HCV DAA Treatment Interruptions

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Conflict of Interest Disclosure Statement

- Speaker has nothing to disclose

Learning Objectives

1. Apply the guidance provided by the AASLD/IDSA on HCV DAA treatment interruptions
2. Identify when patients should have DAA therapy continued vs when DAA therapy should be stopped
3. Describe the data in patients with incomplete adherence

AASLD-IDSA HCV Guidelines

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

IDSA
Infectious Diseases Society of America

ome | Test, Evaluate, Monitor | Treatment-Naive | Treatment-Experienced | Unique & Key Populations | About

New and updated:

Updated Testing Recommendations
Review new HCV screening guidance from the AASLD and IDSA.

Search the Guidance

Enter your keyword | Search

Recent Announcements

24 Oct — What's New, Updates and Changes to the Guidance

29 Sep — What's New, Updates and Changes to the Guidance

Start Here: Choose a patient profile from the menu above.

Welcome to HCVGuidelines.org

The AASLD and IDSA in partnership with the panel have created an updated web experience to facilitate easier and faster access to this important resource. Please select a patient profile from the menu above, click on a guidance section below, or use the search box to begin.

Contents and Introduction - *Select a Page*

Testing, Evaluation, and Monitoring of Hepatitis C - *Browse Topics*

- Testing, Evaluation, and Monitoring of Hepatitis C
- HCV Testing and Linkage to Care
- When and in Whom to Initiate HCV Therapy
- Overview of Cost, Reimbursement, and Cost-Effectiveness Considerations for Hepatitis C Treatment Regimens
- Monitoring Patients Who Are Starting HCV Treatment, Are on Treatment, or Have Completed Therapy
- Incomplete Adherence
- HCV Resistance Primer

Initial Treatment of HCV Infection - *Choose Patient Genotype*

https://www.hcvguidelines.org/evaluate/monitoring/incomplete-adherence; Updated 10/5/21, accessed 6/3/23

Introduction

- Missing medication doses is common
- Minimal data regarding the outcome of patients who have incomplete adherence to DAA therapy
- AASLD-IDSA HCV Guidelines updated 10/5/21
- Recommendations are based on the opinion of the AASLD-IDSA HCV Treatment Guidance Panel

Simplify Study

- International multicenter study to evaluate adherence to sofosbuvir/velpatasvir (12 weeks) in 103 people with recent injecting drug use.
  - One-third (32%) of study participants had <90% adherence
  - Most episodes of nonadherence lasted fewer than 7 days; 11% of episodes lasted ≥7 days
  - Despite nonadherence, SVR12 94% among DAA adherent (≥90% of doses) and nonadherent (<90% of doses) patients.

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.

Italian Retrospective Analysis: NAVIGATORE-Lombardia Network

- Aim to investigate SVR 12 rates in patients who prematurely discontinue DAA therapy , N= 365
- DAA discontinued a median of 1 week before planned EOT
- 45% stopped treatment at least 2 weeks prior to planned EOT
- No cirrhosis:

  <4 weeks of therapy SVR 50% (2/4)

  ≥4 weeks of therapy SVR 99% (109/110)
- Cirrhosis:

  <8 weeks of therapy SVR 83% (25/30)

  ≥8 weeks of therapy SVR 95% (209/221)

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.

