Presenter Disclosure Information

In compliance with the Conflict of Interest Policies, the European AIDS Clinical Society (EACS) requires the following disclosure from the presenters:

Lene Ryom

Research Support: None
Speaker's Bureau: Never
Board Member/Advisory Panel: Never
Stock/Shareholder: Never
Consultant: Never
Employee: Never
Other: Never

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EACS Treatment Guidelines V9.0
An introduction To The 2017 Revisions

Lene Ryom, MD PhD
Assistant EACS Guidelines Coordinator
Centre for Health and Infectious Diseases Research (CHIP),
Department of Infectious Diseases, Section 2100, Rigshospitalet,
Copenhagen, Denmark

Aims of the EACS Guidelines

The scope of the EACS guidelines is to

- Provide easy accessible recommendations to clinicians centrally involved with the care of HIV-positive individuals
- Cover a large and geographically diverse area
- Not to be considered as a full overview of all aspects of HIV-infection, but rather as a continuously updated overview of the most relevant clinical issues in HIV

New Summary of Changes in v9.0

Summary of Changes from v8.2 to v9.0

ART section

- **What to start with:** Older ARVs (LPV/r) have been removed. The order of the listed regimens was changed to reflect the preference of use based on the data available. The structure of the table was changed to facilitate the reading of essential information. Footnotes were added: a note on when to prefer TAF over TDF; a note on the potential CVD toxicity of DRV; a note on ATV and renal toxicity, page 11
- **Primary HIV infection:** Recommendation that all HIV-positive women of reproductive age should have a pregnancy test was added, page 12
- **Switch strategies:** Indications for switch were added (HCV treatment, renal/bone toxicity). DTG+RPV regimen was added as switch option. DTG monotherapy was added in the strategies not recommended. The wording and structure of "Class-sparing strategies" was changed to improve clarity, page 13
- **Virological failure:** Changes in the definition were made to differentiate "incomplete suppression" from "virological rebound". A note on the importance of taking into consideration all the available resistance tests when choosing a new regimen in patient with virological failure was added, page 14
- **ARV in pregnancy:** A recommendation on use of INSTI in pregnant women who start ARVs in the late second or third trimester was added. A warning note on EFV in pregnancy was removed. EFV, RAL, RPV or DRV/r can be continued during pregnancy. Women on EVG/c need to be informed that more monitoring of HIV-VL and drug levels may be necessary during pregnancy. A recommendation against the initial use of TAF and cobicistat was added. A recommendation against breastfeeding was added, page 15
- **Post-Exposure Prophylaxis (PEP):** A note on providing emergency contraception counselling for sexual exposure was added, page 17

Co-morbidities and related sections

- Four entirely new sections were introduced on:
  - Non-Alcoholic Fatty Liver Disease (NAFLD), page 57
  - Chronic lung disease, page 73
  - Prescribing in elderly, page 76
  - Solid Organ Transplantation (SOT), page 77
- New drug-drug interaction tables were included on bronchodilators, pulmonary antihypertensives and immunosuppressants, pages 26, 30 and 31
- The drug-drug interaction table on antimalarial drugs was changed to a format, similar to all remaining drug-drug interaction tables, page 29
- ATV/c data were added to all drug-drug interaction tables
- Ischaemic heart disease was added as a potential adverse effect of DRV/r, page 19
- Recommendations for screening for anal cancer were extended to also include all persons with HPV-associated dysplasia; screening for cervical cancer now includes all HIV-positive women > 21 years of age or within one year after sexual debut, pages 7 and 38
- Blood pressure targets were lowered for high risk individuals and where resources allow to SBT < 130 and DBT < 80 mmHg, pages 40-41
- Diabetes management was revised and sulfonylureas are now only recommended in combination with metformin. Limited data remain for any oral antidiabetic agents in terms of CVD prevention in the HIV-positive population, page 45
- A new lipid lowering drug class of PCSK9-inhibitors was added and is to be considered in high risk individuals inadequately controlled on top statin dose or when statin intolerant, page 46
- Recommendations on clinical situations where TAF may be preferred over TDF were added to the bone and kidney section, pages 47 and 50
- More dynamic measures of kidney function declines were added, page 50
- HPV vaccination is now recommended for all HIV-positive persons up to 26 years of age and up to 40 years if MSM, page 6 and page 64
- A recommendation to screen for STIs not only for those at risk, but also during pregnancy was added, page 65
- As part of an interim update in Jan 2017, we have further included video links to EACS online courses on HIV management, page 101
- In the Introduction to the Guidelines we have further emphasised that the EACS Guidelines aim to cover wide ranges of recommendations as opposed to the often more uniform national guidelines as the Guidelines geographically cover a relatively large and diverse area with different national levels of access to care, page 2

Co-infections section

- HCV core-antigen testing has been added, page 79
- HCC screening recommendations have been updated, pages 56 and 79
- HBV treatment figure has been removed. Footnotes have been converted into full text with new recommendations for individuals with HBV who face immunosuppression
- Evaluation of concurrent causes of liver disease has been added to the diagnostic procedures table, page 81
- Text on HCV treatment has been shortened with emphasis on DAA table
- Recommendations for individuals with failure on DAA treatment have been updated, page 82
- Recommendations for individuals with acute HCV have been updated, page 82
- HCV management figure was removed
- DDI table has been updated and now includes GLE/PIB and SOF/VEL/VOX, boceprevir and telaprevir have been deleted, page 84
- Figure on management of acute HCV has been amended, page 85
- All tables and figures dealing with IFN-containing HCV therapy have been removed. We refer to an older online version of the Guidelines for details on IFN-treatment, page 82

Opportunistic infections section

- A comment for TMP-SMX as preferred therapy for cerebral toxoplasmosis when the oral route is not available was added, page 88
- The preliminary results of the REALITY trial in the cryptococcal disease section were added, page 89. An enhanced infection prophylaxis in severely immunosuppressed individuals (< 50 CD4 cells/µL) including INH 12 weeks, fluconazole 100 mg/day 12 weeks, azithromycin 500 mg/day for 5 days and albendazole 400 mg single dose may decrease overall opportunistic infections (including cryptococcal meningitis) and mortality
- A comment on the possibility to add fluconazole to liposomal amphotericin B during the induction phase for cryptococcal meningitis treatment in countries where flucytosine is not available was added, page 89
- Intermittent TB regimens (2 or 3 times per week) are contraindicated in HIV-positive persons, page 95
- A comment on the possibility to add steroid therapy to avoid IRIS in individuals with TB was added, page 95
- The preliminary results of the Nix-TB trial in the section of treatment for resistant TB (MDR- and XDR-TB) were added, page 96
- A duration of 9-months for latent TB treatment, particularly in countries with high TB prevalence, was emphasised, page 97
- A comment explaining that other preventive regimens are needed for treating latent infection with MDR-/XDR-TB in countries with high resistant TB rates was added, page 97

EACS Guidelines are available online at http://www.eacsociety.org and in the EACS Guidelines App

Imprint

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New Topics in v9.0

Drug-drug Interactions between Bronchodilators (for COPD) and ARVs

Bronchodilators		ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	EVG/c	RAL	ABC	FTC	3TC	TAF	TDF	ZDV
LAMA	aclidinium bromide	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	glycopyrronium bromide	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	tiotropium bromide	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	umeclidinium bromide	↑	↑	↑	↑	↑	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔	↔
SAMA	ipratropium	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
LABA	formoterol	↔[a]	↔[a]	↔	↔	↔[a]	↔	↔	↔	↔[a]	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	indacaterol	↑[d]	↑[d]	↑[d]	↑[d]	↑[d]	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	olodaterol	↑	↑	↑	↑	↑	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔	↔
	salmeterol	↑[b]	↑[b]	↑[b]	↑[b]	↑[b]	↓	↓	↓	↔[a]	↔	↔	↑[b]	↔	↔	↔	↔	↔	↔	↔	↔
	vilanterol	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔	↔
SABA	salbutamol (albuterol)	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
MX	aminophylline	↔	↓	↔	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	theophylline	↔	↓	↔	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
PDE4	roflumilast	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔	↔
ICS	beclometasone	↑[c]	↑[c]	↑?[c]	↓11%	↑[c]	↔	↔	↔	↔	↔	↔	↑[c]	↔	↔	↔	↔	↔	↔	↔	↔
	budesonide	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔	↔
	fluticasone	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔	↔

Legend

↑	potential elevated exposure of the bronchodilator
↓	potential decreased exposure of the bronchodilator
↔	no significant effect
D	potential decreased exposure of ARV drug
E	potential elevated exposure of ARV drug
ATV/c	ATV co-formulated with COBI (300/150 mg qd);
DRV/c	DRV co-formulated with COBI (800/150 mg qd)
a	caution as both drugs can induce QT interval prolongation

Colour legend

- no clinically significant interaction expected
- these drugs should not be co-administered
- potential clinically significant interaction that is likely to require additional monitoring, alteration of drug dosage or timing of administration
- potential interaction likely to be of weak intensity. Additional action/ monitoring or dosage adjustment is unlikely to be required

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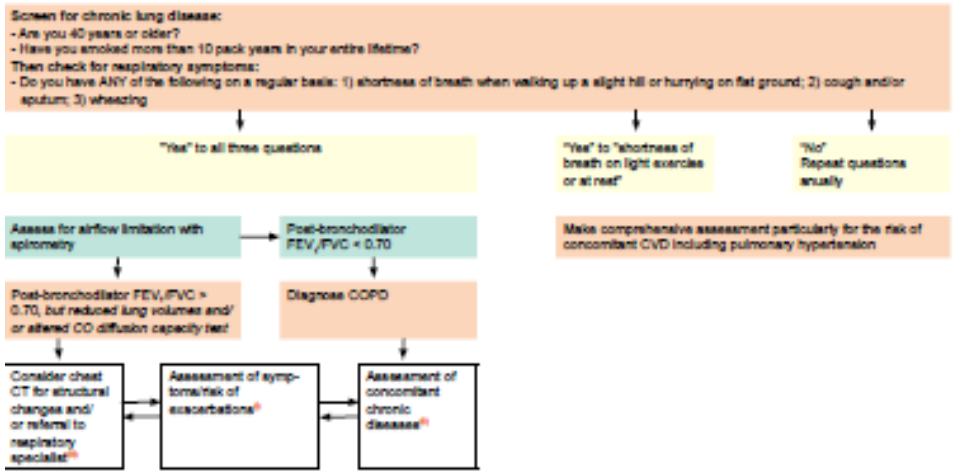
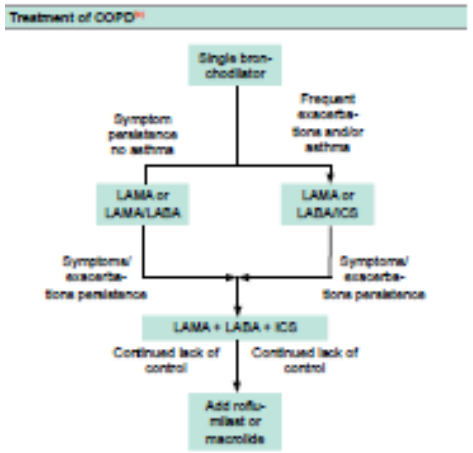
New Topics in v9.0

Chronic Lung Disease in HIV





LABA: long-acting β2-agonist
LAMA: long-acting muscarinic antagonist
ICS: inhaled corticosteroid

There are 3 life saving interventions:
1. Smoking cessation
2. Chronic oxygen when stable (non-exacerbated) resting $SpO_2 \leq 88\%$ (or $PaO_2 \leq 55$ mmHg)
3. Non-invasive ventilation (NIV) in individuals with acute hypercapnic respiratory failure

i Assessment of either dyspnoea using mMRC, see https://www.verywell.com/guidelines-for-the-mmrc-dyspnea-scale-914740 or symptoms using CAT™, see http://www.catestonline.org/ and history of exacerbations (including prior hospitalisations)

ii COPD itself has significant extra-pulmonary (systemic) effects including weight loss, nutritional abnormalities and skeletal muscle dysfunction

iii Based on expert opinion

iv Each pharmacological treatment should be individualised and guided by the severity of symptoms, risk of exacerbations, adverse effects, co-morbidities, drug availability and cost, and the individual's response, preference and ability to use various drug delivery devices. Inhaler technique needs to be assessed regularly.
Long-term use of oral glucocorticoids has no evidence of benefits in COPD. Because of the risk of pneumonia and because of proven superiority of LABA/LAMA over LABA/ICS, the addition of ICS to LABA is recommended only in individuals with history of frequent exacerbations and/or asthma or in individuals not adequately controlled by LAMA/LABA combination. Do not use inhaled glucocorticoids with boosted ART regimens, see Drug-drug Interactions between Corticosteroids and ARVs.
Influenza and pneumococcal vaccination decreases rates of lower respiratory tract infections, see Vaccination

New Topics in v9.0

Non-Alcoholic Fatty Liver Disease (NAFLD)

The prevalence of NAFLD is higher in individuals with HIV infection (30- 40% in the US) than in the general population [9]. Nearly half of the HIV-positive persons that undergo evaluation for unexplained liver test abnormalities are found to have NAFLD. The diagnosis of NAFLD requires the exclusion of both secondary causes and of a daily alcohol consumption ≥ 30 g for men and ≥ 20 g for women.

