

HCV treatment following HCC diagnosis

Jesse Powell PA-C
Hennepin Healthcare



Objectives

- Review recommendations around who should be treated for HCV
- Discuss the optimal time for initiating DAA treatment following HCC treatment
- Analyze the benefits of treatment vs non treatment

AASLD recommendations on who to treat

Recommendation for When and in Whom to Initiate Treatment	
RECOMMENDED	RATING
Treatment is recommended for all patients with acute or chronic HCV infection, except those with a short life expectancy that cannot be remediated by HCV therapy, liver transplantation, or another directed therapy. Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert.	I, A

Which patients with HCC should be treated?

- **Potentially curative treatment options**
 - Resection or single lesions undergoing ablation
- **Transplant candidates**
- **What about those with:**
 - Multiple lesions
 - Undergoing TACE but not transplant candidates
 - Receiving systemic therapies
 - Metastatic disease
 - Decompensated cirrhosis

Definition of cure for HCC

- HCC free 5 years after curative treatment

Odds of Cure following resection

- Meta-analysis by Rveron-Thorton RF etal.
- Reviewed 110 studies and 82,392 participants
 - 1 year survival 89% and 5 year survival 56%
 - Recurrence free survival at 1 year 71% and 35% at 5 years

When should you start treatment?

- HCC recurrence rates are high (15-20% annually)
 - Is this recurrence in part due to active viremia?
- Does treating HCV early decrease the risk for recurrence?
- Several studies were published following the introduction of DAA's that raised concern about early HCC recurrence after DAA therapy.

Does DAA treatment result in early recurrence?

- **Reig et al**

- 58 patients with HCV and prior HCC
 - 5.7 month follow up – 3 had died and 16 had developed recurrence (27.6%)

- **Pei-Chien Tsai et al**

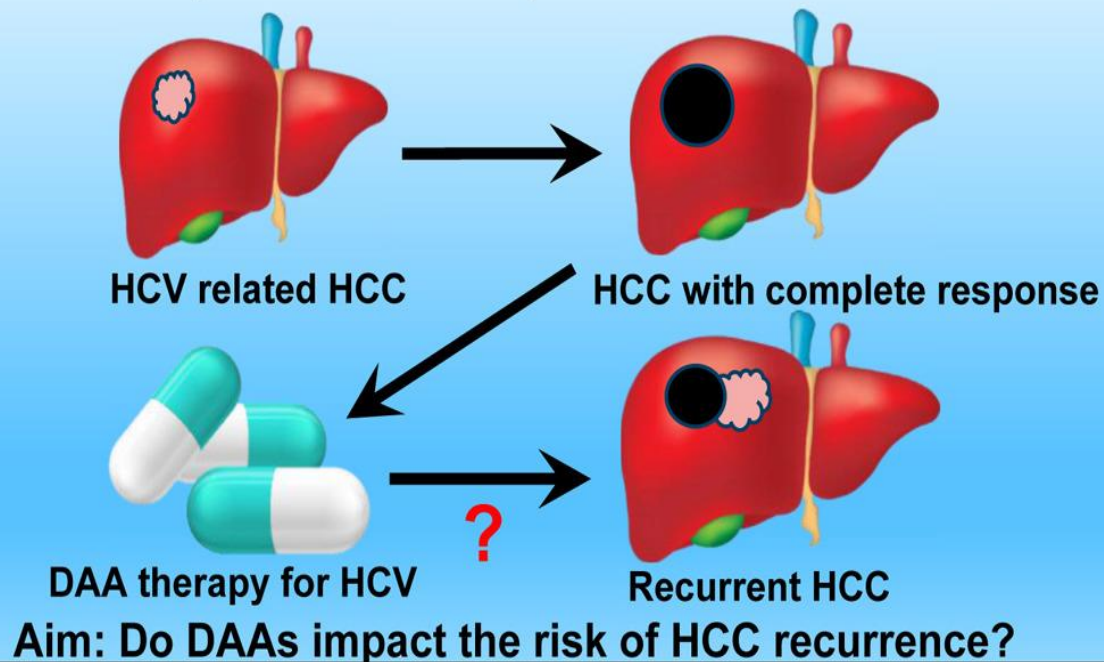
- Recurrence was higher when treatment was starting within 4 months
 - 54.6% vs 21.3%

