Characterization of participants in Canada with Chronic HCV Infection Initiating DAA Therapy Based on Risk For HCV Transmission and Response to Treatment: The Real-World C-RESPECT Study

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BACKGROUND

- The incidence of hepatitis C virus (HCV) infection is higher in certain risk groups, including men who have sex with men (MSM) and people who inject drugs (PWID), identified as Core Transmitters (CT). Other HCV-infected individuals are identified as non-Core Transmitters (non-CT)
- Understanding the characteristics of the infection, the parameters favoring engagement in care and the response to treatment in both CT and non-CT groups is of great importance in the design of comprehensive strategies to address the HCV epidemic in Canada.

OBJECTIVES

- To describe the patient and disease profile of HCV-infected CT and non-CT participants treated with direct-acting antivirals (DAAs) during routine clinical care in Canada as part of the ongoing C-RESPECT study and to compare response to treatment outcomes (SVR/non-response/relapse) as well as rates of recurrent viremia after successful treatment among different groups.

METHODS

STUDY DESIGN

- C-RESPECT is an ongoing, prospective, observational study of HCV-infected individuals treated with DAAs.
- Participants were recruited from the offices of infectious disease specialists, hepatologists, gastroenterologists, and general practitioners across Canada.
- Participants are followed from the time they are prescribed treatment with a DAA, as decided by the treating physician prior to study enrollment, up to the end of treatment, and are continuing to be followed as per routine care until the end of the study (maximum of 3 years post study initiation).
- Participants are managed as per routine Canadian practice and clinician standard of care. Duration of DAA treatment is at the discretion of the treating physician based on the selected DAA, baseline clinical characteristics, and the approved product monograph.

STUDY POPULATION

- Male or female ≥18 years of age at time of informed consent.
- Confirmed viremia with HCV genotype 1, 3 or 4, by RNA assay.
- Participants with chronic HCV infection, defined as detectable HCV RNA for ≥6 months.
- Participants initiating DAA for treatment of HCV. Treatment decision must have been made prior to and independently of study recruitment.
  - DAAs include: daclastavir, dasabuvir, elbasvir, grazoprevir, ledipasvir, ombistasvir, paritaprevir, sofosbuvir, simeprevir, velpatasvir or other approved DAAs in Canada
- Core Transmitter (CT) Specific Inclusion Criteria:
  - PWID injected an illicit drug at least once in the previous 24 months.
  - MSM had unprotected sex with a man of positive or unknown HCV serostatus in the previous 24 months.

ANALYZED STUDY COHORT

- The participants enrolled as part of the ongoing C-RESPECT study between March 2017 and July 2019 were included in this interim analysis.
- A total of 434 participants (CT: 264 [56 HIV co-infected]; and non-CT: 170 [6 HIV co-infected]) from 26 sites across Canada were included in this interim analysis; these participants included those who had at least 1 dose of DAA and met all inclusion/exclusion criteria.

- Participants who completed their DAA treatment regimens were included in the per protocol (PP) analysis population used for the analyses of the primary/secondary objectives.

VARIABLES

- Baseline assessments included patient socio-demographic characteristics, disease characteristics and comorbidities.
- The primary outcome measure was the rate of genetically confirmed reinfection (detectable HCV RNA) after end of treatment (EOT).
- Secondary outcomes included achievement of sustained virologic response at 12/24 (SVR12/24) weeks after the end of HCV treatment and treatment failure (detectable HCV RNA at EOT or post EOT).

STATISTICAL METHODS

- Descriptive statistics, including the mean and standard deviation (SD) for continuous variables and frequency distributions for categorical variables were produced.
- Participants were stratified into two distinct patient subgroups:
  - Core-Transmitters (CTs), defined as men who have sex with men (MSM) and/or people who inject drugs (PWID);
  - Non-Core Transmitters (non-CTs)
- Baseline parameters for CTs and non-CTs groups were compared using independent Student's t-test or Wilcoxon rank sum test for continuous variables, and Chi-square test or Fisher's exact test for categorical variables.
- Primary/secondary outcomes were measured using the proportion of participants. For treatment failure and reinfections, incidence density rates (IDR; per 100 patient-years of follow-up) were produced, along with the 95% CIs. Comparison of SVR achievement between groups was assessed using Fisher's exact test.
- The time to reinfection was assessed using the Kaplan-Meier estimator of the survival function, and compared using the Breslow-Day log-rank test.

