ACS Project

Shoulder

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ACS Project: Shoulder

Title

The efficacy and safety of Autologous Conditioned Serum (ACS)-Orthokine injections, compared to Betamethasone (Diprofos) and placebo injections in the treatment of chronic shoulder joint pain: Prospective, randomizied,double-blind, controlled study.

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Objective

To compare the efficacy and safety of Autologous Conditioned Serum (ACS)-Orthokine injections, versus Betamethasone (Diprofos) and placebo injections in the treatment of chronic shoulder joint pain.

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Study design

Prospective, randomized, double-blind, controlled study.

Patients

Group of 32 patients suffering from chronic supraspinatus tendinopathy and lesions of the supraspinatus tendon.

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Randomisation

16 patients treated with ACS – Orthokine,

- 4 injections (one injection/week)

16 patients will be treated with betamethasone – Diprofos and placebo - saline,

- 3 injections of Diprofos (one injection/week), and one injection od saline on a fourth week

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Methods - Flow Chart

Procedure	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 7
	Week 1	Week 1	Week 2	Week 3	Week 4	Week 24
Blood sampl.	X	Option (safety)	Option (safety)	Option (safety)	Option (safety)	Option (safety)
Clin. Exam.	X				X	X
US int. exam.	X	X	X	X		
US Dg. exam.	X				X	X

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Methods

Blood sample is taken for each patient before the treatment starts. First injection will be administrated 7 hours after the blood collection.

Each injection is administrated under the sonography control, by one sonographer (ND).

Patient were blinded for the treatment option.

The independent rheumatologist (BB), blinded for the treatment option, examined the patients at each visit.

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Inclusion criteria

1. Subjects ≥ 18 years old.
2. Chronic shoulder pain lasting longer than 6 weeks.
3. Patients assessment of pain ≥50 on VAS scale (0 – 100).
4. No treatment for at least two weeks before randomization (patient is allowed to take Paracetamol, up to 500mg every 4 hours, when necessary).
5. No glucocorticoid local injections in the shoulder for at least 24 weeks before the Study entry.

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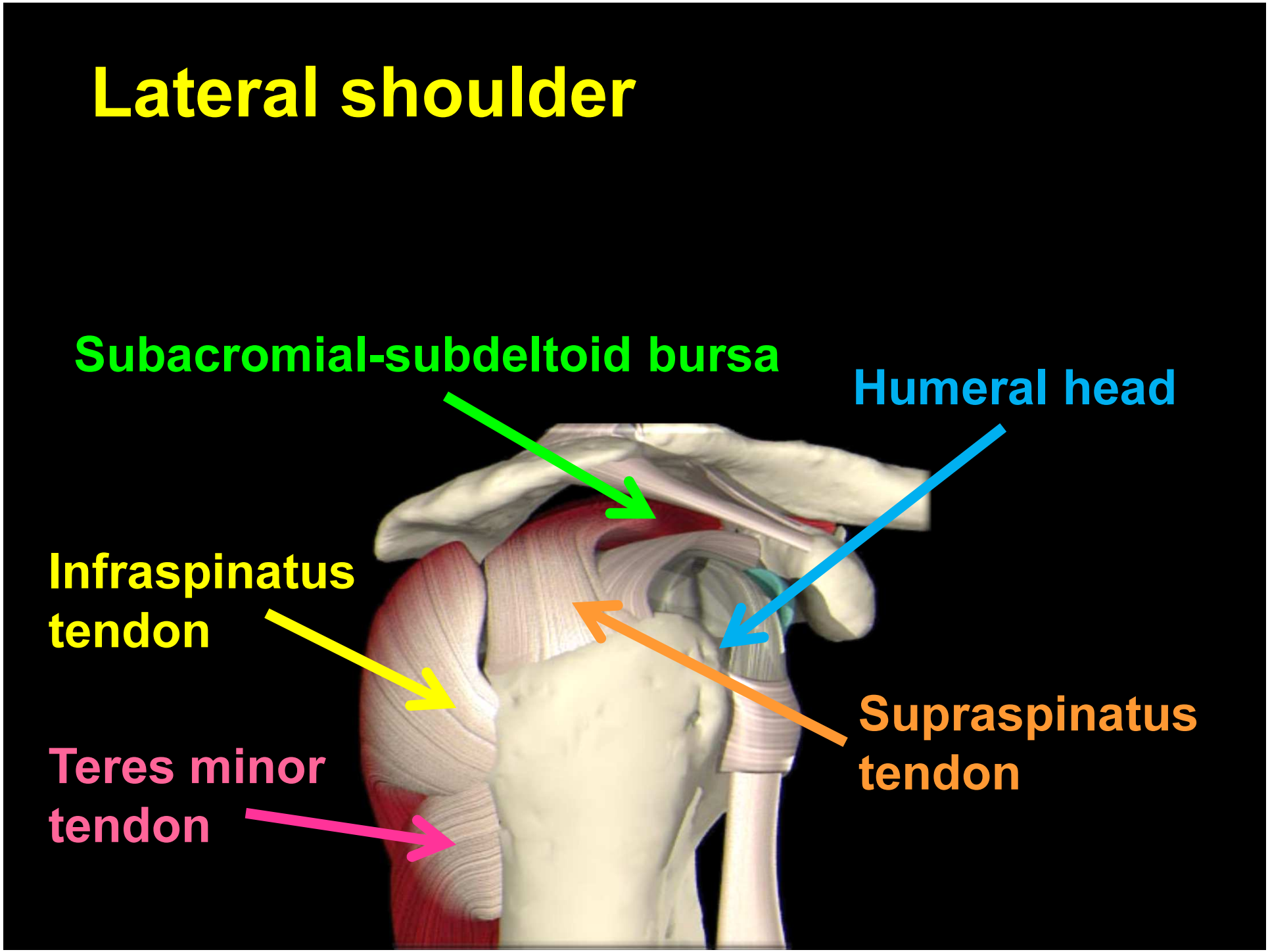
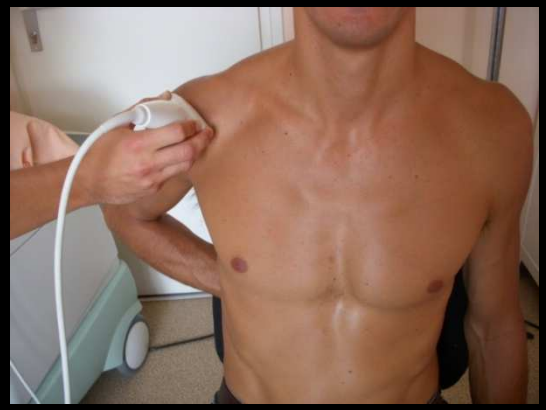
Exclusion criteria

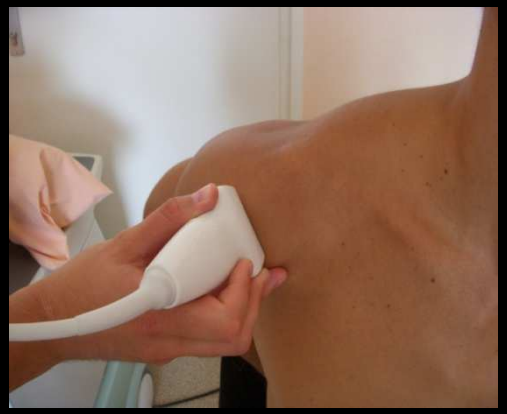
1. Subjects with inflammatory rheumatic diseases, metabolic and autoimmune diseases either of musculoskeletal or other systems.
2. Severe forms of acute or chronic diseases of other organ systems (infections and malignant illnesses included).
3. Subjects with contraindications for treatment with glucocorticoids.
4. Any other condition that could jeopardize the Study Objective or violate the Protocol.

