Antiretroviral resistance at virologic failure in the NEAT 001/ANRS 143 trial: Raltegravir + Darunavir/ritonavir or Tenofovir/Emtricitabine + Darunavir/ritonavir as first line antiretroviral therapy

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Running Head: Resistance of first-line raltegravir + darunavir/r at virologic failure

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OBJECTIVES: To describe the pattern of drug resistance at virologic failure (VF) in the NEAT001/ANRS143 trial (first-line treatment with ritonavir-boosted darunavir plus either tenofovir/emtricitabine or raltegravir).

METHODS: A genotypic testing was performed at baseline for reverse transcriptase (RT) and protease genes and for RT, protease and integrase (IN) genes for patients with a confirmed viral load (VL) > 50 copies/mL or any single VL > 500 copies/mL at or after week 32.

RESULTS: A resistance test was obtained for 110/805 (13.7%) randomised participants qualifying for resistance analysis (61/401 of RAL arm and 49/404 of TDF/FTC arm). No resistance associated mutation (RAM) was observed in the TDF/FTC+DRV/r arm, and all further analyses are limited to the RAL+DRV/r arm. In this group, 15/55 (27.3%) participants had viruses with IN RAM (12 N155H alone, 1 N155H + Q148R, 1 F121Y and 1 Y143C), 2/53 (3.8%) with NtRTI RAM (K65R, M41L), and 1/57 (1.8%) with primary protease RAM (L76V). The frequency of IN mutations at failure was significantly associated with baseline VL: 7.1% for VL <100,000 copies/mL, 25.0% for VL ≥100-500,000 copies/mL, and 53.8% for VL ≥500,000 copies/mL ($P_{TREND}=0.007$). Of note, 4/15 participants with IN RAM had a VL <200 copies/mL at time of testing.

CONCLUSION: In the NEAT001/ANRS143 trial, there were no RAM at VF in the standard DRV/r+TDF/FTC regimen, contrasting with rate of 29.5% in the DRV/r+RAL NtRTI-sparing regimen (mostly IN mutations). Cumulative risk of IN RAM after 96 weeks follow-up in participants initiating antiretroviral therapy with DRV/r + RAL was 3.9%.
In Europe, a combination of 2 nucleoside or nucleotide analogue reverse transcriptase inhibitors (NtRTI) and a non-nucleoside analogue reverse transcriptase inhibitor (NNRTI), a ritonavir boosted protease inhibitor (PI) or an integrase strand transfer inhibitor (ISTI) is recommended for initial therapy for HIV-1 infected patients. The tolerability and toxicity profile of NtRTIs in particular the cardiovascular risk with abacavir and bone and renal toxicity with tenofovir has led to the research of NtRTI-sparing alternative antiretroviral combinations. NEAT 001/ANRS 143 was an European open-label, non-inferiority, phase III randomised trial that evaluated the efficacy of the NtRTI-sparing regimen raltegravir plus darunavir and ritonavir (RAL+DRV/r) versus a standard of care regimen tenofovir/emtricitabine plus darunavir and ritonavir (TDF/FTC+DRV/r) in treatment-naïve adults. This study showed the non-inferiority of the NtRTI sparing strategy (RAL+DRV/r arm) versus the standard arm but only in participants with baseline CD4 cell counts > 200 cells/mm³. As described in the main study report, genotypic analysis was done at screening and at all visits from 32 weeks onwards for participants who had HIV-1 RNA ≥ 500 copies/mL. Among participants who underwent genotype testing to assess emerging resistance at the time of virological failure, treatment-emergent resistance was seen in no participants in the standard of care-group and in six (21%) of 29 in the NtRTI sparing group, five of whom had resistance to integrase (IN) and one to NtRTI. While IN-associated resistance frequency and profile are somewhat well characterized with RAL, when used in combination with TDF/FTC, there is little information when RAL is combined with DRV/r in a randomised study. Therefore, the objective of the present study, was to describe the full resistance profile at virological failure and to determine factors associated with the development of IN-resistance mutations.
METHODS

Study design

NEAT 001/ANRS 143 was an European open-label, non-inferiority, phase III randomised trial conducted in 15 European countries. Eight hundred five participants were randomised in a 1/1 ratio to receive 400 mg twice daily raltegravir plus 800 mg darunavir and 100 mg ritonavir once daily (n=401) or tenofovir/emtricitabine in a 245 and 200 mg fixed dose combination once daily plus 800 mg of darunavir and 100 mg of ritonavir once daily (n= 404).

