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Highlights – Was ist neu für die Praxis?

Hepatitis C

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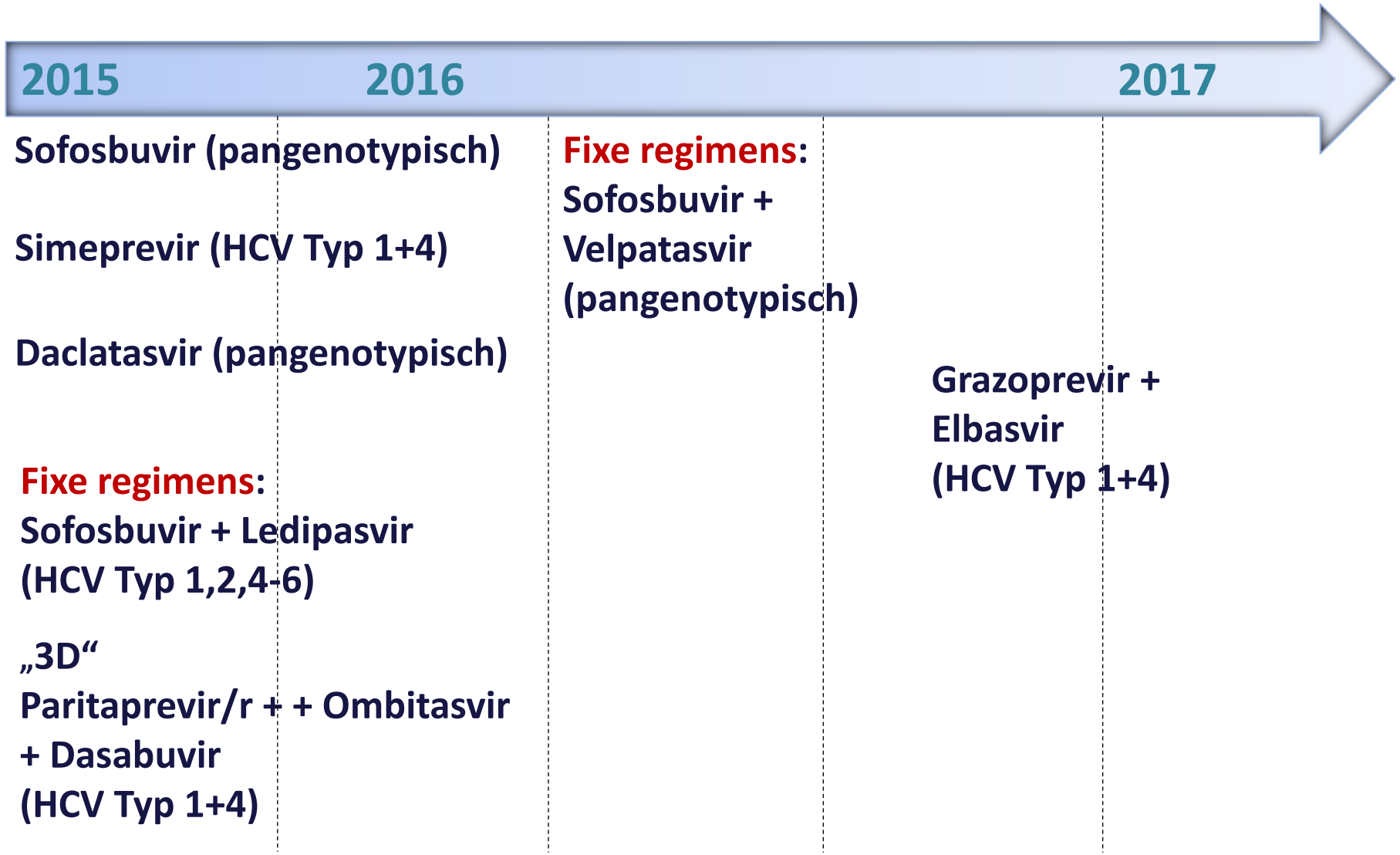
Zugelassene DAAs in Deutschland