Lateral shoulder



Supraspinatus tendon trans

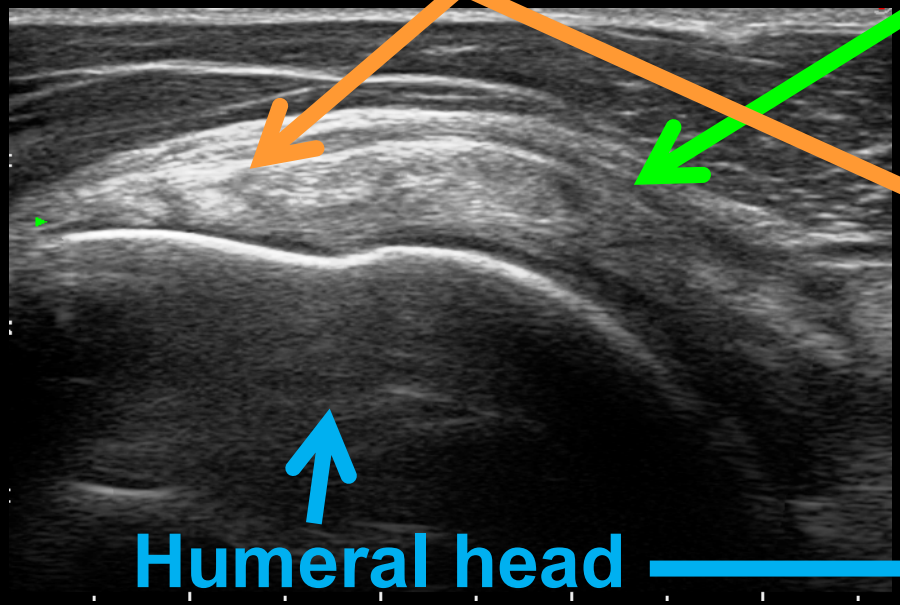


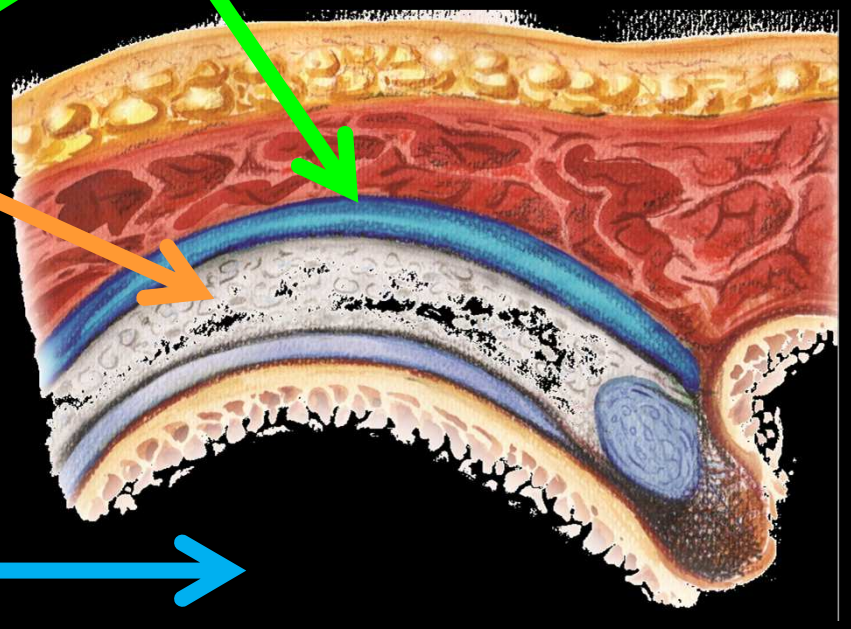


Full internal rotation and adduction

Subacromial-subdeltoid bursa

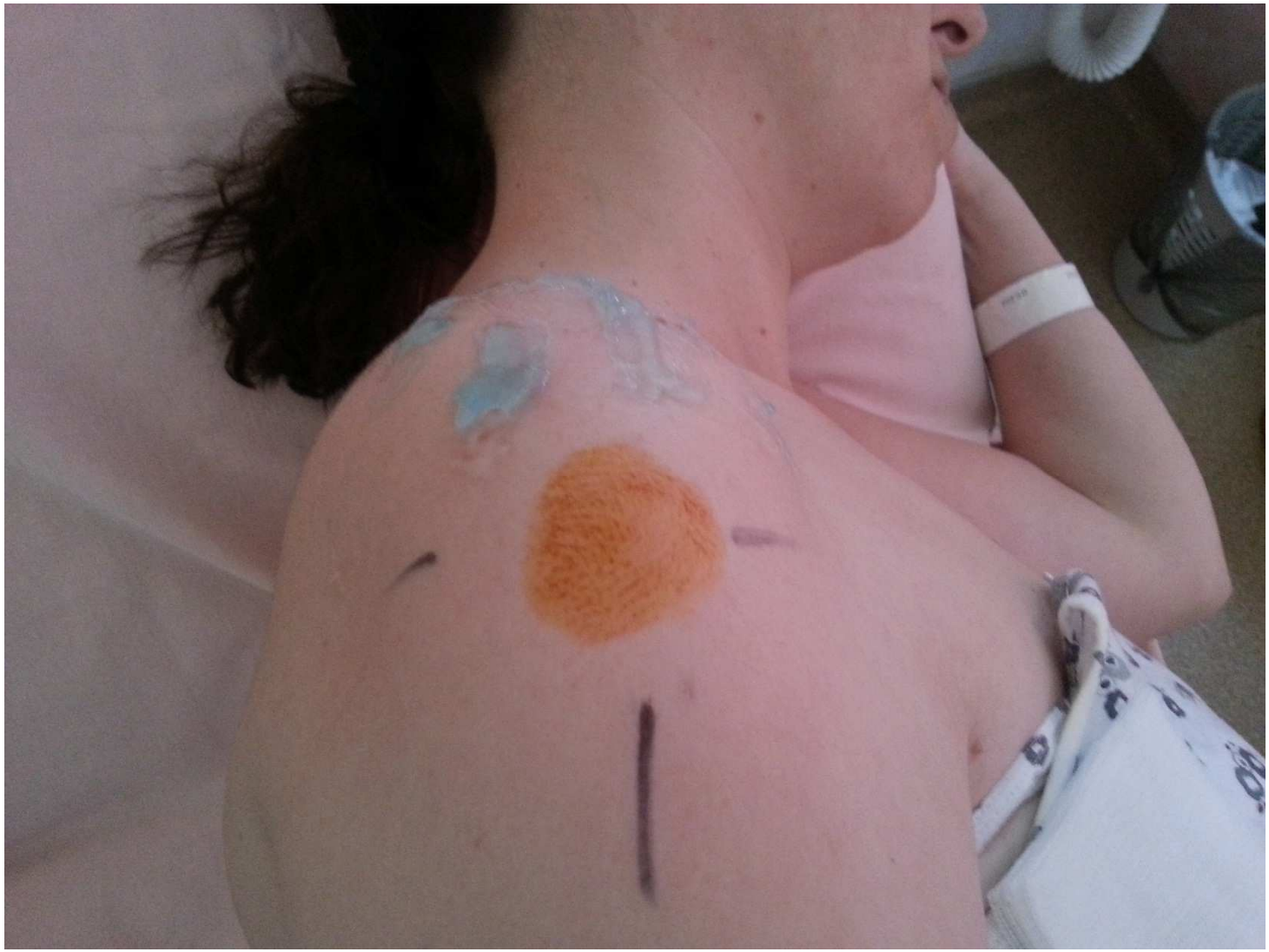
Supraspinatus tendon



