BELATACEPT IN RENAL TRANSPLANTATION: A REAL-WORLD PHARMACOKINETIC STUDY

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A high intervariability of belatacept exposure supports the potential use of belatacept drug monitoring to evaluate in an individualized manner the immunosuppressive burden of KTR

BACKGROUND

Belatacept, a CTLA4-Ig, was designed as an alternative to calcineurin inhibitors (CNI) to prevent rejection and graft loss in kidney transplant recipients. It inhibits T-cell activation by blocking the CD28-CD80/86 costimulatory pathway. (Martin et al., 2011).

Several studies have suggested a long-term clinical benefit for kidney transplant recipients (KTR) mainly on renal function and better glycemic control, after a conversion from CNI to belatacept-based maintenance regimen (Nair et al., 2017)

However belatacept has also been associated with a higher number of severe infectious diseases, particularly CMV disease, and lymphoproliferative disease (Chavarot et al., 2021)

Therapeutic drug monitoring usually guides the benefit-risk assessment of long-term immunosuppression. However, belatacept concentration is not available in clinical routine, and extensive real-world pharmacokinetic data are lacking.

We aimed to provide data about the inter-variability and intra-variability of belatacept concentrations in kidney transplant recipients (KTR), after conversion from a CNI- to a belatacept-based regimen

METHOD

All KTR (N=102) with a signed consent, who were given maintenance belatacept doses at the outpatient transplant clinic of Necker Hospital (Paris, France), between March and June 2022, were enrolled.

Plasma belatacept concentrations were measured by a validated quantitative liquid chromatography tandem mass spectrometry method (MabXmise kit, Promise Proteomics, France).

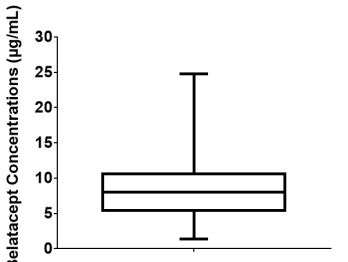

Figure 1 : Through concentrations of 108 KTR (receiving 5 mg/kg every 4 weeks)

RESULTS & CONCLUSION

A total of 252 trough concentrations of belatacept, from 108 KTR (45% women, 25-85 years old) were measured. They all displayed a stable graft function, and received belatacept as maintenance regimen (5mg/kg every 4 weeks) for at least 3 months, in order to assess steady-state belatacept concentrations.

Notably, belatacept trough concentrations greatly varied from 1.4 to 24.8 µg/L, with a mean (±SD) concentration of 8.4±3.9 µg/L. The mean inter-individual variability was 46%.

Belatacept concentrations were assessed at 3 consecutive time points in 37 KTR. The mean intra-patient variability was only 17%.

Despite standardized dosing, based on bodyweight, our study unveiled a high variability of belatacept exposure between patients under maintenance regimen. This finding strongly supports the use of belatacept monitoring to evaluate in an individualized manner the immunosuppressive burden of patients and the low intra-patient variability further reinforce the validity of the measurement. Further studies are needed to evaluate whether belatacept therapeutic drug monitoring, as assessed in a broad population, would correlate with clinical events, such as rates of infections, malignancies, or rejections.

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