Suivi somatique en addictologie

Prof. C. Chuard

Infectiologie

HFR Fribourg – Hôpital cantonal

«Traitements basés sur la substitution»

Grangeneuve, novembre 2015

Hépatite C

Propagation: environ 1,5 pour cent de la population en Suisse est infecté par une hépatite virale.

Hépatite C: 50'000 à 80'000 personnes
Hépatite B: 20'000 à 30'000 personnes

Based on studies in the years 1994 to 1996, the anti-HCV prevalence rates in IDUs in Switzerland ranged from 56.4% to 82.2% [15, 25].

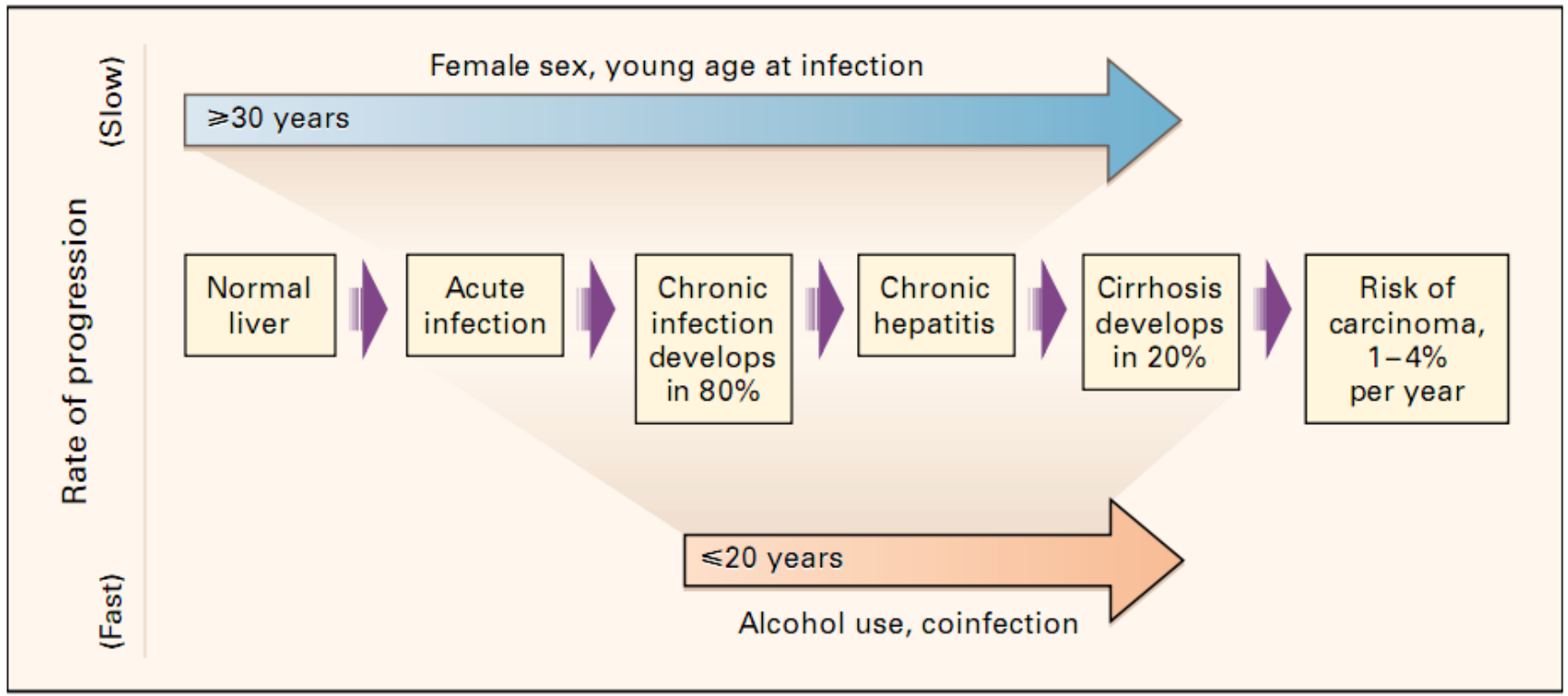
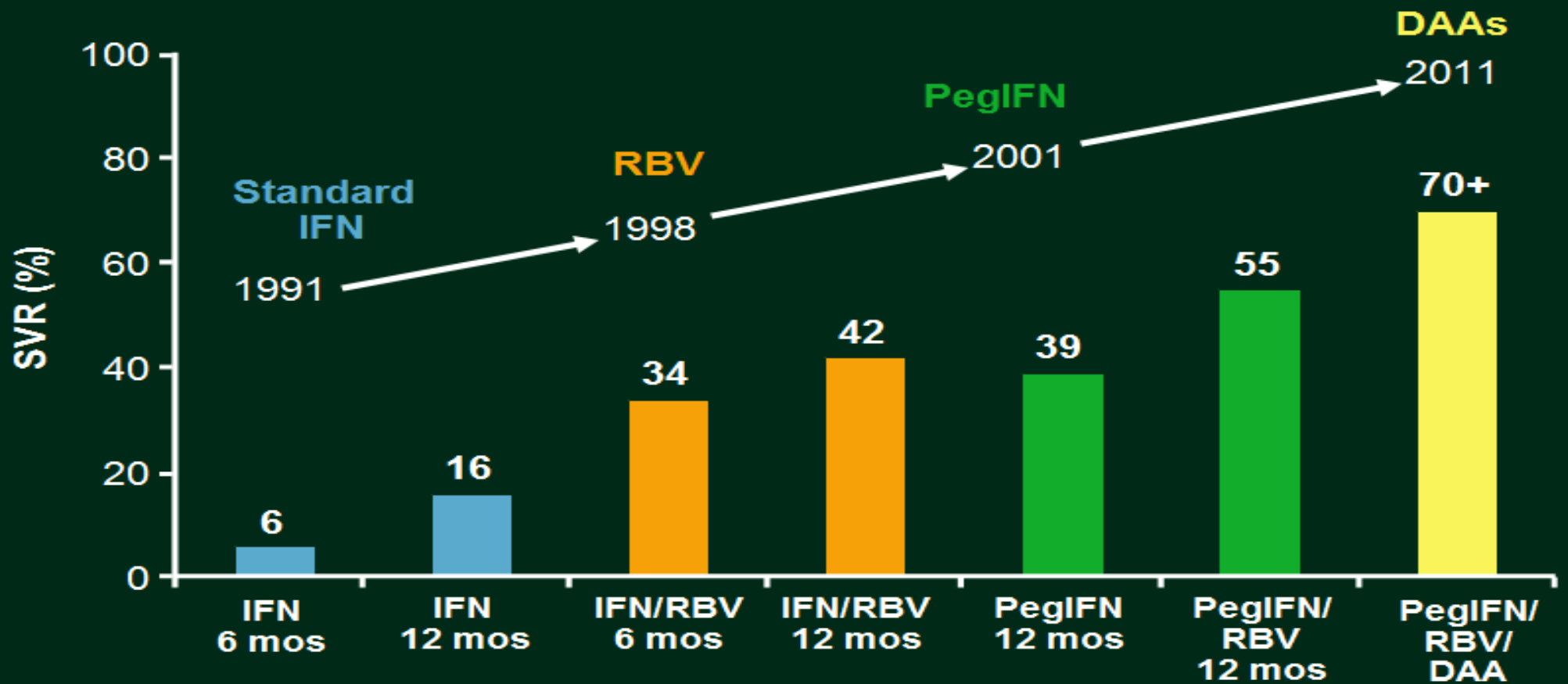


Figure 2. The Natural History of HCV Infection and Its Variability from Person to Person.

