A Phase II Trial of 4 Weeks of Glecaprevir/Pibrentasvir for Early Hepatitis C Virus (ACTG A5380) 00696

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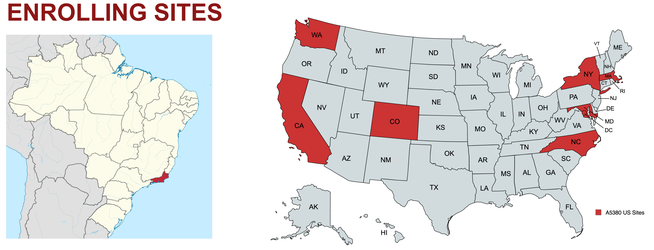
BACKGROUND

- The US CDC reports a doubling of acute HCV infections during 2014-2020 in the United States.[1]
- Acute HCV infections and re-infections threaten elimination efforts in key populations including people with HIV (PWH).
- Eight weeks of glecaprevir/pibrentasvir (G/P) 300 mg/120 mg fixed-dose combination is a safe, effective approved treatment for chronic hepatitis C virus.
- Shorter treatment courses have been effective in early hepatitis C (HCV) but are still longer than optimal.
- Shortening to a single month simplifies treatment and may further facilitate the national plan of HCV elimination.
- A previous trial with 23 participants using a regimen of 4 weeks of glecaprevir/pibrentasvir for HCV diagnosed within past 12 months demonstrated a sustained virologic response (SVR12) of 78% (18/23;95%CI 56–93%).[2]

METHODS

- A5380 (PURGE-C) was a prospective, phase II, single-arm multicenter trial evaluating the efficacy and safety of once daily oral G/P for 4 weeks in adults with early HCV.
- Early HCV was defined as new ALT elevation (≥5x ULN or >250 U/L if normal ALT in prior year, or ≥10x ULN or >500 U/L if no or abnormal ALT in prior year); or detectable HCV RNA with prior negative antibody (1st infection) or HCV RNA (re-infection) within 24 weeks prior to study entry.
- The primary endpoint was SVR12, defined as HCV RNA < LLOQ (lower limit of quantification) at 12 weeks after treatment cessation.
- A5380 was powered to conclude that the SVR12 proportion is >80% using the 90% Wilson confidence interval (CI).
- Participants not achieving SVR12 were offered re-treatment through the study (Step 2) or through their providers.

ENROLLING SITES



Treatment with 4 weeks of glecaprevir/pibrentasvir for early HCV infection resulted in a SVR12 (cure) rate of 84%

Consort Diagram

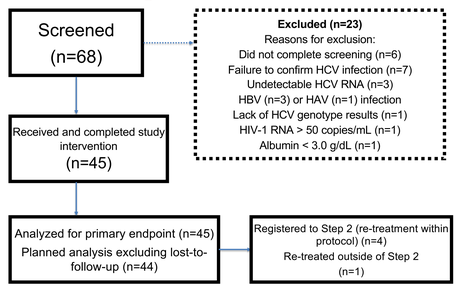


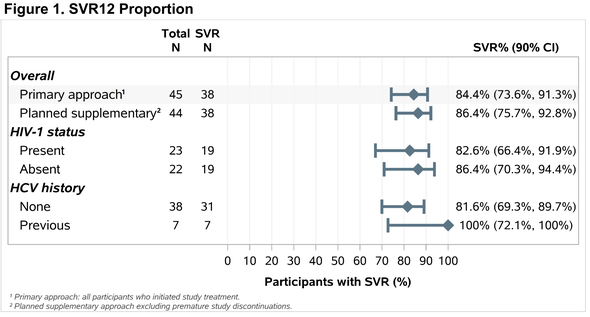
Table: A5380 Baseline Demographic, Behavioral and Virologic Characteristics

Age (years)	Median (IQR)	36 (29-43)
Sex assigned at birth	Female	1 (2%)
	Male	44 (98%)
Gender identity	Cisgender women	1 (2%)
	Cisgender men	43 (96%)
	Non-Binary	1 (2%)
Race	Asian	3 (7%)
	Black	12 (27%)
	White	23 (51%)
	Other/Unknown	7 (16%)
Ethnicity	Hispanic or Latino	14 (31%)
	Not Hispanic or Latino	30 (67%)
History of injection drug use	Yes	12 (27%)
	No	33 (73%)
Living with HIV	Yes	23 (51%)
HIV VL < 40 copies/mL		23/23 (100%)
CD4 count (cells/mm^3)	Median (IQR)	545 (348-820)
HCV history	None	38 (84%)
	Previous	7 (16%)
Time since acute HCV diagnosis (days)	Median (IQR)	31 (15-49)
ALT (U/L)	Median (range)	146 (22-3866)
HCV genotype	1	32 (71%)
	2	2 (4%)
	3	1 (2%)
	4	5 (11%)
	Unable to determine	5 (11%)
HCV RNA ($\log_{10}$ IU/mL)	Median (IQR)	5.3 (3.3-6.0)

RESULTS

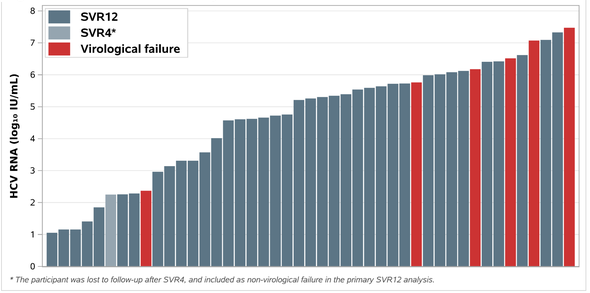
- Participants enrolled between November 2019 and January 2023 at 11 U.S. and 1 Brazilian site, with temporary enrollment closure due to the COVID-19 pandemic from March 18 to October 1, 2020.
- All 45 participants completed treatment.
- No treatment-related serious adverse events.

Figure 1. SVR12 Proportion



¹ Primary approach: all participants who initiated study treatment.
² Planned supplementary approach excluding premature study discontinuations.

Figure 2. Baseline HCV RNA by Outcome



* The participant was lost to follow-up after SVR4, and included as non-virological failure in the primary SVR12 analysis.

RESULTS (post-treatment viremia outcomes)

- Six participants demonstrated recurrent viremia after end-of-treatment at or before SVR12 determination.
  - Analysis of sequencing data are pending to determine relapse vs. reinfection and emergence of resistance.
  - 1 withdrew from the study and is classified as non-SVR
  - 1 was prescribed SOF/VEL/VOX x 12 weeks outside of the study, was determined to have SVR.
  - 4 registered to Step 2 (re-treatment), 3 were prescribed G/P for 16 weeks and 1 prescribed SOF/VEL/VOX for 12 weeks.
    - 2 participants in Step 2 experienced AEs judged related to study treatment by site (grade 2 fatigue, weight increased).
    - 3 achieved SVR; 1 participant discontinued Step 2 treatment due to AE (cellulitis); outcome is unknown.

CONCLUSIONS

- Treatment of early HCV with 4 weeks of G/P resulted in clinically acceptable cure rates in people with or without HIV.
- Although SVR12 >80% could not be concluded from the CI, a planned CI analysis excluding LFU supports that the SVR12 proportion is >75%.
- As simplified treatment approaches are critical for HCV elimination, a 4-week G/P regimen should be tested in implementation programs aiming to cure early HCV.
- Cure with 4-week regimens inform strategies for the deployment of long-acting injectable antivirals for HCV.

TRIAL REGISTRATION https://clinicaltrials.gov/study/NCT04042740

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[2]Martinello et al. JHep Rep 2023

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