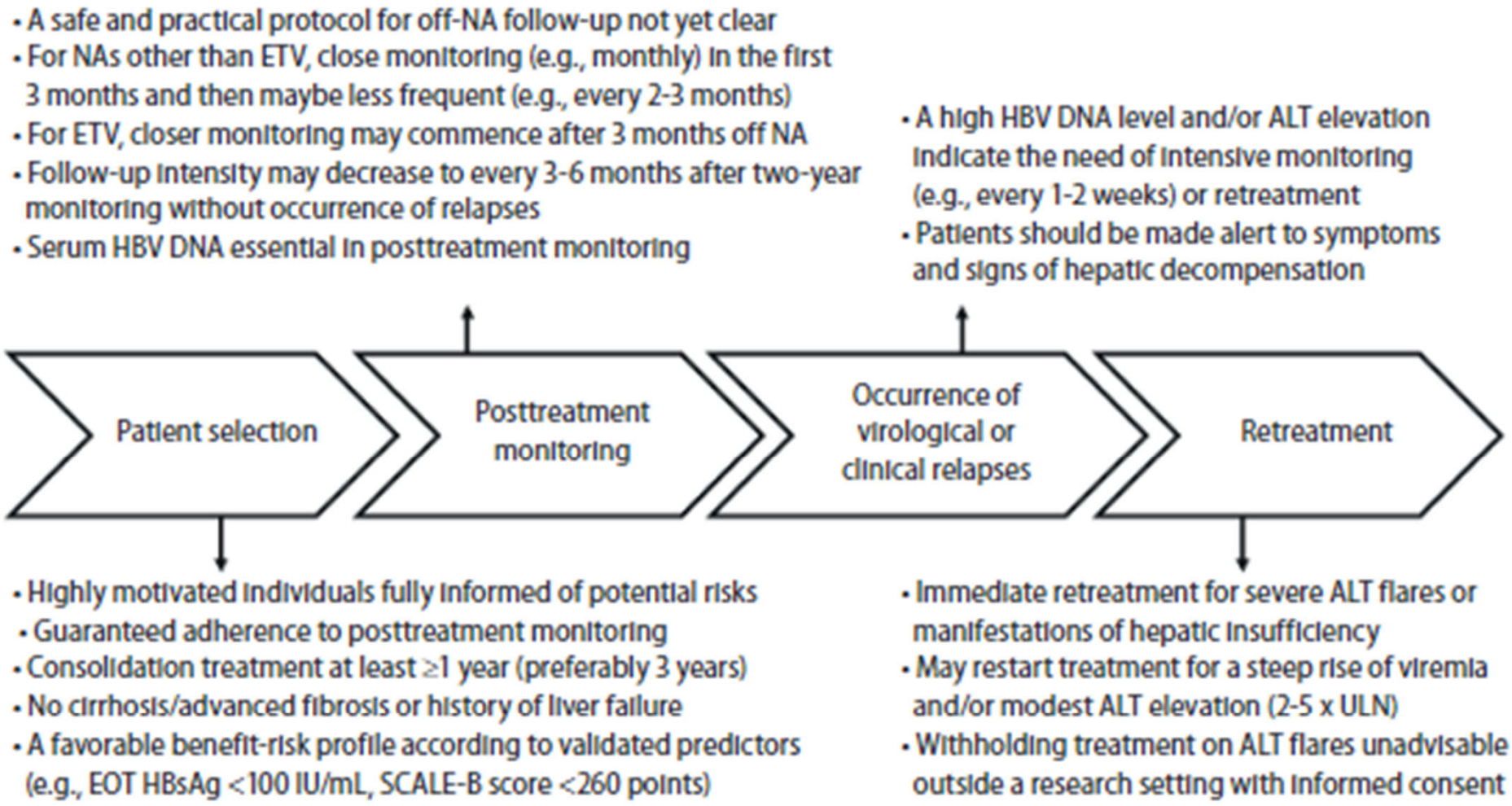

Figure 2. Safety considerations along the proposed scheme for an elective cessation of nucleos(t)ide analogues. ALT, alanine aminotransferase; DNA, DNA, deoxyribonucleic acid; EOT, end of treatment; ETV, entecavir; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; NA, nucelos(t)ide analogue; RNA, ribonucleic acid; TDF, tenofovir disoproxil fumarate; ULN, upper limit of normal.

