A Phase IB Clinical Trial with Dekavil (F8-Il10), an Immunoregulatory 'Armed Antibody' for the Treatment of Rheumatoid Arthritis, Used in Combination with Methotrexate

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A therapeutic strategy based on the selective delivery of an immunoregulatory cytokine to the sites of inflammatory disease has been developed. Dekavil is an 'armed antibody', composed of the human F8 antibody (specific to the EDA domain of fibronectin, a marker of angiogenesis) fused to the anti-inflammatory cytokine interleukin-10 (IL-10), enabling delivery and accumulation of the cytokine at sites of disease [1,2]. A Phase Ib clinical trial is now underway, which features the administration of weekly escalating doses (6, 15, 30, 60, 110, 160, 210 and 300 µg/kg) of Dekavil in combination with a fixed dose of methotrexate (MTX) to cohorts of three to six rheumatoid arthritis (RA) patients who have previously failed at least one line of anti-tumor necrosis factor (TNF) therapy. This is not a placebo-controlled trial. The objective is to establish the maximum tolerated dose (MTD) and the recommended dose (RD) of the combined treatment, to study safety and tolerability, and to obtain preliminary therapeutic information. The treatment is given as a once-weekly subcutaneous injection for up to 8 weeks.

As of today, 24 patients have received at least one drug administration of F8IL10, from dose levels of between 6 and 300 µg/kg, in combination with MTX, and were therefore evaluable for safety. No dose limiting toxicities (DLTs), serious adverse events (SAEs), or Serious unexpected suspected adverse reactions (SUSARs) have been recorded. No MTD has been reached. The dose level of 300 µg/kg is currently being used. Twelve of 24 treated patients reported mild reactions at the injection sites. A single systemic adverse reaction, progressive anemia, was reported in one patient treated with the 160 µg/kg dose level. All adverse reactions recorded resolved after the end of treatment with little to no therapeutic interventions.

Initial signs of therapeutic benefit have been observed in the treated patients, even at the low drug dosages of the initial steps of the dose escalation. Overall, 15 of 23 patients evaluable for efficacy have experienced therapeutic benefit (in terms of American College of Rheumatology responses). Among these, 15 patients experienced ACR 20 response, 7 experienced ACR 50 response, and 3 achieved ACR 70 response (15 µg/kg, 30 µg/kg and 60 µg/kg cohorts). Variation in the duration of the response was observed. Of note, two patients in the 30 µg/kg cohort and in the 60 µg/kg cohort achieved long-lasting remission (ACR 70 maintained in excess of one year from the last study drug administration).

The promising safety data, together with preliminary positive signs of activity, suggest that the targeted delivery of IL-10 to the sites of inflammation may be beneficial to patients with RA with a possibility for a long-lasting therapeutic potential. These results warrant future clinical investigations in dedicated randomized trials.

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