Zugelassene DAAs in Deutschland

Sofosbuvir (pangenotypisch)

Simeprevir (HCV Typ 1+4)

Fixe regimens:
Sofosbuvir +
Velpatasvir
(pangenotypisch)

Heilungsraten in Studien und „real-world“ ≥ 95%

(HCV Typ 1,2,4-6)

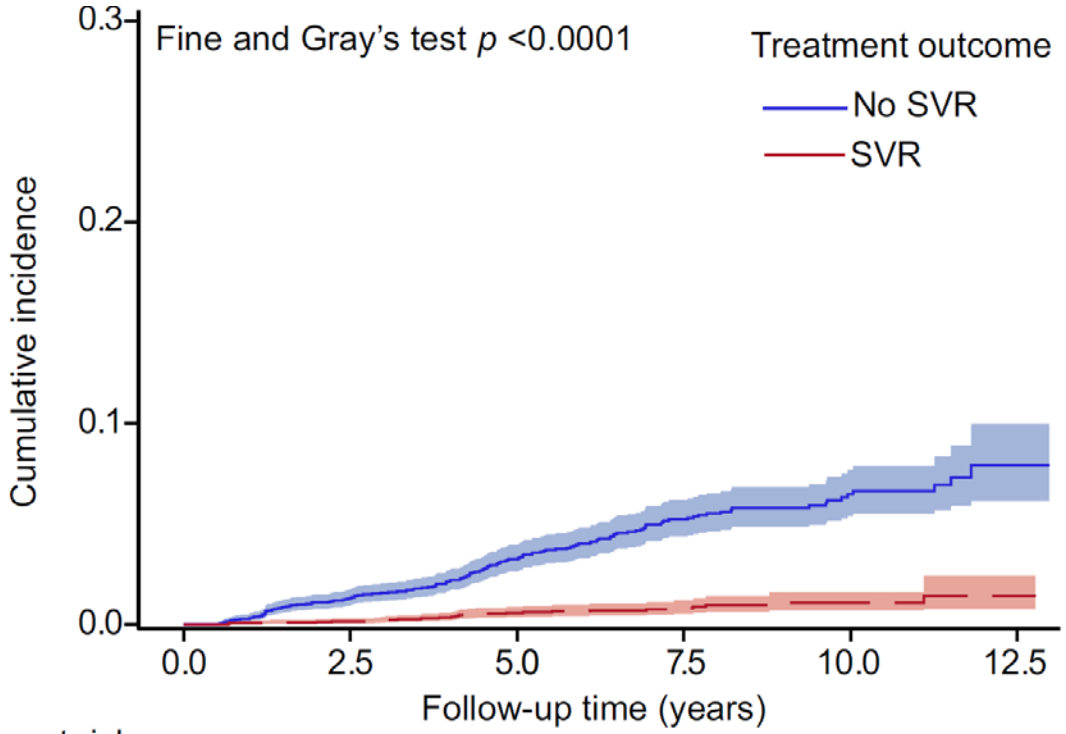
„3D“
Paritaprevir/r + + Ombitasvir
+ Dasabuvir
(HCV Typ 1+4)

Neue Leitlinien: DGVS und EASL
Empfehlungen zur Behandlung der Hepatitis C

Combination regimen	Genotype 1	Genotype 2	Genotype 3	Genotype 4	Genotypes 5 and 6
Sofosbuvir + ribavirin	No	Suboptimal	Suboptimal	No	No
Sofosbuvir/ledipasvir ± ribavirin	Yes	No	No	Yes	Yes
Sofosbuvir/velpatasvir ± ribavirin	Yes	Yes	Yes	Yes	Yes
Ombitasvir/paritaprevir/ritonavir + dasabuvir ± ribavirin	Yes	No	No	No	No
Ombitasvir/paritaprevir/ritonavir ± ribavirin	No	No	No	Yes	No
Grazoprevir/elbasvir ± ribavirin	Yes	No	No	Yes	No
Sofosbuvir + daclatasvir ± ribavirin	Yes	Yes	Yes	Yes	Yes
Sofosbuvir + simeprevir ± ribavirin	Suboptimal	No	No	Yes	No

