Two subjects (GT1b and GT2b) experienced post-treatment relapse. In this first clinical trial of BEM+RZR in HCV-infected subjects, a 127
85
An SVR4 rate of ≥90% in a lead-in cohort of subjects without
99
99
71
43
85
Both low plasma drug levels, and viral populations that were similar
https://clinicaltrials.gov/study/NCT05904470 (accessed May 2024)
141
The regimen was well tolerated, with no drug-related SAEs or
At baseline, most subjects (51/56) in the lead-in had at least one of
113
In this first clinical trial of BEM+RZR in HCV-infected subjects, a
29
85
The combination of BEM+RZR was well tolerated, with no adverse
events (AEs) leading to treatment discontinuation
• One subject in the lead-in cohort experienced non-drug related
serious AEs (SAEs) of cellulitis and subsequent overdose (not study
drug), resulting in death after the SVR4 visit
• Other non-serious AEs were reported in 25% of subjects (15 of 60).
Only headache was reported in more than a single subject (11.7%.
7 of 60 subjects). Non-serious AEs were mild or moderate in
severity. No clinically significant patterns were observed for safety
laboratory or electrocardiogram parameters
Analysis of post-treatment relapse
• Two subjects (GT1b and GT2b) experienced post-treatment relapse.
Viral kinetics, plasma drug levels for AT-273 (sumrgete for the BEM
active triphosphate) and RZR, and resistance sequencing data from
each are presented in Figure 4
• Both low plasma drug levels, and viral populations that were similar
at baseline and SVR12 timepoints, indicate that relapse was due to
lack of treatment non-adherence, rather than viral resistance
• Post-study, both subjects were planned to be treated with SOF/VEL/VOX

Figure 4. Profiles of subjects with relapse
A. GT1b-infected subject
B. GT2b-infected subject

Efficacy analysis
• All subjects completed treatment, with 54/60 (90%) achieving
HCV RNA <LLOQ by Week 4 and all 60 achieving <LLOQ levels
at the end of treatment (Figure 1). These rapid viral kinetics were
observed in all subjects upon initiation of treatment, regardless of
genotype and baseline viral load
• One subject withdrew consent after the Week 8 time point.
SVR4 data were available in all 59 remaining subjects, with one
documented post-treatment relapse, for an SVR4 rate of 58/59
(98%). Of the 58 subjects with SVR4, there was one non-HCV non-
drug-related death before the SVR12 time point, with one additional
post-treatment relapse documented, resulting in an SVR12 rate of
56/59 (97%) (Figure 2)
• High SVR12 rates were observed in both GT1 and historically
difficult-to-treat GT3-infected subjects (Figure 3)

Figure 1. On-treatment viral kinetics: individual subject data

Table 1. Baseline demographic and disease characteristics
Characteristic Subjects (N=60)
Median age, years (range) 47 (25–79)
Median BMI, kg/m2 (range) 26.3 (18.9–47.1)
Male sex, n (%) 34 (56.7)
Race, n (%) White 57 (95.0)
Black or African American 1 (1.7)
Other 2 (3.3)
HCV genotype, n (%) GT1a 6 (10.0)
GT1b 39 (65.0)
GT2b 2 (3.3)
GT3 13 (21.7)
Median baseline viral load, log_{10} (range) 6.3 (2–7.3)
Fibrosis stage, n (%) F0 9 (15.0)
F1 26 (43.3)
F2 15 (25.0)
F3 10 (16.7)

CONCLUSIONS
• In this first clinical trial of BEM+RZR in HCV-infected subjects, a
high SVR12 rate (97%) was observed in the lead-in cohort with a
short 8-week duration of treatment
• BEM+RZR has an excellent clinical resistance profile and has
been shown to overcome baseline pre-existing RAS
• Two post-treatment relapses were linked to treatment
non-adherence as opposed to viral resistance
• Viral kinetics were similar in GT1- and GT3-infected subjects
• 100% SVR12 rate in historically difficult-to-treat GT3-infected
subjects
• The regimen was well tolerated, with no drug-related SAEs or
treatment discontinuations
• Based on these data from the lead-in cohort, the Phase 2 study
continues with the aim of enrolling up to an additional 220
subjects, including those with compensated cirrhosis

Additional sequencing analyses
• At baseline, most subjects (51/56) in the lead-in had at least one of
the most common NS5A RASs, and 13/59 had at least one of
the most common NS5B RASs (such as N142I, L159F, and V321I) with
a 1% assay threshold
— NS5B*30: 24, 26, 28, 29, 30, 31, 32, 37, 38, 52, 54, 58, 62, 64, 92, or 93
155*, 223*, 343*(-RAS) and BEM in (RAS)
• A GT3-infected subject with pre-existing NSSA RASs S62A and
Y93H achieved SVR12 (Figure 5) S62A/Y93H (S62A/Y93H) confer very high resistance to NSSA
inhibitors in GT3 replicons (>1000-fold loss of potency for RZR
and velpatasvir; >100-fold loss of potency for ribavirin)
• Despite pre-existing baseline RASs at both targets, 97% of subjects
achieved SVR12

Figure 5. GT3-infected subject with known NSSA RASs

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