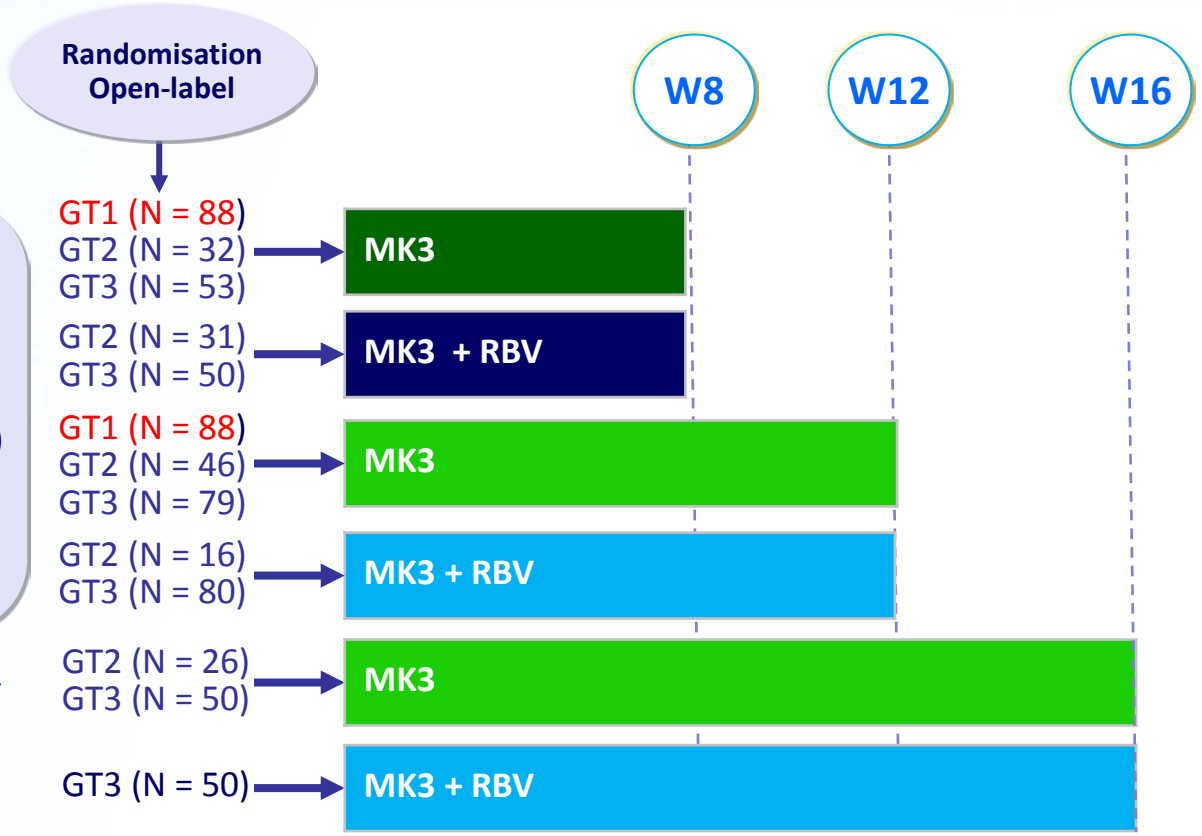
C-CREST study, Part B: uprifosbuvir (MK-3682)/GZR/ruzasvir (MK-8408) fixed-dose combination ± RBV for genotypes 1, 2 and 3 - Phase II

HCV-trials.com

Design

≥ 18 years
Chronic HCV infection
Genotype 1, 2 or 3
Treatment-naïve (GT1 or GT2)
Treatment-naïve or PEG-IFN failure (GT3)
HCV RNA ≥ 10 000 IU/mL
Compensated cirrhosis allowed *
No HBV co-infection

