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Infections émergentes
AFRAVIH
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# Comorbidités et VIH : cas clinique

*Dr Kayembe Kick (RD Congo)*
*Pr Karine Lacombe (France)*

Patiente NK
-Age : 45 ans
-Mariée, 3 enfants en bonne santé
-Tabac : 20PA
-Alcool : 0

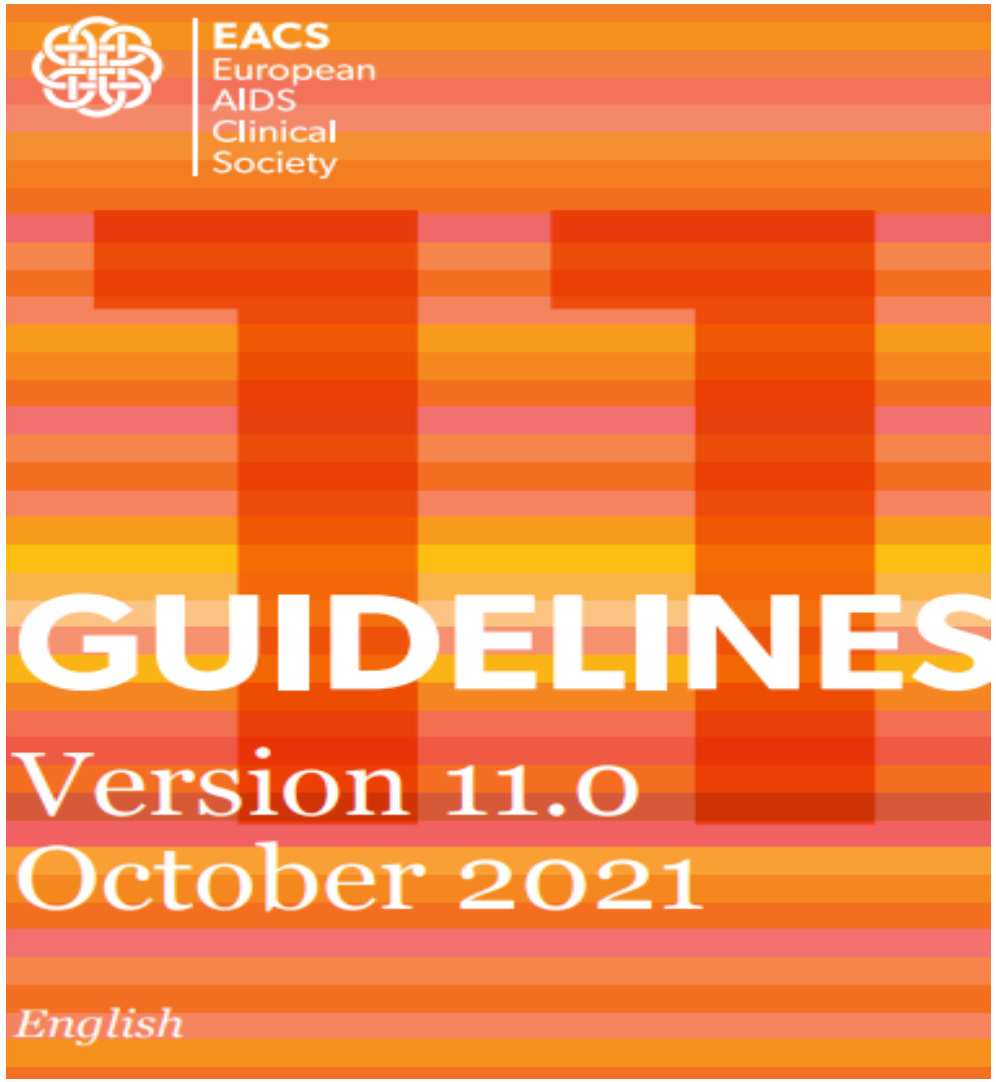
ATCDs : - Infection VIH depuis 2010
- Sous Truvada–Kaletra
- Découverte à l'occasion d'une toxoplasmose cérébrale
- Nadir CD4 : 40 /mm3, zénith CV VIH : 5200 copies/mL
-Dernier bilan immuno-virologique : CD4 607/mm3 , CV VIH < 20 copies/mL

Consultation du 6/7/2015 :

- Se plaint d'un syndrome polyuropolydepsique
- Biologie :

| Paramètres biologiques | Résultats |
|---|---|
| **Glycémie** | 9,1 mmol/L |
| **HbA1c** | 9% |
| **Créatini** | /L |
| **Choleste** | l/L |
| **Triglycér** | l/L |
| **HDLc** | ol/L |
| **LDLc** | 1,5mmol/L |

