Tratamiento antirretroviral de inicio OMS 2017

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SE- COMISCA
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FARMACOS ANTIRRETROVIRALES

- **Inhibidores de la transcriptasa inversa (IT)**
  Inhibidores nucleosidos de TI (ITIANs)
  Inhibidores no nucleosidos de TI (ITINANs)

- **Inhibidores de la proteasa (IP)**

- **Inhibidores de la integrasa**

- **Inhibidores de la fusión**

- **Inhibidores de correceptores**

INHIBIDORES DE LA TRANSCRIPTASA INVERSA

Inhibidores nucleosidos de TI (ITIANs

- Abacavir (ABC)
- Didanosina (ddl)
- Emtricitabina (FTC)
- Lamivudina (3TC)
- Estavudina (d4T)
- Tenofovir (TDF)
- Zidovudina (AZT)

Inhibidores no nucleosidos de TI (ITINANs)

- Efavirenz (EFV)
- Nevirapina (NVP)
- Etravirina (ETV)
- Rilpivirina (RIL)

INHIBIDORES DE LA PROTEASA

- Atazanavirnavir (ATV)
- Darunavir (DRV-TMC 114)
- Fosamprenavir (FPV)
- Indinavir (IDV)
- Lopinavir/ritonavir (LPV/RTN)
- Nelfinavir (NFV)
- Ritonavir (RTV)
- Saquinavir mesilato (SQV hgc)
- Tripanavir (TPV)

Inhibidores de la fusión

Enfuvirtida T-20 (ENF)

Inhibidores de la integrasa

- Raltegravir (RAL)
- Elvitegravir (EVG)
- Dolutegravir (DGV)

Inhibidores de correceptores

Maraviroc (MVC)

OBJETVOS DEL TRATAMIENTO ARV

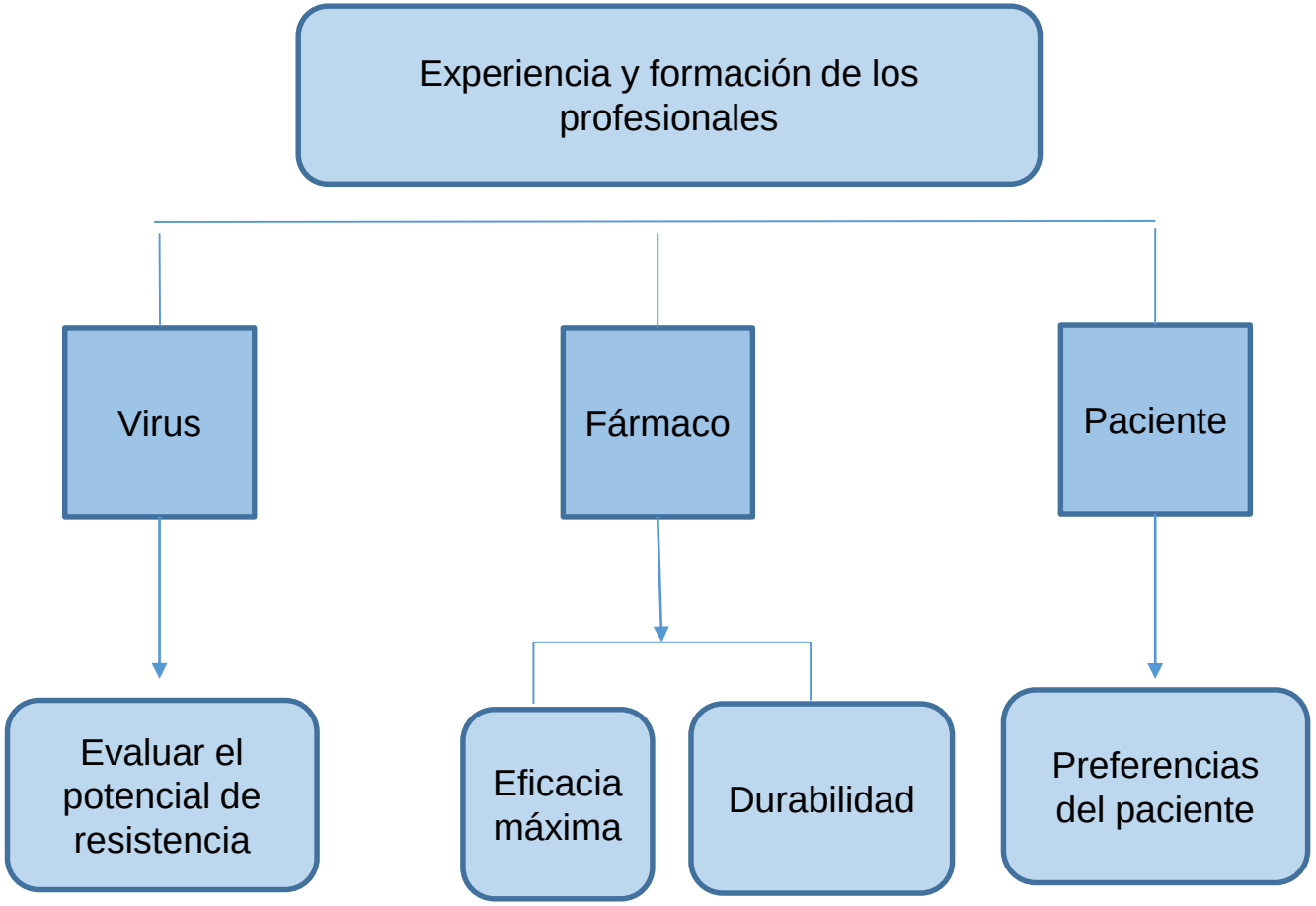
Reducir la carga viral plasmática (CVP) de forma sostenible, por debajo de los límites de detección (<50/20 copias/ml) con técnicas ultrasensibles.

