EACS
European
AIDS
Clinical
Society

Clinical Management and Treatment of Viral Hepatitis Co-infections in PLWH

Charles Béguelin for the Viral Hepatitis Co-infections EACS guidelines panel

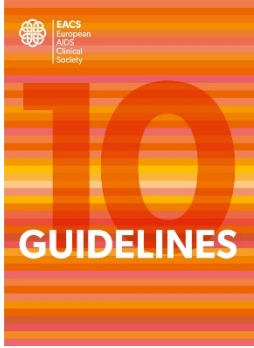
Disclosures

Research Support: Gilead
Educational support: Gilead, MSD
Speaker’s Bureau: Never
Board Member/Advisory Panel: Not in the past 12 months
Stock/Shareholder: Never
Consultant: Never
Employee: Never

Summary of Changes

- New chapter **name**:
  - «Clinical management and treatment of **Viral Hepatitis** Co-infections in PLWH»

- New chapter **structure**:
  - General recomendations
  - Treatment and monitoring of persons with **HBV**/HIV Co-infection
  - Treatment and monitoring of persons with **HCV**/HIV Co-infection
  - **Hepatitis D and E** in PLWH



General recomendation

- **Diagnosing hepatic fibrosis**:

The combination of **liver stiffness** measurement and **blood tests** or repeated assessments may improve accuracy.

Cut-off Values of Non-invasive Tests for the Detection of Significant Fibrosis and Cirrhosis

HIV/Hepatitis C co-infection (according to EASL recommendations on Treatment of Hepatitis C 2018 [1])

Test	Stage of fibrosis	Cut off (kPa)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Fibroscan	F3*	10	72	80	62	89
	F4*	13	72-77	85-90	42-56	95-98
APRI	F4	2	48	94	n.a.	n.a.
		1	77	75	n.a.	n.a.
Fib-4	F4	3.25	55	92	n.a.	n.a.
		1.45	90	58	n.a.	n.a.

These cut-offs were derived from different studies and the optimal values might vary between populations and must be interpreted together with the individual clinical assessment

*The distinction between F3 and F4 is often imprecise and must be interpreted in the individual clinical context

HIV/Hepatitis B co-infection [2], [3], [4]

Test	Stage of fibrosis	Cut off (kPa)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Fibroscan	F3	7.6	85	87	77	92
	F4	9.4	92	94	79	98
APRI	F4	2	35	89	26	92
		1	65	75	22	95

EACS European AIDS Clinical Society

HBV/HIV Co-infection

- **HCC screening**

In HBV-positive non-cirrhotic, HCC screening should follow current HCC EASL guidelines (http://www.easl.eu/research/our-contributions/clinical-practice-guidelines/detail/easl-clinical-practice-guidelines-on-hepatocellular carcinoma). Risk factors for HCC in this population include family history of HCC, ethnicity (Asians, Africans), HDV and **age >45 years**.

Wandeler et al. J. Hepatol. 2019

HBV/HIV Co-infection

- **HBV reactivation**

HBs-Ag negative, anti-HBc positive persons undergoing immunosuppression:

– **Severe immunosuppressive therapy** (chemotherapy for lymphoma/leukaemia or stem-cell or solid-organ transplantation)
➢ **TDF/TAF** therapy to prevent HBV reactivation.

– **B-cell-depleting agents** (rituximab, ofatumumab, natalizumab, alemtuzumab, ibritumomab)
➢ **TDF/TAF** should be part of the ART. If contraindicated, second line options include 3TC and FTC (cave reactivation due to resistance)

– **Other immunosuppressive therapy** (e.g. TNF alpha inhibitor)
➢ **careful monitoring** with HBV DNA and HBsAg is required for HBV reactivation. If this is not possible, addition of TDF/TAF is recommended

Caution with ART simplification strategy without TDF/TAF or NRTI free regimens

HCV/HIV Co-infection

- **DAA table has been split in two parts:**

Preferred treatment options

Preferred DAA HCV treatment options (except for persons pre-treated with Protease or NS5A inhibitors)