Spectrum of NAFLD

Often associated with components of the metabolic syndrome:

Non-Alcoholic Fatty Liver (NAFL)
- Pure steatosis

NAFLD
- Steatosis and mild lobular inflammation

Non-Alcoholic SteatoHepatitis (NASH)
- Early NASH: no or mild (F0-F1) fibrosis
- Fibrotic NASH: significant (≥ F2) or advanced (≥ F3, bridging) fibrosis
- NASH-cirrhosis (F4)
- HCC (can occur in the absence of cirrhosis and histological evidence of NASH)

Most common concurrent diseases
- AFLD-alcoholic fatty liver disease
- Drug-induced fatty liver disease
- HCV-associated fatty liver (GT 3)

Consideration on ARV drugs

- d-drugs (ddI, d4T) are contraindicated in individuals at risk of or with NAFLD
- Consider use of lipid neutral regimens in individuals at risk of or with NAFLD

Diagnosis

- Ultrasound is the preferred first-line diagnostic procedure for imaging of NAFLD.
- Whenever imaging tools are not available or feasible, serum biomarkers and scores are an acceptable alternative for the diagnosis. Fibroscan is not validated for this purpose.
- A quantitative estimation of liver fat can only be obtained by 1H-MRS. This technique is of value in clinical trials and experimental studies, but is expensive and not recommended in the clinical setting.
- NASH has to be diagnosed by a liver biopsy showing steatosis, hepatocyte ballooning and lobular inflammation.

Treatment of NAFLD

- Lifestyle modification and weight reduction is the cornerstone of treatment
- Pharmacotherapy should be reserved for individuals with NASH, particularly for those with significant fibrosis ≥ F2 and individuals with less severe disease, but at high risk of faster disease progression (i.e. with diabetes, metabolic syndrome, persistently increased ALT, high necroinflammation).
- Management and treatment of NASH should be discussed with hepatologists. Options with proven efficacy include pioglitazone, vitamin E and bariatric surgery.
- Statins may be safely used but have demonstrated no impact on liver disease. The same is true for n-3 polyunsaturated fatty acids.

Diagnostic flow-chart to assess and monitor disease severity in case of suspected NAFLD and metabolic risk factors

* Serum fibrosis markers: NAFLD-Fibrosis Score, FIB-4, Commercial tests (FibroTest, FibroMeter, ELF)

These recommendations are largely inspired by the EASL–EASD–EASO Clinical Practice Guidelines for the Management of Non-Alcoholic Fatty Liver Disease: European Association for the Study of the Liver (EASL), European Association for the Study of Diabetes (EASD) and European Association for the Study of Obesity (EASO) [9]

New Topics in v9.0

Solid Organ Transplantation (SOT) in HIV-Positive Persons

General features

- HIV infection is not a contraindication for transplantation consideration.
- Experts in HIV medicine should preferably be members of the multi-disciplinary team, responsible for the pre-transplant evaluation, and take primary responsibility for the management of the HIV infection and the prevention and treatment of OIs.

Organ criteria for SOT

- HIV-positive persons should be considered for organ transplantation using the same indications as used in HIV-negative persons. HIV-positive persons with HCC can be evaluated for liver transplantation if they fulfill the Milan criteria[1].

HIV-infection criteria for SOT

According to most international guidelines, HIV-positive individuals should fulfil the following criteria to be considered for SOT

1. **Clinical criteria.** No active OIs or HIV-related cancers. Individuals with PML, chronic crypto/microsporidiosis, multi-drug resistant fungal or mycobacterial infections, NHL and visceral KS to be excluded. For non-HIV-related cancers same criteria apply as in the general HIV-negative population.
2. **Immunological criteria.** CD4 > 200 cells/µL for all SOT except for liver transplantation where CD4 > 100 cells/µL. Persons with previous opportunistic infections should have a CD4 > 200 cells/µL.
3. **Virological criteria.** Full control of HIV replication prior to and after transplantation should be confirmed/predicted in all cases.
4. **Drug abuse.** Abstinence period: alcohol 6 months; heroin/cocaine 2 years. Former IVDUs can be in methadone programme.

Preparing HIV-positive persons for transplantation

Antiretroviral therapy

- Choice of ART components should avoid drugs known to cause organ dysfunction or drugs with a high potential for drug-drug interactions if at all possible, see Drug-drug interactions between immunosuppressants (for SOT) and ARVs.
- Using a pharmacological booster (RTV or COBI) and some of the NNRTIs are best avoided, see Drug-drug interactions between immunosuppressants (for SOT) and ARVs.
- For individuals nearing indication for transplantation, ART should be modified to ensure this if at all possible.
- RAL (and probably DTG) plus 2 NRTIs is the preferred regimen.
- If the individual has not yet started ART and transplantation is considered, ART should be commenced as soon as possible and preferably before the transplantation is started.

Viral hepatitis co-infection

In liver transplant candidates, every effort should be made to treat the underlying viral hepatitis, see pages 80 and 82-84. Use of DAAs in persons with HCV co-infection may improve their liver function, and possibly lead to them being removed from the transplant waiting list.

Prevention of infections

- While screening and treatment for latent TB is recommended in all HIV-positive persons, see page 97, it is particularly important in persons pre-and post-transplantation due to the additional use of immunosuppres-

Follow-up after transplantation

Antiretroviral therapy

- Same recommendations in individuals under preparation for transplantation.
- Additionally, ARVs may exacerbate immunosuppressive agents' adverse drug effects (kidney impairment, bone marrow suppression, drug-induced liver injury, etc.). Therefore, careful consideration of which drugs to use is essential see Adverse Effects of ARVs & Drug Classes.
- Before starting or restarting abacavir containing ART the HLA-B*5701 status of the donor should be assessed.

Primary and secondary disease-specific chemoprophylaxis

- HIV-positive transplant recipients should receive the same surveillance, prophylaxis and immunisation regimens for OIs as HIV-negative SOT recipients.
- Screening and treatment for latent TB is a priority, see page 97.

Viral hepatitis co-infection

- The efficacy and safety of DAAs in liver transplant HIV-positive recipients with HCV recurrence is the same as in HIV-negative recipients.
- Anti HBV treatment should follow the same schedules of HIV-negative persons.

Immunosuppressive regimens

- Same as in HIV-negative transplant recipients. The risk of acute rejection is however double of that of HIV-negative SOT recipients and, therefore, requires close monitoring.
- Special attention to interaction with ART, see Drug-drug interactions between immunosuppressants (for SOT) and ART.

[1] Milan criteria: solitary tumor smaller than 5 cm or 2–3 tumors of < 3 cm in the absence of macrovascular tumor invasion and extrahepatic metastases.

New Videolinks

Video links

EACS Guidelines	Video lectures	Link to video lecture
Primary HIV Infection	When to Start ART Part 1	https://vimeo.com/197164442/93941a8e75
	When to Start ART Part 2	https://vimeo.com/197167665/3f00ac2634
	What ART to Start Part 1	https://vimeo.com/197374541/32232bd037
	What ART to Start Part 2	https://vimeo.com/197378793/215317ddab
Switch Strategies for Virologically Suppressed Persons	How to Change ART	https://vimeo.com/197161843/ae0c46e0be
Virological Failure	Adherence and Prevention of HIV Drug Resistance	https://vimeo.com/197381327/d7e972c0d5
ART in TB/HIV Co-infection	HIV and the Management of IRIS Part 1	https://vimeo.com/197762901/a147257ffc
	HIV and the Management of IRIS Part 2	https://vimeo.com/197765956/9b61e5d15d
Pre-exposure Prophylaxis	PrEP Part 1	https://vimeo.com/196714648/6a196a71a4
	PrEP Part 2	https://vimeo.com/196716750/a12a32989b
Adverse Effects of ARVs and Drug Classes	Adverse Effects and Monitoring	https://vimeo.com/197275138/3df1c99e55
Cancer: Screening Methods	Clinical Management of Cancers and HIV Part 1	https://vimeo.com/197398883/6cbeebb66e
	Clinical Management of Cancers and HIV Part 2	https://vimeo.com/197748761/68cc01229a
	Epidemiology of Cancers Part 1	https://vimeo.com/197749519/afea560124
	Epidemiology of Cancers Part 2	https://vimeo.com/197749948/e7e5062f2d
Prevention of CVD	HIV and CVD, CKD, Endocrinology	https://vimeo.com/197488153/396253a733
Kidney Disease: Definition, Diagnosis and Management	HIV and CVD, CKD, Endocrinology	https://vimeo.com/197488153/396253a733
Lipodystrophy: Prevention and Management	HIV and CVD, CKD, Endocrinology	https://vimeo.com/197488153/396253a733
Algorithm for Diagnosis and Management of HIV-Associated Neurocognitive Impairment (NCI) in Persons without Obvious Confounding Conditions	CNS and HIV Part 1	https://vimeo.com/197280954/e995f1c097
	CNS and HIV Part 2	https://vimeo.com/197370416/ee3655aa09
Diagnostic Procedures for HCV in Persons with HCV/HIV Co-infection	Hepatitis C and HIV Co-infection Part 1	https://vimeo.com/197259934/bc5cac91d1
	Hepatitis C and HIV Co-infection Part 2	https://vimeo.com/197261826/0462d2df0e
	Hepatitis C and HIV Co-infection Part 3	https://vimeo.com/197262690/a323b6cd72
Introduction to OIs	Pulmonary Infections Part 1	https://vimeo.com/197388161/dc24235ab6
	Pulmonary Infections Part 2	https://vimeo.com/197389876/7c26fb8551
	Pulmonary Infections Part 3	https://vimeo.com/197392161/f90020ae21
	CNS and HIV-related Opportunistic Infections Part 1	https://vimeo.com/197752868/34462456dd
	CNS and HIV-related Opportunistic Infections Part 2	https://vimeo.com/197758431/6b2939c62a
Diagnosis and Treatment of TB in HIV-positive Persons	Tuberculosis and HIV Co-infection Part 1	https://vimeo.com/196723861/7a067d0254
	Tuberculosis and HIV Co-infection Part 2	https://vimeo.com/197161188/4e881b687c

EACS Guidelines Organisation

The guidelines V9.0 consist of:

- Summary of changes from v8.0 to 9.0

- Part I : Visit Assessment
- Part II : ART
- Part III: Co-morbidities
- Part IV: Co-infections
- Part V : Opportunistic Infections

- References

- Videolinks

EACS Guidelines Management

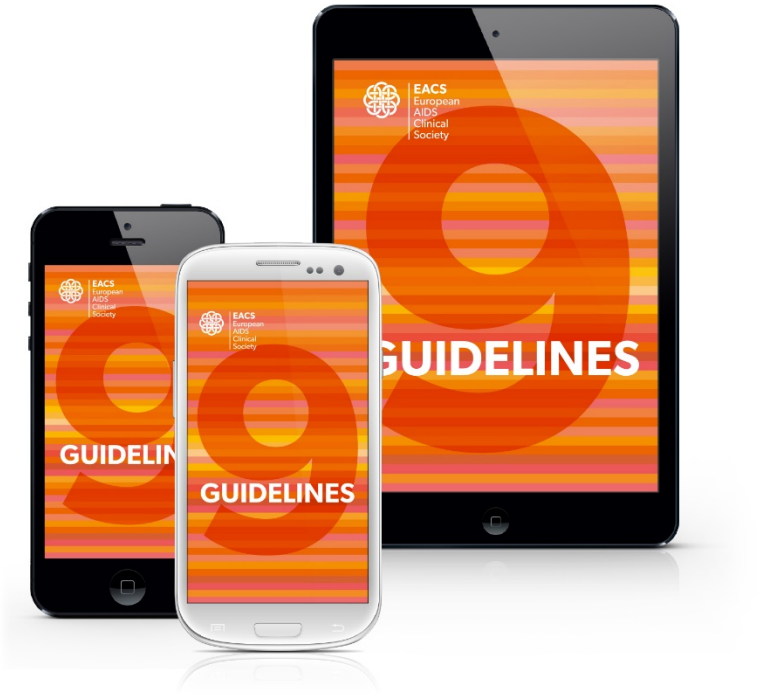
Each individual part of the guidelines is

Managed by
- A Panel of experienced European HIV experts
- External experts (e.g. in the co-morbidity part)
- And Reviewed by community representatives and Wave

Governed by
- A 3-person leadership group
  – Panel Chair, Co-chair and Young Scientist

The guidelines content is managed by
- The EACS Medical Secretariat; guideline coordination chair and assistant working closely with the EACS Secretariat

EACS Guidelines Availabilities



- In print as a booklet
- Since 2015 as a free App for IOS and Android systems
  by the Sanford Guide
- Online on the EACS website

http://www.eacsociety.org/guidelines/eacs-guidelines/eacs-guidelines.html

EACS European AIDS Clinical Society

EACS Guidelines Revisions

- Formal reviews are made annually for the electronic versions, and biennially for the printed version, but updates are also made continuously
  - New important data immerge
  - Feedback from the users

- We warmly welcome feedback on content and translations, can be submitted via guidelines@eacsociety.org

Panel Members

Medical Secretariat

The EACS Medical Secretariat is responsible for the coordination and update of the EACS Guidelines based on the recommendations from the four EACS panels.