When and in Whom to Initiate HCV Therapy Table 3. Factors Associated with Accelerated Fibrosis Progression

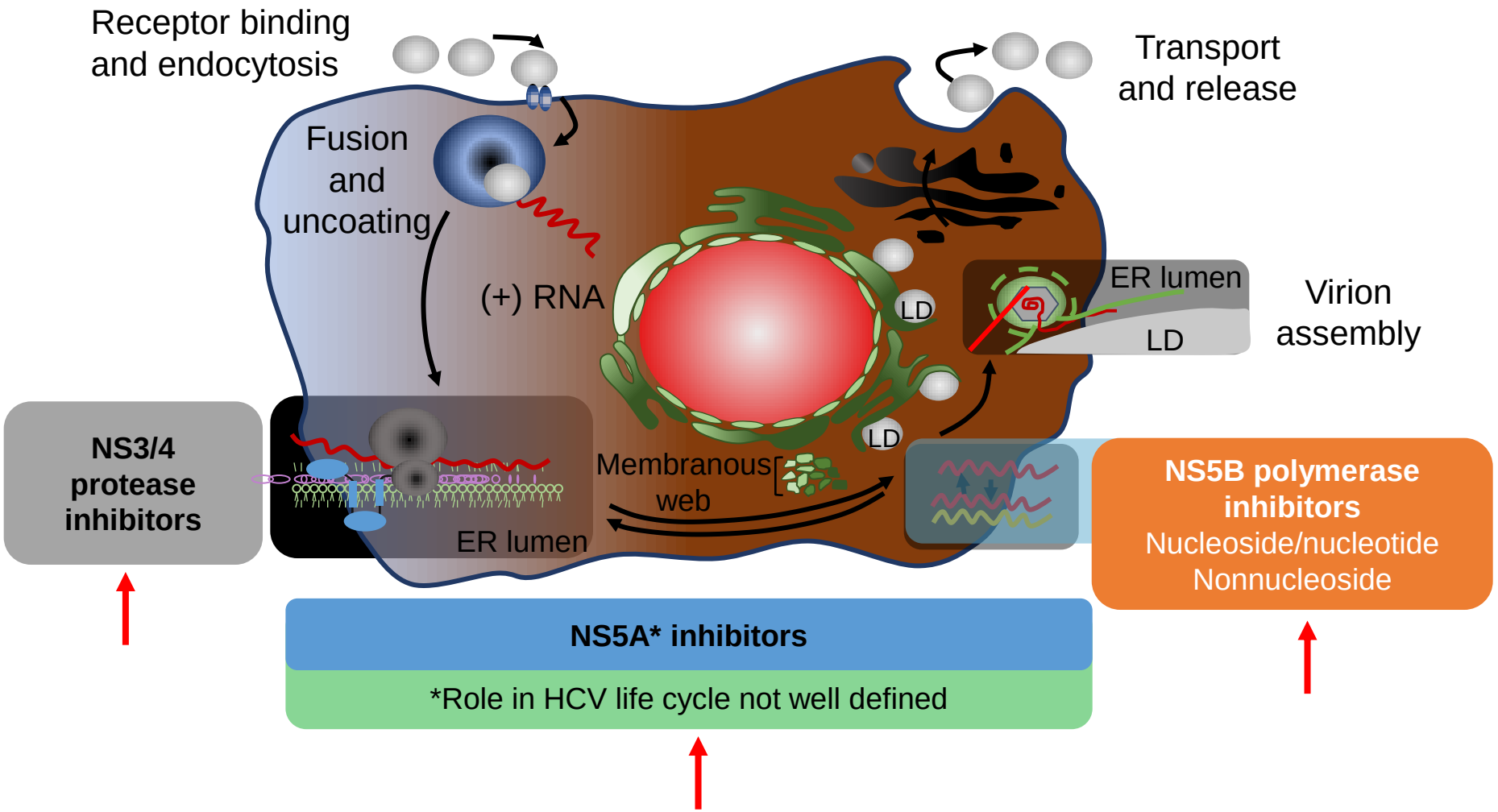
Host	Viral
Non-Modifiable	Genotype 3
Fibrosis stage	Coinfection with hepatisis B virus (HBV) or HIV
Inflammation grade	
Older age at time of infection	
Male sex	
Organ transplant	
Modifiable	
Alcohol consumption	
Nonalcoholic fatty liver disease	
Obesity	
Insulin resistance	

A Major Advance



Adapted from the US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting, April 27-28, 2011, Silver Spring, MD.

HCV Life Cycle and Targets



-buvir, -previr, -asvir:
What do these endings mean?

- **BUVIR = polymerase inhibitors**

  Sofosbuvir, Deleobuvir, Setrobuvir, Mericitabine (!), ABT-072, ABT-333, BMS-791325, GS-9669 and VX-222

  dasabuvir

- **PREVIR = protease inhibitors**

  Boceprevir, Telaprevir, Simeprevir, Asunaprevir, Danoprevir, Faldaprevir, Sovaprevir, ABT-450 and MK-5172

