



ARV treatment Update 2012

Avondseminarie 18 december 2012

Eric Florence

ITG, Antwerpen

Three big conferences in 2012

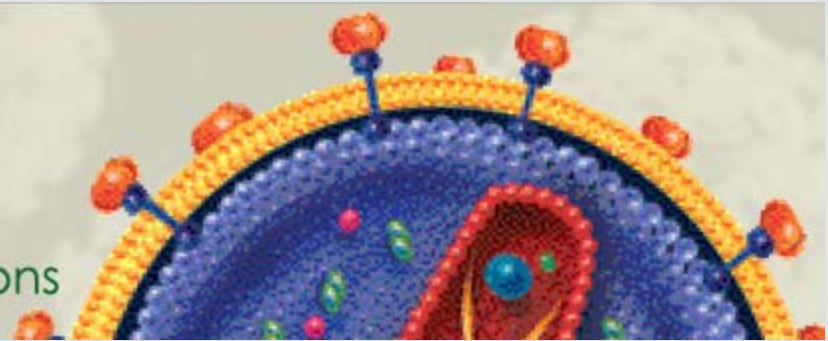


2012
SEATTLE

Washington State
Convention Center

March 5-8, 2012

19th Conference
on Retroviruses and
Opportunistic Infections



XIX INTERNATIONAL AIDS
CONFERENCE JULY 22 - 27
WASHINGTON DC USA

TURNING THE TIDE TOGETHER

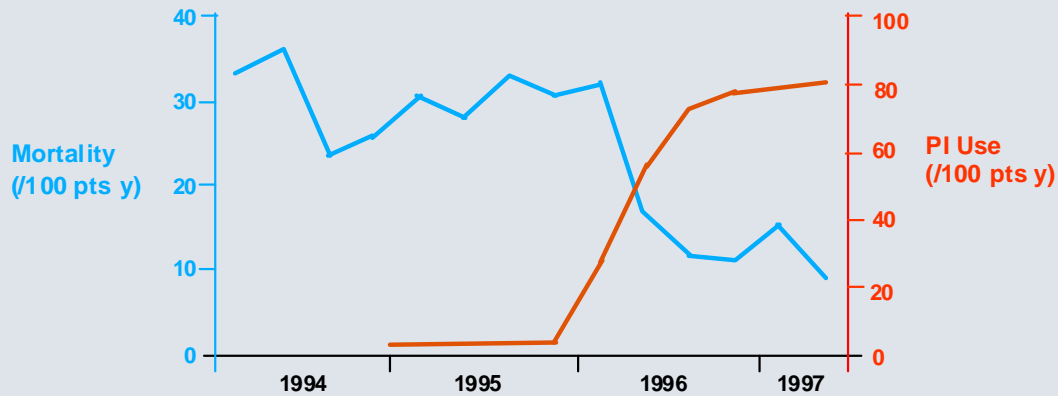
Welcome to **HIV11.com**

Eleventh International Congress on Drug Therapy in HIV Infection
11-15 November 2012 Glasgow, UK



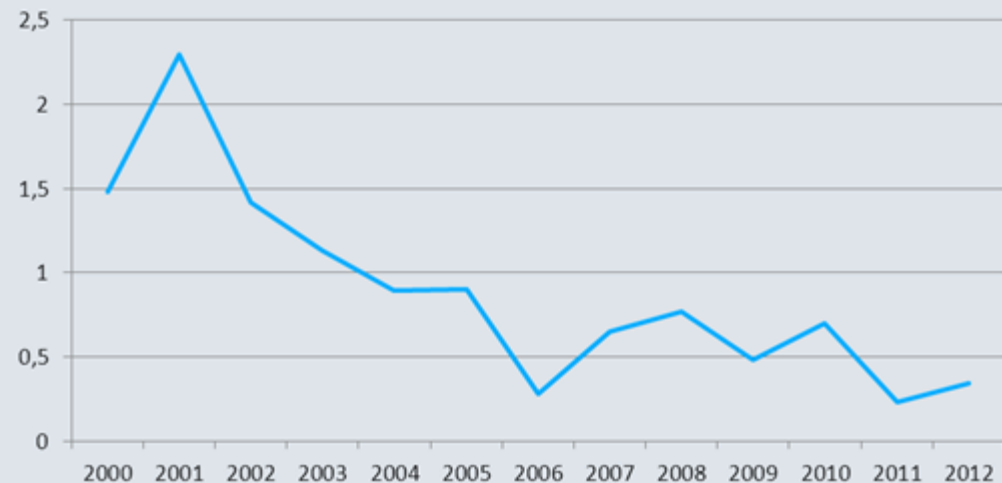
11 International Congress on
Drug Therapy in
HIV Infection

