

# Drug Resistance

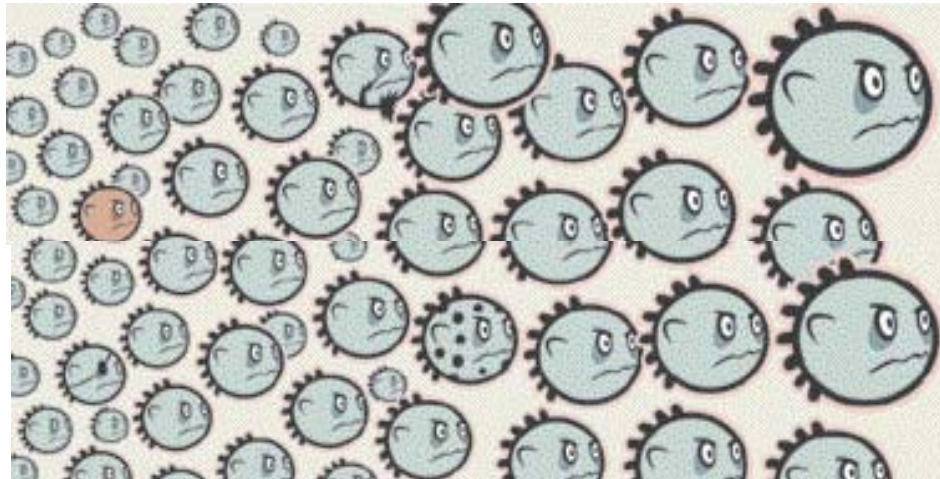
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MTN-009 Training  
Durban, South Africa  
May 7, 2010



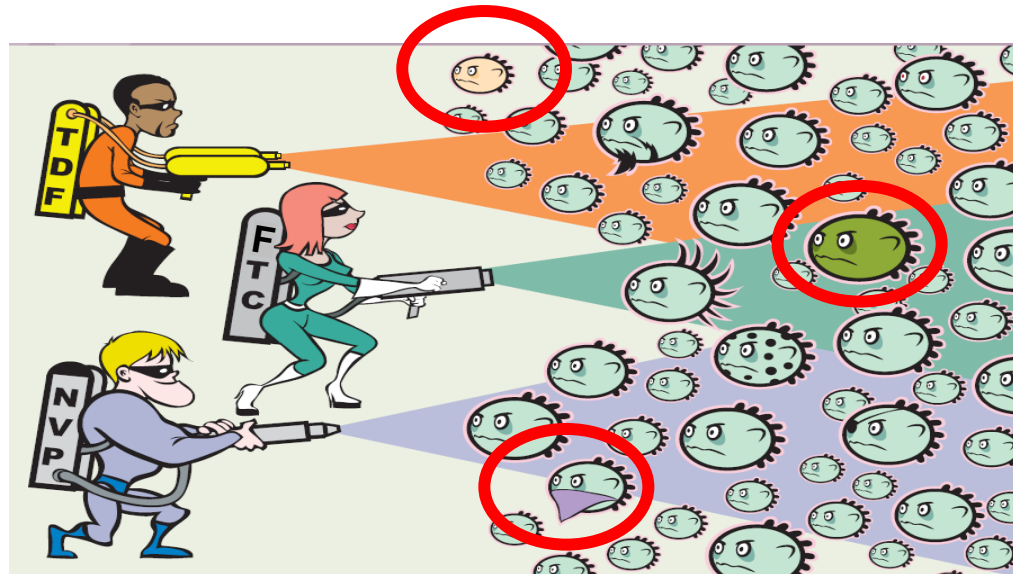
# What is HIV drug resistance?

- ❑ **Drug Resistance** = loss of effectiveness of one or more ARVs (a drug used to treat HIV)
- ❑ Drug resistance is caused by changes in HIV's genetic material
- ❑ These changes are called **MUTATIONS**



# How Drug Resistance Occurs

- HIV medications are best at treating the “wild-type” (regular) not the mutated virus
- HIV makes mistakes each time it copies itself, creating mutations



- If a mutation differs in just the right way, it can render an HIV medication less effective or useless.

