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Study No.: Study OTX113390
Title: Evaluation of the safety and tolerability of re-dosing with intravenous (IV) otelexizumab in adult subjects with newly diagnosed type 1 diabetes mellitus.
Rationale: Study OTX113390 was designed to assess the safety, tolerability, and immunogenicity of re-dosing otelexizumab IV at 6 months (after the initial treatment course) with an 8 consecutive day series of infusions in adult subjects with newly diagnosed type 1 diabetes mellitus (T1DM) and to characterise the pharmacokinetic (PK) and pharmacodynamic (PD) effects following re-dosing.
Phase: IIa
Study Period: The first subject was enrolled on 22 Nov 2010. On 09 Mar 2011, investigators were notified to cease subject recruitment, as efficacy was not seen in the Phase 3 Study OTX115495 ("DEFEND-1") at the 3.1 mg dose of otelexizumab. At the time that recruitment ceased one subject had received a single course of otelexizumab (8 consecutive days of IV otelexizumab at the following doses: 0.1 mg, 0.2 mg, 0.3 mg and 0.5 mg x5); an additional subject was enrolled but never received study medication. No subjects were re-dosed. The subject that received otelexizumab subsequently withdrew from the study on 19 May 2011.
Study Design: Open-label, multi-centre study in eight adults with newly diagnosed T1DM.
Centres: Five sites received Institutional Review Board/Ethics Committee (IRB/EC) approval. One site (Hôpital Bichat Claude Bernard, Service Diabétologie-Endocrinologie, 46 rue Henri Huchard, Paris Cedex 18, France, 75877) enrolled the single subject who received study medication.
Indication: Type 1 diabetes mellitus.
Treatment: Otelexizumab was diluted in 0.9% saline solution for IV infusion over 30 minutes for 8 consecutive days: 0.1 mg on Day 1, 0.2 mg on Day 2, 0.3 mg on Day 3, and 0.5 mg per day on Days 4 to 8. The total dose was 3.1 mg/treatment course. This same dose regimen was to be repeated at Month 6 (though no one received re-treatment in this study).
Objectives: The primary objective was to assess the safety, tolerability, and immunogenicity of re-dosing otelexizumab IV at 6 months (after the initial treatment course) with an 8 consecutive day series of infusions in adult subjects with newly diagnosed T1DM.
Primary Outcome/Efficacy Variable: The primary safety and tolerability endpoints were: <ul style="list-style-type: none"> • Adverse Events (AEs). • Change from baseline and number of subjects outside the normal range for blood pressure (BP), respiration rate (RR), heart rate (HR) and temperature. • Change from baseline in clinical chemistry and haematology parameters. • Epstein-Barr Virus (EBV) viral load. • Change in total lymphocyte, CD4+ and CD8+ T-cell counts (also a secondary PD endpoint). • Immunogenicity: Serum levels of anti-otelexizumab binding antibodies. Where binding antibodies were detected, proportion which were anti-otelexizumab neutralising antibodies.
Secondary Outcome/Efficacy Variable(s): Secondary PD endpoints were: <ul style="list-style-type: none"> • Circulating peripheral T lymphocytes and CD4+ and CD8+ subset counts. • Saturation of CD3 antigen on peripheral blood T cells. Secondary PK endpoints were: <ul style="list-style-type: none"> • Individual serum concentrations of otelexizumab and data permitting summary PK parameters.
Statistical Methods: Data from the pivotal Phase 3 Study OTX115495 ("DEFEND-1") of otelexizumab in type 1 diabetes became available just as this study began recruiting. Study OTX115495 did not meet its primary endpoint. As a result, recruitment was halted for this study. The statistical analyses described in the protocol for the full study were no longer appropriate. No summary analyses were performed.
Study Population: Adult subjects aged 18-45 years with a diagnosis of T1DM (newly-diagnosed T1DM; within 90 days prior to the first dose of study drug administration) who were currently taking insulin or had required insulin therapy at some time since diagnosis were eligible. All subjects required evidence of residual β cell function (stimulated C-peptide level greater than 0.20 nmol/L and less than or equal to 3.50 nmol/L) and a positive test for one or more of the auto-antibodies typically associated with T1DM.
Number of Subjects: It was planned that 8 subjects would be enrolled to achieve a target of 6 subjects completing the study. One subject was enrolled and received a single course of study medication; an additional subject was enrolled

but never received study medication. No subjects were re-dosed. No subjects completed the study. The subject that received otelixizumab subsequently withdrew from the study on 19 May 2011.
Demographics: The subject was a 31-year-old White female.
Primary Efficacy Results: Not applicable.
Secondary Outcome Variable(s): Not applicable.
Safety Results: Adverse events were collected from the start of Investigational Product (IP) and until the follow-up contact. Since no tabular summaries were produced, all AEs are listed here.
All Adverse Events – On-Therapy (Preferred Term/verbatim Term)
Cough/cough (1 report)
Dyspepsia/dyspepsia (1 report)
Pyrexia/fever (1 report)
Headache/headache (1 report)
Serious Adverse Events - On-Therapy
n (%) (n considered by the investigator to be related to study medication): No SAEs were reported.
Conclusion: No conclusions can be made regarding the primary or other objectives of the study.