HCV GT	Treatment regimen	Treatment duration & RBV usage		
		Non-cirrhotic	Compensated cirrhotic	Decompensated cirrhotics CTP class B/C
1 & 4	EBR/GZR	12 weeks[ii]		Not recommended
	GLE/PIB	8 weeks	12 weeks	Not recommended
	SOF/VEL	12 weeks		12 weeks with RBV
	SOF/LDV +/- RBV	8-12 weeks without RBV[iii]	12 weeks with RBV[iii]	
2	GLE/PIB	8 weeks	12 weeks	Not recommended
	SOF/VEL	12 weeks		12 weeks with RBV
3	GLE/PIB	8 weeks[iv]	12 weeks[iv]	Not recommended
	SOF/VEL +/- RBV	12 weeks[v]	12 weeks with RBV[vi] or 24 weeks without RBV	
	SOF/VEL/VOX	-	12 weeks	Not recommended
5 & 6	GLE/PIB	8 weeks	12 weeks	Not recommended
	SOF/LDV +/- RBV	12 weeks +/- RBV[viii]	12 weeks with RBV[iii]	
	SOF/VEL	12 weeks		12 weeks with RBV

Treatment options if preferred not available

DAA HCV treatment options (except for persons pre-treated with Protease or NS5A inhibitors) to be used if preferred option is not avaible

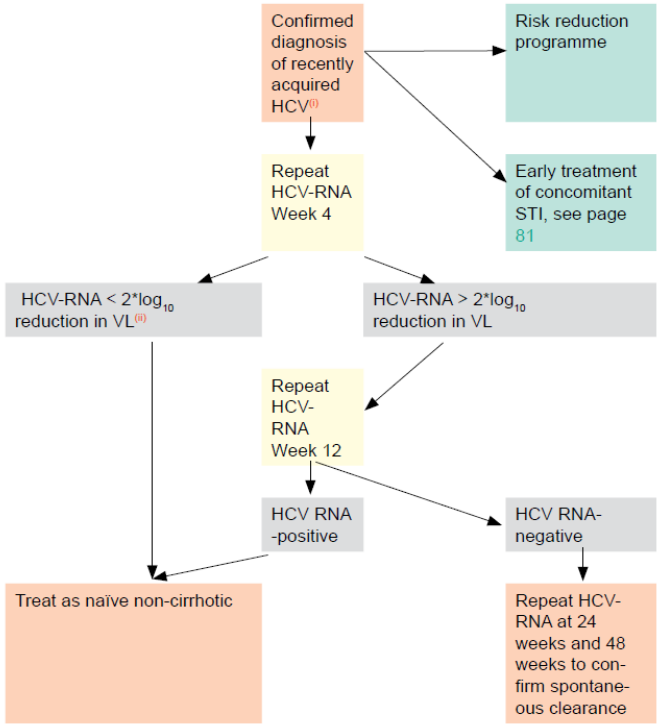
HCV GT	Treatment regimen	Treatment duration & RBV usage		
		Non-cirrhotic	Compensated cirrhotic	Decompensated cirrhotics CTP class B/C
1 & 4	OBV/PTV/r + DSV	8[ix]-12 weeks in GT 1b	12 weeks in GT 1b	Not recommended
	OBV/PTV/r + DSV + RBV	12 weeks in GT 1a	24 weeks in GT 1a	Not recommended
	OBV/PTV/r + RBV	12 weeks in GT 4		Not recommended
	SOF + DCV +/- RBV	12 weeks +/- RBV[x]	12 weeks with RBV[iii]	
	SOF/VEL/VOX	8 weeks[iv]	12 weeks	Not recommended
2	SOF + DCV	12 weeks		12 weeks with RBV
	SOF/VEL/VOX	8 weeks[iv]	12 weeks	Not recommended
3	SOF + DCV +/- RBV	12 weeks +/- RBV[xi] or 24 weeks without RBV	24 weeks with RBV	
	SOF/VEL/VOX	8 weeks[iv]	12 weeks	Not recommended
5 & 6	SOF + DCV +/- RBV	12 weeks +/- RBV or 24 weeks without RBV[xii]	12 weeks with RBV[iii]	
	SOF/VEL/VOX	8 weeks[iv]	12 weeks	Not recommended

EACS European AIDS Clinical Society

HCV/HIV Co-infection

- Figure on management of **recently acquired HCV infection:**

HCV-RNA <2log reduction at 4 weeks is considered as **early chronic HCV infection**



a) Treat with short duration DAAs
b) Enrol in clinical trial for acute HCV treatment

European AIDS Treatment Network (NEAT) consensus conference statement june 2019 (www.neat-id.org).