# How can drug resistance occur?

## □ In an HIV positive person on ARV

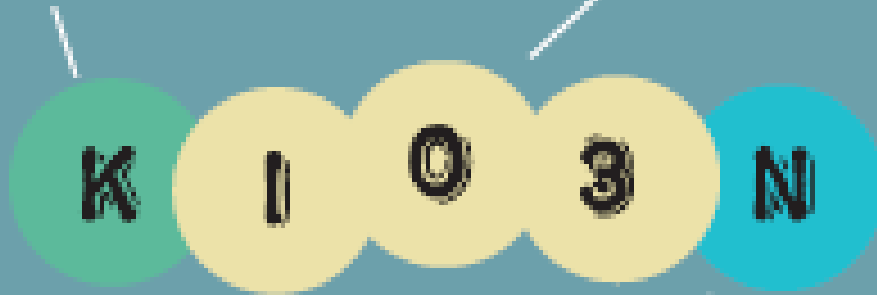
Suppose someone frequently misses a dose. HIV will grab this opportunity to start making more copies of itself. As the amount of HIV in their body increases while they are not taking their medications consistently, so does the amount of mutated HIV—including mutations that make their virus resistant to their medications.

# How can drug resistance occur?

- **Question:** How can someone be resistant to HIV medications if they have never taken them?
- **Answer:** Most likely, the person they got HIV from may have been on HIV treatment and his or her virus may have become resistant to one or more HIV medications

# How to describe mutations

Code letter for the amino acid lysine.



Specific spot or "codon" within HIV's RNA where the mutation is.

Code letter for asparagine, which took lysine's place at codon 103. Because asparagine is there instead of lysine, this copy of HIV is a mutation.

Scientists have given a letter and number to describe HIV's genetic material

The **NUMBER** shows where the mutation occurred.

The **LETTER** shows how it changed.

# Why do I need to know the terminology?

- This is how resistance is reported.
- You will see these letters and numbers on the participant's drug resistance report.
- The mutation pattern will let you know what drugs the participant is “resistant” to
- This also helps the physician know what drugs to prescribe to the participant to treat their HIV infection

# EXAMPLES OF MUTATIONS

HIV that has the mutation...	Makes this drug less effective
K103N	Nevirapine, Efavirenz
M184V	3TC, FTC
K65R	Tenofovir

There are databases and algorithms to try to figure out what mutations cause resistance to which drugs. This is an area where research is ongoing.



# Question

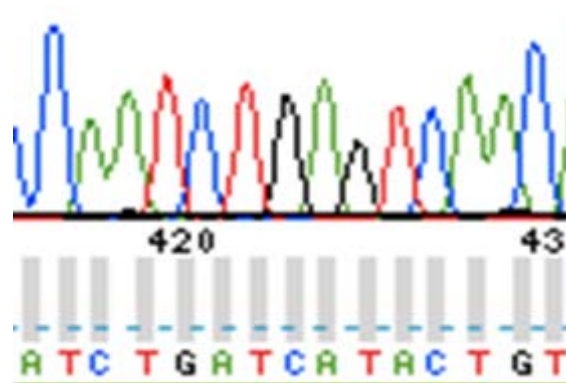
- Can HIV have more than one mutation?
  - YES
  - NO



HIV can be resistant to one drug or multiple drugs

# Drug Resistance Testing in MTN-009

- Participants who are **HIV POSITIVE**
  - Will get a drug resistance test
  - This test will be done at NL
  - Results will be sent ideally within 3 months
  - Participants will need to be counseled on the results of their test



Who will **NOT**  
get a  
resistance  
test result in  
MTN-009?

✓ HIV NEGATIVE  
participants

✓ Participants whose  
VL is  $< 200$  copies/ml  
(there is not enough  
virus to test)