El objetivo de supresión virológica (CPV <50/20 copias/ml) se debe conseguir tanto en pacientes sin TAR previo como en individuos que han experimentado un fracaso previo.

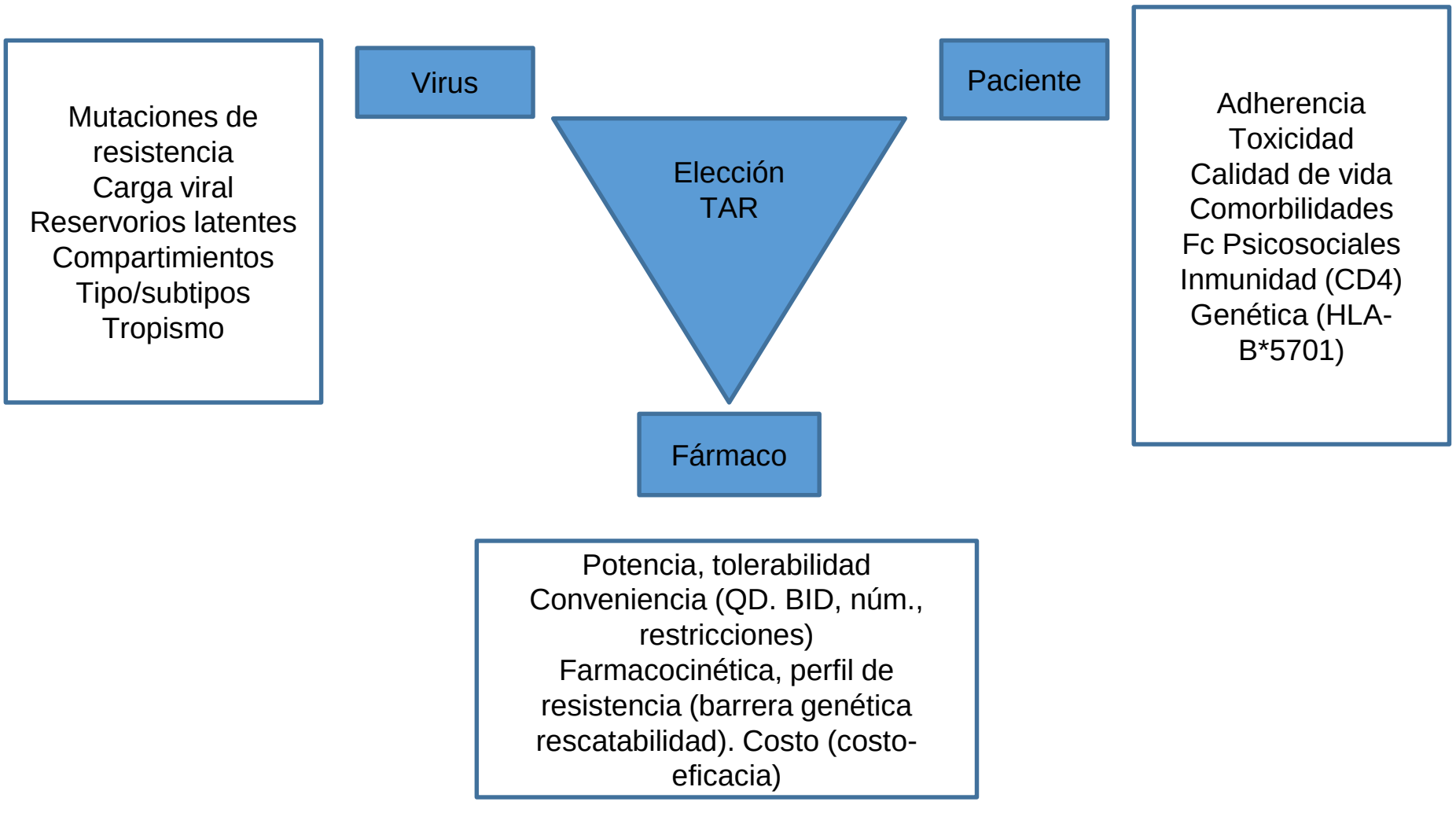
Objetivo: el éxito en terapia de inicio

- Durante el mayor tiempo posible
- Con el menor numero de efectos adversos
- Buena tolerancia
- Pocas interacciones
- Lo más cómodo posible
- Al menor coste