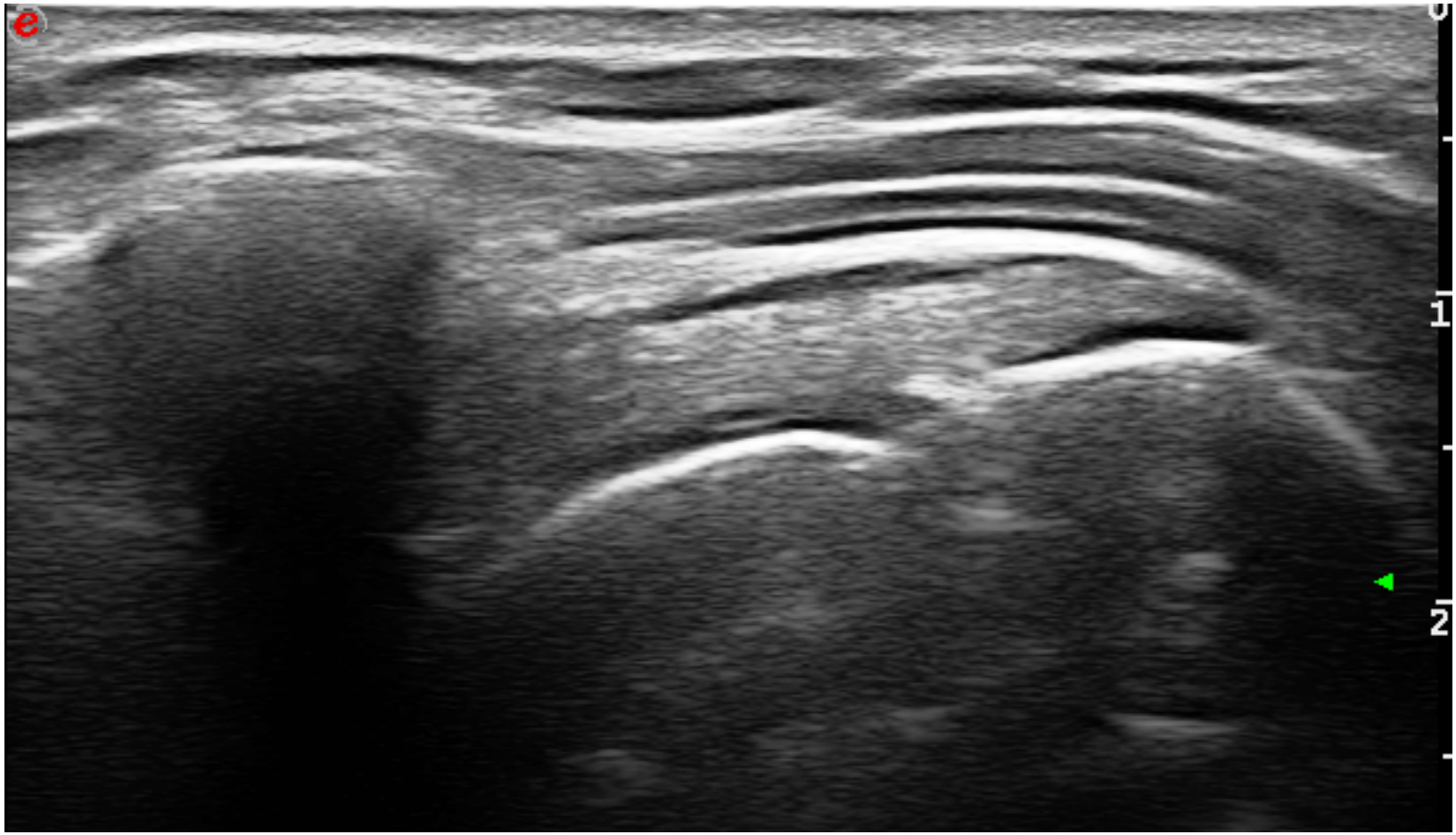


Humeral head

Antiseptic swabbing of the injection site

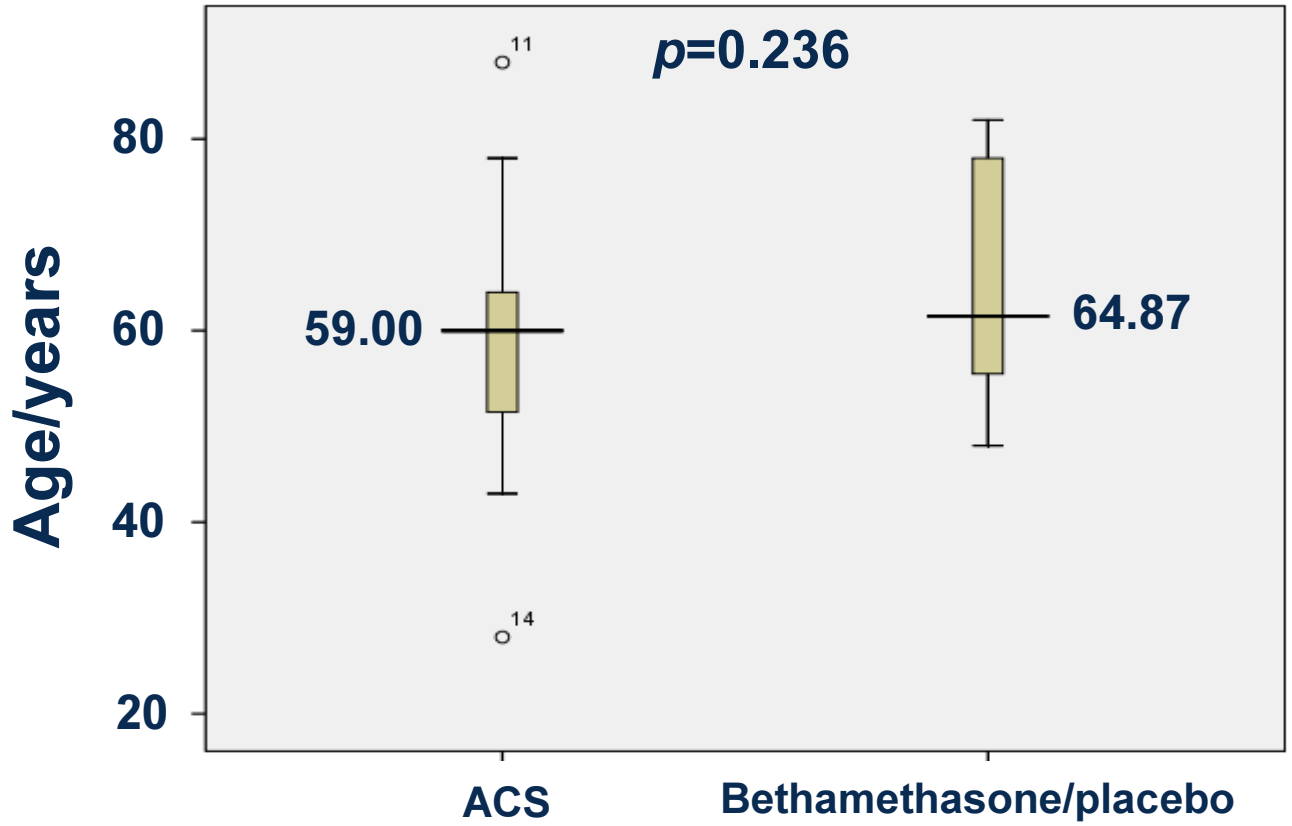


US image of Supraspinatus Tendon



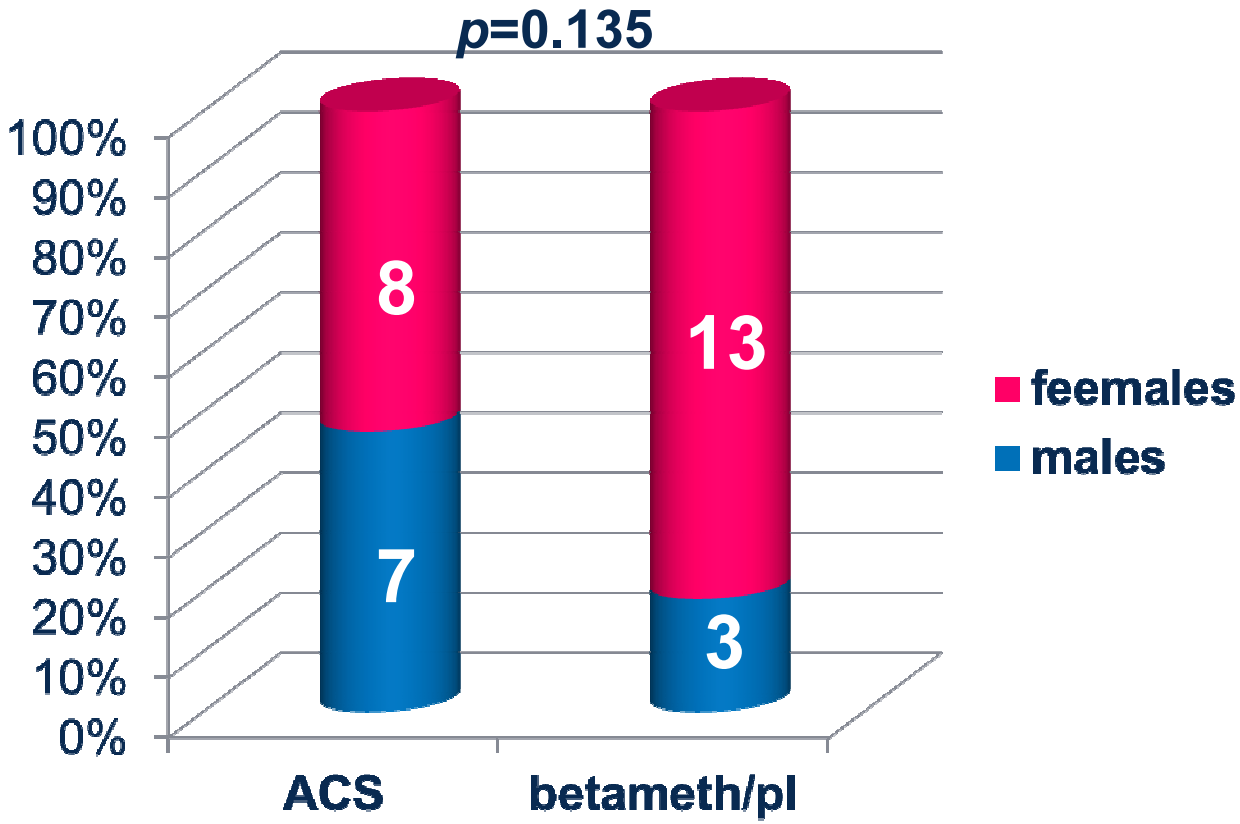
Injection of the supraspinatus tendon under the ultrasonographic guidence

