Arthritis & Rheumatism
AMERICAN COLLEGE OF RHEUMATOLOGY
EDUCATION · TREATMENT · RESEARCH
WILEY-BLACKWELL

Arthritis & Rheumatism, Volume 64, November 2012 Abstract Supplement

Abstracts of the American College of Rheumatology/Association of Rheumatology Health Professionals Annual Scientific Meeting
Washington, DC November 9-14, 2012.

Active Immunization With TNF-Kinoid In Rheumatoid Arthritis Patients With Secondary Resistance To Tumor Necrosis Factor-Alpha Antagonists Is Safe And Immunogenic.

Durez[1], Patrick, Miranda[2], Pedro, Toncheva[3], Antoaneta, Berman Sr.[4], Alberto, Rillo[5], Oscar L., Boutsen[6], Yves, Kehler[7], Tatjana

Université Catholique de Louvain, Brussels, Belgium
APHP-Pitie Salpetriere Hospital/UPMC, Paris, France
Université Paris-Sud, Le Kremlin Bicetre, France
Diagnostic and Consulting Center, Plovdiv, Bulgaria
Centro Investigaciones Reumatológicas, Tucumán, Argentina
University Hospital Split, Split, Croatia
Clinical Hospital Center Sestre Milosrdnice, Zagreb, Croatia
Clinical Hospital Sveti Duh, Zagreb, Croatia
Rehabilitation clinical Hospital Iasi, Iasi, Romania
NEOVACS SA, Paris, France
Hopital Avicenne, Bobigny, France
Centro de Estudios Reumatologicos, Santiago de Chile, Chile
National Multiprofile Transport Hospital, Sofia, Bulgaria
Hospital Padilla, Tucuman, Argentina
Hospital Tornú, Buenos Aires, Argentina
UCL Mont-Godinne, Godinne, Belgium
Thalassotherapia Opatija, Opatija, Croatia
Emergency County Hospital Dr Constantin Opis, Maramures, Romania
Sociedad Medica del Aparato Locomotor SA, Santiago de Chile, Chile

Background/Purpose:

Blocking TNF alpha (TNFa) with monoclonal antibodies (mAbs) has been successful in the treatment of rheumatoid arthritis. However secondary resistances are frequent and impose treatment changes. Active immunization with a TNF-Kinoid that safely induces self polyclonal anti-TNFa antibodies (Abs) could be an alternative to anti-TNFa mAbs. We evaluated the immunogenicity and safety of TNF-K in patients with rheumatoid arthritis and secondary resistance to TNF blockers.

Methods:

TNFa-Kinoid (TNF-K, Neovacs SA, Paris, France) is an immunotherapeutic composed of recombinant human TNFa conjugated to KLH, inactivated and adjuvanted with ISA-51 emulsion. 40 patients with active rheumatoid arthritis (DAS28>=3.2) with history of positive clinical response to at least one TNF-blocker followed by secondary failure (35% IFX, 30 % ADA, 42.5% ETA) were enrolled in a double-blind, placebo-controlled, phase 2 study to evaluate three different intramuscular doses of TNF-K (90, 180, 360 mcg) and two immunization schedules (D0 and 28 or D0, 7 and 28). Humoral immune responses were evaluated through titration of anti-TNFa

and anti-KLH Abs and neutralization assay. The T cell response was assessed by lymphoproliferative assay with tritiated thymidine incorporation. Clinical response was evaluated by the ACR and EULAR core set response.

Results:

No related serious adverse event has been reported. Few minor transient local and systemic reactions have been recorded following immunization. Anti-TNFa Abs were induced in 50%, 75% and 91% of patients at 90 mcg, 180 mcg and 360 mcg, respectively. 100% of patients with three injections of 180 or 360 mcg had immunogenic response against TNF versus 67% in the groups receiving two injections. The anti-TNF antibody geometric mean titres were higher in patients who received 3 injections of 360 mcg. No lymphoproliferative response could be measured after stimulation with native TNF. Among the 21 patients who developed anti-TNF Abs, 48% present a moderate to good response according to EULAR score as opposed to only 31% of the 16 patients without Abs. A mean decrease of -14% of the C reactive protein level is measured in patients with Abs while in patients without Abs, the mean CRP level increased by 5%.

Conclusion:

Active immunization with TNFa kinoid to induce a polyclonal, self-anti-TNFa antibody response is safe and immunogenic. A clear dose-response was observed for the dose of kinoid as well as for the number of administrations. Association of anti-TNF Abs induced by the kinoid with clinical and biological responses were observed in patients included in this preliminary phase 2 study. Further studies are needed to confirm this new approach in RA.

To cite this abstract, please use the following information:
Durez, Patrick, Miranda, Pedro, Toncheva, Antoaneta, Berman Sr., Alberto, Rillo, Oscar L., Boutsen, Yves, et al; Active Immunization with TNF-Kinoid in Rheumatoid Arthritis Patients with Secondary Resistance to Tumor Necrosis Factor-Alpha Antagonists Is Safe and Immunogenic. [abstract]. Arthritis Rheum 2012;64 Suppl 10 :479
DOI: 10.1002/art.38214