BASELINE CHARACTERISTICS

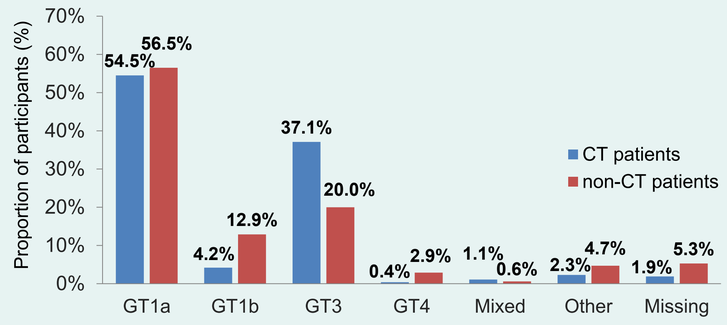
- Statistically significant ($p<0.05$) differences in baseline parameters were observed between CT and non-CT participants, with CT being younger, more often Aboriginal, less often employed and having lower income (most often from social assistance), less stably housed, more likely to have been incarcerated, and more likely to be smokers. **(Table 1)**

Table 1. Patient Socio-Demographics and Baseline Characteristics

Characteristics	CT (N=264)	non-CT (N=170)	p-value
Age (years), mean (SD)	42.4 (11.3)	54.6 (11.9)	**<0.001**
Male, n (%)	167 (63.3%)	121 (71.2%)	0.093
Ethnicity, n (%)			
Caucasian	191 (72.3%)	139 (81.8%)	**<0.001**
Aboriginal	56 (21.2%)	13 (7.6%)	
Other	17 (6.5%)	18 (10.6%)	
BMI (kg/m^2), mean (SD)	25.9 (6.1)	27.4 (7.6)	**0.030**
Employment status, n (%)			
Employed	33 (12.5%)	54 (31.8%)	**<0.001**
Unemployed	52 (19.7%)	37 (21.8%)	
Social assistance	92 (34.8%)	24 (14.1%)	
Disability	71 (26.9%)	27 (15.9%)	
Other	11 (4.2%)	26 (15.3%)	
Missing	5 (1.9%)	2 (1.2%)	
Socioeconomic Status (CAD$), n (%)			
≤ 15,000$	173 (65.5%)	71 (41.8%)	**<0.001**
15,001$ ≤ 25,000$	38 (14.4%)	18 (10.6%)	
25,001$ ≤ 50,000$	14 (5.3%)	27 (15.9%)	
50,001$ ≤ 75,000$	3 (1.1%)	15 (8.8%)	
> 75,000$	1 (0.4%)	15 (8.8%)	
Unknown or missing	35 (13.3%)	24 (14.1%)	
Housing Status, n (%)			
Rented	161 (61.0%)	99 (58.2%)	**<0.001**
Shelter	30 (11.4%)	9 (5.3%)	
Owned	21 (8.0%)	46 (27.1%)	
Detox/therapy	13 (4.9%)	2 (1.2%)	
Homeless	12 (4.5%)	1 (0.6%)	
Prison/jail	3 (1.1%)	0 (0.0%)	
Other or missing	24 (9.1%)	13 (7.6%)	
Currently on income assistance, n (%)	203 (76.9%)	88 (51.8%)	**<0.001**
Have ever been incarcerated, n (%)	160 (60.6%)	61 (35.9%)	**<0.001**
Alcoholic beverages consumer, n (%)	110 (41.7%)	76 (44.7%)	0.597
Current smoker, n (%)	215 (81.4%)	85 (50.0%)	**<0.001**

- GT3 was more common among CT participants. **(Figure 1)**

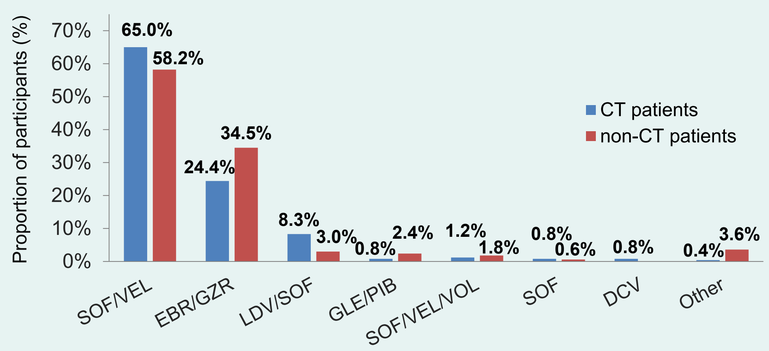
Figure 1. HCV Genotypes by Patient Group



participants may have reported ≥1 genotype

- DAA treatment regimens were similar between treatment groups. SOF/VEL was the most common regimen prescribed, specifically for 65.0% and 58.2% of CT and non-CT participants, respectively, with over 90% in both CT and non-CT groups having received either SOF/VEL or EBV/GZR. **(Figure 2)**

