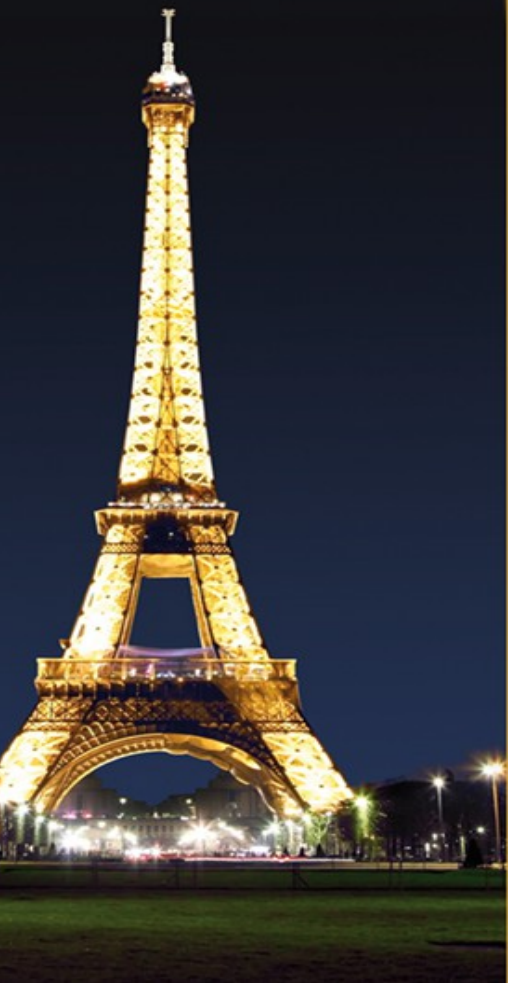


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10th PARIS
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CONFERENCE

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Current Issues in Liver Diseases