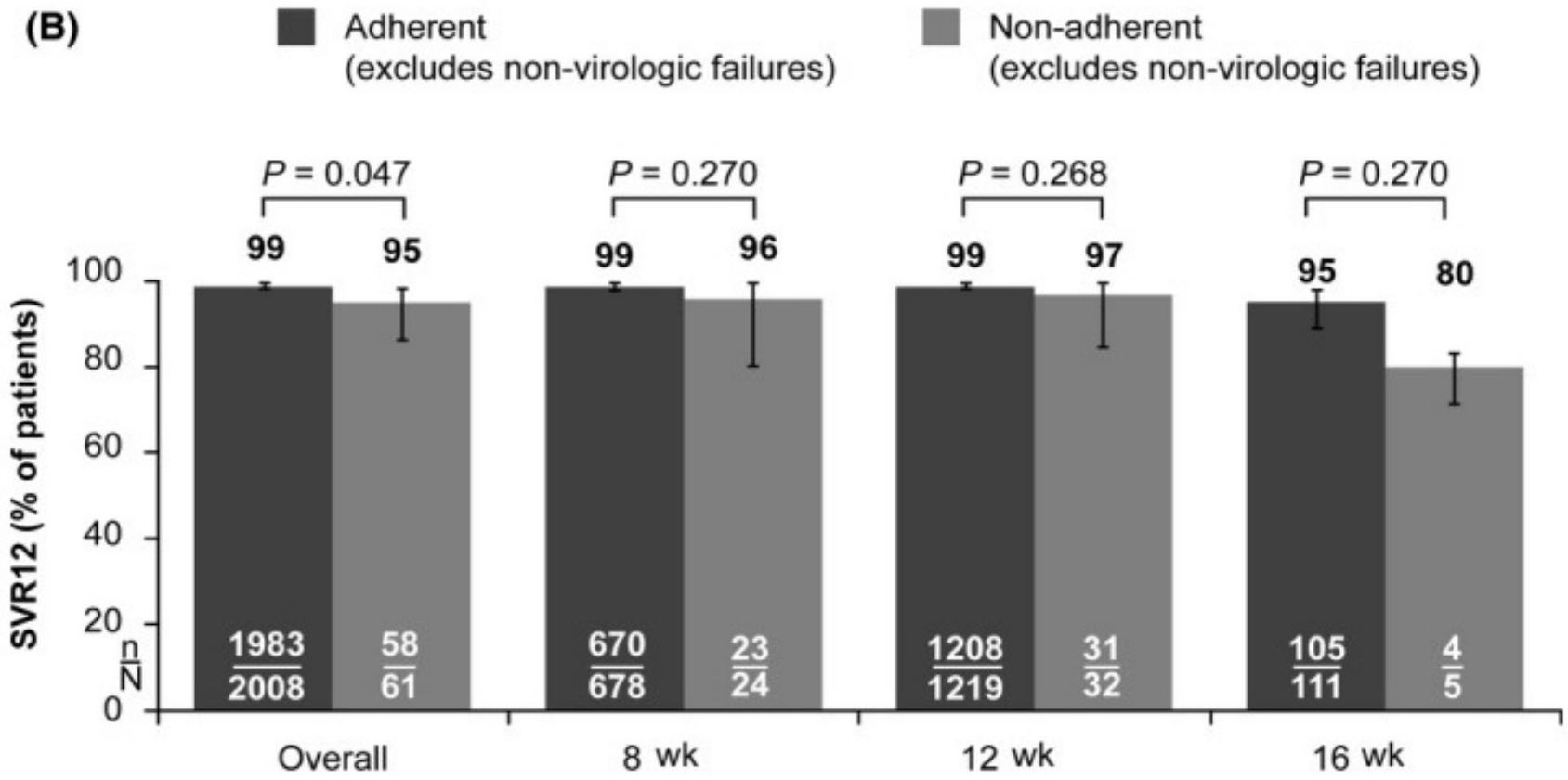
Clinical Trials Data with GLE/PIB

- Pooled analysis of 2091 patients with HCV genotypes 1-6
- Adherence
  - 97% adherent (2024/2091) at all study visits
  - 67% considered non-adherent had <80% adherence during at least 1 study visit

Baseline characteristic, yes vs no	Odds ratio	95% CI	*P* value
Alcohol use (drinker or ex-drinker)	2.38	1.13-5.01	.022
Tobacco use (smoker or ex-smoker)	1.60	0.82-3.13	.167
History of depression	0.98	0.53-1.80	.944
On stable OST	0.81	0.31-2.11	.660
Injecting drug use	1.06	0.61-1.84	.830
On polypharmacy (use of ≥5 concomitant medications)	1.10	0.64-1.87	.737

