Treatment and Care: Product portfolio

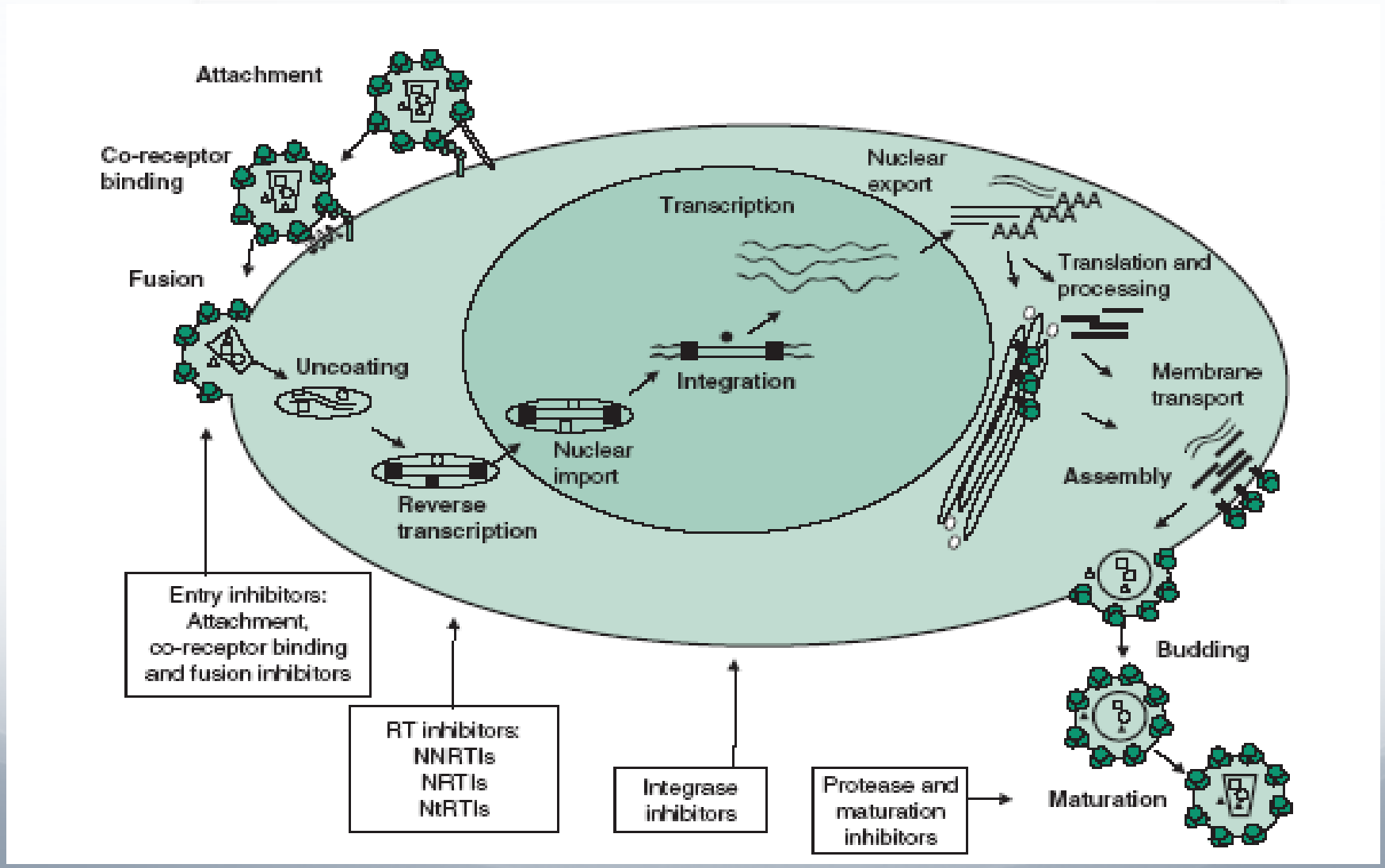
Dr Paula Munderi
MRC/UVRI Uganda Research Unit on AIDS

EDCTP Stakeholder Meeting on HIV/AIDS
3-4 September 2013

Summary

- Brief overview HIV Treatment Pipeline
- Key Questions & Challenges
- EDCTP role

