



Southern African HIV Clinicians Society

3rd Biennial Conference

13 - 16 April 2016
Sandton Convention Centre
Johannesburg

**Our Issues, Our Drugs,
Our Patients**

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ART beyond the second-line regimen: Adult third-line ART

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14 Apr 2016

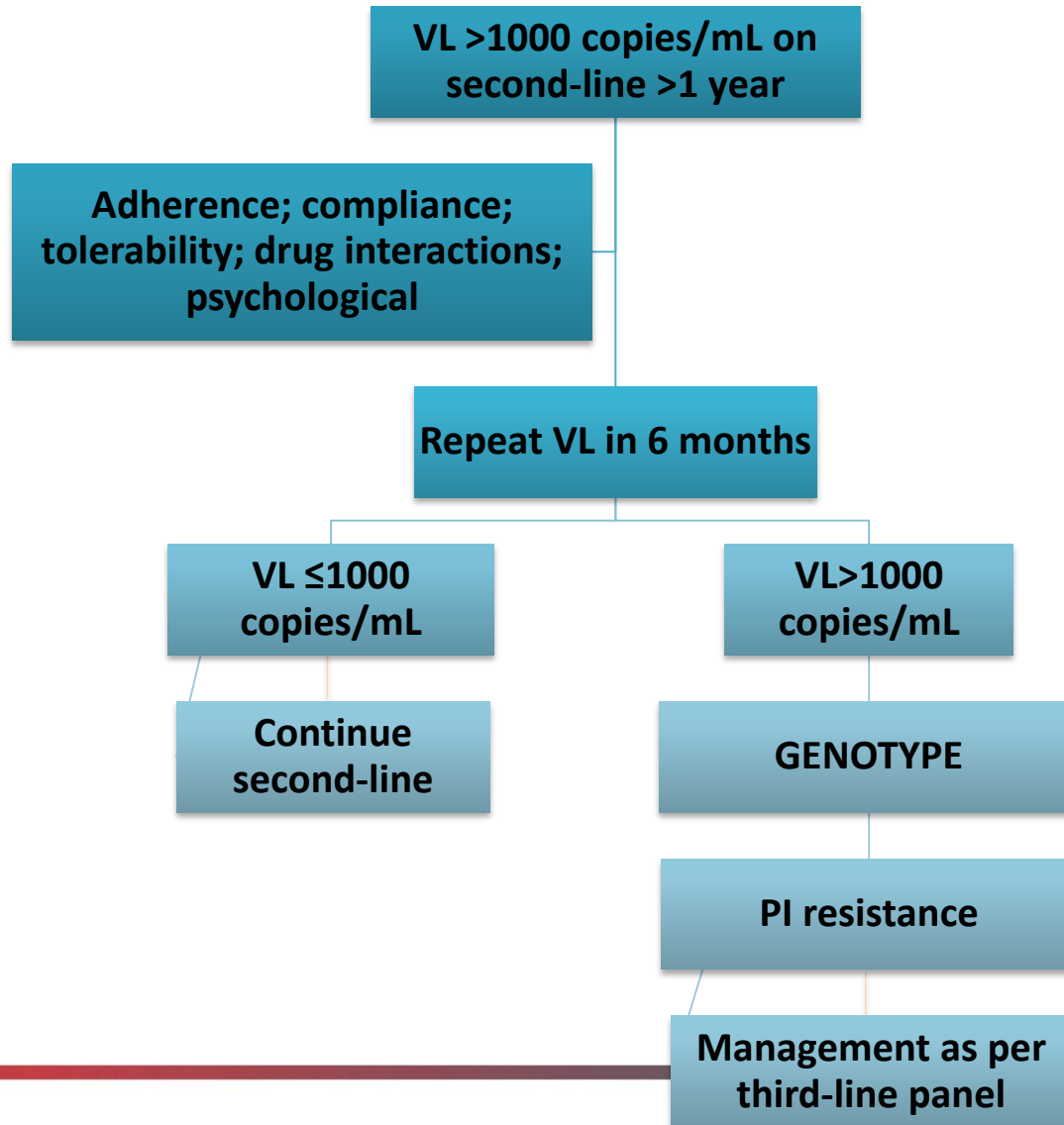


2016

Management of treatment failure after second-line

- Standardised first- and second-line regimens
 - Efficacy, safety and tolerability
 - Predictable resistance mutations that develop after first-line failure
- Second-line should achieve viral suppression
- Provision for third-line, controlled by expert panel
- Third-line drugs approved by panel sent to facility on named patient basis

Diagnosis of second-line failure



Third line eligibility

Adults on PI regimen not fully suppressed at 12 months

Genotype resistance test

PI resistance: full treatment history to third-line panel

Documented resistance to PI/r in current regimen

Access to third-line drugs, including **DRV/r**, **etravirine** and **raltegravir**

Send it to:

Facility completes motivation form and submits to the Secretariat: Third Line ARV Peer Review Committee (PRC)

TLART@health.gov.za

Important to note:

