

A 12 month safety study of second monthly
Intra-articular injections of rh-ASb into hip
joints.

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Background

- ◆ Intravenous Enzyme Replacement Therapy (ERT) with rhASB (Nagalazyme) improves mobility, endurance and general function in patients with MPS VI

- ◆ Bone and joint deformities respond less well than soft tissue problems

Feline models

Human experience



Background (2)

- ◆ Studies in feline MPS VI model have shown improved outcome (bone, cartilage and other joint tissues) in joints treated with direct Intra-articular (IA) injections of rhASB in combination with IV ER
- ◆ Survey studies have shown joint pathology to be a particular issue in MPS VI patients
- ◆ 3 of 11 patients seen in Adelaide had significant hip surgeries (3 of 4 age of patients over 16 years)



Background (3)

- ◆ Significant progress of hip pathology has been noted in some MPS VI patients despite IV ERT



Study Purpose

- ◆ Primary objective assess safety and practicality of IA injections in patients with MPS VI
- ◆ Secondary objective to assess response of hip pathology to IA rhASB



Study Design

- ◆ Two patients with MPS VI, stabilised on regular IV ERT with Naglazyme were selected to have second monthly IA 1mg injections of rhASB (Naglazyme) to each hip joint.
- ◆ Two (younger) patients followed to improve knowledge of progress of hip pathology with regular IV ERT alone



Methods

- ◆ Hip injections were performed by ultrasound guided direct injection (local anaesthetic PRN)
- ◆ Assessments
 - Joint Range of Motion
 - Hip ultrasound
 - Hip X-ray
 - Hip MRI
 - Symptom scores (HOOS, WOMAC)
 - Joint fluid aspiration
 - Routine blood biochem and cell counts
 - Adverse events recorded



Results

- ◆ No significant changes in routine biochemistry, red or white blood cell indices or rheumatoid factor
- ◆ Some initial discomfort with placement of needle for injection reduced with time
- ◆ A slight “sponginess” on walking noted for 2-4 hours post each procedure
- ◆ No other adverse events noted



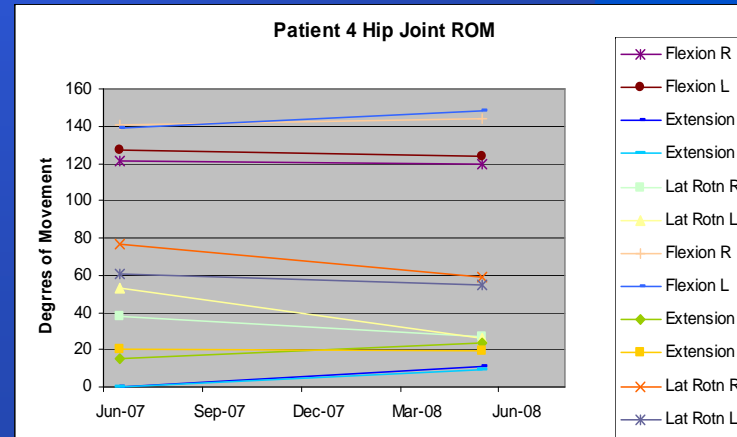
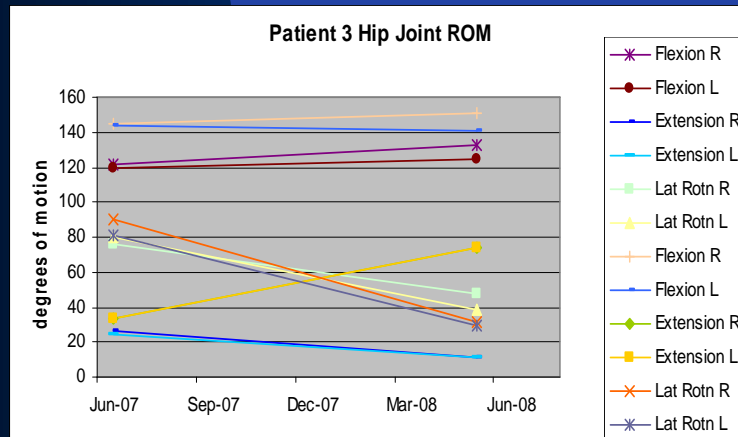
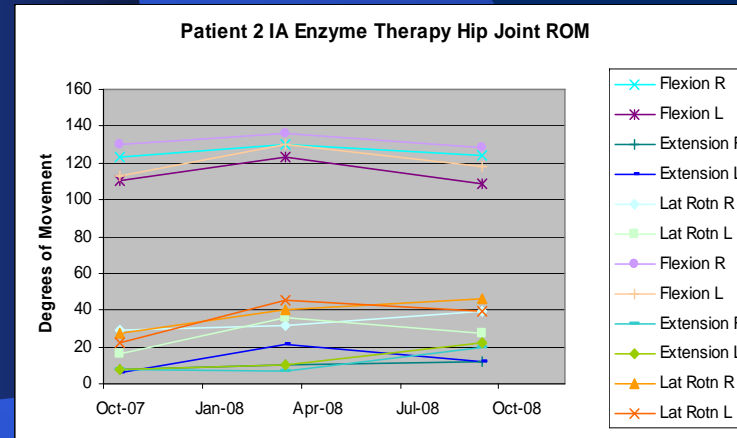
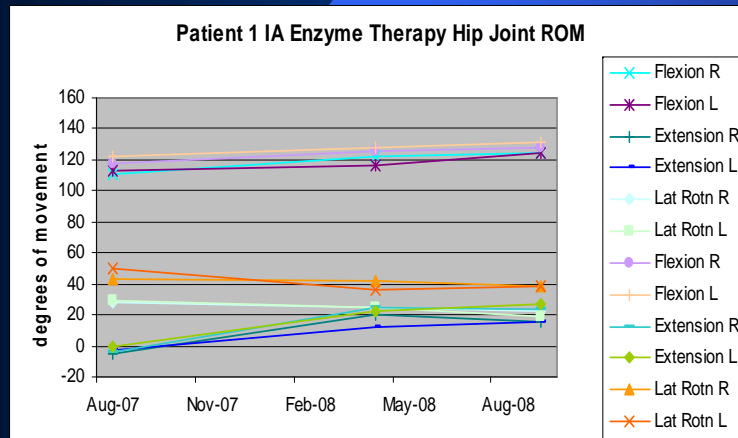
Results