Guidelines Chair and Coordinator:	
Manuel Battegay	**Basel, Switzerland**
Assistant Coordinator:	
Lene Ryom	**Copenhagen, Denmark**

HIV Treatment

Chair: Anton Pozniak	**London, United Kingdom**
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Young scientist: Margherita Bracchi	**London, United Kingdom**
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François Raffi	Nantes, France
Peter Reiss	Amsterdam, The Netherlands
Hans-Jürgen Stellbrink	Hamburg, Germany

Co-morbidities

Chair: Georg Behrens	**Hannover, Germany**
Vice-Chair: Patrick Mallon	**Dublin, Ireland**
Young scientist: Lene Ryom	**Copenhagen, Denmark**
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Giovanni Guaraldi	Modena, Italy
Jens D. Lundgren	Copenhagen, Denmark
Esteban Martinez	Barcelona, Spain
Catia Marzolini	Basel, Switzerland
Socrates Papapoulos	Leiden, The Netherlands
Renaud du Pasquier	Lausanne, Switzerland
Neil Poulter	London, United Kingdom
Peter Reiss	Amsterdam, The Netherlands
Ian Williams	London, United Kingdom
Alan Winston	London, United Kingdom

Co-infections

Chair: Massimo Puoti	**Milan, Italy**
Vice-Chair: Andri Rauch	**Bern, Switzerland**
Young scientist: Christoph Boesecke	**Bonn, Germany**
Juan Berenguer	Madrid, Spain
Sanjay Bhagani	London, United Kingdom
Raffaele Bruno	Pavia, Italy
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ART SECTION
EACS GUIDELINES V9.0

Dr Anton Pozniak
ART Panel Head

ART section updates

- Recommended regimens for naïve patients
- Alternative regimens
- Primary HIV infection
- Switch strategies
- Virological failure
- ARVs in pregnancy
- Post-exposure prophylaxis

Recommended regimens

Regimen	Dosing	Caution	Food requirement
2 NRTIs + INSTI			
ABC/3TC/DTG[i, ii]	ABC/3TC/DG 600/300/50 mg, 1 tablet qd	Al/Ca/Mg-containing antacids or multivitamins should be taken well separated in time (minimum 2h after or 6h before) DTG 50 mg bid with rifampicin	None
TAF/FTC[iii] or TDF/FTC[iii] + DTG	TAF/FTC 25/200 mg, 1 tablet qd or TDF/FTC 300/200 mg, 1 tablet qd + DTG 50 mg, 1 tablet qd		None
TAF/FTC/EVG/c[iii] or TDF/FTC/EVG/c[iii,iv]	TAF/FTC/EVG/c 10/200/150/150 mg, 1 tablet qd or TDF/FTC/EVG/c 300/200/150/150 mg, 1 tablet qd	Al/Ca/Mg-containing antacids or multivitamins should be taken well separated in time (minimum 2h after or 6h before)	With food
TAF/FTC[iii] or TDF/FTC[iii] + RAL	TAF/FTC 25/200 mg, 1 tablet qd or TDF/FTC 300/200 mg, 1 tablet qd + RAL 400 mg, 1 tablet bid	Co-administration of antacids containing Al or Mg not recommended RAL 400 or 800 mg bid with rifampicin.	None
2 NRTIs + NNRTI			
TAF/FTC/RPV[iii] or TDF/FTC/RPV[iii]	TAF/FTC/RPV 25/200/25 mg, 1 tablet qd or TDF/FTC/RPV 300/200/25 mg, 1 tablet qd	Only if CD4 count > 200 cells/µL and HIV-VL < 100,000 copies/mL PPI contra-indicated; H2 antagonists to be taken 12h before or 4h after RPV	With food
2 NRTIs + PI/r or PI/c			
TAF/FTC[iii] or TDF/FTC[iii] + DRV/c[v] or + DRV/r[v]	TAF/FTC 10/200 mg, 1 tablet qd or TDF/FTC 300/200 mg, 1 tablet qd + DRV/c 800/150 mg, 1tablet qd or + DRV 800 mg, 1 tablet qd + RTV 100 mg, 1 tablet qd		

New

- For recommended regimens order = alphabetical
- For alternative regimen order = preference of use
- When to prefer TAF over TDF
- ATV and renal toxicity
- Potential DRV CV toxicity

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Alternative regimens

Regimen	Dosing	Caution	Food requirement
2 NRTIs + INSTI			
ABC/3TC[i, ii] + RAL	ABC/3TC 600/300 mg, 1 tablet qd + RAL 400 mg, 1 tablet bid	Co-administration of antacids containing Al or Mg not recommended. RAL 400 or 800 mg bid with rifampicin	None
2 NRTIs + NNRTI			
ABC/3TC[i, ii] + EFV[vi]	ABC/3TC 600/300 mg, 1 tablet qd + EFV 600 mg, 1 tablet qd	Only if HIV-VL <100,000 copies/mL	At bed time or 2 hours before dinner
TDF/FTC/EFV[iii,vi]	TDF/FTC/EFV 300/200/600 mg, 1 tablet qd		
2 NRTIs + PI/r or PI/c			
TAF/FTC[iii] or TDF/FTC[iii] + ATV/c[vii,viii] or + ATV/r[vii,viii]	TAF/FTC 10/200 mg 1 tablet qd or TDF/FTC 300/200 mg, 1 tablet qd + ATV/c 300/150 mg, 1 tablet qd or + ATV 300 mg, 1 tablet qd + RTV 100 mg, 1 tablet qd		With food
ABC/3TC[i, ii] + ATV/c[vii,viii] or + ATV/r[vii,viii]	ABC/3TC 600/300 mg, 1 tablet qd + ATV/c 300/150 mg 1 tablet qd or + ATV 300 mg, 1 tablet qd + RTV 100 mg, 1 tablet qd	Only if HIV-VL < 100,000 copies/mL	With food
ABC/3TC[i, ii] + DRV/c[v] or + DRV/r[v]	ABC/3TC 600/300 mg, 1 tablet qd + DRV/c 800/150 mg, 1 tablet qd or + DRV 800 mg, 1 tablet qd + RTV 100 mg, 1 tablet qd	Monitor in p allergy	
Other combinations			
RAL[ii] + DRV/c[v] or + DRV/r[v]	RAL 400 mg, 1 tablet bid + DRV/c 800/150 mg, 1 tablet qd or + DRV 800 mg, 1 tablet qd + RTV 100 mg, 1 tablet qd	Only if CD4 100,000 cop Co-administ not recomm	

New

- Older ARVs (LPV/r) removed
- Order = preference of use

Primary HIV Infection

Acute infection: HIV detection (p24 Ag and/or HIV-RNA) in the absence of HIV antibody.

Recent infection: HIV antibody detection; up to 6 months after infection

Circumstances where immediate treatment initiation should be advised

- Acute infection
- Severe or prolonged symptoms
- Neurological disease
- Age ≥ 50 years
- CD4 count < 350 cells/µL

Treatment selection

- Clinical trials (HIV curative strategies)
  .
- Resistance test
- If therapy starts before resistance test available:
- Start a PI/r or PI/c or an INSTI + TDF or TAF/FTC
- Regimen can be adjusted once the resistance test is available and viral load is suppressed

New

All HIV-positive women of reproductive age should have a pregnancy test

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Switch strategies

Pt with VL<50 cp

Indications

- Documented toxicity
- Prevention of long-term toxicity.
- Avoid serious DDIs
- Planned pregnancy
- Ageing and/or co-morbidity
- Simplification
- Starting of HCV treatment (DDIs)

New

- **Indications for switch** (HCV rx, renal/bone toxicity)
- **DTG+RPV included**

DTG monotherapy not recommended

Dual therapy
DTG + RPV
3TC + (DRV/r or DRV/c)
3TC + (ATV/r or ATV/c)

Monotherapy with DRV/r

only if
a) no resistance to the PI
b) suppression of HIV-VL <50 cp for 6 months
c) absence of chronic HBV co-infection

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Virological failure

New
Definition of Virological Failure

INCOMPLETE SUPPRESSION: HIV-VL > 200 copies/mL at 6 months after starting therapy

VIROLOGICAL REBOUND: confirmed HIV VL > 50 copies/mL in patients with previous undetectable vital loads

If HIV-VL > 50 and < 500:

- Check adherence
- Check HIV-VL 1 to 2 months later
- If genotype na, consider changing regimen based on past rx and resistance hx

If HIV-VL confirmed > 500:

- Change regimen as soon as possible based on the resistance testing results
- If no resistance mutations found: re-check for adherence, perform TDM

ARV in pregnancy

1. Women planning to be pregnant/ becoming pregnant while already on ART: Maintain ART

[Contra-indicated during pregnancy: ddI + d4T, triple NRTI]

2. Women becoming pregnant, treatment-naïve: Start ART ASAP

4. Women whose follow-up starts late in II/III trimester: Start ART ASAP / INSTI as the preferred choice rapid HIV-VL decline NEW!

5. Women whose HIV-VL is not <50 cp in III trimester: VRT / consider INSTI if not already on it

ARV in pregnancy

Antiretroviral regimens:

If on RAL, DTG, RPV or DRV/r: could be continued (Among PI/r, prefer ATV/r)

- EFV is a suitable alternative NEW!
- NVP not to be initiated but can be continued
- TAF and Cobicistat in pregnancy: not recommended in initial regimen (limited experience) NEW!
- Caution with EVG/cobi: monitoring of VL and drug levels may be needed (low exposure demonstrated in third trimester) NEW!

Breastfeeding

- We advise against breastfeeding. In case a woman insists on breastfeeding we recommend follow-up with increased clinical and virological monitoring of both the mother and the infant NEW!

Post-Exposure Prophylaxis (PEP)

Rapid testing of the source person for HCV/HIV (if HIV-status unknown):
if Source person HIV-positive on ART, order resistance testing if HIV-VL detectable
For sexual exposure, if HIV-positive source has documented undetectable HIV-VL, PEP is no longer recommended.

- Individualise PEP according to the source's treatment history and previous resistance tests
- PEP to be started ideally < 4 hours after the exposure, and no later than 48/72 hours
- Duration of PEP: 4 weeks (unless discontinued due to lack of indication)

PEP regimen: TDF/FTC + RAL bid

Alternatives: TDF/FTC + DRV/r qd or
+ LPV/r bid or
+ DTG qd

- Full sexual health screen in case of sexual exposure
- Emergency contraception counselling for sexual exposure

New
Emergency contraception counselling for sexual exposure

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Presenter Disclosure Information

In compliance with the Conflict of Interest Policies, the European AIDS Clinical Society (EACS) requires the following disclosure from the presenters:

Georg Behrens

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Speaker's Bureau: Gilead, ViiV, Janssen, Abbvie, MSD, Hexal, Sandoz
Board Member/Advisory Panel: Gilead, BMS, Janssen, ViiV, MSD
Stock/Shareholder: Never
Consultant: Never
Employee: Never
Other: Never

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Part III Prevention and Management of Co-morbidities in HIV-positive Persons

Professor Georg Behrens
Department for Clinical Immunology and Rheumatology
Hannover Medical School, Hannover, Germany

Part III Prevention and Management of Co-morbidities in HIV-positive Persons

Young scientist: Lene Ryom **Copenhagen, Denmark**

Catia Marzolini Basel, Switzerland

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9

We recommend

multi-disciplinary care

for

aging HIV patients

with

multiple co-morbidities

and

chronic immune activation

to maintain

good quality of life

and to prevent

frailty.

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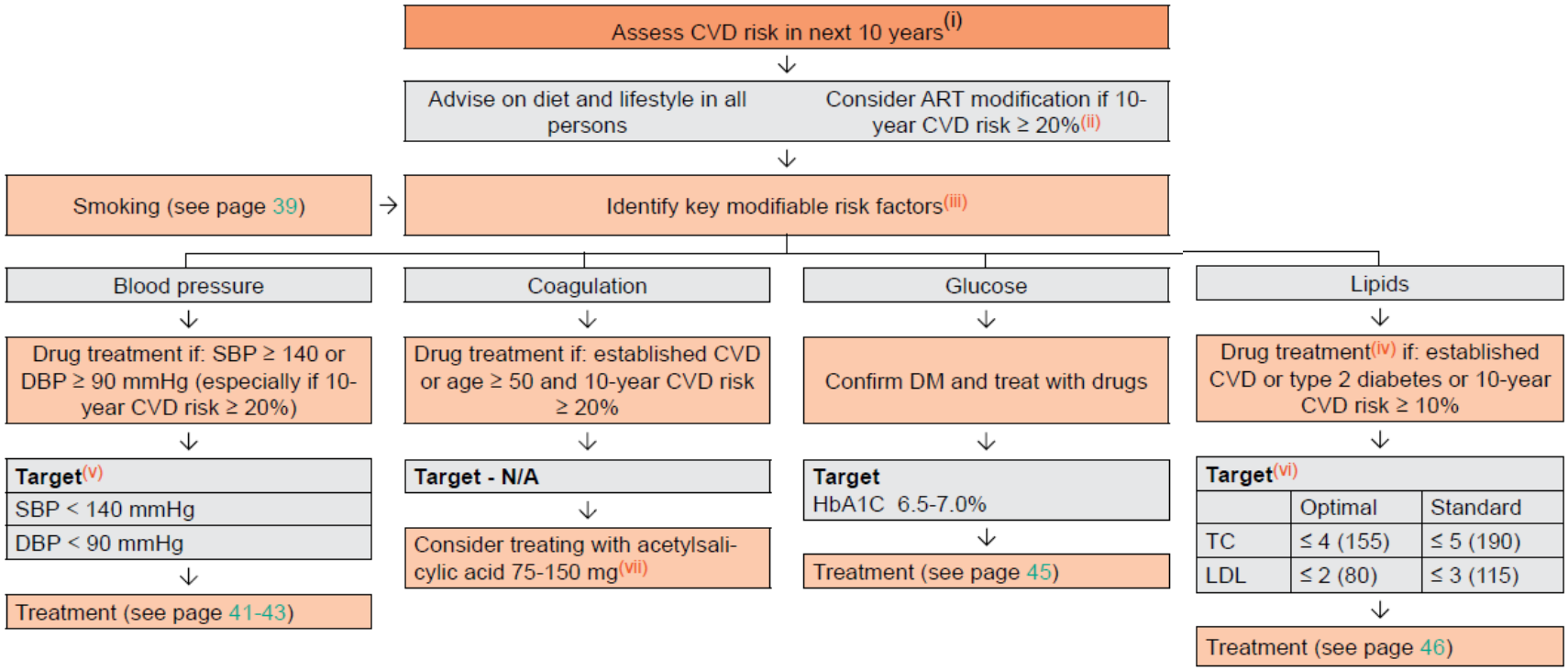
Prevention of CVD

Principles: The intensity of efforts to prevent CVD depends on the underlying risk of CVD, which can be estimated[i]. The preventive efforts are diverse in nature and require involvement of a relevant specialist, in particular if the risk of CVD is high and always in persons with a history of CVD.



v For higher risk individuals (e.g. diabetes) where resources allow target SBP < 130 and DBP < 80 mmHg.

