Anticipating the future: NCCC guidance on DAA treatment interruptions reliably matched AASLD Guidelines prior to their release

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Background & Objective

- Direct-acting antivirals (DAAs) have revolutionized hepatitis C (HCV) treatment, with greater than 90% sustained virologic response (SVR) rates. Despite the short treatment duration, treatment interruptions still occur in the real world setting for a variety of reasons.
- There are few data in the literature[1,2] on how to manage these treatment interruptions, and current HCV treatment guidelines on how to manage incomplete adherence were first published in October 2021[3].
- This retrospective case review aims to compare how National Clinician Consultation Center (NCCC) Hepatitis C Warmline guidance (2017-2021) aligned with the AASLD's 2021 recommendations on treatment interruptions prior to their release.

Methods

- The federally supported NCCC provides free, telephone-based consultation for any U.S. healthcare provider seeking guidance on HCV diagnosis and treatment. Its Hepatitis C Warmline started in July 2017. Deidentified case information, stored in a secure consultation database, include relevant caller information, clinical details, and consultant recommendations.
- All calls involving HCV treatment interruptions received from July 2017 to October 5, 2021 (release of AASLD guidelines) were retrospectively identified and reviewed.
- We aimed to analyze how well NCCC's clinical advice matched with Figure 1[3] of the AASLD guidelines on "Incomplete Adherence". High concordance was defined as fully matching the bullet points delineated in Figure 1. Partial concordance was defined as matching some points but offering alternative suggestions. Finally, not being concordant with the guidelines was defined when our consultation completely differed.

Results

- There were a total of 873 calls that came in between July 2017 to October 5, 2021. 94 of these calls (11%) involved treatment interruptions.
- Patient age ranged from 21-70 years old, and the median patient age was 46 years old. Callers identified the patients 43% as cis-female, 56% as cis-male, and 1% gender information was not available.
- Caller demographics are in the Figures 1 and 2. Patient demographics are displayed in Figures 3-7.

Caller Demographics

Figure 1

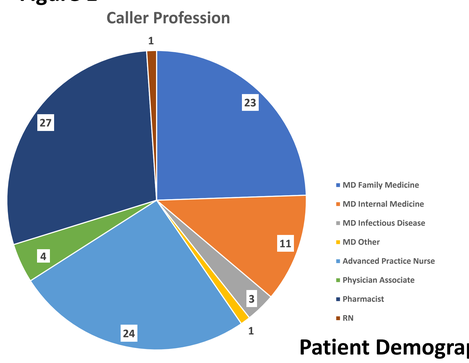
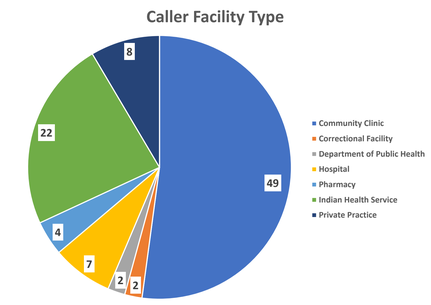


Figure 2



Patient Demographics

Figure 3

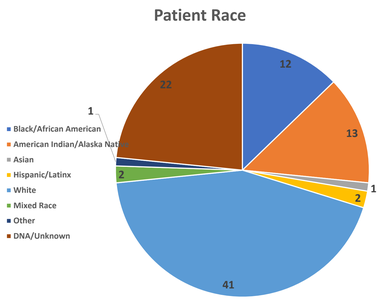
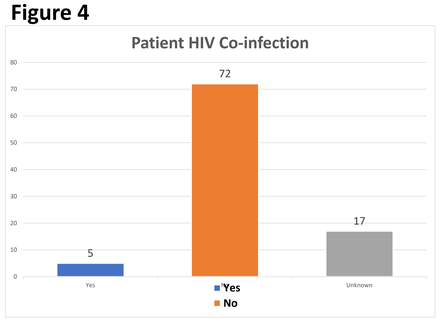