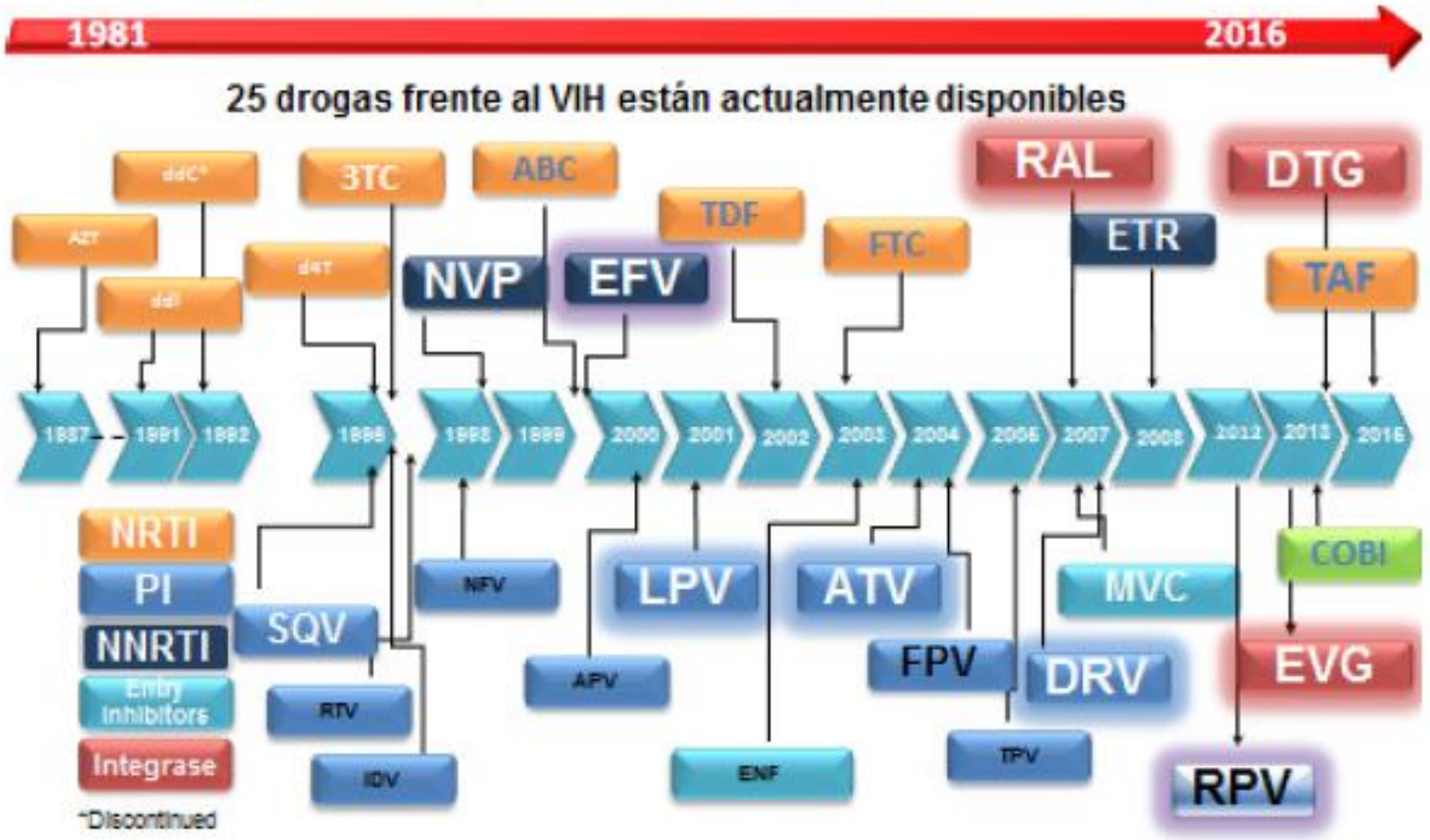
Planificar el éxito del tratamiento



Factores claves para la elección de la TAR



FÁRMACOS ANTIRRETROVIRALES EN LA ACTUALIDAD



Últimas combinaciones en aparecer

- EVOTAZ : Atazanavir/Cobicistat, ATZ/COBI 300mg/150mg

- PREZCOBIX : Darunavir/Cobicistat, DRV/COBI 800mg/150mg
- REZOLTA : Darunavir/Cobicistat, DRV/COBI 800mg/150 mg

- DUTREVIX : Raltegravir/Lamivudina, RAL/3TC 400mg/150mg

Cuando iniciar. Que dicen las guías

Recommendation

- **ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count (strong recommendation, moderate-quality evidence).**

- As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with CD4 count ≤350 cells/mm³ (strong recommendation, moderate-quality evidence).

Sources:

Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV. Geneva: World Health Organization 2015 (http://www.who.int/hiv/pub/guidelines/earlyrelease-arv/en).

Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach Geneva: World Health Organization; 2013 (http://www.who.int/hiv/pub/guidelines/arv2013/download/en).

Cuando iniciar. Que dicen las guías

Categoría Clínica	CD4 cells/mm^3	IAS 12	DHHS 15	GESIDA/PNS 16	EACS 15
Infección sintomática	Cualquier valor	Recomendar	Recomendar	Recomendar	Recomendar
Asintomática	< 350	Recomendar	Recomendar	Recomendar	Recomendar
Asintomática	350–500	Recomendar	Recomendar	Recomendar	Recomendar
Asintomática	>500	Recomendar	Recomendar	Recomendar	Recomendar

EACS Guidelines. Noviembre 2015. www.europeanaidsclinicalsociety.org/guidelines.asp
JAMA 2012;304:321-333
DHHS Guidelines for the use of antiretroviral agents in HIV-1 Infected Adults and Adolescents. Mayo 2015. wwwaidsinfo.nih.gov/guidelines