Diabète type II




# Type 2 Diabetes: Diagnosis

**Diagnostic criteria**(i)

| | Fasting plasma glucose mmol/L (mg/dL)(ii) | Oral glucose tolerance test (OGTT) 2-h value mmol/L (mg/dL)(iii) | HbA1c(iv) (mmol/mol) |
|---|---|---|---|
| **Diabetes** | ≥ 7.0 (126) OR→ | ≥ 11.1 (200) | ≥ 6.5% (≥ 48) |
| **Impaired glucose tolerance (IGT)** | < 7.0 (126) AND→ | 7.8 – 11.0 (140-199) | Prediabetes 5.7-6.4% (39-47) |
| **Impaired fasting glucose (IFG)** | 5.7– 6.9 AND (100-125) | < 7.8 (140) | |

Chez cette patiente, les facteurs favorisant le diabète sont :

A- Son traitement antirétroviral
B- L'infection VIH
C- La prédisposition génétique
D- Le nadir CD4
E- Le zénith de charge virale

# Insulino-résistance et VIH

# HIV, Antiretroviral Therapy and Metabolic Alterations: A Review

2020 Ergin et al. Cureus 12(5): e8059. DOI 10.7759/cureus.8059

Huseyin Ekin Ergin [1] , Evelyn E. Inga [2, 3] , Tun Zan Maung [2] , Mehwish Javed [2] , Safeera Khan [2]

1. Medicine, California Institute of Behavioral Neurosciences and Psychology, Fairfield, USA 2. Internal Medicine, California Institute of Behavioral Neurosciences and Psychology, Fairfield, USA 3. Internal Medicine, LaSante Health Center, Brooklyn, USA

| Author | Drug studied | Number of patients | Type of study | Result | Conclusion |
|---|---|---|---|---|---|
| Araujo et al. (2014) [23] | Predominance of PI in pretreated patients (14 vs 56%), while most first-line patients received non-nucleoside analogs (86 vs 41%). Specifically, DRV or ATV was primarily used in pretreated patients | 265 | Cross-sectional study | Insulin resistance was found to be less prevalent in patients on first-line treatment compared to pretreated patients. | Newer antiretrovirals were demonstrated to be safer than older drugs considering metabolic disorders. |
| Muhammad et al. (2017) [14] | ART | 300 | Cross-sectional study | MS was more prevalent in patients on HAART than HAART-naive patients. Duration of HAART exposure wasn't significantly associated with insulin resistance. | HAART, especially regimens with PIs was associated with the increased risk of MS. |

# HIV, Antiretroviral Therapy and Metabolic Alterations: A Review

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| | | | | | |
|---|---|---|---|---|---|
| Bune et al. (2019) [31] | NRTI + NNRTI + PI | 633 | Cross-sectional study | 31.3% of the ART-exposed patients had DM. DM was prevalent in %28 of the ART-naive patients. DM was the third most frequent component of the MS. | MS was more frequent in ART-exposed patients than ART-naive patients in this study. |

# HIV-associated lipodystrophy: from fat injury to premature aging

Martine Caron-Debarle[1,2], Claire Lagathu[1,2], Franck Boccara[1,2,3], Corinne Vigouroux[1,2,3] and Jacqueline Capeau[1,2,3]

| Class | Molecule | Abbreviation | Lipoatrophy | Lipohypertrophy | Dyslipidemia | Insulin resistance |
|---|---|---|---|---|---|---|
| NRTI | Stavudine | D4T | +++ | ++ | ++ | ++ |
| | Zidovudine | AZT, ZDV | ++ | + | + | ++ |
| | Didanosine | ddI | +/− | +/− | + | + |
| | Lamivudine | 3TC | 0 | 0 | + | 0 |
| | Abacavir | ABC | 0 | 0 | + | 0 |
| | Tenofovir | TDF | 0 | 0 | 0 | 0 |
| | Emtricitabine | FTC | 0 | 0 | 0 | 0 |
| NNRTI | Efavirenz | EFV | +/− | +/− | ++ increased HDL | + |
| | Nevirapine | NVP | 0 | 0 | + increased HDL | 0 |
| PI | Ritonavir | RTV | +/− | + | +++ | ++ |
| | Indinavir | IDV | +/− | + | + | +++ |
| | Nelfinavir | NFV | +/− | + | ++ | + |
| | Lopinavir | LPV | +/− | + | ++ | ++ |
| | Amprenavir Fosamprenavir | APV FPV | +/− | + | + | +/− |
| | Saquinavir | SQV | +/− | + | +/− | +/− |
| | Atazanavir | ATV | 0 | ++ | +/− | 0 |
| | Darunavir | DRV | 0 | + | +/− | +/− |
| Fusion inhibitor | Enfuvirtide | T20 | ? | ? | 0 | 0 |
| CCR5 inhibitor | Maraviroc | MVC | ? | ? | 0 | 0 |
| Integrase inhibitor | Raltegravir | RAL | ? | ? | 0 | 0 |