Figure 2. DAA Treatment Regimens by Patient Group



DCV, daclatasvir; EBR, elbasvir; GLE, glecaprevir; GZR, grazoprevir; LDV, ledipasvir; PIB, pibrentasvir; VEL, velpatasvir; VOL, voxilaprevir

RESULTS

- Among the 434 participants included in the analysis, 263 (60.6%) completed their DAA treatment regimens, specifically 156 (59.1%) CT and 107 (62.9%) non-CT participants, and were included in the per protocol (PP) analysis population for assessment of primary/secondary outcomes.
- SVR was achieved in over 95% of all study participants, with no difference between CT and non-CT groups. **(Figure 3)**
- Reinfections occurred in 8 CT participants, corresponding to 10.1 reinfections per 100 PYs. Most reinfections (n=5) occurred between 6-12 months post end of treatment. **(Table 2)**
- No reinfections occurred among non-CT participants. **(Table 2)**

Figure 3. Achievement of SVR12 by Patient Group

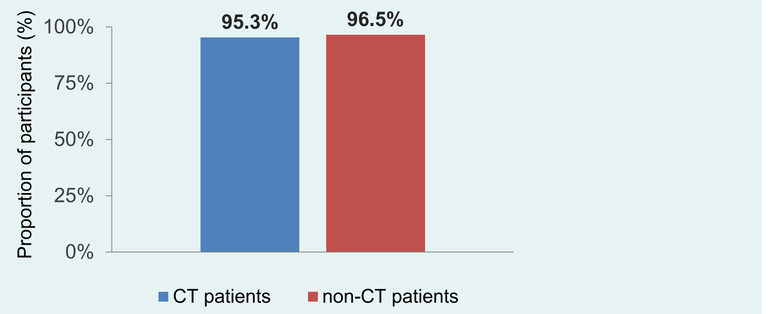


Table 2. Number of Reinfections After End of Treatment by Patient Group

Visit	CT (N=156)	non-CT (N=107)
Overall reinfection rate-(95% CI), 100 PYs	10.1 (5.1–20.2)	-
Total number of reinfections, n	8	0
0-3 months post EOT	2	-
3-6 months post EOT	0	-
6-12 months post EOT	5	-
12-24 months post EOT	1	-

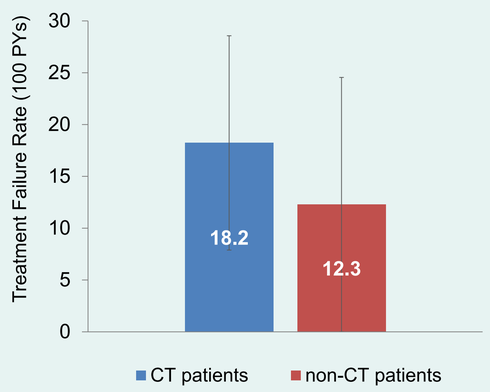
- The median (95% CI) time to reinfection for CT participants was 357 (194–376) days and no reinfections occurred among non-CT participants. **(Table 3)**

Table 3. Time to Reinfection by Patient Group

	CT (N=156)	non-CT (N=107)
Time (days), median (95% CI)	357 (194–376)	No reinfections

- A total of 19 treatment failures were reported among CT participants, corresponding to a treatment failure rate of 18.2 reinfections per 100 patient-years (PYs) of follow-up. **(Figure 4)**
- Among non-CT participants, a total of 8 treatment failures were reported, equivalent to 12.3 reinfections per 100 PYs. **(Figure 4)**

Figure 4. Overall Treatment Failure Rates by Patient Group



CONFLICT OF INTEREST DISCLOSURE

- This study was sponsored by Merck & Co., Inc., Kenilworth, NJ, USA, and sponsored and funded by Merck Canada Inc., Kirkland, QC, Canada.
- Dr. Conway reports grants from Merck during the conduct of the study; grants, personal fees and other from AbbVie; grants, personal fees, and other from Gilead; grants, personal fees, and other from Merck, outside the submitted work.

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CONCLUSIONS

- This interim analysis reports real-world data on 264 CT and 170 non-CT HCV-infected participants who initiated treatment with a DAA in Canada.
- Participants in the CT group represent a more vulnerable group for whom specific strategies for engagement in care may be necessary. Despite this fact, SVR rates were comparable between CT and non-CT groups in this study.
- Reinfections were observed among CT patients at a rate that is higher than reported in a number of meta-analyses of similar populations. Strategies to mitigate this risk will have to be developed to maximize the benefits of HCV treatment in this population.