- **Singal et al**

- 793 patients with HCV associated HCC in North America
 - 304 (38.3%) received DAA and 489 (61.7%) were untreated
 - Recurrence – 41.2% in treated (128 with early recurrence in 52) and 58.9% in untreated (288 with early recurrence in 227).

Direct-Acting Antiviral Therapy is not Associated with HCC Recurrence: A Multicenter North American Cohort Study

Conflicting data on whether direct acting antiviral hepatitis C treatment impacts the risk of hepatocellular carcinoma recurrence



Methods:

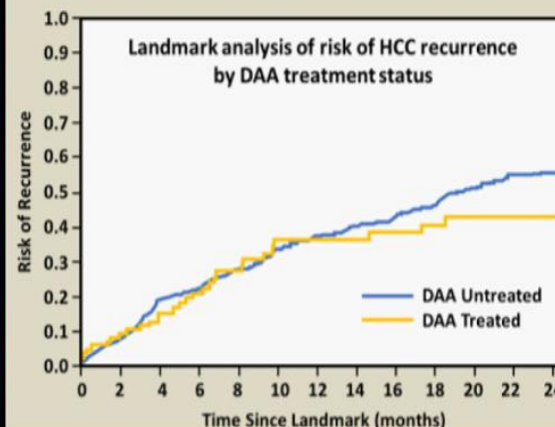
31 centers in North America including patients with HCV-related HCC with complete radiographic response

304 Treated with DAAs
489 Treatment naïve HCV

Results:

DAA therapy has no impact on:

- Overall HCC recurrence (aHR: 0.90 95% CI: 0.70-1.16)
- Early HCC recurrence (aHR: 0.96 95% CI: 0.70-1.34)



Does treatment prevent HCC?

- **Conti et al**
- **344 cirrhotic patients**
 - 59 with previous HCC
- **Followed for 24 weeks**
 - 26 patients developed HCC
 - 17 of the 59 with prior HCC and 9 of the 285 without prior HCC
- **Risk factors:** more severe fibrosis, CP-B, low plts and previous HCC
 - Of those with previous HCC: younger age and more severe fibrosis
- **Conclusion:** DAA treatment did not seem to reduce occurrence of HCC.

Decrease risk of recurrence?

- **Torres Et al**

- No patients (N 20) who received curative procedures followed by DAA showed recurrent HCC at median follow up of 12 months (range 4-60 months)