Targets for Antiretroviral Drugs in HIV Life Cycle



Reeves & Piefer, 2005

Approved products & Sponsors

2003 - 2012

Emtricitabine 2003 Gilead

Etravirine 2008 Janssen
Rilpivirine 2011 Janssen

Atazanavir 2003 BMS
Fosamprenavir 2003 Vertex/GSK
Tipranavir 2005 BI
Darunavir 2006 Janssen

Enfurvitide 2003
Trimeris / Hoffman LaRoche

Maraviroc 2007 Pfizer

Raltegravir 2007 Merck

ARV Class	Total Products	Phase I	Phase II	Phase III	Approved	Submitted	Discontinued
NRTI (NtRTI)	12	1	2		1	1	7
NNRTI	8	1	1		3		3
Protease Inhibitor	6				4		2
Fusion Inhibitor	1				1		
CCR5RI/2RI	4		1		1		2
Intergrase Inhibitor	5	1	1	1	1	1	
Attachment Inhibitor	4		1				3
	40	**3**	**6**	**1**	**11**	**2**	**17**

2012 PIPELINE REPORT, JULY 2012. i-Base/**T**reatment Action Group

FDCs approved in 2003-2012

		Trade name	Sponsor
2003	Abacavir/Lamivudine	*Epzicom*	GSK
2004	Tenofovir/Emtricitabine	*Truvada*	Gilead
2006	Efavirenz/Emtricitabine/Tenofovir	*Atripla*	BMS / Gilead
2011	Rilpivirine/Emtricitabine/Tenofovir	*Complera / Eviplera*	Janssen/Gilead

2012 PIPELINE REPORT, JULY 2012. i-Base/**T**reatment Action Group

25 single products in 6 “classes” & still counting, but key questions remain…

Tolerability

Resistance

Convenience

Special Populations

Cost

Focus of research: to overcome limitations of current regimens

Improving Tolerability …

- new product development
- reformulation

NRTI Class – Tenofovir is preferred product today

Reformulation –Tenofovir Alafenamide (TAF)

similar safety and efficacy to Tenofovir DF
Improved bio availability
potentially reduced side effects.
[CROI 2013]

25 mg dose selected for development as single agent
10 mg dose in FDC with cobicistat (PK booster)

Ongoing studies: co-formulations of TAF, FDC with Darunavir

Dosage Optimisation Studies

Reducing dose of ARVs in current use

- Efavirenz
- AZT
- d4T
- Atazanavir/Ritonavir

+ Cost reduction through reduction in API

? Role for EDCTP in treatment optimisation research

Special Populations

Children

- Appropriate formulations
- Product approval for children

? Dolutegravir /Abacavir/Lamivudine

HIV TB co-infection

- Rifabutin + Boosted PIs & Intergrase Inhibitors

Women of child bearing age

Post registration surveillance

? Role for EDCTP: include post registration surveillance

Clinical Trial Capacity in Africa

- suitable sites with trained personnel
- sufficient resources & infrastructure
- appropriate regulatory & ethical oversight

? Consolidation of clinical trial capacity building started in EDCTP 1

Diagnostic tests

- Toxicity
  - Haematology, Renal function, Lipids & Glucose
- Diagnosis of Co-infections – HepB, HepC
- Efficacy – CD4, Viral Load
- Resistance testing

? Role of EDCTP in development and implemenattion of POCs

HIV Cure Research

Eradication of the “HIV Reservoir”

- Lack of assays to quantify the reservoir
- Products very experimental

- More clarity within next 10 years
- Africa should participate

  ANRS : studies in children & early treatment studies in adults aimed

? EDCTP as a partner in HIV Cure Research Strategy

Questions

How can EDCTP best enhance the HIV treatment product pipeline for developing countries ?

- A role for EDCTP in post marketing research

e.g. dosage - optimisation, reformulation, co-formulation how can this be effected?

- Would it be better to focus on the needs of special populations?

How can EDCTP consolidate contribution to clinical trial capacity building, so African sites to participate in HIV treatment development? What is the best model for this capacity building?

There is a role for EDCTP in the development validation and establishment of diagnostic tests for viral load, CD4, antiviral toxicities and important co-infections, to monitor efficacy and safety of HIV treatement. – how can this be defined ?

Future research in HIV Cure: should EDCTP remain open to this field ?