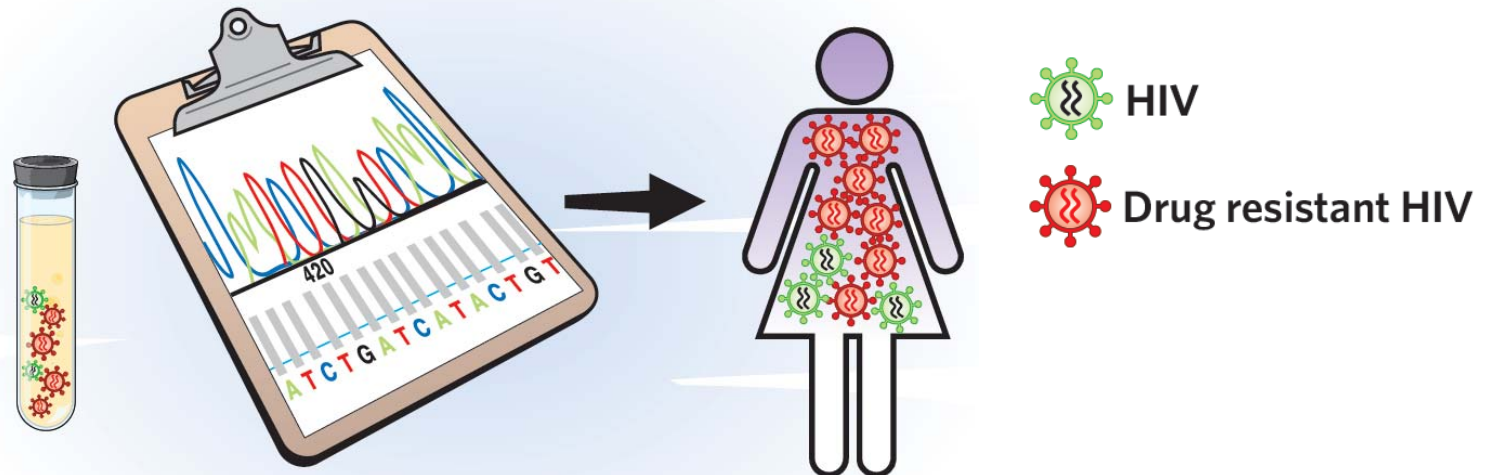
✓ If the resistance  
test fails (this is rare  
but can happen)

# When providing resistance results:

- **Explain to the participant:**
  - What the test measured
  - What the results signify
  - How the results may impact the effectiveness of certain types of antiretroviral medications
  
- **The participant should also know:**
  - If she consents, the study site will share these results with her doctor.

# What does a drug resistance test measure?

- A drug resistance test identifies which mutations are present in the majority of HIV viruses in the plasma



# Resistance Results Interpretation

- The results will indicate which ARVs have reduced effectiveness
- Each HIV drug has its own resistance result, which can be:
  - **NONE**
  - **POSSIBLE RESISTANCE**
  - **RESISTANCE**

# What do results mean?

<b>NONE</b>	There is no evidence of resistance to this drug
<b>POSSIBLE RESISTANCE</b>	There is some evidence of resistance but it may not have been validated or clinically verified
<b>RESISTANCE</b>	This drug is reduced in effectiveness

# Example of Results

(The report will be discussed in detail later this afternoon.)

Drug	Evidence of Resistance
<i>EPIVIR®</i> (lamivudine, 3TC)	<i>Possible Resistance*</i>
<i>EMTRIVA®</i> (emtricitabine, FTC)	<i>Possible Resistance*</i>
RETROVIR® (zidovudine, AZT)	Resistance*
VIDEX® (didanosine, ddl)	Resistance*
ZERIT® (stavudine, d4T)	None
ZIAGEN® (abacavir, ABC)	None
VIREAD® (tenofovir, TDF)	None

Only the participants physician can decide which ARVs she should take.

How would you describe these results?



# Tips for Resistance Counseling

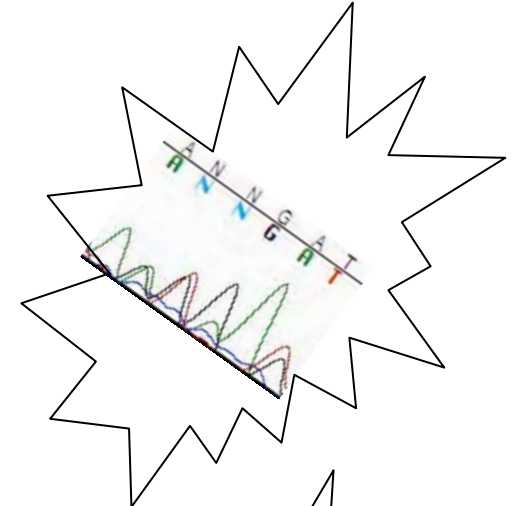
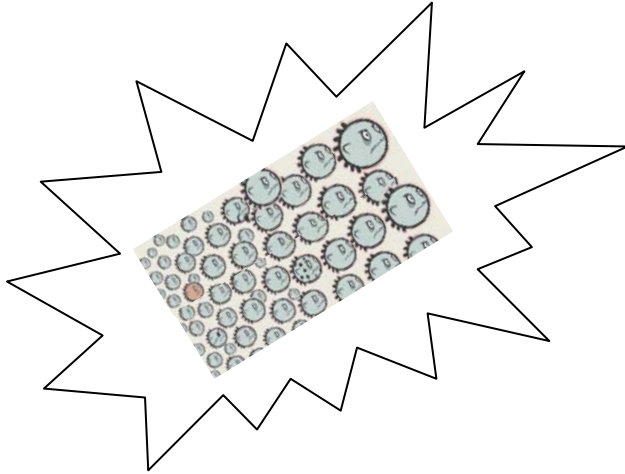
- Resistance could be hard to understand, encourage the participant to ask questions. Assess participant's understanding
- Emphasize the importance of taking medications as instructed
- If a participant's test results show resistance to a medication, explain to her that resistance to a drug does not automatically mean she can no longer use it. There are different degrees of resistance.