Eligible individuals had baseline plasma VL > 1000 copies/mL and no evidence of major IAS-USA resistance mutations on genotype testing, historically or at screening. The primary endpoint was the time to virological or clinical failure, with preplanned subgroup analyses of the primary endpoint by baseline CD4 cell count and HIV-1 RNA concentration. Ethics committee approval was obtained from all participating centres, in accordance with the principles of the Declaration of Helsinki. All trial participants gave written informed consent.

Genotypic resistance analyses and interpretation

The criteria for genotypic testing was a confirmed viral load (VL) > 50 copies/mL or any single VL > 500 copies/mL at or after W32. In addition, insufficient virological response was defined as decrease <1 log_{10} copies per mL in HIV-1 RNA concentration at week 18, or an HIV-1 RNA concentration ≥ 400 copies/per mL at week 24. In this situation of insufficient virological response before week 32, decision to perform genotypic testing and/or change in treatment was optional and left to the clinician. Although protocol-defined virological failure was considered at or after W32, genotypes done before because of insufficient virological response were included in the resistance analysis. In patients with multiple virological
failures, we analysed all available resistance tests available, resistance developed on second-
line therapy was not considered in the analysis. Bulk sequences of the reverse transcriptase
(RT), protease and integrase (IN) genes on RNA were determined using the ANRS consensus
technique primer sequences described at http://www.hivfrenchresistance.org. In the main
results paper,\textsuperscript{7} resistance mutations were interpreted according to the 2009 IAS-USA list of
mutations (reference list used at time of inclusion) and in the present study with the 2014
IAS-USA version \textsuperscript{11}. A genotypic testing at baseline was performed for RT and protease
genes, at each site local laboratory and for RT, protease and IN genes at virological failure,
mainly in the Pitié-Salpêtrière Virology Laboratory. Only data from participants with a
successful genotypic test were available for the analyses. To assess potential factors
associated with resistance development in participants treated with DRV/r + RAL, the
baseline characteristics of viral load and CD4+ T-cell count were evaluated.

\textbf{Statistical analyses}

The Kaplan Meier method was used to estimate cumulative proportion of patients with IN
resistance in the NtRTI-sparing strategy, assuming that patients who did not virologically fail
did not develop resistance. Chi squared tests, rank sum tests and tests for trend were used
to compare characteristics at baseline and failure between participants who developed at
least one IN resistance mutation and those who did not.
Overall, 127 participants (69/401 in the RAL+DRV/r arm and 58/404 in the TDF/FTC+DRV/r arm) met the criteria for genotypic testing with, at or after W32, either a confirmed viral load (VL) > 50 copies/mL or at least one VL > 500 copies/mL. Baseline characteristics of participants are reported in table 1. At least one resistance test was obtained for 110 participants (61 in the RAL+DRV/r arm and 49 in the TDF/FTC+DRV/r arm), although not all tests were successful in all genes. Median (IQR) HIV RNA at time of genotype testing was significantly different in participants who failed between the 2 arms: 373 copies/mL (IQR: 110-1064) in the RAL+DRV/r arm vs 133 copies/ml (IQR: 67-568) in the TDF/FTC+DRV/r arm; p-value=0.02. In the TDF/FTC+DRV/r arm, among the 49 participants who met criteria for genotypic testing and successfully had genotypic resistance test, no major IAS-USA resistance mutations were observed; thus all further analyses are limited to the RAL+DRV/r arm. Of the 61 genotypes tested in the RAL+DRV/r arm, we obtained 55, 53 and 57 sequences for IN, RT and protease gene, respectively. At baseline none had major IAS RT and protease resistance mutations detected by Sanger sequencing. In those with at least one successful genotypic test, 15/55 (27.3%) in the RAL DRV/R arm had viruses with IN resistance mutations (12 N155H alone, 1 N155H + Q148R, 1 F121Y and 1 Y143C), 2/53 (3.8%) with NtRTI resistance mutations (K65R, M41L), and 1/57 (1.8%) with a primary protease mutation (L76V) (Table 2). Three patients presented minor IN resistance mutations (L74M or T97A) that could be interpreted as polymorphisms. The cumulative risk in patients in the DRV/r +RAL to experience virological failure and emergent IN resistance associated mutations was 2.1% (95% CI 1.0-4.1) at week 48 and 3.9% (95% CI 2.4-6.4) at week 96. HIV-1 RNA values at failure were not significantly different in those who failed with or without an IN mutation (median 731 copies/mL (IQR: 192, 14864) vs. 351 copies/mL (IQR: 134-904); p=0.17. The
proportion of patients in the RAL arm who achieved full virological success when switched to a different regimen (mostly RAL changed to TDF/FTC) was similar in those who switched after failure with resistance (13/15 = 86.7 %) and in those those who switched after failure without resistance (27/34 = 79.4 %). The frequency of IN mutations at failure was significantly associated with baseline VL: 7.1% (1/14) for participants harbouring a baseline VL < 100,000 copies/mL, 25.0% (7/28) for a baseline VL ≥ 100-500,000 copies/mL, and 53.8% (7/13) for a baseline VL ≥ 500,000 copies/mL ($P_{TREND}$=0.007). Although prespecified subgroup analysis showed that the NtRTI-sparing regimen was inferior to the standard regimen group in patients with baseline CD4 count of <200 cells/μL there was no statistically significant difference in the proportion of IN resistance between patients with a baseline CD4 count <200 cells/μL compared to those above (36.8 % vs. 22.2%, p-value=0.25). Of note, 4/15 participants with IN resistance mutations had a VL < 200 copies/mL at the time of testing. Figure 1 shows the time to detection of IN resistance mutations on RAL+DRV/r (based on all participants in this arm), that tended to emerge early (between 19 and 96 weeks).