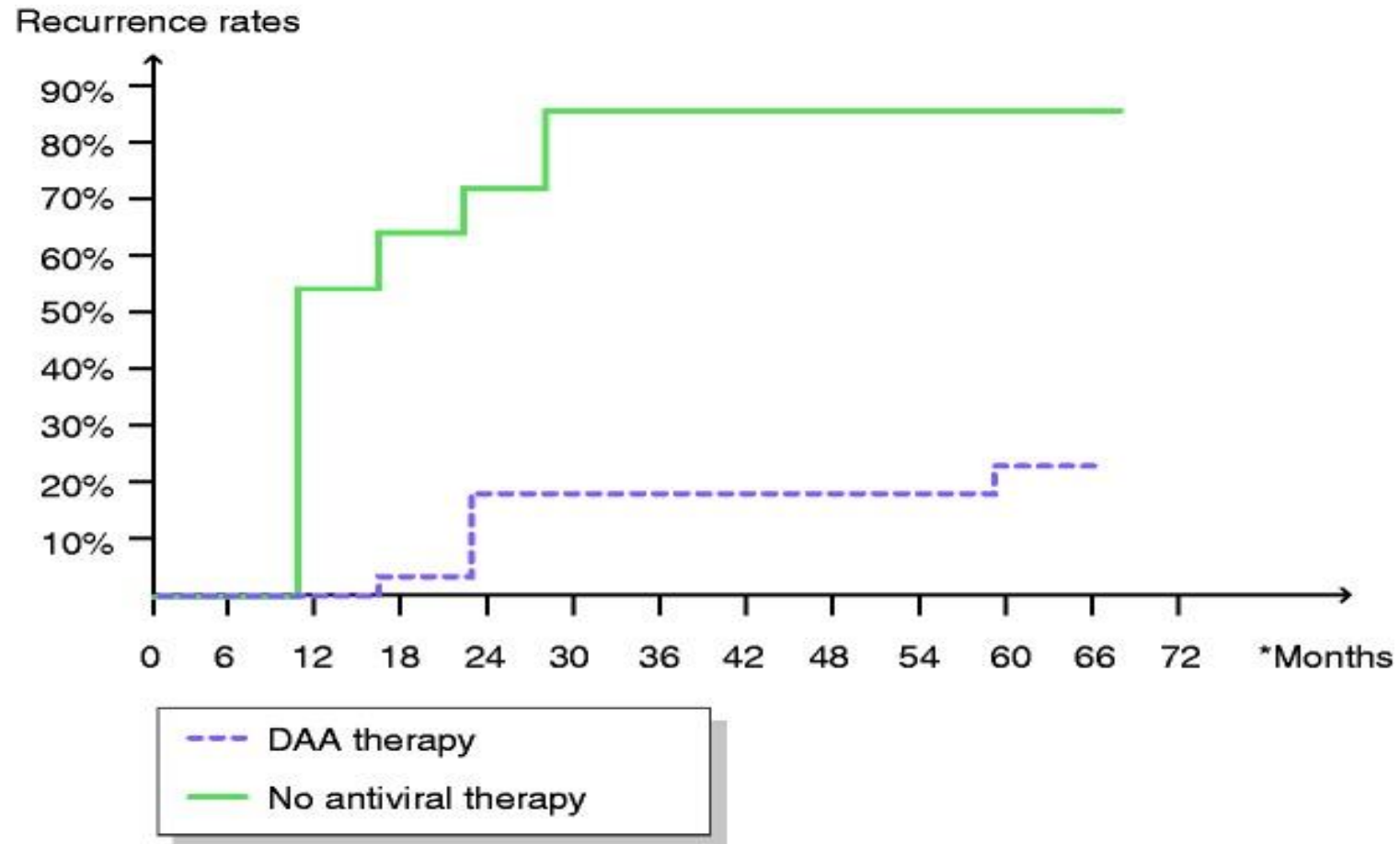
- **Ikeda et al**

- 177 patients received DAA after curative HCC treatment
- 89 underwent HCV treatment
- Recurrence rates at 1 and 2 years for DAA treated vs untreated
 - 18.1 and 25% and 21.8 and 46.5%

- **Preda et al**

- Reoccurrence during 44 month follow up:
- HCC treated with resection, RFA or TACE and given DAA vs HCC treated but no antiviral therapy given (27% vs 91%)

Preda et al



Conclusion

- Treatment of HCV following HCC treatment is beneficial
- Timing of treatment may be debatable

