

Role of Antivirals in HCV-related HCC

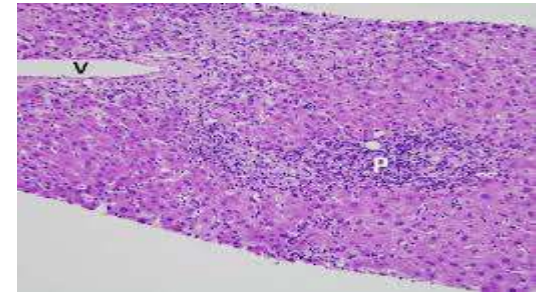
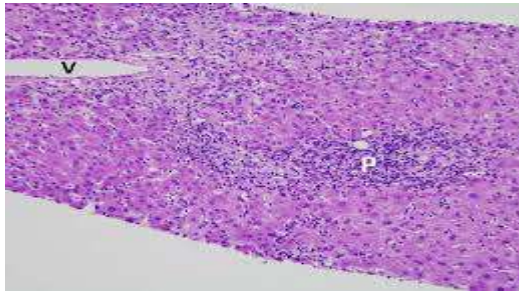
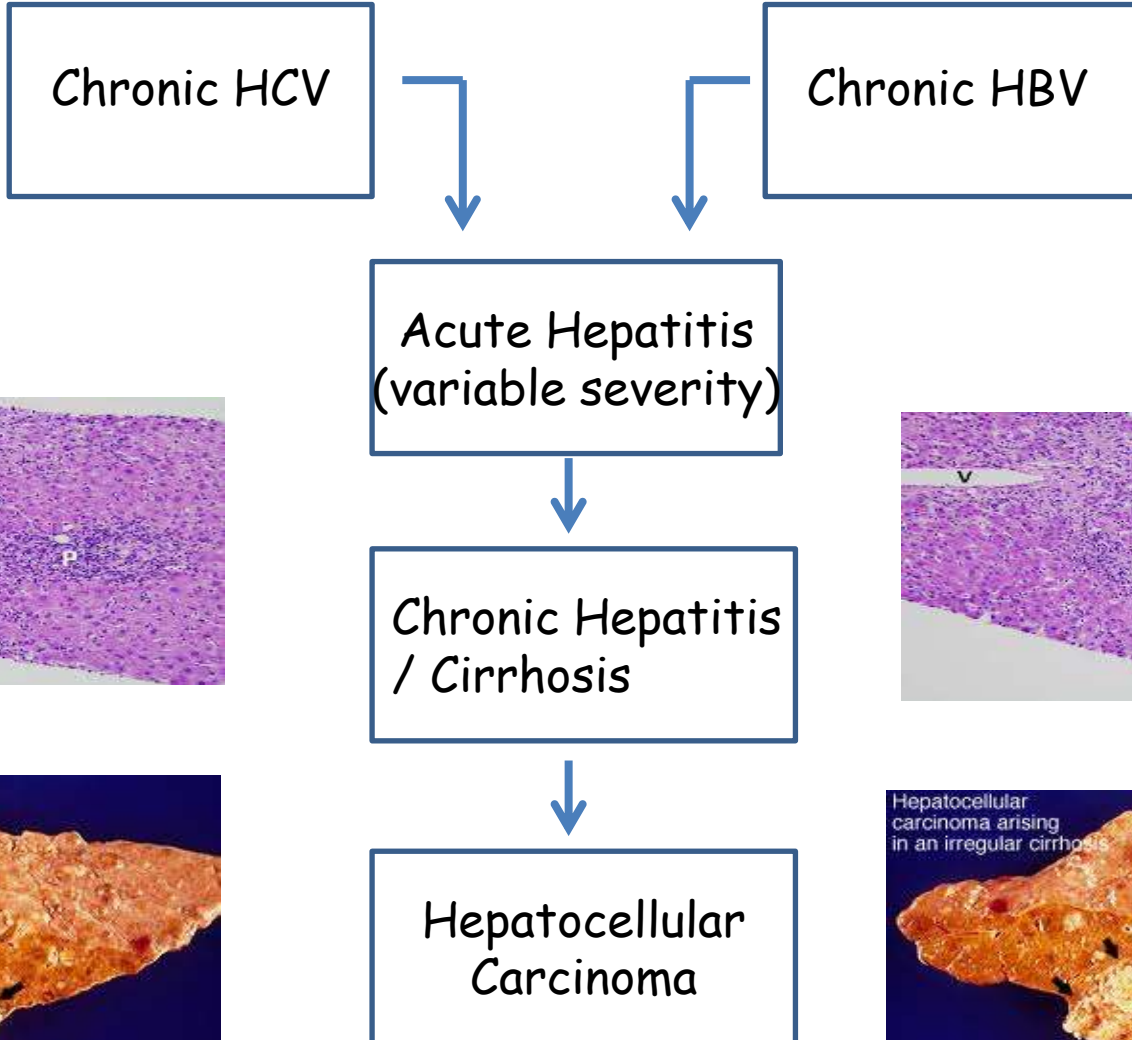
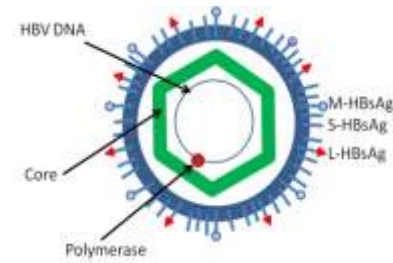
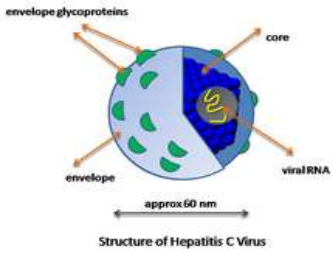
Professor Darrell HG Crawford MD FRACP

Head, School of Medicine.