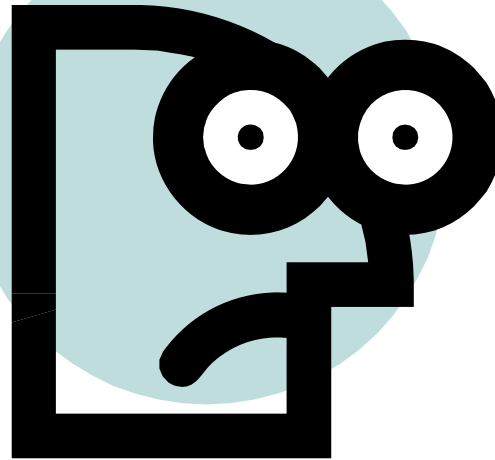
# Tips for Resistance Counseling

- Before the counseling, discuss with clinical staff the meaning of results and the best method forward for this participant
- Remind participants that if needed, additional counseling is available to ensure understanding of the information
- Provide referrals and follow-up on the referrals
- Explain to the participant the importance of these referrals

# Questions?



```
ATTCTGGACATAAAGACAAGGACCAAAG  
AACCCCTTTAGAGACTATGTAGACCGGT  
CTATAAAACTCTAAAGCCGAGCAAGT  
TCACAGGAGGTA AAAAATTGGATGACAG  
AAACCTTGTGGTCCAAAATGCCAAACC  
AGATTGTAAGACTATTTAAAGCATTG  
GGACCAGCAGCTACACTAGAAGAAATGA  
TGACCCATAAGCCAAAGATTTTGGCTGAA  
CGCCATAAGCCAAAGATTTTGGCTGAA  
GCAATAATGATGCAAAAGAGGCAATTTAG  
GAACCAAAGAAAGATTGTTAAGTGTTC  
AATTGTGCCAAAGAAGGGCACATAGCCA
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K103N

# Counseling Role Play

- The participant's resistance report has "NONE" listed for all ARVs.

Drug	Evidence of Resistance
(lamivudine, 3TC)	None
(emtricitabine, FTC)	None
(zidovudine, AZT)	None
(didanosine, ddl)	None
(stavudine, d4T)	None
(abacavir, ABC)	None
(tenofovir, TDF)	None

# Counseling Role Play

- The participant's resistance report shows that the only NNRTI without resistance is etavirine, which is not available in South Africa.

RESCRIPTOR®	(delavirdine, DLV)	Resistance*
SUSTIVA®	(efavirenz, EFV)	Resistance*
VIRAMUNE®	(nevirapine, NVP)	Resistance*
INTELENCE™	(etravirine, ETR)	None

# Counseling Role Play

- The participant's resistance report shows possible resistance to 3TC and FTC.

<b>Drug</b>	<b>Evidence of Resistance</b>
<i>(lamivudine, 3TC)</i>	<i>Possible Resistance*</i>
<i>(emtricitabine, FTC)</i>	<i>Possible Resistance*</i>

# Counseling Role Play

- You see that the result is listed as “None” for all drugs except Nelfinavir. You look at the mutation table, and see that V179D is listed. Should you be worried?

PREZISTA®	(darunavir, DRV)	None
VIRACEPT®	(nelfinavir, NFV)	Possible Resistance
REYATAZ®	(atazanavir, ATV)	None
APTIVUS®	(tipranavir, TPV)	None