HIV Treatment Guidelines

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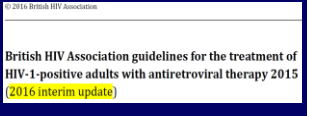
Current HIV Treatment Guidelines

- DHHS: www.aidsinfo.nih.gov 5/30/18

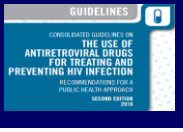
- IAS-USA: Saag JAMA 2018;320:379-396

- BHIVA: www.bhiva.org/guidelines 9/15, 2016
  interim update



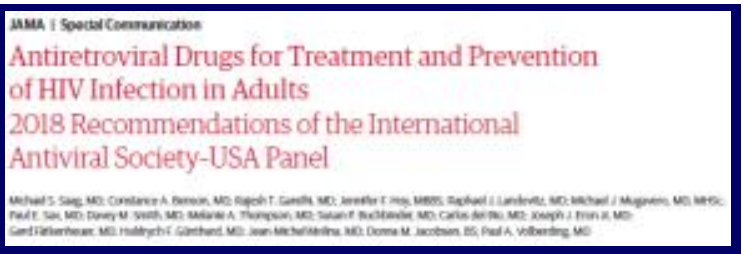
- EACS: www.eacsociety.org 10/17

- WHO:
  http://www.who.int/hiv/pub/guidelines/ARV2018update/en/
  7/30/18 interim guidance



Process – DHHS (+ Australian!)

- continuous review process
- updated as needed
- recommendations based on full panel consensus and votes
- rate the quality of evidence and strength of recommendations
- 298 web-based, searchable document
- Australian panel reviews and annotates recommendations for local context



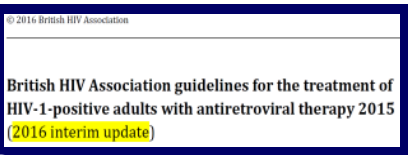
JAMA | Special Communication

Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults 2018 Recommendations of the International Antiviral Society-USA Panel

Process – IAS-USA

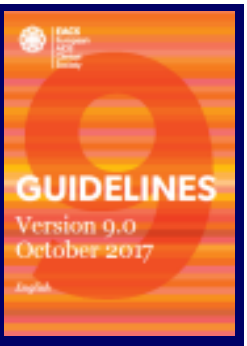
- updated every 2 yrs
- published data or presented abstracts in the past 2 years systematically searched and reviewed by the panel
- recommendations based on full panel consensus
- 18-page article published in JAMA

Process – BHIVA



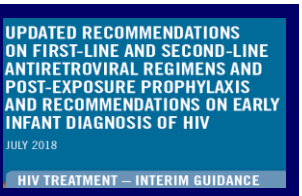
- questions drafted
- search done, including abstracts
- systematic literature review performed by an "informational scientist"; evaluated by writing group
- panel members assess and grade the quality of evidence & develop & grade strength of recommendations – modified GRADE
- GRADE evidence profile and summary of findings tables constructed for some questions
- before final approval, external peer review (n=3) and published online for public consultation
- community consultation
- 151-page document; 5 on-line appendices

Process – EACS



- updated annually in autumn
- process summarized
  - Evidence-based (expert opinion rarely)
  - Consensus or formal votes (not published)
  - No formal grading of evidence
- 101-page document, mostly outline and tables (minimal text)
- translated into 10 languages(!)

Process – WHO



- questions developed
- systematic review teams conducted reviews
- standardized GRADE evidence table used to present quantitative summaries of evidence
- rated the quality of evidence and strength of recommendations
- feasibility considered
- community consultation
- 432-page document; 16-page update

Antiretroviral Therapy: Questions

- When to start?
- What to start?
- What to switch to?
- When to change?
- What to change to?

When to Start?

When to Start?: Chronic Infection

	AIDS/ symptoms	CD4 <200	CD4 200-350	CD4 350-500	CD4 >500
US DHHS 2018 www.aidsinfo.nih.gov	recommended				
IAS-USA 2018 JAMA 2018;320:379	recommended				
EACS 2017 www.europeanaidsclinicalsociety.org/	recommended				
UK 2016 update www.bhiva.org	recommended				
WHO 2016 http://www.who.int/hiv/pub/guidelines/en/	strong recommendation *PRIORITY*			strong recommendation	

When to Start?: Other

	Acute Infection	Elite controllers
US DHHS 2018 www.aidsinfo.nih.gov	recommended	theoretical rationale to start
IAS-USA 2018 JAMA 2018;320:379	recommended	(uncertain; recommended if ↓CD4)
EACS 2017 www.europeanaidsclinicalsociety.org/	recommended	possible exception to start with high CD4 + VL <1000
UK 2016 update www.bhiva.org	offer; recommended for neurologic involvement, AIDS, CD4 <350, dx w/i 12 wks of negative test	(not addressed)
WHO 2016 http://www.who.int/hiv/pub/guidelines/en/	no specific recommendation	(not addressed)

What to Start?