Type 2 Diabetes[i]: Management

i Type 1 diabetes should be treated according to national guidelines.

ii Metformin may worsen lipoatrophy.

No data for any oral antidiabetic agents in terms of CVD prevention in HIV-positive persons. Incretins (DDP-4 inhibitors [e.g. linagliptin, saxagliptin (reduce dose when given with a booster), sitagliptin and vildagliptin], GLP-1 agonists [liraglutide, exenatide], and SGLT-2 inhibitors [e.g. dapagliflozin, canagliflozin, empagliflozin] have not been evaluated in HIV-positive persons, but some (e.g empagliflozin, liraglutide) have shown to reduce mortality from CVD; choice of drugs dependent on a variety of individual- & disease-specific factors; no clinically significant drug-drug-interaction or adverse effects on CD4 counts expected; clinical use of pioglitazone questioned by its side effects; HbA1c targets up to 7.5% can be considered for older persons with long-standing type 2 diabetes and evidence of CVD.

Kidney Disease: Definition, Diagnosis and Management

Diagnosis of kidney disease

		eGFR[i]			
		> 60 mL/min	> 60 mL/min, but accelerated decline of eGFR*	> 30 - ≤ 60 mL/min	≤ 30 mL/min
Proteinuria[ii]	UP/C[iii] < 50	Regular follow-up			• Check risk factors for CKD a medicines including ART[iv] • Discontinue or adjust drug d • Perform renal ultrasound • Urgent referral to nephrologi
	UP/C[iii] 50-100	• Check risk factors for CKD[vi] and nephrotoxic medicines including ART[iv, x] • Discontinue or adjust drug dosages where appropriate[v] • Perform renal ultrasound • If haematuria present with any level of proteinuria refer to nephrologist • Refer to nephrologist if new CKD or progressive decline in eGFR			
	UP/C[iii] > 100				

* Defined as decrease in eGFR of 5 mL/min per year for ≥3 consecutive years or confirmed 25% eGFR decline from baseline

Management of HIV-associated kidney disease[vi]

Prevention of progressive renal disease	Comment
1. ART	Start ART immediately where HIV-associated nephropathy (HIVAN)[vii] or HIV immune complex disease strongly suspected. Immunosuppressive therapy may have a role in immune complex diseases. Renal biopsy to confirm histological diagnosis recommended.
	Consider replacing TDF by non-tenofovir drug or TAF*** if:** • UP/C 20-50 mg/mmol • eGFR > 60 mL/min, but decrease in eGFR by 5 mL/min per year for at least 3 consecutive years or confirmed 25% eGFR decline from baseline • co-morbidities with a high risk of CKD (i.e. diabetes and hypertension) • body weight < 60 kg • use of a PI/r as a third agent **Replace TDF** by non-tenofovir drug or TAF*** if:** • eGFR ≤ 60 mL/min • UP/C > 50 mg/mmol • nephrotoxic comedication • previous TDF toxicity (proximal renal tubulopathy) ** Expert opinion pending clinical data ***There are limited data on use of TAF with eGFR ≤ 30 mL/min, and longer term outcomes are unknown.
2. Start ACE inhibitors or angiotensin-II receptor antagonists if: a. Hypertension and/or b. Proteinuria	**Monitor eGFR and K^+ level closely on starting treatment or increasing dose** a. Blood pressure target: < 130/80 mmHg
3. General measures: a. Avoid nephrotoxic drugs b. Lifestyle measures (smoking, weight, diet) c. Treat dyslipidaemia[viii] and diabetes[ix] d. Adjust drug dosages where necessary[v]	CKD and proteinuria are independent risk factors for CVD

i For eGFR: Use CKD-EPI formula based on age and ethnicity because eGFR quantificat min. The abbreviated modification of diet in the Cockcroft-Gault (CG) equation may be c http://www.chip.dk/Tools. Definition CKD: eGFR ≤ 60 mL/min for ≥ 3 m kdigo.org/clinical_practice_guidelines/pdf/C GL.pdf). If not previously known to have CK eGFR within 2 weeks. Use of DTG, COBI a associated with an increase in serum creati to inhibition of proximal tubular creatinine tr actual glomerular filtration: consider new se

ii Urinalysis: use urine dipstick to screen for h proteinuria, use urine dipstick and if ≥ 1+ ch (UP/C), or screen with UP/C. Proteinuria de firmed on ≥ 2 occasions > 2-3 weeks apart. urine albumin/creatinine (UA/C), see[iii]

iii UP/C in spot urine is preferred to UA/C as d secondary to glomerular and tubular disease merular disease and can be used for screen disease where UP/C is not available, but is for tubular proteinuria secondary to drug ne both UP/C and UA/C are measured, UP/C > proteinuria. Screening values for UA/C are: should be monitored in persons with diabete urine protein (mg/L) / urine creatinine (mmo as mg/mg. Conversion factor for mg to mmo

iv Repeat eGFR and urinalysis as per screeni

v See Dose Adjustment of ARVs for Impaired

vi Joint management with a nephrologist

vii HIVAN suspected if black ethnicity & UP/C > turia

viii See page 46

ix See page 44-46

x Different models have been developed for c risk score while using different nephrotoxic A pendent and HIV-related risk factors [6], [7]

See online video lecture CVD, CKD and En online course Clinical Management of HIV.

Consider replacing TDF by non-tenofovir drug or TAF*** if:**

- UP/C 20-50 mg/mmol
- eGFR > 60 mL/min, but decrease in eGFR by 5 mL/min per year for at least 3 consecutive years or confirmed 25% eGFR decline from baseline
- co-morbidities with a high risk of CKD (i.e. diabetes and hypertension)
- body weight < 60 kg
- use of a PI/r as a third agent

Replace TDF by non-tenofovir drug or TAF*** if:**

- eGFR ≤ 60 mL/min
- UP/C > 50 mg/mmol
- nephrotoxic comedication
- previous TDF toxicity (proximal renal tubulopathy)

** Expert opinion pending clinical data

***There are limited data on use of TAF with eGFR ≤ 30 mL/min, and longer term outcomes are unknown.

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Non-Alcoholic Fatty Liver Disease (NAFLD)

The prevalence of NAFLD is higher in individuals with HIV infection (30- 40% in the US) than in the general population [9]. Nearly half of the HIV-positive persons that undergo evaluation for unexplained liver test abnormalities are found to have NAFLD. The diagnosis of NAFLD requires the exclusion of both secondary causes and of a daily alcohol consumption ≥ 30 g for men and ≥ 20 g for women.

Spectrum of NAFLD

Often associated with components of the metabolic syndrome:

Non-Alcoholic Fatty Liver (NAFL)
- Pure steatosis

NAFLD
- Steatosis and mild lobular inflammation

Non-Alcoholic SteatoHepatitis (NASH)
- Early NASH: no or mild (F0-F1) fibrosis
- Fibrotic NASH: significant (≥ F2) or advanced (≥ F3, bridging) fibrosis
- NASH-cirrhosis (F4)
- HCC can occur in the absence of cirrhosis and histological evidence of NASH

Most common concurrent diseases
- AFLD-alcoholic fatty liver disease
- Drug-induced fatty liver disease
- HCV-as

Considera

- d-drugs NAFLD
- Conside NAFLD

Diagnostic

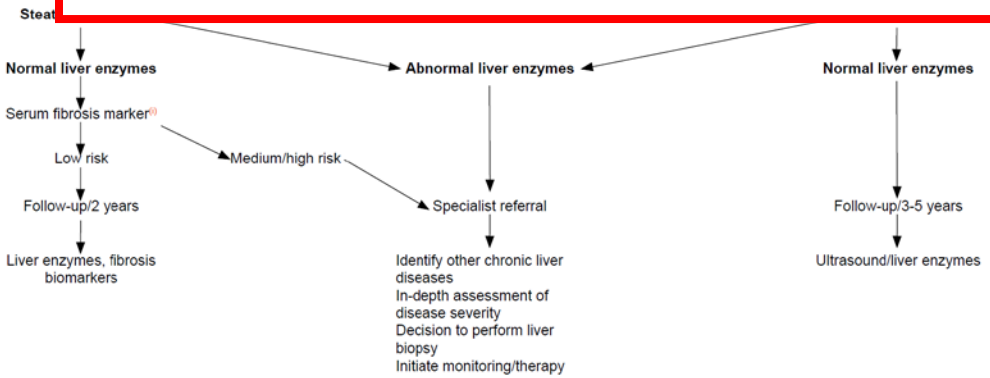
Diagnosis

- Ultrasound is the preferred first-line diagnostic procedure for imaging of NAFLD.
- Whenever imaging tools are not available or feasible, serum biomarkers and scores are an acceptable alternative for the diagnosis. Fibroscan is not validated for this purpose.
- A quantitative estimation of liver fat can only be obtained by 1H-MRS. This technique is of value in clinical trials and experimental studies, but is expensive and not recommended in the clinical setting.
- NASH has to be diagnosed by a liver biopsy showing steatosis, hepatocyte ballooning and lobular inflammation.

Treatment of NAFLD

- Lifestyle modification and weight reduction is the cornerstone of treatment
- Pharmacotherapy should be reserved for individuals with NASH, particularly for those with significant fibrosis ≥ F2 and individuals with less severe disease, but at high risk of faster disease progression (i.e. with diabetes, metabolic syndrome, persistently increased ALT, high necroinflammation).
- Management and treatment of NASH should be discussed with hepatologists. Options with proven efficacy include pioglitazone, vitamin E and bariatric surgery.
- Statins may be safely used but have demonstrated no impact on liver

The prevalence of NAFLD is higher in individuals with HIV infection (30- 40% in the US) than in the general population [9]. Nearly half of the HIV-positive persons that undergo evaluation for unexplained liver test abnormalities are found to have NAFLD. The diagnosis of NAFLD requires the exclusion of both secondary causes and of a daily alcohol consumption ≥ 30 g for men and ≥ 20 g for women.



i Serum fibrosis markers: NAFLD-Fibrosis Score, FIB-4, Commercial tests (FibroTest, FibroMeter, ELF)

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Vaccination

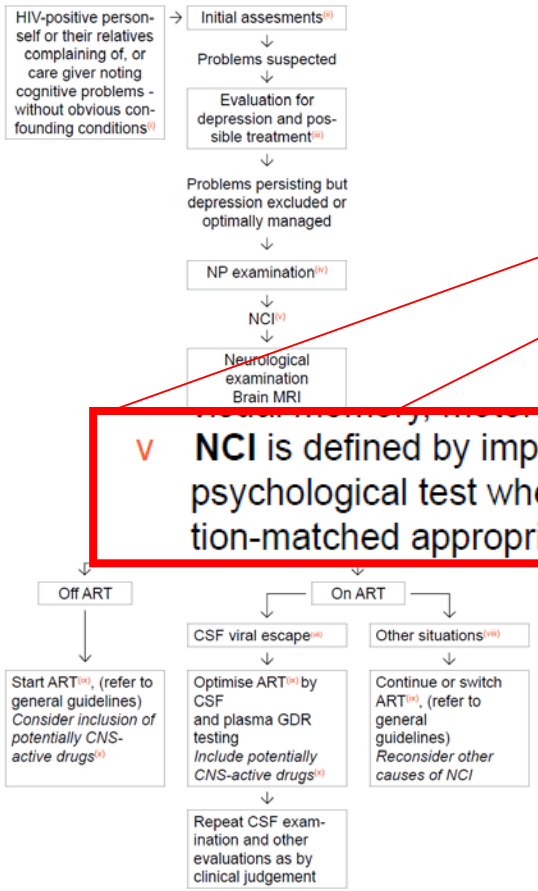
Infection	Comment
Influenza Virus	Yearly
Human Papilloma Virus (HPV)	Vaccinate with 3 doses for all HIV-positive persons up to age 26 / age 40 if MSM (health insurance coverage differs by country according to age, sex, sexual orientation). Use 9-valent vaccine if available. If HPV infection is established, efficacy of vaccine is questionable
Hepatitis B Virus (HBV)	Vaccinate if seronegative. Repeat doses until anti-HBs antibodies ≥ 10 IU/L / ≥ 100 IU/L according to national guidelines. In order to reach ≥ 100 IU/L in non-responders repeat 3 doses if anti-HBs < 10 IU/L, 1 dose if anti-HBs < 100 IU[ii]; consider double dose (40 µg) in particular with low CD4 count and high HIV-VL. See page 79
Hepatitis A Virus (HAV)	Vaccinate if seronegative. Consider checking antibody titres in individuals with high risk. Weaker immune response expected with HAV/HBV co-vaccine. See page 79
Neisseria meningitidis	Use conjugated[iii] vaccine (2 doses 1-2 months apart) if available. Booster every five years if exposure continues. Polysaccharide vaccine not recommended anymore.
Streptococcus pneumoniae	One dose of conjugated[iii] 13-valent vaccine (CPV-13) for all individuals, also if pre-vaccinated with PPV-23 polysaccharide vaccine. No general recommendation for any booster dose. Some national guidelines consider one dose of PPV-23 at least 2 months after CPV-13 for all individuals.
Varicella Zoster Virus (VZV)	Perform serology if exposure history negative. Vaccinate if seronegative. For contraindications, see*
Yellow Fever Virus	Contraindicated if past or current haematological neoplasia or thymus affection (thymoma, resection/radiation) For other contraindications, see*. Booster q 10 years.

[...]