* Liver biopsy or Fibroscan® > 12.5 kPa or Fibrotest® ≥ 0.75 + APRI > 2



– Uprifosbuvir 225 mg/GZR 50 mg/ruzasvir 30 mg FDC (MK3) = 2 tablets QD

Objective

– Primary endpoint: SVR_{12} (HCV RNA < 15 IU/mL), full analysis set (patients having received ≥ 1 dose of study drug)

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Baseline characteristics

	Genotype 1 N = 176	Genotype 2 N = 151	Genotype 3 N = 337
Median age, years	55	57	52
Female, %	39	43	41
Race, white, %	89	89	90
HCV genotype 1a / 1b, %	51 / 49	-	-
Metavir F4, %	43	38	35
HCV RNA log_{10} IU/mL, median	6.2	6.4	6.3
Treatment-naïve, % PEG-IFN experienced, %	100 0	100 0	56 44
HIV co-infection, %	6	3	4

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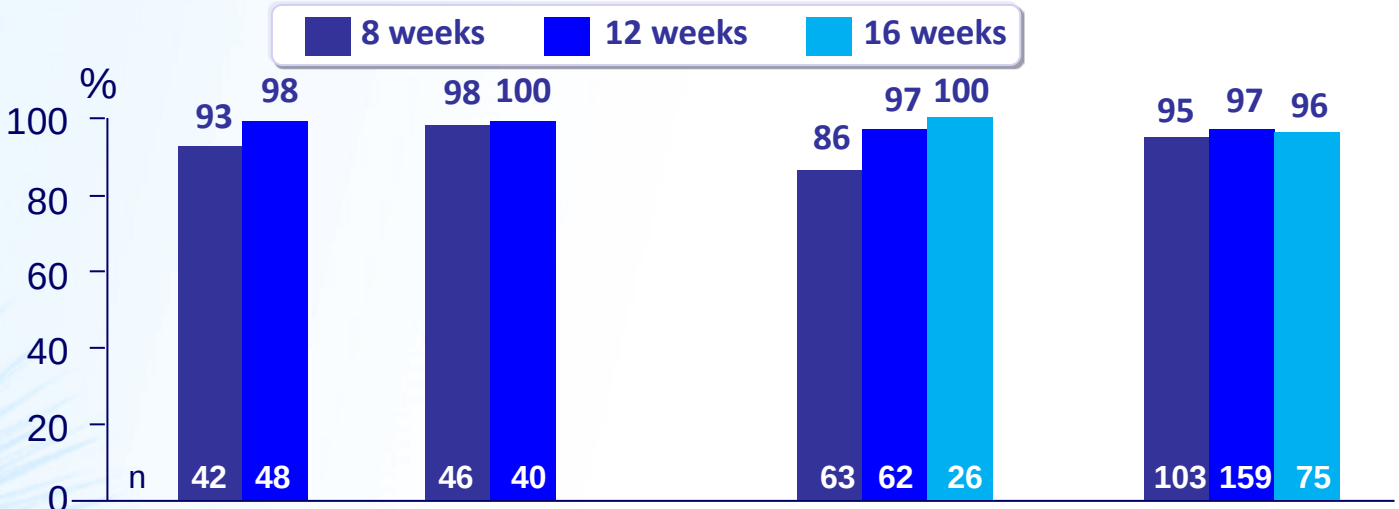
SVR_{12} (Full Analysis Set)



Relapse	**2**	**0**		**1**	**0**		**7**	**0**	**0**	**4**	**3**	**2**
Discontinuation (DR-AE)*	**0**	**0**		**0**	**0**		**1**	**0**	**0**	**0**	**0**	**0**
Reinfection*	**1**	**0**		**0**	**0**		**0**	**0**	**0**	**0**	**0**	**0**
Non-virologic failure*	**0**	**1**		**0**	**0**		**1**	**2**	**0**	**1**	**1**	**1**