Recomendaciones de GeSIDA/PNS. Enero 2016. www.msssi.es

Con qué empezar

- La selección de una pauta inicial tiene consecuencias a largo plazo sobre los tratamientos futuros.

- Individualizar la decisión en base a resistencias, tolerancia, número de pastillas y frecuencia de dosis, interacciones, comorbilidades y preferencias.

- Las guías deben considerar los resultados de ensayos clínicos seleccionados por criterios de calidad y nivel de evidencia.

Pautas para inicio de TAR según GESIDA/PNS

3er Fármaco	Pauta†	Comentarios‡
Preferentes. Pautas aplicables a la mayoría de los pacientes y que en ensayos clínicos aleatorizados han mostrado una eficacia superior frente a otras o mostrando no-inferioridad presentan ventajas adicionales en tolerancia, toxicidad o un bajo riesgo de interacciones farmacológicas.		
INI	ABC/3TC/DTG	- ABC está contraindicado en pacientes con HLA-B*5701 positivo; cuando se prescriba se deben tomar las medidas necesarias para tratar de minimizar todos los FRCV modificables - Información escasa en pacientes con CD4+ <200 células/µL
	TDF/FTC+DTG	- Usar TDF con precaución en pacientes con factores de riesgo para insuficiencia renal; no indicado en pacientes con FGe <50 mL/min - Información escasa en pacientes con CD4+ <200 células/µL
	TDF/FTC+RAL	- Usar TDF con precaución en pacientes con factores de riesgo para insuficiencia renal; no se recomienda en pacientes con FGe <50 mL/min a menos que no exista otra alternativa
	TAF/FTC/EVG/COBI*	- No indicado en pacientes con FGe <30 ml/min. - Información escasa en pacientes con CD4+ < 200 células/µL - Mayor potencial de interacciones que otras pautas basadas en INI

