



**HAL**  
open science

## Conversion From Belatacept to Another Immunosuppressive Regimen in Maintenance Kidney-Transplantation Patients

Anna Gouin, Rebecca Sberro-Soussan, Cécile Courivaud, Dominique  
Bertrand, Arnaud del Bello, Amandine Darres, Didier Ducloux, Christophe  
Legendre, Nassim Kamar

► **To cite this version:**

Anna Gouin, Rebecca Sberro-Soussan, Cécile Courivaud, Dominique Bertrand, Arnaud del Bello, et al.. Conversion From Belatacept to Another Immunosuppressive Regimen in Maintenance Kidney-Transplantation Patients. *Kidney International Reports*, 2020, 5, pp.2195 - 2201. 10.1016/j.ekir.2020.09.036 . hal-03492621

**HAL Id: hal-03492621**

**<https://hal.science/hal-03492621v1>**

Submitted on 15 Dec 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

## **Conversion from belatacept to another immunosuppressive regimen in maintenance kidney-transplant patients**

Anna Gouin<sup>1</sup>, Rebecca Sberro Soussan<sup>2</sup>, Cécile Courivaud<sup>3</sup>, Dominique Bertrand<sup>4</sup>, Arnaud Del Bello<sup>1,5</sup>, Amandine Darres<sup>1</sup>, Didier Ducloux<sup>3</sup>, Christophe Legendre<sup>2</sup>, Nassim Kamar<sup>1,5,6</sup>

<sup>1</sup> Department of Nephrology and Organ Transplantation, CHU Rangueil, Toulouse, France

<sup>2</sup> Service de néphrologie-Transplantation, Hôpital Necker, AP-HP, Paris et Université Paris Descartes, Paris

<sup>3</sup> Service de néphrologie, dialyse et transplantation rénale, FHU INCREASE, CHU de Besançon, Besançon, France.

<sup>4</sup> Service de néphrologie, dialyse et transplantation rénale, CHU de Rouen, Rouen, France.

<sup>5</sup> INSERM U1043, IFR-BMT, CHU Purpan, Toulouse, France

<sup>6</sup> Université Paul Sabatier, Toulouse, France

**Corresponding author:**

Nassim KAMAR, MD, PhD

Department of Nephrology and Organ Transplantation

CHU Rangueil

TSA 50032

31059 Toulouse Cedex 9

France

Tel.: +33 5 61 32 23 35

Fax: +33 5 61 32 39 89

Email: [kamar.n@chu-toulouse.fr](mailto:kamar.n@chu-toulouse.fr)

**Running title:** Belatacept cessation in maintenance patients

**Keywords:** Belatacept, conversion, DSA, kidney function, safety, CNI

**Abstract word count:** 193

**Manuscript word count:** 2274

**Tables:** 2

**Figure:** 2

**Supplementary tables:** 1

### **Authors' contributions**

AG collected the data from Toulouse, pooled the data from all centers, and wrote the paper.

RSS and CL collected the data from Necker Hospital and reviewed the paper.

CC and DD collected the data from Besançon Hospital and reviewed the paper.

DB collected the data from Rouen Hospital and reviewed the paper.

ADB, AD reviewed the paper.

NK designed the study, did the statistical analyses, and wrote the paper.

### **Abbreviations:**

CNI: calcineurin inhibitors

DSA: donor-specific antibody

eGFR: estimated glomerular-filtration rate

HLA: human leukocyte antigen

MDRD: modification of the diet in renal disease

MPA: mycophenolic acid

mTORi: mammalian target of rapamycin inhibitor

## **Abstract**

Background: The effect of the conversion from belatacept to another immunosuppressive regimen is underreported. The aim of the present retrospective study was to assess the effect on kidney function and the clinical outcome of the conversion from belatacept to another regimen.

Patients: We have identified 44 maintenance kidney-transplant patients from five French kidney transplant centers who were converted from belatacept to another regimen either because of a complication ( $n=28$ ) or another reason (patients' request or belatacept shortage,  $n=13$ ). The follow-up after the conversion from belatacept was  $27.5\pm 25.3$  months.

Results: Overall, mean estimated glomerular filtration rate (eGFR) decreased from  $44.2\pm 16$  mL/min/1.73m<sup>2</sup> at conversion from belatacept to  $35.7\pm 18.4$  mL/min/1.73m<sup>2</sup> at last follow-up ( $p=0.0002$ ). eGFR significantly decreased in patients who had been given belatacept at transplantation as well as in those who had been converted to belatacept earlier. The decrease was less significant in patients who had stopped belatacept without having experienced any complications. Finally, eGFR decreased more severely in patients who were converted to calcineurin inhibitors, compared to those who received mammalian target of rapamycin inhibitors. Few patients also developed diabetes and hypertension.

Conclusion: Thus, transplant physicians should avoid stopping belatacept when not clinically required.

## Introduction

Although calcineurin inhibitor (CNI)-based immunosuppression has dramatically improved the outcome of kidney transplantation, its use is responsible for nephrotoxicity and increased risk for tumoral proliferation. This has prompted transplant physicians to try using CNI-free regimens. A mammalian target of rapamycin (mTORs) inhibitor CNI-free regimen was used in *de novo* and maintenance kidney-transplant patients<sup>1 2 3</sup>. It was associated with significantly improved kidney function in patients who tolerated this therapy compared to those who remained on CNI-based therapy<sup>1 2 2 3</sup>. However, mTOR inhibitor CNI-free regimens were associated with an increased risk of occurrence of acute rejection and *de novo* donor-specific anti-human leukocyte (HLA) antibodies (DSAs)<sup>4 5 6</sup>. Thus, they are now rarely used. Conversely, CNI-avoiding regimens based on the use of belatacept were confirmed to be effective in preventing acute rejection and safe after kidney transplantation<sup>7 8</sup>. In *de novo* kidney-transplant patients, long-term use of belatacept was associated with better kidney function and an increase in patient and graft survivals compared to patients who were given cyclosporin A-based immunosuppression<sup>9</sup>. In maintenance kidney-transplant patients, several studies, including a phase II trial and a large retrospective real-life study, have shown that the conversion from CNI to belatacept leads to an improvement in kidney function<sup>10 11</sup>. To our knowledge, the effect on kidney function and the clinical outcome of the conversion from belatacept to another regimen has not been assessed. Thus, this was the aim of the present retrospective study.