*Genotype 1a 8W, No RBV: 1 patient achieved SVR_8 but was reinfected with a different HCV strain at FW12
Genotype 1a 12W, No RBV: 1 patient died due to study-drug unrelated bacterial sepsis
Genotype 2 8W + RBV: 1 patient discontinued at D5 due to drug-related AEs of fatigue, malaise; 1 patient lost to FU
Genotype 2 12W, No RBV: 2 patients lost to follow-up
Genotype 3 8W + RBV: 1 patient lost to follow-up
Genotype 3 12W, No RBV: 1 patient withdrew due to pregnancy, lost to follow-up
Genotype 3 16W: 1 patient lost to follow-up

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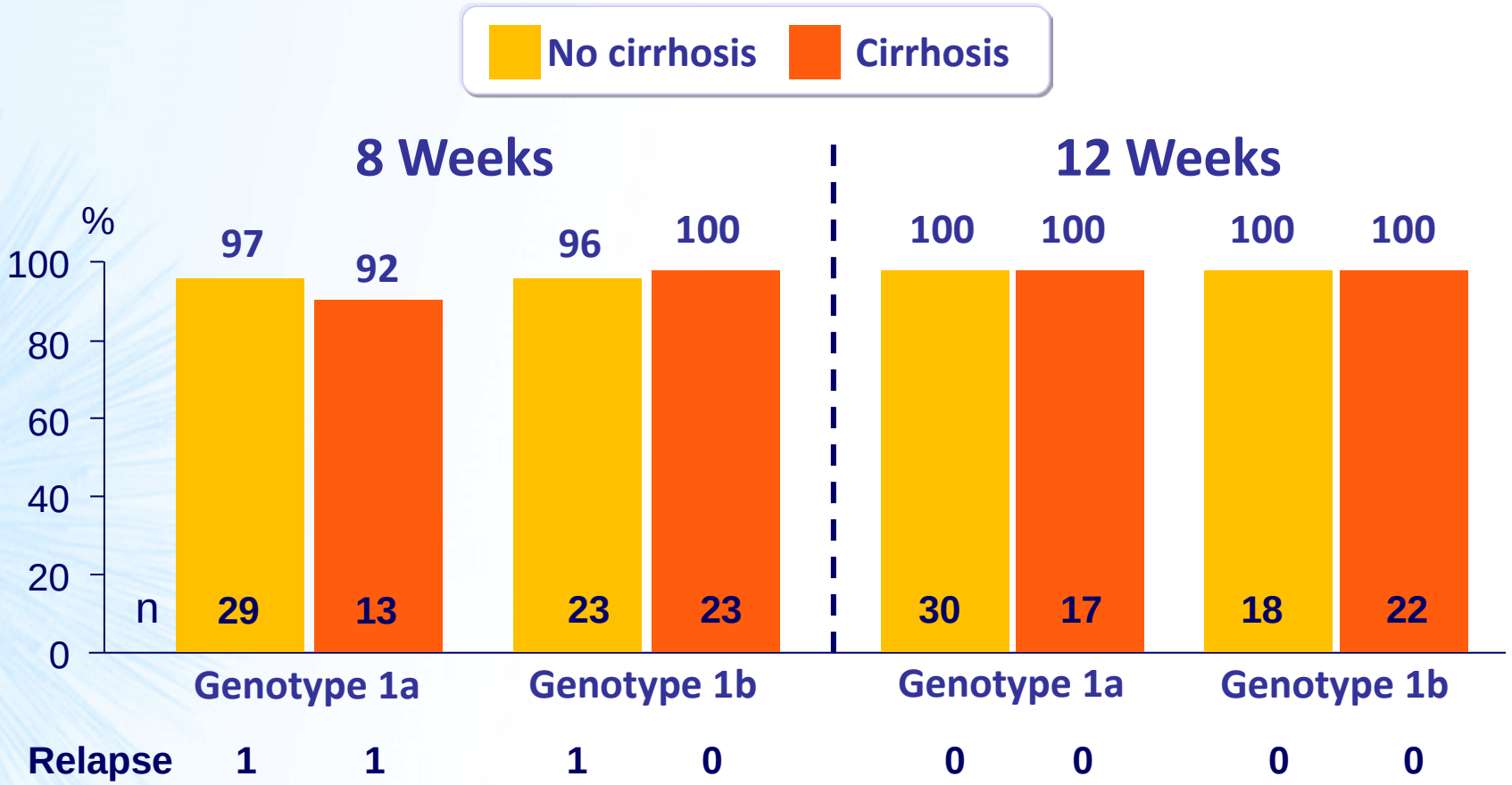
SVR_{12} (per protocol), genotype 1 patients with or without cirrhosis