**DISCUSSION**

NEAT 001/ANRS 143 was a phase 3 trial of NtRTI sparing regimen which compared an integrase strand transfer inhibitor (raltegravir) to a NtRTI standard backbone (tenofovir/emtricitabine) in first line therapy with a boosted protease inhibitor (darunavir/r). This trial showed that RAL+DRV/r regimen was overall non inferior to standard treatment for antiretroviral-naïve participants, but inferior for those with a CD4 count < 200 cells/μL. Through week 96, a high proportion of participants treated with either regimen had viral load suppression (HIV-1 RNA < 50 copies/mL in 78.6% and 82.2% for NtRTI-sparing group and
However the NtRTI-sparing regimen RAL+DRV/r was associated with higher rates of virological failure in those with baseline CD4 counts < 200 cells/μL and was associated with selection of resistance mutations at virological failure, especially to IN. Whereas no resistance mutations were found in genotype of participants with virological failure from the standard arm, IN mutation resistance was observed in more than one-quarter of samples at failure in the RAL+DRV/r arm. Our results confirm very well established data on the almost absence of development of protease resistance-associated mutations at virological failure in patients on a first-line ritonavir boosted protease inhibitor combined with 2 NtRTI, while such resistance mutations is more likely when a ritonavir-boosted protease inhibitor is combined with NNRTI, or, to a lesser extent, with integrase strand transfer inhibitor. These data suggest a mutual bidirectional protection of NtRTI and PI/r when combined with regards to resistance selection, as illustrated by the total absence of selection of reverse transcriptase or protease resistance-associated mutations in the 49 virological failures on ritonavir-boosted darunavir + tenofovir/emtricitabine.

However we cannot exclude that resistance mutations are selected outside the protease gene such as gag-pol cleavage sites and gp41 and this question should be examined in future studies. In NEAT 001, the cumulative risk of integrase resistance at virological failure in patients treated with DRV/r + RAL at W48 was 2.1%, which is higher than the cumulative risk of resistance development reported in other studies with raltegravir + tenofovir/emtricitabine given as first-line therapy, ranging from 0.2% to 1.4% at W48. Such higher rate of integrase resistance has been reported in previous studies of raltegravir + ritonavir-boosted protease inhibitor. In the Spartan study, a randomised controlled multicentre pilot study in 94 naïve HIV infected participants received atazanavir plus RAL or ritonavir-boosted atazanavir plus TDF/FTC. After 24 weeks of follow-up, 4 (6.3%) participants...
in the NRTI-sparing arm failed with development of IN resistance mutations, while no resistance mutations were observed in the control arm. Three of the 4 participants with resistance at failure had baseline HIV-1 RNA > 500,000 copies/mL.\textsuperscript{21}

