



# **Immunotherapeutics in the Treatment of Chronic Hepatitis B**

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**HBV Forum & ICE-HBV  
Therapeutic Vaccines Webinar**

18 January 2022



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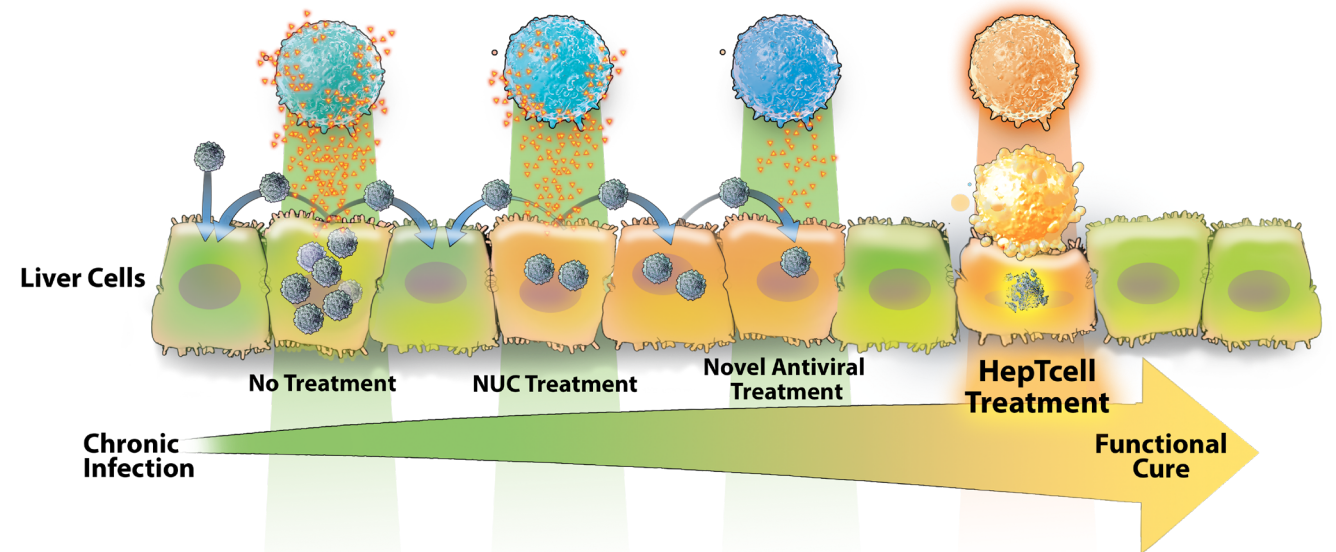
# FOCUS ON LIVER AND METABOLIC DISEASES

PRODUCT NAME	PRECLINICAL	PHASE 1	PHASE II	PHASE III	STATUS
Pemvidutide	NASH				Readouts on Phase 1 NAFLD and T2DM studies H12022
Pemvidutide	Obesity				US IND filing Q4 2021, with trial initiation expected Q1 2022
HepTcell™	Chronic Hepatitis B				In Phase 2, data readout expected H2 2022

# CURRENT HBV THERAPEUTICS DO NOT LEAD TO FUNCTIONAL CURE

Immune activation will be required for significant impact

- Current antivirals prevent disease progression but rarely clear chronic infection
- Newer direct-acting antivirals unlikely to result in immune reactivation alone
- Breaking T cell immune tolerance is key to functional cure
- Immunotherapy is designed to “wake up” dormant T-cells to eliminate infection