Figure 4



Patient Demographics Continued

Figure 5

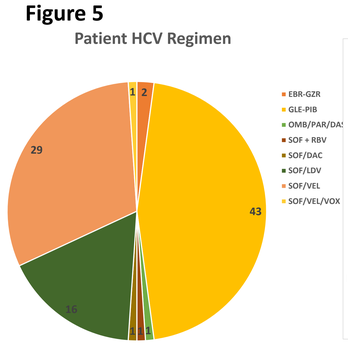


Figure 6

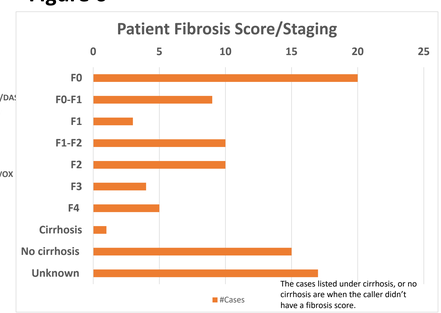
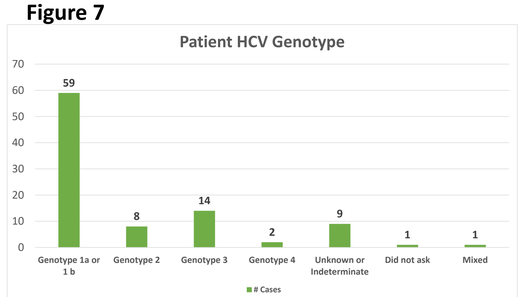
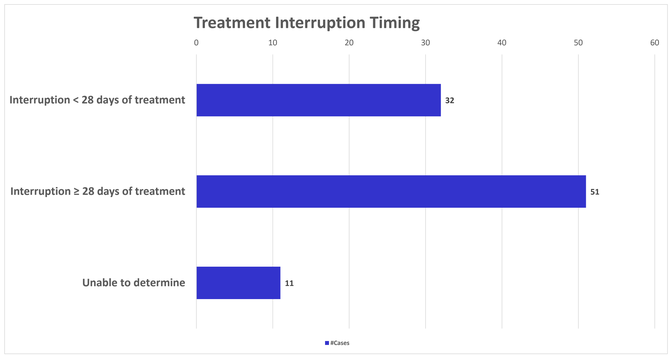


Figure 7



Results, Continued:

- Timing of treatment interruptions was categorized according to Figure 1 of the AASLD guidelines on "Incomplete Adherence". 32/94 calls (34%) involved treatment interruptions within the first 28 days of therapy, 51/94 (54%) involved treatment interruption after 28 days of therapy, and timing of treatment interruption could not be determined in 11/94 (12%).



- NCCC guidance was highly concordant with AASLD guidelines for 43% of cases, partially concordant for 35%, and differed for 13%; in 9%, recommendations could not be provided due to insufficient information.

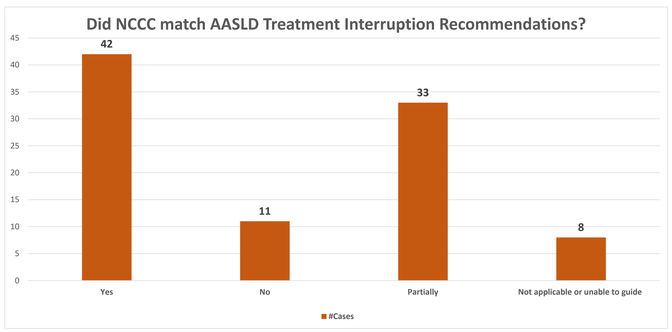


Figure 1. Recommended Management of DAA Treatment Interruptions for Treatment-Naive Patients, Without Cirrhosis or With Compensated Cirrhosis, Receiving Glecaprevir/Pibrentasvir or Sofosbuvir/Velpatasvir

Interruptions During First 28 Days of DAA Therapy

Missed ≤7 Days
- **Restart** DAA therapy immediately. Complete therapy for originally planned duration (8 or 12 weeks).

