



Leading By Example in the Public Health Approach to Antiretroviral Therapy

Industry Participants:

Abbott

Boehringer Ingelheim

Bristol-Myers Squibb

Gilead

GlaxoSmithKline

Merck

Schering-Plough

Tibotec

Industry Perspective: Current Strategies, Knowledge Gaps and Barriers in Delivering ART using the Public Health Approach

February 12, 2009

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Director, Commercial Development
Abbott International

Industry Perspective on the Delivery of ART

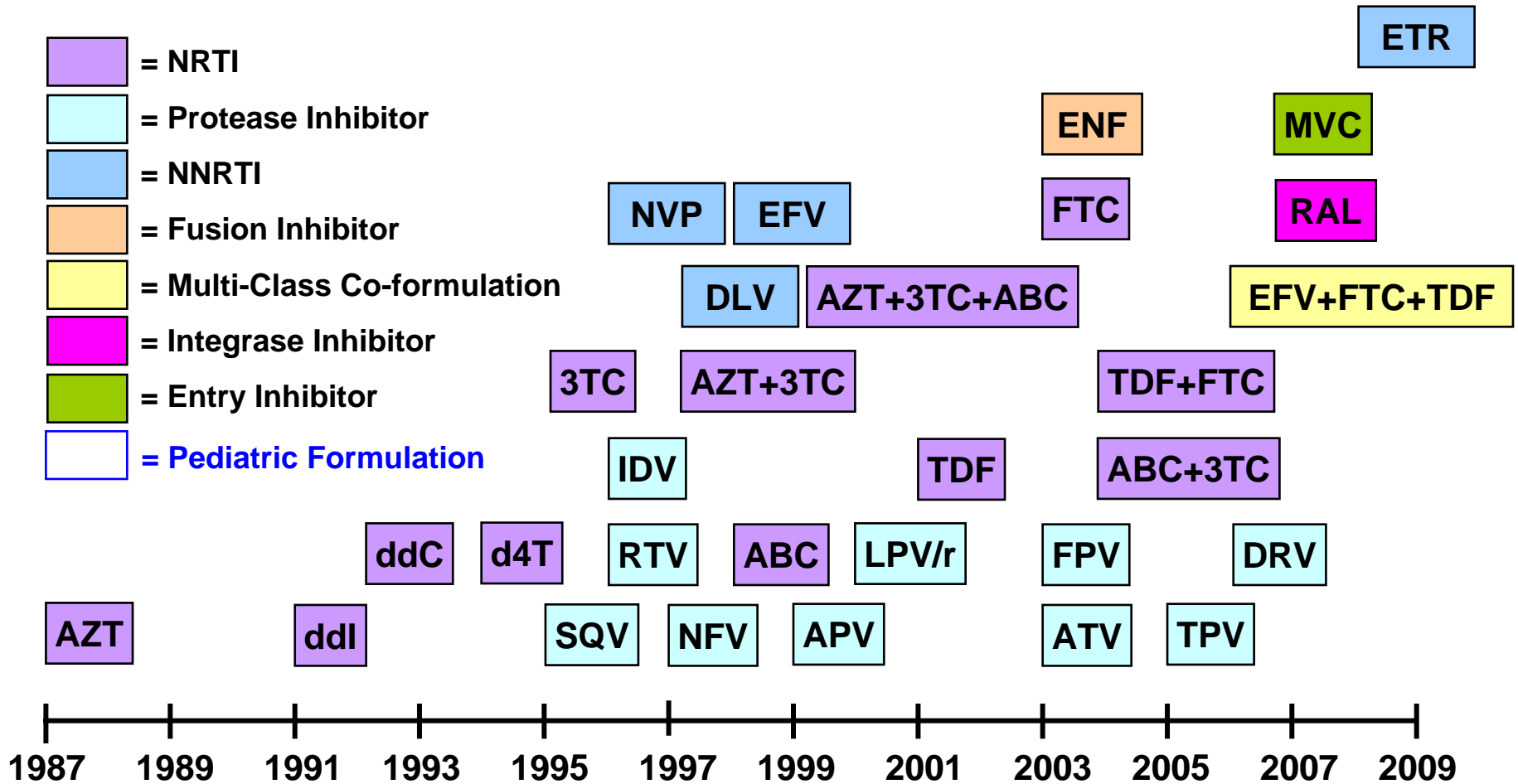
- ❑ The role of industry and current strategies
- ❑ Key challenges
- ❑ Funding ARV therapy
- ❑ Care and treatment must evolve with the pandemic
 - ❑ The goal of treatment programs is changing
 - ❑ Is more emphasis on quality of care needed?
- ❑ Access and product quality
 - ❑ Regulation and regulatory harmonization
 - ❑ Pharmacovigilance