HCC Risiko und SVR

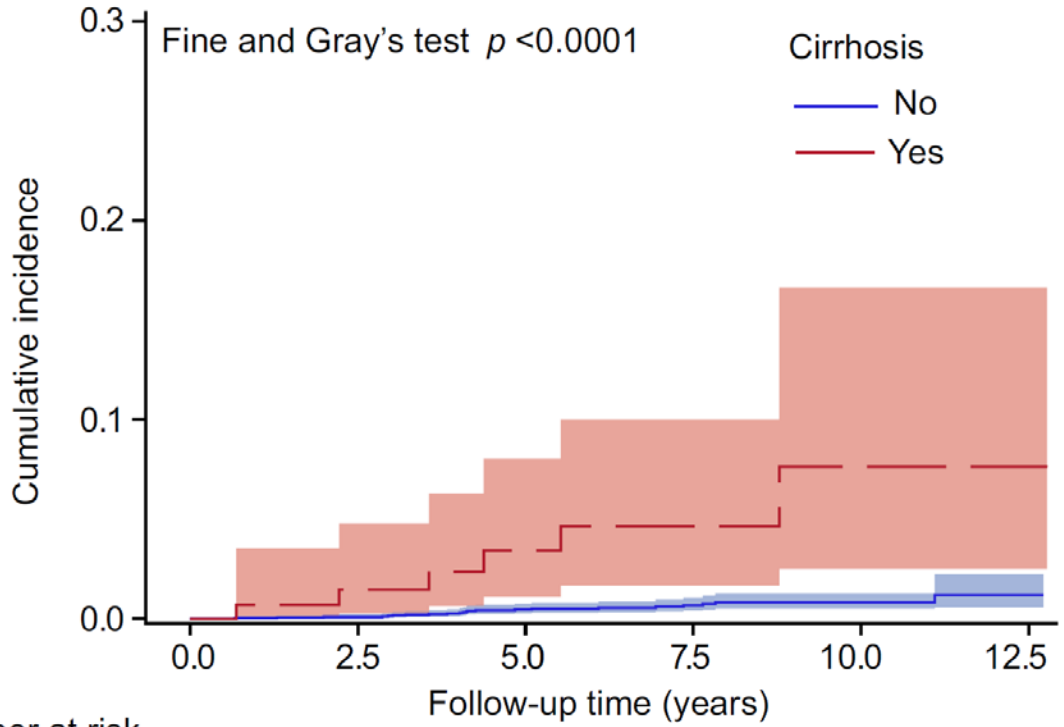
Bedeutung der SVR für das HCC Risiko



Number at risk

SVR	4663	3788	2637	1453	518	10
No SVR	3454	2778	1939	1152	478	26

Bedeutung der Cirrhose für das HCC Risiko nach SVR

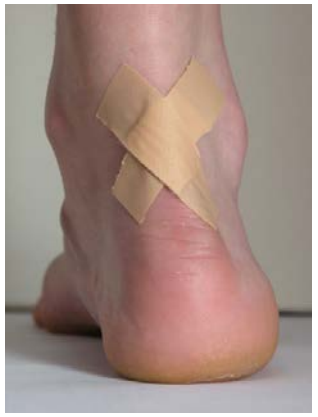


Number at risk

Cirrhosis	145	122	81	52	20	2
No cirrhosis	4518	3666	2556	1401	498	8

Janjua NZ et al J Hepatol 2017; 66: 504

Resistenzen



Die Achillesferse der Interferon-freien DAA Therapie

The importance of resistance to direct antiviral drugs in HCV infection in clinical practice

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The next HCV regimens?

