3e édition

AFRAMED

VIH / HÉPATITES

CASABLANCA

du 27 au 29 | sept 2019

Comorbidités et VIH : cas clinique

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Vendredi 27 Septembre 2019

CASABLANCA
du 27au 29 sept. 2019

Cas clinique

Patiente SM
-Age : 44 ans
-Mariée, 3 enfants en bonne santé
-Tabac : 20PA
-Alcool : 0

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

Cas clinique

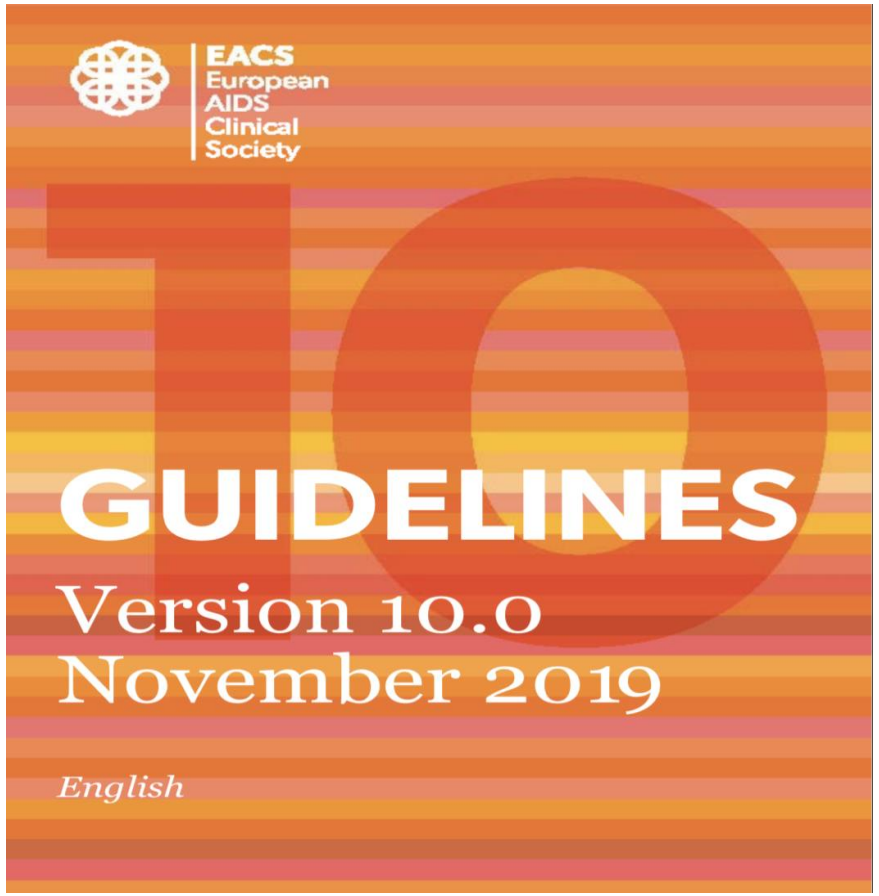
Consultation du 6/7/2015 :

- Se plaint d'un syndrome polyuropolydepsique
- Biologie :

Paramètres biologiques	Résultats
Glycémie	9,1 mmol/L
HbA1c	9%
Créatin	l/L
Cholest	ol/L
Triglyc	ol/L
HDLc	nol/L
LDLc	1,5mmol/L

Diabète type II

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)	

Question 1

Chez cette patiente, les facteurs favorisants le diabète sont :

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

Insulino-résistance et VIH

Prevalence of insulin resistance and risk of diabetes mellitus in HIV-infected patients receiving current antiretroviral drugs

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Table 3 Factors associated with insulin resistance (HOMA ≥3.8).