## Patients and Methods

We have identified 44 maintenance kidney-transplant patients from five French kidney-transplant centers who were converted from belatacept: Besançon University Hospital ( $n=10$ ), Necker University Hospital (Paris, France) ( $n=15$ ), Rouen University Hospital ( $n=1$ ), and Toulouse University Hospital (France) ( $n=18$ ). Conversion was conducted between December 2006 and June 2018. The 44 patients had been given belatacept—MPA—steroids ( $n=37$ ), belatacept—MPA ( $n=2$ ), or belatacept—mTORi—steroids ( $n=5$ ) for 14 (2-137) months. Fourteen patients (31.8%) had been given *de novo* belatacept at transplantation, and 30 patients had been converted at 7.2 (0.6-223) months from CNI to belatacept for impaired kidney function and/or histology ( $n=29$ ) or posttransplant diabetes mellitus ( $n=1$ ). All 14 *de novo* kidney-transplant patients were given belatacept—MPA—steroids. For the 30 patients who were converted to belatacept, initial immunosuppression was based on CNI-MPA-S ( $n=11$ ), CNI-MPA-mTORi-steroids ( $n=2$ ), or CNI-mTORi-S ( $n=3$ ). The patients' characteristics at and before conversion from belatacept to other immunosuppressive regimens are presented in Table 1. No specific anti-microbial prophylaxis was given after conversion from belatacept. Kidney parameters were assessed at conversion to belatacept (in the 30 patients who were converted to belatacept) 6 and 3 months before the conversion from belatacept, at conversion from belatacept, and at 3, 6, and 12 months after conversion, as well as at the last follow-up. eGFR was estimated using the abbreviated Modification of the Diet in Renal Disease (MDRD) formula. In all centers, DSAs were assessed yearly or in case of impaired kidney function and/or increased proteinuria. Efficacy and safety parameters were assessed after the conversion from belatacept until last follow-up, i.e.  $27.5 \pm 25.3$  months [median 20 (6-138)].

According to French law (Loi Jardé), anonymous retrospective studies do not require Institutional Review Board (IRB) approval. In each center, patients were identified and data were obtained from the local database, and then electronic medical records were shared by all institutions.

### Statistical analyses

Reported values represent either means ( $\pm$ SD) or medians (ranges). Proportions were compared by the  $\chi^2$  test or Fisher's exact test. The non-parametric Friedman test for serial measurements was used to compare quantitative variables. Student's t-test was used to compare quantitative variables. A  $p < 0.05$  was considered to be statistically significant.

## **RESULTS**

### Conversion from belatacept

Belatacept was stopped in 44 patients. The description of baseline characteristics of all patients as well as their outcomes are presented in the Supplementary Table. They had been given belatacept for 14 (2-137) months. Their mean age at conversion from belatacept was  $57 \pm 12.6$  months. The reasons for stopping belatacept are detailed in Table 2 and the Supplementary Table. In 28 patients (63.6%), it was stopped because of a complication; in 13 patients, it was ceased without patients having experienced any complications; and in the last 3 patients, belatacept was interrupted because no improvement in kidney function was observed. In 34 patients, belatacept was replaced by a CNI-based regimen, and 10 patients were given an mTORi CNI-free-based regimen. Post-conversion from belatacept

immunosuppression was as follows: CNI + MPA  $\pm$  steroids ( $n=21$ , 47.7%), CNI + mTORi  $\pm$  steroids ( $n=7$ , 15.9%), CNI + Azathioprine  $\pm$  steroids ( $n=3$ , 6.8%), CNI + steroids ( $n=3$ , 6.8%), mTORi + MPA  $\pm$  steroids ( $n=8$ , 18.2%), and mTORi + Azathioprine  $\pm$  steroids ( $n=2$ , 4.6%). Tacrolimus was the most commonly used CNI after belatacept cessation (94%). Its median trough level was 6 (4-8) ng/mL. Everolimus was the most commonly used mTORi after belatacept cessation. Its median trough level was 3 (2-6) ng/mL when associated with CNI and 5 (4-8) when given without CNI.

### **Kidney function outcome**

Overall, in the whole population ( $n=44$ ), eGFR decreased after belatacept cessation ( $p=0.0002$ ). Mean eGFR decreased from  $44.2\pm 16$  mL/min/1.73m<sup>2</sup> at conversion from belatacept to  $39.3\pm 18.5$  mL/min/1.73m<sup>2</sup> at 12 months post-conversion ( $p=0.01$ ), and  $35.7\pm 18.4$  mL/min/1.73m<sup>2</sup> at last follow-up ( $p=0.0002$ ) (Figure 1A). eGFR decreased in 29 patients (66%), remained stable in 8 patients (18%), and improved in 7 patients (16%). Proteinuria remained unchanged, i.e. 0.09 (0-2.1) g/d at conversion from belatacept vs. 0.13 (0-1.7) g/d at last follow-up,  $p=0.27$ .

Since some patients were given belatacept at transplantation (*de novo* patients) while others were converted to belatacept mainly because of impaired kidney function and/or histology, and since in some patients belatacept was ceased because of complications that can negatively impact kidney function, we have analyzed the outcome of different subgroups of patients separately.



De novo kidney-transplant patients who were given belatacept: Fourteen patients who were given belatacept immediately after transplantation stopped it 12.5 (3-137) months later. The mean follow-up after conversion from belatacept was 41.5±38.4 months. eGFR decreased after belatacept cessation ( $p=0.054$ ). Mean eGFR decreased from 51.4±16.6 mL/min/1.73m<sup>2</sup> at conversion from belatacept to 44.5±18.6 mL/min/1.73m<sup>2</sup> at 12 months post-conversion ( $p=0.03$ ), and 43.3±19.4 mL/min/1.73m<sup>2</sup> at last follow-up ( $p=0.03$ ) (Figure 1B).

Maintenance kidney-transplant patients who were converted to belatacept: Thirty patients were converted to belatacept at 7.2 (0.6-223) months. The mean follow-up after conversion from belatacept was 21±13.1 months. eGFR decreased after belatacept was stopped ( $p=0.0009$ ). Mean eGFR initially improved from 32.4±13.6 mL/min/1.73m<sup>2</sup> at conversion to belatacept to 40.8±14 mL/min/1.73m<sup>2</sup> at conversion from belatacept ( $p=0.004$ ). Thereafter, it decreased to 36.9±18.7 mL/min/1.73m<sup>2</sup> at 12 months post-conversion from belatacept ( $p=0.035$ ) and 32.1±17.4 mL/min/1.73m<sup>2</sup> at last follow-up ( $p=0.0002$ ) (Figure 1C).