# GOAL OF IMMUNOTHERAPY IN CHB

## Limitations of prior immunotherapeutic approaches

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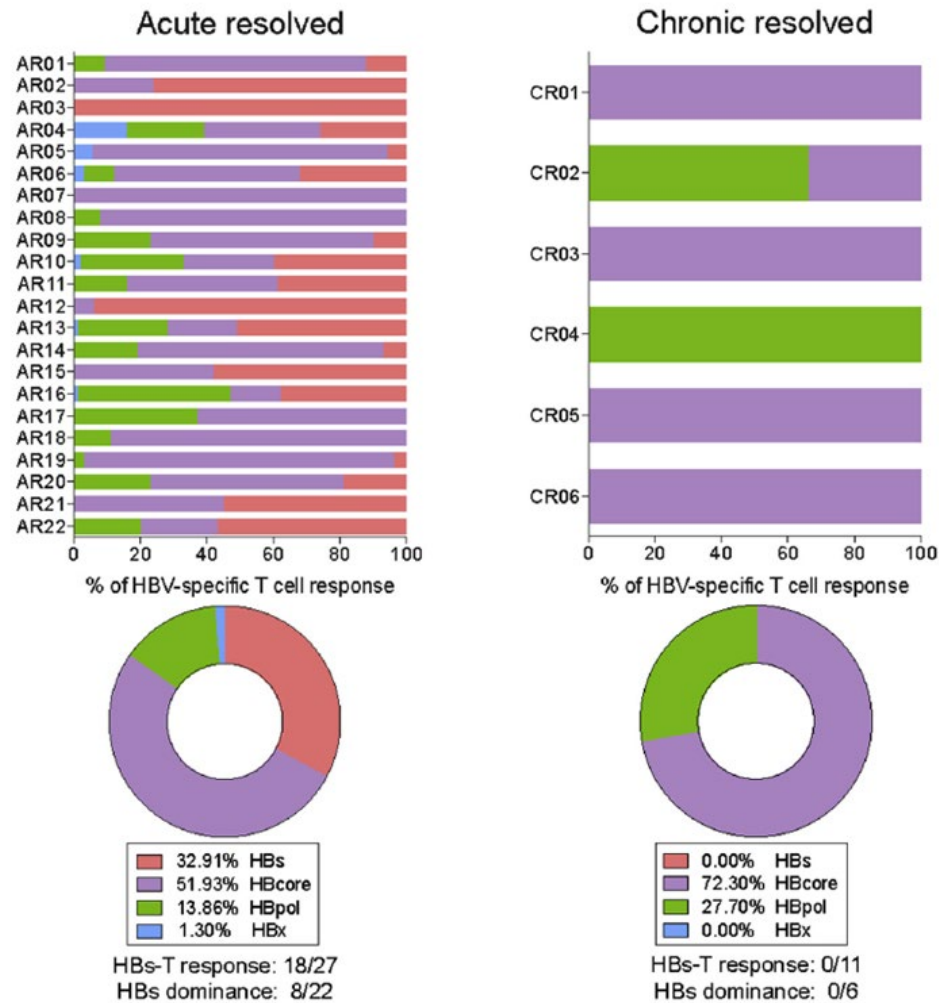
- Many therapeutic vaccines have failed
  - Limited to or biased towards Surface Antigen-specific tolerance barrier
  - Vaccine based on full length antigens - T cell responses bias towards less-conserved domains
  - Weak immunogens/vaccine formulation
- Non-specific immunomodulators (checkpoint inhibitors or TLR agonists) carry risk of off-target effects

Li et al PLoS One. 2011;6(6):e20479.



