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Managing cognitive impairment in PLWH

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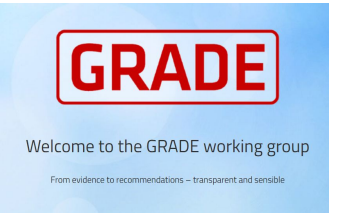
Evidence base



Grade of recommendation Conclusions of evidence	I Strong recommendation to do Benefits >>> risk & burdens	IIa Moderate recommendation to do Benefits >> risk & burdens	IIb Weak recommendation to do Benefits >= risks & burdens	III Recommendation not to do No benefit / Potentially harm
A High level of evidence Consistent evidence from well performed and high quality studies or systematic reviews (low risk of bias, direct, consistent, precise)	Strong recommendation based on high level of evidence	Moderate recommendation based on high level of evidence	Weak recommendation based on high level of evidence	Recommendation based on high level of evidence
B Moderate /Low level of evidence Evidence from studies or systematic reviews with few important limitations	Strong recommendation based on moderate/ low level of evidence	Moderate recommendation based on moderate/ low level of evidence	Weak recommendation based on moderate/ low level of evidence	Recommendation based on moderate/ low level of evidence
C Very low level of evidence Evidence from studies with serious flaws. Only expert opinion, or standards of care	Strong recommendation based on expert opinion	Moderate recommendation based on very low level of evidence Diverging expert opinions	Weak recommendation based on very low level of evidence Diverging expert opinions	Recommendation based on very low level of evidence Expert opinion

Example

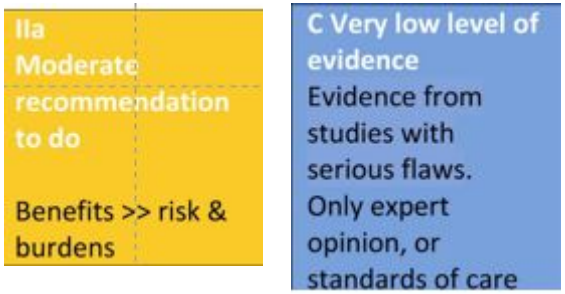
British HIV Association BHIVA

BHIVA guidelines for the treatment of HIV-1-positive adults with ART 2015 (2016 interim update)

8.6 Cardiovascular disease

In individuals with a high CVD risk

- We suggest avoiding abacavir if an acceptable alternative is available
- 2C



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Managing cognitive impairment

1	Starting ART

Question:

- Should all PLWH with HIV associated cognitive impairment commence ART?

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Managing cognitive impairment

1	Starting ART

Question:

- Should all PLWH with HIV associated cognitive impairment commence ART

Evidence for:

1. START main study
2. HIV encephalopathy improves with ART

Evidence against:

1. START neurology sub-study showed no benefit

Recommendation:

- We recommend commencing ART in all PLWH with HIV associated cognitive impairment
- A1

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Managing cognitive impairment

1	Starting ART
2	Triple therapy or novel strategies

Question:

- Should all PLWH with HIV associated cognitive impairment receive standard triple ART or can novel strategies be utilised?

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Managing cognitive impairment

1	Starting ART
2	Triple therapy or novel strategies

Question:

- Should all PLWH with HIV associated cognitive impairment receive standard triple ART or can novel strategies be utilised?

Evidence for triple therapy:

- Recovery from HIV encephalopathy mainly with triple therapy
- Case reports and series of problems with PI monotherapy

Evidence against triple therapy:

- In large PI monotherapy studies, no differences in cognitive function

Recommendation:

- Recommend triple therapy
- Best practice management

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Managing cognitive impairment

1	Starting ART
2	Triple therapy or novel strategies
3	Antiretroviral toxicity

Question:

- Should efavirenz be replaced by another agent in PLWH with HIV associated cognitive impairment?

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Managing cognitive impairment

1	Starting ART
2	Triple therapy or novel strategies
3	Antiretroviral toxicity

Question:

- Should efavirenz be replaced by another agent in PLWH with HIV associated cognitive impairment?