The University of Queensland. Brisbane. Australia.



Pathways to HCC



Prevention of CVH Infection and Progression will Limit HCC -Related Deaths

- HCC - 6th most common cancer
- 600,000 deaths per year
- 75-80% of global HCC is attributed to CVH
- Prevention of CVH might prevent 450,000 deaths per annum from HCC
- Strong data to show that vaccination for HBV reduces HCC risk
- Difficult to prove that treatment of established CVH also reduces the risk

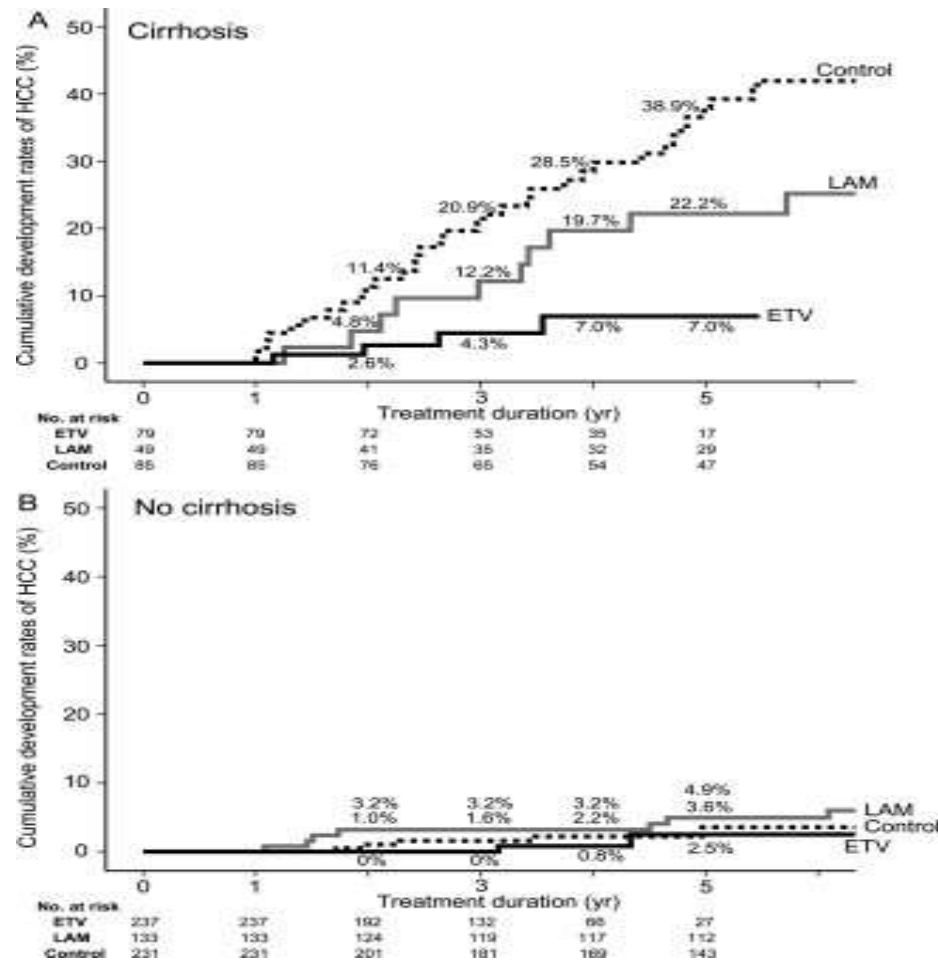
Implementation of Trials to Prove HCV Therapy Reduces Incidence of HCC is Difficult

- Progression to HCC is over decades
- Not all patients with CVH develop HCC
- Study cohort will have to be huge and followed for years
- Withholding antiviral therapy from patients in the control arm is unethical
- Rely on cohort follow up studies or retrospective analyses
- Low frequency of events has led to meta-analyses