Caron-Debarle, Trends in Molecular Medicine. 2010

# Diabète type II



EACS European AIDS Clinical Society

GUIDELINES

Version 11.0
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*English*

## Type 2 Diabetes: Management

First-line therapy is metformin[i] and comprehensive lifestyle modification

Indicators of high-risk or established ASCVD[ii], CKD or HF

NO

Consider independently of baseline HbA1c or HbA1c target[iii]

HbA1c above individualised target

ASCVD[ii] predominates

HF or CKD[iv], predominates

DPP-4i | GLP-1RA[vii] | SGLT2i[viii] | TZD

**Preferably**
GLP-1 RA with proven CVD benefit[v],

**OR**

SGLT2i with proven CVD benefit if eGFR adequate

**Preferably**
SGLT2i with evidence of reducing HF and/or CKD progression if eGFR adequate[vi],

**OR**

If SGLT2i not tolerated or contraindicated of if eGFR less than adequate add / switch to GLP-1 RA with proven CVD benefit

HbA1c above target

SGLT2i **OR** TZD | SGLT2i **OR** TZD | GLP-1RA **OR** DPP-4i **OR** TZD | SGLT2i **OR** DPP-4i **OR** GLP-1RA

HbA1c above target

HbA1c above target

HbA1c above target

If further intensification is required:
- For those on a GLP-1RA consider adding SGLT2i with proven CVD benefit[vi]
- DPP-4i if not on GLP-1RA
- Basal insulin
- TZD
- SU

Avoid TZD in the setting of HF
- For those on a SGLT2i consider adding GLP-1RA with proven CVD benefit[vi]
- DPP-4i (not saxigliptin) in the setting of HF (if not on GLP-1RA)
- Basal insulin
- SU

Continue with addition of other agents as outlined above / see EASD/ADA Guidelines for more details / refer to a specialist

Lors de son contrôle habituel le 7/4/2019 :

Examen : Poids : 89 Kg Taille 1m65. ➔ BMI : 32,72 kg/m²

Tour de taille 110 cm

TA : 13/7 cmHg

Biologie :

| Paramètres biologiques | Résultats |
|---|---|
| Glycémie | 5,5 mmol/L |
| HbA1c | 6% |
| ASAT/ ALAT | 35UI/ 24UI/L |
| GGT | 30 UI/L |
| PAL | 70UI/L |
| Créatinine | 85 µmol/L |
| Cholesterol | 6,4 mmol/L |
| Triglycérides | 2,6 mmol/L |
| HDLc | 0,5 mmol/L |
| LDLc | 4,3 mmol/L |

Lors de son contrôle habituel le 7/4/2019 :

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| Glycémie | 5,5 mmol/L |
| HbA1c | 6% |
| ASAT/ ALAT | 35UI/ 24UI/L |
| GGT | 30 UI/L |
| PAL | 70UI/L |
| Créatinine | 85 mol/L |
| **Cholesterol** | **6,4 mmol/L** |
| **Triglycérides** | **2,6 mmol/L** |
| **HDLc** | **0,5 mmol/L** |
| **LDLc** | **4,3 mmol/L** |

Cette dyslipidémie est favorisée par :

A- Le vieillissement physiologique
B- L’ âge
C- Son traitement antirétroviral
D- La durée d’évolution du VIH
E- Le nadir CD4

# Changes in lipidomic profile by anti-retroviral treatment regimen

## An ACTG 5257 ancillary study

Chaudhary et al. Medicine (2021) 100:30

Ninad S. Chaudhary, MBBS[a], Tobias Kind, PhD[b], Amanda L. Willig, PhD[c], Michael S. Saag, MD[c], Sadeep Shrestha, PhD[a], Nicholas Funderburg, PhD[d], Howard W. Wiener, PhD[a], E. Turner Overton, MD[c], Marguerite R. Irvin, PhD[a,*]