Pautas preferentes según DHHS

Recommended Regimen Options (Drug classes and regimens within each class are arranged in alphabetical order.)
INSTI-Based Regimens: • DTG/ABC/3TC[a]—**only** for patients who are HLA-B*5701 negative **(AI)** • DTG plus TDF/FTC[a] **(AI)** • EVG/c/TDF/FTC—only for patients with pre-treatment estimated CrCl ≥70 mL/min **(AI)** • RAL plus TDF/FTC[a] **(AI)**
PI-Based Regimens: • DRV/r plus TDF/FTC[a] **(AI)**

Pautas preferentes según EACS

Initial Combination Regimen for ART-naïve Adult HIV-positive Persons

A) Recommended regimens (one of the following to be selected)[*,**]

Regimen	Dosing	Food requirement	Caution
2 NRTIs + INSTI			
ABC/3TC/DTG[i, ii]	ABC/3TC/DTG 600/300/50 mg, 1 tablet qd	None	Al/Ca/Mg-containing antacids should be taken well separated in time (minimum 2h after or 6h before).
TDF/FTC[iii, iv] + DTG	TDF/FTC 300[vii]/200 mg, 1 tablet qd + DTG 50 mg, 1 tablet qd	None	
TDF/FTC/EVG/c[iii, iv, v]	TDF/FTC/EVG/c 300[vii]/200/150/150 mg, 1 tablet qd	With food	Al/Ca/Mg-containing antacids should be taken well separated in time (minimum 2h after or 6h before).
TDF/FTC[iii, iv] + RAL	TDF/FTC 300[vii]/200 mg, 1 tablet qd + RAL 400 mg, 1 tablet bid	None	Al/Ca/Mg-containing antacids should be taken well separated in time (minimum 2h after or 6h before).
2 NRTIs + NNRTI			
TDF/FTC/RPV[viii]	TDF/FTC/RPV 300[vii]/200/25 mg, 1 tablet qd	With food (min 390 Kcal required)	Only if CD4 count >200 cells/µL and HIV VL <100,000 copies/mL. PPI contraindicated, H2 antagonists to be taken 12h before or 4h after RPV.
2 NRTIs + PI/r			
TDF/FTC[iii, iv] + DRV/r	TDF/FTC 300[vii]/200 mg, 1 tablet qd + DRV 800 mg, 1 tablet qd + RTV 100 mg, 1 tablet qd	With food	Monitor in persons with a known sulfonamide allergy.

Cuando iniciar según OMS

Recommendation

- **ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count (strong recommendation, moderate-quality evidence).**

NEW

- As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with CD4 count ≤350 cells/mm^3 (strong recommendation, moderate-quality evidence).

Sources:

Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV. Geneva: World Health Organization 2015 (http://www.who.int/hiv/pub/guidelines/earlyrelease-arv/en).

Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach Geneva: World Health Organization; 2013 (http://www.who.int/hiv/pub/guidelines/arv2013/download/en).

FDC Terapia ARV combinada con dosis fijas OMS

4.4.2 Fixed-dose combinations and once-daily regimens

NEW

Recommendation

Fixed-dose combinations and once-daily regimens are preferred for antiretroviral therapy (strong recommendation, moderate-quality evidence).

Cuando iniciar embarazadas y mujer lactando. OMS

4.3.2 When to start ART in pregnant and breastfeeding women

NEW

Recommendation

ART should be initiated in all pregnant and breastfeeding women living with HIV regardless of WHO clinical stage and at any CD4 cell count and continued lifelong (strong recommendation, moderate-quality evidence).

Source: HIV and adolescents: guidance for HIV testing and counselling and care for adolescents living with HIV. Geneva: World Health Organization; 2013 (http://www.who.int/hiv/pub/guidelines/adolescents/en).

Conque pautas iniciar según OMS

Table 4.1. First-line ART regimens for adults, pregnant or breastfeeding women, adolescents and children

First-line ART	Preferred first-line regimens	Alternative first-line regimens[a,b]
Adults	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + DTG[c] TDF + 3TC (or FTC) + EFV_{400}[c,d,e] TDF + 3TC (or FTC) + NVP
Pregnant or breastfeeding women	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + NVP
Adolescents	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV (or NVP) TDF (or ABC) + 3TC (or FTC) + DTG[c,d] TDF (or ABC) + 3TC (or FTC) + EFV_{400}[c,d,e] TDF (or ABC) + 3TC (or FTC) + NVP
Children 3 years to less than 10 years	ABC + 3TC + EFV	ABC + 3TC + NVP AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + EFV (or NVP)
Children less than 3 years	ABC (or AZT) + 3TC + LPV/r	ABC (or AZT) + 3TC + NVP

[a] For adults and adolescents, d4T should be discontinued as an option in first-line treatment.