The Role of Industry

- ❑ R & D roots – Discovery, development and introduction of ARVs
- ❑ Contributions in the fight against HIV/AIDS and the evolution of therapy
 - ❑ Significant philanthropic efforts
 - ❑ Innovation: Providing products with greater efficacy, tolerability and convenience
 - ❑ Formulations and dosing for special populations (e.g. pediatrics)
 - ❑ HIV diagnostics and therapy monitoring
 - ❑ Programs to increase access to treatment and diagnostic tools
- ❑ Leveraging industry expertise
 - ❑ Distribution and logistics
 - ❑ Post-marketing studies
 - ❑ Medical education



The Role of Industry

Development of Antiretrovirals



Key Participants and Current Strategies to provide ARVs in Resource-Limited Settings

Global Price Reporting Mechanism Database*								
Products with two or more shipments (Sub-Saharan Africa Only)								
Jan 2007 – Jan 2009								
		Aspen	Aurobindo	Cipla	Hetero	Matrix	Ranbaxy	Strides
Abbott	LPV/r							
	RTV							
B-I	NVP							
BMS	ddl							
	d4T							
Gilead	TDF-FTC							
	TDF							
GSK	ABC							
	AZT							
	AZT-3TC							
	AZT-3TC-ABC							
	3TC							
Merck	EFV							
	IDV							
Roche	NFV							
	SQV							
Various	FDCs							

-  = Shipments of approved products
-  = Product shipped, but in the absence of WHO pre-qualification or FDA tentative approval



* GPRM Database (as of 29Jan09):
<http://www.who.int/hiv/amds/price/hdd/>

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Strategic Approaches:

- Affordable tiered pricing (est. 2000-2001)
- Product licensing
- Technology transfer
- “Non-assert” or “Immunity from suit”
- Broad registration and supply of adult and pediatric formulations

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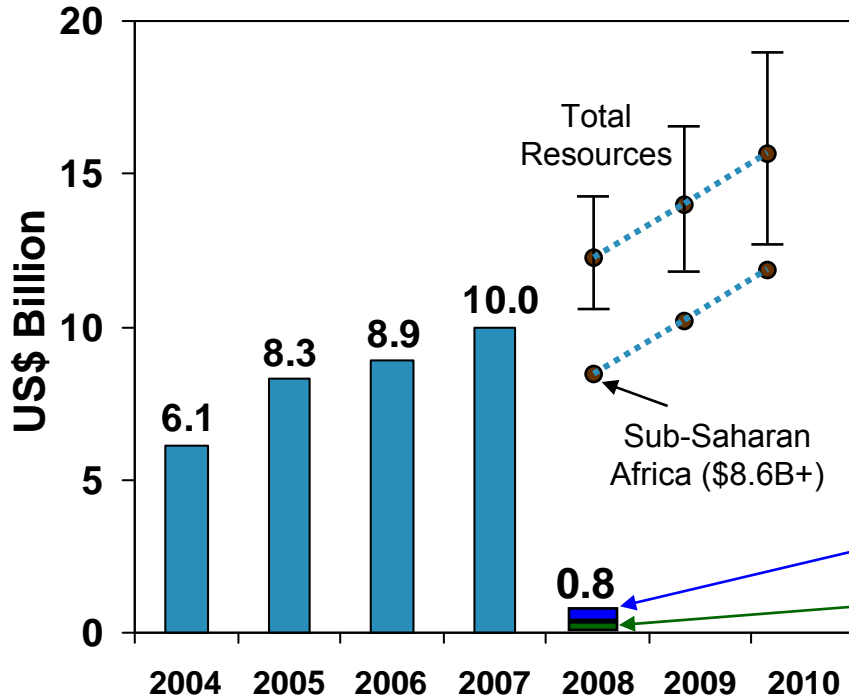
 = Protease inhibitors