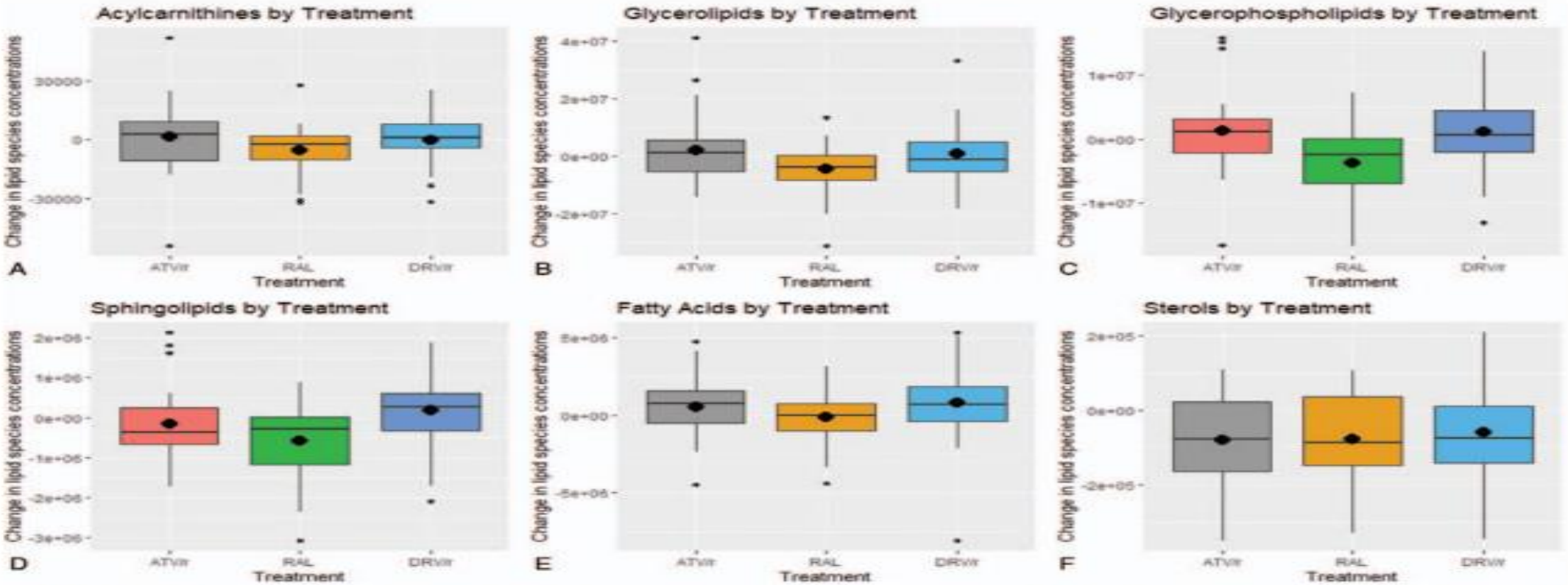


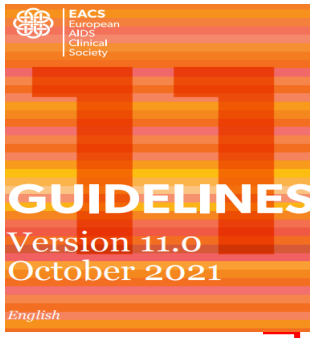

**Figure 1.** Distribution of lipid class concentrations by treatment group. Footnote: Y axis indicates change in the concentration of lipidomic classes before and after treatment; X axis denotes treatment group; * denotes outliers; Glycerophospholipids class (Plot C) and Sphingolipids class (Plot D) represents change in lipid class concentrations that are statistically different by treatment group; ATV/r = ritonavir-boosted atazanavir, DRV/r = ritonavir-boosted darunavir, RAL = raltegravir; Group (number of lipid species within class): AcylCarnithines (7), Glycerolipids (82), Glycerophospholipids (208), Sphingolipids (92), fatty acids (19), sterols (9). The statistical *P* value from a one-way anova test each lipid class are: Acylcarnithines (*P* = .28), Glycerolipids (*P* = .06), Glycerophospholipids (*P* = .007), Sphingolipids (*P* = .028), Fatty acids (*P* = .35), Sterols (*P* = .82).