ART: What to Start? – Recommended/Preferred: 2 NRTI + 3rd Drug

	NRTI
US DHHS 2018 www.aidsinfo.nih.gov	TAF/FTC TDF/FTC ABC/3TC+
IAS-USA 2018 JAMA 2018;320:379	TAF/FTC ABC/3TC+
EACS 2017 www.europeanaidsclinicalsociety.org/	TAF/FTC TDF/FTC ABC/3TC+
UK 2016 update www.bhiva.org	TAF/FTC TDF/FTC
WHO 2018 http://www.who.int/hiv/pub/guidelines/ARV2018update/en/	TDF/3TC

+ only with DTG; * performs less well/not recommended for baseline HIV RNA >100,000 and/or CD4 <200

ART: What to Start? – Alternative: 2 NRTI + 3rd Drug

	NRTI	NNRTI	PI	INSTI	other
US DHHS 2018 www.aidsinfo.nih.gov	ABC/3TC	EFV RPV*	ATV/c ATV/r DRV/c		DRV/r + RAL* LPV/r + 3TC or FTC
IAS-USA 2018 JAMA 2018;320:379	TDF	EFV RPV	DRV/c DRV/r	EVG/c RAL	DRV/r + RAL* or 3TC (DTG + 3TC)
EACS 2017 www.europeanaidsclinicalsociety.org/	ABC/3TC	EFV	ATV/c ATV/r		DRV/c or /r + RAL
UK 2016 update www.bhiva.org	ABC/3TC*	EFV			DRV/r + RAL*
WHO 2018 http://www.who.int/hiv/pub/guidelines/ARV2018update/en/	FTC	EFV 400 or 600		RAL	

+ with DRV/c or DRV/r only
* performs less well/not recommended for baseline HIV RNA >100,000, CD4 <200 (except ABC/3TC/DTG)

Switch

Switch (with VS) Regimens

Guideline	Recommended	NOT recommended
US DHHS 2018 www.aidsinfo.nih.gov	DTG + RPV Boosted PI + 3TC or FTC	Boosted PI mono, DTG mono, boosted ATV + RAL, MVC regimens
IAS-USA 2018 JAMA 2018;320:379	DTG + RPV Boosted PI + 3TC DTG + 3TC	Monotherapy with boosted PI or DTG
EACS 2017 www.europeanaidsclinicalsociety.org/	DTG + RPV Boosted DRV + 3TC Boosted ATV + 3TC	ATV/r mono, DTG mono, 3 NRTIs, other 2-drug regimens (boosted PI + MVC; boosted ATV + RAL; MVC + RAL)

When to Change?

When to Change?

US DHHS 2018 www.aidsinfo.nih.gov	confirmed HIV RNA ≥200
IAS-USA 2018 JAMA 2018;320:379	confirmed HIV RNA >200
EACS 2017 www.europeanaidsclinicalsociety.org/	(rebound: confirmed HIV RNA >50 with prior VS) confirmed HIV RNA >500
UK 2016 update www.bhiva.org	confirmed HIV RNA >200
WHO 2016 http://www.who.int/hiv/pub/guidelines/en/	2 consecutive HIV RNA >1000 over 3 months

What to Change to?

What to change to?

US DHHS 2017 www.aidsinfo.nih.gov	At least 2, and preferably 3, fully active agents
IAS-USA 2018 JAMA 2018;320:379	NNRTI failure → 2 NRTI + DTG INSTI failure → 2 NRTI + boosted PI Do not add single active agent
EACS 2017 www.europeanaidsclinicalsociety.org/	At least 2 and preferably 3 active drugs (at least 1 fully active PI/r [e.g. DRV/r] + new class [FI, II, CCR5 or NNRTI e.g. ETR])
UK 2016 update www.bhiva.org	At least 2 and preferably 3 fully active agents (at least 1 active PI/r – preferably DRV/r -- and 1 with novel mechanism – II, CCR5, or FI)
WHO 2018 http://www.who.int/hiv/pub/guidelines/en/	NNRTI or PI failure → 2 NRTI + DTG DTG failure → 2 NRTI + [LPV/r or ATV/r] 3rd-line failure → 1-2 NRTI + DRV/r + DTG bid

Treatment Guidelines: Conclusions

- When to start?: any CD4
- What to start?: integrase inhibitors
- When to change?: confirmed viremia (≥200)
- What to change to?: at least 2, preferably 3, active drugs

Acknowledgments

- Weill Cornell Medicine
  - Cornell HIV Clinical Trials Unit (CCTU)
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- HIV Prevention Trials Network (HPTN)
- NIH, NIAID, Division of AIDS
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