Key Challenges in the Delivery of ART

- PMTCT capacity and routine testing of pregnant women
- Initiation of first-line therapy
 - Potential changes to therapy
 - When should therapy start?
- Keeping patients on therapies that work
 - Adherence counseling and support to sustain first-line treatment
 - Appropriate therapy monitoring
 - Unencumbered switching to second-line therapies as needed
- Ensuring Quality of Care
 - Care and treatment algorithms
 - Product integrity
 - Pharmacovigilance

Funding ARV Therapy and Monitoring

Estimated total annual resources available for HIV services



First Line:

2,640,000 patients x \$130 ppy = \$343MM

Second Line:

110,000 patients x \$794 = \$87MM

Viral Load:

2.8MM patients x \$50 (1 per year) = \$140MM

CD4:

2.8MM patients x \$16 x 4 per year = \$180MM

Total for ARVs and Monitoring = \$750MM

Total cost of ARVs

Total cost of Monitoring

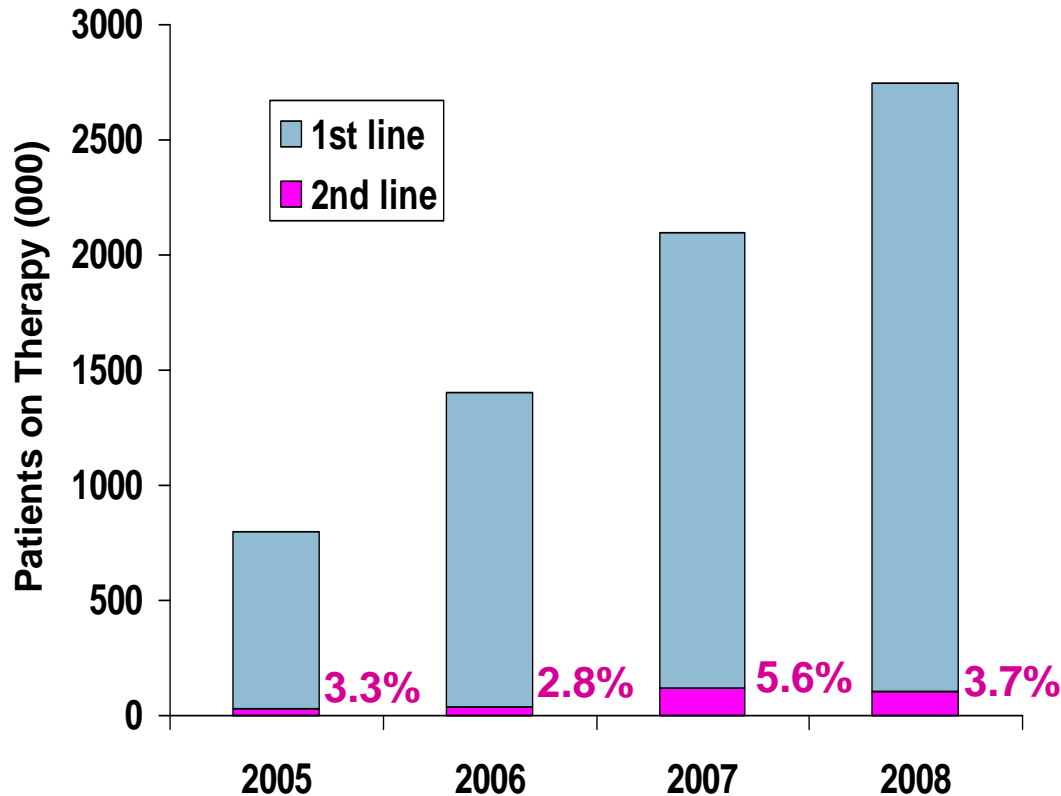
Source: 08 Report on the global epidemic; UNAIDS p. 179