Patients - age



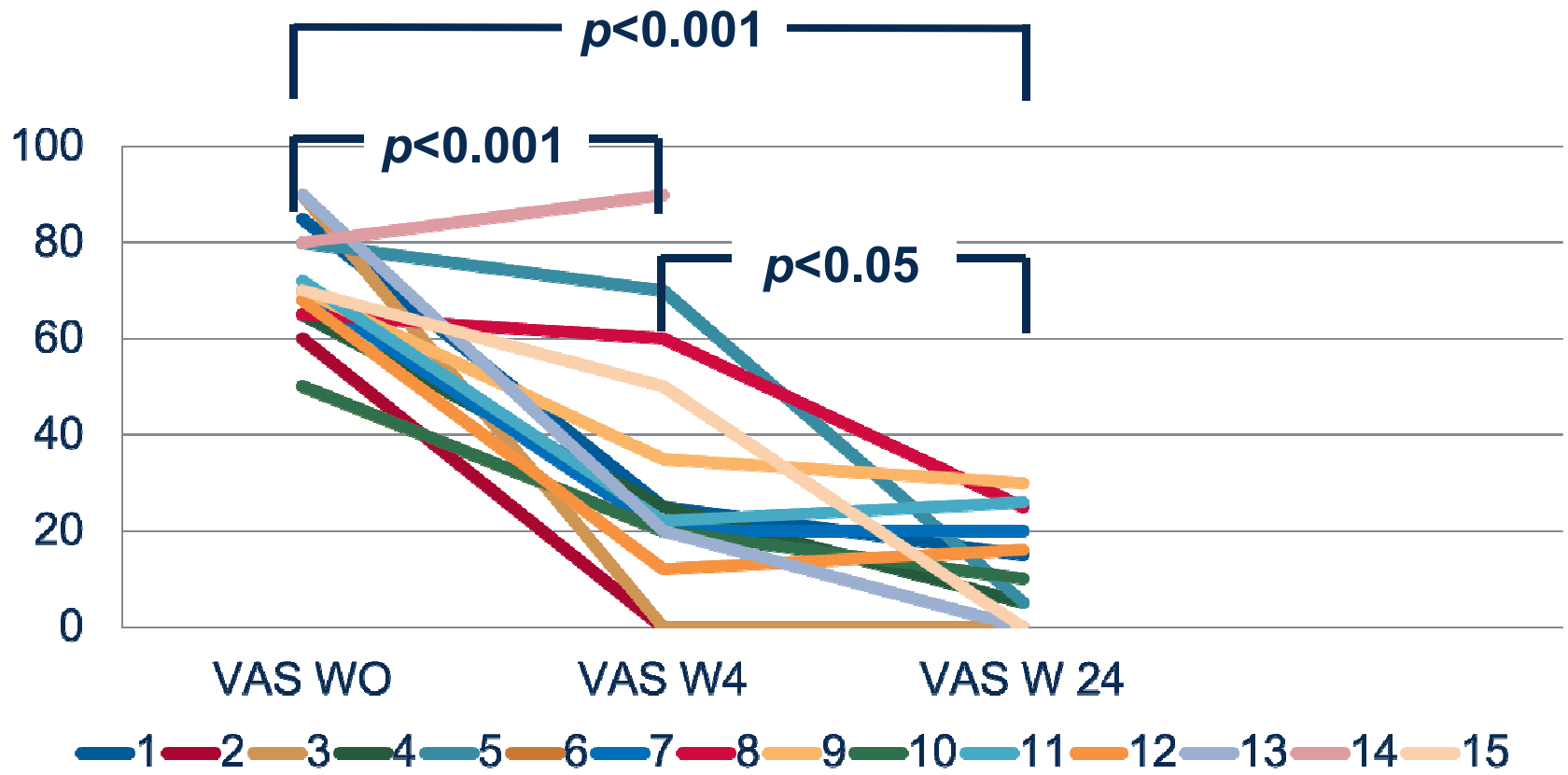
There was no significant difference in age between group of patients treated with ACS (Orthokine) and group treated with betamethasone (Diprofos)/placebo (student t test; *p*=0.236).

Patients - gender



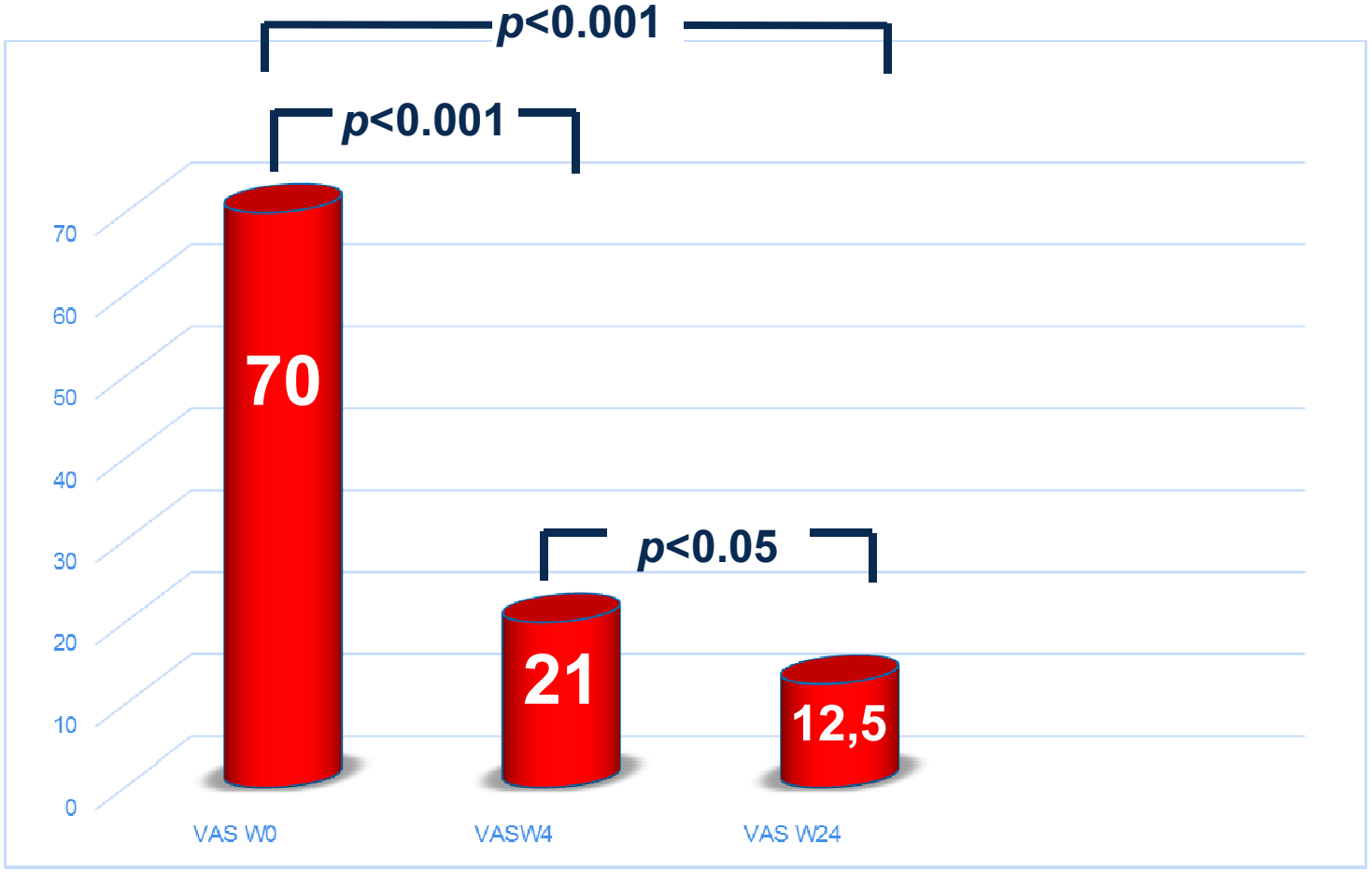
There was no significant difference in gender ditribution between group of patients treated with ACS (Orthokine) and group treated with betamethasone (Diprofos)/placebo (Fisher's Exact Test; p=0.135).