	Univariate analysis			Multivariate analysis		
Variable	RR	95% CI	*P* value	RR	95% CI	*P* value
Age (year)	1.03	0.99–1.06	0.08	1.05	0.88–1.16	0.25
Gender, male	0.66	0.34–1.27	0.21			
Mean BMI (kg/m^2)	**1.17**	**1.06–1.28**	**<0.01**	1.03	0.76–1.5	0.87
CD4+ count nadir	1.05	0.57–1.93	0.19	1.6	0.44–5.05	0.8
Time of HIV infection (months)	**1.005**	**1.001–1.009**	**0.01**	1.001	0.98–1.014	0.9
Cumulative time on HAART (months)	**1.007**	**1.002–1.012**	**0.01**	1.002	0.99–1.02	0.75
Time on current HAART (months)	1.006	0.99–1.019	0.15	1.15	0.98–1.04	0.3
Current use of PI	**2.32**	**1.24–4.44**	**<0.01**	1.49	0.39–5.88	0.56
HCV coinfection	**3.03**	**1.64–5.88**	**<0.01**	2.19	0.57–8.34	0.24
Vitamin D deficiency	1.01	0.54–1.83	0.9			
Waist (cm)	**1.08**	**1.04–1.12**	**<0.01**	1.04	0.92–1.17	0.49
Waist/hip ratio	**12.8**	**1.5–19.1**	**<0.01**	**10**	**1.66–16**	**<0.01**
Trunk fat (kg)	**1.07**	**1.004–1.14**	**0.037**	1.01	0.83–1.19	0.9
Trunk fat (%)	**1.08**	**1.04–1.13**	**<0.01**	**1.08**	**1.01–1.17**	**0.04**
Total fat (%)	**1.07**	**1.02–1.13**	**<0.01**	1.05	0.88–1.13	0.2
FMR	**3.18**	**1.7–6.06**	**<0.01**	2.32	0.56–9.1	0.2

HAART, highly active antiretroviral therapy; PI, protease inhibitors; HCV, hepatitis C virus; FMR, fat mass ratio (defined in the text). Values with a *P* value of <0.2 were included into the multivariate analysis.

Araujo S. 2014 european journal of endocrinologie

Insulino-résistance et VIH

Table 2. Glycaemia, insulin resistance markers, body fat distribution and adipokine levels according to the baseline CD4⁺ T-cell counts in the HIV-infected patients included in the metabolic substudy of the ANRS COPANA cohort

	CD4⁺ T-cell counts at baseline per mm³				
Markers	≤200 (*n*=42)	201–350 (*n*=43)	351–500 (*n*=60)	>500 (*n*=69)	*P*-value
T0 glucose, mmol/l	4.6 (4.2–4.9)	4.9 (4.4–5.2)	4.9 (4.4–5.3)	4.7 (4.3–5.2)	0.70
T120 glucose, mmol/l	5.3 (4.2–6.8)	5.0 (4.6–5.7)	5.1 (4.2–5.3)	4.9 (4.2–5.6)	0.17
T0 insulin, mU/l	6.6 (4.8–11.0)	5.8 (4.1–8.0)	4.8 (3.7–8.5)	4.8 (3.4–7.0)	0.02
T120 insulin, mU/l	33.3 (18.7–53.6)	17.5 (7.8–25.2)	16.6 (6.7–37.6)	13.8 (9.0–24.0)	<0.001
HOMA-IR (*n*=202)	1.4 (1.1–2.6)	1.3 (0.8–1.7)	1.1 (0.8–1.7)	1.0 (0.7–1.6)	0.004
SAT (*n*=139), cm²	111.0 (44.2–160.8)	136.1 (98.7–213.3)	158.8 (74.4–200.5)	128.9 (84.6–190.9)	0.29
VAT (*n*=139), cm²	63.2 (38.0–87.5)	70.5 (48.5–103.3)	84.2 (46.2–130.3)	60.5 (43.4–99.0)	0.31
SAT/VAT (*n*=139)	1.57 (1.06–2.17)	1.68 (1.26–3.35)	1.52 (1.16–2.18)	1.92 (1.33–3.86)	0.28
Total body fat (*n*=102), %	16.0 (9.5–33.7)	24.9 (15.3–37.1)	20.9 (14.4–28.5)	22.3 (10.0–38.4)	0.61
Trunk fat (*n*=102), %	18.1 (8.8–35.7)	24.1 (12.2–36.3)	22.4 (11.6–30.9)	24.7 (12.2–38.9)	0.59
Limb fat (*n*=102), %	13.1 (8.3–31.9)	19.0 (12.6–38.8)	18.9 (13.2–25.1)	19.3 (7.9–39.9)	0.60
HOMA-B (*n*=200)	115.2 (76.0–173.1)	95.1 (45.4–133.3)	84.4 (52.9–117.5)	94.3 (59.2–125.0)	0.02
Leptin, µg/l	2.7 (1.2–10.9)	4.6 (1.5–14.1)	5.3 (2.2–9.4)	3.1 (0.7–12.2)	0.15
Adiponectin, mg/l	14.5 (11.3–16.8)	15.4 (9.0–17.9)	12.7 (9.2–16.4)	14.9 (9.0–17.9)	0.58