Associés aux règles hygiéno-diététiques , vous indiquez

A- Le remplacement du traitement antirétroviral
B- L'arrêt du traitement antirétroviral ( patiente indétectable depuis 8 ans )
C- La prescription d'une statine
D- Un contrôle biologique dans 3 mois
E- Un bilan thyroïdien

# Prevention of Cardiovascular Disease (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.




Assess CVD risk in next 10 years[i]

Advise on diet and lifestyle in all persons

Consider ART modification if 10-year CVD risk ≥ 10%[ii]

Smoking (see page 61)

Identify key modifiable risk factors[iii]

## Blood pressure

Drug treatment if: SBP ≥ 140 or DBP ≥ 90 mmHg (especially if 10-year CVD risk ≥ 10%)

**Target**[iv]

SBP < 130 mmHg

DBP < 80 mmHg

Treatment (see pages 63-65)

## Coagulation

Drug treatment if: established CVD or DM with very high/high CVD risk[v]

**Target - N/A**

Consider treating with acetylsalicylic acid 75–150 mg[vi]

## Glucose

Confirm DM and treat with diet and drugs

**Target**
HbA1C 6.5-7.0%

Treatment (see page 68)

## Lipids

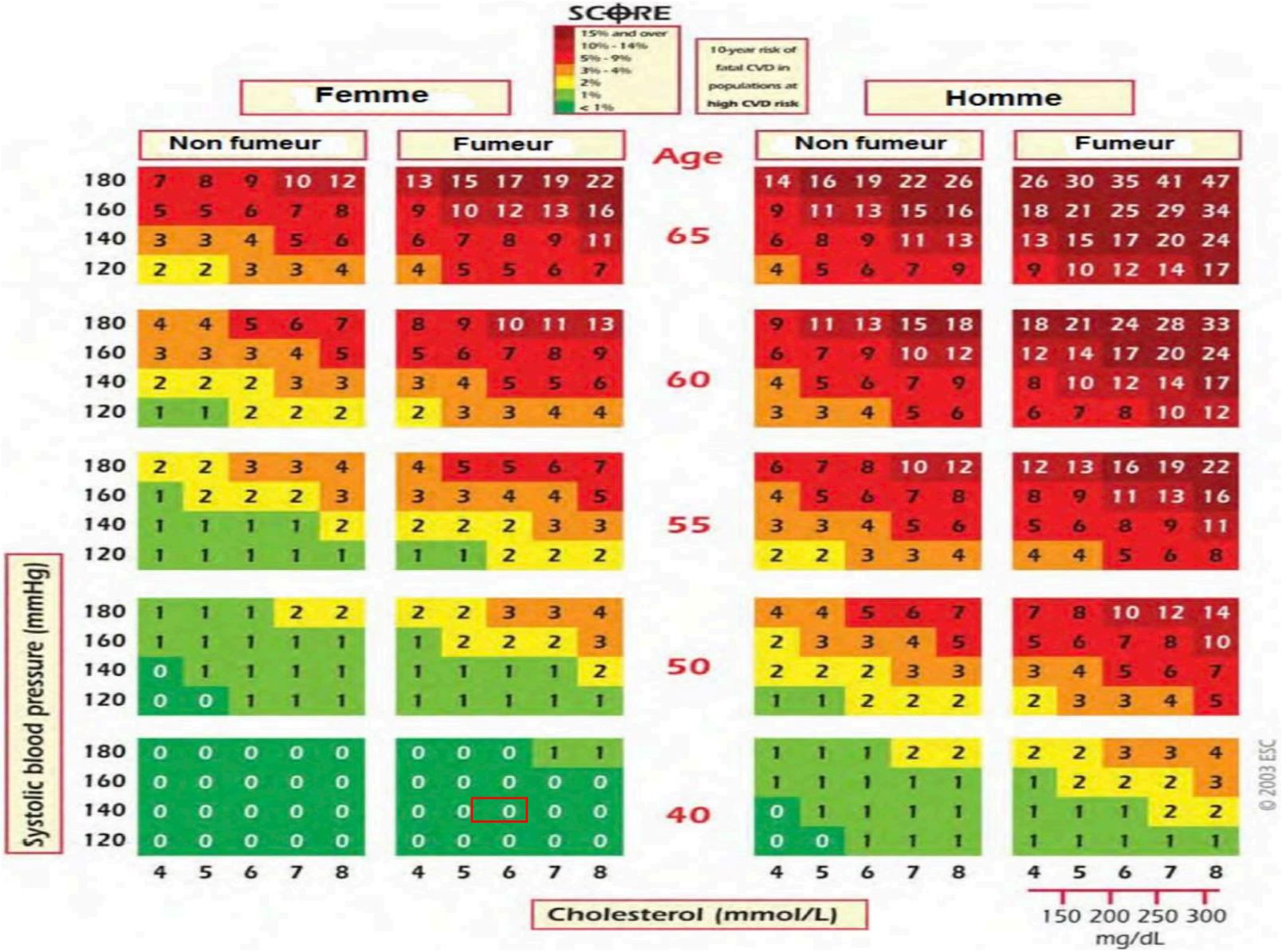
Drug treatment if: established CVD or DM or 10-year CVD risk ≥ 10%