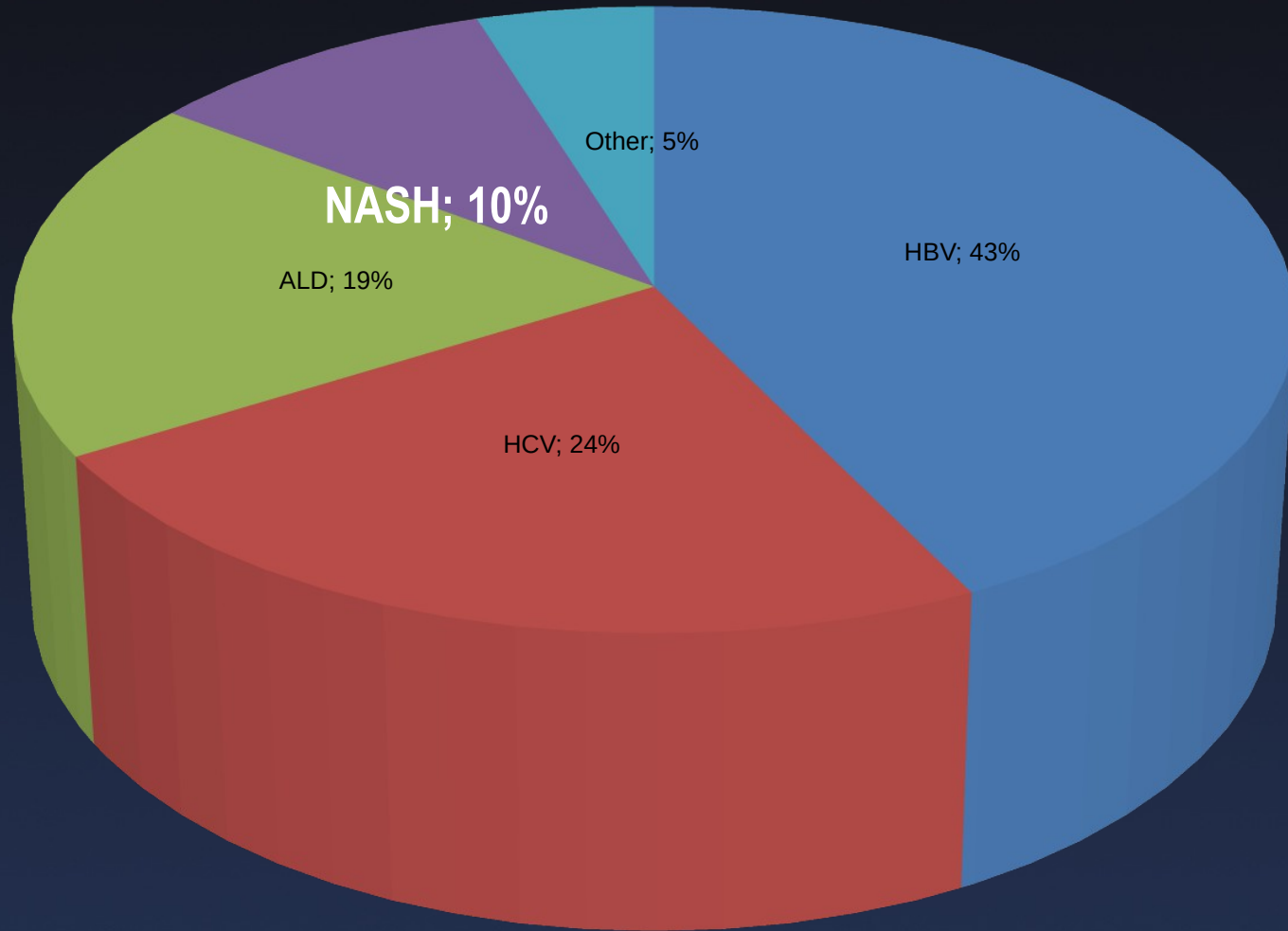
Challenges in Liver Patients

- **Improvement of treatment in HBV patients**
- **Improve management of end-stage liver disease**
- **The future of liver transplantation**
- **Optimal management of HCC**