Data are medians and 25th to 75th percentiles (IQR) unless otherwise indicated. *P*-values are adjusted for sex. Subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT), were assessed by L4 CT scans in 139 patients. Percentage of total, trunk and limb fat were assessed by DEXA in 102 patients. HOMA-B, homeostasis model assessment of pancreatic β-cell function; HOMA-IR, homeostasis model assessment of insulin resistance.

Boufassa F et al Antiviral Ther 2011

Insulino-résistance et Antirétroviraux

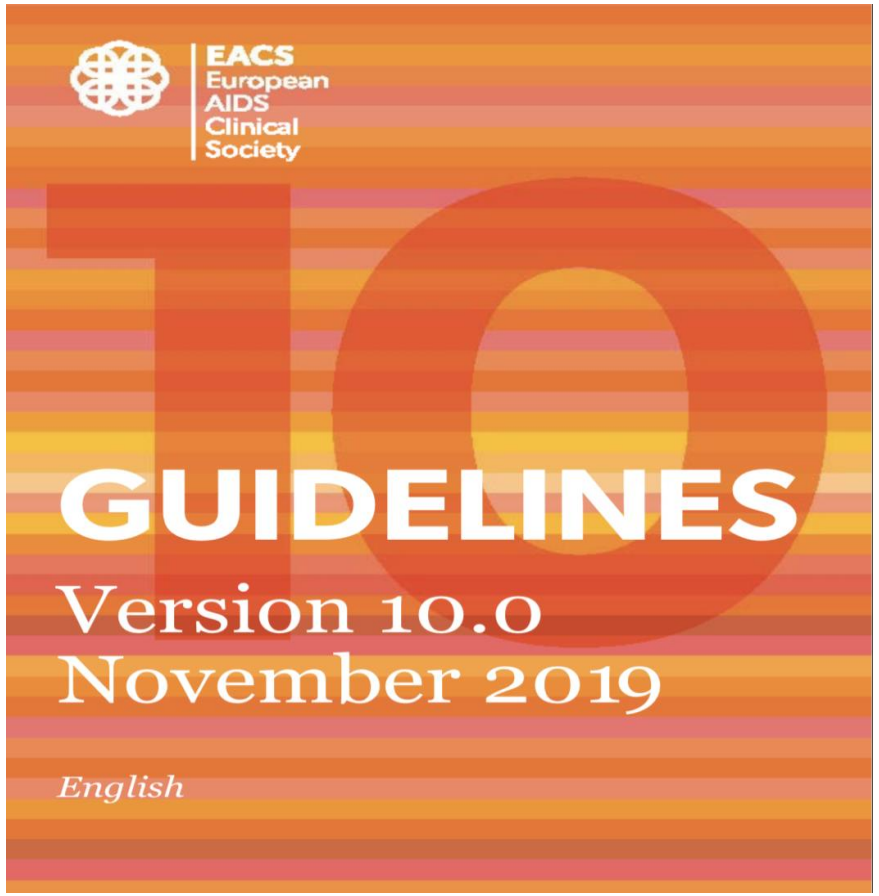
HIV-associated lipodystrophy: from fat injury to premature aging