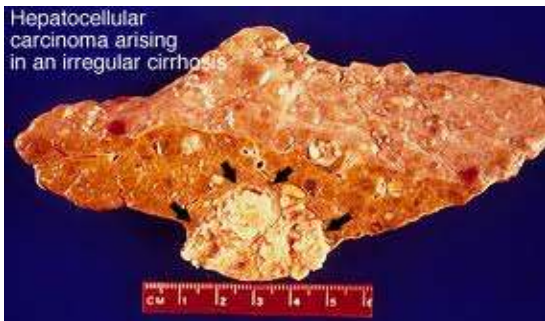
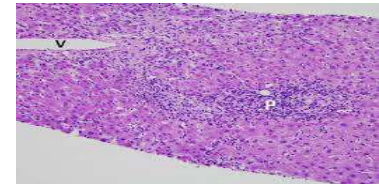
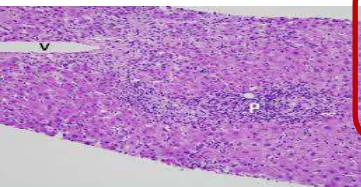
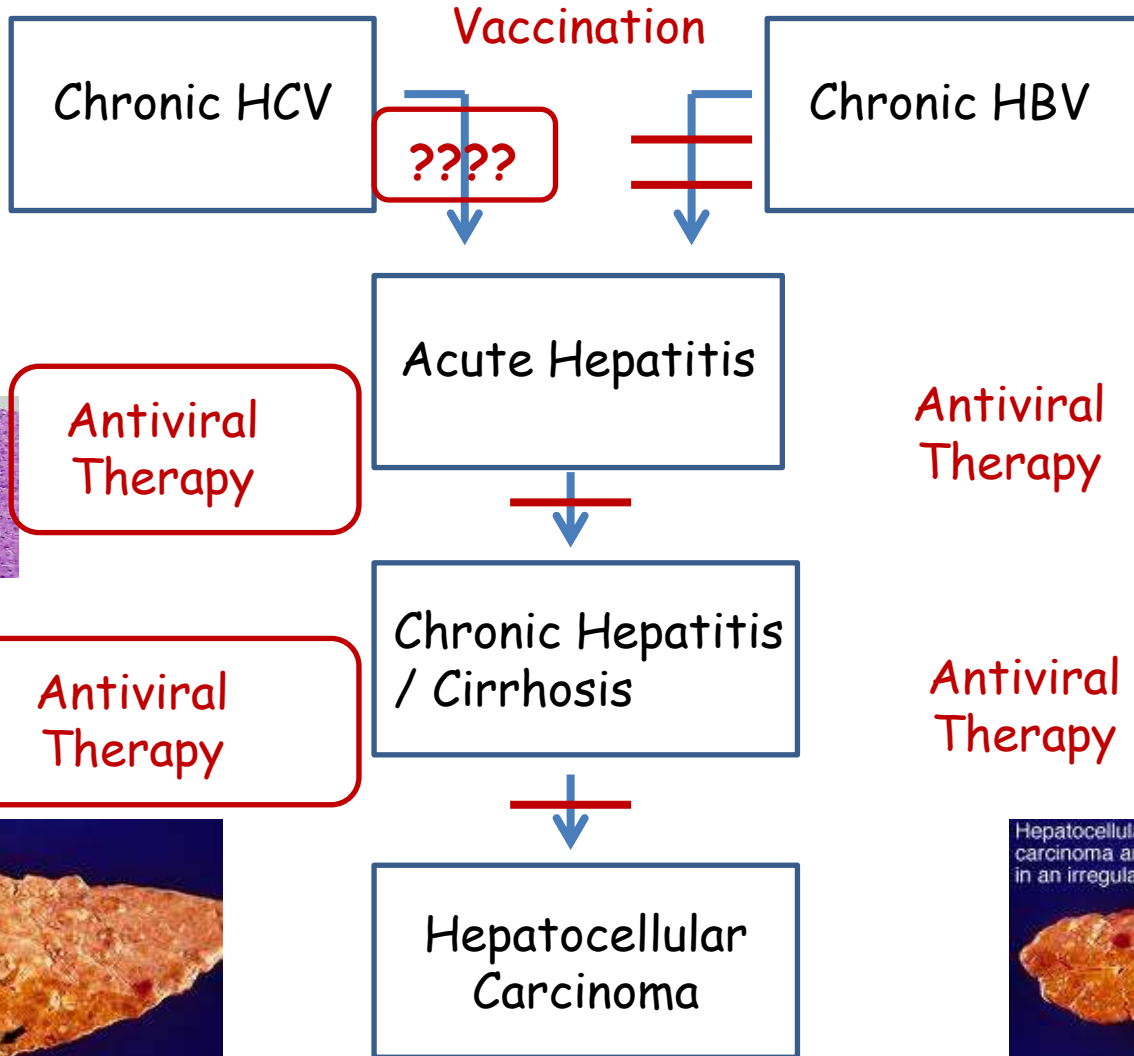
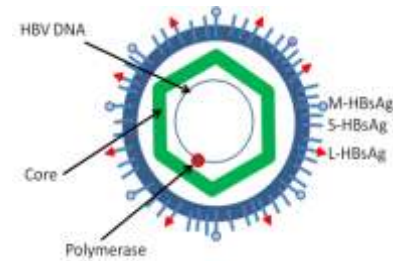
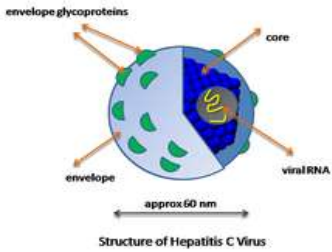
Examples for HCV from HBV Treatment and reduction in the incidence of HCC?

- Potent oral antivirals have had a major impact on treatment of this disease
- Risk of HCC is ultimately related to viral load, and given the efficacy these agents, reasonable to expect a decrease in risk of HCC