# IMMUNE RESOLUTION OF CHB

Importance of core and polymerase as target antigens



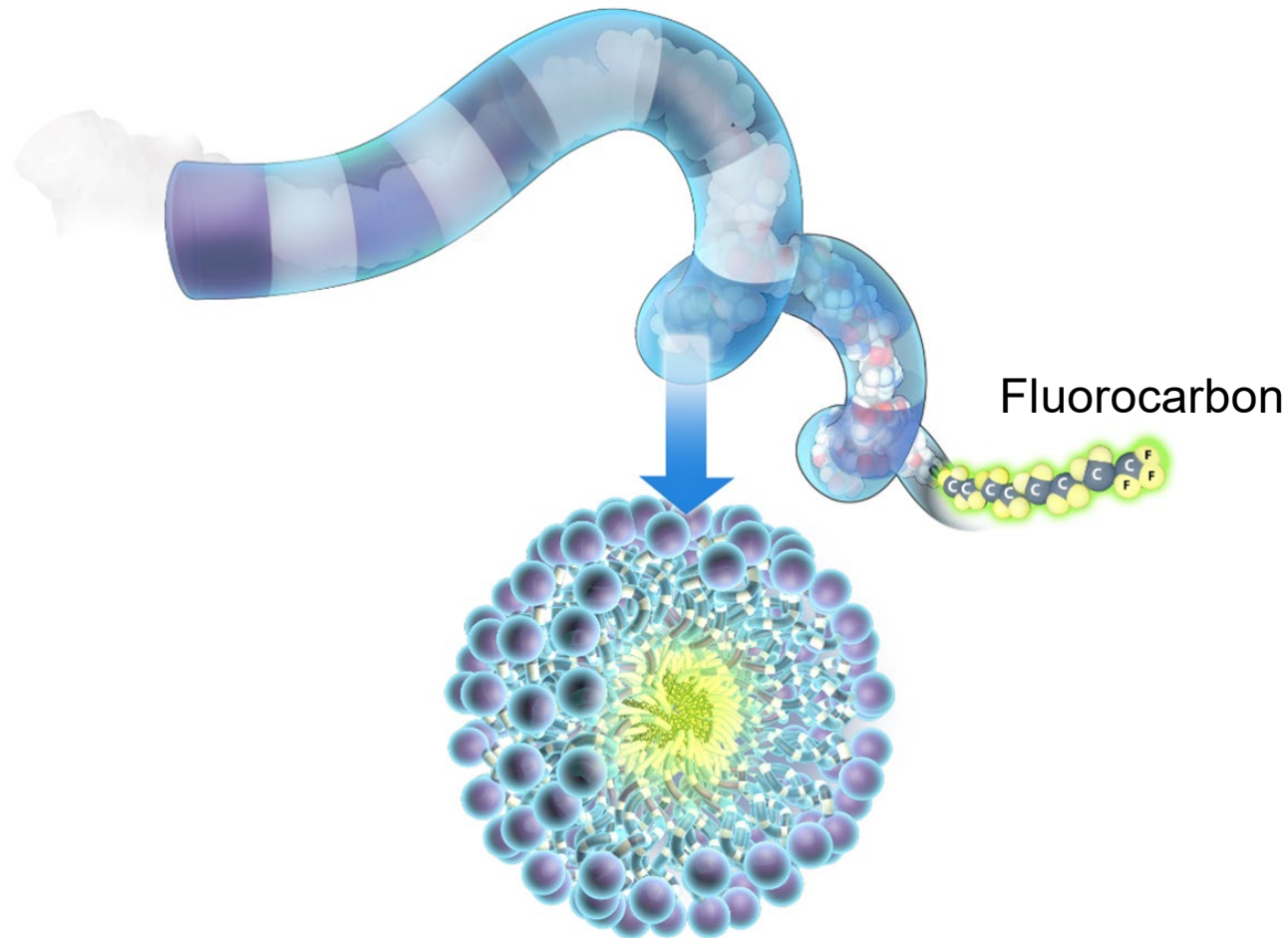
- T cell responses against HBsAg are strongly affected by duration of exposure
- T cell responses against core and polymerase are dominant in chronic resolved infection
- Baseline T cell responses against core and polymerase are associated with virological control following NA discontinuation

Le Bert Gastroenterology 2020; García-López J Hepatol. 2021, Rivino J Clin Invest. 2018

# HEPTCELL IMMUNOTHERAPEUTIC TECHNOLOGY

Long synthetic peptides to promote CD4+ and CD8+ T cell responses

T cell epitope containing peptide



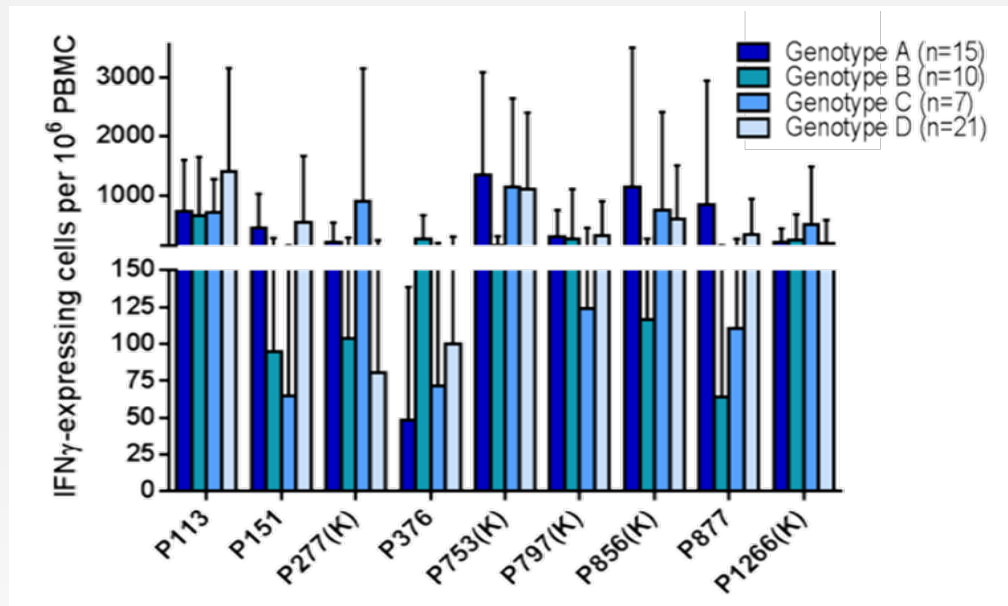
- 30 to 40 a.a. long peptides manufactured by solid phase synthesis
- Contain CD4+ and CD8+ T cell epitopes to overcome HLA restriction
- Fluorocarbon moiety promotes micelle formation and improves immunogenicity
- Robust immunogenicity observed with this peptide platform in young and older adults