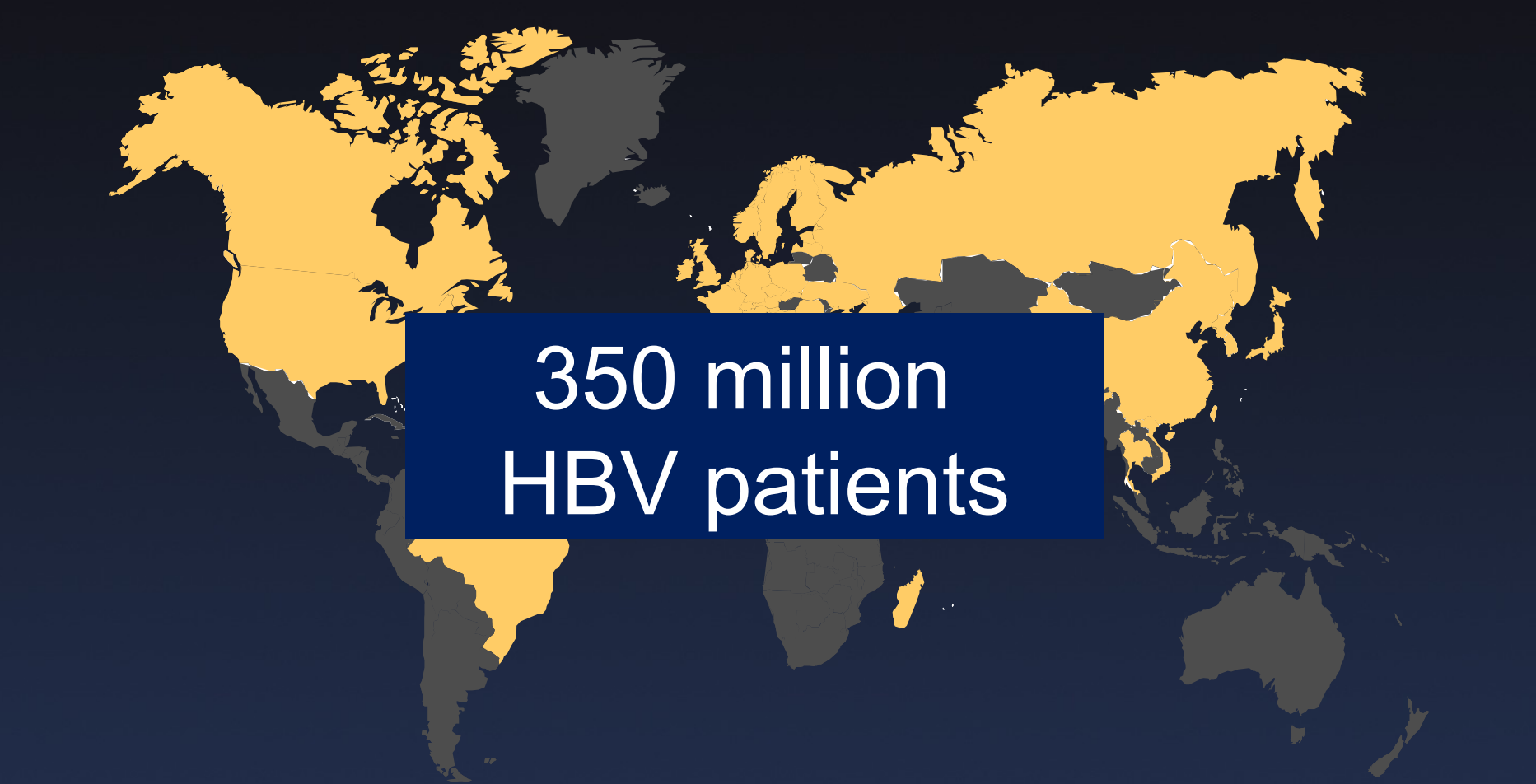
Hepatitis B

THE COME BACK

Distribution of Causes of CLD



Hepatitis B : Very High Prevalence



350 million
HBV patients

HBV is Coming Back

Researchers and Investments focus now on HBV

- **High prevalence**
(350 million carriers / >600 000 deaths/year)
- **More contagious than HCV (vertical transmission)**
- **Increased prevalence in countries welcoming immigrants**
- **More complex virus (ccc DNA and integration of DNA)**
- **More complex disease (from inactive carriers to cirrhosis)**

HBV is Coming Back

- Current therapies: remission and not cure
- Significant cost (indefinite therapy)
- HBsAg loss is the ultimate end-point
- HBsAg loss=clinical cure with improved outcome
- HBsAg loss rare with NUCs
- Persistence of cccDNA
- 2 innovative concepts:
 - qHBsAg
 - Combination therapy PEG IFN+NUC

Innovative Concept: qAgHBS

Standardized and simple test

Identification of inactive carriers

Assessment of severity of liver disease

Probability of HBsAg loss

NPV 97%: HBsAg decline >1log at 12 weeks

Indication of treatment

Choice of the drug :IFN Peg vs Nuc

When to stop NUCs?

Innovative Concept: PEG IFN + NUC

Proof of concept of combination

Accelerates HBsAg decline

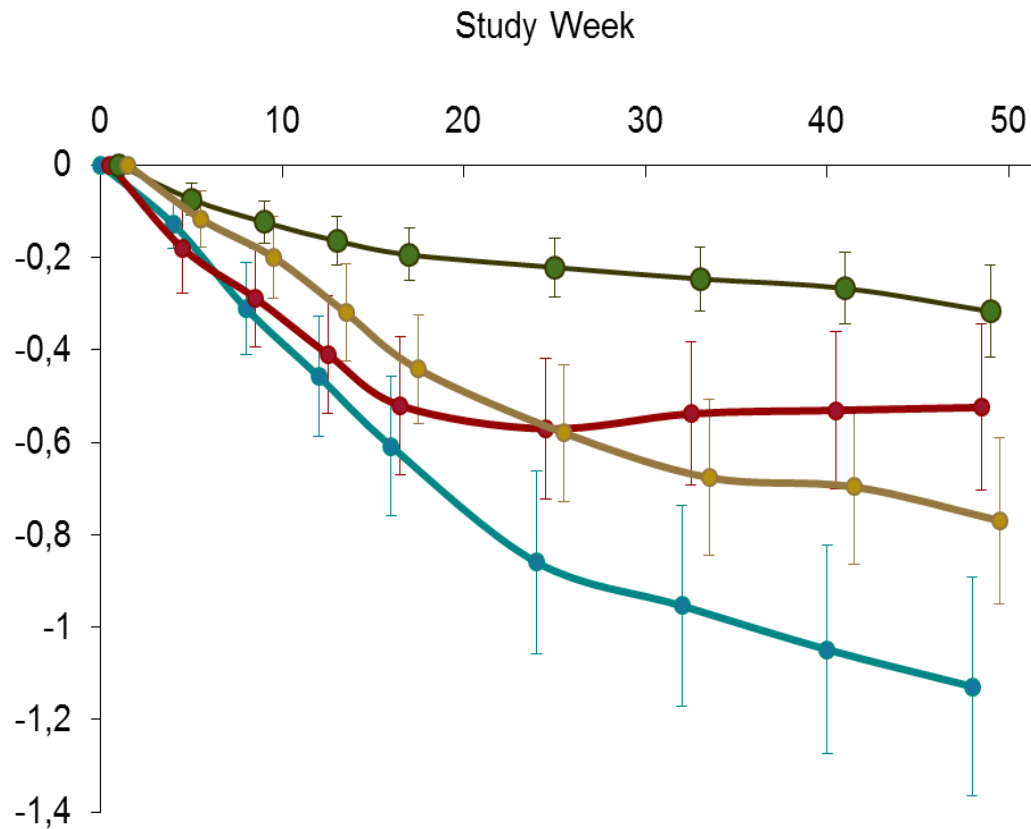
Increases HBsAg loss

Good tolerance and safety

Simultaneous better than add on?