  paritaprévir

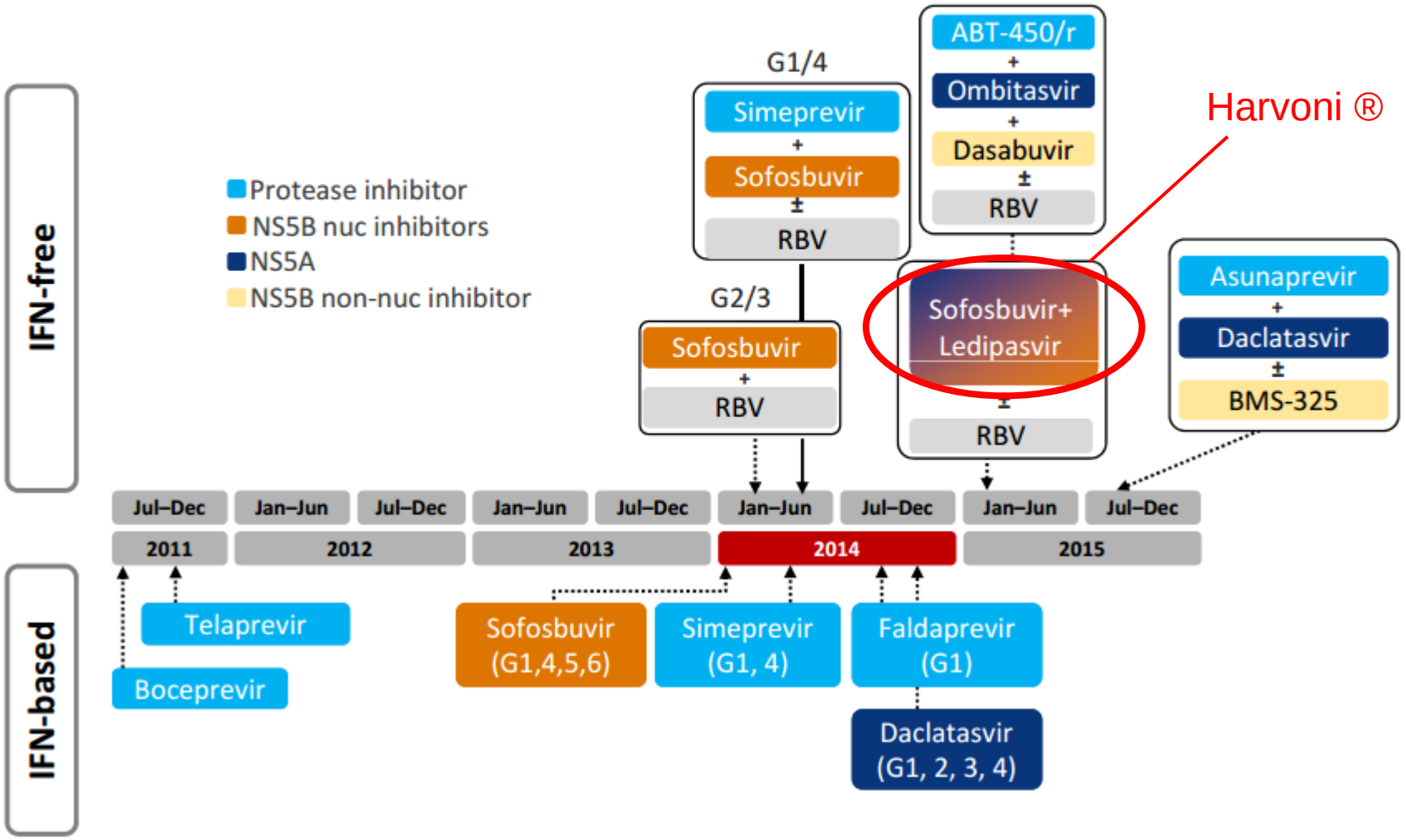
- **ASVIR = NS5A inhibitors**

  Daclatasvir, Ledipasvir, ABT-267, MK-8742 and PPI-668

  ombitasvir

Sovaldi®, Harvoni®, Exviera®,
Viekirax®, Daklinza®, Olysios®

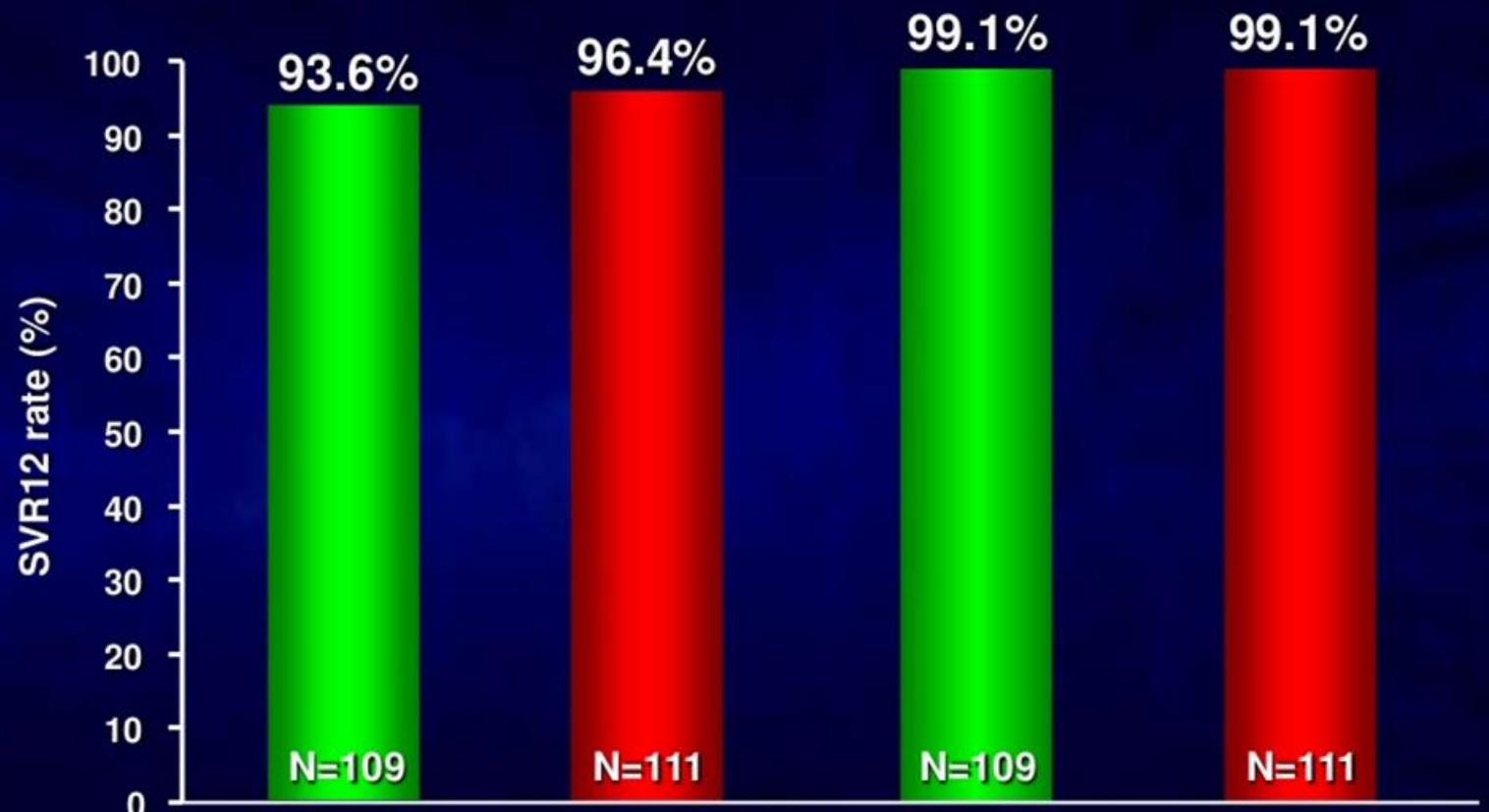
Direct-acting antivirals against HCV: a rich pipeline



2015 : l'année de l'explosion des thérapies anti-HCV

Sofosbuvir/Ledipasvir FDC ± RBV

ION-2-Phase III, Gen 1, Rx-experienced, 20% cirrhosis



Research Article

EASL | JOURNAL OF HEPATOLOGY

Ombitasvir/paritaprevir/r and dasabuvir plus ribavirin in HCV genotype 1-infected patients on methadone or buprenorphine

Conclusions: The interferon-free regimen of ombitasvir/paritaprevir/ritonavir and dasabuvir + ribavirin for 12 weeks was well tolerated and achieved sustained virologic response in 97.4% of patients on opioid substitution therapy in this study. This all-oral regimen may provide an effective alternative to interferon-based therapies for HCV-infected patients with a history of injection drug use.