Brown A et al. Liver Int. 2020:40:778-786

SVR Based on Treatment Duration and Adherence – GLE/PIB



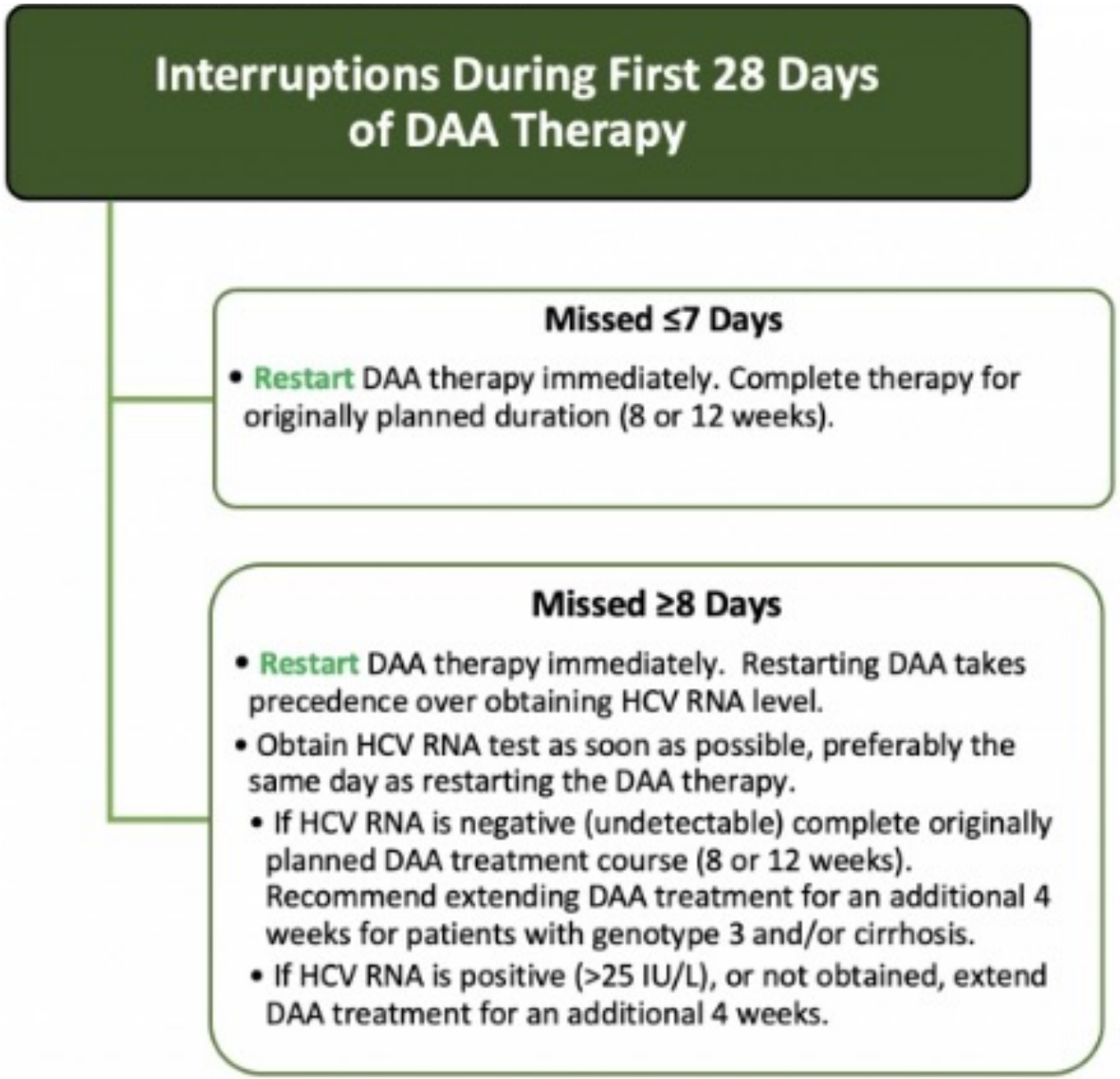
Brown A et al. Liver Int. 2020:40:778-786

Updated Guidance

- Recommendations for :
  - treatment-naive patients
  - no cirrhosis or compensated cirrhosis
  - receiving either glecaprevir/pibrentasvir or sofosbuvir/velpatasvir.
- Recommendations are based on the opinion of the AASLD-IDSA HCV Treatment Guidance Panel

https://www.hcvguidelines.org/evaluate/monitoring/incomplete-adherence
Updated 10/5/21