Estimate of resources for for Sub-Saharan Africa (~70%) is based on Global Fund disbursements of 55-60% for sub-Saharan Africa in rounds 4-7 (<http://www.theglobalfund.org/en/distributionfunding/>); and the distribution of patients treated (72% in sub-Saharan Africa) (http://www.theglobalfund.org/documents/publications/factsheets/ARV_Factsheet_2008.pdf); 97.8% of PEPFAR patients treated in the 15 focus countries reside in sub-Saharan Africa (Celebrate Life: Latest PEPFAR Results, as of 30Sep08)

Funding ARV Therapy and Monitoring

- ❑ Currently ARV expense is a relatively low percentage of total aid for HIV but...
 - ❑ First line regimens will change to eliminate d4T and become more costly
 - ❑ More patients will move to second-line regimens (also more costly)
 - ❑ Therapy initiation at higher CD4 counts will increase patient numbers and add to the cost
- ❑ Locally, the implementers and governments who have long-term responsibility to patients are voicing concern over the predictability of aid
- ❑ It is important to anticipate a significant change in funding requirements to avoid any lapse in care for patients and continue the scale up

The Slow Pace of Second-line Therapy



Estimates of Patients on Therapy
Sub-Saharan Africa

Second-line therapy currently represents less than 5% of the total patients on therapy

- How large is the *need* for second-line therapy?
- What are the consequences of a delay in moving to second-line therapy?

Source: Total on therapy: WHO; Toward Universal Access, Progress Report 2008 pp. 18-19; 2008 is an estimate based on the trend
Second-Line: Estimates from internal (Abbott) shipment data in fiscal 4Q of each year

Extensive Resistance After First-Line Failure in Malawi

- ❑ >150,000 individuals are on ART
 - ❑ First line: NVP + d4T + 3TC
 - ❑ Second line: LPV/r + ZDV/3TC + TDF
- ❑ ART failure defined as:
 - ❑ Clinical: New/progressive WHO Stage IV condition
 - ❑ Immunologic: CD4+ decline either >50% from peak or to <BL
- ❑ Among 96 patients who failed and had confirmatory RNA >1000 c/mL, 94 had amplifiable samples for GT with extensive resistance
- ❑ Up to 50% had no active drugs left by phenotype according to second-line NRTI backbone chosen

Type and prevalence of RT mutations among 94 patients failing first-line ART

Type of mutation	Prevalence
TAMs – total	56%
Of which:	
1	16%
2	16%
≥3	24%
Q151M or 69 insertion	17%
M184V/I	81%
K65R or K70E	23%
NNRTI mutations (median of 2)	93%

Hosseinipour M, *et al.* XVII IAC, Mexico 2008, #TUAB0105

Evolution of Care and Treatment Strategies in Resource-Limited Settings

Increasing Patient Base

Vancouver Summit

Public Health Approach

WHO
3 X 5
Initiative

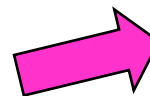
Current issues:

- Late initiation of first-line treatment
- High death rate in year 1
- Broad use of d4T
- Limited use of viral load
- First-line patients with OIs