Table 2. Drug-Drug Interactions (DDIs)[a] Between DAAs, Methadone, and Buprenorphine.[b]

HCV Antiviral Agents	Methadone	Buprenorphine
HCV protease inhibitors		
Boceprevir	No clinically significant DDI[c,64]	No clinically significant DDI[c,64]
Simeprevir	No clinically significant DDI[c,97]	NI (monitor for adverse events of buprenorphine)
Telaprevir	*R*-methadone AUC 21% ↓. Monitor for withdrawal; ↑ in dose may be required, *S*-methadone in the racemic mixture has potential for QT prolongation, ECG useful[c,70]	No clinically significant DDI[c,68]
Grazoprevir MK-5172 (investigational)	No clinically significant DDI[c,66]	No clinically significant DDI[c,66]
Paritaprevir/ritonavir	No clinically significant DDI[c,65]	No clinically significant DDI[c,65]
NS5B nucleoside inhibitor		
Dasabuvir	No clinically significant DDI[c,65]	No clinically significant DDI[c,65]
Sofosbuvir	No clinically significant DDI[c,98]	NI (DDI not expected)
NS5A inhibitors		
Daclatasvir	No clinically significant DDI[c,99]	No clinically significant DDI[c,99]
Ledipasvir	NI (DDI not expected)	NI
Elbasvir MK-8742 (investigational)	No clinically significant DDI[c,68]	NI
Ombitasvir	No clinically significant DDI[c,65]	No clinically significant DDI[c,65]

Abbreviations: AUC, area under the (concentration-time) curve; DAA, direct-acting antiviral; ECG, electrocardiogram; HCV, hepatitis C virus; NI, not investigated; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PK, pharmacokinetic.

[a]May not be all inclusive.

[b]Modified from HEP-Druginteractions.org,[8] Tseng,[9] and Gruber and McCance-Katz.[11]

[c]PK-study; drug-drug interaction between antiretroviral drug and DAAs has to be considered in HIV/HCV-coinfected patients.[100]

3 règles pour l’hépatite C :

- Tout patient toxicomane doit avoir une sérologie HCV. En cas de positivité, il faut demander une virémie HCV et la détermination du génotype du virus.

- Tout patient avec une virémie positive doit être encouragé à discuter de sa situation avec un infectiologue (ou un gastro-entérologue). Ils décideront ensemble de la suite des investigations : ponction –biopsie du foie ou élastographie (*Fibroscan®* à Lausanne, Berne ou Neuchâtel).

- En cas de fibrose de stade ≥2, un traitement (généralement sans interféron) sera proposé au patient.

Hépatite B

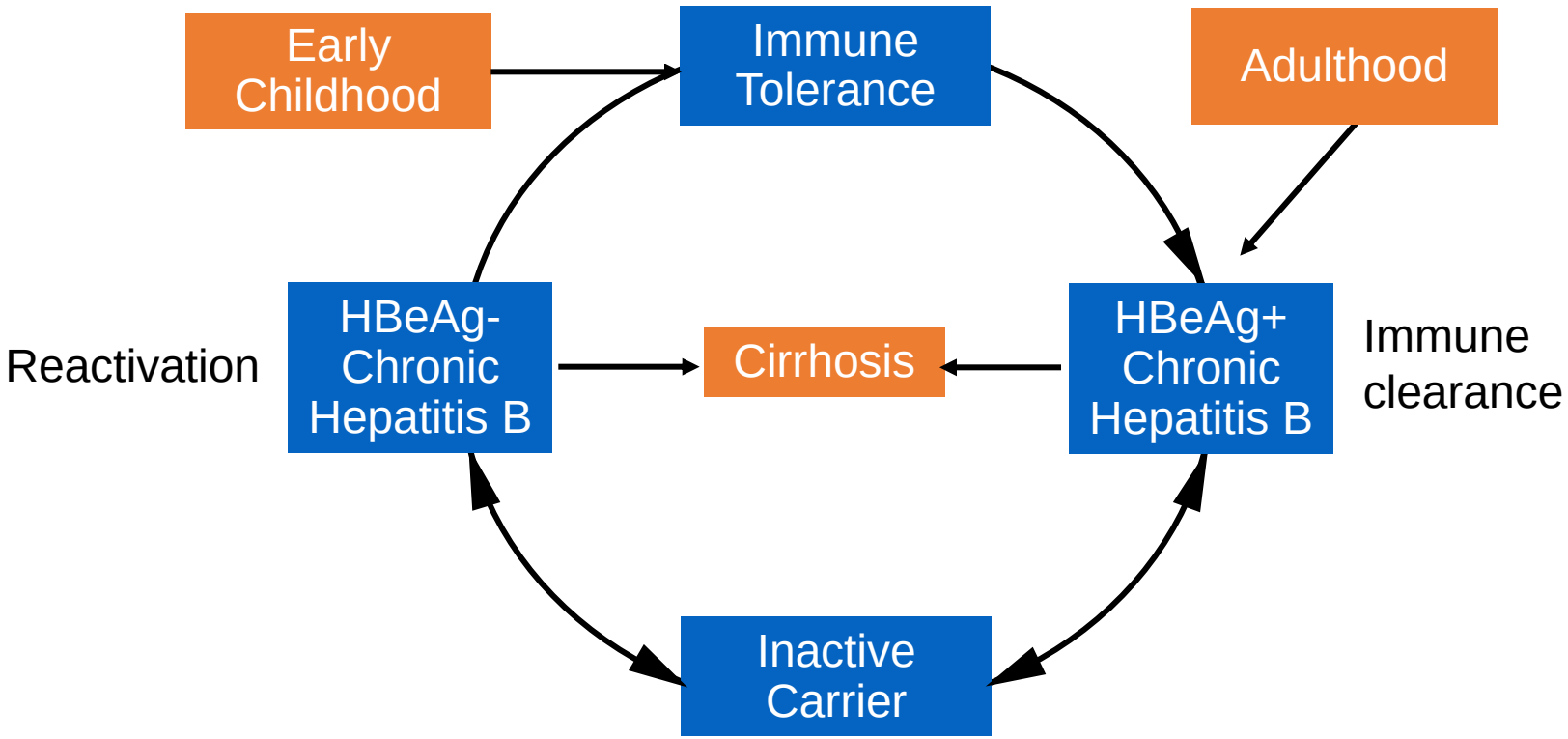
Propagation: environ 1,5 pour cent de la population en Suisse est infecté par une hépatite virale.