AASLD/IDSA Guidance on Incomplete Adherence:
First 28 days of therapy



AASLD/IDSA Guidance on Incomplete Adherence: After initial 28 days of treatment

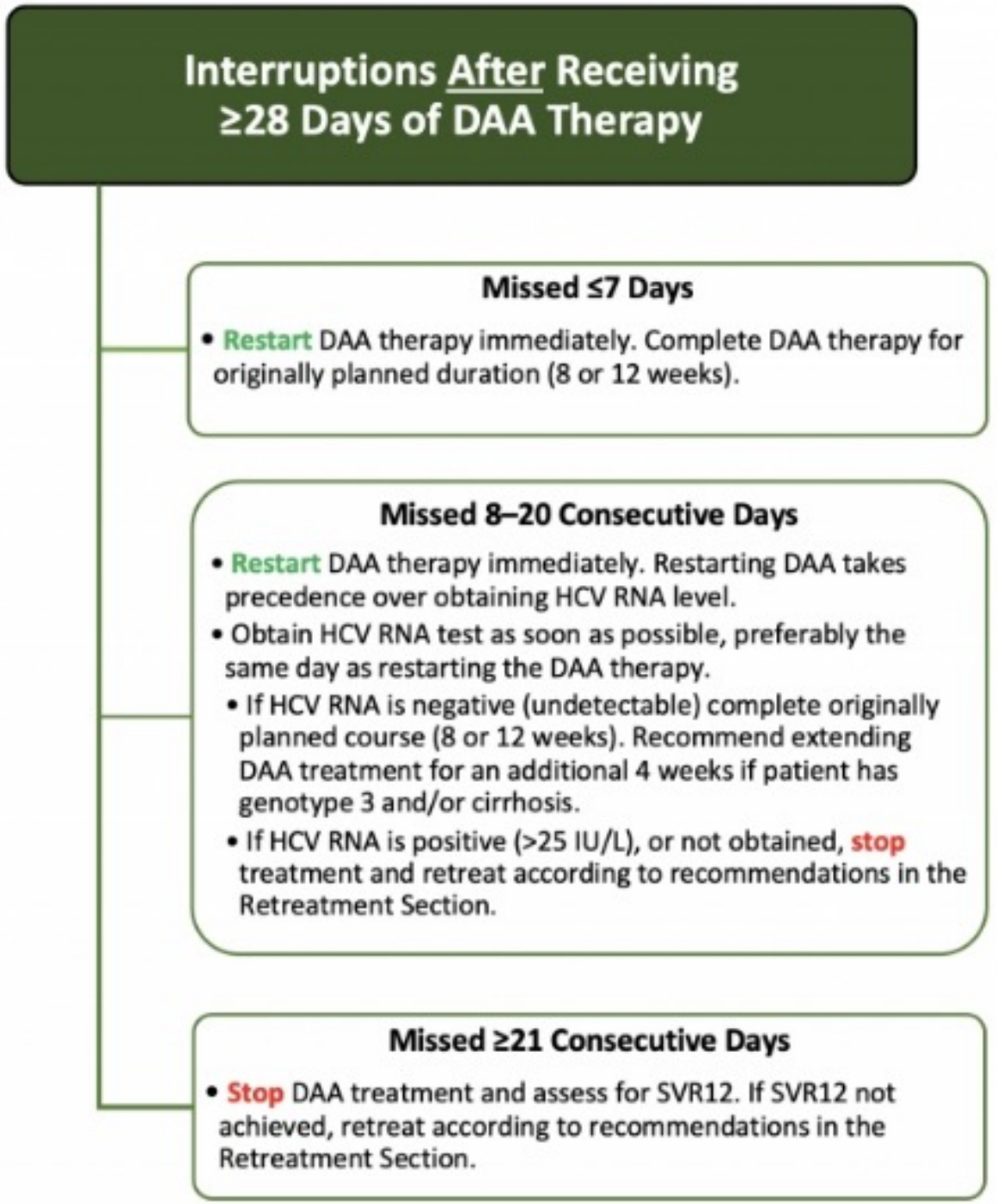
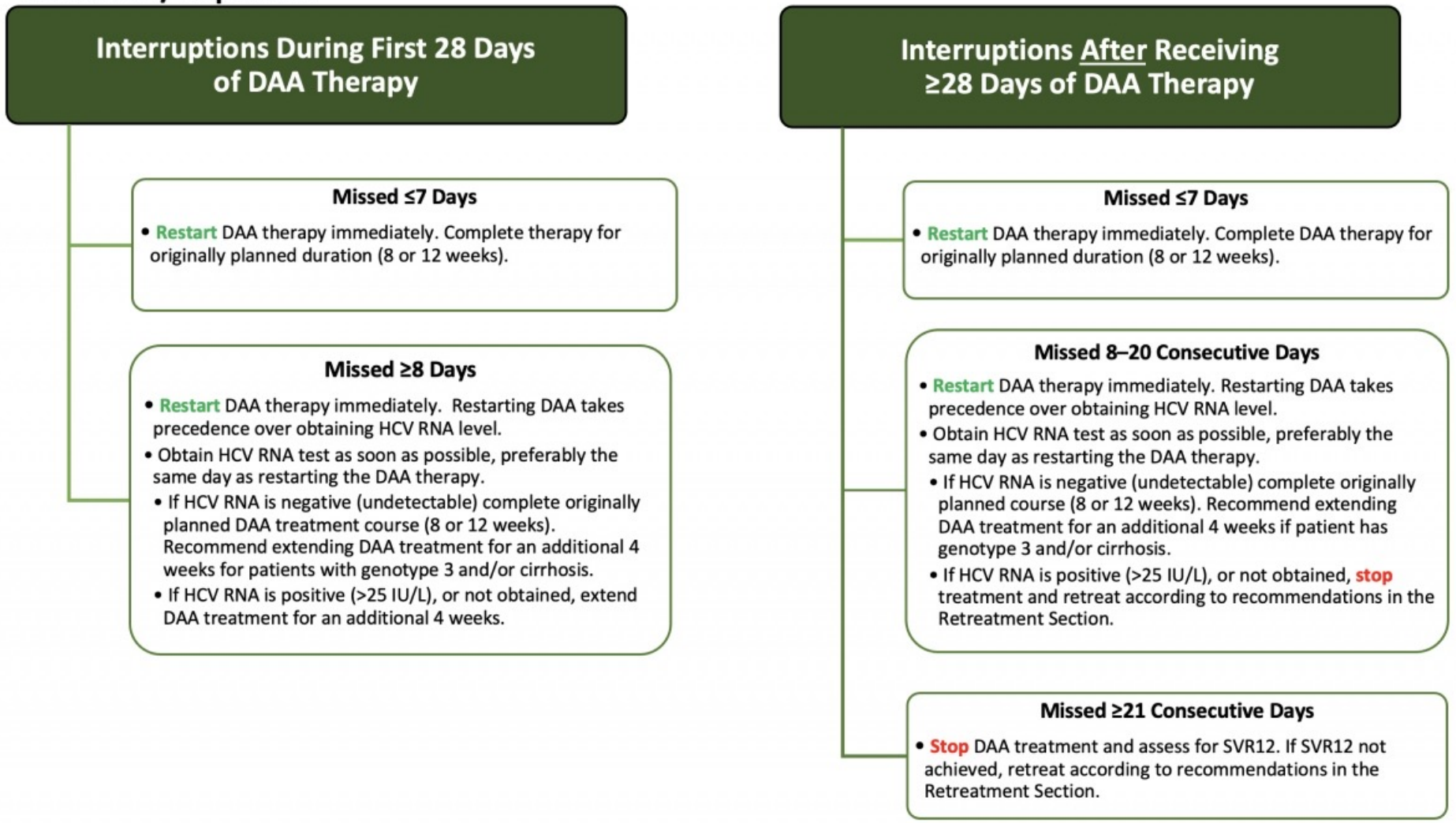


