Study finds bortezomib to be promising treatment for rheumatoid arthritis

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A new study by Greek researchers suggests that the biologic drug bortezomib (Velcade), a proteasome inhibitor used to treat multiple myeloma (bone marrow cancer), may represent a promising treatment for rheumatoid arthritis (RA). In this study, bortezomib displayed favorable effects in an animal model of inflammatory arthritis that mimics RA, in reducing disease severity and inflammation, and promoting bone healing. Full findings of this study are published in the November issue of *Arthritis & Rheumatism*, a journal of the American College of Rheumatology (ACR).

RA is a chronic, systemic, autoimmune disease characterized by inflammation and joint destruction. The newer biologics, such as the tumor necrosis factor (TNF) inhibitors and monoclonal antibodies, have increased the therapeutic options for patients with RA. However, studies have shown that more than 50% of patients treated with a TNF inhibitor do not meet the ACR 50 improvement criteria-a standard set of measures developed by the college to determine efficacy of drugs in clinical trials.

"The definitive role of biologic agents in treating this difficult-to-cure population has yet to be defined in prospective trials comparing the available therapeutic options," explained study leader Evangelia Yannaki, M.D., of George Papanicolaou Hospital in Thessaloniki, Greece. "Given the lack of options for poor responders and the increased risk of infections and malignancies with available biologic agents for RA, there is a great need for novel therapies that are safe and effective."

The research team explored bortezomib as an optimal treatment for RA because the drug targets multiple pathways. In RA, the most important proinflammatory mediators are regulated by the transcription factor NF-KB-proteins that control genes involved in inflammation and the immune response to infection. Where bortezomib inhibits NF-KB, researchers speculate that the drug may improve autoimmune conditions, such as RA, which are characterized by chronic inflammation.

The analysis demonstrated that in vitro, bortezomib significantly reduced proliferation and increased death of the inflammatory cells in rats with adjuvant induced arthritis (AIA), thereby reducing invasiveness of fibroblast-like cells that are responsible for the damage to the lining of the joints; it also modified the pattern of protein cell signaling (cytokine secretion) in T-lymphocytes that are involved in the immune system response. In vivo, bortezomib significantly improved clinical manifestations of arthritis in these animals, even when administered during the advanced disease phase. Researchers noted that joints in animals treated with the drug displayed limited damage and inflammation, and an obvious bone healing effect was observed.

"Our research showed that bortezomib is a useful treatment in targeting critical cell populations involved in the development of inflammation and autoimmunity in RA," concluded Dr. Yannaki. "We believe that bortezomib should be further explored in a clinical setting, as it represents an attractive intervention for inflammatory conditions and a highly promising agent in the treatment of RA."

More information: "The Proteasome Inhibitor Bortezomib Drastically Affects Inflammation and Bone Disease in a Rat Model of Adjuvant-Induced Arthritis." Evangelia Yannaki, Anastasia Papadopoulou, Evangelia Athanasiou, Panayotis Kaloyannidis, Argyro Paraskeva, Dimitris Bougiouklis, Panayotis Palladas, Minas Yiangou, and Achilles Anagnostopoulos. Arthritis & Rheumatism; Published Online: October 29, 2010 (DOI: 10.1002/art.27690); Print Issue Date: November 2010.

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