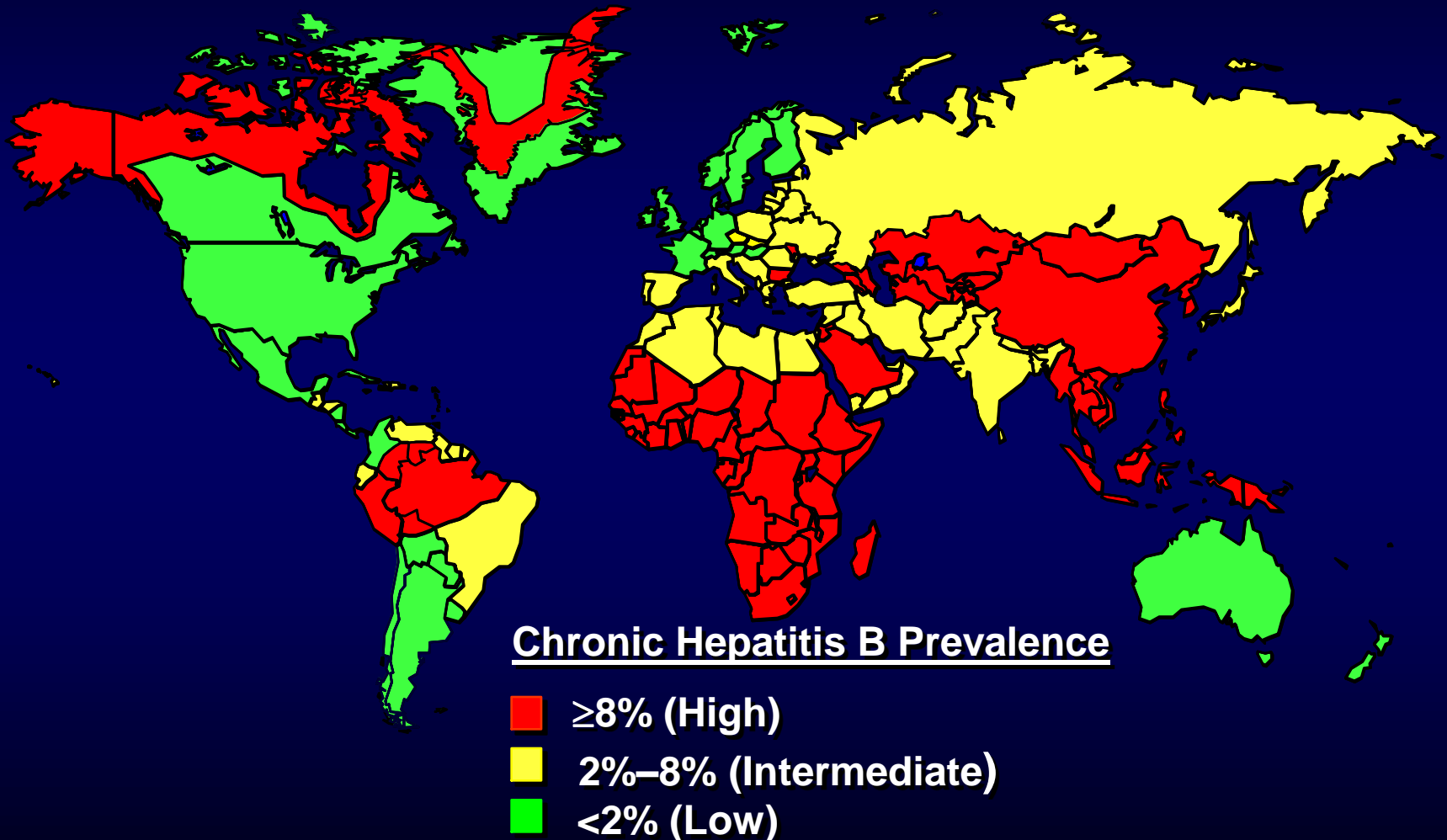


New Data from AASLD, 2009

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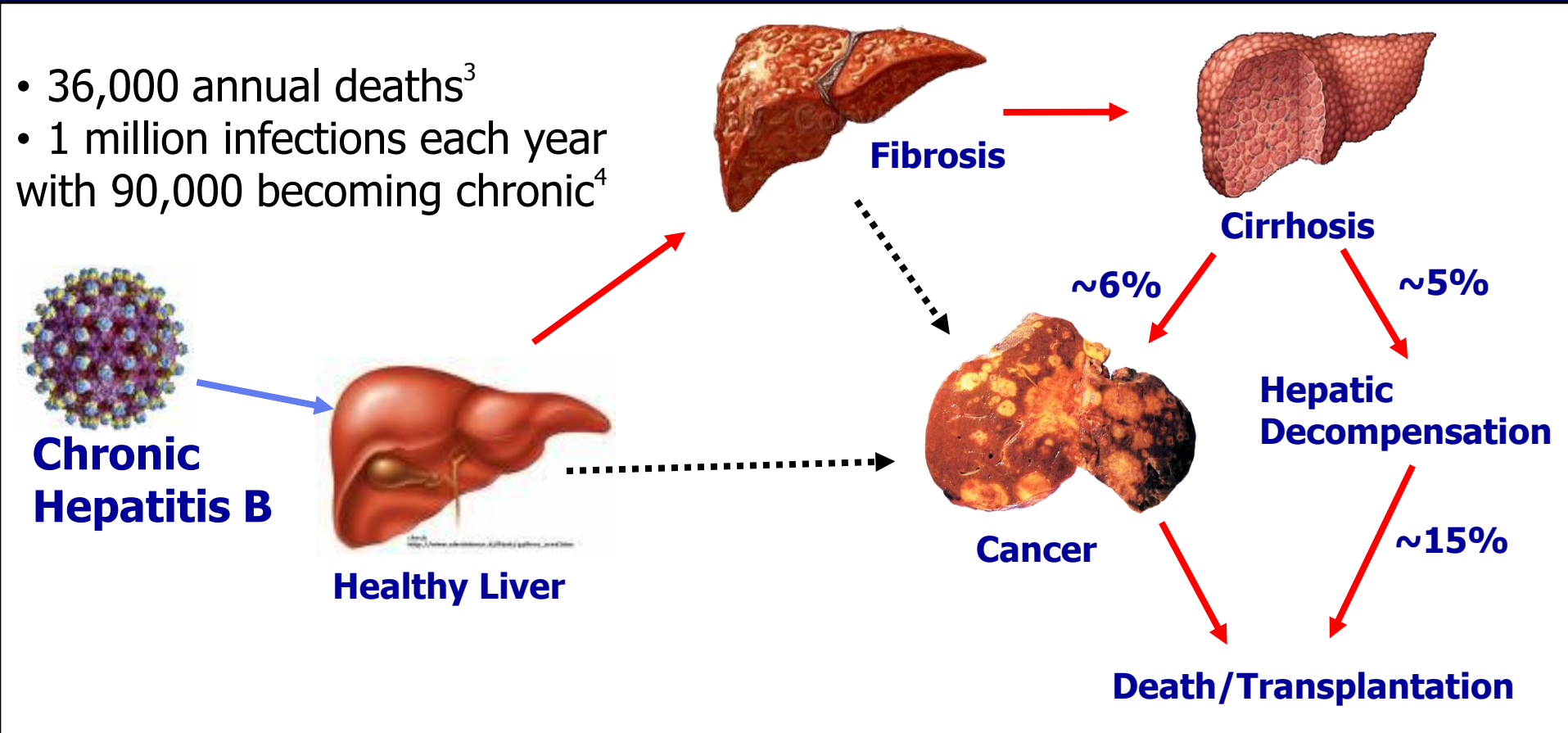
Worldwide, 350 - 370 Million Persons Have Chronic Hepatitis B Infection, Prevalence varies by Region



The stages of liver disease progression

If left untreated, the liver will deteriorate, permanently interfering with its ability to function properly and sustain life

- 36,000 annual deaths³
- 1 million infections each year with 90,000 becoming chronic⁴



Estimated annual incidence (% per year) in perinatally-acquired chronic HBV infection

Source: Liaw F-Y. *Antivir Ther* 2006;11:669-79.