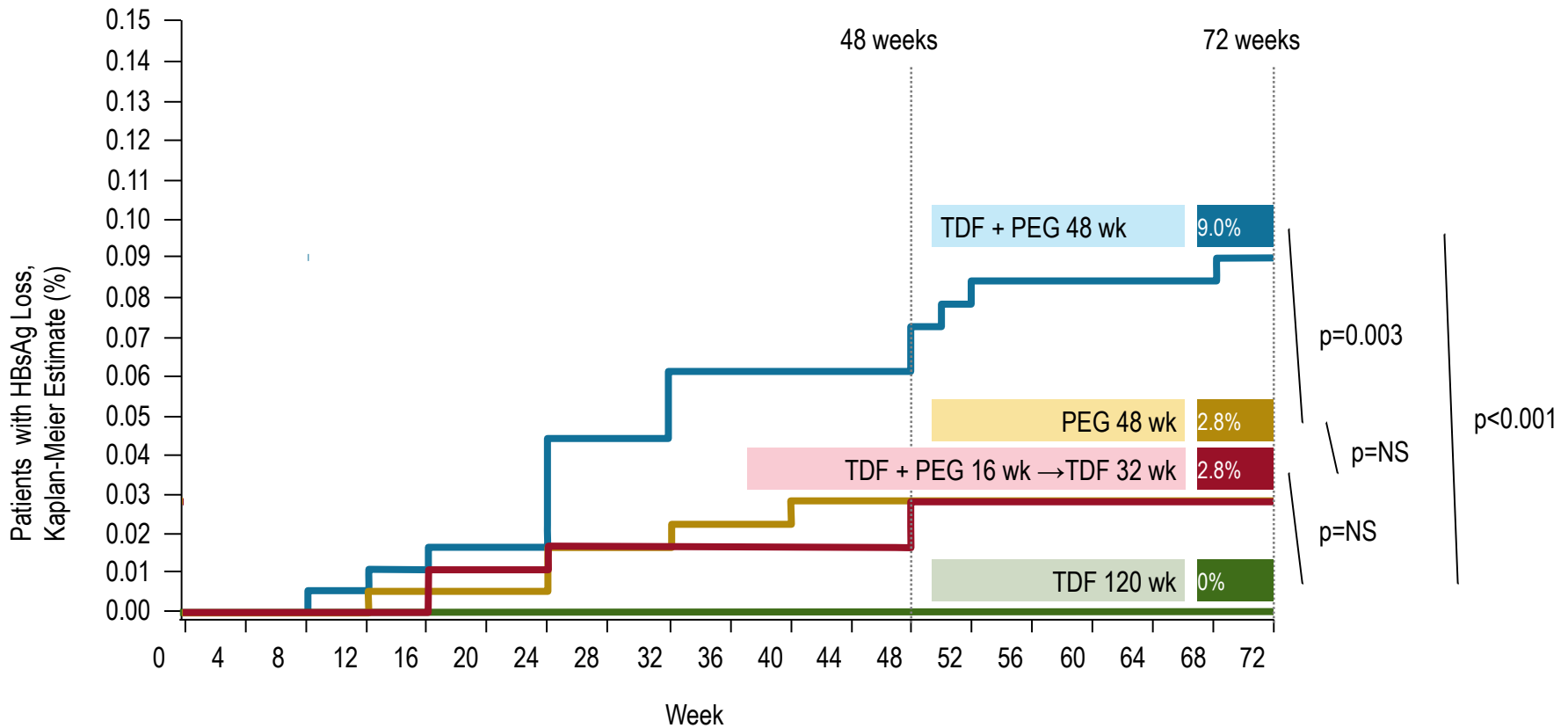
Duration of treatment?

On-Treatment Changes in HBsAg Levels at Week 48



Mean Change

Results: HBsAg Loss Over Time (Week 72)



Future Therapeutic Innovation Pipe Line

- **Early stage development**
- **More potent NUCs**
- **New immunomodulators**
- **New antiviral compounds acting on different targets (receptors, proteins, capsid, cccDNA ...)**

TRIPLE THERAPY

TODAY
INDIVIDUALIZED TREATMENT

TOMORROW
COMBINATION

Triple therapy in 5 years?