**Target**[vii] *

| | 2ry prevention or very high risk[viii] | High risk [ix] |
|---|---|---|
| LDL-c** | < 1.4 (55) | < 1.8 (70) |
| non-HDL-c | < 2.2 (85) | < 2.6 (100) |

Treatment (see page 69)

* Fasting or non-fasting samples may be used
** and ≥ 50% reduction from baseline




# Risque cardio- vasculaire : Evaluation du risque d'évènement cardiovasculaire fatal à 10 ans

**Mais ne tient pas compte de:**
**- Facteurs liés au VIH.**
**- Insulinorésistance (syndrome métabolique).**

**Drugs used to lower LDL-c**

| Drug class | Drug | Dose | Adverse effects | Advice on use of lipid lowering therapy together with ART | |
|---|---|---|---|---|---|
| | | | | use with PI/r | use with NNRTIs |
| Statin[i,viii] | Atorvastatin[ii] | 10-80 mg qd | Gastrointestinal symptoms, headache, insomnia, | Start with low dose[v] (max daily dose: 10 mg (ATV/r); 20 mg (LPV/r); 40 mg (DRV/r) | Consider higher dose[vi] |
| | Fluvastatin[iii] | | | higher dose[vi] | Consider higher dose[vi] |
| | Pravastat | | | | Consider higher dose[vi] |
| | Ro | | | | Start with low dose[v] |
| | Simva | | | | |
| | Pitavastatin | | | xpected | |
| Intestinal cholesterol absorption inhibitor[i,ix] | Ezetimibe[iv] | | | teraction expected | |
| PCSK9-inhibitors[x] | Evolocumab | 140 mg 2 weekly or 420 mg monthly | Nil | No interaction expected | |
| | Alirocumab | 75 mg or 150 mg 2 weekly | | | |

Interaction médicamenteuse
+++++

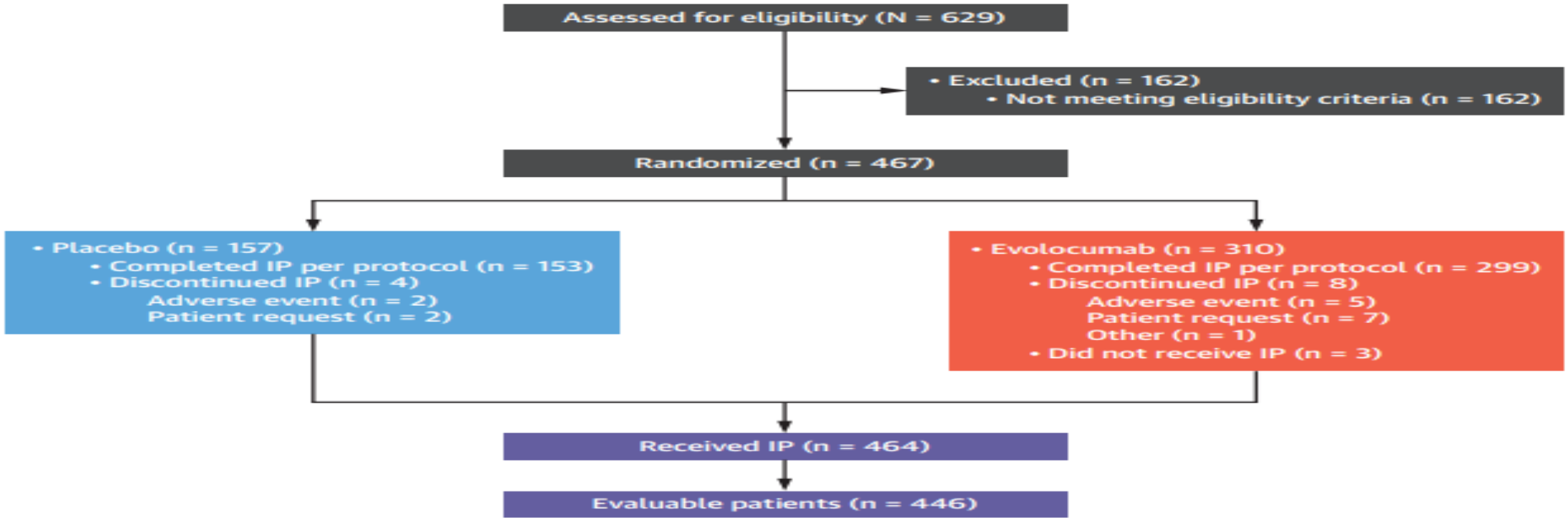
# Dyslipidémies : Nouvelles recommandations