Regímenes primera línea adultos OMS

Table 4.2. First-line ART regimens for adults (see Annex 11 for doses)

Preferred regimen	TDF + 3TC (or FTC) + EFV
Alternative regimens	AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + DTG[a] TDF + 3TC (or FTC) + EFV_{400}[b] TDF + 3TC (or FTC) +NVP
Special circumstances[c,d]	Regimens containing ABC and boosted PIs

[a] Safety and efficacy data on DTG for pregnant and breastfeeding women and TB coinfection are still pending.

[b] Efficacy data for EFV at a lower dose of 400 mg/day in the case of pregnant and breastfeeding women and TB coinfection are still pending.

[c] Special circumstances may include situations where preferred or alternative regimens may not be available or suitable because of significant toxicities, anticipated drug–drug interactions, drug procurement and supply management issues, or for other reasons.

[d] Using stavudine (d4T) as an option in first-line treatment should be discontinued.

3TC lamivudine, ABC abacavir, ATV atazanavir, AZT zidovudine, DTG dolutegravir, EFV efavirenz, FTC emtricitabine, NVP nevirapine, PI protease inhibitor, TDF tenofovir.

Pautas preferentes según OMS

4.4.3 First-line ART for adolescents

Recommendations

First-line ART for adolescents should consist of two NRTIs plus an NNRTI or an INSTI:

- TDF + 3TC (or FTC) + EFV as a fixed-dose combination is recommended as the preferred option to initiate ART (strong recommendation, low-quality evidence).
- **TDF + 3TC (or FTC) + DTG or TDF + 3TC (or FTC) + EFV_{400}[a] may be used as alternative options to initiate ART (conditional recommendation, low-quality evidence).** NEW

If preferred regimens are contraindicated or not available, one of the following alternative options is recommended (strong recommendation, moderate-quality evidence):

ABC + 3TC + EFV
ABC + 3TC + NVP
AZT + 3TC + EFV
AZT + 3TC + NVP
TDF + 3TC (or FTC) + NVP

[a] EFV at a lower dose (400 mg/day).

Pautas preferentes para niños de 3 a 10 años. OMS

Table 4.5. Summary of recommended first-line ART regimens for children 3–10 years of age

Preferred	ABC + 3TC + EFV
Alternatives	ABC + 3TC + NVP AZT + 3TC + EFV AZT + 3TC + NVP TDF + 3TC (or FTC) + EFV TDF + 3TC (or FTC) + NVP

3TC lamivudine, ABC abacavir, AZT zidovudine, EFV efavirenz, FTC emtricitabine, NVP nevirapine, TDF tenofovir