Hépatite C: 50'000 à 80'000 personnes
Hépatite B: 20'000 à 30'000 personnes

The reported HBsAg prevalence in injection drug users (IDUs) in the EU varied widely, ranging from 0% in Belgium to 11.6% in Bulgaria in 2006. Generally, the HBsAg prevalence among IDUs is higher in countries in Central and Eastern Europe, when compared with those in Western Europe [9]. A prevalence study in Switzerland amongst patients with a history of long-term injection drug use in the years 1994 to 1996 documented a seroprevalence of the hepatitis B core antibodies ~~antigen (HBcAg)~~ as high as 73.2%, suggesting that the majority of individuals were, or had been, in contact with the virus [15].

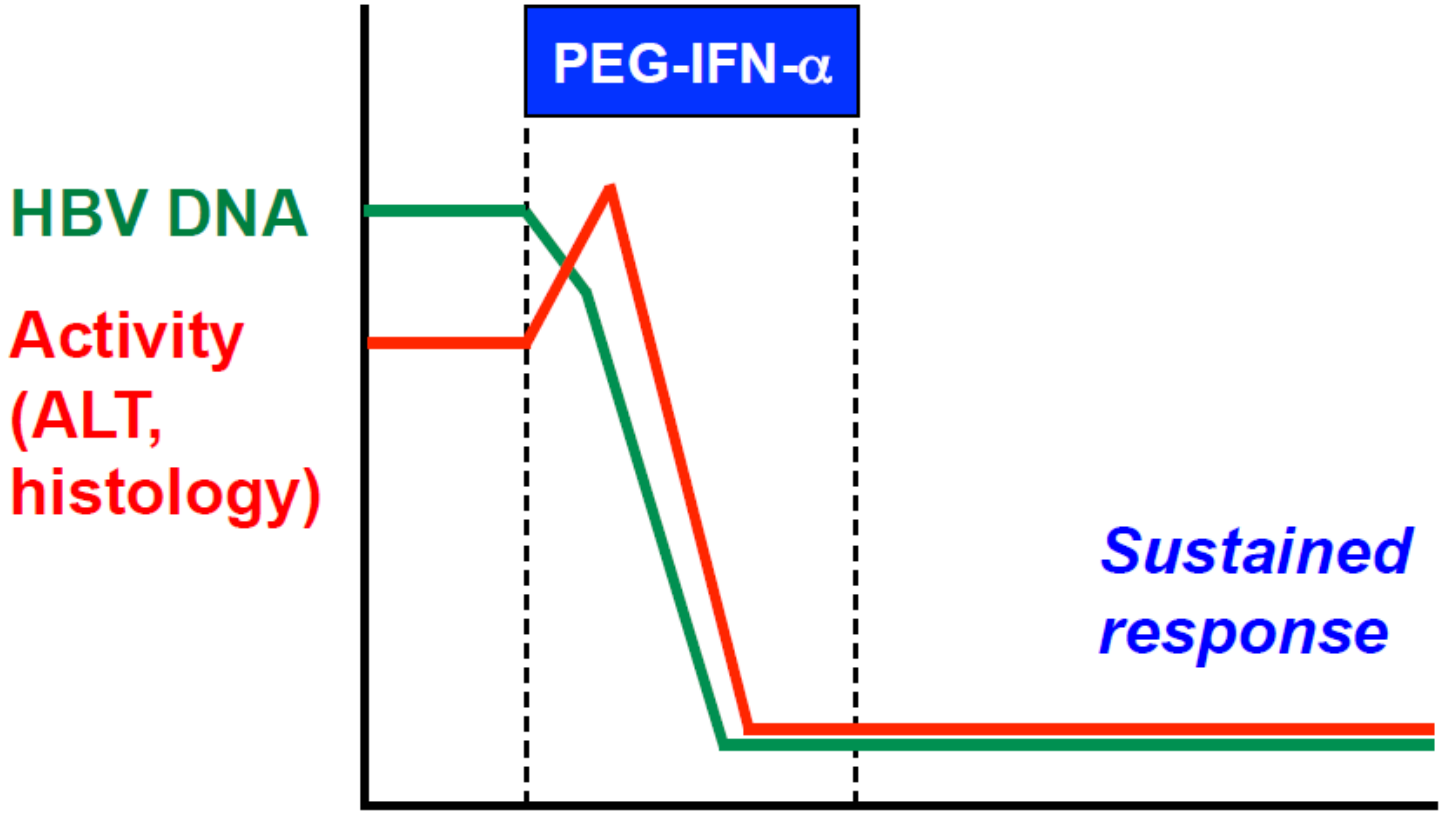
Swiss Med Wkly. 2013;143:w13793

Histoire naturelle de l'infection chronique par le HBV



Transaminases normales, virémie <2'000 U/l

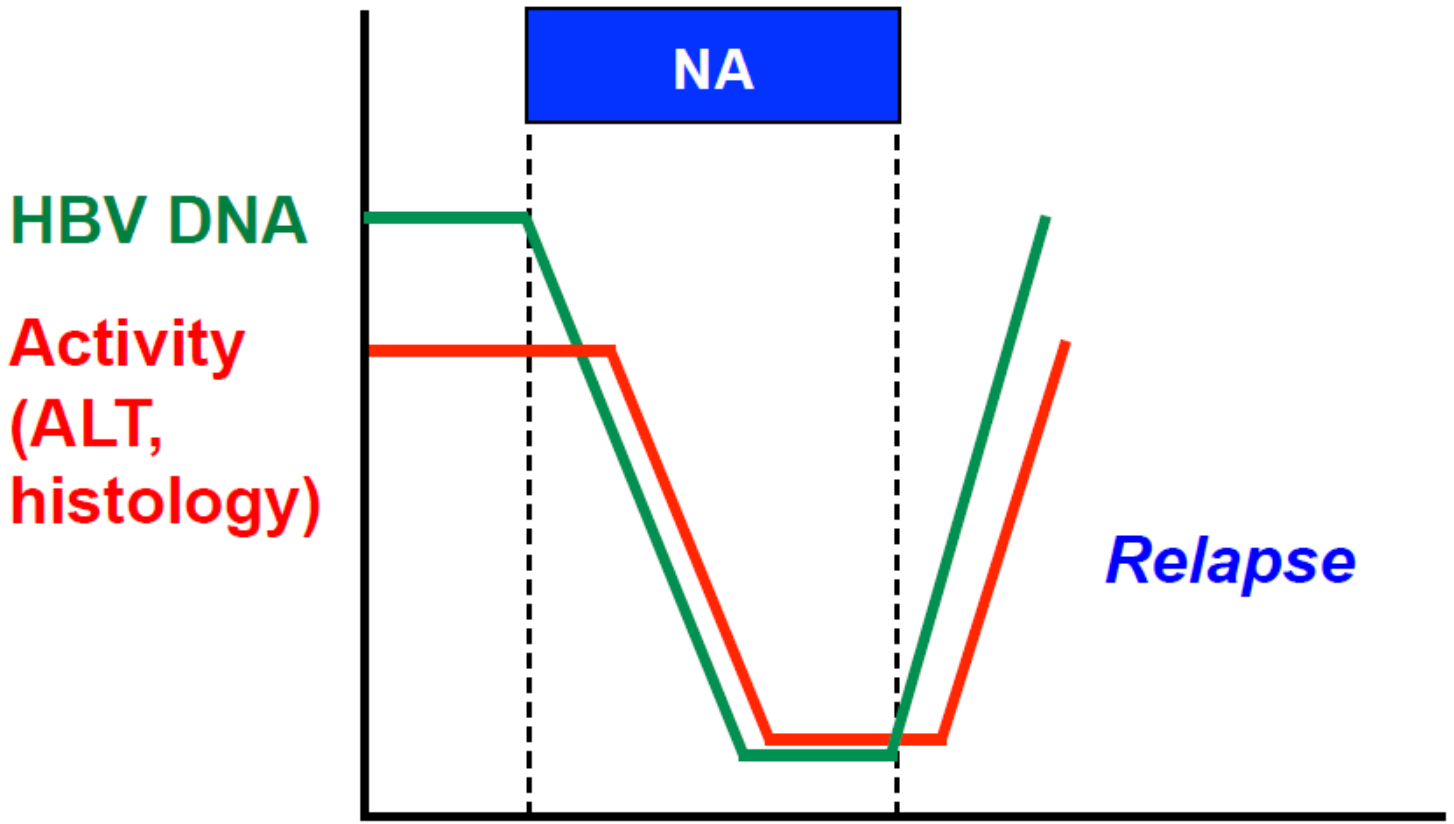
Therapy of Chronic Hepatitis B
PEG-IFN-α



30%

Moradpour

Therapy of Chronic Hepatitis B
Nucleos(t)ide Analogs



Moradpour

			Status CH 01/2013
PEG-IFN-α2a		Pegasys®	licensed 1st line
Lamivudine	LAM	Zeffix®	licensed 1st line
Adefovir	ADV	Hepsera®	licensed 2nd line
Telbivudine	LdT	Sebivo®	licensed 1st line
Entecavir	ETV	Baraclude®	licensed 1st line
Tenofovir	TDF	Viread®	licensed 1st line

Moradpour

3 règles pour l’hépatite B :

- Tout patient toxicomane doit avoir une sérologie HBV. En d’antigène HBs positif, il faut demander une virémie HBV et de transaminases.

- Tout patient avec une virémie >2’000 U/l positive ou des transaminases élevées (=hépatite active) doit être encouragé à discuter de sa situation avec un infectiologue (ou un gastro-entérologue). Ils décideront ensemble de la suite des investigations.
- Les hépatites actives doivent généralement être traitées.