Anforderungen:

Pangenotypisch

SVR stabil ≥ 98%

Wirksam bei NS5A Resistenz

Wirksam bei HCV Typ 3 Cirrhose

8 Wochen bei „unkomplizierter“ Infektion

Sicher – auch bei Niereninsuffizienz

1 Tablette pro Tag

Nächste Generation von NS5A und NS3A/4a Inhibitoren

Next Generation Direct-Acting Antivirals

Glecaprevir
(formerly ABT-493)
pangenotypic NS3/4A protease inhibitor

Collectively: G/P

Pibrentasvir
(formerly ABT-530)
pangenotypic NS5A inhibitor

In vitro:[1,2]

- High barrier to resistance
- Potent against common NS3 polymorphisms (eg, positions 80, 155, and 168) and NS5A polymorphisms (eg, positions 28, 30, 31 and 93)
- Additive/synergistic antiviral activity

Clinical PK & metabolism:

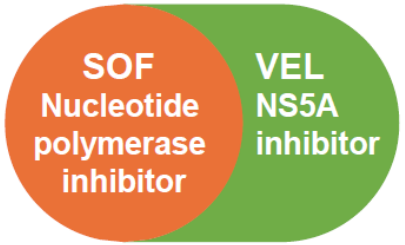
- Once-daily oral dosing
- Minimal metabolism and primary biliary excretion
- Negligible renal excretion (<1%); no dose adjustment for CKD[3]

G/P is coformulated and dosed once daily as three 100 mg/40 mg pills for a total dose of 300 mg/120 mg
Glecaprevir was identified by AbbVie and Enanta

1. Ng TI, et al. Abstract 636. CROI, 2014.
2. Ng TI, et al. Abstract 639. CROI, 2014.
3. Kosloski M, et al. Abstract THU-230. EASL 2016.

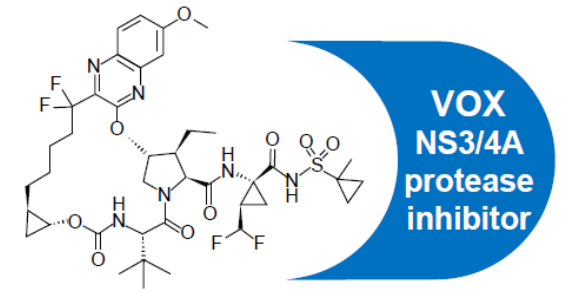
Zeuzem S et al. Hepatology 2016; 64 (Suppl) 132A

Neue pangenotypische Sofosbuvir Triple Therapie – POLARIS Studien



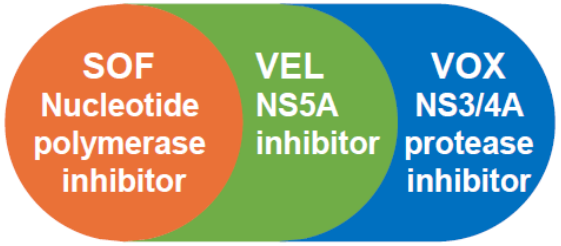
Sofosbuvir (SOF)/Velpatasvir (VEL)

- **SOF**: Nucleotide polymerase inhibitor with activity against HCV GT 1–6
- **VEL**: Potent pangenotypic NS5A inhibitor



Voxilaprevir (VOX)

- HCV NS3/4A PI with potent antiviral activity against GT 1–6, including most RASs



SOF/VEL/VOX

- Once daily, oral, fixed-dose combination (400/100/100 mg) for GT 1–6

Foster GR et al. Hepatology 2016; 64 (Suppl) Abstract (AASLD 2016)

Cure for all HCV-infected patients – a tailored strategy

Treatment duration		Disease characteristics
	Easy-to-treat	
(6-) 8 weeks		No advanced fibrosis, no co-morbidities, tx-naive
12 weeks		Compensated cirrhosis HCV type 3
12 (-24) weeks + ribavirin	Difficult-to-treat	Decompensated cirrhosis, DAA failure, Type 3 cirrhosis plus BL NS5A RAVs

Cure for all HCV-infected patients – a tailored strategy