Poster

[P25-7] P25-7: Immunosuppressive drugs (2): Monoclonal antibody and genotyping

Chair: Toru Hashida, Japan

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[P25-7-2] Determination of belatacept pharmacokinetics in renal transplant patients using a novel automated assay

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Background

Belatacept (Nulojix®) is an alternative to calcineurin inhibitors for immunosuppression following kidney transplantation. Available data on belatacept pharmacokinetics is sparse and therapeutic drug monitoring is currently not practiced. We have developed and validated an automated assay to determine belatacept pharmacokinetics in renal transplant recipients.

Methods

A time-resolved fluorescence assay was developed using recombinant CD80 (coated onto 96-well microplates) as belatacept capture reagent. An anti-immunoglobulin tracer labeled with europium was used to detect bound drug. The assay was automated on the AutoDELFIA® immunoassay platform (Perkin Elmer). Renal transplant patients previously treated with tacrolimus, who were switched to belatacept, were included in the study. Belatacept was given every two or four weeks. Blood samples were taken immediately prior to infusion and at 40, 70, 100 and 130 minutes and 2-3 days and 7-14 days after.

Results

The assay was validated according to EMA guidelines, with a range of 0.3 mg/L –30 mg/L. Inaccuracy was below 9.0 % and the coefficient of variation (CV) was below 3.6 %. Samples with high drug concentrations (130 mg/L) showed linearity upon dilution with mean inaccuracy of 9.7 % and a CV of 3.8 %. Values were unaffected by storage at 4 C for 14 days and two freeze/thaw cycles. Five patients were included in the ongoing study and preliminary results (mean, [SD]) showed peak concentration of 96.4 mg/L [19.8], volume of distribution 4.3 L [0.9] and half-life of 6.9 days [0.70]. Trough concentration was 2.9 mg/L [1.3] in patients receiving drug every four weeks (n=2) and 11.3 mg/L [3.8] in patients receiving drug every second week (n=4). The AutoDELFIA® platform was capable of analyzing a total of 120 samples could be analyzed with a runtime of 4 hours, allowing for large volume analysis.

Conclusions

An automated assay for measuring belatacept in serum has been developed, validated and applied in an ongoing pharmacokinetic study. Preliminary results show little variation in belatacept pharmacokinetics among patients.

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