Ottimizzazione terapeutica in differenti contesti clinici

Terapia duplice: quando semplificare

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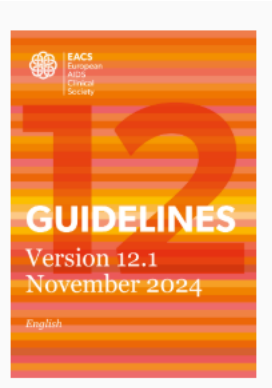
What does simplification mean?



- To reduce pill burden
- To start an injectable regimen
- Adjust food restrictions
- Improve adherence
- Reduce monitoring needs

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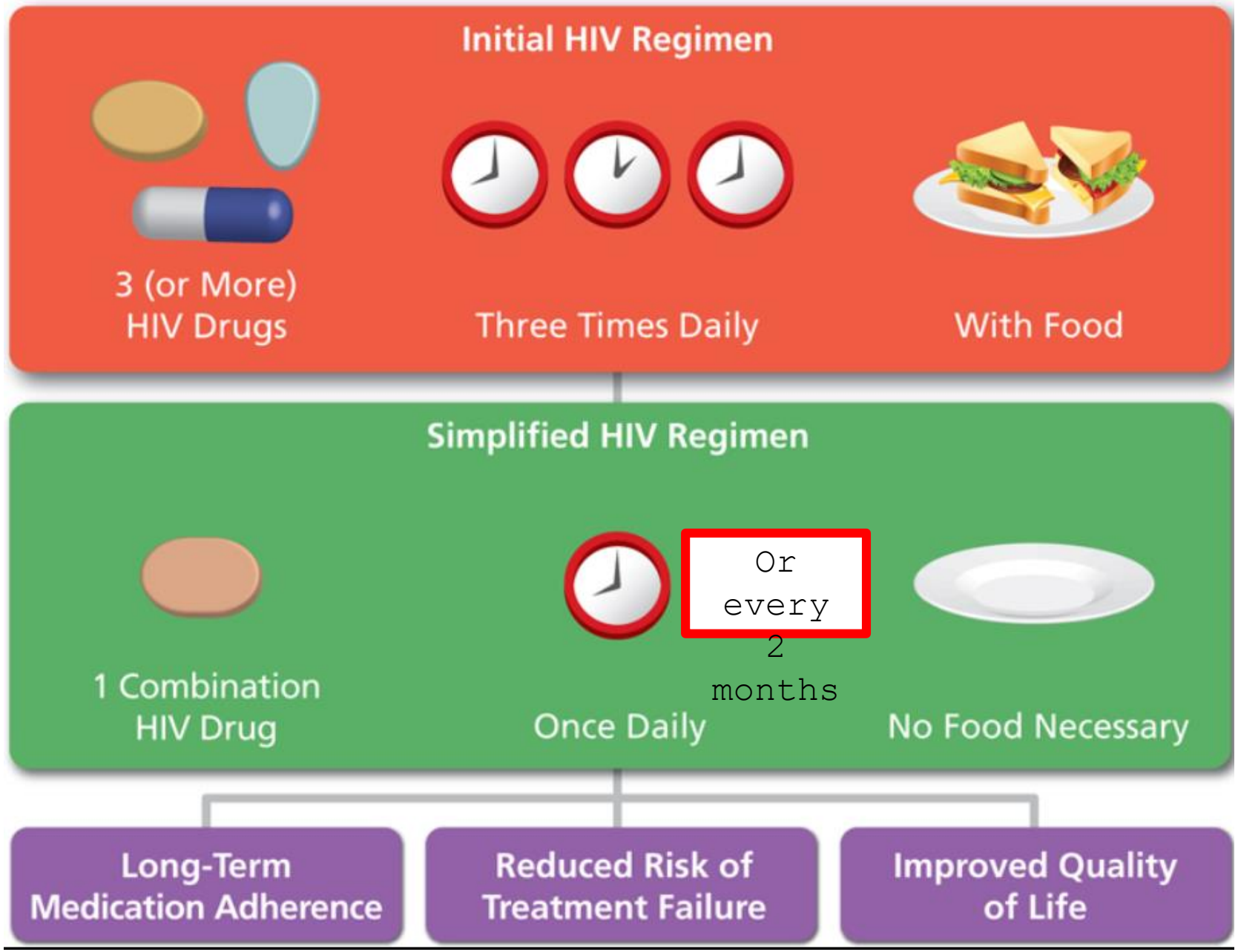
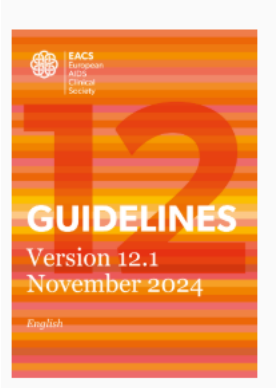
- Making changes to an HIV treatment regimen to make medication adherence easier.
- Simplifying an HIV regimen can include reducing the number of ARV drugs in the regimen or changing to a combination ARV drug that provides a one-pill, once-daily complete regimen.
- Other changes can include switching to ARV drugs that cause fewer adverse effects or to ARV drugs that can be taken without food.