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



Type 2 Diabetes[i]: Management

If modification of lifestyle measures is insufficient

↓

Metformin[ii] start dose (500-850 mg qd), increase to maximum tolerated dose of 2(-3) g/day over 4-6 weeks[iii]

↓

HbA1c > 6.5-7% (> 48-53 mmol/mol)

↓

Metformin[ii] + sulfonylureas or thiazolidinedione or DPP-4 inhibitor or SGLT-2 inhibitor or GLP-1 agonist or insulin

↓

HbA1c > 6.5-7% (> 48-53 mmol/mol)

↓

Refer to specialist for triple therapy – use insulin

Cas clinique

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 mol/L
Cholesterol	6,4 mmol/L
Triglycérides	2,6 mmol/L
HDLc	0,5 mmol/L
LDLc	4,3 mmol/L

Cas clinique

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

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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 mol/L
Cholesterol	**6,4 mmol/L**
Triglycérides	**2,6 mmol/L**
HDLc	**0,5 mmol/L**
LDLc	**4,3 mmol/L**

Question 2

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

Dyslipidémie et VIH

Research Article

Changes in Lipid Indices in HIV+ Cases on HAART

Shujing Ji,[1,2] Yufan Xu,[1,2] Dating Han,[1,2] Xiuming Peng,[1,2] Xiangyun Lu,[1,2] Norbert H. Brockmeyer,[3,4] and Nanping Wu[1,2]

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[3] *Department of Dermatology and Allergology, St. Josef-Hospital, Ruhr-University Bochum, 44791 Bochum, Germany*
[4] *St. Elisabeth-Hospital Ruhr-Universität Bochum Große Beckstr, 12,44787 Bochum, Germany*

Table 3: Model-based estimated factors correlated with TC levels.

	estimate	Standard error	P value
Sex (male vs. female)	4.44	14.17	0.755
IFG vs. euglycemia	27.84	11.09	0.014
DM vs. euglycemia	45.41	11.80	0.000
age	0.45	0.49	0.355
nevirapine	24.79	11.07	0.028
lgVL	39.10	22.12	0.077
CD4	0.004	0.001	0.000

TC: total cholesterol; IFG: impaired fasting glucose; DM: diabetes mellitus; VL: viral load.

Shujing et al, BioMed Research International, 2019.

Dyslipidémie et Antirétroviraux

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]

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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

Question 3

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

Prise en charge des dyslipidémies : Nouvelles recommandations

Prevention of 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 53) → 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(v)

SBP < 130 mmHg

DBP < 80 mmHg

↓

Treatment (see page 56-57)

Coagulation

↓

Drug treatment if: established CVD only

↓

Target - N/A

↓

Consider treating with acetylsalicylic acid 75-150 mg(vii)

Glucose

↓

Confirm DM and treat with diet and drugs

↓

Target
HbA1C 6.5-7.0%

↓

Treatment (see page xx)

Lipids

↓

Drug treatment(iv) if: established CVD or type 2 diabetes or 10-year CVD risk ≥ 10%