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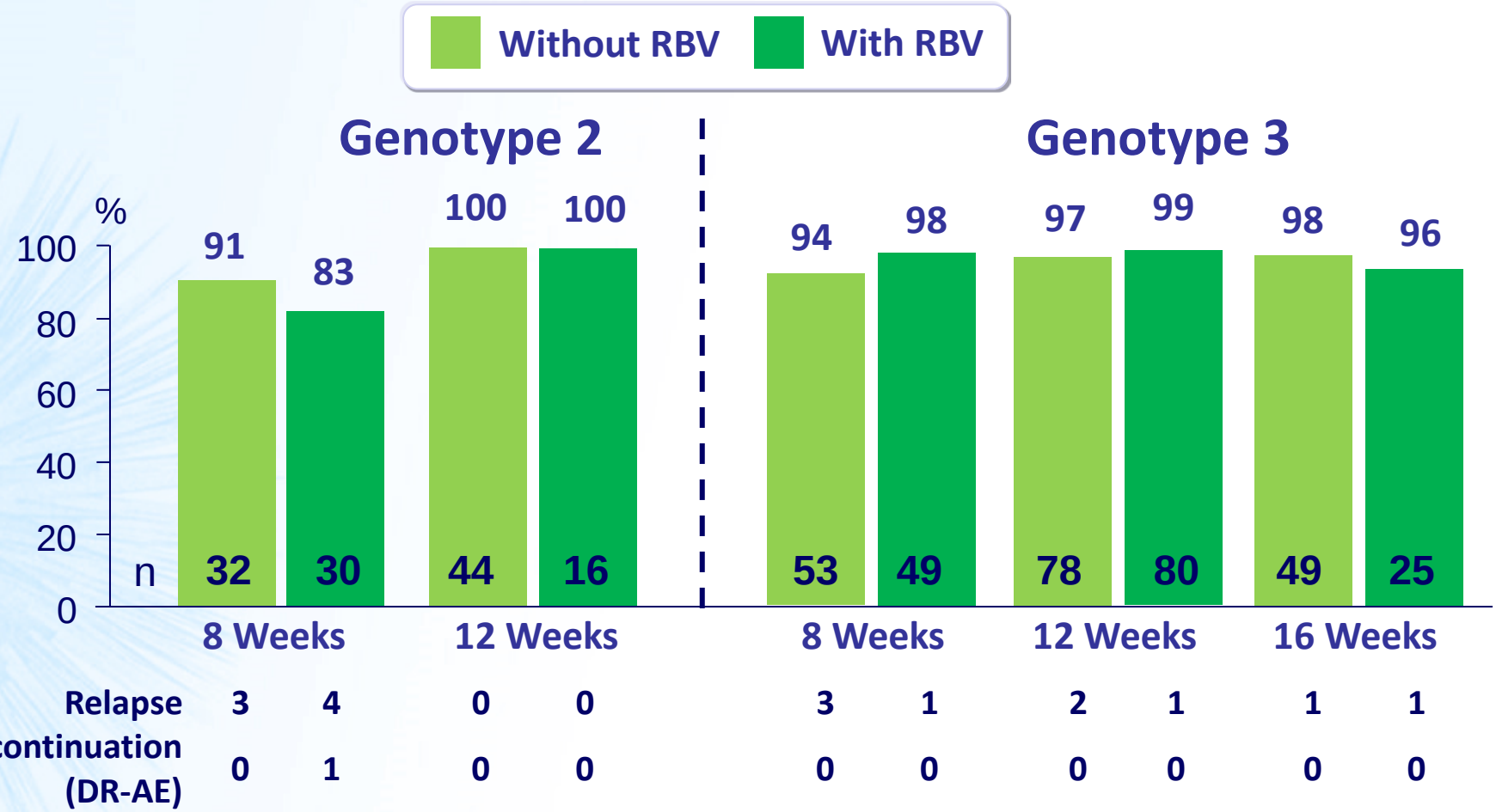
SVR_{12} (per protocol), genotype 2 or 3 or patients ± RBV