Benefits of regimen simplification include **long-term medication adherence, reduced risk of treatment failure, and improved quality of life**.

Regimen Simplification



Switch Strategies for Virologically Suppressed Persons

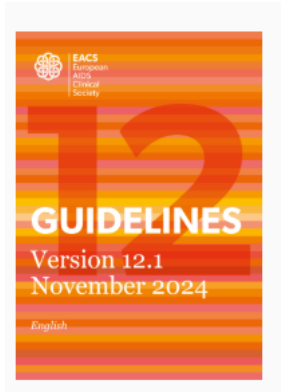


Definition of Virologically Suppressed

Clinical trials exploring switching strategies have generally defined suppression as an HIV-VL < 50 copies/mL for at least 6 months

Definition of Virologically Suppressed

A confirmed HIV RNA level below the LLOD of available assays.



Indications

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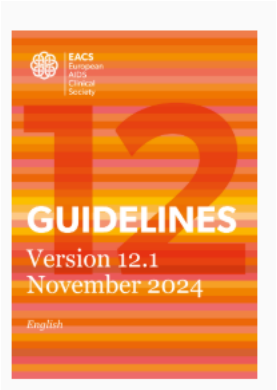
1. **Documented toxicity**
2. **Prevention of long-term toxicity** (This may include person's concerns about safety)
3. **Avoidance of drug-drug interactions**
4. **Ageing and/or co-morbidity**
5. **Simplification :** to reduce pill burden or to start an injectable regimen, adjust food restrictions, improve adherence and reduce monitoring needs
6. **Regimen fortification (**Increasing the barrier to resistance)
7. **Cost reduction**

1. **Adverse events**
2. **Drug–drug or drug–food interactions**
3. **Pill burden**
4. **Stigma**
5. **Inconvenience from taking oral medications**
6. **The desire to simplify a regimen**
7. **Cost**

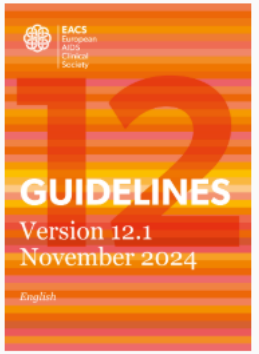


Principeles

- Sustain and not to jeopardize virological suppression
- The complete ARV history with HIV-VL, tolerability issue, cumulative genotypic resistance history and/or phases of viremia on previous regimens with the potential of resistance development should be evaluated prior to any drug switch
- Remaining treatment options in case of potential virological failure of the new regimen should be taken into consideration
- If someone receives and tolerates a regimen that is no longer a preferred option, and none of the other reasons for change applies, there is no need to change. Example: persons tolerating EFV-containing regimens

- To maintain viral suppression without jeopardizing future treatment options.
- Full ARV history, including virologic responses, past ARV-associated toxicities and intolerances, and cumulative resistance test

Dual therapies



In persons with suppression of HIV-VL < 50 copies/mL for the past 6 months these dual therapy strategies should only be given if there is
a) no historical resistance (recent data suggest possible use of DTG or DRV/b + XTC even when M184V is detected) and
b) HBV immunity with anti-HBs antibodies

Oral dual therapies supported by large randomized clinical trials or meta-analyses:

- DTG + RPV
- XTC + DTG
- XTC + DRV/b

Long-acting intramuscular dual therapy CAB + RPV

The following baseline factors, when combined, are associated with risk of virologic failure and resistance:

- Archived RPV-associated mutations
- HIV subtype A6/A1 (Recent data suggest possible use in people with subtype A1)
- BMI ≥ 30 kg/m^2

Dual therapies

- People with HIV who have no history of drug-resistance mutations or virologic failure can likely switch to any regimen that has been shown to be highly effective in people who are ARV-naïve (DTG+3TC) or to NRTI-sparing options extensively researched in switch studies, such as dolutegravir (DTG) plus rilpivirine (RPV) or long-acting cabotegravir plus rilpivirine (LA CAB/RPV).
- For regimen optimization in the setting of **existing nucleoside reverse transcriptase inhibitor (NRTI) resistance**, if an NRTI is to be included in the new regimen, two NRTIs (tenofovir alafenamide [TAF] or tenofovir disoproxil fumarate [TDF] plus emtricitabine [FTC] or lamivudine [3TC]) should be included, along with a fully active drug with a high resistance barrier, such as DTG, bictegravir (BIC), or boosted darunavir. Alternatively, as noted above, an NRTI-sparing regimen (such as DTG/RPV or LA CAB/RPV) is possible if there is no evidence of prior integrase strand transfer inhibitor (INSTI) or RPV resistance.

Open questions: When to simplify to 2DR?

1. Should we be reactive or proactive?
2. How should we address patient's preferences and desires?
3. Do you usually consider stigma when proposing a new regimen?
4. What should we do with older or "other" regimens when the patient is doing well?
5. How do you consider M184V and TAMs in light of a potential switch to 2DRs?

Thanks for your attention