↓

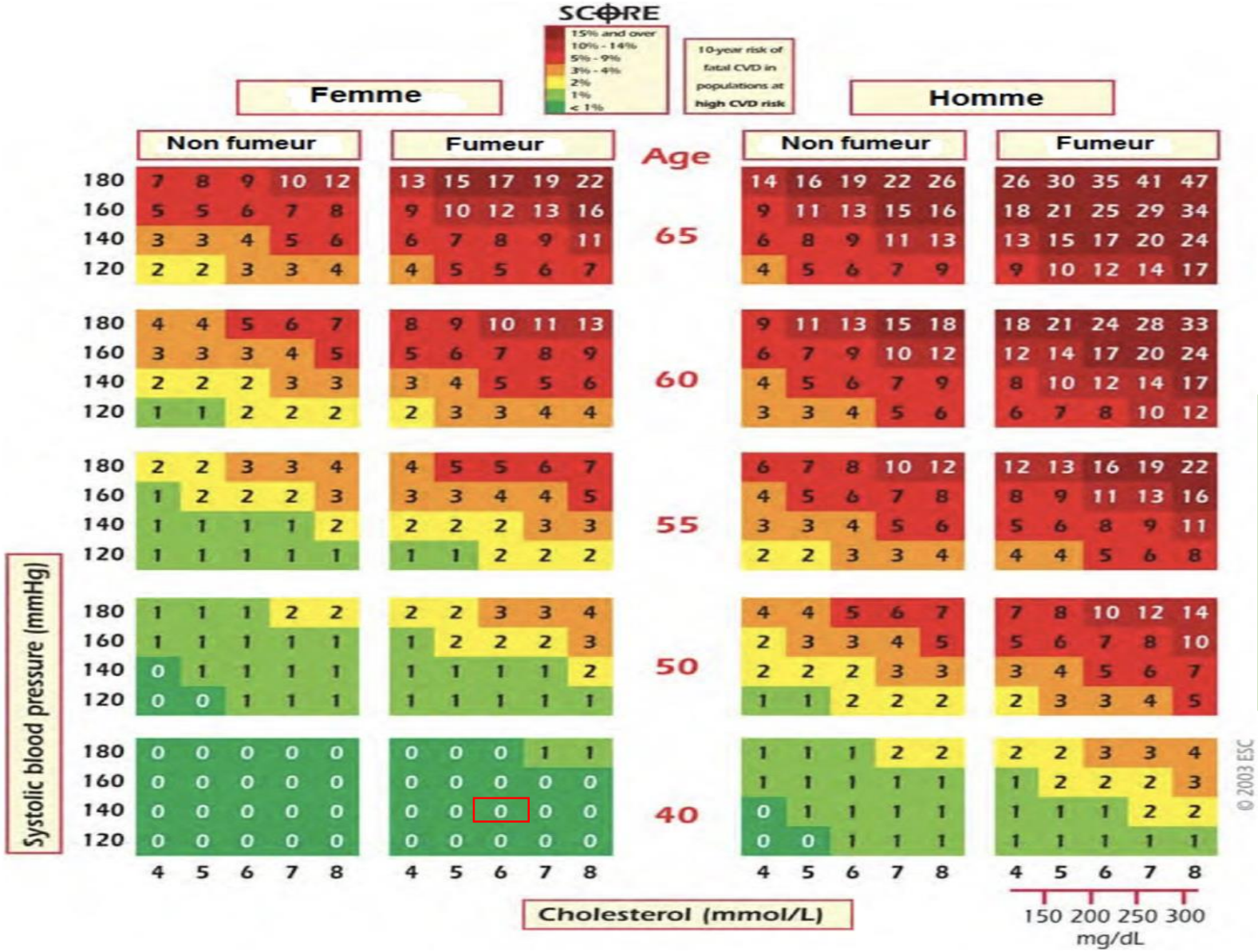
Target*

	2ry prevention or very high risk	1ry Prevention
LDL**	< 1.4 (55)	< 2.0 (80)
Non LDL	< 2.2 (85)	< 3.0 (115)

↓

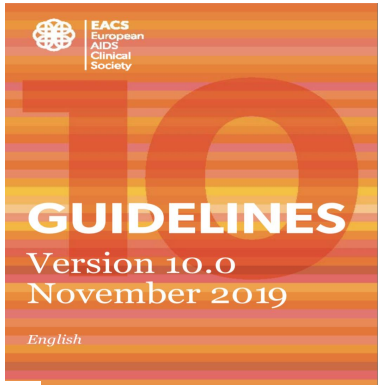
Treatment (see page 60)

Risque cardioo- vasculaire : Évaluation du risque d'événement cardiovasculaire fatal à 10 ans



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

Prise en charge des dyslipidémies : Nouvelles recommandations



Drugs used to lower LDL-c

Drug class	Drug			Statin together with ART
				Use with NNRTIs
Statin[i,ix]	atorva			sider higher dose[vi]
	fluva			der higher dose[vi]
	prava			sider higher dose[vi]
	rosuvastatin			Start with low dose[v]
	simvastatin[ii]	10-40		traindicated
Intestinal cholesterol absorption inhibitor↓[i,viii]	ezetimibe[iv]	10 mg qd	Gastrointestinal symptoms	No known drug-drug interactions with ART
PCSK9-inhibitor[x]	evolocumab	140 mg 2 weekly or 420 mg monthly	Nil	No drug-drug interactions anticipated