Patients who stopped belatacept without experiencing a complication: Thirteen patients stopped belatacept because of the shortage of belatacept that occurred a couple of years ago ( $n=5$ ), upon their request ( $n=7$ ), or because kidney function had improved after the initiation of belatacept given because of prolonged delayed graft function ( $n=1$ ). The mean follow-up after conversion from belatacept was 27.9±21.9 months. Overall, no significant change was observed in eGFR ( $p=0.3$ ). Mean eGFR decreased from 56.4±15.6 mL/min/1.73m<sup>2</sup> at conversion from belatacept to 47.7±20 mL/min/1.73m<sup>2</sup> at last follow-up ( $p=0.07$ ) (Figure 1D).

Patients who were converted from belatacept to calcineurin inhibitors: Thirty-four patients were converted from belatacept to a CNI-based regimen. eGFR decreased after belatacept cessation ( $p=0.001$ ). Mean eGFR decreased from  $44.1\pm 15.3$  mL/min/1.73m<sup>2</sup> at conversion from belatacept to  $38.9\pm 19.5$  mL/min/1.73m<sup>2</sup> at 12 months post-conversion ( $p=0.006$ ) and  $34.8\pm 18.9$  mL/min/1.73m<sup>2</sup> at last follow-up ( $p<0.0001$ ) (Figure 2A).

Patients who were converted from belatacept to mTOR inhibitors: Ten patients were converted from belatacept to an mTORi-based regimen. No significant change in eGFR was observed after belatacept stop ( $p=0.17$ ). Mean eGFR decrease was at  $44.6\pm 17.4$  mL/min/1.73m<sup>2</sup> at conversion from belatacept,  $40.7\pm 16.8$  mL/min/1.73m<sup>2</sup> at 12 months post-conversion ( $p=0.22$ ), and  $38.5\pm 18.3$  mL/min/1.73m<sup>2</sup> at last follow-up ( $p=0.2$ ) (Figure 2B).

### **Immunological and kidney allograft outcomes after conversion from belatacept**

Only one patient, who was given CNI—MPA—Steroids, developed a *de novo* donor-specific antibody (2.3%) 6 months after conversion from belatacept that led to antibody-mediated rejection (AMR) and graft loss. Another patient who had a DSA at conversion to belatacept developed a chronic AMR. A third patient experienced a T-cell-mediated rejection 16 months after conversion from belatacept. Thus, overall 3 patients (6.8%) developed an acute rejection after belatacept cessation. Four patients (9.1%) lost their graft during follow-up: the first patient because of chronic AMR, a second patient due to the development of the acute AMR, a third one due to poor kidney function and severe interstitial fibrosis/tubular atrophy, and a last patient because of a cardio-renal syndrome. After the exclusion of patients who presented an acute rejection and/or a graft loss ( $n=5$ ), eGFR significantly decreased in the remaining 39

patients from  $46.1 \pm 14.6$  mL/min/ $1.73\text{m}^2$  at conversion to  $39.3 \pm 16.2$  mL/min/ $1.73\text{m}^2$  at last follow-up,  $p=0.0002$ .

### **Clinical outcomes after conversion from belatacept**

During follow-up, 10 patients (22.3%) experienced an infectious episode: cytomegalovirus replication ( $n=3$ ), flu ( $n=2$ ), norovirus infection ( $n=1$ ), *pneumocystis jiroveci* pneumonitis ( $n=1$ ), pyelonephritis ( $n=2$ ), and arthritis ( $n=1$ ).

Eight patients (18.2%) developed *de novo* cancer after conversion from belatacept: 6 patients developed skin cancer 4 to 66 months after conversion from belatacept; one patient presented lung cancer 11 months after conversion from belatacept; and one patient developed an EBV-positive cerebral posttransplant lymphoma disease (PTLD) 12 months after the conversion from belatacept.

Two patients (4.5%) developed *de novo* diabetes mellitus 1 and 3 months after belatacept cessation.

Two patients (4.5%) developed *de novo* hypertension 1 and 3 months after the conversion from belatacept, whereas a worsening of hypertension defined by adding anti-hypertension medications was observed in 10 other patients (22.7%).

Finally, 6 patients (13.6%) died during follow-up with a functioning graft. The causes for death were colon cancer ( $n=1$ ), lung cancer ( $n=1$ ), cerebral PTLD ( $n=1$ ), stroke ( $n=1$ ), vascular dementia ( $n=1$ ), and acute respiratory distress syndrome due to flu virus ( $n=1$ ).

## DISCUSSION

The effect of the conversion from belatacept to another immunosuppressive regimen is underreported. The aim of the present retrospective study was to assess the effect on kidney function and the clinical outcome of the conversion from belatacept to another regimen. Our findings were threefold: (i) the conversion from belatacept to another regimen was associated with a decrease in eGFR of  $\sim 8$  mL/min/1.73 m<sup>2</sup>; (ii) the decrease was less significant in patients who were converted from belatacept for a reason that wasn't a complication, and in those who were converted to an mTORi-based CNI-free regimen; and (iii) some patients developed diabetes and hypertension after conversion from belatacept.

In maintenance kidney-transplant patients, a phase II randomized controlled study showed an improvement in kidney function at one year in patients converted to belatacept (given with MPA and steroids) compared to those who were maintained on CNI- ( $7 \pm 11.99$  mL/min/1.73 m<sup>2</sup>)<sup>13</sup>. This gain was maintained at 3 years, i.e.  $+1.9$  mL/min/1.73 m<sup>2</sup> per year<sup>10</sup>. In a large retrospective real-life European multicenter study that included 219 maintenance kidney-transplant patients, mean eGFR significantly increased from  $32 \pm 16.4$  at conversion to belatacept to  $38 \pm 20$  mL/min/1.73 m<sup>2</sup> at  $21.9 \pm 20.2$  months later<sup>11</sup>. In the present study, we observed another way that eGFR decreases by  $\sim 8$  mL/min/1.73 m<sup>2</sup> after conversion from belatacept. This decrease was observed in patients who had received belatacept at transplantation and in those who had been converted to belatacept earlier because of impaired kidney function and/or histology.

In nearly two thirds of patients, belatacept was stopped because of a complication, mainly because of a viral infection. It was recently shown that CMV infection is the main opportunistic infection observed in belatacept-treated kidney transplant patients<sup>12 14</sup>. Conversely, in thirty percent of patients, belatacept was stopped either at the patients' request or because of belatacept shortage. In these patients in whom belatacept was stopped without having experienced any complication, eGFR also decreased from  $56.4 \pm 15.6$  mL/min/1.73m<sup>2</sup> at conversion from belatacept to  $47.7 \pm 20$  mL/min/1.73m<sup>2</sup> at last follow-up ( $p=0.07$ ). Due to the small number of patients, the decrease in eGFR was not statistically significant. An improvement in eGFR was observed in some few patients after belatacept cessation. Most of them were converted because of a complication. Thus, we speculate that the improvement is related to the resolution of the complication.