## Evolocumab in HIV-Infected Patients With Dyslipidemia

### Primary Results of the Randomized, Double-Blind BEIJERINCK Study

Franck Boccara, MD, PhD,[a] Princy N. Kumar, MD,[b] Bruno Caramelli, MD, PhD,[c] Alexandra Calmy, MD, FMH, PhD,[d] J. Antonio G. López, MD,[e] Sarah Bray, PhD,[e] Marcoli Cyrille, MD,[e] Robert S. Rosenson, MD,[f] for the BEIJERINCK Investigators

**FIGURE 1** BEIJERINCK Study Profile




Consort flow chart of patient disposition in the BEIJERINCK study. Patients were screened for eligibility (n — 629) and randomized (n — 467) into the placebo (n — 157; **blue box**) or evolocumab (n — 310; **red box**) groups of the study. A total of 446 patients who received IP were evaluable for the primary endpoint. IP — investigational product.

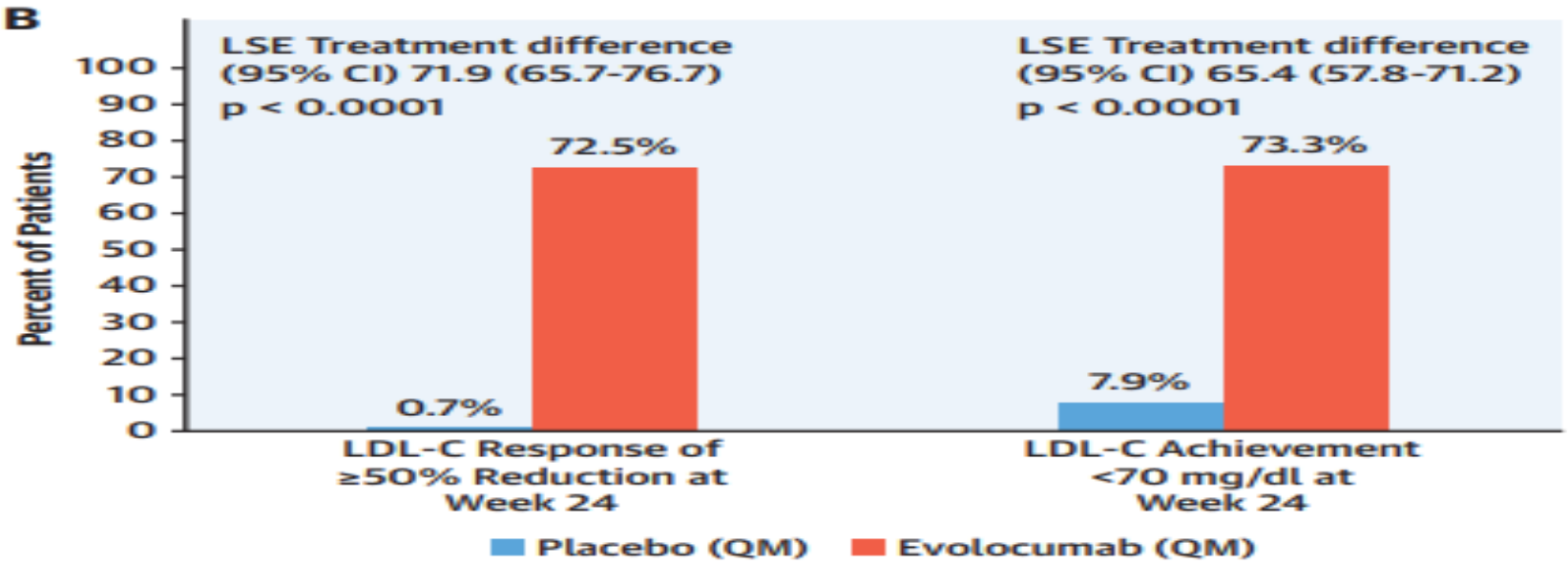
# Prise en charge des dyslipidémies : Nouvelles recommandations

## Evolocumab in HIV-Infected Patients With Dyslipidemia

### Primary Results of the Randomized, Double-Blind BEIJERINCK Study

Franck Boccara, MD, PhD,[a] Princy N. Kumar, MD,[b] Bruno Caramelli, MD, PhD,[c] Alexandra Calmy, MD, FMH, PhD,[d] J. Antonio G. López, MD,[e] Sarah Bray, PhD,[e] Marcoli Cyrille, MD,[e] Robert S. Rosenson, MD,[f] for the BEIJERINCK Investigators