ACS treatment - Assessment of pain (VAS scale)



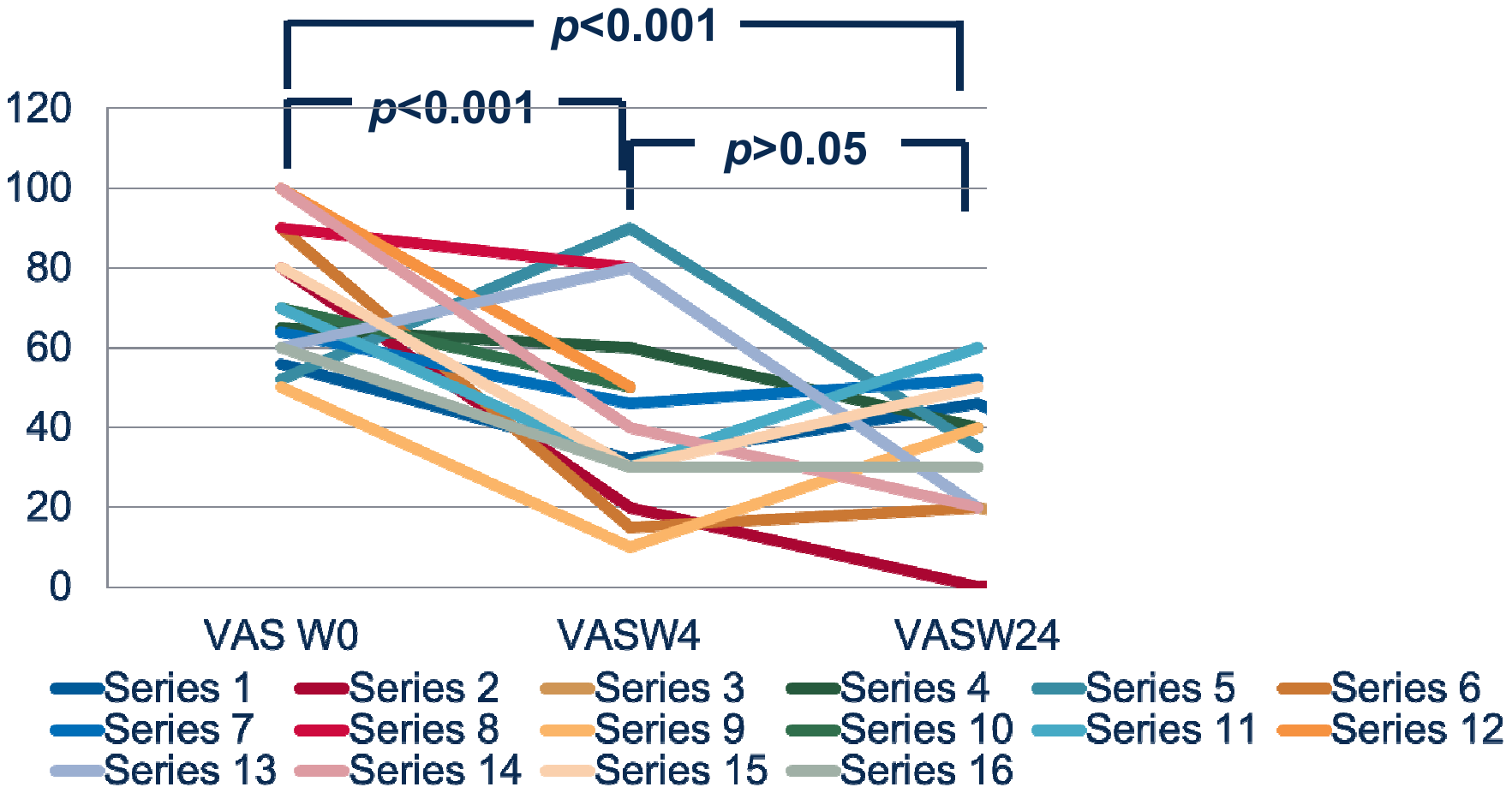
There was significant decrease in intesity of pain between week 0 and week 4 ($p<0.001$), as well as between week 0 and week 24 ($p<0.001$) and between week 4 and week 24 ($p<0.05$) (Wilcoxon test)

ACS treatment - Assessment of pain (VAS scale)



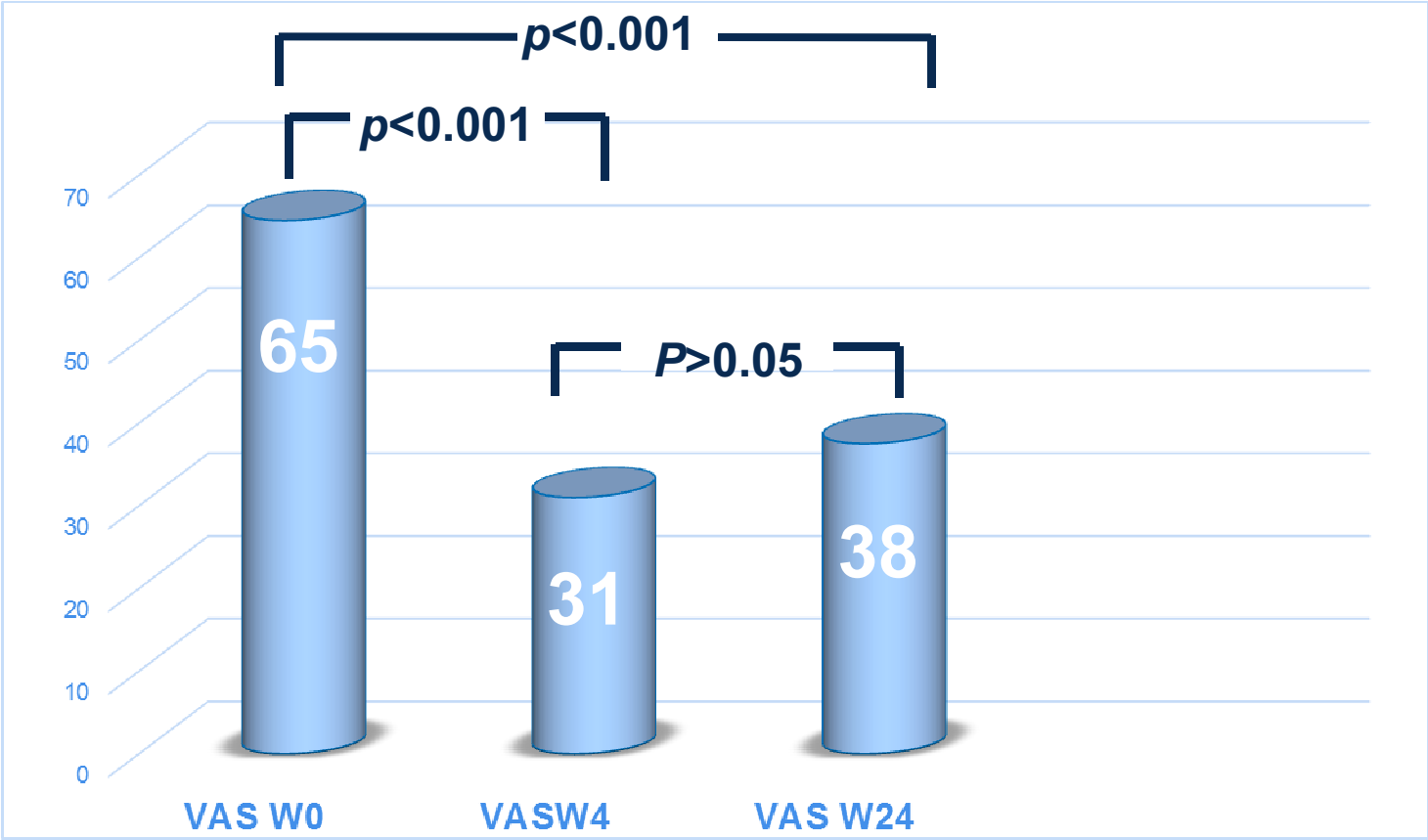
There was significant decrease in intesity of pain between week 0 and week 4 ($p<0.001$), as well as between week 0 and week 24 ($p<0.001$) and between week 4 and week 24 ($p<0.05$) (Wilcoxon test)