Treating Chronic Hepatitis B

- Goals of Treatment are to improve quality of life and survival by preventing progression of the disease to cirrhosis, liver cancer and death
- The most potent drugs with the optimal resistance profile should be used as the treatment of choice
 - Rapid viral load suppression
 - High genetic barrier to resistance

Entecavir for NUC-naïve chronic hepatitis B patients in clinical practice: long-term effectiveness from a large multicenter cohort study in 376 patients

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Background and Aim

- Registration trials showed Entecavir (ETV) to be a safe and effective therapy for NUC-naïve patients with chronic hepatitis B
- However, the long-term effectiveness ETV in field practice patients is unknown
- Aim of the study was to assess the long-term efficacy and safety of ETV in a large cohort of NUC-naïve patients with CHB
 - This is the first study that assesses efficacy based on the new European guidelines
 - Guidelines published April 2009 in the Journal of Hepatology

Patients and methods

<u>Study</u>	retrospective/prospective cohort, multicenter (16 Italian centers)
<u>Patients</u>	376 consecutive NUC-naive patients with CHB
<u>Enrolment:</u>	2007-2008
<u>Treatment</u>	ETV 0.5 mg
<u>Follow-up</u>	21 months (5-24)
<u>Assays:</u>	HBV-DNA (LLQ 12 U/mL) ETV-resistance (INNO-LiPA HBV DR V2-3)
<u>Monitoring:</u>	every 3 months

Endpoints of the study

Efficacy

- Virological response (HBV DNA <12 U/ml)*
- Primary Non Response (<1 log decline at wk 12)*
- Partial Virological Response (HBV DNA pos at wk 48)*
- Virological breakthrough (> 1 log HBV DNA vs nadir)
- ETV resistance (rt180, 184, 202, 204, 250)
- HBeAg/HBsAg seroconversion
- ALT normalization (< ULN)