The improvement in kidney function after stopping CNI was often attributed to the loss of CNI-associated intra-renal vasoconstriction<sup>15</sup>. In the present study, in patients converted from belatacept to CNI, eGFR decreased from  $44.1 \pm 15.3$  mL/min/1.73m<sup>2</sup> to  $34.8 \pm 18.9$  mL/min/1.73m<sup>2</sup> at last follow-up ( $p < 0.0001$ ), while in those converted from belatacept to an mTORi-based CNI-free regimen, no significant change in eGFR was observed, i.e.  $44.6 \pm 17.4$  mL/min/1.73m<sup>2</sup> at conversion from belatacept and  $38.5 \pm 18.3$  mL/min/1.73m<sup>2</sup> at last follow-up ( $p=0.2$ ). Thus, after belatacept cessation, the less eGFR decrease was observed in patients who stopped it without having experienced a complication and in patients who were given mTORi without CNI. Although the risk of *de novo* DSAs is increased in kidney transplant patients who receive the latter combination<sup>4 5</sup>, several studies have shown improved kidney function in patients given an mTORi-based therapy compared to those on CNI-based immunosuppression.

The use of belatacept was associated with a decreased risk of metabolic syndrome, posttransplant diabetes mellitus, and hypertension<sup>16 17</sup>. In the present study, some patients developed *de novo* diabetes and *de novo* hypertension in the first three months after conversion from belatacept.

There are several limitations for the present study. It is retrospective uncontrolled study that included a small number of patients. The evolution of eGFR should be interpreted with caution since in 28 out of 44 patients, belatacept was stopped because of a complication that could have had a negative impact on kidney function. Finally, we acknowledge the lack of kidney allograft histology at conversion from belatacept and at last follow-up.

In summary, ceasing belatacept is associated with a significant decrease in kidney function.

**ACKNOWLEDGMENT:** No funding was obtained for this study

**DISCLOSURES:**

AG, RSS, CC, AD, ADB, and DB have nothing to declare

DD has received grants from Astellas and Neovii.

CL has received lecture fees from Astellas, Novartis, Chiesi, CSL Behring, and Hansa Medical and travel grants from Astellas, CSL Behring, and Alexion.

NK has received lecture fees from Astellas, Novartis, Gilead, Neovii, MSD, Octapharma, and Amgen and travel grants from Astellas, CSL Behring, Novartis, and Alexion.

**Supplementary Table:** Clinical course of all 44 patients who were included in the study (PDF).

Supplementary information is available at the *KI Reports* website

## **REFERENCES:**

1. Flechner SM, Kurian SM, Solez K, *et al.* De novo kidney transplantation without use of calcineurin inhibitors preserves renal structure and function at two years. *Am J Transplant* 2004; **4**: 1776-1785.
2. Campistol JM, Eris J, Oberbauer R, *et al.* Sirolimus therapy after early cyclosporine withdrawal reduces the risk for cancer in adult renal transplantation. *J Am Soc Nephrol* 2006; **17**: 581-589.
3. Budde K, Becker T, Arns W, *et al.* Everolimus-based, calcineurin-inhibitor-free regimen in recipients of de-novo kidney transplants: an open-label, randomised, controlled trial. *Lancet* 2011; **377**: 837-847.
4. Liefeldt L, Brakemeier S, Glander P, *et al.* Donor-Specific HLA Antibodies in a Cohort Comparing Everolimus with Cyclosporine After Kidney Transplantation. *Am J Transplant* 2012; **12**: 1192-1198.
5. Kamar N, Del Bello A, Congy-Jolivet N, *et al.* Incidence of donor-specific antibodies in kidney transplant patients following conversion to an everolimus-based calcineurin inhibitor-free regimen. *Clin Transplant* 2013; **27**: 455-462.
6. Rostaing L, Hertig A, Albano L, *et al.* Fibrosis progression according to epithelial-mesenchymal transition profile: a randomized trial of everolimus versus CsA. *Am J Transplant* 2015; **15**: 1303-1312.
7. Vincenti F, Charpentier B, Vanrenterghem Y, *et al.* A phase III study of belatacept-based immunosuppression regimens versus cyclosporine in renal transplant recipients (BENEFIT study). *Am J Transplant* 2010; **10**: 535-546.
8. Durrbach A, Pestana JM, Pearson T, *et al.* A phase III study of belatacept versus cyclosporine in kidney transplants from extended criteria donors (BENEFIT-EXT study). *Am J Transplant* 2010; **10**: 547-557.
9. Vincenti F, Rostaing L, Grinyo J, *et al.* Belatacept and Long-Term Outcomes in Kidney Transplantation. *The New England journal of medicine* 2016; **374**: 333-343.
10. Grinyo JM, Del Carmen Rial M, Alberu J, *et al.* Safety and Efficacy Outcomes 3 Years After Switching to Belatacept From a Calcineurin Inhibitor in Kidney Transplant

- Recipients: Results From a Phase 2 Randomized Trial. *Am J Kidney Dis* 2017; **69**: 587-594.
11. Darres A, Ulloa C, Brakemeier S, *et al.* Conversion to Belatacept in Maintenance Kidney Transplant Patients: A Retrospective Multicenter European Study. *Transplantation* 2018; **102**: 1545-1552.
  12. Bertrand D, Chavarot N, Gatault P, *et al.* Opportunistic infections after conversion to belatacept in kidney transplantation. *Nephrol Dial Transplant* 2020; **35**: 336-345.
  13. Rostaing L, Massari P, Garcia VD, *et al.* Switching from calcineurin inhibitor-based regimens to a belatacept-based regimen in renal transplant recipients: a randomized phase II study. *Clin J Am Soc Nephrol* 2011; **6**: 430-439.
  14. Karadkhele G, Hogan J, Magua W, *et al.* CMV high-risk status and posttransplant outcomes in kidney transplant recipients treated with belatacept. *Am J Transplant* 2020.
  15. Shihab FS. Cyclosporine nephropathy: pathophysiology and clinical impact. *Semin Nephrol* 1996; **16**: 536-547.
  16. Vanrenterghem Y, Bresnahan B, Campistol J, *et al.* Belatacept-based regimens are associated with improved cardiovascular and metabolic risk factors compared with cyclosporine in kidney transplant recipients (BENEFIT and BENEFIT-EXT studies). *Transplantation* 2011; **91**: 976-983.
  17. Rostaing L, Neumayer HH, Reyes-Acevedo R, *et al.* Belatacept-versus cyclosporine-based immunosuppression in renal transplant recipients with pre-existing diabetes. *Clin J Am Soc Nephrol* 2011; **6**: 2696-2704.