Limited treatment

Private Market

Goal: Treat as many as possible



Goal: Suppress as much virus as possible

1998

2002

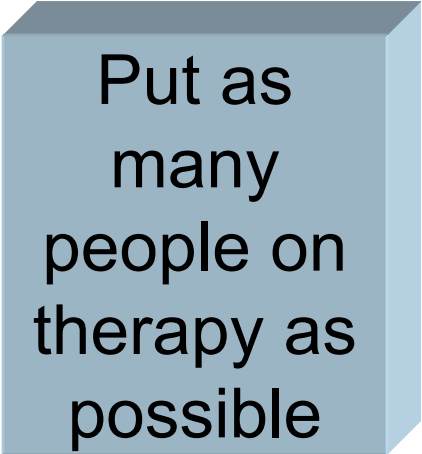
2006

2010

2014

Evolution of Care and Treatment Strategies in Resource-Limited Settings

The objective of antiretroviral treatment programs



Put as many people on therapy as possible

Activity



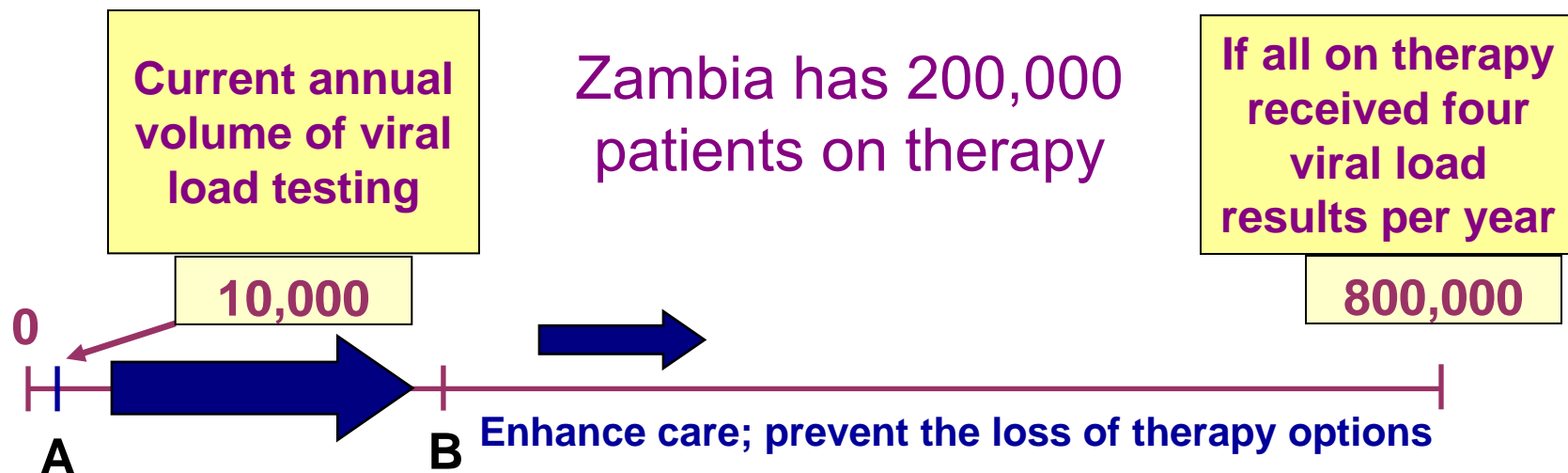
Patient-months of virus suppression per \$ million spent on therapy

Result



Viral Load

Providing Treatment that Endures Appropriate Initiation of Second-Line Therapy



- Taking viral load monitoring from point A to point B will enhance patient care
- Research to discover the approach that finds the most patients in need
 - Those on therapy longest
 - Those most likely to have an elevated viral load
 - 6 mos; 18 mos; 60 mos

Importance of Viral Load Monitoring

- ❑ When VL monitoring is not utilized, patients:
 - ❑ Don't benefit from knowing that they are controlling the virus
 - ❑ Delay benefits provided by an alternate regimen
 - ❑ Lose drug options
 - ❑ Encounter more opportunistic infections
- ❑ Economic arguments
 - ❑ Patients on failing regimens continue to take drugs that they do not benefit from (wasted resources)
 - ❑ Waiting for clinical symptoms increases the likelihood of an OI that must also be treated (at some cost and risk of mortality)
 - ❑ Using only clinical symptoms and CD4 may cause a premature switch to a more costly therapy that is not necessary

Algorithms that Assess patients with possible ART failure

PEPFAR Implemented program – Zambia

- Evaluate patient for clinical and immunological indicators of failure
- Skip viral load if both are present
- Test for viral load if evaluation is inconclusive

Government Hospital - Lusaka

- Viral Load monitoring is offered, but not free of charge
- Samples are collected; batches are run in groups of about 10
- Frequency: ~ one run per week
- Patients pay 200,000 Kwacha (~US\$40)
- Samples from other provinces are rare