Evidence for:

- Two randomised controlled studies report poorer cognitive performance with efavirenz
- Cohort data

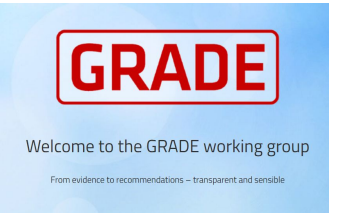
Evidence against:

- Some cohort studies

Recommendation:

- Replacing with a different third agent is generally possible
- 1B

Evidence base



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Managing cognitive impairment

1	Starting ART
2	Triple therapy or novel strategies
3	Antiretroviral toxicity
4	Management of comorbidities and lifestyle

Question:

- How important is comorbidity and lifestyle management

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Comorbidities and lifestyle

Question:

- How important is comorbidity and lifestyle management

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AMERICAN ACADEMY OF NEUROLOGY®

RESeptember 07, 2010; 75 (10) ARTICLES

Cardiovascular risk factors associated with lower baseline cognitive performance in HIV-positive persons

E.J. Wright, B. Grund, K. Robertson, B.J. Brew, M. Roediger, M.P. Bain, F. Drummond, M.J. Vjecha, J. Hoy, C. Miller, A.C. Penalva de Oliveira, W. Pumpradit, J.C. Shlay, W. El-Sadr, R.W. Price and ; For the INSIGHT SMART Study Group

First published August 11, 2010, DOI: https://doi.org/10.1212/WNL.0b013e3181f11bd8

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Comorbidities and lifestyle

Question:

- How important is comorbidity and lifestyle management

Depression and HIV

Recreational drug and Chemsex

Public Health England

Chemsex

"We lack robust and timely data on 'Chemsex', a term describing sex that occurs under the influence of drugs. However, there is evidence that Chemsex is associated with risky sexual behaviour and that MSM in London are more likely to use the common Chemsex drugs, such as crystal methamphetamine, GHB/GBL and mephedrone"

HIV and STIs in men who have sex with men in London PHE Report September 2014

Why are drugs being used?

- Ability to boost self-confidence
- Remove insecurities
- Increased sexual desire though dependence on drugs to have sex is widely reported

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Managing cognitive impairment

1	Starting ART
2	Triple therapy or novel strategies
3	Antiretroviral toxicity
4	Management of comorbidities and lifestyle

Question:

- How important is comorbidity and lifestyle management

Recommendation:

- Although evidence lacking, optimal management of comorbidities, mental health and lifestyle factors should be undertaken

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Managing cognitive impairment

1	Starting ART
2	Triple therapy or novel strategies
3	Antiretroviral toxicity
4	Management of comorbidities
5	Specific ART considerations • Include specific agents • Dosing of ART, CSF escape and pharmacokinetic scoring systems

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Specific ART agents

Class	Drug	Advantage	Disadvantage
NRTIs	zidovudine	• Evidence from monotherapy days	• No evidence with triple therapy • Potential neurotoxicity
	abacavir	• High CSF to plasma ratio	• CVD signal
NNRTI	nevirapine	• High CSF to plasma ratio	
PIs	lopinavir/r darunavir/r/c	• CSF exposure above IC_{50}	• CVD signal / metabolic signal
INSTI	dolutegravir	• CSF HIV RNA decay data	• CNS toxicities
EI	maraviroc	• Anti-inflammatory potential	• No strong evidence as anti-inflammatory • Antiviral activity questionable

Dose consideration, CSF escape and pharmacokinetic scoring systems

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Class	Drug	Usual clinical dose	Alternative(s) and rationale
NRTIs	abacavir	• 600 mg once daily	• 300 mg twice daily • 600 mg twice daily
PIs	darunavir/r/c	• 800 mg / 150 mg cobicistat once daily	• 800 mg / 100 mg ritonavir once daily • 600 mg / 100 mg ritonavir twice daily If PI resistance detected or suspected consider twice daily
INSTI	dolutegravir	• 50 mg once daily	• 50 mg twice daily If INSTI resistance detected or suspected in CSF and/or plasma
PK scoring systems		In cases of CSF escape, sequencing and basing regimen on resistance testing is of greater importance *	

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Managing cognitive impairment

1	Starting ART
2	Triple therapy or novel strategies
3	Antiretroviral toxicity
4	Management of comorbidities
5	Specific ART considerations • Include specific agents • Dosing of ART, CSF escape and pharmacokinetic scoring systems
6	Adjunctive therapies

Adjunctive therapies:

- Many have been trialled
- No positive signals to date in larger scale studies
- Of future research interest
- Not current clinical practice

Managing cognitive impairment

Summary

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	Question	Recommendation
1	Starting ART	All should commence
2	Triple therapy or novel strategies	Standard triple therapy
3	Antiretroviral toxicity	Avoid efavirenz
4	Management of comorbidities	Challenging but optimise management
5	Specific ART considerations • Include specific agents • Dosing of ART, CSF escape and pharmacokinetic scoring systems	Evidence is lacking to recommend specific ART agents or strategies Balance between toxicity and theoretical benefits
6	Adjunctive therapies	Future research interest

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Thank you

HIV CNS UK·MEETING

http://hivcns.co.uk/