Betameth/pl. treatment - Assessment of pain (VAS scale)



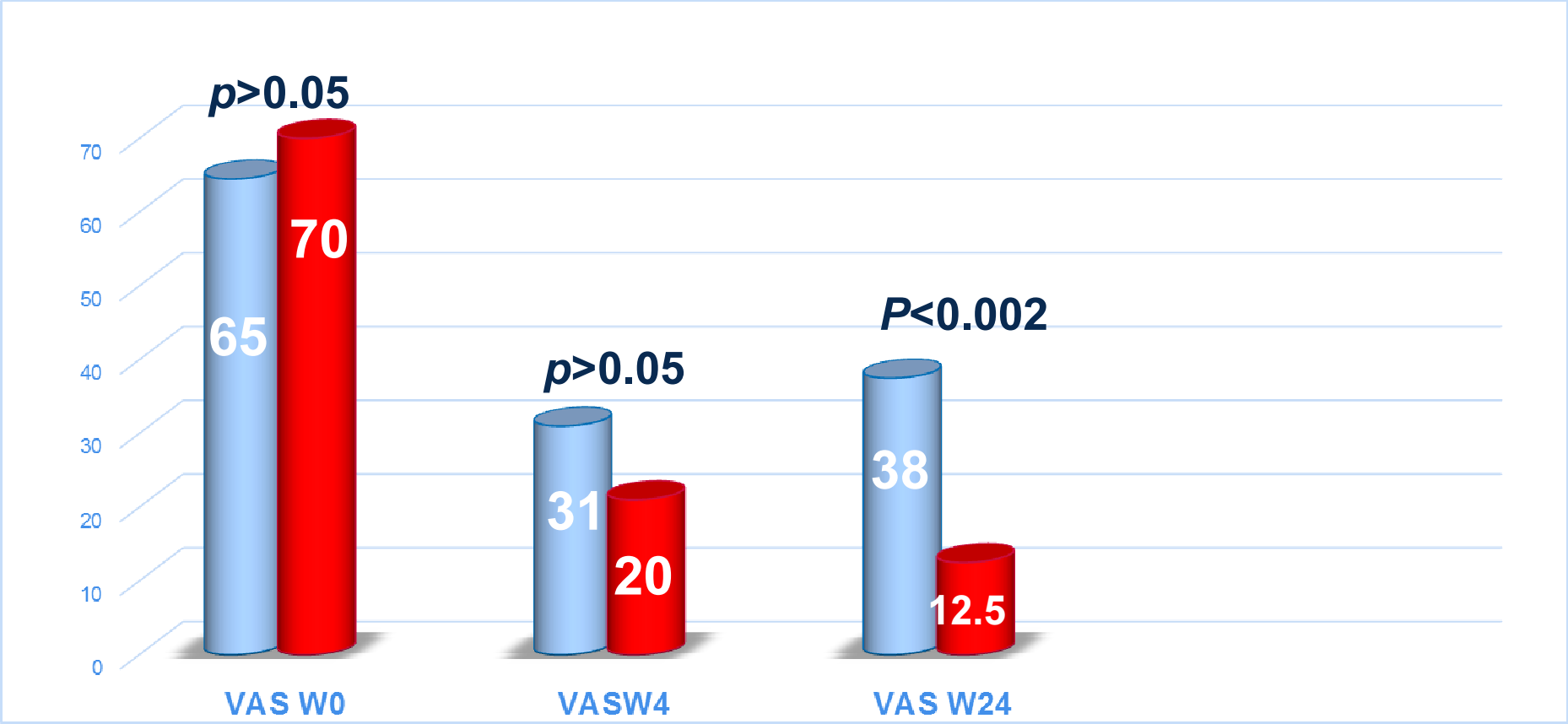
There was significant decrease in intesity of pain between week 0 and week 4 ($p<0.05$), as well as between week 0 and week 24 ($p<0.001$), but there was slight unsignificant deterioration between week 4 and week 24 ($p>0.05$) (Wilcoxon test)

Betameth/pl. treatment - Assessment of pain (VAS scale)



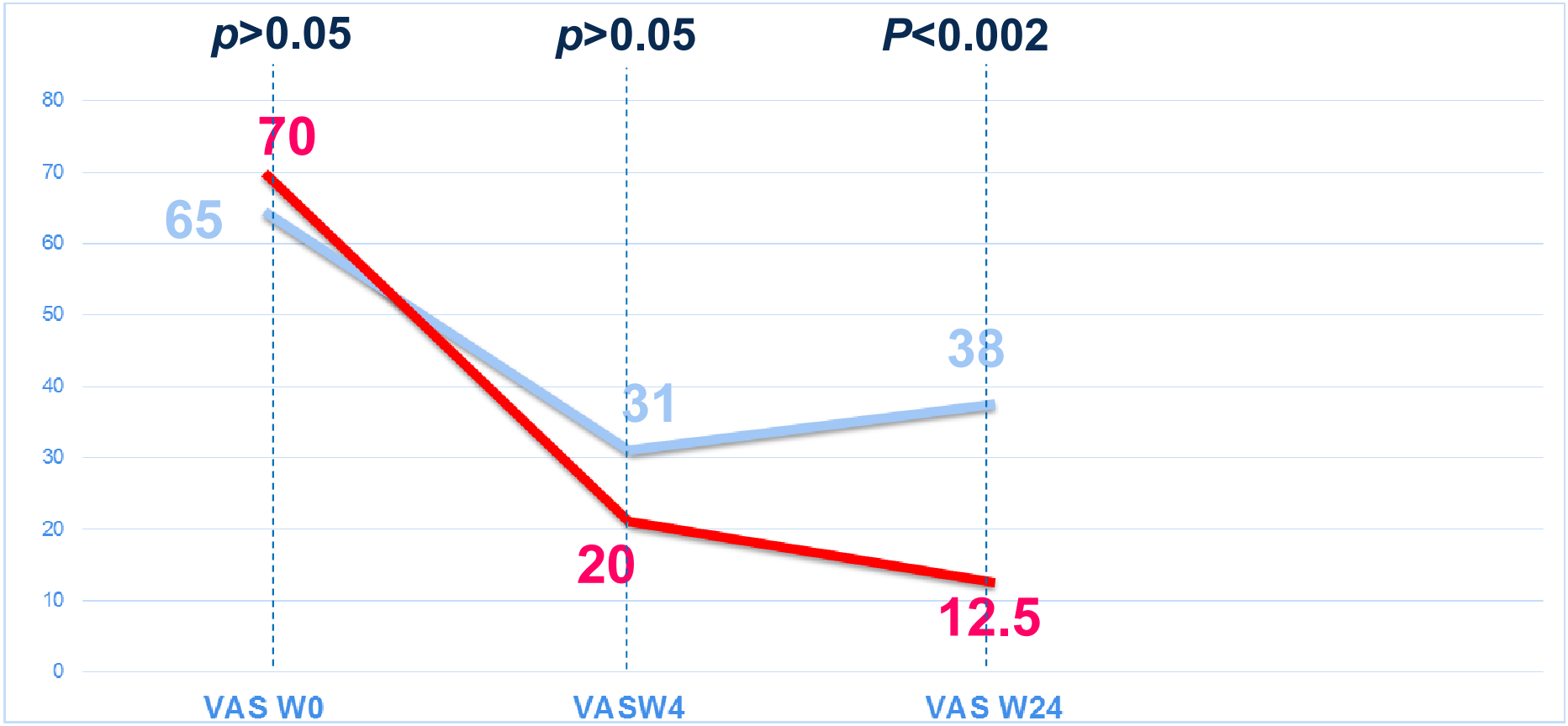
There was significant decrease in intesity of pain between week 0 and week 4 ($p<0.05$), as well as between week 0 and week 24 ($p<0.001$), but there was unsignificant deterioration bewteen week 4 and week 24 ($p>0.05$) (Wilcoxon test)

