# Is Kivexa with rilpivirine as effective as Eviplera for switch in clinical practice?

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## Background

- In December 2013 the UK license for Eviplera® (tenofovir DF-emtricitabine-rilpivirine, EVP) was extended to include switch.
- The license for rilpivirine (RPV, Edurant®) as a single component was not extended.
- Several studies and cohorts report favorable outcomes when switching to EVP, however there are no data for switching to abacavir-lamivudine (Kivexa®, KIV) with RPV.
- We aimed to describe the characteristics, indications and outcomes of those switching to RPV with Kivexa (KIV-RPV) compared to Eviplera.

## Methods

- Retrospective, observational cohort looking at all patients switching to KIV-RPV at six UK HIV units from June 2012 to February 2015, and comparing these to a cohort switching to EVP at one centre.
- Patients were identified using clinic databases, and information regarding ART history, demographics, switch indication and short term outcomes was identified using local information systems and case note review. This was recorded using Excel 2003.
- Only first use of RPV included. Change in NRTI backbone was considered failure.
- Patients re-starting ART with RPV were excluded.
- Time to treatment discontinuation was assessed using standard survival methods.
- Comparisons were made using $\chi^2$, Fishers Exact test or Mann-Whitney U test as appropriate.
- Those with the potential for 24 weeks' follow-up (i.e. those who had started ART more than 24 weeks prior to data collection) were included in snapshot analysis of outcomes at 24 weeks. Similarly, only those with the potential for 48 weeks' follow-up were included in 48-week snapshot analysis.

## Results (1)

- We identified a total of 280 patients who switched, 118 (42%) switching to KIV-RPV.

**Table 1: Baseline demographics of patients switching to KIV-RPV or EVP**

| % (N) unless stated | KIV-RPV | EVP | P |
|---|---|---|---|
| Number patients, n | 118 | 162 | - |
| Male | 72 (85) | 77 (125 | 0.33 |
| Age (median) | 43 | 42 | 0.66 |
| White ethnicty | 60 (71) | 56 (91) | 0.004 |
| MSM | 59 (70) | 61 (99) | 0.76 |
| HCV IgG Ab positive<br>HBS Ag positive | 9 (11)<br>2 (2) | 13 (21)<br>7 (4) | 0.34<br>0.31 |
| VL<50c/ml at switch | 96.6 (114/117) | 96.3 (156) | 0.44 |
| Nadir CD4 prior to ART* | 255 (0-1160) | 234 (0-749) | 0.43 |
| CD4 at switch (cells/mm$^3$)* | 626 (107-1468) | 659 (26-1546) | 0.59 |
| Switched from:<br>NNRTI + 2NRTI<br>PI/r + 2NRTI<br>Other regimen | <br>66 (78)<br>24 (28)<br>10 (12) | <br>52 (85)<br>41 (66)<br>7 (11) | 0.011 |
| Maintained NRTI backbone at switch | 86.4 (102) | 84.6 (137) | 0.66 |
| *median (range) | | | |

## Results (2)

**Table 2: Indication for switch, % (N)**

| Indication | KIV-RPV | EVP |
|---|---|---|
| CNS side effects | 48 (57) | 33 (54) |
| Gastrointestinal disturbances | 9 (11) | 12 (19) |
| Hyperlipidaemia | 7 (8) | 11 (18) |
| Other drug intolerance | 12 (14) | 4 (6) |
| Simplification<br>Due to adherence<br>Without adherence concerns | <br>1 (1)<br>5 (6) | <br>3 (5)<br>19 (30) |
| Other indication | 27 (32) | 22 (36) |
| Not documented | 8 (9) | 5 (8) |
| More than one indication for switching ART possible | | |

- Of those switching to KIV-RPV 115 (97%) had the potential for 24 weeks' follow-up (i.e. started ART before 1st Jun 2015). 113 (96%) had the potential for 48 weeks' follow-up (i.e. started ART before 1st Jan 2015).

**Figure 1: 24 and 48 week snapshot analysis (+/-10 weeks) of viral load outcomes according to regimen status (ITT, M=E, S=F)**