Francis et al. Vaccine. 2015 Jan 3;33(2):396-402.

# HEPTCELL PRECLINICAL ACTIVITY

Broad cross-genotype coverage

HepTcell covers 4 predominant HBV genotypes and all other genotypes by homology



- Most individual peptide components of HepTcell can cross-react with multiple HBV genotypes
- Collectively, the peptides in HepTcell cross-react with genotypes A-D
- Based on HBV homology, HepTcell expected to cross-react with all HBV genotypes



# HEPTCELL: PHASE 1 SAFETY AND IMMUNOGENICITY STUDY

Study in subjects chronically infected with HBV

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## Population (n=60)

- 18-65 yo with eAg negative chronic HBV for  $\geq 2$  years
- Tenofovir or entecavir for  $\geq 2$  years
- HBV DNA  $< 50$  IU/ml for  $\geq 1$  year
- No history of cirrhosis and current Fibroscan  $< 11.5$  kPa

## Treatment

- 3 double blind dose escalating cohorts enrolled from sites in UK and Korea
- Low (150  $\mu$ g) or high dose (500  $\mu$ g) peptides, with or without IC31, c/w IC31 or saline
- 3 IM injections 28 days apart, followed by 6-month observation

## Endpoints

- Safety: Routine labs, AEs, injection site assessment
- Cultured IFN- $\gamma$  Elispot
- qHBsAg

# HEPTCELL: PHASE 1 SAFETY AND IMMUNOGENICITY STUDY

## Safety

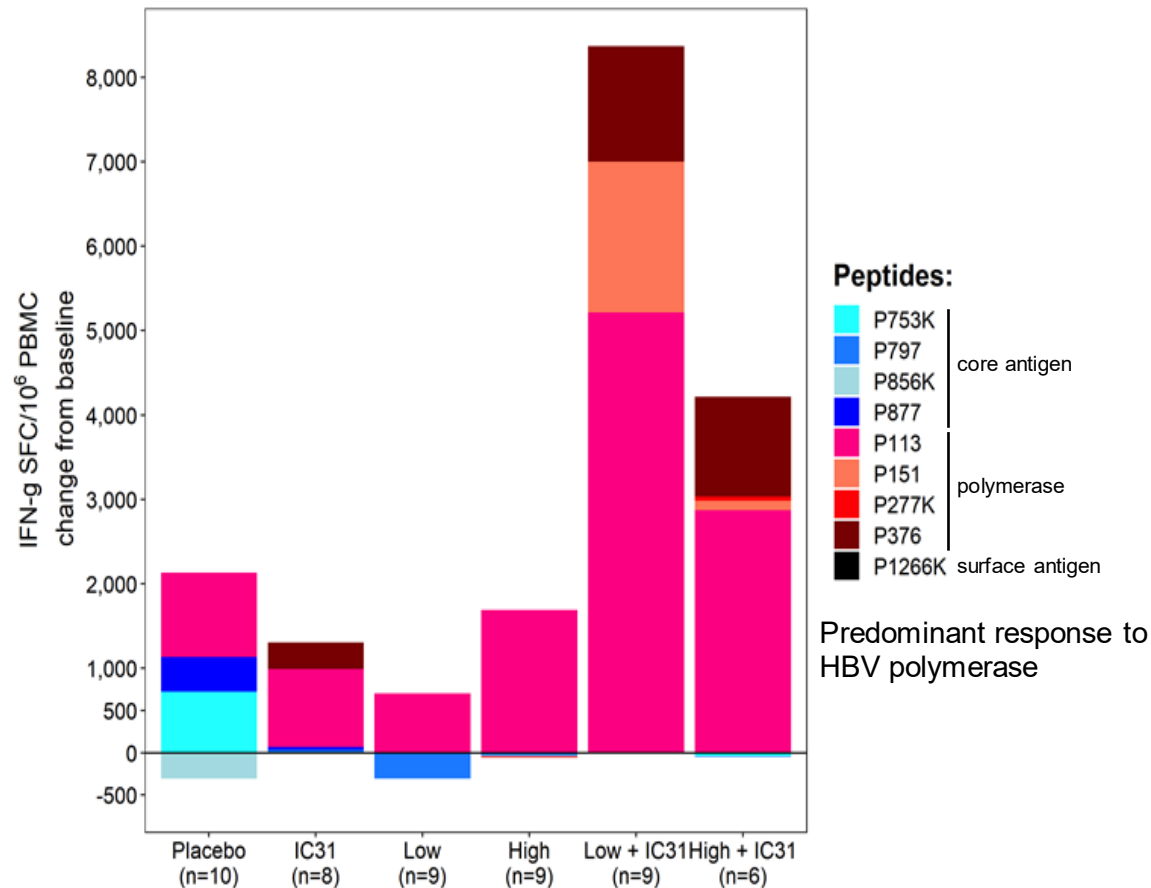
- 1 SAE (infectious colitis between dose 2 and 3) in High + IC31 subject
- No autoimmune events
- No hepatitis flares
- No trends in other AEs
- Injection site reactions were self-limited and mild-moderate except for one patient with severe tenderness in the low + IC31 group

