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Titel des Beitrags:
Pharmacokinetics and antibody responses to the CD3 antibody otelixizumab used in the treatment of type 1 diabetes.

Abstract:
Otelixizumab is a chimeric CD3 antibody that has been genetically engineered to remove the glycosylation site in the Fc domain. This limits its ability to bind to complement or Fc receptors and reduces the risk of adverse clinical reactions due to cytokine release. In a trial for treatment of type 1 diabetes, a short treatment with otelixizumab resulted in a reduced requirement for insulin lasting at least 18 months. In the course of this trial, the blood concentrations of the antibody were measured by flow cytometry to determine its pharmacokinetic profile. Dose-dependent accumulation of otelixizumab was demonstrated and modeling of the data indicated that the terminal half-life was approximately 1.5 days. Antibody responses to otelixizumab were measured by 2 methods: a bridging enzyme-linked immunosorbent assay and surface plasmon resonance. The surface plasmon resonance method had a greater sensitivity and was able to detect responses in all patients, starting at 8 days after the commencement of therapy. Neutralizing antibodies were detected in a significant proportion of patients by days 22 to 29. Although no adverse clinical effects were associated with these antibody responses and they did not appear to affect the clearance of the drug, they might have important
implications for possible retreatment of the patients.

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