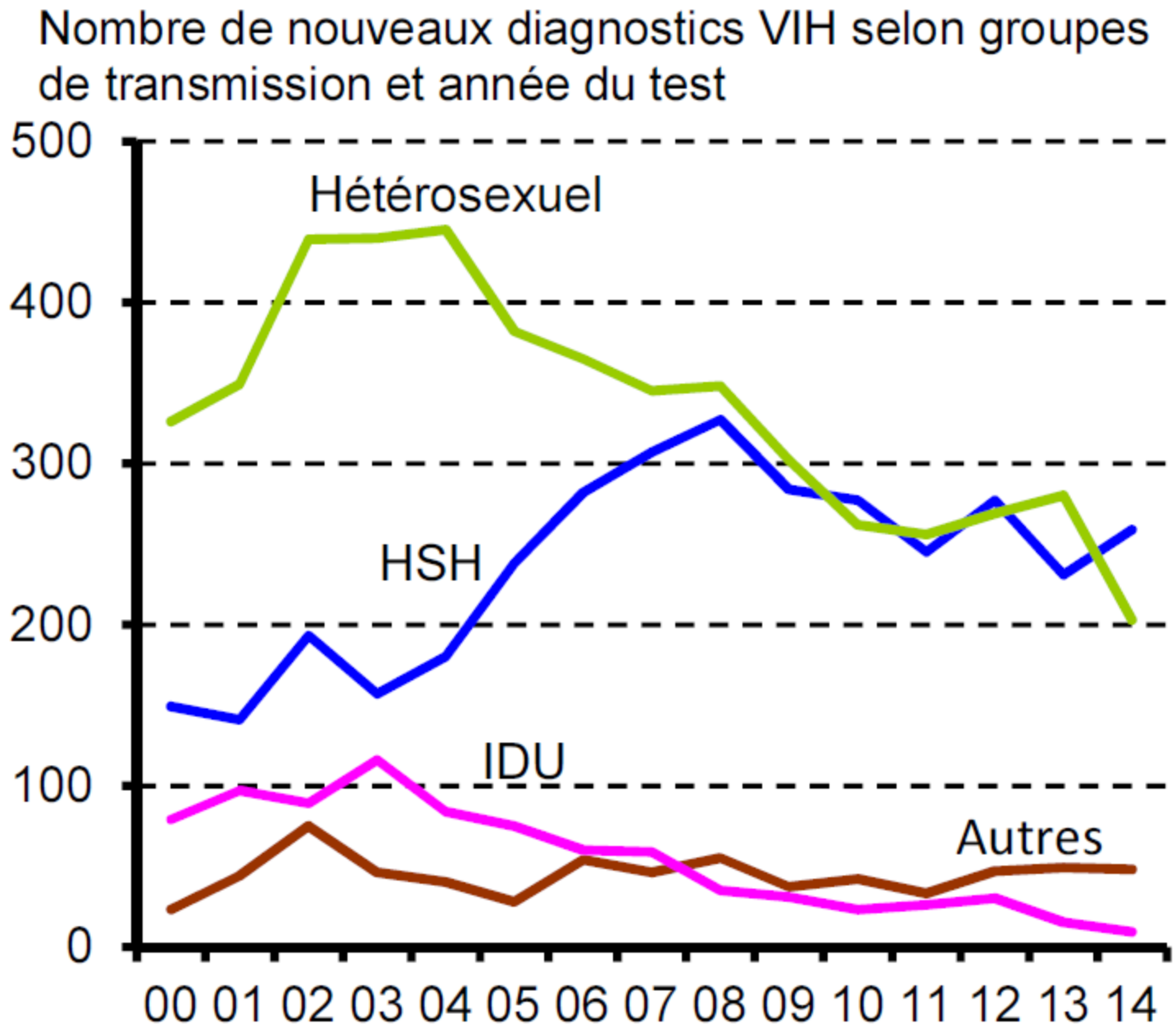
VIH

Suisse , 2014

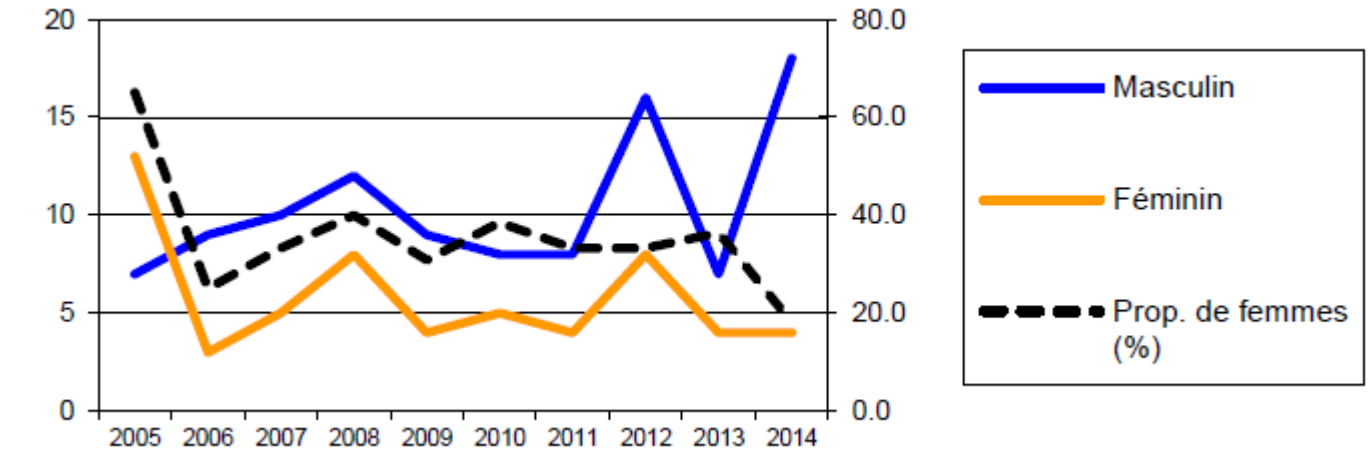
Modes d'infection (proportions estimées pour les nouvelles infections)

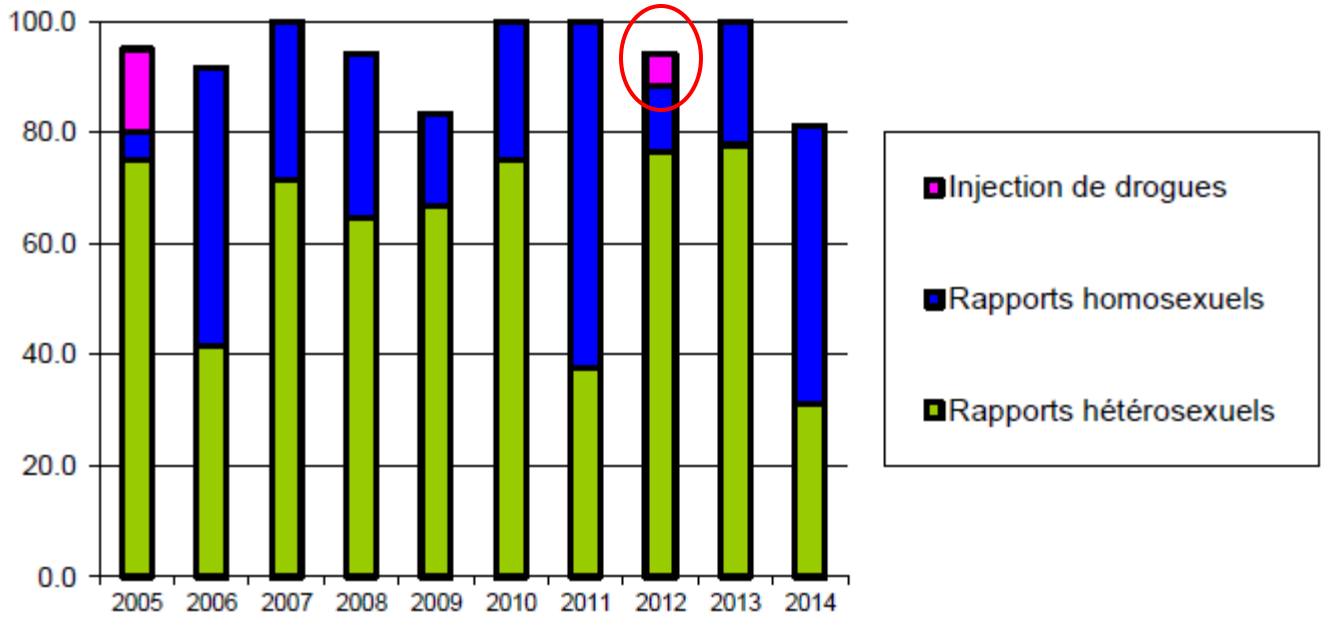
- Rapports hétérosexuels	~42%
- Rapports sexuels entre hommes	~57%
- Injection de drogues	~2%
- Transmission de la mère à l'enfant	~0%
- Transfusions de sang et produits sanguins§	~0%

§ (survenu en Suisse)


Nombre de nouveaux diagnostics VIH selon groupes de transmission et année du test
500
400
300
200
100
0
Hétérosexuel
HSH
IDU
Autres
00 01 02 03 04 05 06 07 08 09 10 11 12 13 14

Canton de Fribourg :





Médicament anti-HIV en Suisse, 2015

Generic name	Trade name		Formulation
Single-tablet regimens			
Dolutegravir/ abacavir / lamivudine	*Triumeq*		Tablet comprising 50mg dolutegravir, 600mg abacavir and 300mg lamivudine
Efavirenz / emtricitabine / tenofovir	*Atripla*		Tablet comprising 600mg efavirenz, 200mg emtricitabine and 245mg tenofovir
Elvitegravir / cobicistat / emtricitabine / tenofovir	*Stribild*		Tablet comprising 150mg elvitegravir, 150mg cobicistat, 200mg emtricitabine, 245mg tenofovir
Rilpivirine / emtricitabine / tenofovir	*Eviplera*		Tablet comprising 25mg rilpivirine, 200mg emtricitabine and 245mg tenofovir
Fixed-dose combinations			
Abacavir / lamivudine	*Kivexa*		Tablet comprising 600mg abacavir and 300mg lamivudine
Abacavir / lamivudine / zidovudine	*Trizivir*		Tablet comprising 300mg abacavir, 150mg lamivudine and 300mg zidovudine
Emtricitabine / tenofovir	*Truvada*		Tablet comprising 200mg emtricitabine and 245mg tenofovir
Lamivudine / zidovudine	*Combivir*		Tablet comprising 150mg lamivudine and 300mg zidovudine