**Table 1:** Patients' characteristics

	<b>N= 44</b>
<b>Characteristics at transplantation</b>	
Recipients' gender: male	27 (61.4%)
Deceased donor	36 (81.8%)
Rank of transplantation (First/Second)	41/3
Initial kidney disease	
Glomerulopathy	18 (40.9%)
Interstitial nephropathy	7 (15.9%)
Diabetes mellitus and/or nephroangiosclerosis	4 (9.1%)
Genetic disease	7 (15.9%)
Other	8 (18.2%)
EBV serostatus	
Donor positive/Recipient positive	42 (95.4%)
Donor negative/Recipient positive	1 (2.3%)
Donor positive/Recipient negative	1 (2.3%)
<b>Immunologic recipient status, n (%)</b>	
Anti-HLA antibodies at kidney transplantation	8 (18.2%)
Donor-specific antibodies at kidney transplantation	5 (11.4%)
Donor-specific antibodies at conversion to belatacept	4 (9.3%)
<b>Start of belatacept</b>	
Age upon starting belatacept (years)	54.8±13
<i>De novo</i> belatacept/Conversion to belatacept	14 (13.6%)/30 (68.2%)
Time from transplantation to conversion to belatacept (months)	7.2 [0.6-223]
Induction therapy at transplantation	
Anti-interleukin 2 receptor blocker	34 (77.3%)
Polyclonal antibodies	6 (13.6%)
None	4 (9.1%)
Calcineurin inhibitors before conversion to belatacept	30 (100%)
Cyclosporine A	3 (10%)
Tacrolimus	27 (90%)
mTORi-based therapy before conversion to belatacept	5 (16.7%)
MPA before conversion to belatacept	27 (90%)
Steroids before conversion to steroids	30 (100%)

Abbreviations: EBV: Epstein-Barr virus; HLA: human leukocyte antibodies; mTORi: mammalian target of rapamycin inhibitor; MPA: mycophenolic acid

**Table 2:** Reasons for conversion from belatacept

	<b><i>N</i> = 44</b>
<b><u>Conversion for a complication</u></b>	<b><u>28</u></b>
<b>Infections §</b>	<b>15</b>
Cytomegalovirus	13
Human herpes virus 8	1
BK virus	1
<b>Acute rejection</b>	<b>7</b>
T-cell-mediated rejection	5
Antibody-mediated rejection	1
Mixed T-cell and antibody-mediated rejection	1
<b>T-cell-mediated rejection and cytomegalovirus infection</b>	<b>1</b>
<b>Colon cancer</b>	<b>2</b>
<b>T-lymphoma and human papilloma virus infection</b>	<b>1</b>
<b>No improvement in kidney function and recurrent cytomegalovirus infection</b>	<b>1</b>
<b>No improvement in kidney function and BK virus infection</b>	<b>1</b>
<b><u>Conversion without a complication</u></b>	<b><u>13</u></b>
<b>Belatacept shortage</b>	<b>5</b>
<b>Patients' request</b>	<b>7</b>
<b>Improvement in kidney function</b>	<b>1</b>
<b><u>No improvement in kidney function after conversion to belatacept</u></b>	<b><u>3</u></b>

§ Among patients who were converted from belatacept because of a complication, cytomegalovirus replication persisted in patients having resistant CMV infection ( $n=3$ ) while no CMV replication recurrence occurred in the nine remaining patients. All other viruses were cleared after conversion from belatacept

**Figures legends:**

Figure 1: Outcome of kidney function before and after conversion from belatacept.

A- in the whole population ( $n=44$ )

B- in *de novo* kidney transplant patients who were given belatacept ( $n=14$ )

C- in maintenance kidney transplant patients who were converted to belatacept earlier ( $n=30$ )

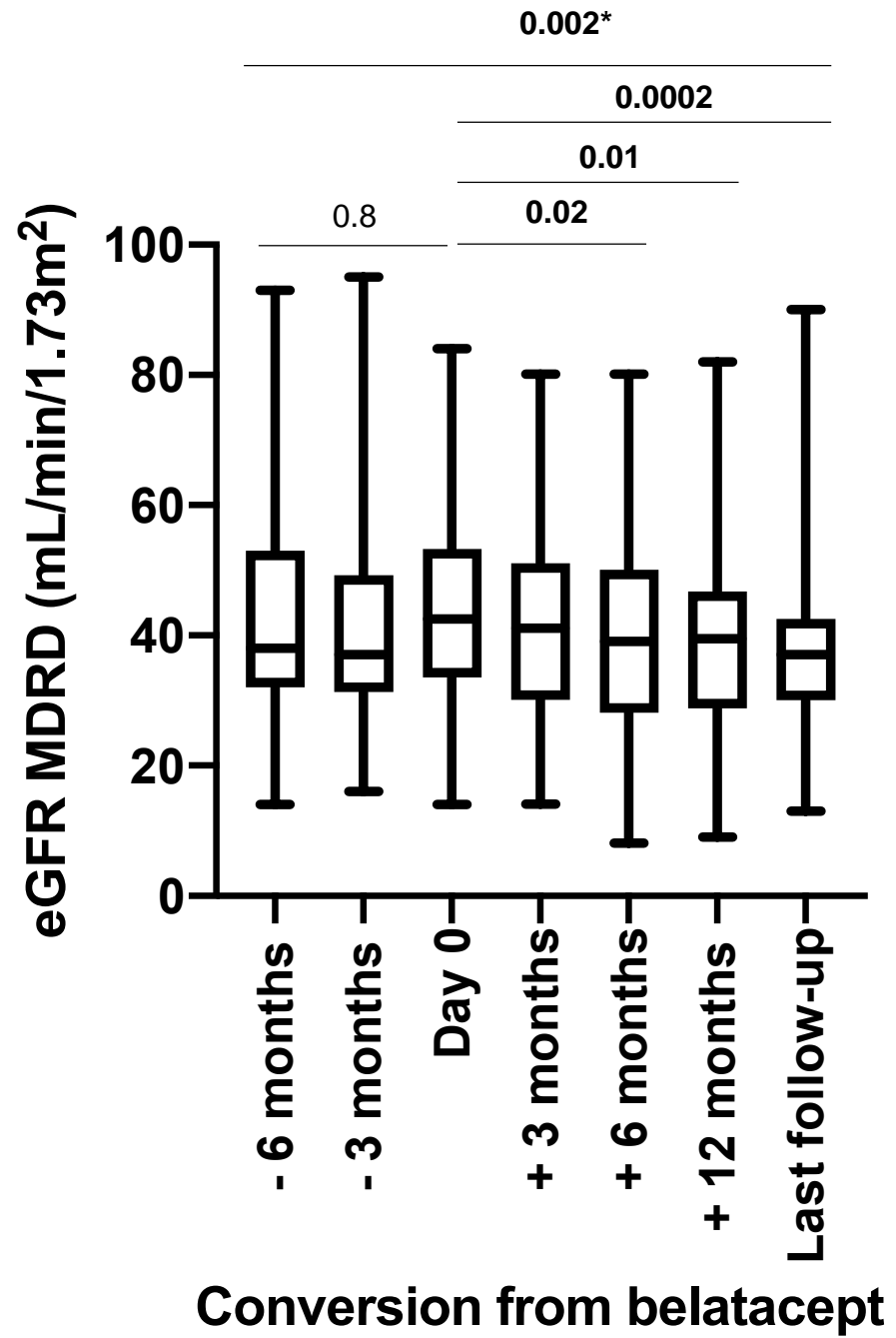
D- in patients who stopped belatacept without experiencing a complication ( $n=13$ )

