Novel noninvasive molecular imaging for monitoring rheumatoid arthritis

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Comparison of Tc-99m tilmanocept radiopharmaceutical uptake on planar imaging in subjects with active RA (A: 200 µg tilmanocept / 10 mCi Tc-99m; B-C: 400 µg tilmanocept / 10 mCi Tc 99m) versus healthy controls (D-F: 400 µg tilmanocept / 10 mCi Tc-99m) at three hours post-IV administration). Credit: A Kardan et al., University Hospitals/Case Western Reserve University, Cleveland, OH

A first-in-human Phase 1/Phase II study demonstrates that intravenous administration of the radiopharmaceutical imaging agent technetium-99m (99mTc) tilmanocept promises to be a safe, well-tolerated, noninvasive means of monitoring rheumatoid arthritis disease activity. At present, there is no reliable noninvasive way to directly monitor inflammation in joints of RA patients. The study was presented at the 2019 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI).

According to the Rheumatoid Arthritis Support Network, rheumatoid arthritis (RA)—a chronic, autoimmune, inflammatory joint disease—affects more than 1.3 million Americans. Activated macrophages release pro-inflammatory cytokines and chemokines that significantly contribute to the initiation and propagation of RA. 99mTc tilmanocept (TCT) binds to the macrophage mannose receptor CD206, which is highly expressed on activated macrophages in RA. Previous clinical studies have shown subcutaneous administration of TCT to be safe and effective.

"Intravenous (IV) administration of TCT provides a novel noninvasive molecular imaging marker that demonstrates joint-specific, CD206-expressing synovial macrophage involvement," explains Arash Kardan, associate professor of radiology at Case Western University in Cleveland, Ohio. "It reveals potentially significant qualitative and quantitative immunodiagnostic information regarding the distribution and severity of active disease involvement in RA patients."

For the study, 39 subjects (33 with active RA and six healthy controls) were divided into 11 groups and received various combinations of intravenous 99mTc at 1, 5 and 10 mCi with 50, 200, or 400 µg of tilmanocept. They then had standard gamma camera whole-body planar imaging, as well as spot view of the hands and wrists from front to back at one hour and three hours post-injection. Twelve of the 39 subjects (six RA/six healthy controls) underwent whole-body planar scans for radiodosimetry assessment and pharmacokinetic analysis.

No adverse drug reactions or serious adverse events were observed in any dose group. Planar imaging revealed that TCT localizes specifically in the inflamed joints of RA patients and not in the joints of healthy individuals. Qualitative and quantitative data analysis and modeling established an optimal mass dose of 134 µg tilmanocept/10 mCi of 99m TC, stable over an imaging time frame of one to three hours post-injection.

For the purposes of accuracy and streamlining practice, a mass dose of 150 µg and imaging time frame of one to three hours post-injection are...
recommended for future use.

Kardan says, "These results enable the initiation of further clinical studies to assess if intravenous 99mTc tilmanocept imaging can provide physicians with a noninvasive, receptor-specific molecular imaging marker of rheumatoid arthritis disease activity status to guide the most effective therapeutic strategy for their patients. This includes when to initiate therapy and evaluation of response to therapy, thereby improving outcomes for all patients with rheumatoid arthritis."

More information: Abstract 89: "A Phase I/Phase II Study of Intravenously (IV) Administered Tc 99m Tilmanocept (TCT) to Determine Safety, Tolerability, Optimal Clinical Dose Selection, and Imaging Timepoint in Patients Clinically Diagnosed with Rheumatoid Arthritis (RA)"

Provided by Society of Nuclear Medicine and Molecular Imaging


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