Figure 1. Recommended Management of DAA Treatment Interruptions for Treatment-Naive Patients, Without Cirrhosis or With Compensated Cirrhosis, Receiving Glecaprevir/Pibrentasvir or Sofosbuvir/Velpatasvir



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

https://www.hcvguidelines.org/evaluate/monitoring/incomplete-adherence
Updated 10/5/21

Other recommendations

- Patients with prior DAA treatment, or receiving other DAAs should be managed in consultation with an expert
- All patients with incomplete adherence should be asked about factors contributing to adherence or nonadherence, and counseled regarding the importance of adherence
- In general, the panel considers a treatment interruption of <7 days unlikely to impact SVR12

Key Points

- Patients who miss consecutive doses of DAAs should be restarted on therapy as soon as possible
- Therapy should be stopped if patients have missed more than 21 days of consecutive doses
- Optimal treatment outcomes observed with >90% treatment adherence and full course of HCV therapy **but**
  - *SVR can be achieved with imperfect adherence and shorter courses of therapy*
- Patients with incomplete treatment adherence should be asked about factors which impair adherence and every attempt made to address and minimize these barriers

References

- AASLD-IDSA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. [accessed 6/5/23].
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- Cunningham, E. B., Amin, J., Feld, J. J., Bruneau, J., Dalgard, O., Powis, J., et al. (2018). Adherence to sofosbuvir and velpatasvir among people with chronic HCV infection and recent injection drug use: The SIMPLIFY study. *Int J Drug Policy.* 62*;* 2018:14-23.
- Fabbiani M, Lombardi A, Colaneri M, Del Poggio P, Perini P, 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*. 2021:28:558-563.

Questions