Algorithm for Diagnosis and Management of HIV-Associated Neurocognitive Impairment (NCI) in Persons without Obvious Confounding Conditions

Abbreviations

CSF	cerebrospinal fluid
GDR	genotypic drug resistance test
HAD	HIV-associated dementia
MND	mild neurocognitive disorder
MRI	brain magnetic resonance imaging
NP	neuropsychological
OIs	opportunistic infections



i **Obvious confounding conditions:**
1. Severe psychiatric conditions
2. Abuse of psychotropic drugs
3. Alcohol abuse
4. Sequelae from previous CNS-OIs or other neurological diseases
5. Current CNS-OIs or other neurological diseases

ii **The following questions may be used to guide doctor assessment**
1. Do you experience frequent memory loss (e.g. do you forget the occurrence of special events even the more recent ones, appointments, etc.)?
2. Do you feel that you are slower when reasoning, planning activities, or solving problems?
3. Do you have difficulties paying attention (e.g. to a conversation, book or movie)?

Answering "yes" to one or more of these questions may suggest the presence of cognitive disorders, although not necessarily linked to HIV.

iii See Depression: Screening and Diagnosis

iv **NP examination** will have to include tests exploring the following cognitive domains: fluency, executive functions, speed of information processing, attention/working memory, verbal and visual learning, verbal and visual memory, motor skills plus assessment of daily functioning.

v **NCI** is defined by impairment in cognitive function on the above neuropsychological test where performance is compared to age- and education-matched appropriate controls and is considered clinically significant.

vi **Neurological examination, brain MRI and CSF examination** are required to exclude other pathologies and to further characterise HIV-associated NCI by including assessment of CSF HIV-VL level and, where appropriate, evidence for genotypic drug resistance (GDR) in a paired CSF and plasma sample.

vii **CSF escape definition:**
either CSF HIV-VL detectable and plasma HIV-VL undetectable; or both CSF HIV-VL and plasma HIV-VL detectable, with CSF HIV-VL higher than

v **NCI** is defined by impairment in cognitive function on the above neuropsychological test where performance is compared to age- and education-matched appropriate controls and is considered clinically significant.

HIV-positive populations (concentration above the IC90 in > 90% examined persons)
2. proven short-term (3-6 months) efficacy on cognitive function or CSF HIV-VL decay when evaluated as single agents or in controlled studies in peer-reviewed papers

- Drugs with demonstrated clear CSF penetration:
  —NRTIs: ZDV, ABC*
  —NNRTIs: EFV**, NVP
  —PI/r: LPV/r, DRV/r*
  —INSTI: DTG
  —Other classes: MVC
- Drugs with proven clinical efficacy:
  —NRTIs: ZDV, ABC
  —PI/r: LPV/r

* When administered bid. Once-daily administration of these drugs, although common in clinical practice, has not been studied extensively with regard to CNS effects/CSF penetration and may have different CNS activity. RTV is preferred as PI booster

** Avoid EFV because of its detrimental effects on neurocognitive function in a RCT and potentially confounding CNS effects due to neuropsychiatric effects.

See online video lectures CNS and HIV-Part 1 and CNS and HIV-Part 2 from the EACS online course Clinical Management of HIV.

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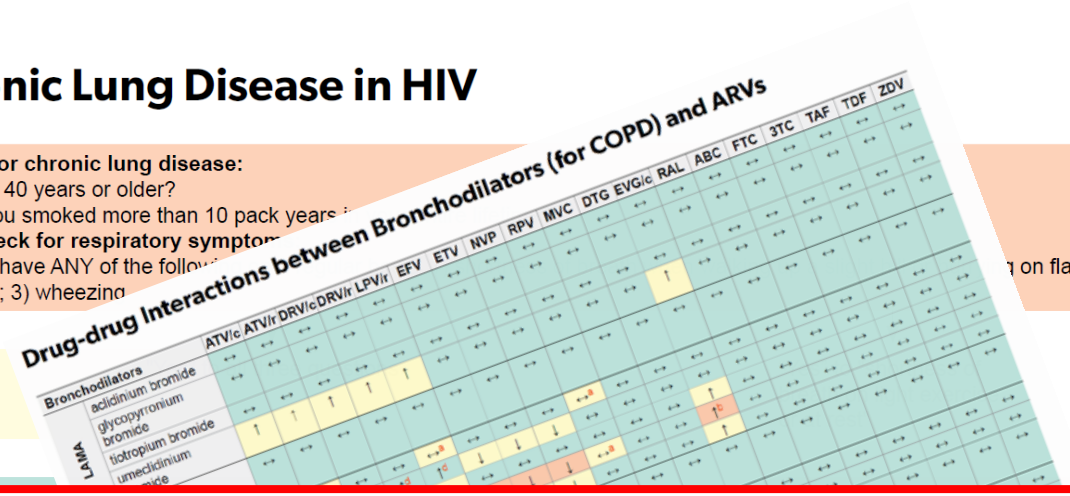
Chronic Lung Disease in HIV

Screen for chronic lung disease:
- Are you 40 years or older?
- Have you smoked more than 10 pack years
Then check for respiratory sympto
- Do you have ANY of the follo
  sputum; 3) wheezing

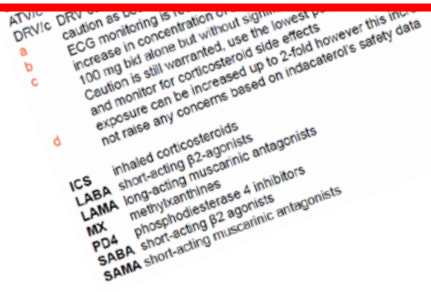
on flat ground; 2) cough and/or

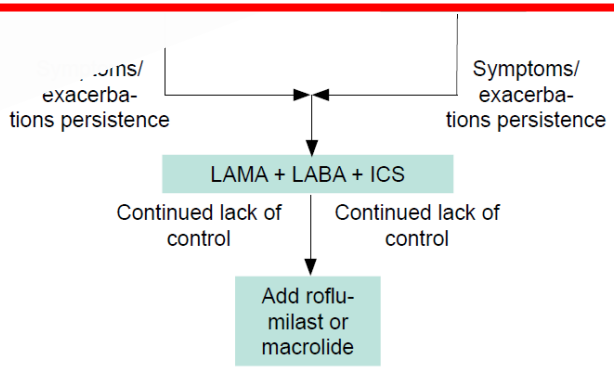
"No"
Repeat questions anually



There are 3 life saving interventions:

1. Smoking cessation
2. Chronic oxygen when stable (non-exacerbated) resting $SpO_2 \leq 88\%$ (or $PaO_2 \leq 55$ mmHg)
3. Non-invasive ventilation (NIV) in individuals with acute hypercapnic respiratory failure





LABA: long-acting β2-agonist
LAMA: long-acting muscarinic antagonist
ICS: inhaled corticosteroid

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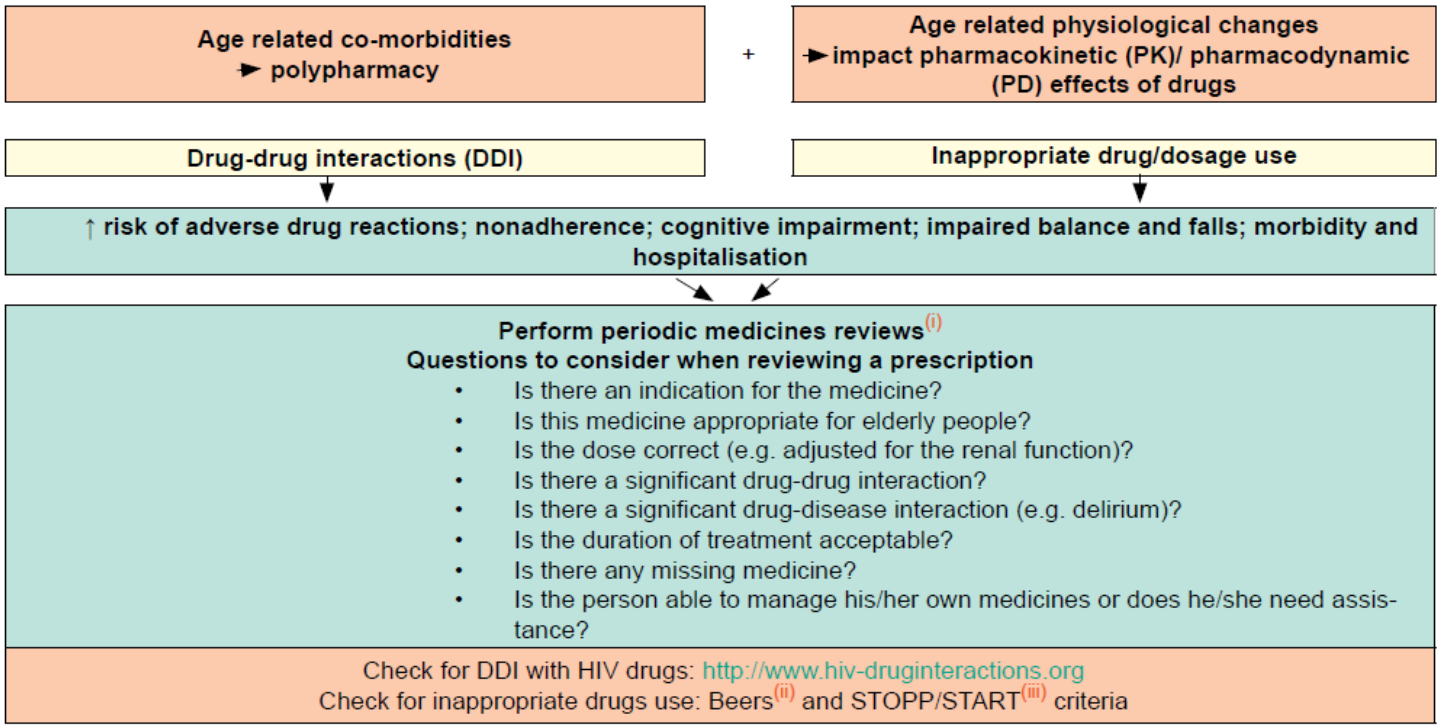
Prescribing in the Elderly



Adapted from [10], [11], [12]

i-iii The Beers and STOPP criteria are tools established by experts in geriatric pharmacotherapy to detect and reduce the burden of inappropriate prescribing in elderly. Inappropriate medicines include, for instance, those which in elderly persons with certain diseases can lead to drug-disease interactions, are associated with a higher risk of adverse drug reactions in the elderly, medicines that predictably increase the risk of falls in the elderly or those to be avoided in case of organ dysfunction. The START criteria consist of evidence-based indicators of potential prescribing omission in elderly with specific medical conditions.

Organ criteria for SOT

- HIV-positive persons should be considered for organ tra… using the same indications as used in HIV-negativ… persons with HCC can be evaluated for liver … the Milan criteria[i].

HIV-infection criteria fo…

According to … fulfill th…

1. …

2. …ells/μL for all SOT except for liver t… cells/μL. Persons with previous opport… tu… have a CD4 > 200 cells/μL.
3. **Viro…** …full control of HIV replication prior to and after plant… …uld be confirmed/predicted in all cases.
4. **Drug …buse.** Abstinence period: alcohol 6 months; heroin/cocaine 2 years. Former IVDUs can be in methadone programme.

…ungal …cluded. For …e general HIV-nega-

Drug-drug Interactions between Immunosuppressants (for SOT) and ARVs

Immunosuppressants		ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	EVG/c	RAL	ABC	FTC	3TC	TAF	TDF	ZDV
CS	prednisone	↔	↓	↔	↓	↓	↓	↓	↓	↓E13%	E	E	↑	↓	↔	↔	↔	↔	↔	↔
AM	azathioprine	↔	↑[a]	↔	↑[a]	↑[a]	↑[a]	↑[a]	↑[a]	↓[a]	↔	↔	↔	↑[a]	↔	↔	↔	↔	↔	↔
	mycophenolate	↔	↑[a]	↔	↑[a]	↑[a]	↑[a]	↑[a]	↑[a]	↓[a]	↔	↔	↔	↑[a]	↔	↔	↔	↔	↔	↔
CNI	cyclosporine	↓	↑[a]	↓	↑[a]	↑[a]	↑[a]	↑[a]	↑[a]	↓[a]	↔	↔	↔	↑[a]	↔	↓?	↔	↔	↔	↔
	tacrolimus*	↓	↑[a]	↓	↑[a]	↑[a]	↑[a]	↑[a]	↑[a]	↓[a]	↔	↔	↔	↑[a]	↔	↔	↔	↔	↔	↔
mTOR	everolimus	↓	↑[a]	↓	↑[a]	↑[a]	↑[a]	↑[a]	↑[a]	↓[a]	↔	↔	↔	↑[a]	↔[c]	↔	↔	↔	↔	↔
	sirolimus	↓	↑[a]	↓	↑[a]	↑[a]	↑[a]	↑[a]	↑[a]	↓[a]	↔	↔	↔	↑[a]	↔	↔	↔	↔	↔	↔
Other	anti-thymocyte globulin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	basiliximab	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	belatacept	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔

		RIF	RBT	RPT
CS	prednisone	↓	↓	↓
AM	azathioprine	↔	↔	↔
	mycophenolate	↓	↓	↓
CNI	cyclosporine	↓	↓	↓
	tacrolimus*	↓	↓	↓
mTOR	everolimus	↓	↓	↓
	sirolimus	↓	↓	↓
Other	anti-thymocyte globulin	↔	↔	↔
	basiliximab	↔	↔	↔
	belatacept	↔	↔	↔

Online only

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Clinical Management and Treatment of HBV and HCV Co-infection in HIV-positive Persons

Massimo Puoti for the coinfections EACS guidelines panel

Presenter Disclosure Information

In compliance with the Conflict of Interest Policies, the European AIDS Clinical Society (EACS) requires the following disclosure from the presenters:

Massimo Puoti

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Temporary Board Member/Temporary Advisory Panel: MSD, Abbvie, Gilead Sciences, BMS
Stock/Shareholder: Never
Consultant: No
Employee: Never
Other: Never

Panel Members

Co-infections

Chair: Massimo Puoti	**Milan, Italy**
Vice-Chair: Andri Rauch	**Bern, Switzerland**
Young scientist: Christoph Boesecke	**Bonn, Germany**
Juan Berenguer	Madrid, Spain
Sanjay Bhagani	London, United Kingdom
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
Jürgen K. Rockstroh	Bonn, Germany

Summary: HBV

- All persons with HBV/HIV co-infection should receive ART including TDF or TAF, unless history of tenofovir intolerance.
- Life-long therapy is recommended if anti-HBV nucleos(t)ides are given as part of ART.
- In case of non-response to HBV vaccinations, ART should contain TDF or TAF
- Anti HBV treatment should be considered in selected pts undergoing immune suppression and immunosuppressive chemotherapy

Anti HBV treatment and Immmune suppressive Tx or Chemotherapy (CTX)

	Severe immunosuppressive (CTX for Haem. Malignancy or SOT)	Other immunosuppressive Tx (eg Rituximab, anti-TNF)
HBsAg	Add TDF/ TAF	
Anti HBc+/anti HBs±	Add TDF/TAF	Monitoring with HBVDNA or HBsAg; if not possible add TDF/TAF
Anti HBs isolated not vaccinated	Monitoring for HBV reactivation	

Summary: HCV

- Alternatively to HCVRNA HCVAg could be performed in anti HCV+ to confirm chronic infection
- Evaluation of concurrent causes of liver disease and/or extra-hepatic HCV disease is mandatory in HCV infected patients
- Every person with HCV/HIV co-infection should be considered for interferon-free DAA therapy to eradicate HCV
- In HCV/HIV treatment indication and regimens are the same as in HCV mono-infected
- Immediate treatment of persons with acute or chronic hepatitis at high risk of transmission could be considered at diagnosis. IFN-free treatment with DAAs is recommended as in non-cirrhotic chronic HCV/HIV co-infection

HCV Treatment Options in HCV/HIV Co-infected Persons

IFN-free HCV Treatment Options				
HCV GT	**Treatment regimen**	**Treatment duration & RBV usage**		
		Non-cirrhotic	**Compensated cirrhotic**	**Decompensated cirrhotics CTP class B/C**
1 & 4	SOF + SMP +/- RBV	GT 4 only: 12 weeks with RBV or 24 weeks without RBV[i]		Not recommended
	SOF/LDV +/- RBV	8 weeks without RBV[ii] or 12 weeks +/- RBV[iii]	12 weeks with RBV[iv]	
	SOF + DCV +/- RBV	12 weeks +/- RBV[iii]	12 weeks with RBV[iv]	
	SOF/VEL	12 weeks		12 weeks with RBV
	SOF/VEL/VOX	8 weeks	Not recommended	
	OBV/PTV/r + DSV	8[v]-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
	EBR /GZR	12 weeks[vi]		Not recommended
	GLE/PIB	8 weeks	12 weeks	Not recommended
2	SOF + DCV	12 weeks		12 weeks with RBV
	SOF/VEL	12 weeks		12 weeks with RBV
	SOF/VEL/VOX	8 weeks	Not recommended	
	GLE/PIB	8 weeks	12 weeks	Not recommended
3	SOF + DCV +/- RBV	12 weeks +/- RBV[vii] or 24 weeks without RBV	24 weeks with RBV	
	SOF/VEL +/- RBV	12 weeks +/- RBV[vii] or 24 weeks without RBV		24 weeks with RBV
	SOF/VEL/VOX	8 weeks		Not recommended
	GLE/PIB	8 weeks	12 weeks	Not recommended
5 & 6	SOF/LDV +/- RBV	12 weeks +/- RBV or 24 weeks without RBV[i]	12 weeks with RBV[iv]	
	SOF + DCV +/- RBV	12 weeks +/- RBV or 24 weeks without RBV[i]	12 weeks with RBV[iv]	
	SOF/VEL	12 weeks		12 weeks with RBV
	SOF/VEL/VOX	8 weeks	Not recommended	
	GLE/PIB	8 weeks	12 weeks	Not recommended

Re-treatment of DAAs failures

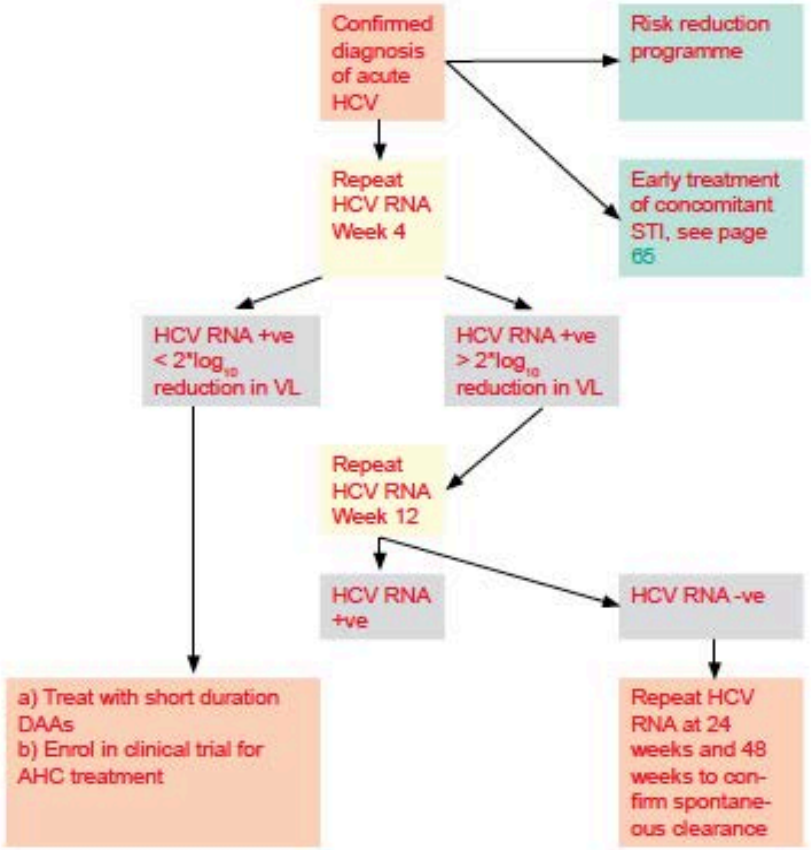
- At least 2 drugs active according to RASs testing

- New options
- SOF/VEL/VOX 12 weeks in NS5Ai and/or NS3i failures

- SOF + G/P 12 weeks in NS5Ai and/or NS3i failures

- G/P in SOF based Tx failures HCV G1,2,4-6 8 weeks in Non Cirrhotics 12 weeks in Cirrhotics and 16 weeks in HCV G3

Algorithm for Management of Acute HCV in Persons with HCV/HIV Co-infection



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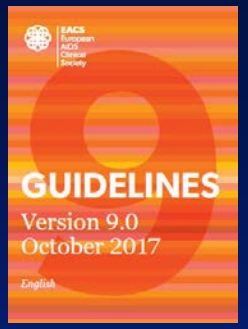

EACS Treatment Guidelines V9.0 Oct. 2017

Part V: Opportunistic Infections Update

Jose M. Miro, Chair
Juan Ambrosioni, Young Scientist
Infectious Diseases Service
Hospital Clínic – IDIBAPS
University of Barcelona
Barcelona, Spain

E-mail address: jmmiro@ub.edu

CLÍNIC BARCELONA Hospital Universitari

UNIVERSITAT DE BARCELONA

Part V – Opportunistic Infections Panel

Opportunistic Infections

Chair: José M. Miro	**Barcelona, Spain**
Vice-Chair: Ole Kirk	**Copenhagen, Denmark**
Young scientist: Juan Ambrosioni	**Barcelona, Spain**
Paola Cinque	Milan, Italy
Gerd Fätkenheuer	Cologne, Germany
Hansjakob Furrer	Bern, Switzerland
Amanda Mocroft	London, United Kingdom
Philippe Morlat	Bordeaux, France
Anton Pozniak	London, United Kingdom
Alain Volny-Anne	Paris, France

Special thanks to Tschabi and Valentin Gisler (Bern, Switzerland)

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Jose M. Miro MD PhD

Research Support: Angelini, Abbvie, BMS, Cubist, Gilead, MSD, Novartis, Pfizer, Theravance, ViiV Healthcare

Speaker's Bureau: None

Board Member/Advisory Panel: Genentech, Medtronic

Stock/Shareholder: Never

Consultant: None

Employee: Never

Other: Never

Part V – Opportunistic Infections

Toxoplasma gondii Encephalitis

Treatment			
Treat 6 weeks, then secondary prophylaxis until CD4 count > 200 cells/µL over 6 months Diagnosis: - **Definitive diagnosis:** clinical symptoms, typical radiology of the cerebrum AND cytological / histological detection of organism - **Presumptive diagnosis:** clinical symptoms, typical radiology AND response to empirical treatment. It is the standard in most clinical settings.			
	Drug	**Dose**	**Comments**
Preferred therapy	**pyrimethamine**	Day 1: 200 mg po, **then** • If ≥ 60 kg: 1 x 75 mg/day po • If < 60 kg: 1 x 50 mg/day po	Monitor for myelotoxicity of pyrimethamine, mostly neutropenia
	+ sulfadiazine	• If ≥ 60 kg: 2 x 3000 mg/day po/iv • If < 60 kg: 2 x 2000 mg/day po/iv	Sulfadiazine is associated with crystalluria and may lead to renal failure and urolithiasis. Good hydration is essential. Check renal function and urine sediment for microhematuria and crystalluria
	+ folinic acid	1 x 10-15 mg/day po	
Alternative therapy	**pyrimethamine**	Day 1: 200 mg/day po, **then** • If ≥ 60 kg: 1 x 75 mg/day po • If < 60 kg: 1 x 50 mg/day po	Monitor for myelotoxicity of pyrimethamine, mostly neutropenia
	+ clindamycin	4 x 600-900 mg/day po/iv	Additional PcP prophylaxis is necessary
	+ folinic acid	1 x 10-15 mg/day po	
	+ atovaquone	2 x 1500 mg/day po (with food)	
	+ folinic acid	1 x 10-15 mg/day po	
	or **sulfadiazine**	• If ≥ 60 kg: 2 x 3000 mg/day po/iv • If < 60 kg: 2 x 2000 mg/day po/iv	Sulfadiazine is associated with crystalluria and may lead to renal failure and urolithiasis. Good hydration is essential. Check renal function and urine sediment for microhematuria and crystalluria
	+ atovaquone	2 x 1500 mg/day po (with food)	
	or **pyrimethamine**	Day 1: 200 mg po, **then** • If ≥ 60 kg: 1 x 75 mg/day po • If < 60 kg: 1 x 50 mg/day po	Monitor for myelotoxicity of pyrimethamine, mostly neutropenia
	+ azithromycin	1 x 900-1200 mg/day po	
	+ folinic acid	1 x 10-15 mg/day po	

A comment was added for TMP-SMX as preferred therapy for *T. gondii* encephalitis when the oral route is not available.

Part V – Opportunistic Infections

Cryptococcal meningitis

Treatment			
14 days induction therapy, then 8 weeks consolidation therapy, then secondary prophylaxis for at least 12 months. Stop, if CD4 count > 100 cells/µL and HIV-VL undetectable over 3 months			
Diagnosis: positive microscopy, OR detection of antigen, OR culture from CSF			
Other organ manifestations: Infection may also involve othe			
Primary prophylaxis: One lar persons (< 50 CD4 cells/µL) in single dose may decrease over			
Pre-emptive therapy: Early st support determination of serum is detected, CSF should be exa two weeks is recommended be			
Pre-emptive therapy			
Induction therapy	**liposomal amphotericin B + flucytosine**	3 mg/kg/day iv 4 x 25 mg/kg/day po	**14 days** - Then perform lumbar puncture (LP): if CSF culture is sterile, switch to oral regimen - Opening pressure should always be measured, when LP is performed - Repeated LPs or CSF shunting are essential to effectively manage increased intracranial pressure which is associated with better survival - Corticosteroids have no effect in reducing increased intracranial pressure, could be detrimental and are contraindicated - Flucytosine dosage must be adapted
	or amphotericin B deoxycholate + flucytosine	0.7 mg/kg/day iv 4 x 25 mg/kg/day po	

In severely immunosuppressed patients (<50 CD4 cells/µL) primary prophylaxis including INH 12 weeks, fluconazole 100mg/d 12 weeks, azithromycin 500mg/d 5 days and albendazole 400mg single dose (in addition to TMP-SMX) may decrease overall opportunistic infections (including cryptococcal meningitis) and mortality

Add fluconazole to liposomal amphotericin B during the induction phase for cryptococcal meningitis treatment, in countries were flucytosine is not available.

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Reality Trial Team. NEJM. 2017;377:233-245

Part V – Opportunistic Infections
Treatment of TB in HIV-positive Persons
Preventing TB-IRIS on ART

Disease	Drug	Dose	Comments*
Susceptible *Mycobacterium tuberculosis*			
Initial phase	**rifampicin** **+ isoniazid** **+ pyrazinamide** **+ ethambutol**	Weight based	**Initial phase** for 2 months, then **Continuation phase** (rifampicin+isoniazid) according to TB type (see below) Possibility to omit ethambutol, if *M. tubercu-*
Alternative	**rifabutin** **+ isoniazid** **+ pyrazinamide** **+ ethambutol**	Weig	**Continuation phase** according to TB type (see below) Possibility to omit ethambutol, if *M. tuberculosis* is known to be fully drug sensitive
Continuation phase	**rifampicin/rifabutin** **+ isoniazid** according to TB type		Total duration of therapy: 1. Pulmonary, drug susceptible TB: 6 months 2. Pulmonary TB & positive culture at 8 weeks of TB treatment: 9 months 3. Extrapulmonary TB with CNS involvement or disseminated TB: 9-12 months 4. Extrapulmonary TB with bone/joint in-

A comment on the possibility to add steroid therapy to avoid IRIS in patients with TB on ART was added

Intermittent TB regimens (2 or 3 times per week) are contraindicated in HIV-infected persons.