Reference

- Reveron-Thornton RF, Teng MLP, Lee EY, Tran A, Vajanaphanich S, Tan EX, Nerurkar SN, Ng RX, Teh R, Tripathy DP, Ito T, Tanaka T, Miyake N, Zou B, Wong C, Toyoda H, Esquivel CO, Bonham CA, Nguyen MH, Huang DQ. Global and regional long-term survival following resection for HCC in the recent decade: A meta-analysis of 110 studies. *Hepatol Commun*. 2022 Jul;6(7):1813-1826. doi: 10.1002/hep4.1923. Epub 2022 Mar 2. PMID: 35234371; PMCID: PMC9234624.
- Gao X, Zhan M, Wang L, Ding Y, Niu J. Timing of DAA Initiation After Curative Treatment and Its Relationship with the Recurrence of HCV-Related HCC. *J Hepatocell Carcinoma*. 2020 Dec 1;7:347-360. doi: 10.2147/JHC.S279657. PMID: 33299823; PMCID: PMC7720283.
- Reig M, Mariño Z, Perelló C, Iñarrairaegui M, Ribeiro A, Lens S, Díaz A, Vilana R, Darnell A, Varela M, Sangro B, Calleja JL, Forns X, Bruix J. Unexpected high rate of early tumor recurrence in patients with HCV-related HCC undergoing interferon-free therapy. *J Hepatol*. 2016 Oct;65(4):719-726. doi: 10.1016/j.jhep.2016.04.008. Epub 2016 Apr 13. PMID: 27084592.
- Conti F, Buonfiglioli F, Scuteri A, Crespi C, Bolondi L, Caraceni P, Foschi FG, Lenzi M, Mazzella G, Verucchi G, Andreone P, Brillanti S. Early occurrence and recurrence of hepatocellular carcinoma in HCV-related cirrhosis treated with direct-acting antivirals. *J Hepatol*. 2016 Oct;65(4):727-733. doi: 10.1016/j.jhep.2016.06.015. Epub 2016 Jun 24. PMID: 27349488.
- Singal AG, Rich NE, Mehta N, Branch A, Pillai A, Hoteit M, Volk M, Odewole M, Scaglione S, Guy J, Said A, Feld JJ, John BV, Frenette C, Mantry P, Rangnekar AS, Oloruntoba O, Leise M, Jou JH, Bhamidimarri KR, Kulik L, Tran T, Samant H, Dhanasekaran R, Duarte-Rojo A, Salgia R, Eswaran S, Jalal P, Flores A, Satapathy SK, Wong R, Huang A, Misra S, Schwartz M, Mitrani R, Nakka S, Nouredine W, Ho C, Konjeti VR, Dao A, Nelson K, Delarosa K, Rahim U, Mavuram M, Xie JJ, Murphy CC, Parikh ND. Direct-Acting Antiviral Therapy Not Associated With Recurrence of Hepatocellular Carcinoma in a Multicenter North American Cohort Study. *Gastroenterology*. 2019 May;156(6):1683-1692.e1. doi: 10.1053/j.gastro.2019.01.027. Epub 2019 Jan 18. PMID: 30660729; PMCID: PMC6598433.
- Preda CM, Baicus C, Sandra I, Oproiu A, Manuc T, Constantinescu I, Gavrilă D, Dicuțescu M, Dumitru R, Vasilescu C, Tieranu C, Istratescu D, Voiosu T, Manuc M. Recurrence rate of hepatocellular carcinoma in patients with treated hepatocellular carcinoma and hepatitis C virus-associated cirrhosis after ombitasvir/paritaprevir/ritonavir+dasabuvir+ribavirin therapy. *United European Gastroenterol J*. 2019 Jun;7(5):699-708. doi: 10.1177/2050640619841254. Epub 2019 Mar 29. PMID: 31210948; PMCID: PMC6545706.
- Ikeda K, Kawamura Y, Kobayashi M, Kominami Y, Fujiyama S, Sezaki H, Hosaka T, Akuta N, Saitoh S, Suzuki F, Suzuki Y, Arase Y, Kumada H. Direct-Acting Antivirals Decreased Tumor Recurrence After Initial Treatment of Hepatitis C Virus-Related Hepatocellular Carcinoma. *Dig Dis Sci*. 2017 Oct;62(10):2932-2942. doi: 10.1007/s10620-017-4739-z. Epub 2017 Sep 7. PMID: 28884320.