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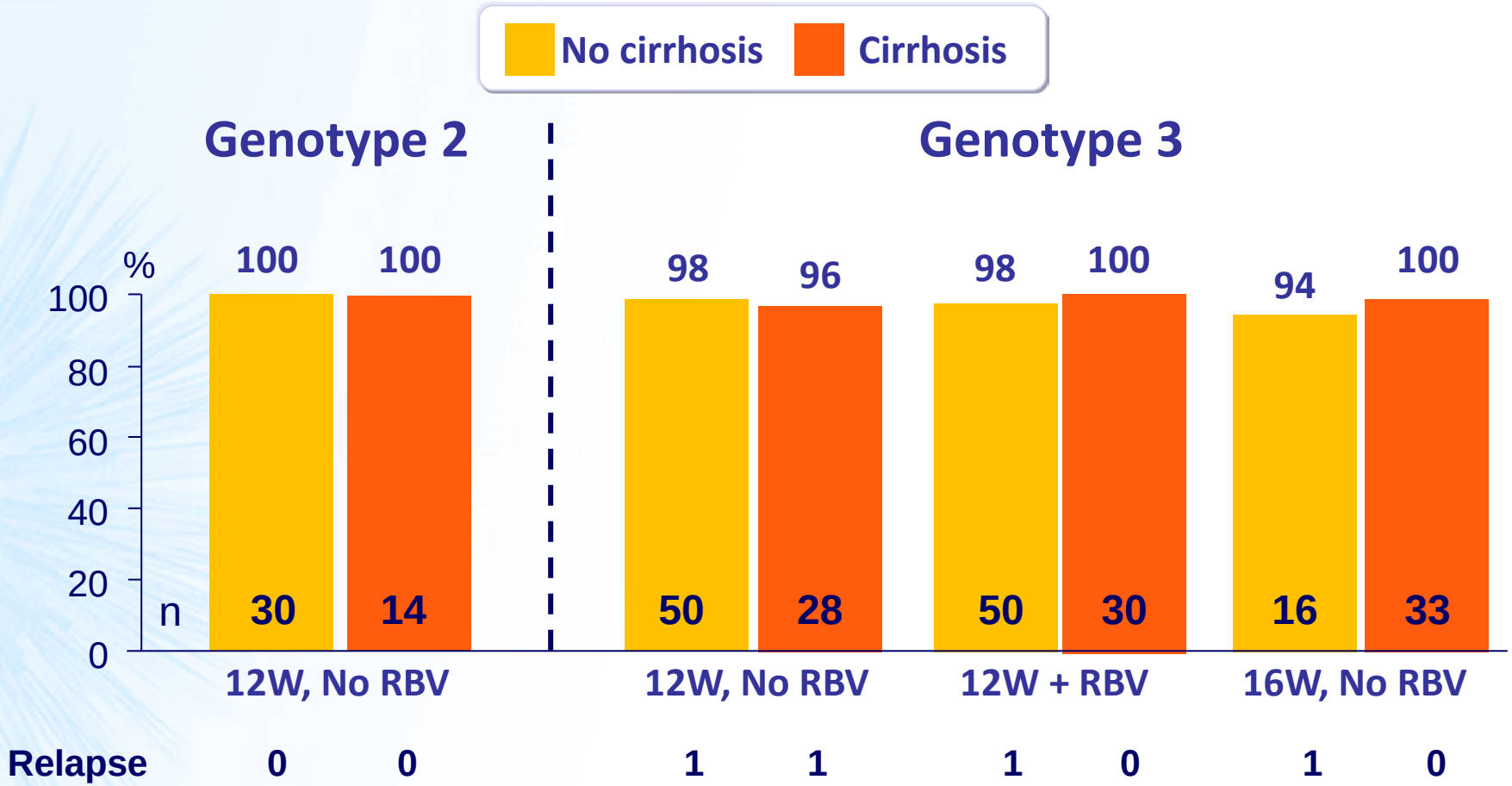
C-CREST study, Part B: uprifosbuvir (MK-3682)/GZR/ruzasvir (MK-8408) fixed-dose combination ± RBV for genotypes 1, 2 and 3 - Phase II