Review

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Hepatitis B core-related antigen: A novel and promising surrogate biomarker to guide anti-hepatitis B virus therapy

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The current requirement for biomarkers to detect hepatitis B virus (HBV) infection is polarized. One is a fully-automated and highly sensitive measurement system; the other is a simple system for point-of-care testing (POCT) in resource-limited areas. Hepatitis B core-related antigen (HBcrAg) reflects intrahepatic covalently closed circular DNA and serum HBV DNA. Even in patients with undetectable serum HBV DNA or HBsAg loss, HBcrAg may remain detectable. Decreased HBcrAg levels are associated with reduction of the occurrence of hepatocellular carcinoma (HCC) in chronic hepatitis B. Recently, a fully-automated, novel high-sensitivity HBcrAg assay (iTACT-HBcrAg, cut-off value: 2.1 logIU/mL) has been developed. This attractive assay has been released in Japan very recently. iTACT-HBcrAg can be useful for monitoring HBV reactivation and prediction of HCC occurrence, as an alternative to HBV DNA. Moreover, monitoring HBcrAg may be suitable for determining the therapeutic effectiveness of approved drugs and novel drugs under development. Presently, international guidelines recommend anti-HBV prophylaxis for pregnant women with high viral loads to prevent mother-to-child transmission of HBV. However, >95% of HBV-infected individuals live in countries where HBV DNA quantification is not available. Worldwide elimination of HBV needs the scaling-up of examination and medication services in resource-limited areas. Based on this situation, a rapid and easy HBcrAg assay as a POCT is valuable. This review provides the latest information regarding the clinical use of a new surrogate marker, HBcrAg, in HBV management, based on iTACT-HBcrAg or POCT, and introduces novel agents targeting HBV RNA/protein. **(Clin Mol Hepatol 2023;29:851-868)**

Keywords: Hepatitis B core-related antigen (HBcrAg); Covalently closed circular DNA (cccDNA); HBV reactivation; Point-of-care testing; RNA destabilizer