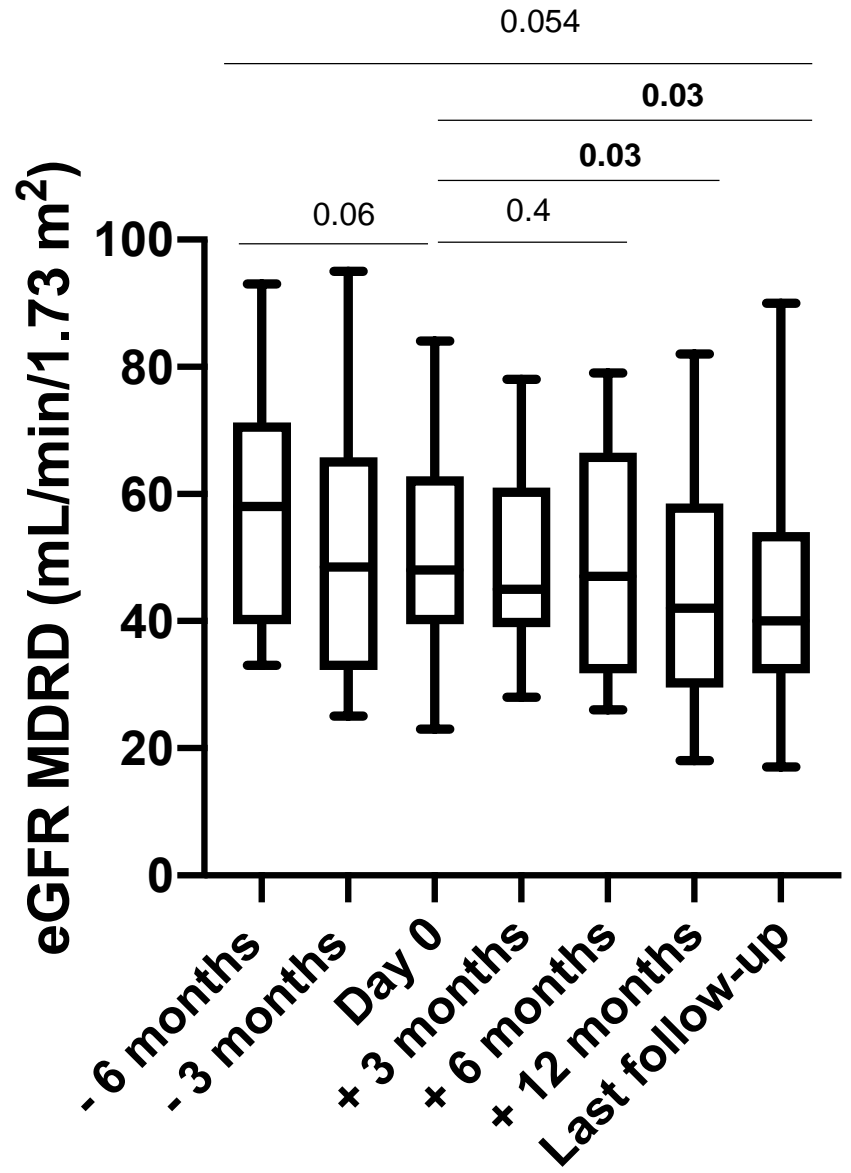
Figure 2: Outcome of kidney function before and after conversion from belatacept.

A- in patients who were converted from belatacept to calcineurin inhibitors ( $n=34$ )

B- in patients who were converted from belatacept to mTOR inhibitors ( $n=10$ )