Current situation: some positive things....



Palella FJ et al. N Engl J Med 1998;338:853–860

mortaliteit ITG(/100pts/y)

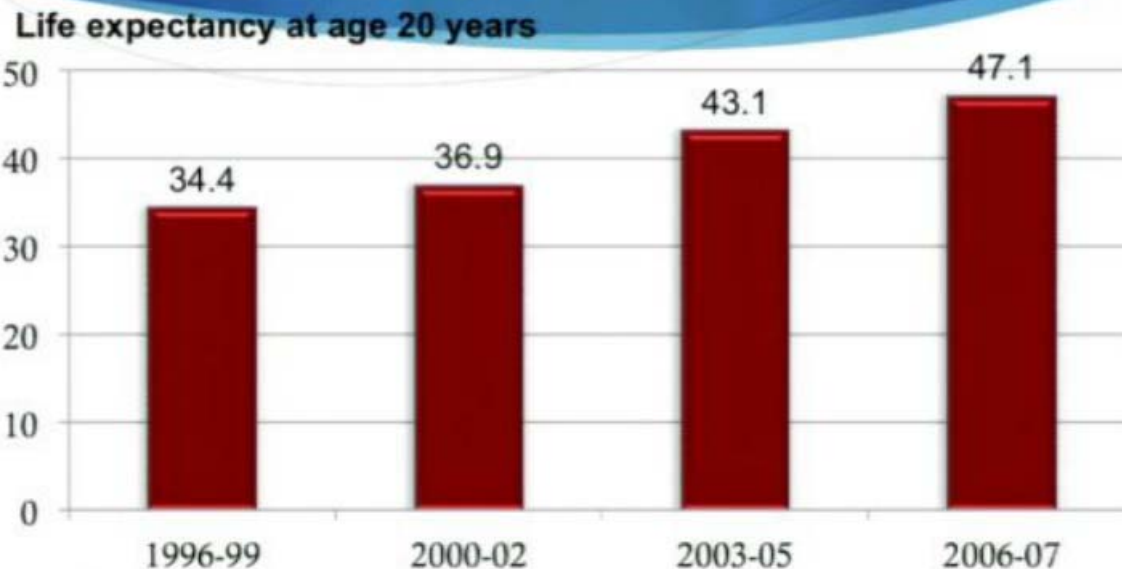


ITM data

Life expectancy



Temporal changes in life expectancy, 1996-2007



Virological control



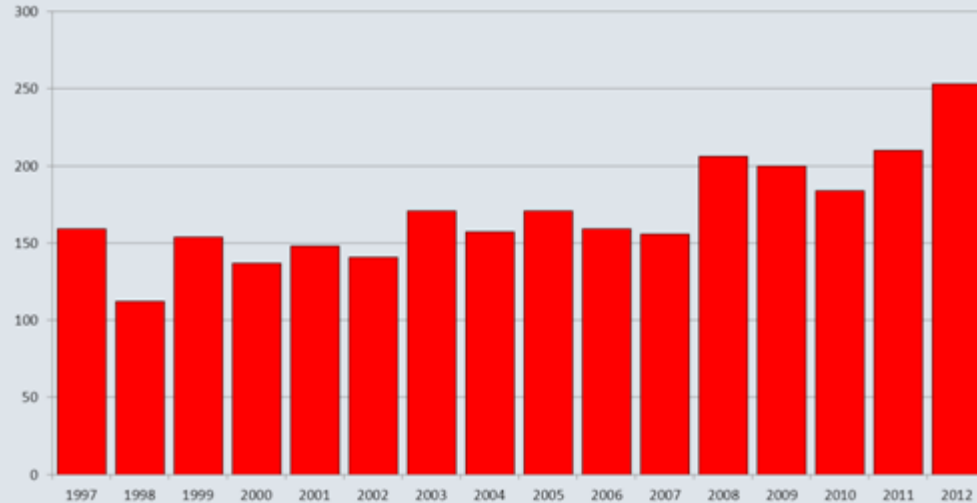
Last viral load below detection limit (%)