In the PROGRESS pilot study, comparing the NtRTI sparing regimen of lopinavir/r plus RAL with the standard of care regimen of lopinavir/r plus TDF/FTC in naïve HIV infected patients, 8 subjects in the LPV/r+RAL failed, 3 of them with IN resistance mutations (3.7%). One of them had also an emergent major protease mutation; conversely, in the TDF/FTC arm only 1/5 patients who failed had a M184V mutation.\textsuperscript{15} Whether these differences are related to the different backbones, 2 NtRTI or ritonavir-boosted protease, in combination with raltegravir, or to differences in resistance testing and analysis is unknown. One could hypothesize that, similarly to what is observed with PI/r therapy, TDF/FTC confers some protection to the risk of resistance emergence at virologic failure with raltegravir therapy. The mechanism of this NtRTI protection could be an undiscovered molecular interaction within the HIV replication cycle or more probably a consequence of the very long half-life of intracellular tenofovir and emtricitabine, providing forgiveness to the great variability of raltegravir exposure. On the contrary, despite its high genetic barrier to resistance, darunavir/ritonavir, with relative short half-life, might confer less forgiveness to raltegravir, especially in situations of partial or intermittent non-adherence. Further analyses will assess adherence and raltegravir plasma concentrations in NEAT 001 to elucidate reasons for the high rate of resistance emergence, especially in patients with high baseline viral load. On the other hand, differences in assays used for resistance testing in the various studies should be considered, and more importantly, different timepoints of analysis (first of confirmed virological failure sample) and level of viral load at the time of genotyping, which might greatly influence genotype results.\textsuperscript{22} This renders cross study comparisons hazardous with
regards to the prevalence of resistance at virologic failure. Indeed, in NEAT 001, resistance analysis population differed from those of previous studies of raltegravir + tenofovir/emtricitabine,\textsuperscript{19,20} or of a pilot uncontrolled study of raltegravir + darunavir/ritonavir.\textsuperscript{23} In the latter study, ACTG 5262, rate of integrase resistance at virologic failure was 4.5%; 5 out of 25 patients with virological failure and genotype testing had integrase resistance mutations at virological failure and a baseline viral load > 100,000 copies/ml. In NEAT 001, the proportion of participants in the DRV/r + RAL group with baseline viral load > 100,000 copies/ml who experienced virological failure and emergent integrase resistance-associated mutations was 9.6% versus 10.4% in ACTG 5262.\textsuperscript{23} Initiating antiretroviral therapy with the combination of ritonavir-boosted darunavir + raltegravir in patients with high baseline viral load is associated with an unacceptable high risk of raltegravir resistance on treatment, particularly in those with HIV-1 RNA > 500,000 copies/ml; 27.3% developed resistance on treatment in our study. The main selected IN mutation in our study was the N155H raltegravir signature mutation alone, so most viruses at virological failure remained, in theory, susceptible to dolutegravir, except for the one harbouring the F121Y mutation which confers phenotypic resistance to dolutegravir as well.\textsuperscript{24} The uncontrolled pilot VIKING 3 study have shown the efficacy of dolutegravir twice a day on raltegravir failure with the mutation N155H alone.\textsuperscript{25} However, great caution and more clinical studies are needed, as recent data suggest that dolutegravir might also select for N155H and that viruses harbouring such mutation might have diminished susceptibility to dolutegravir when used once daily.\textsuperscript{26} One limitation of our study is the absence of genotypic information, due to either absence of available sample or failure to obtain sequence in 12% of participants qualifying for resistance testing in the RAL + DRV/r arm. This proportion was 16% in the TDF/FTC + DRV/r arm. Another limitation of our study is that the
protocol did not ask for IN gene sequence at baseline, as at the time of recruitment there
was little clinical use of integrase inhibitors and a risk of transmitted drug resistance was
very low for the integrase class (1.7% for IN resistance mutation in the PRIMO cohort of
recently infected patients). Although we cannot formally exclude that some participants
might have had IN resistance pre-existing to initiation of therapy, this is highly unlikely, as
N155H mutation confers high level phenotypic resistance to raltegravir and in such
circumstance, virological failure would have occurred much more rapidly, without the early
virological suppression seen in 9/13 patients with N155H mutation. Although none of the RT
(n = 2) and protease (n = 1) resistance mutations evidenced at failure were detected at
baseline using Sanger sequencing, ultradeep sequencing on those baseline samples could
help to determine if these emergent RT (M41L, K65R) and protease (L76V) mutations are
due to selection or re-emergence of transmitted minority resistant variants. Of clinical
relevance, IN resistance was seen in patients (4/15) with very low-level viremia (HIV RNA
between 50 and 200 copies/mL), a phenomenon already described in the ACTG 5262 study.
In another study on risk factors for raltegravir resistance development in clinical practice,
we showed that 7.7% (6/78) of patients with HIV RNA between 50 and 200 copies/mL had
IN resistance mutations. Thus, viral rebound with 2 consecutive HIV RNA values > 50
copies should be considered as definite virological failure in patients receiving DRV/r + RAL,
and genotypic resistance testing should be performed without delay in these patients.