- Facility name and address
- Patient information



2016

COMPILING A THIRD-LINE REGIMEN



2016

Stanford score

| | ATV/r | DRV/r | FPV/r | IDV/r | LPV/r | NFV | SQV/r | TPV/r |
|---------------|--------------|--------------|--------------|--------------|--------------|------------|--------------|--------------|
| I54V | <u>15</u> | <u>0</u> | <u>10</u> | <u>15</u> | <u>15</u> | <u>20</u> | <u>15</u> | <u>20</u> |
| V82A | <u>15</u> | <u>0</u> | <u>15</u> | <u>30</u> | <u>30</u> | <u>30</u> | <u>15</u> | <u>0</u> |
| L10F | <u>0</u> | <u>5</u> | <u>10</u> | <u>10</u> | <u>5</u> | <u>10</u> | <u>0</u> | <u>0</u> |
| T74S | <u>0</u> | <u>0</u> | <u>0</u> | <u>0</u> | <u>0</u> | <u>15</u> | <u>0</u> | <u>0</u> |
| I54V+V82A | 10 | - | 10 | 10 | 10 | 10 | 10 | - |
| V82A+L10F | - | - | 10 | - | - | - | - | - |
| Total: | 40 | 5 | 55 | 65 | 60 | 85 | 40 | 20 |

| RT | 3TC | ABC | AZT | D4T | DDI | FTC | TDF | EFV | ETR | NVP | RPV |
|---------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| M184V | <u>60</u> | <u>15</u> | <u>-10</u> | <u>-10</u> | <u>10</u> | <u>60</u> | <u>-10</u> | - | - | - | - |
| T215F | <u>5</u> | <u>15</u> | <u>45</u> | <u>45</u> | <u>15</u> | <u>5</u> | <u>15</u> | - | - | - | - |
| K219Q | <u>0</u> | <u>5</u> | <u>10</u> | <u>10</u> | <u>5</u> | <u>0</u> | <u>5</u> | - | - | - | - |
| K103C | - | - | - | - | - | - | - | <u>0</u> | <u>0</u> | <u>0</u> | <u>0</u> |
| V106M | - | - | - | - | - | - | - | <u>60</u> | <u>0</u> | <u>60</u> | <u>0</u> |
| Y188F | - | - | - | - | - | - | - | <u>60</u> | <u>0</u> | <u>30</u> | <u>30</u> |
| M230L | - | - | - | - | - | - | - | <u>45</u> | <u>30</u> | <u>60</u> | <u>45</u> |
| Total: | 65 | 35 | 45 | 45 | 30 | 65 | 10 | 165 | 30 | 150 | 75 |



**Eligible for third
line ART?**
PI score ≥ 15

DRV/r
PLUS
3TC/FTC
PLUS
AZT/TDF
(lowest score)

TDF/AZT 30-59
OR
DRV ≥ 15

Add RAL

TDF/AZT > 29
AND
DRV ≥ 15
AND
ETR ≤ 29

Add ETR



ADULT THIRD-LINE COHORT OVERVIEW



2016

Applications received to date

| | No of applications | Outcome |
|--------------|--------------------|--------------------------------|
| Adult | 470 | 392 prescribed TLART |
| Paeds | 191 | 78 prescribed TLART |
| | | 82 prescribed holding regimens |

Methodology

- Cross sectional analysis and descriptive statistics
- Criteria for third-line eligibility
 - At least one year PI-based ART
 - Virological failure despite adherence optimisation
 - Genotypic ARV resistance
 - Stanford PI score >15 for LPV/ATV
- Data on age, gender, duration prior ART and 3 previous CD4 counts and viral loads collected
- Ethics approval

Cohort description

| Factor | Median | IQR |
|--------------------------------|--------------------|---------------|
| Age | 41 | 24- 47 |
| CD4 at submission | 170 | 127 - 337 |
| VL at submission | 17 013 | 396 – 104 178 |
| | | % |
| Male | | 40 |
| Year of ART initiation | <2004 | 14 |
| | 2004 - 2007 | 53 |
| | 2008 – 2011 | 33 |
| | | |
| Year of second-line initiation | <2004 | 5 |
| | 2004 - 2007 | 22 |
| | 2008 - 2011 | 62 |
| | 2012 – 2013 | 11 |

Resistance profiles of cohort

| ARV class | ARV | % |
|-----------|------------|----|
| NNRTI | efavirenz | 74 |
| | nevirapine | 77 |
| | etravirine | 37 |
| NRTI | lamivudine | 85 |
| | zidovudine | 72 |
| | tenofovir | 69 |
| | abacavir | 92 |
| PI | lopinavir | 97 |
| | atazanavir | 98 |
| | darunavir | 57 |

CHOICE OF REGIMENS



2016

**Eligible for third
line ART?**
PI score ≥ 15 **145**

DRV/r **145**
PLUS
3TC/FTC
PLUS
AZT/TDF (lowest
score)

TDF/AZT 30-59
OR
DRV ≥ 15

Add RAL **106**

TDF/AZT > 29
AND
DRV ≥ 15
AND
ETR ≤ 29

Add ETR **33**



Outcome

152 applications

146 resistance tests

145 received third-line ART

117 with ≥ 1 VL

102 with VL < 400 copies/mL (94%)

Conclusions

- Patients failing second-line with PI resistance have high level of resistance to drugs available in public sector
- NOT surveillance of resistance in community
- Algorithm developed to streamline process
- 102/117 patients with follow up VL are virologically suppressed (<400 copies/mL)

Acknowledgements

- TLART committee
- Francesca Conradie
- Matt Fox
- Natisha Jagaroo
- DOH



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