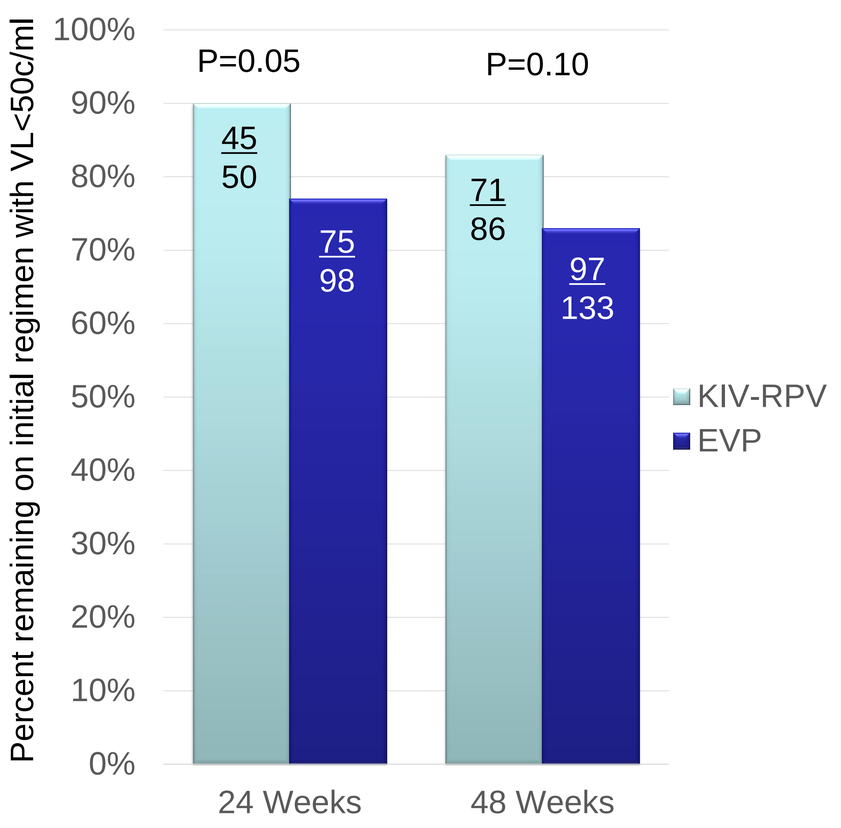



**Table 3: 24 and 48 week snapshot analysis (+/-10 weeks) of viral load outcomes according to regimen**

| Week | Analysis | KIV-RPV % (n/N) | EVP % (n/N) | P |
|---|---|---|---|---|
| 24 | ITT, M=E, S=I | 96 (48/50) | 92 (90/98) | - |
| | ITT, M=E, S=F | 90 (45/50) | 77 (75/98) | 0.05 |
| | OT, M=E, S=E | 100 (45/45) | 95 (75/79) | - |
| 48 | ITT, M=E S=I | 99 (85/86) | 94 (125/133) | - |
| | ITT, M=E S=F | 83 (71/86) | 73 (97/133) | 0.10 |
| | OT, M=E, S=E | 99 (71/72) | 95 (97/102) | - |

ITT: Intent-to-treat; OT: on-treatment,
M=E: Missing=Excluded; M=F: Missing=Failure, S=I: ART switches/discontinuations ignored; S=F: switch=failure

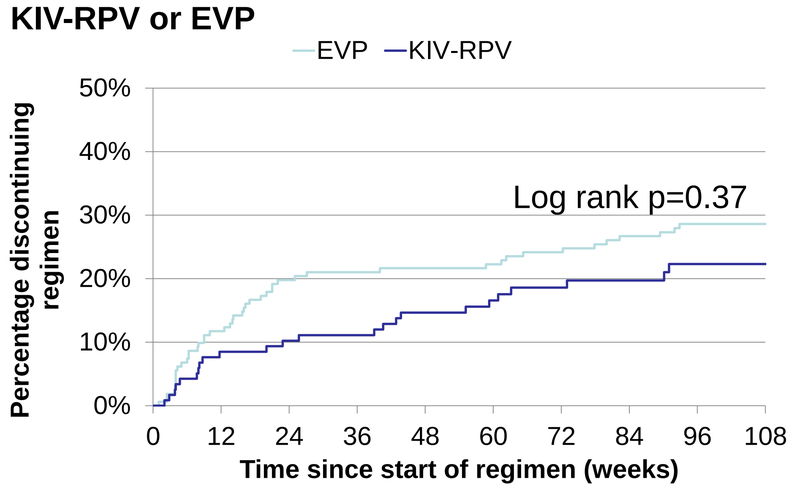
- The main toxicity leading to discontinuation from RPV within the first 48 weeks was gastrointestinal events (EVP 7/17, KIV-RPV 2/11). Central nervous system or psychiatric adverse effects were similar (EVP 4/17, KIV-RPV 3/10).
- 7 patients switched off RPV-based ART to avoid drug-drug interactions, 6/7 due to need for proton pump inhibitors (5/6 from EVP)

## Results (3)

**Table 4: Indication and outcomes of discontinuation by 48 weeks, % (N)**

| | KIV-RPV | EVP | P |
|---|---|---|---|
| Discontinued regimen<br>24 weeks<br>48 weeks | <br>10 (12/115)<br>15 (17/113) | <br>20 (32/161)<br>22 (35/160) | 0.37 |
| Median N weeks to discontinuation (IQR) | 9 (5-26) | 9 (4-17) | - |
| Viral load on discontinuation<br>>50 c/ml<br><50 c/ml<br>Unknown | <br>13 (2)<br>88 (14)<br>[1] | <br>17 (6)<br>83 (29)<br>[0] | <br>0.67 |
| Emergent resistance on failure<br>Any, % (n/N)<br>discontinue<br>New M184I/V<br>New E138K<br>2 class resistance | <br><br>50 (1/2)<br>1/1<br>1/1<br>1/1 | <br><br>66 (4/6)<br>4/4<br>1/4<br>4/4 | - |
| Primary indication for discontinuation, n<br>Toxicity/intolerance<br>Drug interaction<br>Patient choice<br>Virological failure<br>Other | <br>9<br>1<br>3<br>0<br>4 | <br>17<br>6<br>4<br>3<br>5 | - |

**Figure 2: Kaplan-Meier estimate for discontinuation KIV-RPV or EVP**




## Discussion

- In this relatively small, non-randomised retrospective cohort there were no significant differences in outcome of switch to KIV-RPV compared to EVP.
- A relatively high rate of overall discontinuation was noted irrespective of the NRTI backbone, mainly relate to toxicity or intolerance.
- There was a trend towards higher discontinuation from EVP (figure 1). This may reflect the single centre from which the EVP control were drawn.
- Viral failure on discontinuation from both regimens was low.

## Limitations

- Non-randomised comparison.
- Relatively small numbers and short follow up.
- Eviplera control group taken from single centre.

## Conclusions

- In this diverse cohort, switching to KIV-RPV was as effective as EVP at maintaining virological suppression with no key difference observed.
- Despite differences in licenses for Eviplera and Edurant, this data suggests that rilpivirine plus Kivexa may be an alternative where TDF/FTC based therapy is not suitable.