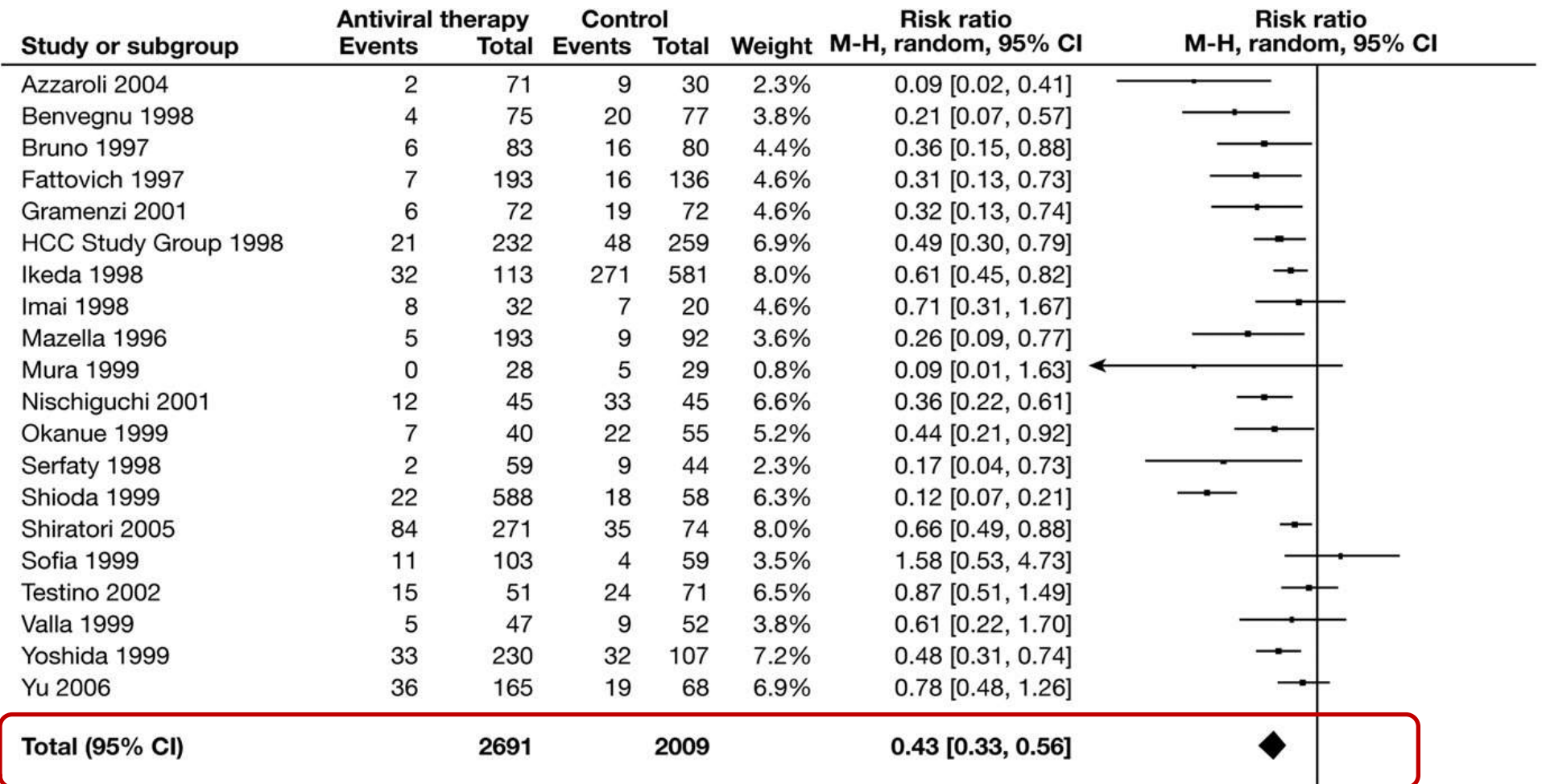
Long-term entecavir treatment reduces HCC incidence in patients with hepatitis B virus infection



Prevention of HCC



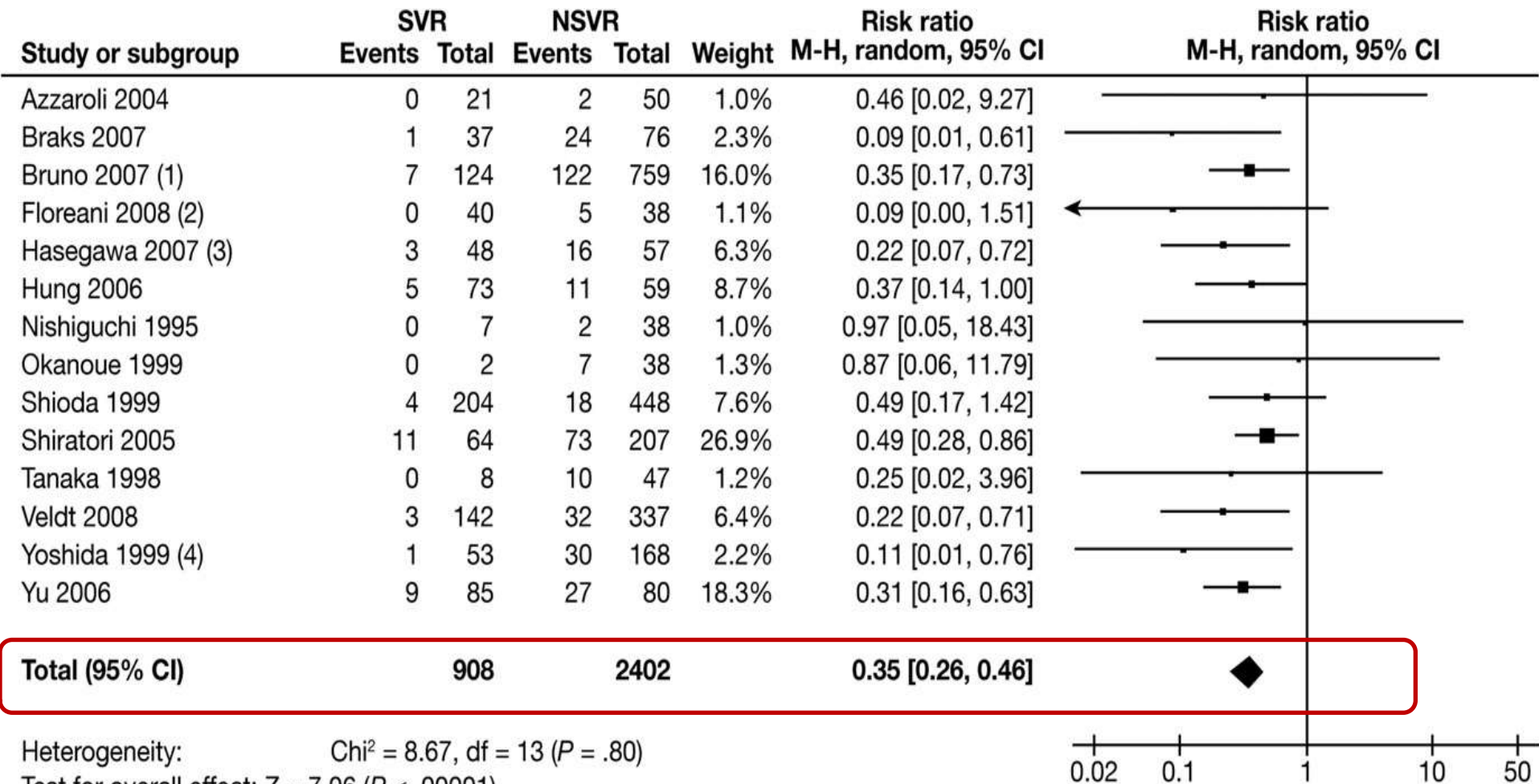
Chronic Hepatitis C and HCC Meta-Analysis: Treated vs Non Treated Patients