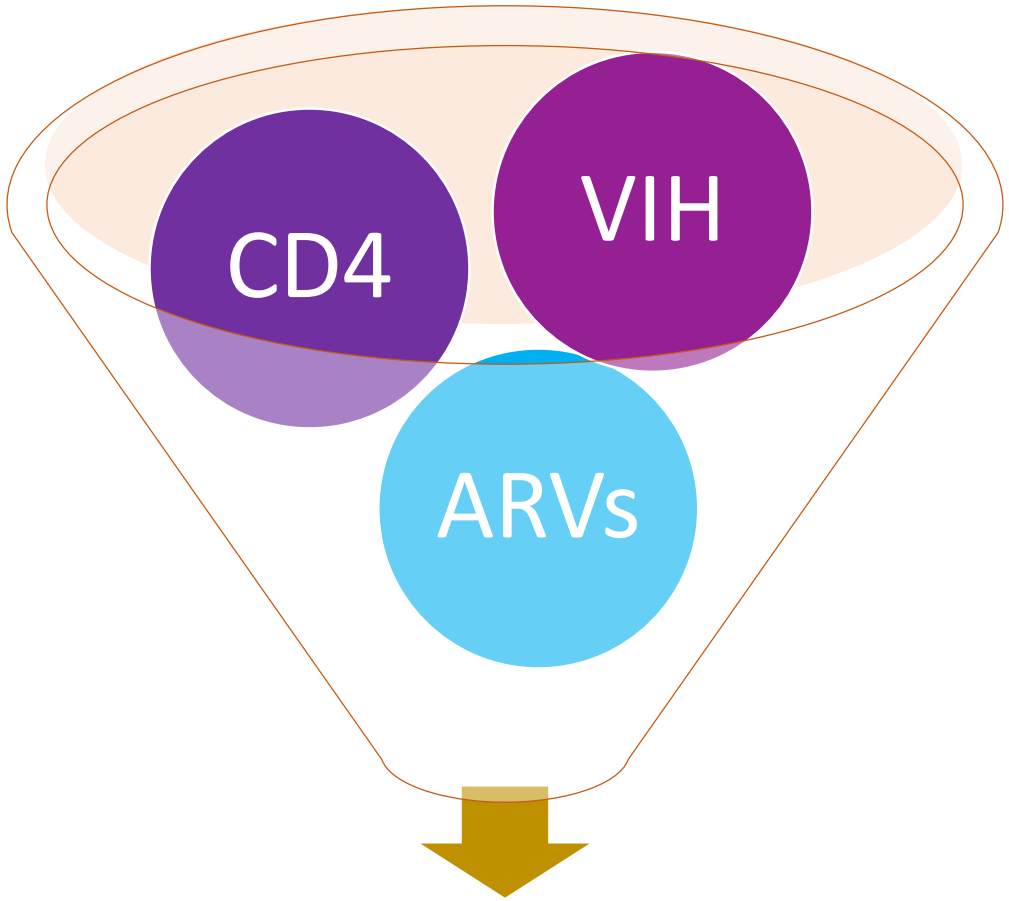
Interaction médicamenteuse
+++++

Question 4

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

A- Tenofovir/ emtricitabine/efavirenz (Atripla)
B- Zidovudine/ lamivudine/ atazanavir/ritonavir (combivir+ reyataz/norvir)
C-Abacavir/lamivudine/ atazanavir/ritonavir (Kivexa+ reyataz/norvir)
D- Tenofovir/ emtricitabine/ raltégravir (truvada+ isentress)
E- Dolutégravir/ darunavir/ritonavir (tivicay+prezista+norvir)

Conclusion



Comorbidités


Merci de
votre
attention