* Intermittent regimens (2 or 3 times per week) are contraindicated in HIV-positive [redacted] acquired drug resistance.

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Nahid P et al. Clin Infect Dis. 2016; 63:853-67;
Gopalan N et al. IAS 2016 Durban. Abstract # WEAB0201
Meintjes G et al. PreART Team. CROI 2017. Abstract #81LB.

Part V – Opportunistic Infections
Treatment of MDR/XDR TB in HIV-positive Persons

INH-resistant TB

- RIF or RFB + Z+ E for 2 months and RIF or RFB + E for 10 months

Some experts recommend to add a FQ in the intensive phase and replace E by the FQ in the maintenance phase.

Each dose of MDR/XDR-TB regimen should be given as DOT throughout the whole treatment.

- In persons with rifampicin-resistant or MDR-TB, a regimen with at least five effective TB medicines during the intensive phase is recommended, including pyrazinamide and four core second-line TB medicines - one chosen from group A, one from group B, and at least two from group C.
- If the minimum of effective TB medicines cannot be composed as above, an agent from group D2 and other agents from D3 may be added to bring the total to five.
- In persons with rifampicin-resistant or MDR-TB, it is recommended that the regimen be further strengthened with high-dose isoniazid and/or ethambutol.
- Preliminary results of a recent RCT (Nix-TB trial) suggest that a 3-drug combination of pretomanid 200 mg/day, bedaquiline 200 mg tiw after a 3-week load, and linezolid 1200 mg/day during 6 months (3 additional months if culture positive at 4th month) may be at least as effective as the 5-drug regimens suggested above. Majority of cases included were pulmonary TB.

- thioacetazone (THZ)

Duration of MDR/XDR treatment

8 months of intensive phase using 5 or more drugs, followed by 12 months of 3 drugs depending on response.
E.g. 8 months of Z, MFX, Km, OFX, PTO and CS, followed by 12 months of MFX, PTO and CS.
In persons with rifampicin-resistant or MDR-TB who have not been previously treated with second-line drugs and in whom resistance to fluoroquinolones and second-line injectable agents has been excluded or is considered highly unlikely, a shorter MDR-TB regimen of 9-12 months may be used instead of a conventional regimen.

Drug interactions with ART and MDR/XDR regimens

Unless RFB is being used, use normal doses but with caution as few data are available on potential drug interactions, see ART in TB/HIV Co-infection

The preliminary results of the Nix-TB trial were added in the section of treatment for resistant TB (MDR/XRD-TB)

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Conradie F et al. Nix TB Trial. CROI; 2017. Abstract #80LB

Part V – Opportunistic Infections

Treatment of LTBI in HIV-positive Persons

Latent tuberculosis	
Indication: TST > 5 mm or positive IGRA or close contacts to persons with sputum smear positive tuberculosis Some national guidelines consider the ethnicity, CD4 count and ART usage to define indication for latent tuberculosis treatment.	
Regimen*	**Comments**
isoniazid 5 mg/kg/day (max 300 mg) po + **pyridoxine** (Vit B6) 25 mg/day po	6-9 monti Consider high-prev
rifampicin 600 mg/day po or **rifabutin** po (dose according to current cART)	4 months ARVs, se between ARVs and Non-ARVs
rifampicin 600 mg/day po or **rifabutin** po (dose according to current cART) + **isoniazid** 5 mg/kg/day (max 300 mg) po + **pyridoxine** (Vit B6) 25 mg/day po	3 months, check interactions with ARVs, see Drug-drug Interactions between ARVs and Non-ARVs
rifampicin 600 mg 2 x/week po + **isoniazid** 900 mg 2 x/week po + **pyridoxine** (Vit B6) 300 mg 1 x/ week po	3 months, check interactions with ARVs, see Drug-drug Interactions between ARVs and Non-ARVs
rifapentine 900 mg 1 x/week po + **isoniazid** 900 mg 1 x/week po	3 months ARVs, se between Rifapenti Europe.

A duration of 9-months for latent TB treatment was stressed, particularly in countries with high TB prevalence

A comment was added explaining that other preventive regimens are needed for treating latent infection with MDR/XDR-TB in countries with high resistant TB rates.

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* Other preventive regimens may be considered if high risk of latent infection with MDR/XDR-TB.

Thank you !

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Drug-drug interactions

Disclosure Information

Research Support: Janssen
Educational support: Janssen, Gilead, AbbVie, Merck
Speaker's Bureau: Never
Board Member/Advisory Panel: Janssen, Gilead
Stock/Shareholder: Never
Consultant: Never
Employee: Never

Organization of the information on DDIs

DDIs for commonly prescribed co-medications and of particular clinical relevance

- Drug-drug interactions between ARVs and Non-ARVs

DDIs within a given therapeutic area

- Drug-drug interactions between **Antidepressants** and ARVs
- Drug-drug interactions between **Antihypertensives** and ARVs
- Drug-drug interactions between **Analgesics** and ARVs
- Drug-drug interactions between **Anticoagulants/antiplatelets agents** and ARVs
- Drug-drug interactions between **Bronchodilatators (for COPD)** and ARVs **New**
- Drug-drug interactions between **Contraceptives** and ARVs
- Drug-drug interactions between **Corticosteroids** and ARVs
- Drug-drug interactions between **Antimalarial drugs** and ARVs **New**
- Drug-drug interactions between **Pulmonary Antihypertensives** and ARVs **New**
- Drug-drug interactions between **Immunosuppressants (for SOT)** and ARVs **New**
- Drug-drug interactions between **DAAs** and ARVs

Format of DDIs tables

	Bronchodilators	ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	EVG/c	RAL	ABC	FTC	3TC	TAF	TDF	ZDV
LAMA	aclidinium bromide	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
LAMA	glycopyrronium bromide	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
LAMA	tiotropium bromide	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
LAMA	umeclidinium bromide	↑	↑	↑	↑	↑	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
SAMA	ipratropium	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
LABA	formoterol	↔[a]	↔[a]	↔	↔	↔[a]	↔	↔	↔	↔[a]	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
LABA	indacaterol	↑[d]	↑[d]	↑[d]	↑[d]	↑[d]	↓	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
LABA	olodaterol	↑	↑	↑	↑	↑	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
LABA	salmeterol	↑[b]	↑[b]	↑[b]	↑[b]	↑[b]	↓	↓	↓	↔[a]	↔	↔	↑[b]	↔	↔	↔	↔	↔	↔	↔
LABA	vilanterol	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
SABA	salbutamol (albuterol)	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
MX	aminophylline	↔	↓	↔	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
MX	theophylline	↔	↓	↔	↓	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
PDE4	roflumilast	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
ICS	beclometasone	↑[c]	↑[c]	↑?[c]	↓11%	↑[c]	↔	↔	↔	↔	↔	↔	↑[c]	↔	↔	↔	↔	↔	↔	↔
ICS	budesonide	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
ICS	fluticasone	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔

Legend

↑ potential elevated exposure of the bronchodilator
↓ potential decreased exposure of the bronchodilator
↔ no significant effect
D potential decreased exposure of ARV drug
E potential elevated exposure of ARV drug

Colour legend

no clinically significant interaction expected
these drugs should not be co-administered
potential clinically significant interaction that is likely to require additional monitoring, alteration of drug dosage or timing of administration
potential interaction likely to be of weak intensity. Additional action/ monitoring or dosage adjustment is unlikely to be required

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Assessment of DDI potential and clinical relevance

Step 1: evaluation of likelihood of having DDI

- PK/PD characteristics of coadministered drugs
- clinical DDI studies
- case reports

No DDI

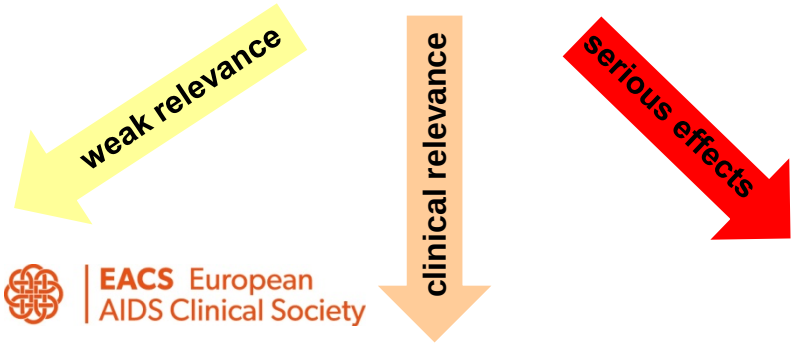
- different elimination pathways
- no significant PK change
- no safety concern

evidence that DDI may occur

Step 2: evaluation of clinical relevance

- magnitude of PK change
- therapeutic index
- possibility to monitor the drug effect
- recommendation on dose adjustment
- length of treatment required

\+ recommendations of product label



Highlights on DDIs in the revised version

DDIs with anticoagulants

		ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	EVG/c	RAL
Anticoagulants	acenocoumarol	↔	↓	↔	↓	↓	↓	↑	↓	↔	↔	↔	↓	↔
	apixaban	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔
	dabigatran	↑	↑	↑	↑	↑?	↔	↔	↔	↑?	↔	↔	↑	↔
	dalteparin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	edoxaban	↑	↑	↑	↑	↑	↔	↔	↔	↔	↔	↔	↑	↔
	enoxaparin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	fondaparinux	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	heparin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	phenprocoumon	↑	↑or↓[a]	↑	↑or↓	↑or↓	↓	↑or↓	↓	↔	↔	↔	↑or↓	↔
	rivaroxaban	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔
	warfarin	↑	↑or↓[a]	↑	↓	↓	↑or↓	↑	↑or↓	↔	↔	↔	↓	↔
Antiplatelet agents	aspirin	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	clopidogrel	↓[c]	↓[c]	↓[c]	↓[c]	↓[c]	↑[d]	↓[c]	↑[d]	↔	↔	↔	↓[c]	↔
	dipyridamole	↑	↓[e]	↔	↓	↓	↓	↓	↔	↔	↔	↔	↔	↔
	prasugrel	↓[f]	↓[f]	↓[f]	↓[f]	↓[f]	↔	↔	↔	↔	↔	↔	↓[f]	↔
	ticagrelor	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔

cobicistat has no inducing properties but ritonavir does

➔ dosage adjustments of co-medications might be needed when switching PK booster

www.hiv-druginteractions.org, Marzolini C et al. JAC 2016

DDIs with DAAs

	HCV drugs	ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	EVG/c
DAAs	daclatasvir	↑[i]	↑110%[ii]	↑	↑41%	↑15%	↓32%[v]	↓	↓	↔	↔	E33%	↑[i]
	elbasvir/ grazoprevir	↑	↑	↑	↑	↑	↓54/83%	↓	↓	↔	↔	↔	↑
	glecaprevir/ pibrentasvir	↑	↑553/64%	↑	↑397%/-	↑338/146%	↓	↓	↓	E84%	E	↔	↑205/57% E47%
	parita-previr/r/ ombitasvir/ dasabuvir	↑	↑94%[iii]	↑	D[v]	↑	[vi]	↓E	↓E	E[vii]	E	↔	↑
	paritaprev-ir/r/ombi-tasvir	↑	↑[iii]	↑	↑[v]	↑	[vi]	↓E	↓E	E[vii]	E	↔	↑
	simeprevir	↑	↑	↑	↑	↑	↓71%	↓	↓	↑6% E12%	↔	↔	↑
	sofosbuvir/ ledipasvir	↑[viii]	↑8/113%[viii]	↑[viii]	↑34/ 39%[viii]	↔[viii]	↓-/34%	↔	↔	↔[viii]	E	↔	↑36/ 78%E[viii]
	sofosbuvir/ velpatasvir	↔[viii]	↑-/142%[viii]	↔[viii]	↓28%/-[viii]	↓29%/-[viii]	↓-/53%	↓	↓	↔	E	↔	↑[viii]
	sofosbuvir/ velpatasvir/ voxilaprevir	↑	↑40/93/331%	↑[viii]	↑-/ /143% [viii]	↑	↓	↓	↓	↔	E	↔	↑-/-/171% [viii]
	sofosbuvir	↔	↔	↑	↑34%	↔	↔	↔	↔	↔	↔	↔	↔

DDIs with corticosteroids

	Corticosteroids	ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	EVG/c	RAL
Inhaled, oral, topic and/or injected corticosteroids	beclometasone (inhalation)	↑[a]	↑[a]	↑?[a]	↓[b]	↑[a]	↔	↔	↔	↔	↔	↔	↑[a]	↔
	betamethasone	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓	↓	↓	D	D	↔	↑[c]	↔
	budenoside (inhalation)	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓	↓	↓	↔	↔	↔	↑[c]	↔
	clobetasol (topical)	↑[c,d]	↑[c,d]	↑[c,d]	↑[c,d]	↑[c,d]	↔	↔	↔	↔	↔	↔	↑[c,d]	↔
	dexamethasone	↑[c] D	↑[c] D	↑[c] D	↑[c] D	↑[c] D	↓D	↓D	↓D	D	D	↔	↑[c] D	↔
	fluocinolone (topical)	↑[c,d]	↑[c,d]	↑[c,d]	↑[c,d]	↑[c,d]	↔	↔	↔	↔	↔	↔	↑[c,d]	↔
	fluticasone (inhalation)	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓	↓	↓	↔	↔	↔	↑[c]	↔
	hydrocortisone (oral)	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓	↓	↓	↔	↔	↔	↑[c]	↔
	hydrocortisone (topical)	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	methylpredni-solone	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓	↓	↓	↔	↔	↔	↑[c]	↔
	mometasone (inhalation)	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓	↓	↓	↔	↔	↔	↑[c]	↔
	prednisolone (oral)	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓40%	↓	↓	↔	↔	↔	↑[c]	↔
	prednisone	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓40%	↓	↓	↔	↔	↔	↑[c]	↔
	triamcinolone	↑[c]	↑[c]	↑[c]	↑[c]	↑[c]	↓	↓	↓	↔	↔	↔	↑[c]	↔

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Highlights on DDIs in the revised version

Drug interactions between hormonal contraceptives and antiretrovirals

Kavita Nanda[a], Gretchen S. Stuart[b], Jennifer Robinson[c], Andrew L. Gray[d], Naomi K. Tepper[e] and Mary E. Gaffield[f]

AIDS 2017

Results: Most antiretrovirals whether used for therapy or prevention, have limited interactions with hormonal contraceptive methods, with the exception of efavirenz.