- ◆ No joint fluid was able to be aspirated despite injection of 2 ml of sterile saline prior to each joint injection
- ◆ Clinically no joint swelling or inflammation



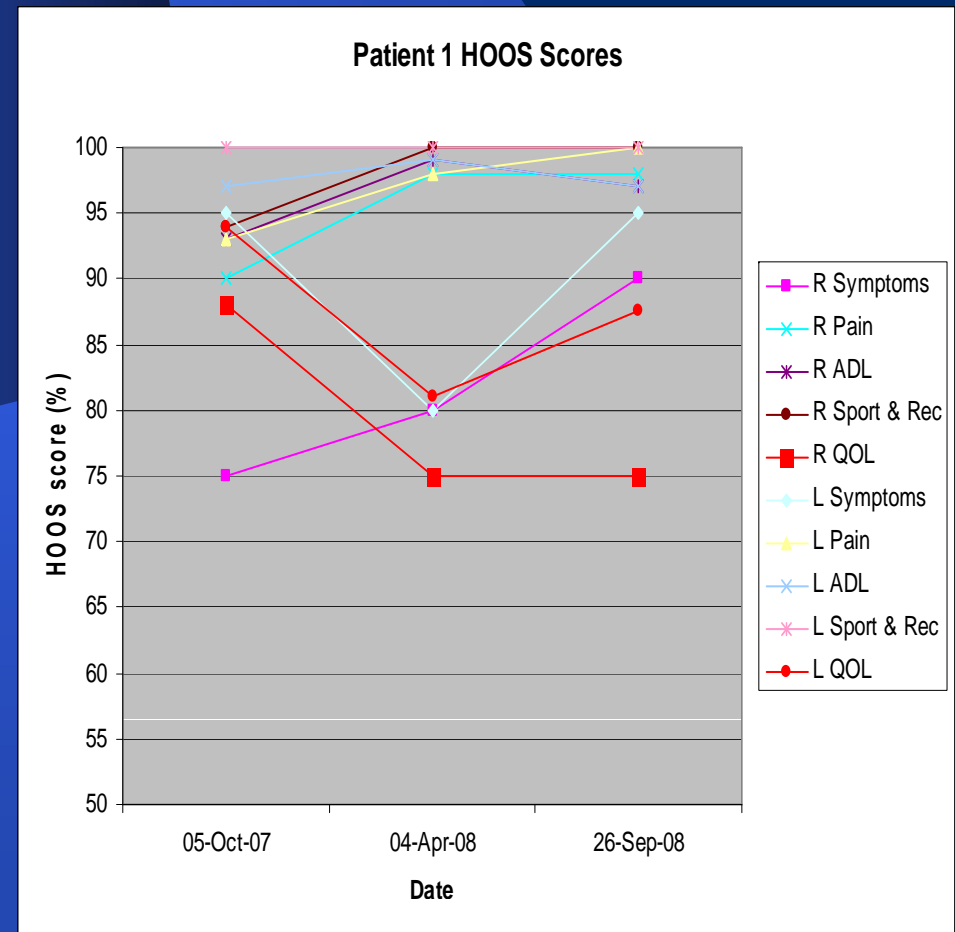
Joint range of motion

Sample size too small for statistical analysis
Possibly some improvement in treated joints



Symptom Scores

- ◆ No specific tools available for MPS Joint Disease
- ◆ HOOS and WOMAC adult tools, validated for arthritis surgery
- ◆ HOOS Data shown for adult patient
- ◆ Suggestive of improvement in Pain, Symptoms, Activities of Daily Life
- ◆ Deterioration in Quality of Life
- ◆ WOMAC scores also suggested symptomatic improvement in adult patient
- ◆ Scoring for WOMAC/HOOS in the younger patients performed by parents so difficult to assess validity, and no standardisation to allow for developmental levels/skills



Radiology

◆ Plain radiology

- Patient 1 “appearances essentially unchanged” over study duration, “slight increase in sclerosis along (bone) fragment margins”
- Patient 2 “bony fragments appear better defined”

◆ MRI

- Patient 1 “essentially unchanged in appearance” over study duration
- Patient 2 “perhaps an increase in bony consolidation in the fragmented femoral heads”



Radiology (patient 1)

Baseline

12 months



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Ultrasound

- ◆ Hip ultrasound performed to assess joint capsule thickness.
- ◆ Longitudinal studies in one MPS VI patient have shown progressive increase in capsule thickness with time, even with (late) use of IV ERT
- ◆ Reduction in thickness in one treated patient, increasing thickness in the other.
- ◆ Untreated patients both showed increasing joint capsule thickness - ? validity as different departments



Conclusions

- ◆ Intra-articular injection of Naglazyme is technically possible and was not associated with adverse events after 12 months of second monthly injections
- ◆ Joint range of movement and bony sclerosis may improve but further studies are required, dose, frequency and timing of treatment all require further assessment.
- ◆ Improved knowledge of progress of joint disease in both untreated patients and those treated with IV Naglazyme is required
- ◆ Paediatric versions of WOMAC and HOOS or similar tools are required to assist monitoring disease progress and treatment outcomes



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