FIGURE 2 Continued

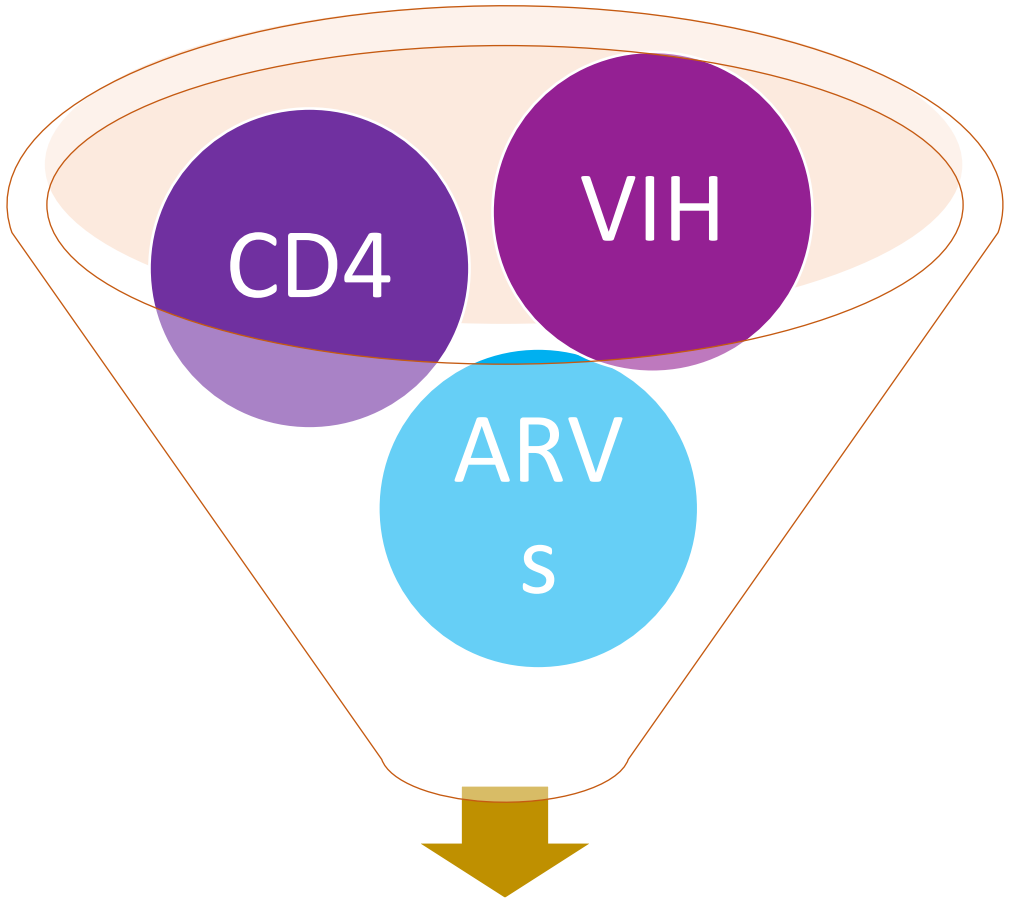



The effect of evolocumab, compared with placebo, on LDL-C, triglycerides, and atherogenic lipoproteins was tested. **(A)** Evolocumab significantly reduced LDL-C, non–HDL-C, ApoB, total cholesterol, VLDL-C, triglycerides, and Lp(a), and increased HDL-C. **(B)** Evolocumab treatment resulted in significantly more patients achieving the secondary efficacy endpoints of LDL-C reduction of ≥50% and LDL-C <70 mg/dl compared with placebo. apoB = apolipoprotein B; CI = confidence interval; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; Lp(a) = lipoprotein(a); LSE = least squares estimate; QM = monthly; VLDL-C = very low–density lipoprotein cholesterol.

Vous décidez de changer le traitement antirétroviral, quelle combinaison choisissez vous?

A- Abacavir/ lamivudine/Dolutégravir (Triumeq)
B- Zidovudine/ lamivudine/ atazanavir/ritonavir ( combivir+ reyataz/norvir)
C-Abacavir/lamivudine/ atazanavir/ritonavir ( Kivexa+ reyataz/norvir)
D- Tenofovir/ emtricitabine/ rilpivirine ( truvada+ edurant)
E- Dolutégravir/ darunavir/ritonavir ( tivicay+prezista+norvir)

# Conclusion




## Comorbidités


Merci de votre attention