In summary, during 96-weeks of follow up, resistance to IN was detected in 15/401
participants randomised to DRV/r+RAL (3.7%). One quarter (27%) of samples at failure had
IN resistance mutations, with risk of resistance related to baseline HIV RNA. Most patients
with resistance mutations achieved complete suppression when switched to other regimens,
most often TDF/FTC instead of RAL, with continuation of ritonavir-boosted darunavir.
It would be interesting to investigate other NtRTI sparing strategies combining an ISTI with a higher genetic barrier to resistance and a longer half-life such as dolutegravir, in combination with a boosted-protease inhibitor. Based on these results on resistance, initiation of antiretroviral therapy with the alternative regimen of ritonavir-boosted darunavir and raltegravir in patients with CD4 > 200/μL should be limited to patients with HIV RNA < 500,000 copies/ml, and discussed in patients with HIV RNA between 100,000 and 500,000 copies/ml.

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Asterisk (*) indicates staff who left during the trial.

Transparency declarations

FR has received honoraria for advisories or invited talks or conferences and research grants from Abbvie Labs, Bristol-Myers Squibb, Gilead Sciences, Merck Laboratories, MSD, Janssen Pharmaceuticals and Viiv Healthcare.

AP (A Pozniak) has been an advisor and invited speaker and received honoraria, research grant, travel and education from Abbvie, GSK, Viiv, BMS, Gilead Sciences, Janssen Pharmaceuticals, Merck & Company, Tobira.
AM has received honoraria for advisories or invited talks or conferences and research grants from Abbvie Labs, Bristol-Myers Squibb, Gilead Sciences, Merck Laboratories, MSD, Janssen Pharmaceuticals and ViiV healthcare.

VC has received honoraria for advisories or invited talks or conferences and research grants from Abbvie Labs, Bristol-Myers Squibb, Gilead Sciences, Merck Laboratories, MSD, Janssen Pharmaceuticals and ViiV healthcare.

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The other authors declare that they have no conflicts of interest.
References


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### Table 1: Baseline characteristics of patients meeting criteria for genotypic testing

<table>
<thead>
<tr>
<th></th>
<th>RAL+DRV/r (n=69)</th>
<th>TDF+FTC+DRV/r (n=58)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>65 (94%)</td>
<td>50 (86%)</td>
</tr>
<tr>
<td>Median (IQR) age (years)</td>
<td>37 (32-44)</td>
<td>39 (31-52)</td>
</tr>
<tr>
<td><strong>Ethnic origin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>53 (77%)</td>
<td>45 (78%)</td>
</tr>
<tr>
<td>Black</td>
<td>12 (17%)</td>
<td>10 (17%)</td>
</tr>
<tr>
<td>Asian</td>
<td>1 (1%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (4%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>Mode of HIV infection</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homosexual/bisexual sex</td>
<td>40 (63%)</td>
<td>32 (58%)</td>
</tr>
<tr>
<td>Heterosexual</td>
<td>23 (37%)</td>
<td>20 (36%)</td>
</tr>
<tr>
<td>IVDU</td>
<td>0</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>HIV CDC clinical stage</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>54 (78%)</td>
<td>47 (81%)</td>
</tr>
<tr>
<td>B</td>
<td>10 (15%)</td>
<td>7 (12%)</td>
</tr>
<tr>
<td>C</td>
<td>5 (7%)</td>
<td>4 (7%)</td>
</tr>
<tr>
<td>Median (IQR) CD4 cell count (cells per μL)</td>
<td>295 (150-378)</td>
<td>316 (205-379)</td>
</tr>
<tr>
<td>CD4 cell count category (cells per μL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>3 (4%)</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>50-199</td>
<td>19 (28%)</td>
<td>11 (19%)</td>
</tr>
<tr>
<td>200-349</td>
<td>24 (35%)</td>
<td>21 (36%)</td>
</tr>
<tr>
<td>350-499</td>
<td>20 (29%)</td>
<td>22 (38%)</td>
</tr>
</tbody>
</table>
≥500 HIV-1 RNA concentration at baseline (log_{10} copies per mL) 5.25 (4.85-5.58) 5.19 (4.80-5.54)
Median (IQR) HIV-1 RNA concentration at baseline (log_{10} copies per mL)