Heterogeneity: Chi² = 59.10, df = 19 (*P* < .00001)
 Test for overall effect: Z = 6.27 (*P* < .00001)

0.02 0.1 1 10 50
 Favours experimental Favours control

Chronic Hepatitis C: SVR vs Non-SVR in Treated Patients



(1) NSVR patients were retreated with SVR in 38 leaving 759 patients with NSVR

(2) 9 patients with NSVR lost to follow-up

(3) 18 patients continued to receive treatment and could not be evaluated for response

(4) 9 patients with NSVR lost to follow-up

Risk Factors for HCV-Related HCC

- Older Age
- Male Gender
- Black Race
- **Cirrhosis**
- Advanced Fibrosis
- HBV Coinfection
- Diabetes
- Alcohol
- Cigarettes

Risk of HCC Following SVR in Patients with Cirrhosis

Retrospective Study

	Number	Patient Years	No of HCC	Rate /100 patient years	Rate Ratio
No SVR	759	5805	122	2.106	3.12
SVR	124	1055	7	0.66	

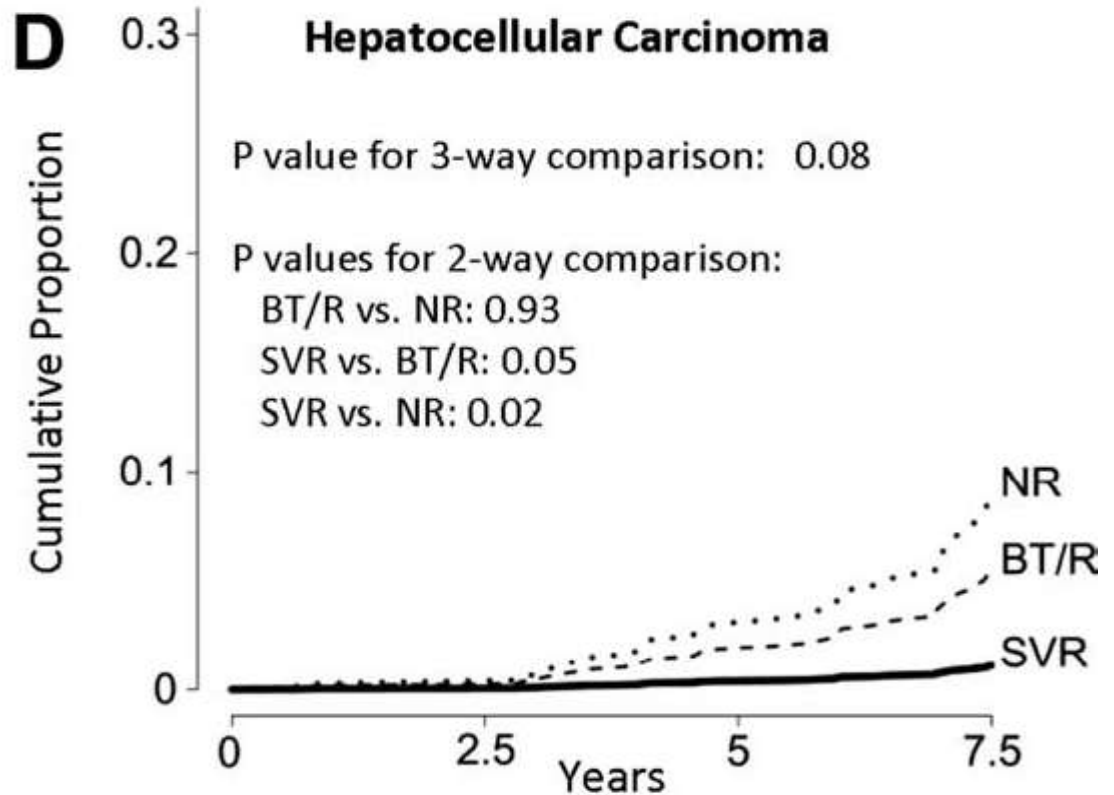
Bruno et al. Hepatology 2007

HALT C Study:

Risk decreased but persists in patients with \geq F3

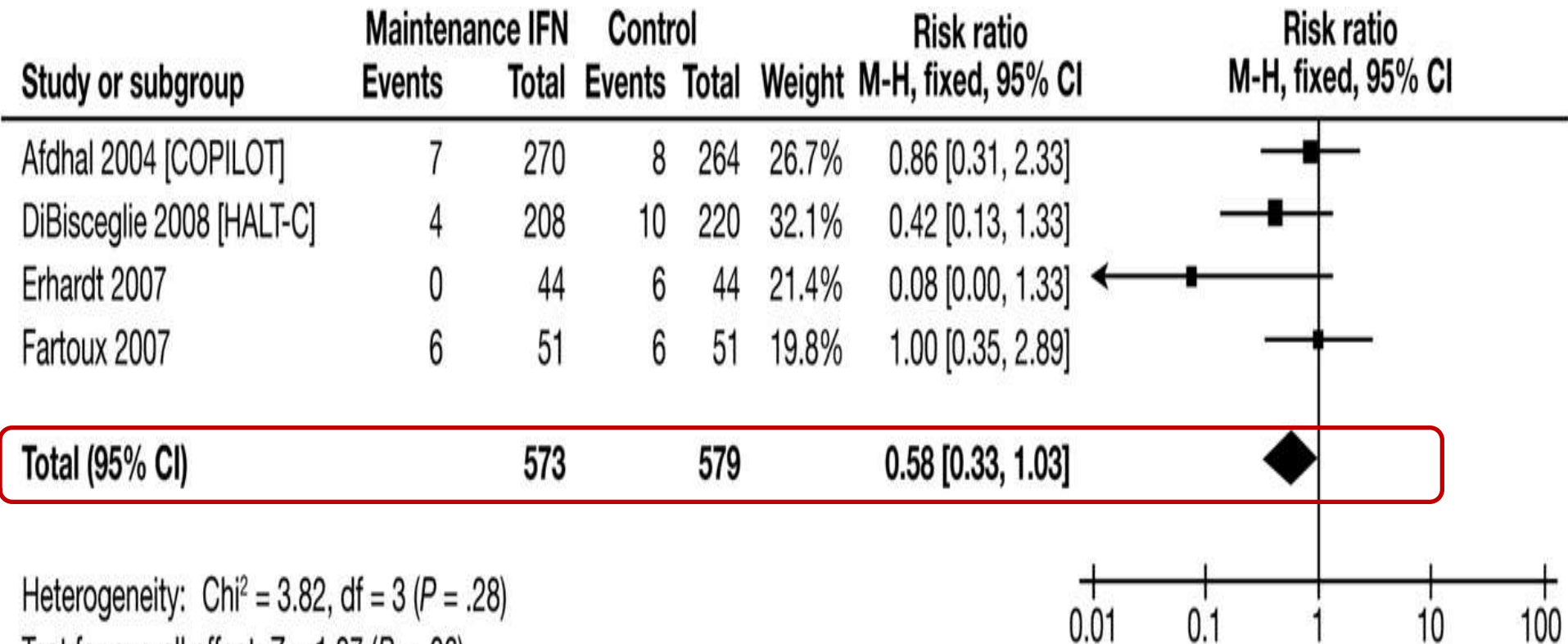
Outcome of sustained virological responders with histologically advanced chronic hepatitis C

