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BACTAF-Prospective Randomized Study & BACTAF-Retrospective Cohort Study

EGFR Recovery 96 Weeks After a TDF to TAF or ABC Switch for TDF-Associated EGFR Decline

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

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

Erasmus MC
University Medical Center Rotterdam

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; a prospective randomized study (NCT02957864) and a retrospective cohort study, with similar goals:

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

Methods

For the prospective randomized study patients from 3 Dutch centers were included and randomized for a switch to ABC or TAF, if a significant eGFR decline had occurred during TDF use. Additionally, we performed the retrospective 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, defined as:

- 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

Exclusion criteria (to exclude other possible causes for eGFR decline):
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 switch
Secondary endpoint: eGFR recovery of >50% at week 96 after switch

Baseline characteristics	TAF (n=130)	ABC (n=120)
Male sex (N (%))	114 (88%)	98 (82%)
Age*	47 (±12)	49 (±11)
eGFR at TDF initiation mL/min*	108 (±16)	104 (±17)
eGFR at TDF discontinuation mL/min*	73 (±15)	68 (±15)
Duration of TDF use in years†	7.5 (5.2, 9.4)	5.5 (4.2, 8.6)
Proportion eGFR<60 mL/min at TDF discontinuation (%)	20%	28%

Table 1. Baseline demographic characteristics and eGFR decline during TDF use.
*Mean (±SD), †Median (IQR)

Main findings

At *week 48* after discontinuation of TDF, eGFR had significantly increased with a median *5.0 mL/min* in patients on *TAF* and *6.0 mL/min* in patients on *ABC* (*p>0.1 for TAF vs ABC*). Proportion with *>50% recovery of eGFR* was 23% for TAF and 26% for ABC.

Median eGFR increase at *week 96* was 6.0 mL/min for TAF and 8.5 mL/min for ABC (p>0.1 for TAF vs ABC).

Discontinuation for *drug-related AE* was more frequent in patients switched to ABC than TAF (13% vs 2%).

Week 48 results	TAF (n=121)	ABC (n=94)	P-value
eGFR increase at W48 in mL/min†	5.0 (-2.0, 14.5)	6.0 (1.0, 13.0)	>0.1
Proportion with >50% eGFR recovery (N(%))	29 (23%)	27 (26%)	>0.1

Table 2. Week 48 results concerning eGFR.
†Median (IQR)

Week 96 results	TAF (n=101)	ABC (n=88)	P-value
eGFR increase at W96 in mL/min†	6.0 (-1.0, 12.0)	8.5 (-1.0, 16.0)	>0.1
Proportion with >50% eGFR recovery (N(%))	18 (18%)	24 (27%)	>0.1
cART discontinuation for drug-related AE (%)	2%	13%	0.002

Table 3. Week 96 results concerning eGFR and adverse events.
†Median (IQR)

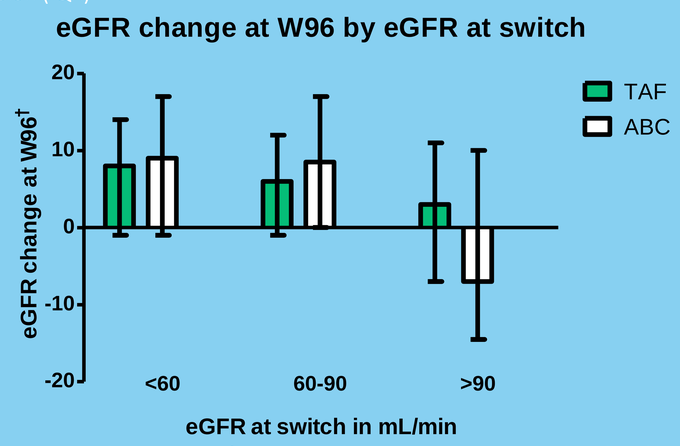

Figure 1. eGFR change in mL/min at week 96 on TAF or ABC, by height of eGFR at switch. †Median with IQR

Results

250 patients were included, of whom 35 in the prospective study. 130 switched to TAF and 120 to ABC (table 1). eGFR had declined by a mean of 4.4mL/min/yr and 5.9mL/min/yr during a median of 7.5 and 5.5 yrs of TDF use respectively. The mean eGFR was 73mL/min at TAF and 68mL/min at ABC initiation, and 20% and 28% had an eGFR <60mL/min. W48 results were available for 213 while data were not available for 37 (discontinuation of TAF or ABC before w48 in 17, LTFU in 4, other reasons in 16).

Week 48 eGFR results (table 2):

- >50% eGFR recovery observed in 29/121 (23%) with TAF and 27/94 (26%) with ABC (p>0.1).
- In 33 of 52 patients (57%) with w48 results available and eGFR<60 at TDF discontinuation, a recovery to >60mL/min was observed.

Week 96 eGFR results (table 3 and figure 1):

- A >50% recovery was observed in 18% and 27%, respectively (p>0.1).
- Of the 44 pts with an eGFR<60ml/min at TDF discontinuation, 30(68%) recovered to >60ml/min at w96.
- Median eGFR increase differed in subgroups with eGFR <60, 60-90 and >90 mL/min at switch to ABC or TAF.

More patients discontinued ABC than TAF (15% vs 2%, p<0.001) and this was mostly driven by discontinuations for drug-related AE (13% vs 2%, p<0.01).

HIV-RNA remained suppressed in all but 3 patients.

Conclusion

Although improvements in eGFR were observed after TDF discontinuation, only a minority recovered >50% of the eGFR lost during TDF use. Recovery of eGFR on TAF and ABC was comparable.

Due to the exclusion of patients with other possible causes of eGFR decline and the relatively large patient population with a clinically relevant eGFR decline during TDF use, this study provides important data for clinical decision-making.

After discontinuation of TDF for an eGFR decline, switching to TAF is non-inferior to switching to ABC considering eGFR recovery. However, discontinuation of cART for possibly drug-related adverse events is more frequent after a switch to ABC.

Contact: n.verwijs@erasmusmc.nl, b.rijnders@erasmusmc.nl

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