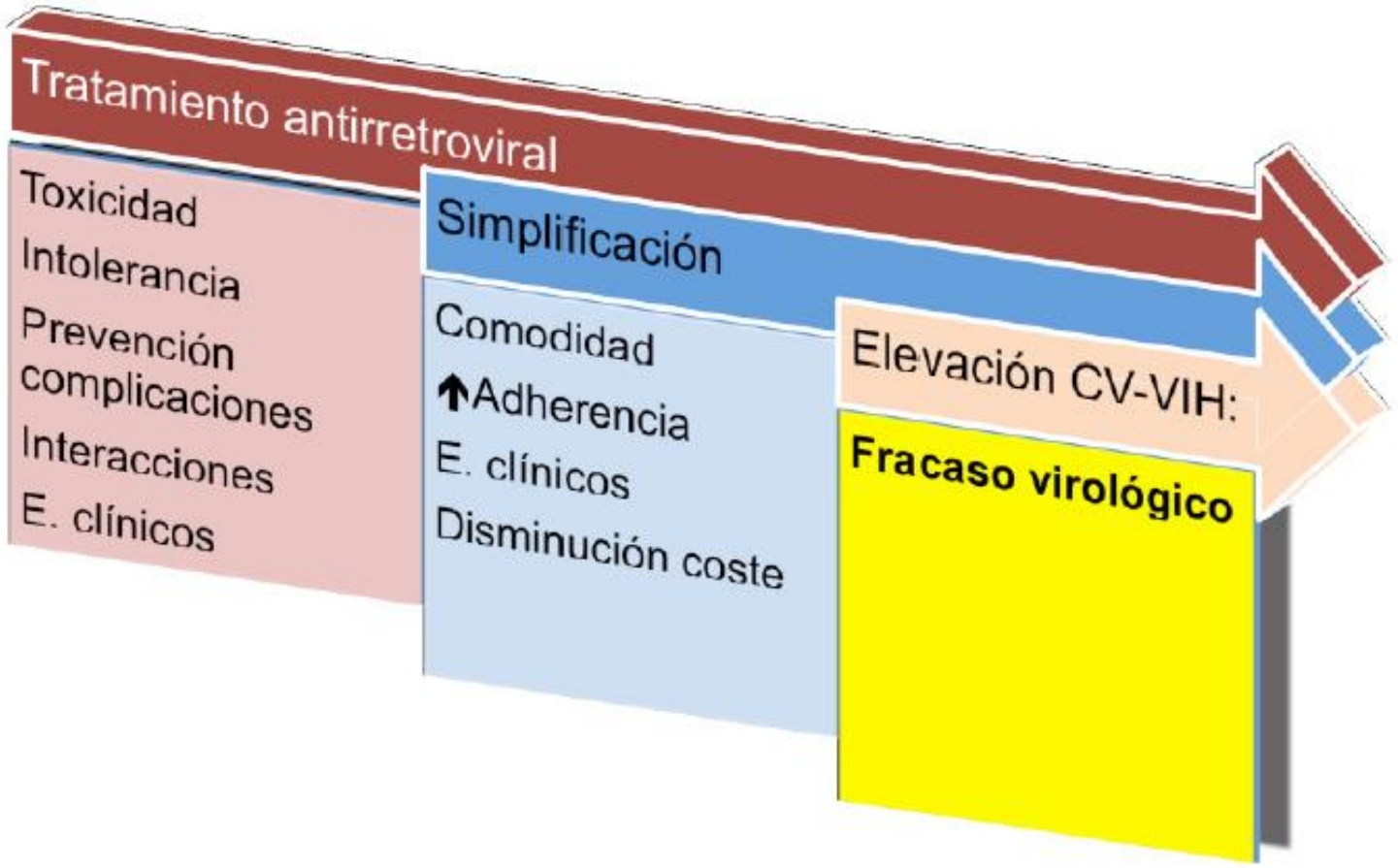
Pautas preferentes niños menores de 3 años
OMS

Table 4.7. Summary of first-line ART regimens for children younger than 3 years

Preferred regimens	ABC[a] or AZT + 3TC + LPV/r[b]
Alternative regimens[c]	ABC[a] or AZT + 3TC + NVP
Special circumstances[d]	ABC[a] or AZT + 3TC + RAL[a]

[a] Based on the general principle of using non-thymidine analogues in first-line regimens and thymidine analogues in second-line regimens, ABC should be considered as the preferred NRTI whenever possible. Availability and cost should be carefully considered.

MOTIVOS DE CAMBIO DE TAR



Regímenes segunda línea adultos y adolescentes. OMS

Table 4.16. Summary of preferred second-line ART regimens for adults and adolescents

Target population	Preferred second-line regimen[a]	
Adults and adolescents	If d4T or AZT was used in first-line ART	TDF + 3TC (or FTC) + ATV/r or LPV/r[b,c]
	If TDF was used in first-line ART	AZT + 3TC + ATV/r or LPV/r[b,c]
Pregnant or breastfeeding women	Same regimens as recommended for adults and adolescents	
HIV and TB coinfection	If rifabutin is available	Standard PI-containing regimens as recommended for adults and adolescents
	If rifabutin is not available	Same NRTI backbones as recommended for adults and adolescents plus double-dose LPV/r (that is, LPV/r 800 mg/200 mg twice daily)[d]
HIV and HBV coinfection	AZT + TDF + 3TC (or FTC) + (ATV/r or LPV/r)[b]	

[a] ABC and didanosine (ddI) can be used as NRTI back-up options but add complexity and cost without clinical advantages.

Pautas preferentes según OMS

Table 4.15. Preferred second-line ART regimens for adults, adolescents, pregnant women and children

Population		Failing first-line regimen	Preferred second-line regimen	Alternative second-line regimens
Adults and adolescents		2 NRTIs + EFV (or NVP)	2 NRTIs[b] + ATV/r or LPV/r	2 NRTIs[b] + DRV/r[c]
		2 NRTIs + DTG		
Pregnant or breastfeeding women		2 NRTIs + EFV (or NVP)	2 NRTIs[b] + ATV/r or LPV/r	2 NRTIs[b] + DRV/r
Children	Less than 3 years	2 NRTIs + LPV/r	2 NRTIs[b] + RAL	Maintain the failing LPV/r-based regimen and switch to 2 NRTIs[b] + EFV at 3 years of age
		2 NRTIs + NVP	2 NRTIs[b] + LPV/r	2 NRTIs[b] + RAL[d]
	3 years to less than 10 years	2 NRTIs + LPV/r[a]	2 NRTIs[b] + EFV	2 NRTIs[b] + RAL[d]
		2 NRTIs + EFV (or NVP)	2 NRTIs[b] + LPV/r	2 NRTIs[b] + ATV/r[d]

[a] ATV/r can be used as an alternative PI for children older than 3 months of age.