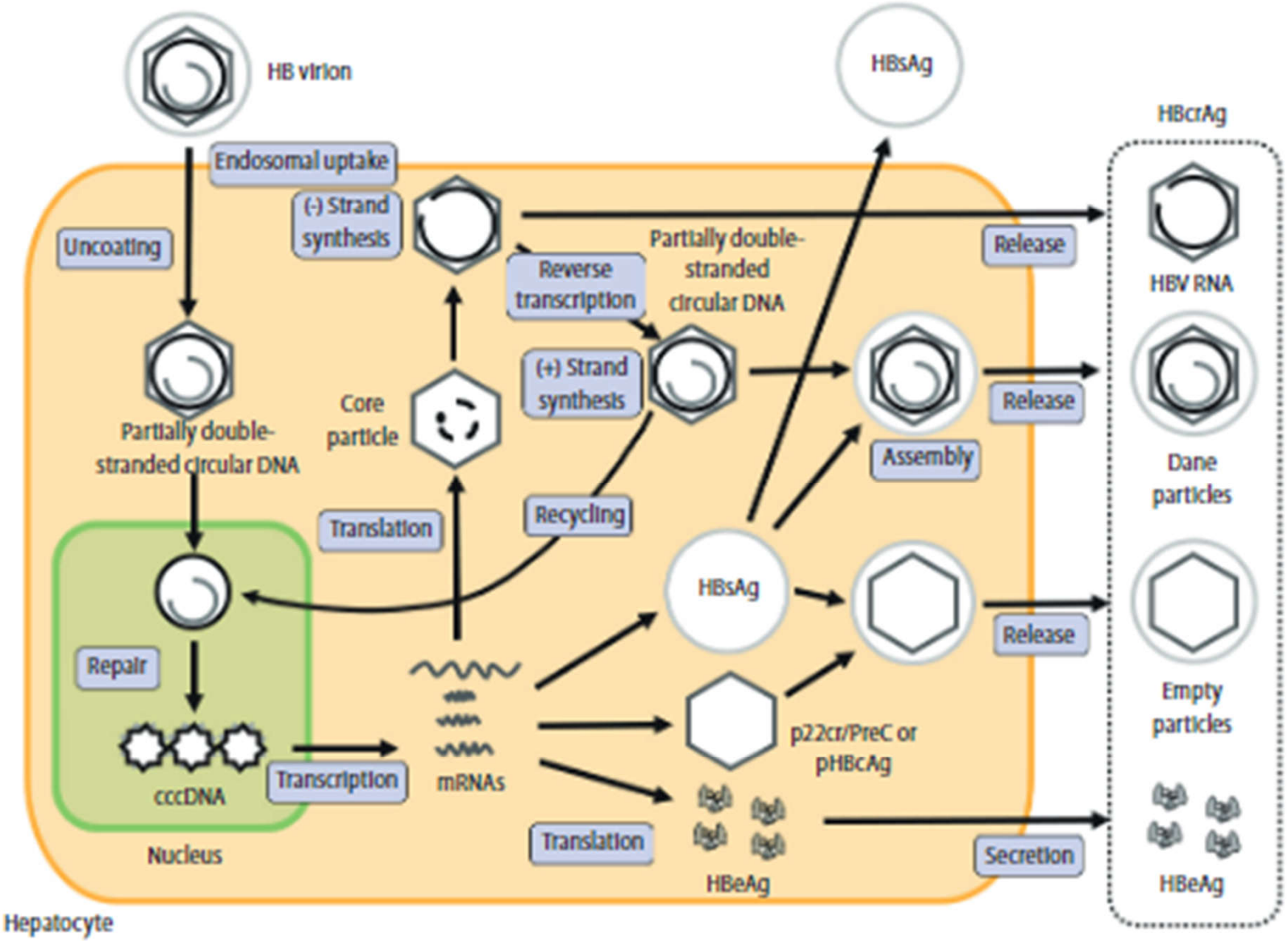

Figure 1. Schema of the life cycle of HBV and HBcrAg. The cccDNA is present as minichromosomes. There are 5 to 50 per hepatocyte. The minichromosomes are recycled as cccDNA to maintain the amount of cccDNA.[13] HBcrAg is produced from cccDNA. HBcrAg is coded from the

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Diagnostic Performance of Artificial Intelligence–Based Computer-Aided Detection Software for Automated Breast Ultrasound

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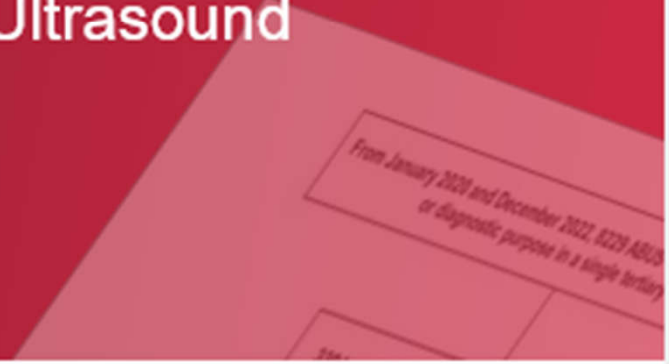

0.870 (95% confidence interval [CI], 0.832–0.908). The AUC significantly improved to 0.919 (95% CI, 0.890–0.947; *P* = 0.001) using AI-aided 1, whereas it improved without significance to 0.884 (95% CI, 0.844–0.923), 0.890 (95% CI, 0.852–0.929), and 0.890 (95% CI, 0.853–0.928) using AI-aided 2, 3, and 4, respectively. AI-CAD-negative cancers were smaller, less frequently exhibited retraction phenomenon, and had lower BI-RADS category. Among nonmass lesions, AI-CAD-negative cancers showed no posterior shadowing.

Conclusion

AI-CAD implementation significantly improved the radiologists' diagnostic performance and may serve as a valuable diagnostic tool.

THE END