Nucleoside reverse transcriptase inhibitors (NRTIs)			
Abacavir	*Ziagen*		300mg tablet
Emtricitabine	*Emtriva*		200mg capsule
Lamivudine	*Epivir*		150* and 300mg tablets
Zidovudine	*Retrovir*		100 and 250mg* capsules
Nucleotide reverse transcriptase inhibitor (NtRTI)			
Tenofovir	*Viread*		245mg tablet
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)			
Efavirenz	*Sustiva Stocrin*		600mg tablet* and 200mg capsule
Etravirine	*Intelence*		100 and 200mg* tablet
Nevirapine	*Viramune*		200mg tablet
Nevirapine	*Viramune prolonged-release*		400mg tablet
Rilpivirine	*Edurant*		25mg tablet

Protease inhibitors			
Atazanavir	*Reyataz*		150, 200 and 300mg* capsule
Darunavir	*Prezista*		600, and 800mg* tablet
Fosamprenavir	*Telzir*		700mg tablet
Lopinavir / ritonavir	*Kaletra*		Tablet comprising 200mg lopinavir and 50mg ritonavir
Ritonavir	*Norvir*		100mg tablet
Tipranavir	*Aptivus*		250mg capsule
CCR5 inhibitor			
Maraviroc	*Celsentri*		150* and 300mg tablets
Integrase inhibitors			
Dolutegravir	*Tivicay*		50mg tablet
Elvitegravir	*Vitekta*		85, 150mg* tablet
Raltegravir	*Isentress*		400mg tablet


123
NEW

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 27, 2015 VOL. 373 NO. 9

Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection

The INSIGHT START Study Group*

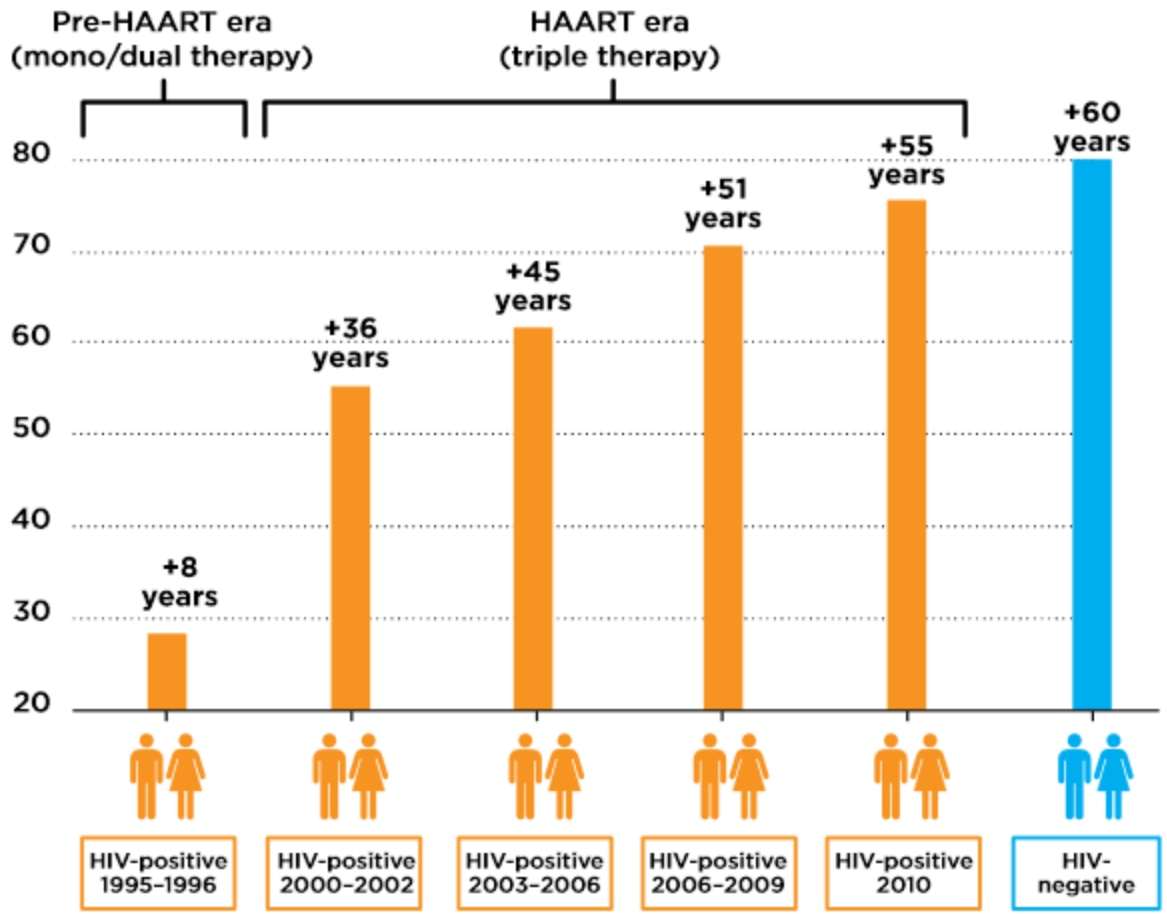
CONCLUSIONS

The initiation of antiretroviral therapy in HIV-positive adults with a CD4+ count of more than 500 cells per cubic millimeter provided net benefits over starting such therapy in patients after the CD4+ count had declined to 350 cells per cubic millimeter. (Funded by the National Institute of Allergy and Infectious Diseases and others; START ClinicalTrials.gov number, NCT00867048.)

New UN treatment guidelines say all people with HIV should get antiretrovirals

30 September 2015 – Anyone infected with HIV should begin antiretroviral treatment as soon after diagnosis as possible, the United Nations World Health Organization (WHO) announced today, as it issued new guidelines that could help avert more than 21 million deaths and 28 million new infections by 2030.

Expected impact of HIV treatment on survival of a 20-year-old person living with HIV in a high-income setting (different periods)



Source: Lohse N, Hansen AB, Pedersen G, et al. Survival of persons with and without HIV infection in Denmark, 1995-2005. Ann Intern Med. 2007;146(2):87-95.

Gestion des interactions : le site indispensable

3 règles pour le VIH :

- Tout patient toxicomane doit avoir une sérologie VIH.

- En 2015, toute sérologie VIH positive confirmée amène un traitement immédiat.

- On diagnostique actuellement très peu de nouvelles infections chez les toxicomanes. Le suivi des patients VIH-positifs connus doit être réalisé par un infectiologue. Le médecin de premier recours veillera à vérifier les éventuelles interaction médicamenteuses en cas d'introduction de nouveaux médicaments.