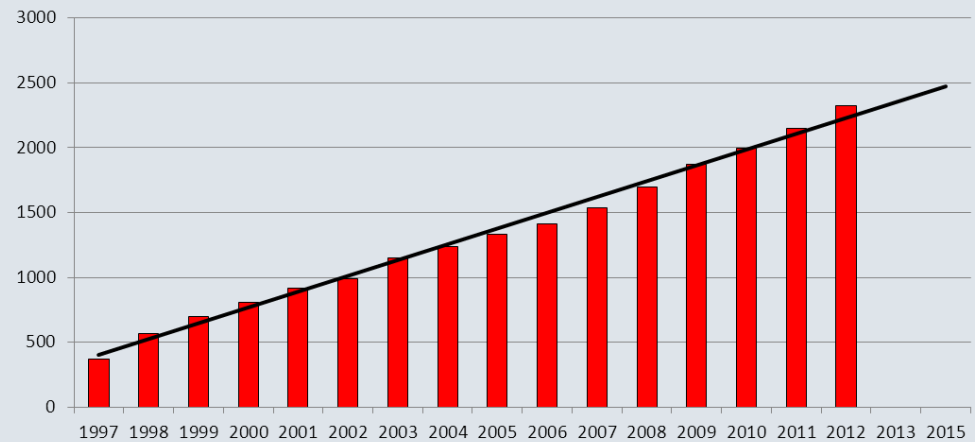
And some negative!



New pts seen at ITM (n)



Total pts followed at ITM (n)



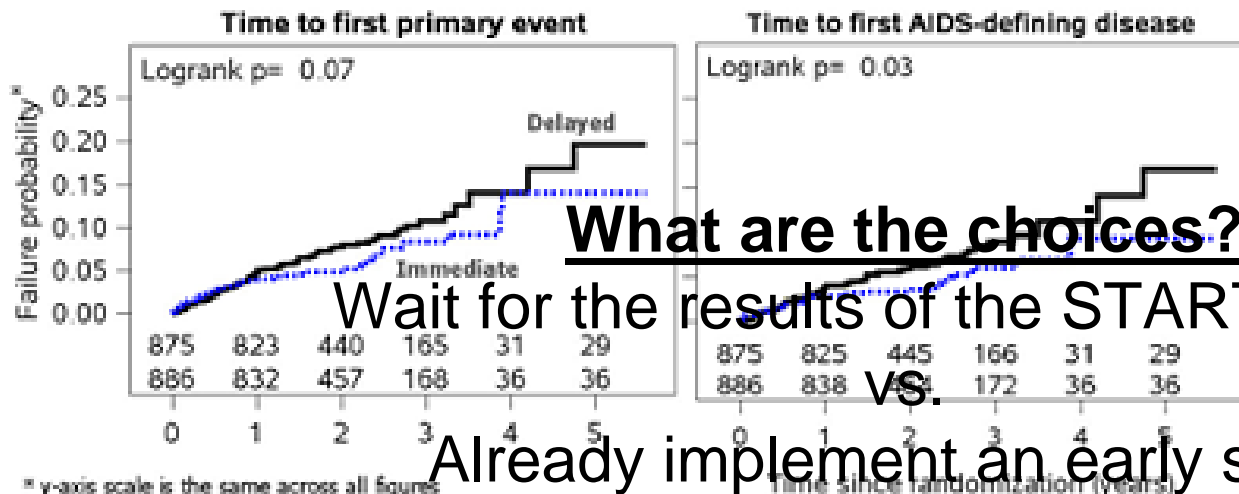
When to start ARV treatment?