EACS European AIDS Clinical Society

HDV and HEV in PLWH

- Screen for HDV antibodies in all HBsAg postive PLWH
- Use non invasive markers with caution
- Refer early to university centers

Hepatitis D and E in PLWH

Hepatitis Delta Virus (HDV)

1. HDV antibodies should be screened for in all HBsAg positive PLWH
2. In PLWH with positive HDV antibodies, HDV-RNA should be measured in order to assess activity of the disease
3. In PLWH with chronic HDV co-infection and significant liver fibrosis (≥ F2), long-term (at least 12 months) treatment with PEG-IFN might be considered in association with TDF-based ART
4. Non-invasive fibrosis markers (transient elastography and serum markers) should be used with caution in PLWH with chronic HDV infection as there are no well-established thresholds
5. Because of its anti-HBV activity, TDF/TAF should be added to PEG-IFN in order to reduce HBV-DNA load
6. PLWH without response to PEG-IFN treatment should be referred to university centers and if possible enrolled in trials on new drugs active against HDV
7. Treatment efficacy should be monitored with HBV-DNA and HDV-RNA measurements, when available, and with follow-up of biochemical and liver fibrosis estimates
8. Persistent off-treatment HDV-RNA negativity and anti-HBs seroconversion are the ideal goals of antiviral treatment for HDV even if they can only be obtained in a minority of PLWH. Histological remission of liver disease is a less ambitious but more likely achievable goal
9. In PLWH with HDV and ESLD or HCC, liver transplantation from HBsAg negative donors should be strongly considered. Transplant with anti-HBV prophylaxis post-OLTX cures HBV and HDV infection

Hepatitis E Virus (HEV)

10. Screening for HEV infection is warranted in PLWH with symptoms consistent with acute hepatitis, unexplained flares of aminotransferases (even if suspected drug induced liver injury), unexplained elevated liver function tests, neuralgic amyotrophy, Guillain-Barrè, encephalitis or proteinuria
11. Screening should include anti-HEV IgG and IgM and HEV-RNA in blood and if possible in stool
12. Treatment with RBV (600 mg daily) may be considered in cases of severe acute HEV, acute-on-chronic liver failure, extrahepatic HEV related disease or in persons with persisting HEV replication three months after first detection of HEV-RNA. RBV should be given for a duration of 12 weeks followed by HEV-RNA measurements in serum and stool. If HEV-RNA is undetectable in both, RBV can be stopped. In PLWH in whom HEV-RNA is still detectable in serum and/or stool, RBV may be continued for an additional three months. In the setting of chronic HEV infection in immunosuppressed persons, reduction in immunosuppression should be considered

EACS European AIDS Clinical Society

10 GUIDELINES

Acknowledgements

Viral Hepatitis Co-infections	
Chair: Andri Rauch	**Bern, Switzerland**
Vice-Chair: Sanjay Bhagani	**London, United Kingdom**
Young scientist:	
Charles Béguelin	**Bern, Switzerland**
Juan Berenguer	Madrid,Spain
Christoph Boesecke	Bonn, Germany
Raffaele Bruno	Pavia, Italy
Svilen Konov	London, United Kingdom
Karine Lacombe	Paris, France
Stefan Mauss	Düsseldorf, Germany
Luís Mendão	Lisbon, Portugal
Lars Peters	Copenhagen, Denmark
Massimo Puoti	Milan, Italy
Jürgen K. Rockstroh	Bonn, Germany

Lene Ryom

Co-morbidity panel

EACS European AIDS Clinical Society

EACS European AIDS Clinical Society

10 GUIDELINES