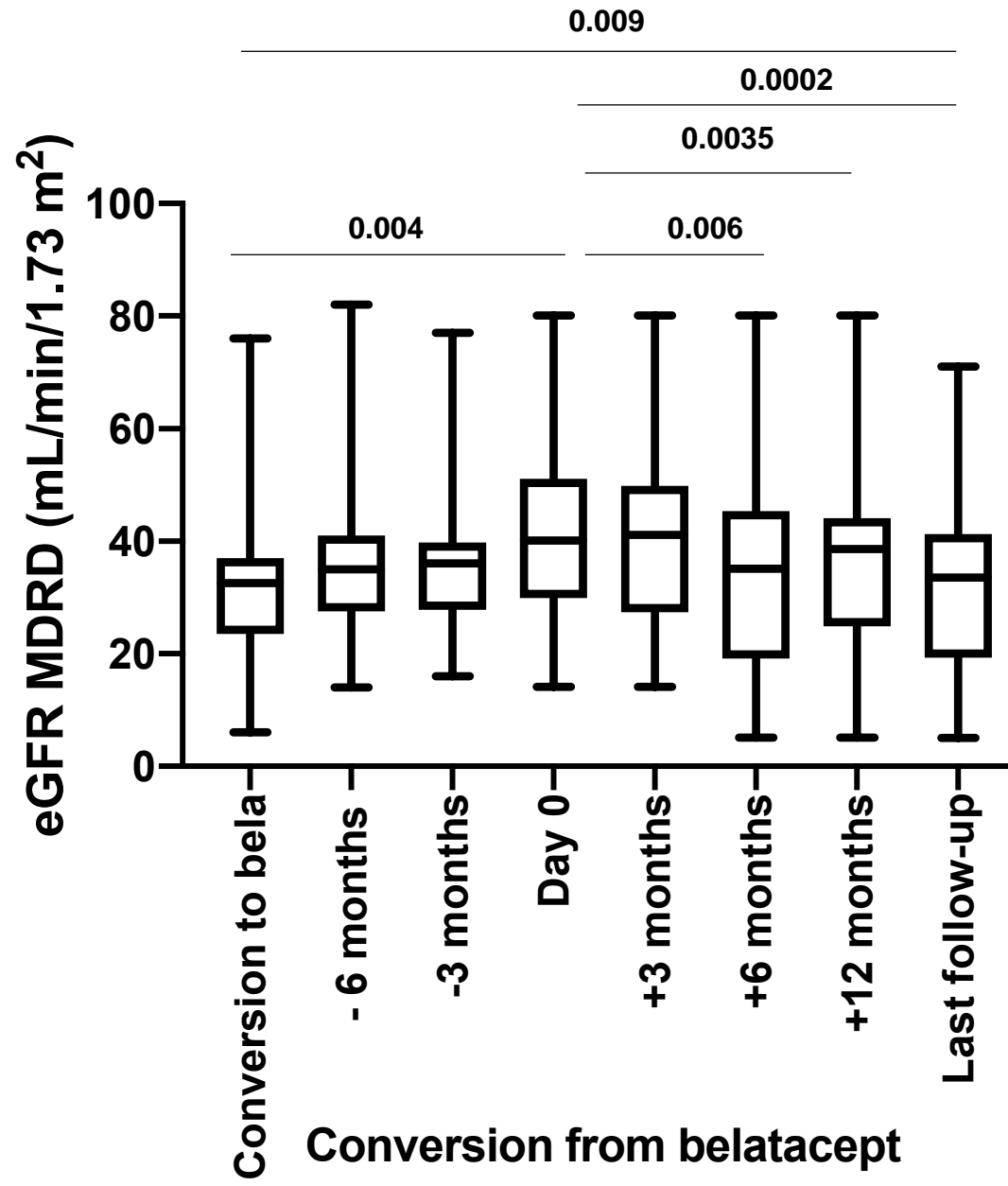
1A

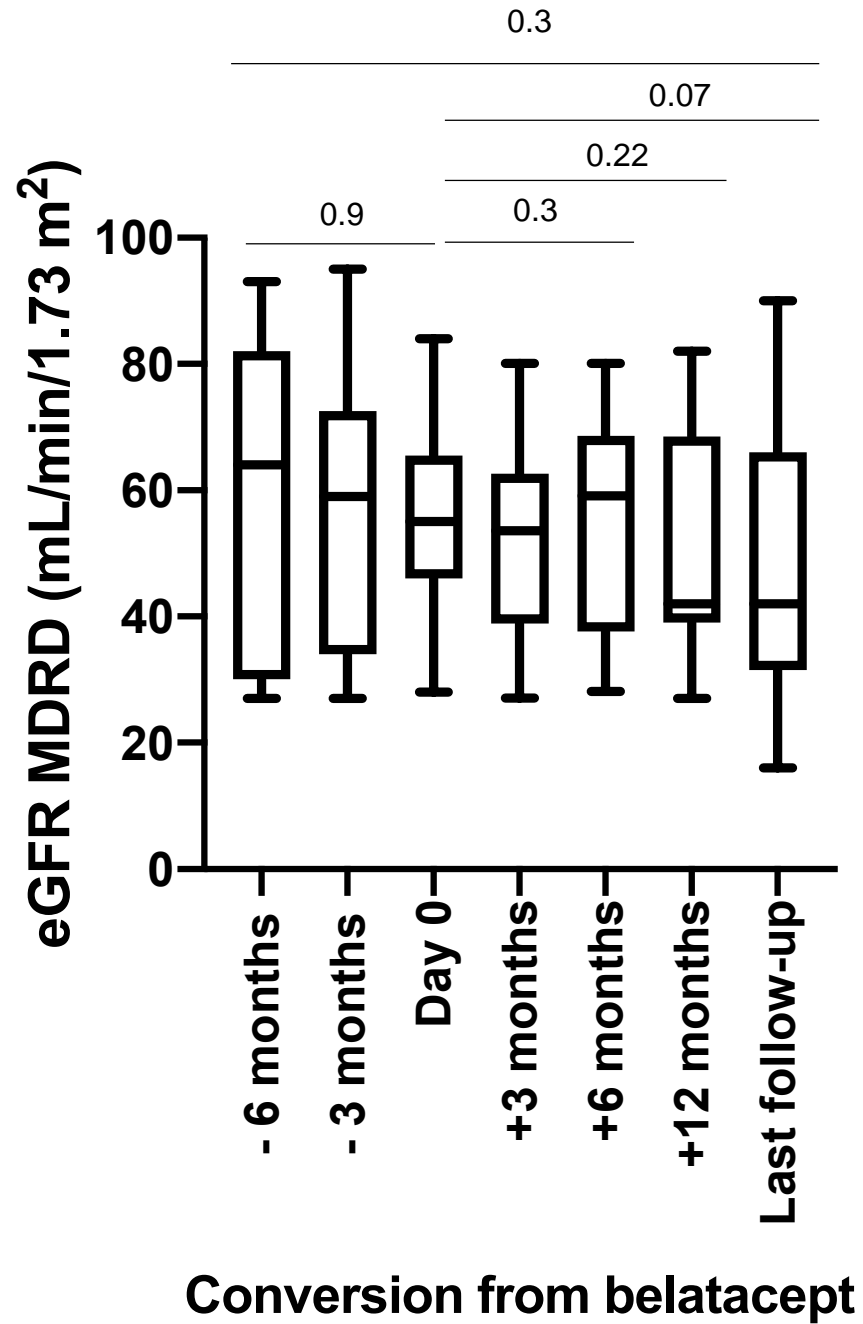




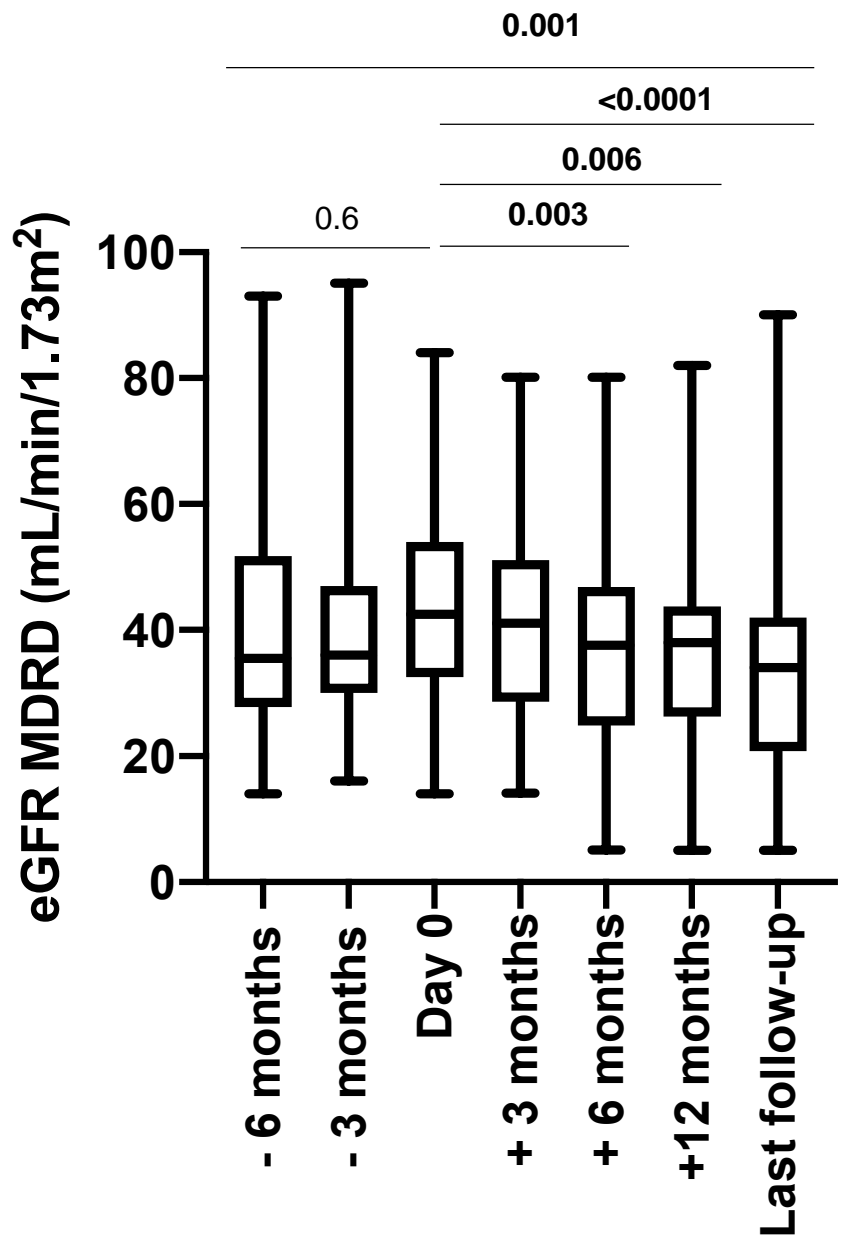
Conversion from belatacept