Guideline	year	AIDS	CD4<350	CD4 350-400	
DHHS	2012	Yes	Yes	Yes	
IAS-USA	2012	Yes	Yes	Yes	Yes
EACS	2012	Yes	Yes	some pts	some pts
WHO	2010	Yes	Yes	No	No

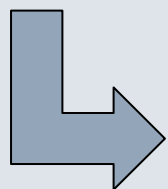
Still not reimbursed in Belgium

- US guidelines (DHHS): <http://aidsinfo.nih.gov/guidelines/>
- Int. AIDS Society guidelines: <https://www.iasusa.org/guidelines>
- European guidelines (EACS): <http://www.european aids clinical society.org/>
- WHO guidelines: <http://www.who.int/hiv/pub/arv/adult2010/en/index.html>

When to start ARV treatment?



(surely a good option to decrease transmission risk
 Expanded analysis of HPTN052 trial*
 Whether this is good for the patient remains maybe controversial)

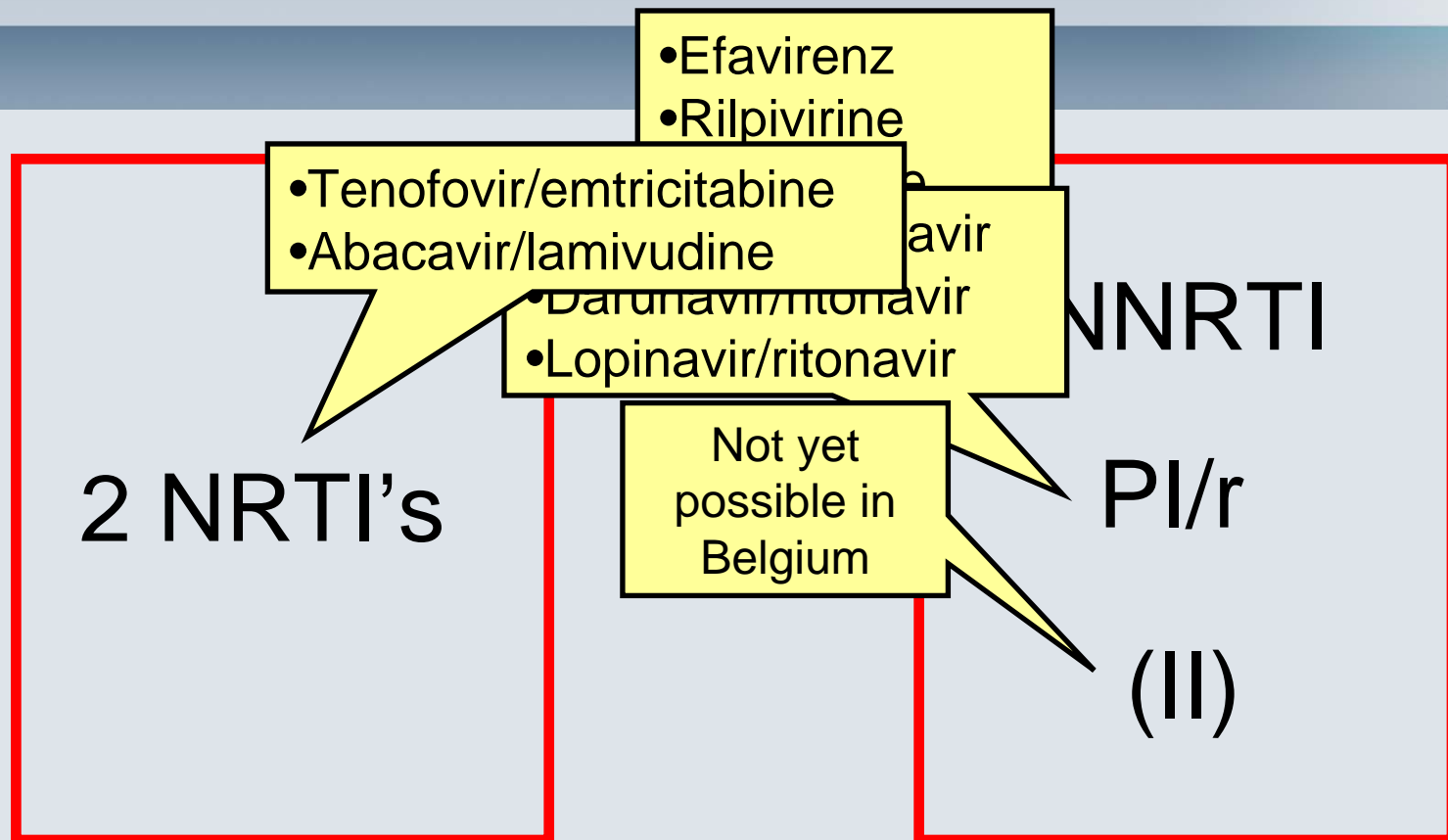


Jury still not out!

See webcast pro/contra session from Glasgow congress

<http://www.hiv11.com> (Monday 12 november)

What to start with?



“Backbone”

“3rd Agent”

What to start with?



- A lot of comparative trials, mostly “non-inferior” results.
- ACTG 5202 (JID 2011)
 - Backbone: ABC/3TC vs. TDF/FTC
 - Third agent: ATV/r vs. EFV
- Single Study (ICAAC 2012)
 - DTG + ABC/3TC vs. EFV/TDF/FTC
- ACTG 5257 (ongoing)
 - ATV/r vs DRV/r vs. Ral (backbone of TDF/FTC)

When to change?



Guideline	year	Change treatment in case of:	Change to:
DHHS	2012	Persistent VL >200 copies/ml	2 (preferably 3) fully active drugs
IAS-USA	2012	Sustained VL > 50-200 copies/ml	3 active drugs
EACS	2012	Confirmed VL >500-1000 copies/ml	2 (preferably 3) fully active drugs

Detectable Viral load under treatment is infrequent
But what is clinically significant?

When to change?



Recent results against an early switch:

- Charpentier C: no risk of subsequent virological failure with viral loads 20-50 c/ml.
- Wolf E: idem with VL 50-200 c/ml.
- Eron: long-term outcome of experienced pts on raltegravir (VL <50 vs 50-400 vs >400).
- Grennan JT, JID 2012 (VL<500).

Influence of Viral load test (real time PCR)?

Always assess adherence & drug interactions

What's new in antiviral therapy?



