Treatment of Knee Osteoarthritis with Intraarticular Infliximab May Improve Knee Function and Reduce Synovial Infiltration by Macrophages

Jeremy R. Schue, Ossama Tawfik, Donald D. Smith, Gary Hinson, Rebecca Bolce, Jo A. Wick and Herbert B. Lindsley

Disclosures
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- No other disclosures relevant to OA

Background
- Benito et al found increased mononuclear cell infiltration, such as CD4+ and CD68+ cells and overexpression of mediators of inflammation (TNFα, IL-1β) in early osteoarthritis versus late osteoarthritis.¹
- IA infliximab used successfully in seven patients with rheumatoid arthritis (6) or spondyloarthropathy (1).² ³

3. Nikas NS et al., Ann Rheumatic Dis 2004

Hypothesis
- In patients with osteoarthritis of the knee, an intraarticular TNFα (tumor necrosis factor alpha) antagonist will suppress inflammation locally.

Objectives—following IA anti-TNF therapy:
- Measure change in WOMAC scores.
- Measure changes in serum levels of inflammatory markers.
- Measure changes in cellular infiltrates and cytokines in synovial tissue.
- Measure changes in circulating subsets of T cells and monocytes expressing intracellular cytokines.
Study Design

- Population: mild to moderate osteoarthritis

- 8 Patients received infliximab (IFX) 100 mg
- 4 patients received methylprednisolone acetate (MPA) 80 mg
- 4 patients received placebo solution (PLA)

Baseline MRI Grade 0-5: Medial vs Lateral Tibial Plateau

Patient Self Reports

- On all scheduled visits, patients completed:
  - WOMAC scale (Western Ontario McMaster Assessment Scale)
    - Validated instrument for assessing OA
    - Focuses on pain, stiffness, and function

WOMAC Total by Treatment Across all Groups

Change in WOMAC Total: each Group at Day 28 compared with its Individual Baseline
Change in WOMAC Total: each Group at Day 56 compared with its Individual Baseline

Serum CRP Levels (mg/dl)

Synovial Biopsies. Selected.

Synovial Bx. Immunostains

Changes in Synovial Cellularity Day 0 to Day 28

Synovial Tissue: Change in TNF Expression from baseline to Day 28 by Treatment Group
**PBMCs: Subjects with ↓ TNFα Expression on Day 28 vs Baseline by Treatment Group**

- IFX (N=8)
- MPA, PLA (N=4 each)

**Synovial Tissue: Change in IL-1β Expression from baseline to Day 28 by Treatment Group**

- IFX
- MPA, PLA

**Conclusions (1)**
- WOMAC improvement
  - IFX: delayed, persistent
  - MPA: quick but transient
  - Placebo: transient only
- Acute phase reactant (CRP) improvement
  - IFX: mild persistent
  - MPA: transient
  - Placebo: none

**Conclusions (2)**
- No consistent trends noted in synovial cellularity
- TNF not found in synovium in 10/15 patients at baseline; however IL-18 was found in the synovium of all patients.
- TNF expression in PBMCs was reduced in B lymphocytes and monocytes with IFX.

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- Principal Investigator: Herbert B. Lindsley, MD, Divn Rheumatology
- Sub-Investigator(s):
  - Jeremy Schue, MD, Divn Rheumatology
  - Osama Tawfik, MD, PhD, Dept Pathology
  - Gary Hinson, MD, Dept Radiology
  - Jo Wick, PhD, Dept Biostatistics
  - Donald Smith, MS, Rheumatology
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- Study Coordinators:
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  - Gall Dreiseszun, LPN, Divn Rheumatology
  - Brandy Macan, Divn Rheumatology

**References**