1C



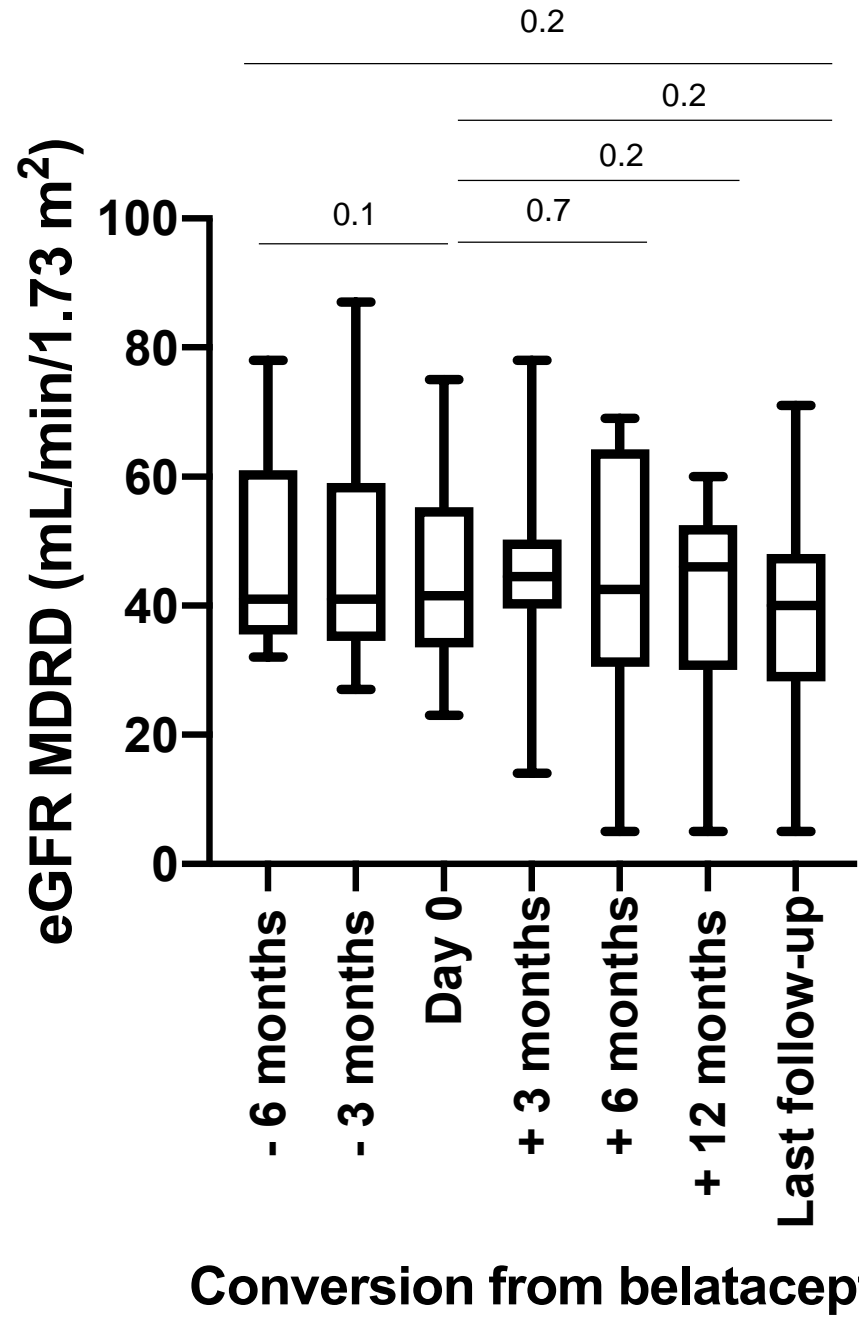


Conversion from belatacept



Conversion from belatacept





Conversion from belatacept