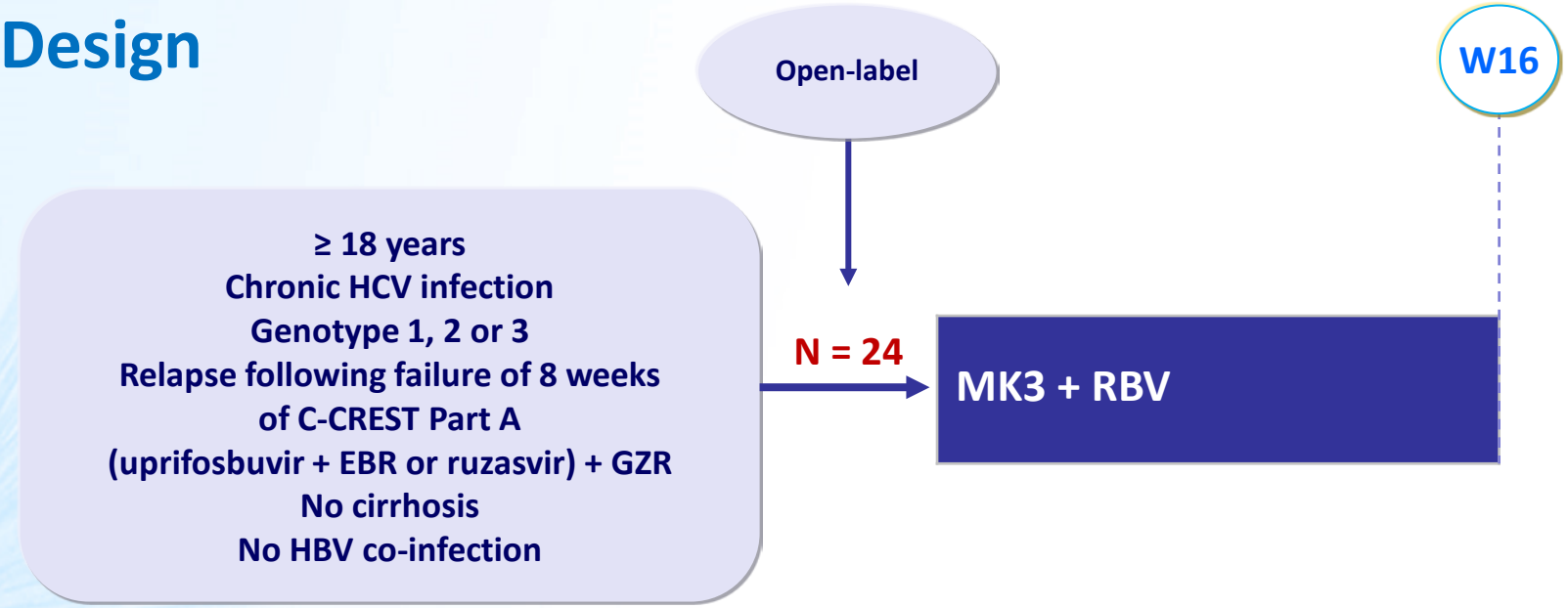
C-CREST study, Part C: 16 weeks of uprifosbuvir/GZR/RZR fixed-dose combination + RBV for genotypes 1, 2 and 3 after failure of 8 weeks of treatment

Design



* Liver biopsy or Fibroscan ≤ 12.5 kPa or Fibrosure® ≤ 0.48 + APRI ≤ 1

- Uprifosbuvir 225 mg/GZR 50 mg/RZR 30 mg FDC (MK3) = 2 tablets QD

Objective

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

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Baseline characteristics (N = 24)

	N = 24
Median age, years	53
Female, %	50
Race, white, %	88
HCV genotype 1a / 1b / 2 / 3, %	1 / 1 / 14 / 8
Metavir F0-F2, %	96
HCV RNA log_{10} IU/mL, median	6.6
NS5A inhibitor in part A regimen EBR RZR	 GT2 = 9/14 ; GT3 = 5/8 GT1 = 2/2 ; GT2 = 5/14 ; GT3 = 3/8
RAVs at retreatment baseline, % NS3 NS5A NS5B	 96 83 4

SVR_{12}, full analysis set, %

Genotype 1, N = 2	Genotype 2, N = 14	Genotype 3, N = 8
100%	93% (1 withdrawal after single dose for AE)	100%

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Adverse events (N = 24)

Treatment-related adverse events, %	**83**
Serious adverse events, N (%) **Treatment-related, N (%)**	**2 (8%) *** **1 (4%) ***
Treatment-discontinuation due to AE, N (%)	**2 (8%) ****
AE occurring in ≥ 20% of patients, % **Headache** **Fatigue** **Nausea** **Rash** **Insomnia**	 **33** **25** **25** **21** **21**
Laboratory abnormalities **Hemoglobin < 10 g/dL, N (%)** **Direct bilirubin > 5 x baseline** **Late ALT/AST > 5 x ULN** **Creatinine grade 1 (1.1-1.3 x ULN)**	 **2 (8%)** **0** **0** **0**

* 2 subjects had 3 SAEs:
  - 1 genotype 2-infected patient withdrew after a single dose with SAEs of vomiting and tachycardia considered related to MK3 + RBV
  - 1 genotype 3-infected patient was hospitalized for severe anxiety, unrelated to MK3 + RBV

** 1 genotype 2-infected patient withdrew after a single dose with SAEs as above ;
1 genotype 2-infected patient discontinued RBV 4 days before the completion of 16 weeks of therapy due to rash considered RBV-related, but completed 16 weeks of MK3

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Summary

- MK3 (uprifosbuvir/grazoprevir/ruzasvir) plus RBV for 16 weeks was highly effective in genotype 1, 2, and 3-infected patients without cirrhosis who had previously failed 8 weeks of treatment with a regimen of uprifosbuvir + EBR or RZR + GZR
- 100% SVR_{12} in 23 patients who completed treatment
- High efficacy despite a high prevalence of baseline NS3 and NS5A RAVs in this DAA failure population
- Treatment was generally safe and well-tolerated

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