- Three products approved in 2011
- A few interesting drugs in the pipeline



Drug Approval in 2011



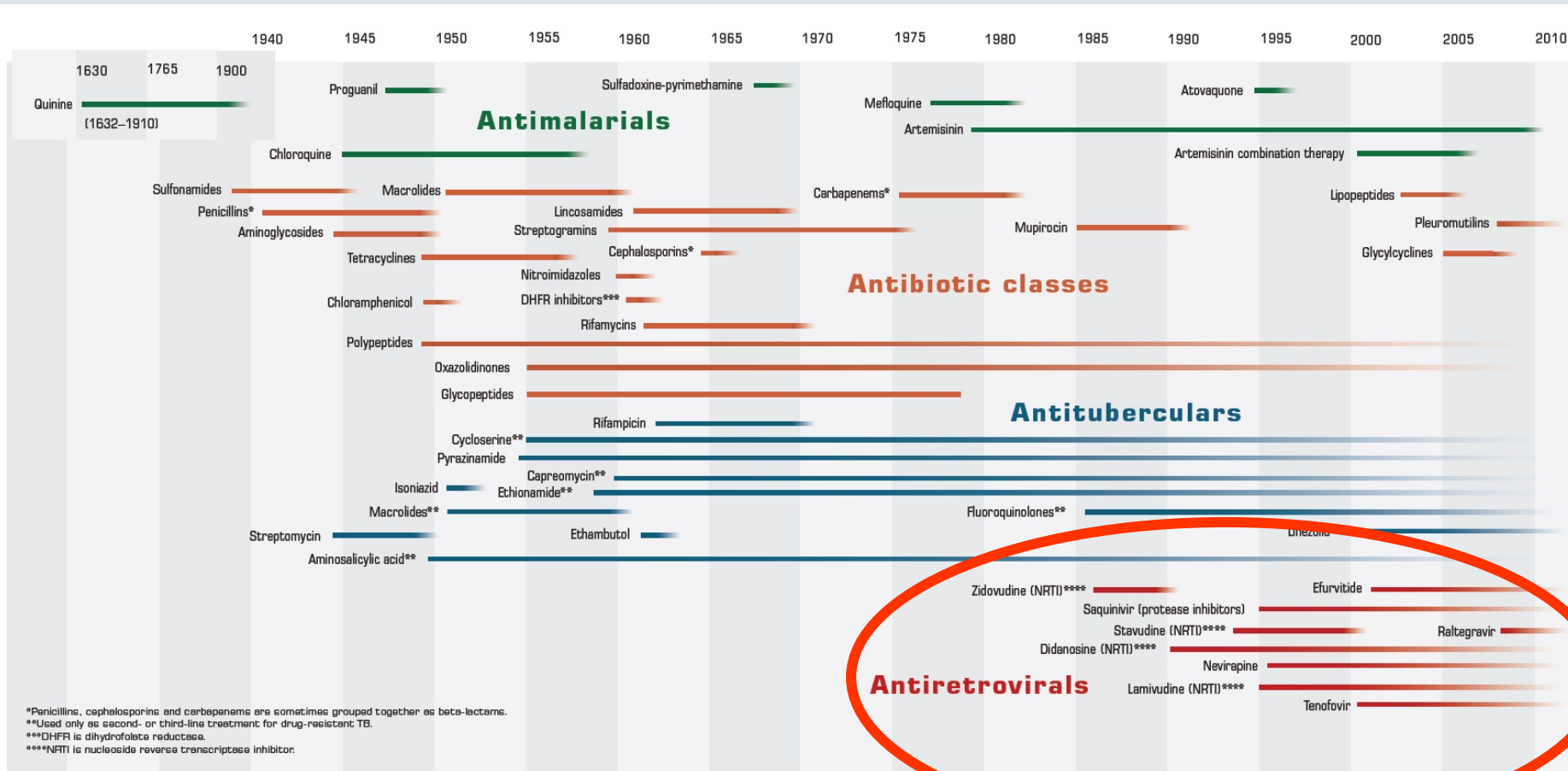
- Rilpivirine (Edurant®)
- Viramune XR (Viramune®)
- Rilpivirine/Emtricitabine/Tenofovir (Eviplera®)

Pipeline for antiviral drugs in 2012



	Class	Drug	Sponsor	Phase
	NRTI	BMS986001	BMS	II
	NRTI	CMX-157	Chimerix	I
	NRTI	GS-7340	Gilead	II
	NNRTI	Lersivirine	Pfizer	II
	NNRTI	Rilpivirine LA	Janssen	I
→	CCR5/CCR2I	Lenacapavir	Takeda	II
→	II	Dolutegravir (DTG)	ViiV	III
→	II	Elvitegravir (EVG)	Gilead	Submitted
	II	GSK-1265744	GSK	II
	II	GSK-1265744 LA	GSK	I
→	AI	BMS663068	BMS	II
→	PK booster	Cobicistat	Gilead	Submitted
	PK booster	SPI-251	Sequoia	Discontinued
	PK booster	CTP-518	GSK	On Hold
→	FDC	"QUAD"	Gilead	Submitted
	FDC	EVG/cobi/FTC/GS7340	Gilead/Tibotec	II
	FDC	DRV/cobi/FTC/GS7340	Janssen/Gilead	II
→	FDC	DTG/ABC/3TC ("Trii")	ViiV	III

Pipelines in infectious diseases



New treatment strategies



- **Start earlier** (“ Test & Treat”, START study...)