Baseline HIV-1 RNA category

≥100 000 copies per mL
49 (71%) 36 (62%)
≥500 000 copies per mL
14 (20%) 9 (16%)

Baseline HIV-1 RNA category

HCV co-infection
3 (4%) 4 (7%)

Figure 1: time to detection of IN resistance mutations, RAL + DRV/r arm, NEAT 001/ANRS 143 trial
Table 2: Resistance mutations in the RAL+DRV/r arm

<table>
<thead>
<tr>
<th>Patients</th>
<th>Genotypic testing</th>
<th>RT</th>
<th>PROT</th>
<th>IN</th>
<th>Subsequent regimen</th>
<th>VL at W96 (copies/mL)</th>
<th>Suppressed before resistance test</th>
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</thead>
<tbody>
<tr>
<td>1 W47</td>
<td>247</td>
<td>L76V</td>
<td></td>
<td></td>
<td>RAL+DRV/r</td>
<td>&lt;50</td>
<td>Y</td>
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<tr>
<td>2 W38</td>
<td>340</td>
<td>M41L</td>
<td></td>
<td></td>
<td>TDF/FTC+EFV then TDF/FTC+DRV/r</td>
<td>&lt;50</td>
<td>N</td>
</tr>
<tr>
<td>3 W65</td>
<td>3800</td>
<td>K65R</td>
<td></td>
<td></td>
<td>TDF/FTC+DRV/r</td>
<td>&lt;50</td>
<td>Y</td>
</tr>
<tr>
<td>4 W24</td>
<td>64041</td>
<td>N155H</td>
<td></td>
<td></td>
<td>TDF/FTC+DRV/r</td>
<td>107</td>
<td>N</td>
</tr>
<tr>
<td>5 W58</td>
<td>60</td>
<td>Y143C</td>
<td></td>
<td></td>
<td>TDF/FTC+DRV/r</td>
<td>90</td>
<td>Y</td>
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<tr>
<td>6 W32</td>
<td>85</td>
<td>N155H</td>
<td></td>
<td></td>
<td>TDF/FTC+DRV/r</td>
<td>&lt;50</td>
<td>N</td>
</tr>
<tr>
<td>7 W34</td>
<td>148</td>
<td>N155H</td>
<td></td>
<td></td>
<td>No treatment after W67</td>
<td>227185</td>
<td>Y</td>
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<tr>
<td>8 W64</td>
<td>192</td>
<td>N155H</td>
<td></td>
<td></td>
<td>TDF/FTC+DRV/r</td>
<td>68</td>
<td>Y</td>
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<td></td>
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<tr>
<td>9</td>
<td>W62</td>
<td>406</td>
<td>N155H</td>
<td>TDF/FTC+DRV/r</td>
<td>&lt;50</td>
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<tr>
<td>10</td>
<td>W29</td>
<td>442</td>
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<td>11</td>
<td>W49</td>
<td>498</td>
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<td>RAL+DRV/r</td>
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<tr>
<td>12</td>
<td>W79</td>
<td>731</td>
<td>N155H</td>
<td>ABC/3TC+DRV/r</td>
<td>&lt;50</td>
<td>Y</td>
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<tr>
<td>13</td>
<td>W32</td>
<td>1311</td>
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<td>TDF/FTC+DRV/r</td>
<td>&lt;50</td>
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<td>14</td>
<td>W34</td>
<td>1900</td>
<td>N155H</td>
<td>TDF/FTC+ETR</td>
<td>&lt;50</td>
<td>Y</td>
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<tr>
<td>15</td>
<td>W21</td>
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<td>16</td>
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<td>52857</td>
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<td>N</td>
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<tr>
<td>17</td>
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<tr>
<td>18</td>
<td>W96</td>
<td>1470</td>
<td>F121Y</td>
<td>RAL+DRV/r</td>
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<td></td>
</tr>
</tbody>
</table>

RT: reverse transcriptase; PROT: protease; IN: integrase; VL: viral load; W96: 96 week; copies/mL: copies/milliliter; Y: yes; N: No; RAI: raltegravir; DRV/r: darunavir/ritonavir; TDF: tenofovir; EFV: efavirenz; FTC: emtricitabine; ABC/3TC: abacavir/lamivudine; ETR: etravirine; NVP: nevirapine; RPV: rilpivirine