SVR_{12} (per protocol), genotype 2 or 3 patients with or without cirrhosis



C-CREST – Part B

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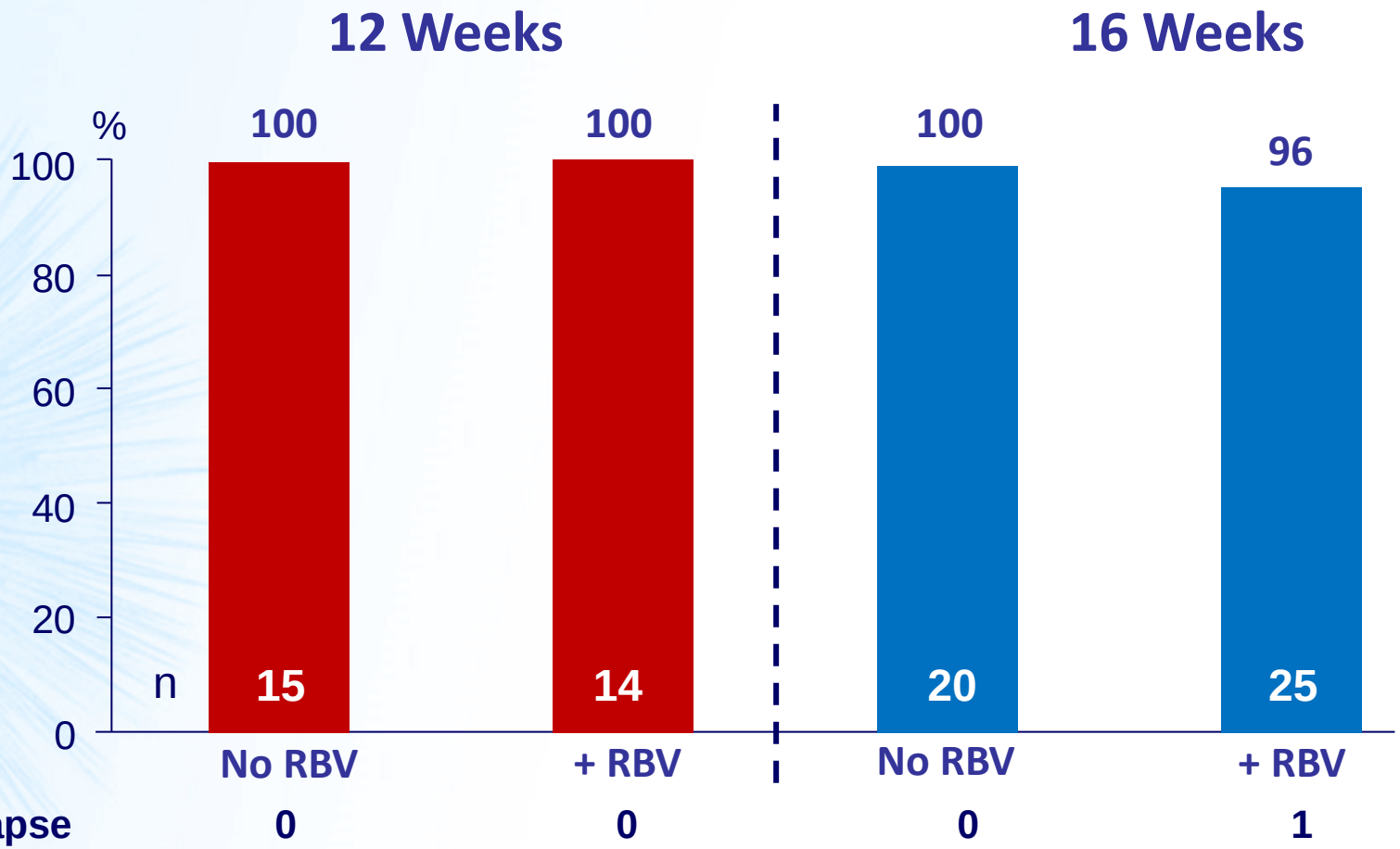
C-CREST study, Part B: uprifosbuvir (MK-3682)/GZR/ruzasvir (MK-8408) fixed-dose combination ± RBV for genotypes 1, 2 and 3 - Phase II