New treatment strategies



- **Start earlier** (“ Test & Treat”, START study...)
- **Modify the third agent** (PI- or NNRTI free)
 - 2 Nucl. analogues + Integrase inhibitor
 - 2 Nucl. analogues + CCR5 inhibitors

New treatment strategies



- **Start earlier** (“ Test & Treat”, START study...)
- **Modify the third agent** (PI- or NNRTI free)
 - 2 Nucl. analogues + Integrase inhibitor
 - 2 Nucl. analogues + CCR5 inhibitors
- **Modify the backbone** (“NRTI sparing”):
 - Protease inhibitor + NNRTI
 - Protease inhibitor + Integrase inhibitors
 - Protease inhibitor + CCR5 inhibitors
 - Simplification (PI/r monotherapy)

NRTI sparing therapy: a holy grail?



1. PI + NNRTI

- ~~• EFV + LPV/r → study A5142 (Riddler SA, NEJM 2008)~~

2. PI + Integrase inhibitor

- ~~• Ral + LPV/r → Progress trial (Reynes J, HIV Clin Trials 2011)~~
- ~~• Ral + ATV/r → Spartan trial (Kozal MJ, HIV Clin Trials 2012)~~
- ~~• Ral + DRV/r → Radar study (Bedimo R, 6th IAS, Rome 2011)~~
- ~~• Ral + DRV/r → ACTG5262 trial (Taiwo B, AIDS 2011)~~
- Ral + DRV/r → NEAT001 trial (ongoing)

3. PI + CCR5 inhibitor

- MVC + ATV/r → Study A4001078 (Mills A XIX AIDS conf TUAB0102)
- ~~• MVC + DRV/r → Midas trial (Taiwo B XIX AIDS conf TUPE099)~~
- MVC + DRV/r → Study A4001095 (ongoing)

PI Monotherapy



Is it still a valuable option?

See:

- Mathis S Plos One 2011 (meta-analysis)
- Guiguet M AIDS 2012 (long term observational study)

Generic antiviral drugs



End patent in the coming years for some antiviral drugs.

- Zidovudine 2005
- Lamivudine 2011
- Combivir® 2013
- Nevirapine 2013
- Efavirenz 2013
- Abacavir 2014
- Lopinavir/ritonavir 2015
- Emtricitabine 2016

Will it affect the way we prescribe antiviral drugs in Belgium?

Interesting [presentation](#) on how to deal with ARV in time of crisis
[Another](#) on the use of generic ARV's in Europe

New (co-)formulations: STR*



STR: Single Tablet Regimen

Till 2011

- Atripla®

Since 2012

- Eviplera® (Ralpivirine/tenofovir/emtricitabine)

In the future

- Elvitegravir/cobicistat/tenofovir/emtricitabine= « QUAD » (Submitted)
- Dolutegravir/Lamivudine/Abacavir (« Trii ») (phase III)
- Darunavir/cobicistat/GS7340/emtricitabine (phase II)
- Elvitegravir/cobicistat/GS7340/emtricitabine (phase II)

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Is STR better than QD?*

Long-Acting drugs



- Rilpivirine LA
- SGSK 1265744

Both phase I studies


Take Home Message



- Tritherapy remains the gold standard
- But:
- Products works far better than in 1996.
 - Better safety profile, much better tolerance.
 - Administration is much easier (Once a day, STR).
- Big questions remains
 - What is the optimal timing to start antiretroviral treatment?
 - Is there something better than the classical tritherapy?
 - ...

Bedankt voor jullie aandacht

Contactgegevens:

 eflorence@itg.be

 03/247.66.42