Investigator Assessed Injection Site Reactions						
	Low (N=10)	Low + IC31 (N=10)	High (N=10)	High + IC31 (N=11)	IC31 (N=10)	Placebo (N =10)
Any Reaction (%)	60	60	50	46	10	20
Burning (%)	0	30	20	0	0	10
Erythema (%)	0	10	0	9	0	20
Induration (%)	0	0	10	0	10	20
Swelling (%)	20	0	0	0	0	20
Pain (%)	60	30	30	36	0	10
Tenderness (%)	50	40	50	10	0	20

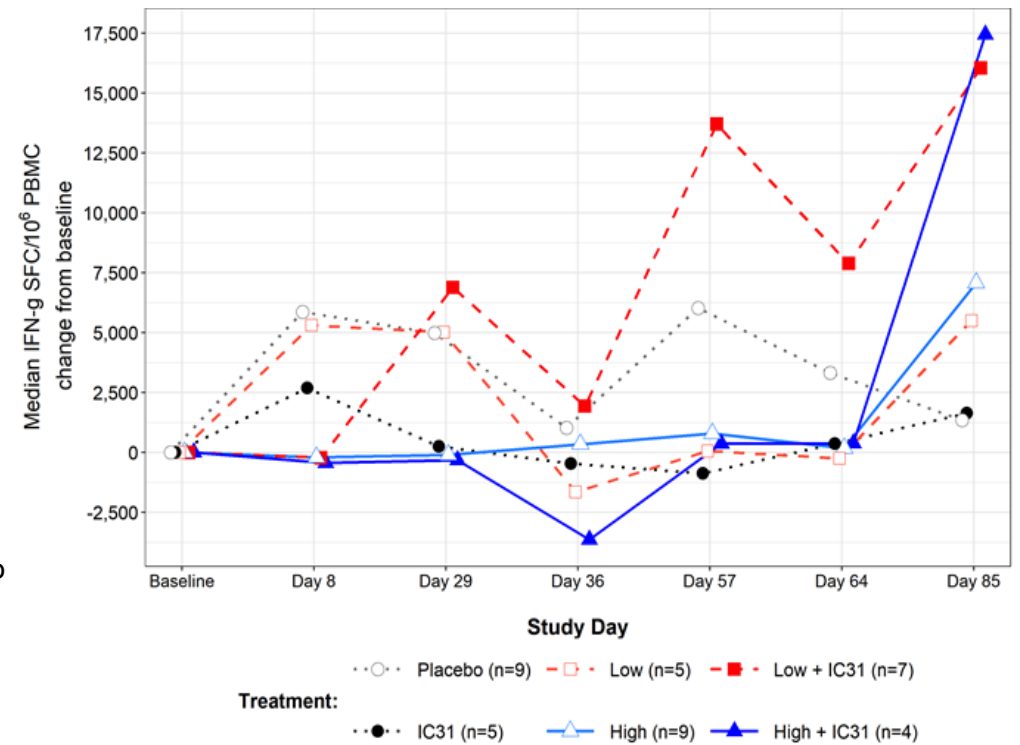
# HEPTCELL: PHASE 1 SAFETY AND IMMUNOGENICITY STUDY

Robust IFN- $\gamma$  ELISpot Responses that Increase over Time

Change from Baseline, Day 85



Change from Baseline over Successive Administrations



# HEPTCELL – PHASE 2 CLINICAL TRIAL

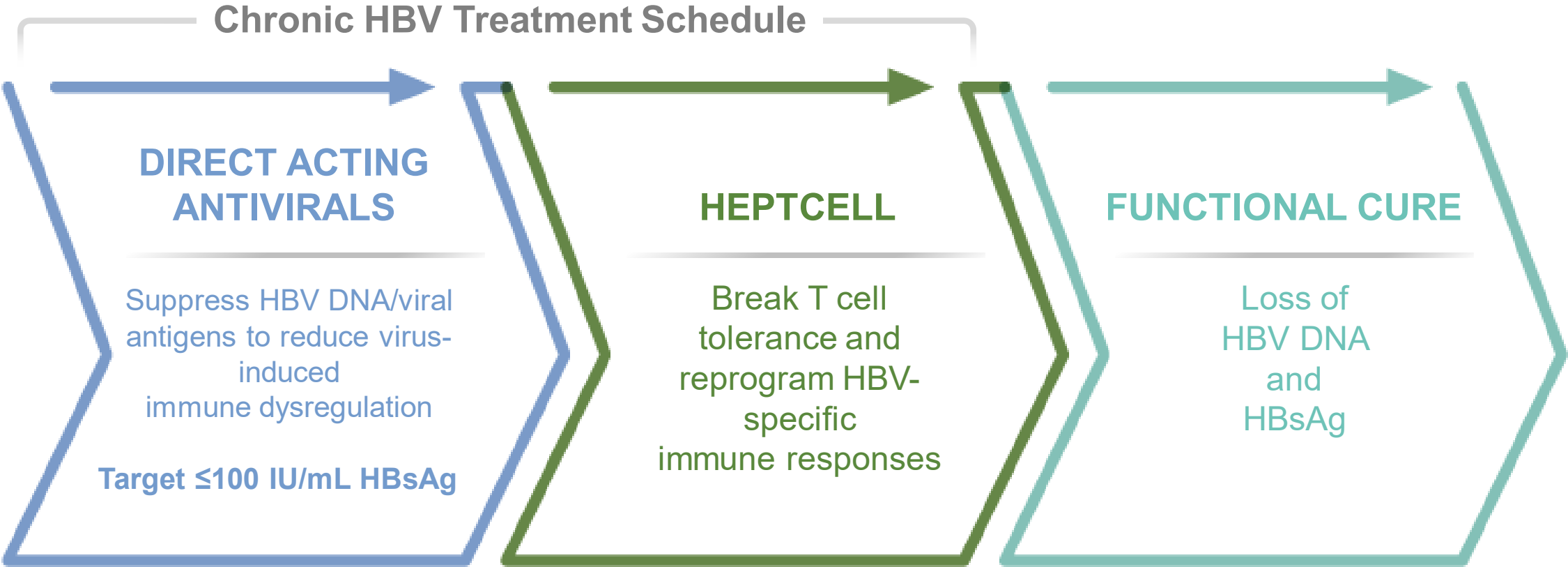
Multinational, multicenter trial of HepTcell in inactive chronic hepatitis B (CHB)

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- Patients with inactive CHB and HBsAg levels  $\leq 100$  IU/mL is a subpopulation that might demonstrate a response to immunotherapy
- Virologic response appears to be more likely to occur with a longer duration of immunotherapy
- 80 patients with HBeAg negative inactive CHB and HBsAg  $\leq 100$  IU/mL randomized 1:1 to HepTcell or placebo administered every 4 weeks for 24 weeks
- Follow-up at 48 weeks after the last dose will assess the safety and durability of response
- Efficacy endpoints
  - Primary: proportion of patients with 1.0-log reduction in HBsAg from baseline at Week 24
  - Secondary: HBsAg clearance, changes from baseline in HBsAg, HBV DNA, HBcrAg, pg-RNA at Week 24
- Data readout expected in H2 2022

# HEPTCELL – KEY COMPONENT OF COMBINATION APPROACH

Combination with novel direct-acting antivirals for improved activity







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