Conclusion: Women taking antiretrovirals, for treatment or prevention, should not be denied access to the full range of hormonal contraceptive options, but should be counseled on the expected rates of unplanned pregnancy associated with all contraceptive methods, in order to make their own informed choices.

DDI with contraceptives

		ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	EVG/c	RAL	ABC	FTC	3TC	TAF	TDF	ZDV
Es	ethinylestradiol (COC, TS, VR)	↔	↓19%[a]	↓30%	↓44%[b]	↓42%[b]	↔[c]	↑22%	↓20%	↑14%	↔	↑3%	↓25%[d]	↔	↔	↔	↔	↔	↔	↔
Progestins	desogestrel (COC)	↑	↑[e,a]	↑	↑[f]	↑[f]	↓[g]	↓	↓	↔	↔	↔	↑[d,e]	↔	↔	↔	↔	↔	↔	↔
	desogestrel (POP)	↑	↑	↑	↑	↑	↓[g]	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
	drospirenone (COC)	↑	↑[e,a]	↑[f]	↑[f]	↑[f]	↓[g]	↓	↓	↔	↔	↔	↑[d,e]	↔	↔	↔	↔	↔	↔	↔
	etonogestrel (IP)	↑	↑	↑	↑	↑52%	↓63%[g]	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
	etonogestrel (VR)	↑	↑[h]	↑	↑[h]	↑[h]	↓[g]	↓	↓	↔	↔	↔	↑[h]	↔	↔	↔	↔	↔	↔	↔
	gestodene (COC)	↑	↑[e,a]	↑	↑[f]	↑[f]	↓[g]	↓	↓	↔	↔	↔	↑[d,e]	↔	↔	↔	↔	↔	↔	↔
	levonorgestrel (COC)	↑	↑[e,a]	↑	↑[f]	↑[f]	↓[g]	↓	↑	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
	levonorgestrel (IP)	↑	↑	↑	↑	↑	↓47%[g]	↓	↑14%	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
	levonorgestrel (POP)	↑	↑	↑	↑	↑	↓[g]	↓	↑	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔
	levonorgestrel (IUD)	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	medroxyprogesterone (POI)	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	norelgestromin (TS)	↑	↑[e,a]	↑	↑[f]	↑83%[f]	↓[g]	↓	↓	↔	↔	↔	↑[d,e]	↔	↔	↔	↔	↔	↔	↔
	norethisterone (COC)	↑	↑[e,a,i]	↑	↓14%[f]	↓17%[f]	↓[g]	↓5%	↓19%	↓11%	↔	↔	↑[d,e]	↔	↔	↔	↔	↔	↔	↔
	norethisterone (POI)	↔	↔	↔	↔	↔	↓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	norethisterone (POP)	↑	↑50%	↑	↑50%	↑50%	↓[g]	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔	↔	↔
	norgestimate (COC)	↑	↑85%[e,a]	↑	↑[f]	↑[f]	↓64%[g]	↓	↓	↔	↔	↔	↑126%[d,e]	↑14%	↔	↔	↔	↔	↔	↔
	norgestrel (COC)	↑	↑[e,a]	↑	↑[f]	↑[f]	↓[g]	↓	↑	↔	↔	↔	↑[d,e]	↔	↔	↔	↔	↔	↔	↔	↔
Other	levonorgestrel (EC)	↑[j]	↑[j]	↑[j]	↑[j]	↑[j]	↓58%[k]	↔	↔	↔	↔	↔	↑[j]	↔	↔	↔	↔	↔	↔	↔
	mifepristone	↑[j]	↑[j]	↑[j]	↑[j]	↑[j]	↓	↓	↓	E[j]	E[j]	↔	↑[j]	↔	↔	↔	↔	↔	↔	↔
	ulipristal	↑[j]	↑[j]	↑[j]	↑[j]	↑[j]	↓[l]	↓[l]	↓[l]	↔	↔	↔	↑[j]	↔	↔	↔	↔	↔	↔	↔

Contraceptive methods:

COC combined oral contraceptive

IP implant

IUD intrauterine device

POI progestin only injectable

POP progestin only pill

TS transdermal patch

VR vaginal ring

EC emergency contraception

interaction likely to be of weak intensity or unlikely to impair contraceptive efficacy

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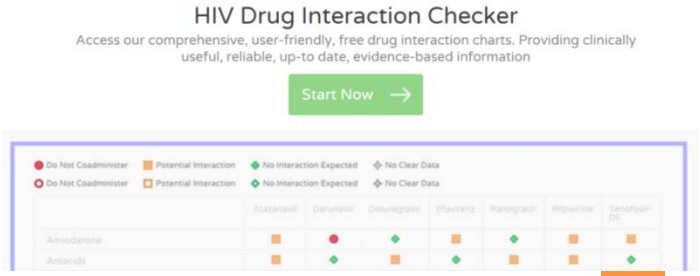
Tables are linked to DDIs websites

HIV Drug Interactions

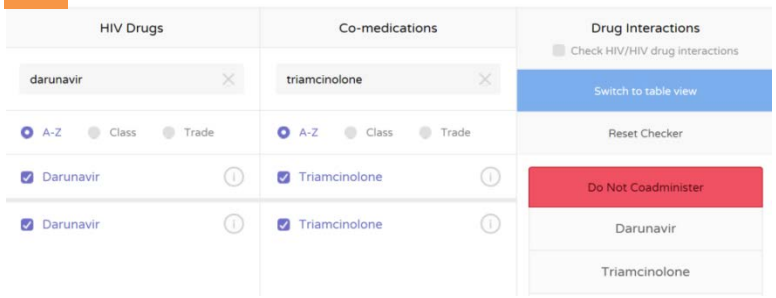
www.hiv-druginteractions.org

HEP Drug Interactions

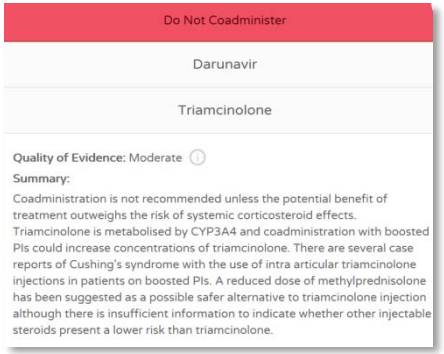
www.hep-druginteractions.org



1 selection of drugs



2 detailed information on DDI



+ **DDI documents related to specific topics** (DDI with PrEP; DDI and PK boosters; DDI with hormones for gender transitioning, DDI with non-oral corticosteroids and management of suspected DDI, …)

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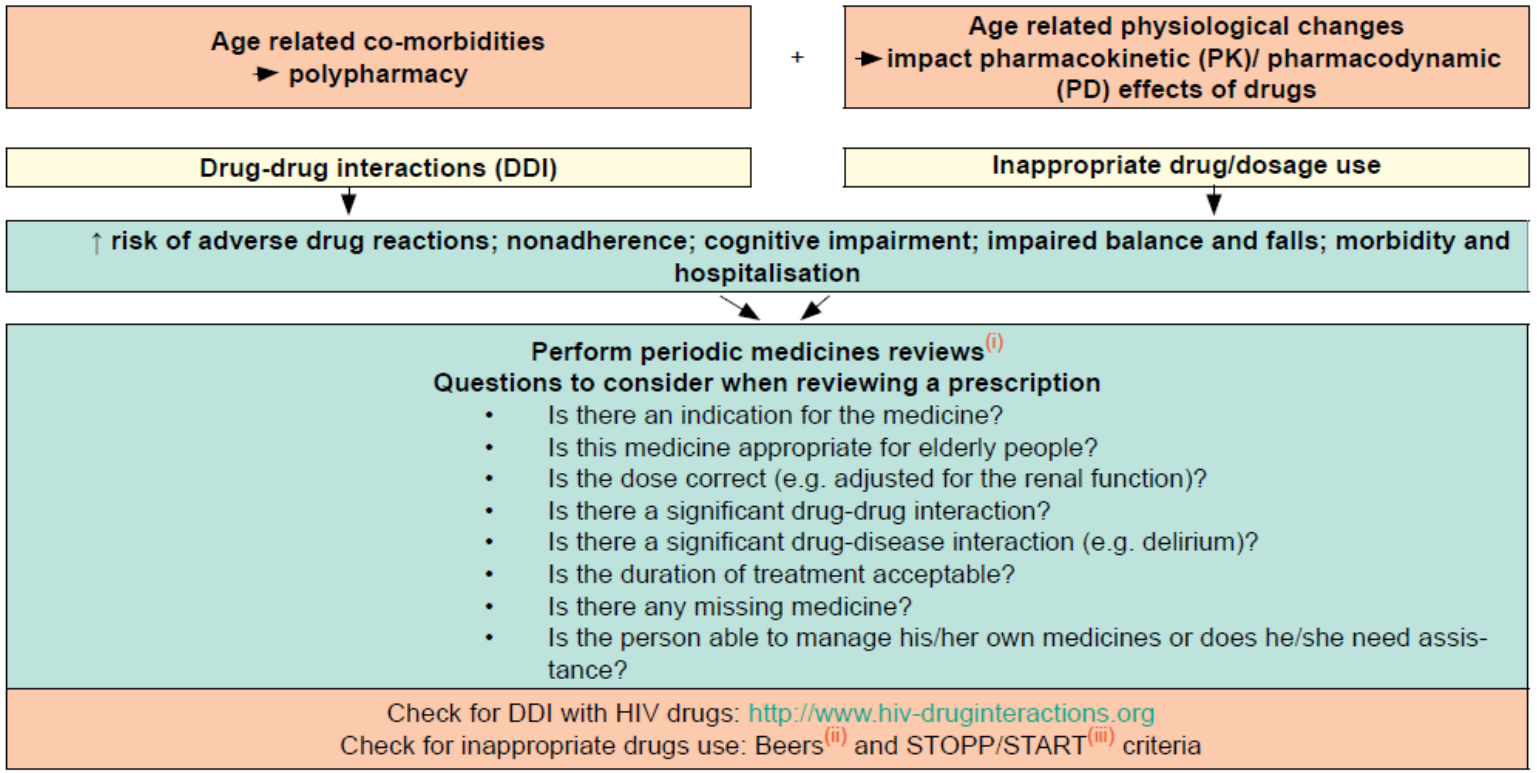
Prescribing in the elderly



The Beers and STOPP criteria are tools established by experts in geriatric pharmacotherapy to detect and reduce the burden of inappropriate prescribing in elderly. Inappropriate medicines include, for instance, those which in elderly persons with certain diseases can lead to drug-disease interactions, are associated with a higher risk of adverse drug reactions in the elderly, medicines that predictably increase the risk of falls in the elderly or those to be avoided in case of organ dysfunction. The START criteria consist of evidence-based indicators of potential prescribing omission in elderly with specific medical conditions.

Acknowledgements

EACS panel members

Co-morbidities

Chair: Georg Behrens	**Hannover, Germany**
Vice-Chair: Patrick Mallon	**Dublin, Ireland**
Young scientist: Lene Ryom	**Copenhagen, Denmark**
Manuel Battegay	Basel, Switzerland
Mark Bower	London, United Kingdom
Paola Cinque	Milan, Italy
Simon Collins	London, United Kingdom
Juliet Compston	Cambridge, United Kingdom
Stéphane De Wit	Brussels, Belgium
Christoph A. Fux	Aarau, Switzerland
Leonardo M. Fabbri	Modena, Italy
Giovanni Guaraldi	Modena, Italy
Jens D. Lundgren	Copenhagen, Denmark
Esteban Martínez	Barcelona, Spain
Catia Marzolini	Basel, Switzerland
Socrates Papapoulos	Leiden, The Netherlands
Renaud du Pasquier	Lausanne, Switzerland
Neil Poulter	London, United Kingdom
Peter Reiss	Amsterdam, The Netherlands
Ian Williams	London, United Kingdom
Alan Winston	London, United Kingdom

Co-infections

Chair: Massimo Puoti	**Milan, Italy**
Vice-Chair: Andri Rauch	**Bern, Switzerland**
Young scientist: Christoph Boesecke	**Bonn, Germany**
Juan Berenguer	Madrid, Spain
Sanjay Bhagani	London, United Kingdom
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
Jürgen K. Rockstroh	Bonn, Germany

Liverpool HIV/HEP Drug Interactions websites team

David Back
Saye Khoo

Sara Gibbons	Alison Boyle
Fiona Marra	Justin Chiong
Katie McAllister	Kay Seden

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