Regímenes segunda línea niños. OMS

Table 4.18. Summary of recommended first- and second-line ART regimens for children

	Children (including adolescents)	First-line ART regimen	Second-line ART regimen
LPV/r-based first-line regimen	Younger than 3 years	ABC + 3TC + LPV/r	AZT or ABC+ 3TC + RAL[a]
		AZT + 3TC + LPV/r	
	3 years and older	ABC + 3TC + LPV/r	AZT + 3TC + EFV or RAL
		AZT + 3TC + LPV/r	ABC or TDF[b] + 3TC + EFV or RAL
NNRTI-based first-line regimen	All ages	ABC + 3TC + EFV (or NVP)	AZT + 3TC + ATV/r or LPV/r[c]
		TDF[b] + 3TC (or FTC) + EFV (or NVP)	
		AZT + 3TC + EFV (or NVP)	ABC or TDF + 3TC[c] (or FTC) + ATV/r or LPV/r[c]

[a] If RAL is not available, no change is recommended unless in the case of advanced clinical disease progression or lack of adherence specifically due to poor palatability of LPV/r. In this case, switching to a second-line NVP-based regimen should be considered. Based on approval of the use of EFV in children less than 3 years, an EFV-based regimen could be considered as an alternative. However, more data are needed to inform how best to use EFV in this population.

Regímenes segunda y tercera línea. OMS

Table 4.19. Summary of sequencing options for first-, second- and third-line ART regimens in adults, adolescents, pregnant women and children

Population	First-line regimens	Second-line regimens	Third-line regimens
Adults and adolescents (>10 years)	2 NRTIs + EFV	2 NRTIs + ATV/r or LPV/r[a]	DRV/r[b] + DTG[c] (or RAL) ± 1–2 NRTIs
		2 NRTI + DRV/r[b]	
	2 NRTIs + DTG	2 NRTIs + ATV/r or LPV/r	DRV/r[b] + 2 NRTIs ± NNRTI
		2 NRTI + DRV/r	Optimize regimen using genotype profile
Pregnant or breastfeeding women	2 NRTIs + EFV	2 NRTIs + ATV/r or LPV/r[a]	DRV/r[b] + DTG[c] (or RAL) ± 1–2 NRTIs
		2 NRTIs + DRV/r[b]	
Children (0–10 years	2 NRTI + LPV/r	If less than 3 years: 2 NRTIs + RAL[d]	RAL (or DTG)[f] + 2 NRTIs DRV/r[g] + 2 NRTIs DRV/r[g] + RAL (or DTG)[f] ± 1–2 NRTIs
		If older than 3 years: 2 NRTIs + EFV or RAL	
	2 NRTI + EFV	2 NRTIs + ATV/r[a] or LPV/r	

[a] RAL + LPV/r can be used as an alternative second-line regimen in adults and adolescents.

Monitoreo de estudio virológico e inmunológico OMS

4.5.2 Monitoring the response to ART and diagnosis of treatment failure

NEW

Recommendations for routine monitoring

Routine viral load monitoring can be carried out at 6 months, at 12 months and then every 12 months thereafter if the patient is stable on ART to synchronize with routine monitoring and evaluation reporting[a] (conditional recommendation, very low-quality evidence).

In settings where routine viral load monitoring is available, CD4 cell count monitoring can be stopped in individuals who are stable on ART and virally suppressed[b] (conditional recommendation, low-quality evidence).

[a] Viral load testing should be performed early after initiating ART (within 6 months), at 12 months and then at least every 12 months to detect treatment failure. If viral load testing is not routinely available, CD4 count and clinical monitoring should be used to diagnose treatment failure, with targeted viral load testing to confirm viral failure where possible.

[b] WHO defines people stable on ART according to the following criteria: on ART for at least 1 year, no current illnesses or pregnancy, good understanding of lifelong adherence and evidence of treatment success (two consecutive viral load measurements below 1000 copies/mL). For service delivery recommendations in these guidelines (*see* Chapter 6 "Service delivery"), an additional criterion is that there are no adverse drug reactions requiring regular monitoring, but this is not relevant to this recommendation.

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¡MUCHAS GRACIAS!

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