Missed ≥8 Days
- **Restart** DAA therapy immediately. Restarting DAA takes precedence over obtaining HCV RNA level.
- Obtain HCV RNA test as soon as possible, preferably the same day as restarting the DAA therapy.
- If HCV RNA is negative (undetectable) complete originally planned DAA treatment course (8 or 12 weeks). Recommend extending DAA treatment for an additional 4 weeks for patients with genotype 3 and/or cirrhosis.
- If HCV RNA is positive (>25 IU/L), or not obtained, extend DAA treatment for an additional 4 weeks.

Interruptions After Receiving ≥28 Days of DAA Therapy

Missed ≤7 Days
- **Restart** DAA therapy immediately. Complete therapy for originally planned duration (8 or 12 weeks).

Missed 8-20 Consecutive Days
- **Restart** DAA therapy immediately. Restarting DAA takes precedence over obtaining HCV RNA level.
- Obtain HCV RNA test as soon as possible, preferably the same day as restarting the DAA therapy.
- If HCV RNA is negative (undetectable) complete originally planned course (8 or 12 weeks). Recommend extending DAA treatment for an additional 4 weeks if patient has genotype 3 and/or cirrhosis.
- If HCV RNA is positive (>25 IU/L), or not obtained, **stop** treatment and retreat according to recommendations in the Retreatment Section.

Missed ≥21 Consecutive Days
- **Stop** DAA treatment and assess for SVR12. If SVR12 not achieved, retreat according to recommendations in the Retreatment Section.

DAA, direct-acting antiviral; HCV RNA, hepatitis C virus ribonucleic acid; SVR12, sustained virologic response 12 weeks after end of treatment.

Case Examples:

Case description	NCCC Guidance	2021 HCV Guidelines Recommendations	Concordance
31 yo cis-F, genotype not provided, treatment naive, low-level fibrosis. Prescribed 8-week course of Glecaprevir-Pibrentasvir (G/P) Completed first 28 d then missed 10 d.	Restart therapy, check HCV RNA now	Restart therapy, check HCV RNA now, additional steps dependent on RNA results	High
34 yo cis-M, GT 1a, treatment naive, low-level fibrosis, took G/P x 5 weeks then stopped. Now 3 weeks later.	Check an HCV RNA now, could either stop now or complete the remaining 3 weeks and assess for SVR12	Stop treatment and assess for SVR12	Partial
59 yo cis-M, GT1a, treatment naive, low-level fibrosis; took 1 mo SOF/LDV, now 7 mos later and VL detectable	Check resistance, consider re-treatment with G/P x 12 weeks if no resistance	Re-treat as treatment failure (SOF/VEL/VOX x 12 w or G/P x 16w)	Not concordant

Conclusions

- Questions on how to manage treatment interruptions were relatively common.
- Despite limited data to guide clinician decision-making around DAA treatment interruptions, NCCC recommendations made prior to the release of formal guidelines on how to manage them matched or partially matched these guidelines for ~80% of calls.
- Major limitations of this analysis are the lack of SVR outcomes, no verification of patient data provided by clinicians, and variability in NCCC consultant's treatment recommendations.
- These findings highlight the NCCC's role and potential value in providing easily-accessible decision support for "real world" scenarios, and the need for further research on treatment interruptions given the variability in recommendations even among subject-matter experts and ongoing areas of uncertainty not specifically addressed in the guidelines.

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References

1) Fabbiani M, Lombardi A, Colaneri M, et al. High rates of sustained virological response despite premature discontinuation of directly acting antivirals in HCV-infected patients treated in a real-life setting. J Viral Hepat. 2021;28(3):558-568.
2) Cunningham EB, Amin J, Feld JJ, et al. Adherence to sofosbuvir and velpatasvir among people with chronic HCV infection and recent injection drug use: the SIMPLIFY study. Int J Drug Policy. 2018;62:14-23.
3) https://www.hcvguidelines.org/evaluate/monitoring#incomplete-adherence