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Abatacept found ineffective in treatment of non-life threatening lupus

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Results from a 12-month multi-center clinical trial did not show therapeutic benefit of abatacept over placebo in patients with non-life threatening systemic lupus erythematosus (SLE). Abatacept failed to prevent new disease flares in SLE patients tapered from corticosteroids in an analysis where mild, moderate and severe disease flares were evaluated together. Full details of the phase IIb clinical trial are published in the October issue of Arthritis & Rheumatism, a journal of the *American College of Rheumatology (ACR).*

The ACR estimates that 161,000 to 322,000 adults in the U.S. have SLE, an autoimmune disease that can affect multiple systems in the body. Those with SLE may experience periods of increased disease activity (flares). Manifestations of lupus range from mild, single-organ involvement to more severe involving multiple organs, which can also lead to organ failure. Treatments for SLE include the off-label clinical use of immunosuppressives such as azathioprine, methotrexate, and cyclophosphamide, which may still require the use of high-dose corticosteroids. Corticosteroids, such as prednisone, are effective in treating flares, but are associated with toxicities and long-term use place patients at risk for severe comorbidities.

Prior studies have shown that abatacept is safe and effective in patients with rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA). The Food and Drug Administration (FDA) and European Medicines Agency (EMA) currently approve abatacept for the treatment of moderate to severe RA and JIA, leading researchers to believe it may be

an appropriate therapy for other autoimmune diseases such as SLE. "Corticosteroids have serious side effects, so treatments that are targeted and could control disease activity while allowing steroid tapering would represent an advance in lupus therapy," said lead author of the current study, Joan T. Merrill, M.D. of the Oklahoma Medical Research Foundation.

Dr. Merrill and colleagues conducted the first trial to assess the effects of abatacept on disease flares in patients with non-life threatening SLE. There were 175 patients included in the trial whose primary symptoms included active polyarthritis, chronic discoid skin lesions, pleuritis, and/or pericarditis. Participants were randomized with 118 administered abatacept (10mg/kg of body weight) by intravenous (IV) infusion on days 1, 15, 29 and every 4 weeks throughout the 12-month period. There were 57 patients in the placebo group who received normal saline IV infusion. Prednisone (30 mg/day) was administered to both groups for 1 month and then tapered.

At the completion of the study 68.6% of participants remained in the abatacept group and 61.4% in the placebo group. Researchers found the most frequent reason for discontinuation was lack of efficacy—17.8% in the abatacept group and 21.1% in the placebo cohort. Further more, the proportion of patients with a new flare following the steroid taper was 79.7% and 82.5% in the abatacept and placebo groups, respectively. In ad hoc analyses, there were greater differences when severe flares or physician-reported flares were analyzed separately, and in the subset of patients who entered the study with active arthritis, but these findings are considered exploratory and would require confirmation in future studies.

The research team also found that the frequency of patients with serious adverse events (SAEs) was higher in participants receiving abatacept (19.8%) than with those in the placebo group (6.8%). SAEs were single events ranging from nausea to lupus nephritis, and most often occurred

during the first 6 months of the study, including the 2-month steroid taper period. Researchers suggest that the majority of SAEs could be attributed to SLE disease activity.

"While there is potential for clinical application of abatacept, further studies are needed to evaluate whether there are subsets of patients for whom this treatment might be useful, and then to determine the best way to treat and monitor such patients," concluded Dr. Merrill.

More information: "The Efficacy and Safety of Abatacept in Patients with Non-Life Threatening Manifestations of Systemic Lupus Erythematosus." J. T. Merrill, R. Burgos-Vargas, R. Westhovens, A. Chalmers, D. D'Cruz, D. J. Wallace, S. C. Bae, L. Sigal, J.-C. Becker, S. Kelly, K. Raghupathi, T. Li, Y. Peng, M. Kinaszczuk, and P. Nash. Arthritis & Rheumatism; Published Online: June 8, 2010 (DOI: 10.1002/art.27601); Print Issue Date: October 2010.

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