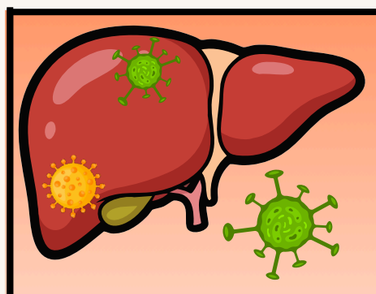

RNA INTERFERENCE VS ANTISENSE OLIGONUCLEOTIDES IN CHRONIC HEPATITIS B

"From Viral Suppression to Functional Cure"

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Abstract No. 47

Aims and Objectives

1. Compare the efficacy of siRNA and ASO therapies in reducing HBsAg and HBV RNA.
2. Evaluate their potential to achieve HBV functional cure.
3. Compare safety profiles and future combination strategies.

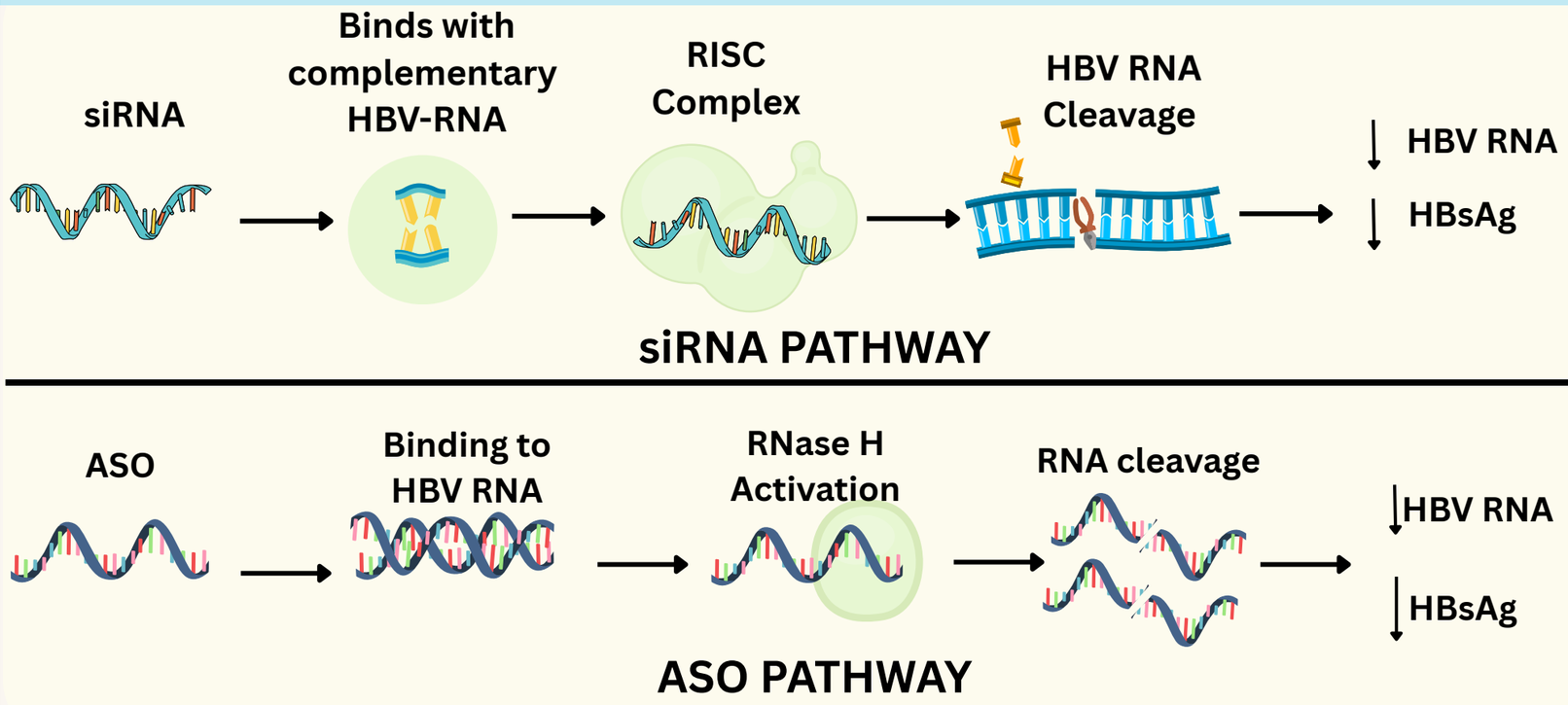
Background

1. Functional cure in chronic hepatitis B remains challenging because sustained HBsAg loss is uncommon.
2. Emerging siRNA and ASO therapies aim to achieve deeper HBsAg and HBV RNA suppression.

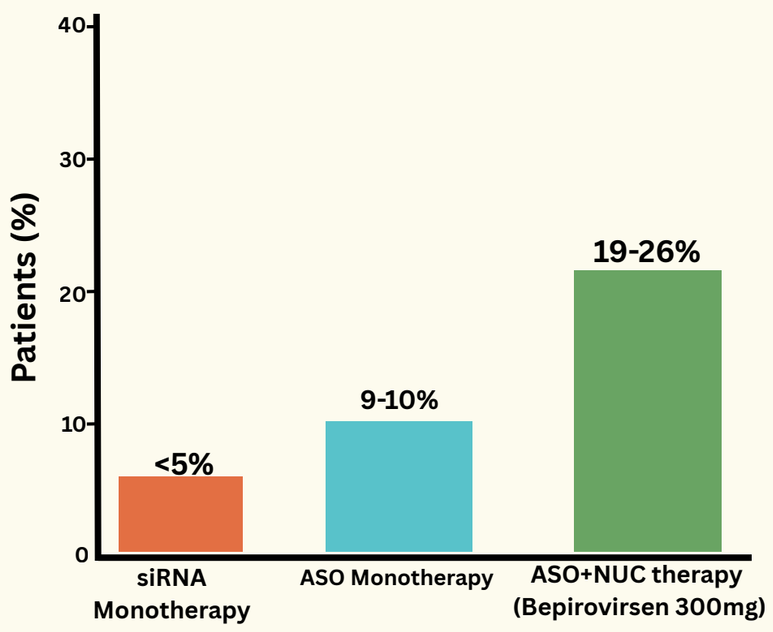
Methodology

- A comparative evaluation of RNA interference and antisense oligonucleotide therapies in chronic hepatitis B, assessing HBsAg and HBV RNA levels, therapeutic efficacy, safety, and treatment-related adverse effects.

Mechanism of Action



Functional cure rates (%)



Comparison of therapies

Parameters	siRNA Therapy	ASO Therapy
Agents	JNJ-3989,AB-729, VIR-2218	Bepirovirsen (300mg)
Mechanism	RISC-mediated cleavage of HBV RNA	RNase H-mediated degradation of HBV RNA
HBsAg Reduction	>75% decline in HBsAg	Significant reduction in HBsAg
Functional cure	<5% with siRNA monotherapy	19-26% with NUCs
Safety	Injections site reactions <8%,fewer hepatic flares	Good safety profile reversible ALT elevations
Key strength	Potent viral suppression and excellent safety	Higher functional cure potential

Results

- Both siRNA and ASO therapies demonstrated significant reductions in serum HBsAg and HBV RNA.
- siRNAs achieved profound on-treatment HBsAg suppression, while bepirovirsen demonstrated a stronger functional-cure signal, including sustained off-treatment HBsAg clearance.
- siRNAs showed favorable overall tolerability, whereas bepirovirsen was associated with reversible ALT flares accompanying antigen decline.
- These findings support future combination strategies integrating RNA-targeting therapies with immunomodulation to improve durable HBV cure.

Conclusion

- RNA-silencing therapies achieve substantial viral-antigen reduction in chronic hepatitis B.
- siRNAs provide potent and sustained antigen suppression, while bepirovirsen has provided the strongest clinical evidence to date for finite-treatment functional cure among RNA-targeting therapies.
- Rational combinations of RNA-targeting agents with immunomodulatory therapies may represent a promising strategy for achieving sustained, off-treatment functional cure.

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