SVR_{12} (per protocol), genotype 3 treatment-experienced patients with cirrhosis



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SVR_{12} according to the presence of NS5A RAVs

	Genotype 1a		Genotype 1b		Genotype 2		Genotype 3	
Duration of treatment	8W	12W	8W	12W	8W	12W	8W	12W
No RAVs *	33/35 (94%)	41/41 (100%)	38/39 (97%)	24/24 (100%)				
RAVs *	3/3 (100%)	6/6 (100%)	6/6 (100%)	16/16 (100%)				
No L31M					31/33 (94%)	23/23 (100%)		
L31M					20/25 (80%)	28/28 (100%)		
No Y93H							95/97 (98%)	147/148 (95%)
Y93H							2/4 (50%)	5/7 (71%)

* RAVs : 28, 30, 31, 93

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Adverse events

	MK3 without RBV	MK3 with RBV
Drug-related adverse event, %	36	67
Serious adverse event, %	2	2
Drug-related serious adverse event, N (%)	0	2 (1) *
Death, N (%)	1 (0.2) **	0
Discontinuation due to adverse event, N (%)	3 (0.6)	6 (3)
Adverse event in > 10% of patients, %		
Headache	19	27
Fatigue	15	29
Nausea	11.3	15
Laboratory abnormalities, %		
Hemoglobin < 10 g/dL	0.4	3
Bilirubin > 5 x baseline	0.2	3
Late AST/ALT > 5 x ULN	1	0
Creatinine elevation, grade 1 /grade 2	0.6 / 0.2	0 / 0

* 1 genotype 3-infected patient had an exacerbation of chronic obstructive pulmonary disease related to RBV ; 1 genotype 2-infected patient had a worsening of depression related to RBV

** 1 genotype 1-infected patient died due to a study drug-unrelated bacterial sepsis

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Summary

- MK3 (uprifosbuvir/grazoprevir/ruzasvir) for 8 or 12 weeks was highly effective in genotype 1 patients (SVR_{12} = 97%)
- MK3 for 12 or 16 weeks was highly effective in genotype 2 patients (SVR_{12} = 98%)
  - The addition of RBV did not increase SVR_{12}
- MK3 for 8, 12 or 16 weeks was highly effective in genotype 3 treatment-naïve or treatment-experienced patients (SVR_{12} = 96%)
  - The addition of RBV did not increase SVR_{12}
  - Efficacy was maintained in genotype 3 treatment-experienced patients with cirrhosis (SVR_{12} = 99%)
- Treatment with MK3 was generally safe and well-tolerated

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