



Rosanne Verwijs<sup>1</sup>, Ingeborg Wijting<sup>1</sup>, Marjo van Kasteren<sup>2</sup>, Jan G. den Hollander<sup>3</sup>, Inge Derdelinckx<sup>4</sup>, Guido van den Berk<sup>5</sup>, Saskia Vrouwenraets<sup>6</sup>, Mark Claassen<sup>7</sup>, Wouter Bierman<sup>8</sup>, Casper Rokx<sup>1</sup>, Bart Rijnders<sup>1</sup>

<sup>1</sup>Erasmus University Medical Center, Rotterdam, Netherlands, <sup>2</sup>Elisabeth-TweeSteden Ziekenhuis, Tilburg, Netherlands, <sup>3</sup>Maasstad Hospital, Rotterdam, Netherlands, <sup>4</sup>University Hospitals Leuven, Leuven, Belgium, <sup>5</sup>OLVG, Amsterdam, Netherlands, <sup>6</sup>Slotervaart MC, Amsterdam, Netherlands, <sup>7</sup>Rijnstate Hospital, Arnhem, Netherlands, <sup>8</sup>University Medical Center Groningen, Groningen, Netherlands.

## Background

Tenofovir-disoproxil fumarate (TDF) containing cART can be associated with an accelerated decline of the estimated glomerular filtration rate (eGFR). Limited data are available on the extent of the reversibility of this eGFR decline and whether using T-alafenamide (TAF) is non-inferior to abacavir (ABC) regarding eGFR recovery after TDF discontinuation.

## Aim

The BACTAF-studies are 2 multicenter studies; an ongoing prospective randomized study (NCT02957864) and a retrospective cohort study. Both have similar goals:

1. Evaluate the reversibility of TDF-associated eGFR decline
2. Compare the eGFR recovery in patients switching to TAF or ABC

## Methods

We performed a retrospective cohort study in 7 Dutch and 1 Belgian center in which patients were included if they had switched from TDF to TAF or ABC for a significant eGFR decline:

- eGFR decline of >3mL/min/yr during ≥5yrs of TDF use or
- >25% eGFR decline or
- eGFR<70mL/min with eGFR>90mL/min at TDF initiation

To exclude other possible causes of the eGFR decline as much as possible (whether HIV related or unrelated), patients with any of the following were excluded: Detectable HIV-RNA, diabetes, history of cardiovascular disease, uncontrolled hypertension, use of >1 antihypertensive drug, use of potentially nephrotoxic medication, HBV/HCV coinfection or any diagnosed kidney disease that may partially explain the eGFR decline.

To correct for the inhibition of the tubular export of creatinine by rilpivirine, dolutegravir or cobicistat we added +10ml/min to the measured eGFR if any of these drugs were started together with ABC or TAF

Primary endpoint: eGFR recovery of >50% at week 48 after TDF discontinuation

Baseline characteristics	ABC (n=101)	TAF (n=114)
Male sex (N (%))	80 (79.2%)	98 (86.0%)
Age *	50 (±11)	52 (±38)
eGFR at TDF initiation mL/min*	103 (±17)	108 (±17)
eGFR at TDF discontinuation mL/min*	67 (±15)	73 (±15)
Duration of TDF use in year†	5 (3, 7)	7 (4, 9)
eGFR<60 mL/min at TDF discontinuation (N (%))	33 (32.7%)	25 (21.9%)

Table 1. Baseline demographic characteristics and eGFR decline during TDF use.

\*Mean (±SD), †Median (IQR)

## Results

Of the 215 patients included, 114 switched to TAF and 101 to ABC. eGFR had declined by a mean of 5.1mL/min/yr and 6.7mL/min/yr during a median of 7 and 5yrs of TDF use respectively. The mean eGFR was 73mL/min at TAF and 67mL/min at ABC initiation, and 22% and 33% had an eGFR <60mL/min.

Week 48 eGFR results (available for 187 pts):

Significant eGFR increase by 6.7mL/min with TAF and 6.5mL/min with ABC (p<0.001 compared to baseline for both, p>0.1 for TAF versus ABC).

>50% eGFR recovery observed in 28/100 (28%) and 23/85 (27%) respectively (p>0.1).

In 23 of 46 patients with w48 results available and eGFR<60 at TDF discontinuation, a recovery to >60mL/min was observed.

More patients discontinued ABC than TAF (11% vs 2%, p=0.008) and this was mostly driven by discontinuations for drug-related AE (10% vs 2%, p=0.014).

HIV-RNA remained suppressed in all but 2 patients.