ACS vs betameth/pl. treatment - Assessment of pain (VAS scale)



There was no significant diference in intesity of pain between ACS and betameth/pl. group before treatment; there was no significant diference between two groups after treatment week 4, but there was significant diference in intesity of pain between ACS and betameth/pl. group after week 24 of follow up ($p<0.002$ (Wilcoxon test)

ACS vs betameth/pl. treatment - Assessment of pain (VAS scale)

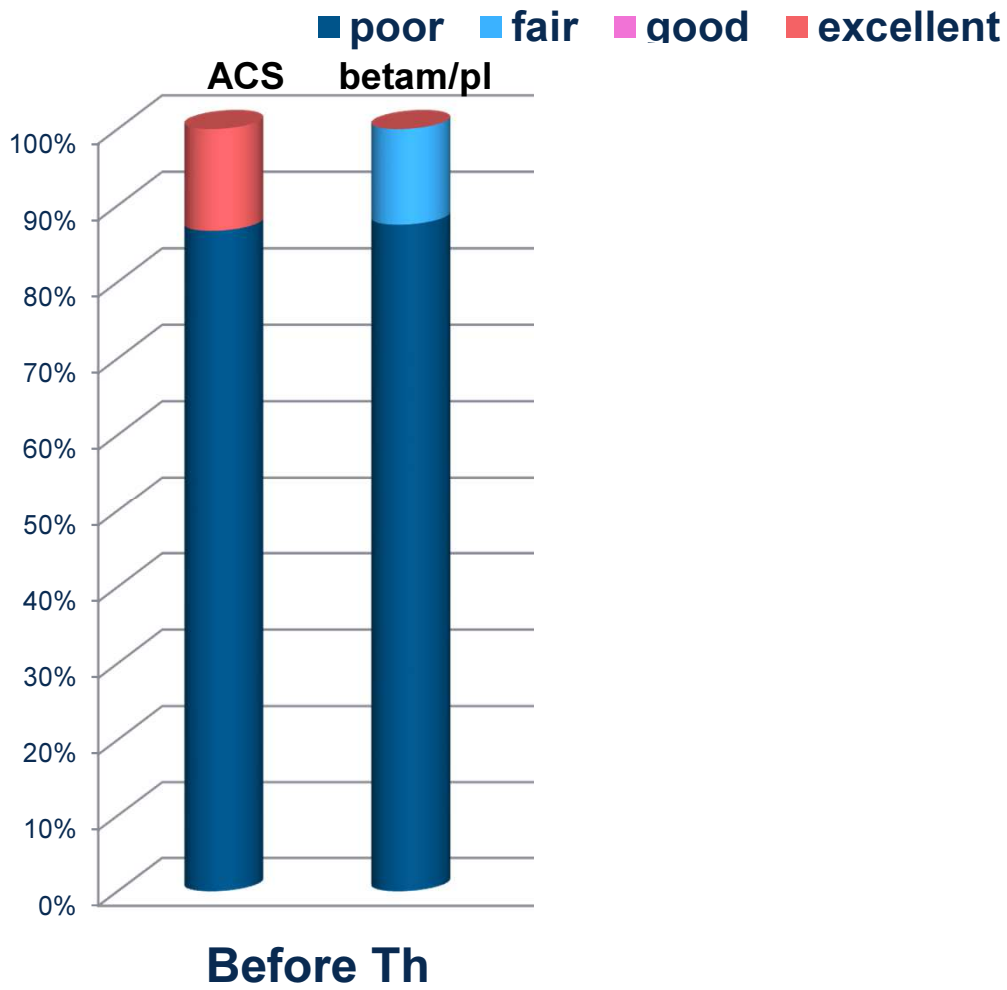


There was no significant diference in intesity of pain between ACS and betameth/pl. group before treatment; there was no significant diference between two groups after treatment week 4, but there was significant diference in intesity of pain between ACS and betameth/pl. group after week 24 of follow up ($p<0.002$ (Wilcoxon test)

Results: CSS Score Orthokine & glucocorticoids

Chi-Square test

p=0.235



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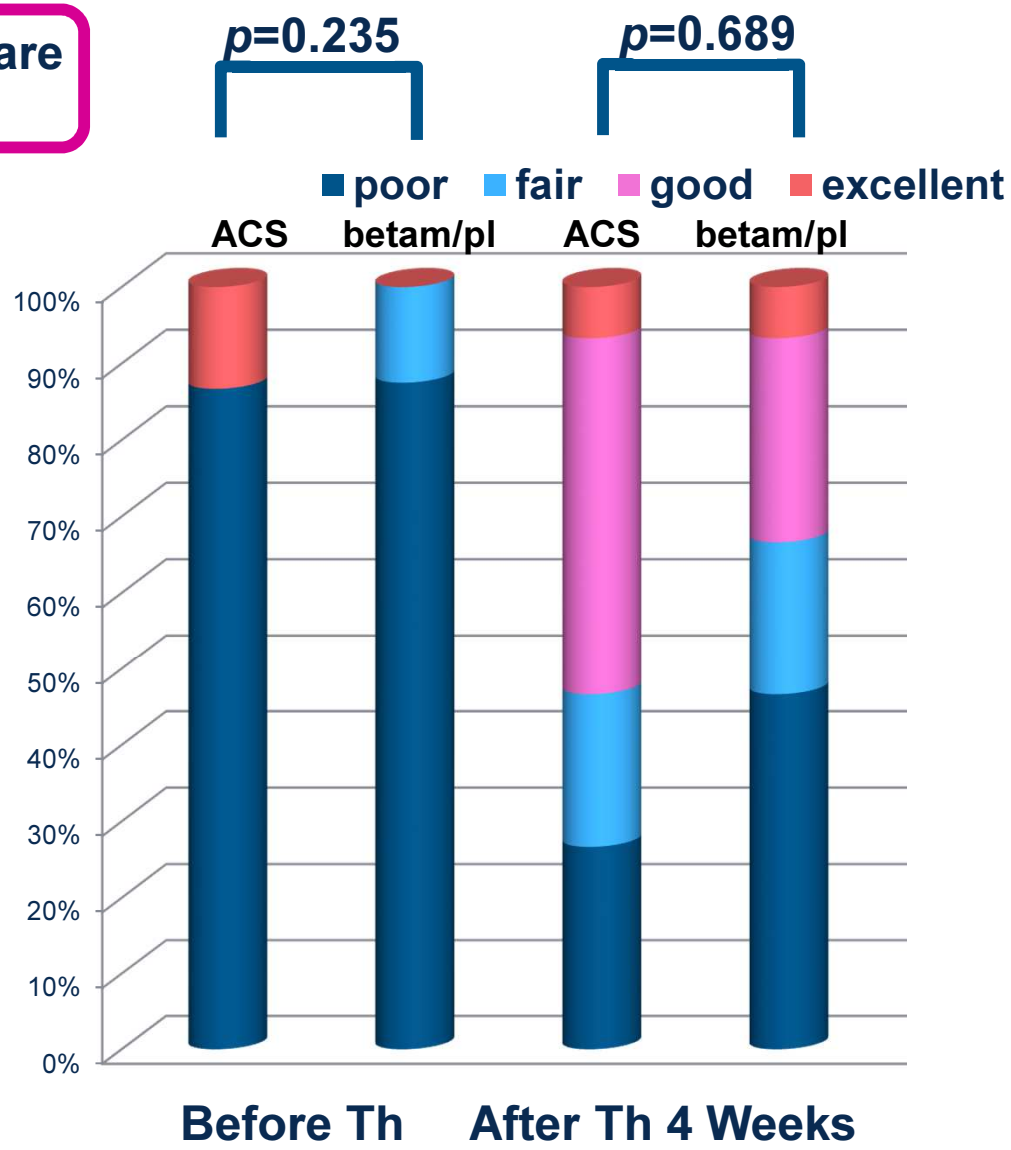