Kenya

- Limited number of centers running viral load
- Yet viral load is often required before changing to a second-line therapy
- Difficulty reaching rural areas

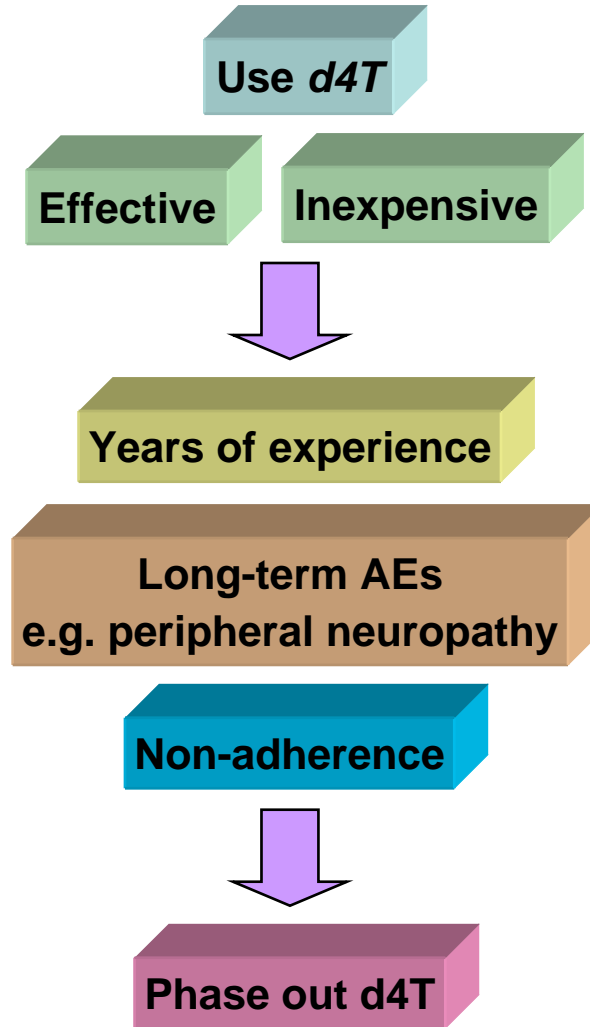
Providing Treatment that Endures

Appropriate Initiation of Second-Line Therapy

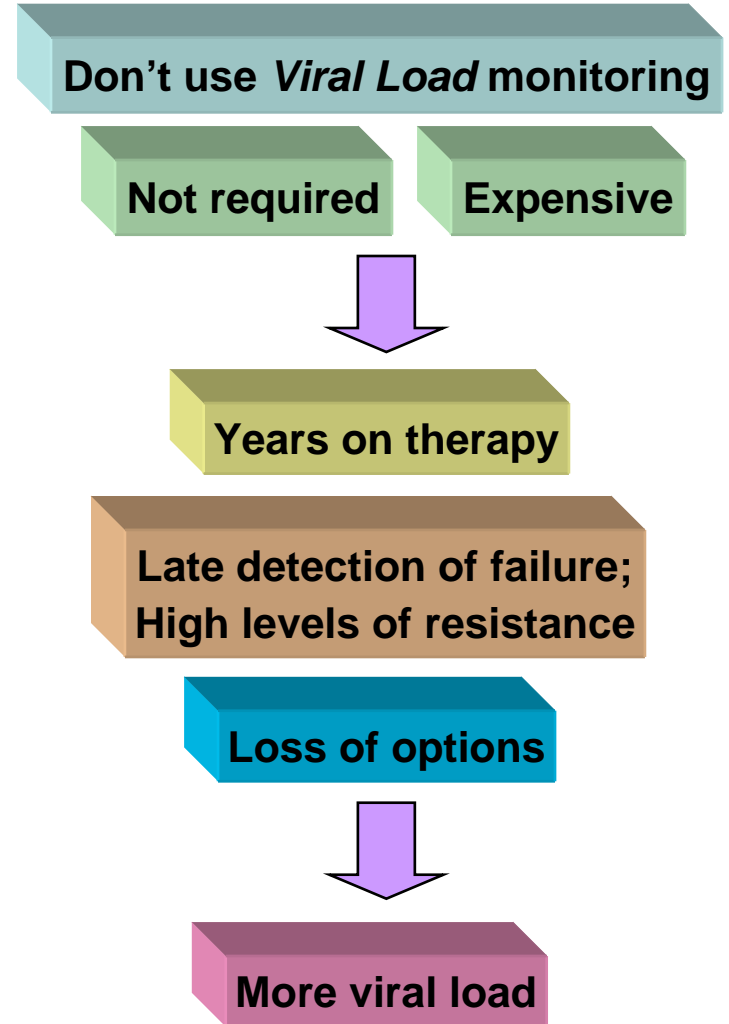
- ❑ The switch to second-line therapy starts with a patient and an assessment of therapy viability
- ❑ Hesitation to switch patients is due to barriers rooted in policy, infrastructure, knowledge, and funding (often in that order)
- ❑ Physicians need algorithms that promote appropriate, timely and cost-effective switching of failing first-line regimens (policy)
- ❑ Programs need laboratory capacity and tools that are more readily available such as a simpler CD4, viral load and DBS sampling
- ❑ All involved need greater knowledge of the complexities associated with a switch to second-line
- ❑ To achieve better healthcare access (to therapy and monitoring) there must be appropriate financial support