Week 48	ABC (n=86)	TAF (n=101)
eGFR increase at W48 in mL/min†	5.5 (0.0, 12.3)	5.0 (-1.5, 15.5)
Proportion with >50% eGFR recovery (N(%))	28 (28%)	25 (27%)
Discontinuation of cART for drug-related AE (N (%))	10 (9.9%)	2 (1.7%)

Table 2. Week 48 results concerning eGFR and adverse events.

\*Mean (±SD), †Median (IQR)

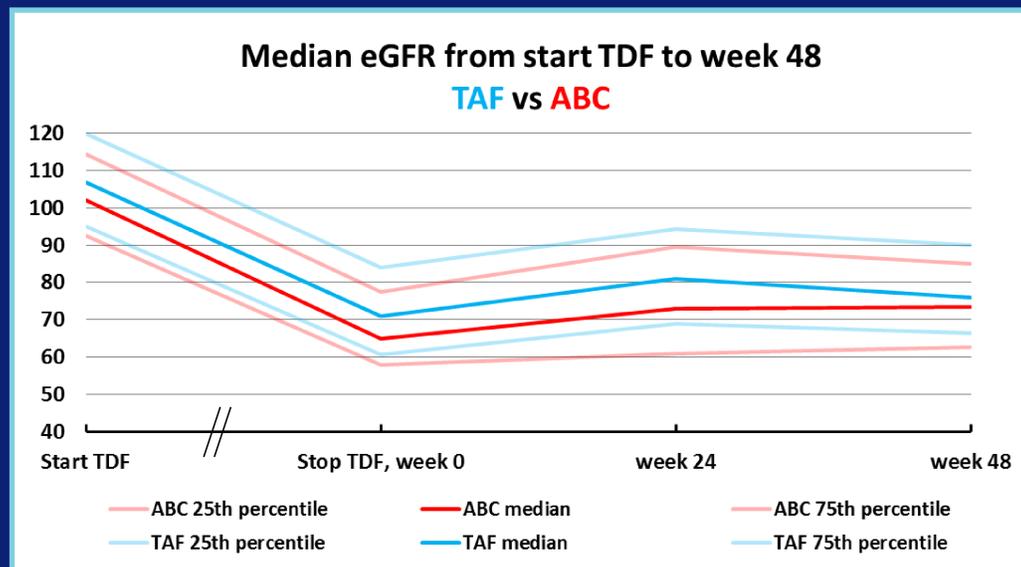


Figure 2. eGFR course from start TDF until week 48

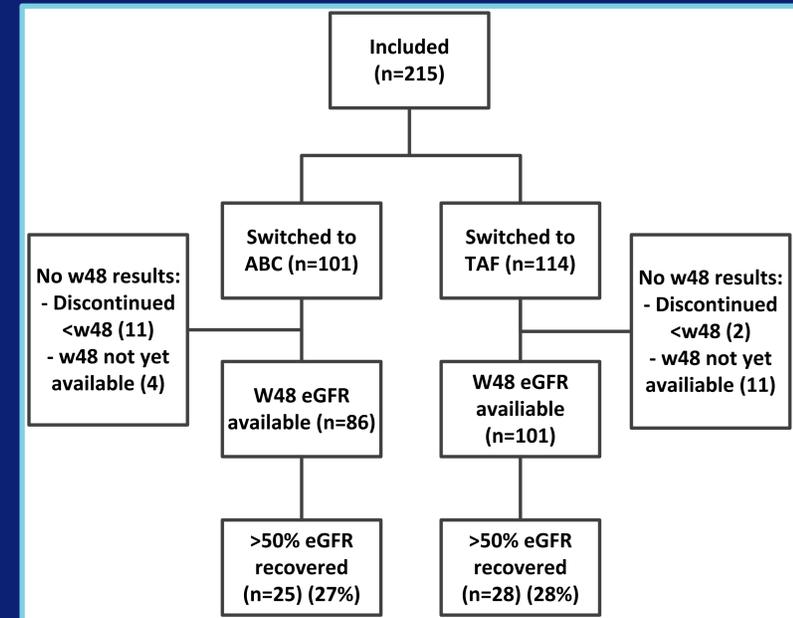


Figure 1. Patient flow concerning primary endpoint

## Discussion

Strengths:

- Selection to exclude patients with other possible causes for eGFR decline
- Relatively large patient population with clinically relevant eGFR decline during TDF use

Limitations:

- TDF as cause for eGFR decline can never be proven
- Follow up still relatively short: Further recovery?
- Baseline differences between ABC and TAF groups
  - BACTAF prospective randomized controlled trial
  - Multivariable analysis with W96 follow up planned

## Conclusion

Although a modest improvement in eGFR was observed after TDF discontinuation, few patients recovered >50% of their eGFR one year after TDF discontinuation. The recovery rate in patients that switched to TAF and ABC was comparable.