Safety

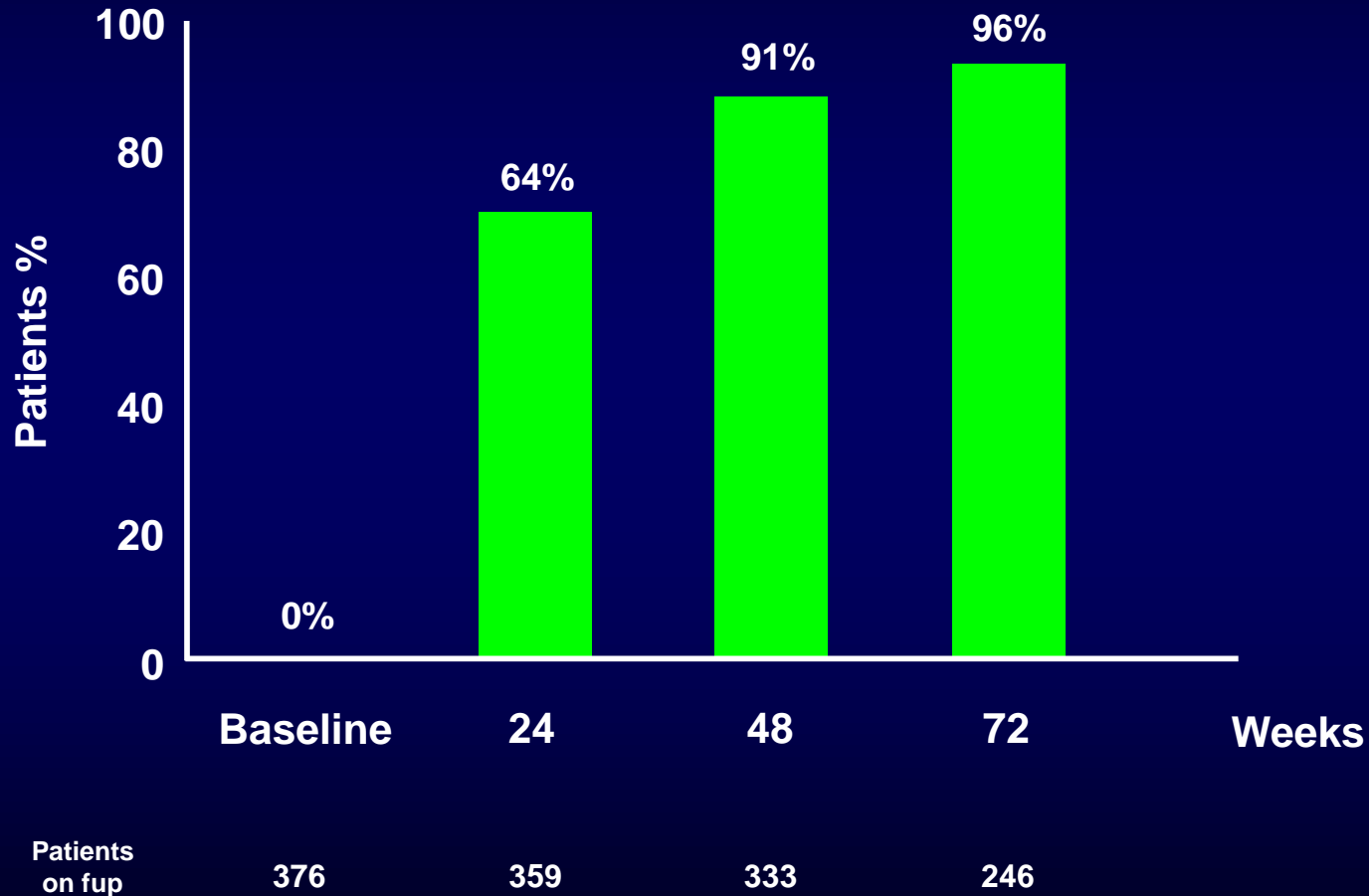
- side effects

Baseline clinical and virological characteristics of the 376 Patients

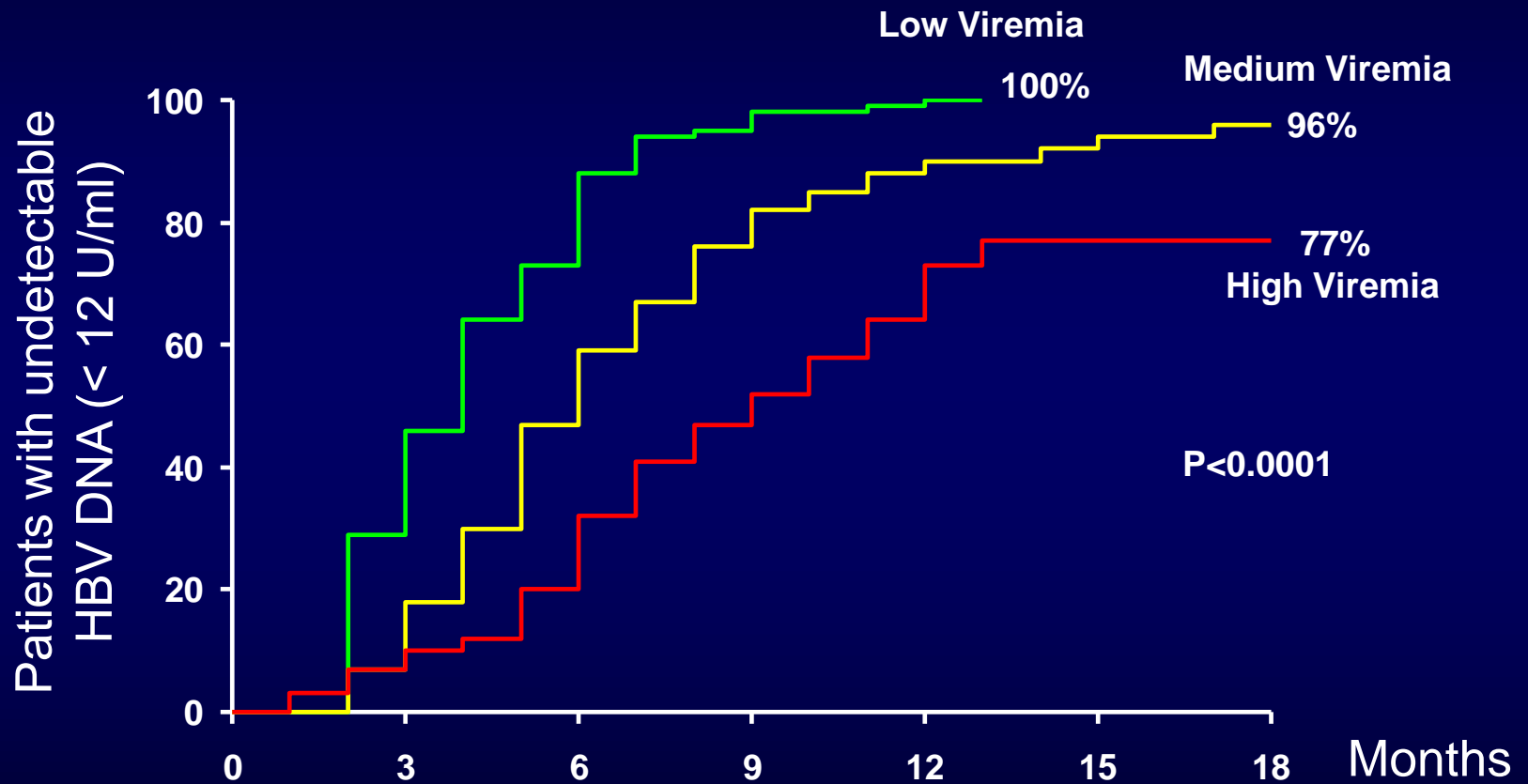
Age*	58 (18-82)
Male	283 (75%)
HBeAg negative	315 (84%)
HBV-DNA, log U/ml*	6.0 (1.5-9)
ALT, median U/ml*	89 (11-2441)
Cirrhosis	178 (47%)
BMI > 25	138/314 (44%)
Concomitant diseases	202 (54%)

* Median (range)

Virological response through week 72 (HBV DNA < 12 U/ml)