Results: CSS Score Orthokine & glucocorticoids

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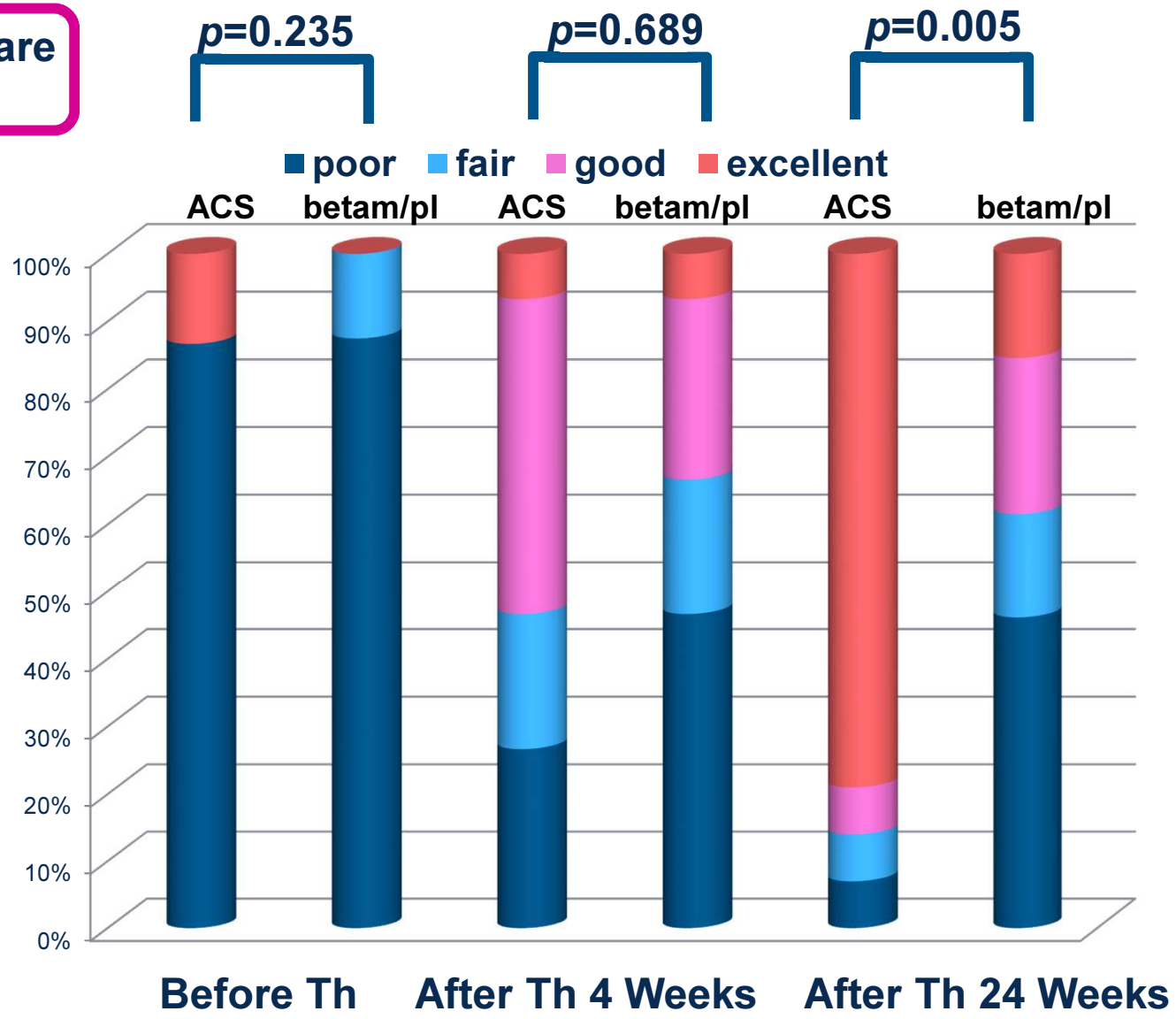

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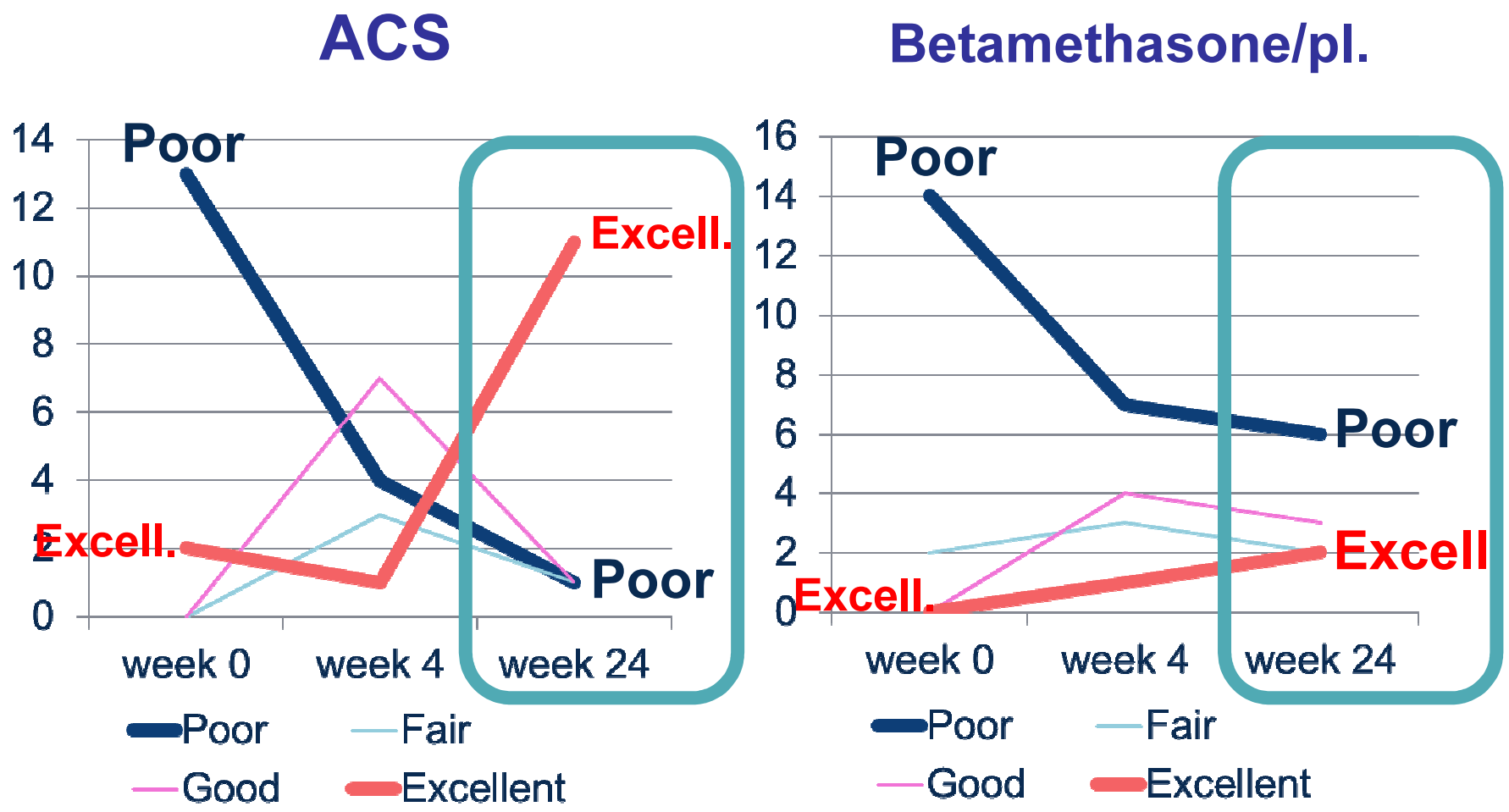

Results: Safety

Adverse event	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 12	Week 24
Headache*	No	Yes 3	Yes 2	No	No	No	No	No
Artheriar hyprtens.*	No	Yes 2	Yes 1	Yes 1	No	No	No	No
Facial erythema*	No	No	Yes 2	No	No	No	No	No
Facies lunata*	No	No	Yes 1	Yes 1	Yes 1	Yes 1	No	No

***All adverse events were reported in patients treated with bethamethasone.**

Conclusions I

Intensity of pain (VAS scale) in the shoulder was lower after 4 weeks, and significantly lower after 24 weeks of treatment with 4 injections of ACS , compared to treatment with 3 injections of betamethasone + 1 injection of placebo.

Shoulder function (Constant Shoulder Score) was more improved after 4 weeks, and significantly more improved after 24 weeks of treatment with 4 injections of ACS, compared to treatment with 3 injections of betamethasone + 1 injection of placebo.

Conclusions II

Eight transient adverse events were reported in three patients in Bethamethasone group, while no adverse events were observed in Orthokine group during the 24 weeks of follow up period.