Understanding unsuccessful direct-acting antiviral hepatitis C treatment among people with HIV: An international cohort study

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BACKGROUND

- Historically people with HIV were considered "difficult to treat" for hepatitis C

- However, direct acting antivirals (DAA) for hepatitis C cure 90-95% of people with HIV

- In previous studies, factors associated with unsuccessful treatment has included cirrhosis, mental health illness, frequent injecting drug use and CD4+ cell count

- As a somewhat rare outcome, smaller studies have limited power and have reported various and sometimes conflicting results; some have also included no SVR test as unsuccessful treatment

- Large international collaborations are needed to understand rare outcomes with more precision

METHODS

Data and eligibility

- Individual level data were from the **In**ternational **C**ollaboration on **H**epatitis C **E**limination in **H**IV **C**ohorts (InCHEHC)
- Six countries: Australia, Canada, France, the Netherlands, Spain, Switzerland
- People with interferon free DAA treatment data between 2014 and 2019 were eligible
- People who had a hepatitis C RNA test 12+ weeks after end of treatment were included in analyses of unsuccessful treatment, including sub-analysis of unsuccessful treatment due to relapse and unsuccessful treatment due to non-response

Definitions

- Unsuccessful treatment defined as detectable HCV RNA at first RNA test 12+ weeks following end of treatment
- Relapse defined as the detection of HCV RNA following a negative test after treatment commencement
- Non-response defined as having no evidence of ever being HCV RNA negative during treatment

Statistical analyses

- Mixed-effects logistic regression used to examine factors associated with no SVR12 test and unsuccessful treatment
- Multinomial mixed-effects logistic regression to examine factors associated with unsuccessful treatment due to relapse and non-response
- Age and cirrhosis were included in unsuccessful treatment multivariable models *a priori*, others based on *p-value 0.10*

RESULTS

A total of 4,510 people had DAA treatment data.

81% were male, with a median age of 51 (21-85)

46% were gay or bisexual men, or other men who have sex with men

36% were people with a history of injection drug use

Of the 4,510 people, 3,945 people had an SVR 12+ test and were included in further analyses

Among these 3,945 people, 217 (5.5%) were defined as unsuccessfully treated

146 (67%) were defined as relapse

Multivariable analyses

Adjusted for age, population group, CD4+ cell count, years since HIV diagnosis and HIV viral load, previous interferon-based treatment was associated with a _reduced_ odds of having no SVR12 plus test (Table 1)

In the multinomial analysis adjusted for age, population group, and cirrhosis, a CD4+ cell count 200-349 was associated with unsuccessful treatment compared to a cell count 350+ (Table 2)

In our multinominal analysis, a CD4+ cell count 200-349 was specifically associated with relapse (aOR 1.46, 95%CI 1.02-2.09); there were no significant associations with non-response

Table 1. No SVR12 testing

	Adjusted Odds Ratio (95%CI)
Age	0.99 (0.98-1.00)
Key population group	
Gay and bisexual males	1
Males w/ history of IDU	1.07 (0.83-1.38)
Females w/ history of IDU	1.33 (0.96-1.84)
Heterosexual & other males	1.24 (0.86-1.81)
Heterosexual & other females	1.24 (0.86-1.79)
Previous HCV treatment	
No	1
Yes	0.67 (0.52-0.87)
CD4+ cell count	
350+	1
200-349	1.00 (0.82-1.24)
<200	1.18 (0.80-1.76)
Years since HIV diagnosis	
<10	1
10-19	1.13 (0.90-1.45)
20-29	0.87 (0.64-1.19)
30+	1.32 (0.89-1.96)
HIV viral load	
<200 copies/ml	1
>200 copies/ml	1.40 (0.95-2.08)

Table 2. Unsuccessful treatment

	Adjusted Odds Ratio (95%CI)
Age	1.01 (0.99-1.03)
Key population group	
Gay and bisexual males	1
Males w/ history of IDU	1.35 (0.94-1.94)
Females w/ history of IDU	0.63 (0.35-1.14)
Heterosexual & other males	1.46 (0.88-2.42)
Heterosexual & other females	1.01 (0.55-1.87)
CD4+ cell count	
350+	1
200-349	1.40 (1.03-1.93)
<200	1.35 (0.74-2.46)
Cirrhosis	
No	1
Yes	0.93 (0.65-1.34)

CONCLUSION

Unsuccessful DAA hepatitis C treatment among people with HIV is rare. However, it was associated with a lower CD4+ cell count. It is difficult to delineate whether the lower CD4+ cell counts were a result of suboptimal HIV treatment adherence or a reflection of a lack of CD4+ cell count restoration following HIV treatment. Given the very high cure rate with DAA treatment, less on-treatment and post-treatment monitoring has been proposed; based on our findings from the largest ever study of unsuccessful treatment specifically among people with HIV, this may be pre-mature advice among people with lower CD4+ cell counts.

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