A Tale of Two Decisions

2000 - 2004



\$



2008 - 2012

Viral Load and the Enhancement of Care and Treatment



**Johns Hopkins Medicine (Press Release)
February 6, 2009**

VIRAL-LOAD TESTING: A BETTER WAY TO PREDICT ANTI-HIV, DRUG-TREATMENT FAILURES IN AFRICA

Call made for changes in World Health Organization monitoring guidelines

Access and Product Quality

- ❑ Product registrations facilitate access
- ❑ Regulatory harmonization facilitates registrations
- ❑ Quality built into products will facilitate harmonization efforts
 - ❑ Importance of human bioequivalence studies
 - ❑ Trust through regulation is essential in markets where counterfeits find a home
- ❑ Pharmacovigilance
 - ❑ Involves manufacturers, physicians, and regulatory authorities in monitoring product safety and effectiveness
 - ❑ ARV scale up is associated with less thorough drug surveillance than in traditional markets. Safety/efficacy issues may arise and be undetected.

Pharmacovigilance Challenges in Resource-Limited Settings

- ❑ Regulation (and pharmacovigilance) of licensed drugs is frequently weak
- ❑ Confusion due to generic and proprietary versions of the same ARV
- ❑ Drug use patterns differ
 - ❑ Therapy combinations
 - ❑ Use of traditional medicines
- ❑ Drug use in certain co-morbidities, and special populations may not have been evaluated
- ❑ Consequences
 - ❑ Potential failure to recognize a significant issue in safety/effectiveness (false negative)
 - ❑ Opportunities for inappropriate concern about a specific drug (false positive)

Pharmacovigilance

Potential solutions

- ❑ Standardized approach to pharmacovigilance across different countries
- ❑ Regional networks
- ❑ Novel surveillance approaches (e.g. active sentinel surveillance)
- ❑ Effective data pooling, pooled analyses
- ❑ Novel communication strategies - data collection and dissemination

Delivering ART in Resource-Limited Settings

Conclusions

- ❑ Industry plays a critical role
- ❑ Challenges and knowledge gaps abound
 - ❑ PMTCT
 - ❑ First-line: changing the regimen and making first line more durable
 - ❑ The slow pace of second-line initiation
- ❑ Treatment program objectives require a “results orientation”
 - ❑ Promote “virus suppression” along with maximum coverage
 - ❑ Develop algorithm recommendations that accurately assess patient status
 - ❑ A higher level of care will require more resources
- ❑ Expand the use of viral load to optimally enhance patient care
- ❑ Encourage regulatory harmonization
- ❑ Focus on both quality and quantity including an appropriate emphasis on human bioequivalence and pharmacovigilance



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Tibotec

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