	SVR	BT/R	NR
HCC	1.4%	6.5%	9.1%

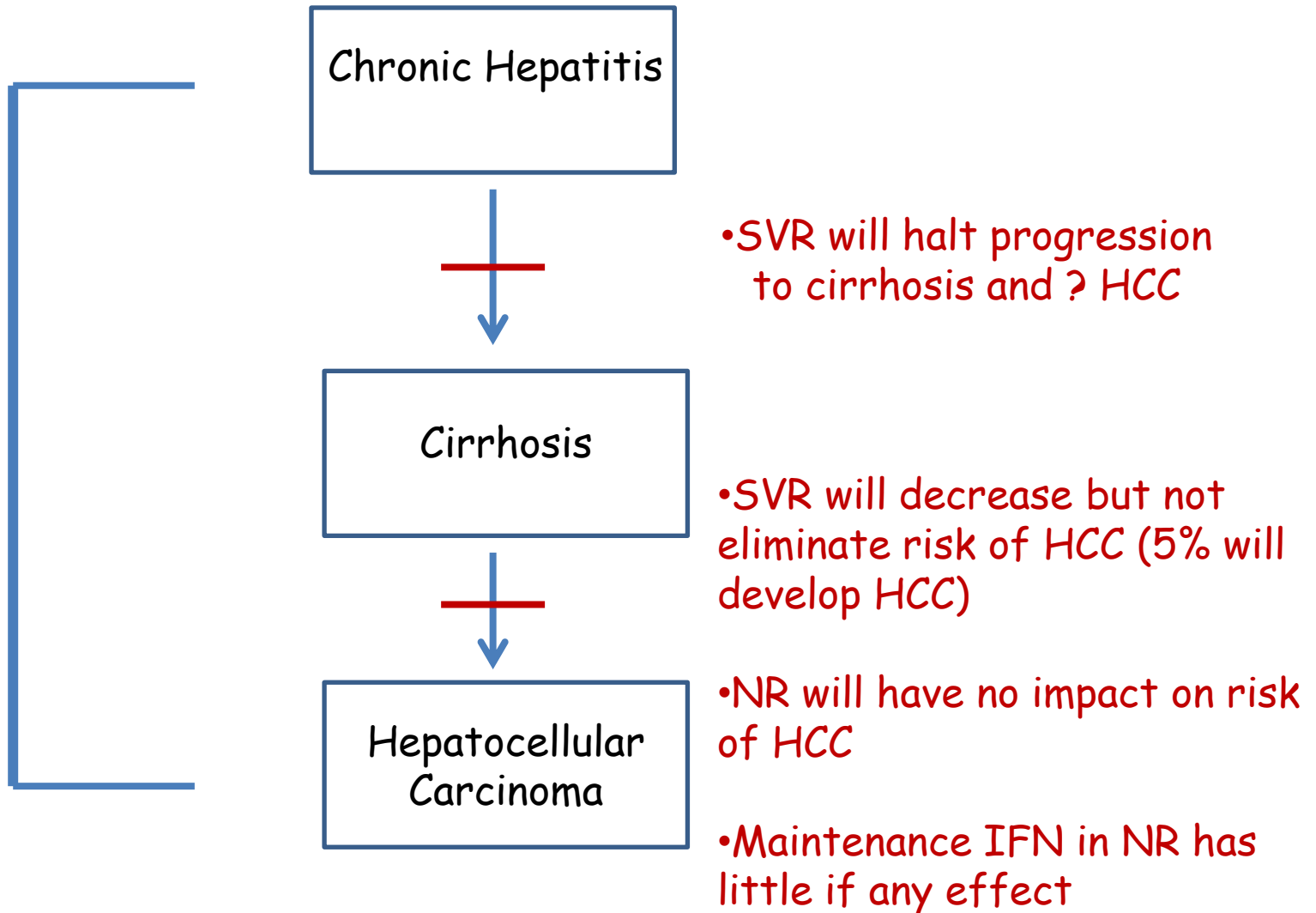


Morgan et al. HEPATOLOGY. 2010

Maintenance Interferon



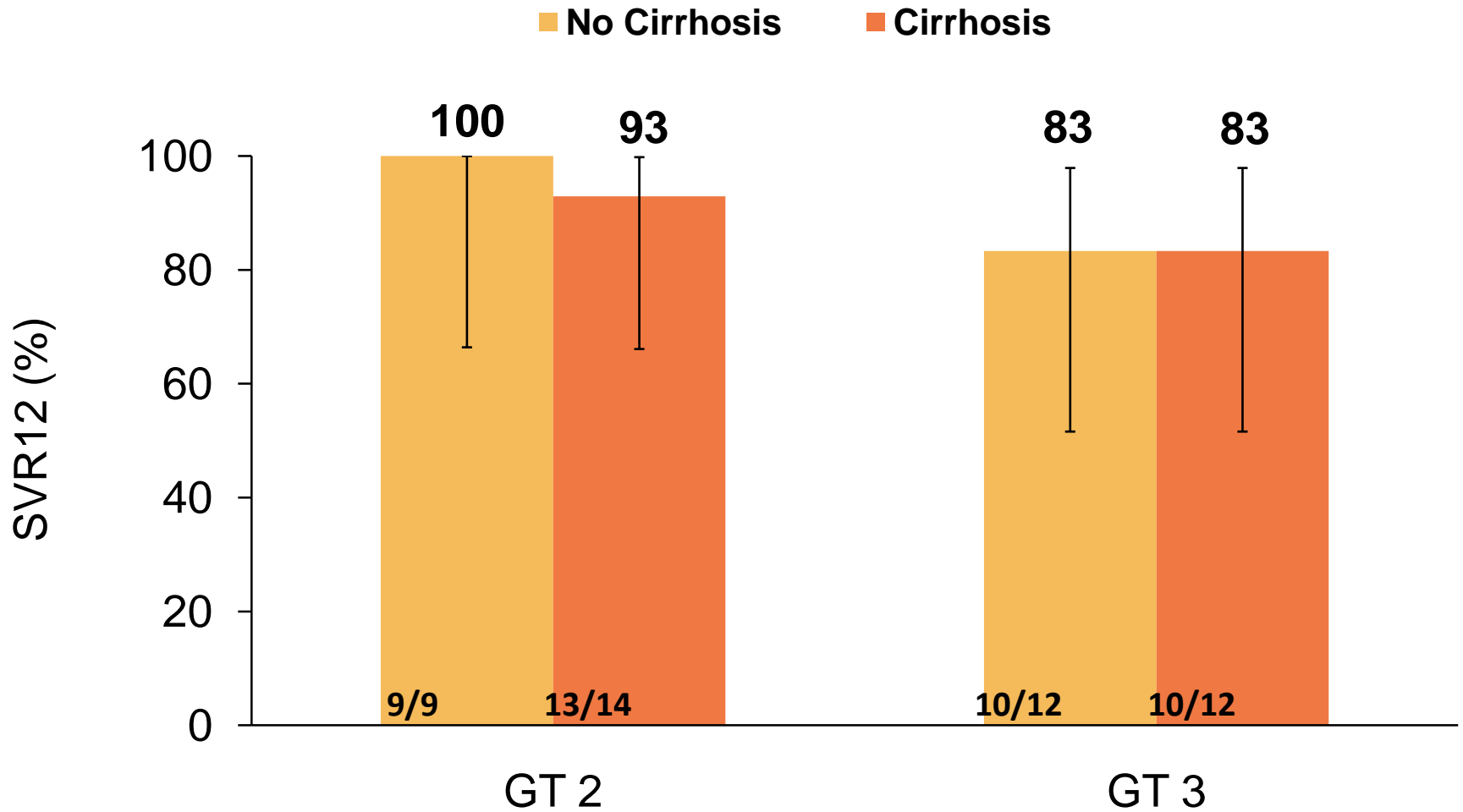
Does HCV Treatment Prevent HCC



The New Era of DAAS

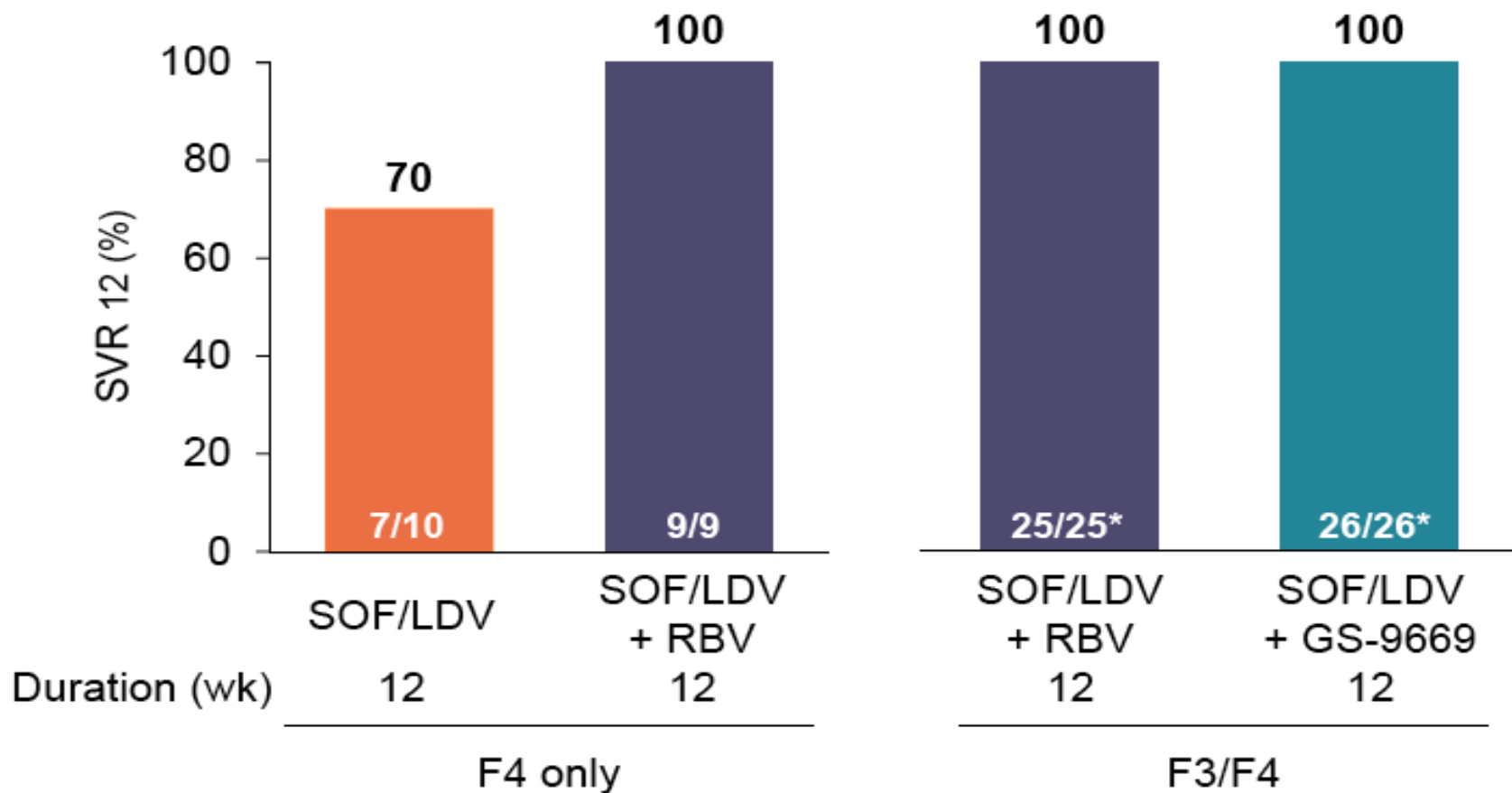
Effective in patients with
cirrhosis

Sofosbuvir/Peg IFN/RVN: SVR12 by Cirrhosis Status



Error bars represent 95% confidence intervals.

SVR12 Results: GT 1 Treatment-Experienced Patients with Advanced Fibrosis/Cirrhosis



*From ELECTRON 2. SOF Nuc Polym Inhib, Ledipasvir NS5A, GS9669 NonNuc Inhib Gane et al. AASLD 2013

The New Era of DAAS

- Effective in patients with cirrhosis
- Uptake likely to be high where funded
- Safe to presume that the effect of DAAs on incidence of HCC in HCV will mimic that of HBV

Advances in antiviral therapy for HCV will have a major impact on the incidence of HCC