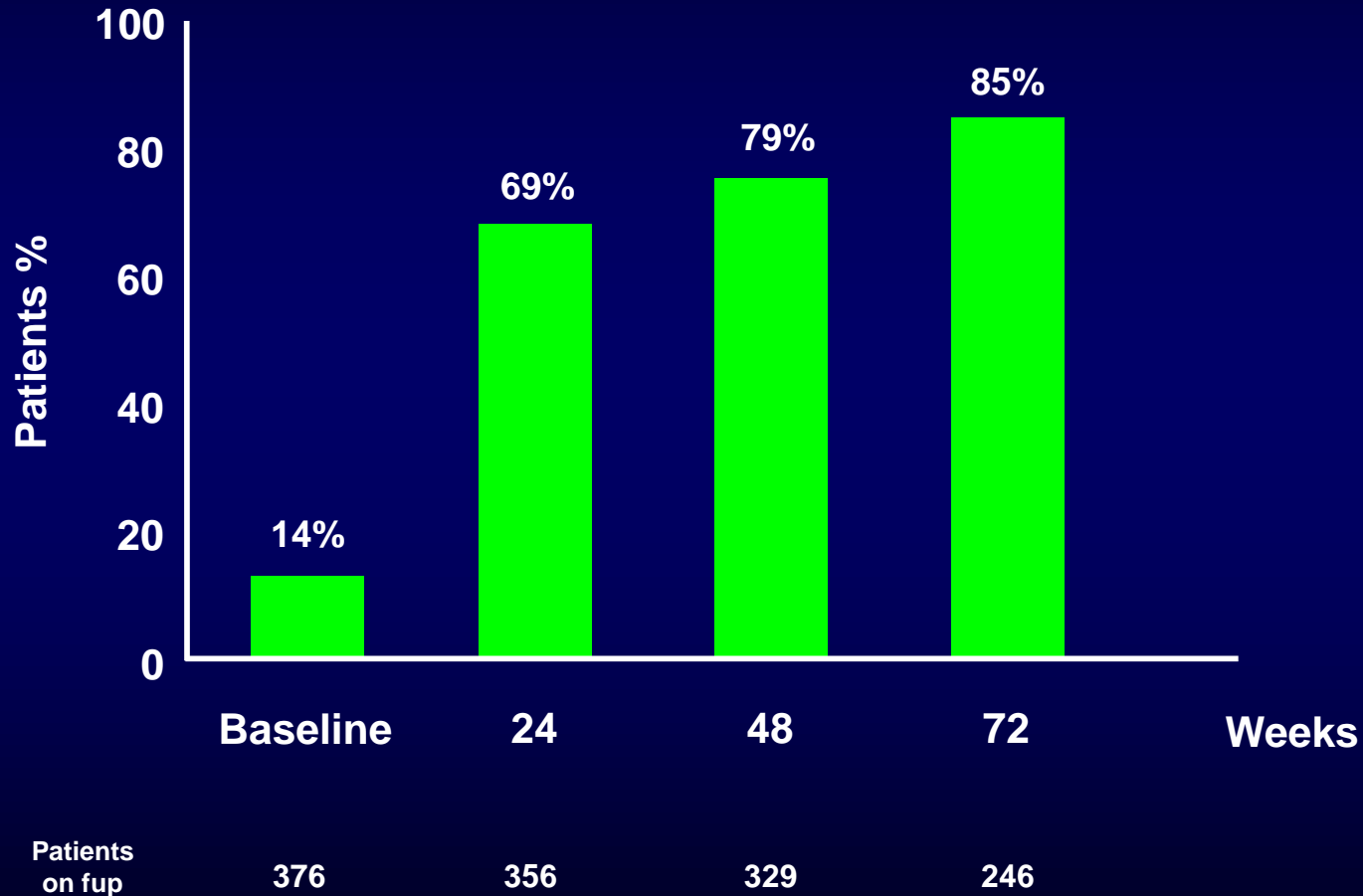


Virological response* by baseline viremia



* Kaplan-Meier estimates

Biochemical response through week 72 (Normal ALT)



New European Guidelines Efficacy Assessment: Partial Virological Responders*

**Few patients with partial response at
week 48: 30 (9%)**

- **Patients with low viremia: all cleared the virus spontaneously within few months**
- **Patients with medium viremia: approximately 50% spontaneously cleared the virus**
- **Patients with high viremia: most did not clear the virus**

* HBV DNA > 12 U at week 48 (EASL HBV Guidelines, J Hepatol 2009)

Further Results

- Few patients had a virological breakthrough: 2 patients (0.5%)
 - Likely due to poor compliance
- S antigen loss: 3 patients (0.7%) cleared HBsAg, 2 patients stopped ETV successfully
- Liver stiffness, assessed by Fibroscan in 73 patients, decreased from 9.3 (4-29) to 7.0 (5-24) KPa, independently of cirrhosis

Overall Safety

- **No serious adverse events related to ETV have been reported**
- **No patients had to withdraw from treatment due to safety reasons**

Conclusions

- **For NUC-naive patients treated in field practice for 72 weeks, ETV monotherapy showed high virological response rates, low treatment failures, progressive decline of liver stiffness and an excellent safety profile**
- **This study provides new perspectives for the management of patients in their first two years of treatment**

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