Bucharest 2-4 October 2025

Evidence and Opportunity of Polyacrylamide in the treatment of OA

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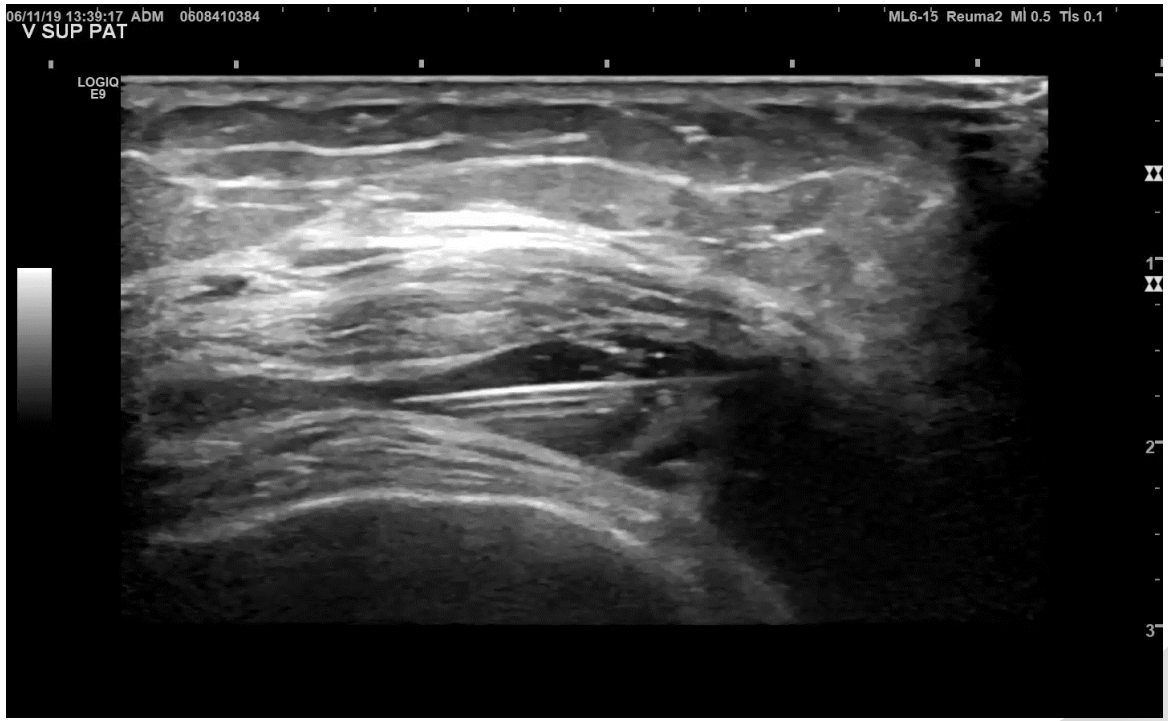
HB is not employed by and holds no shares in Contura

Agenda

- What is Arthrosamid
- Mode of action
- Early treatment and results
  - Off label use
- Long term safety
- Conclusion

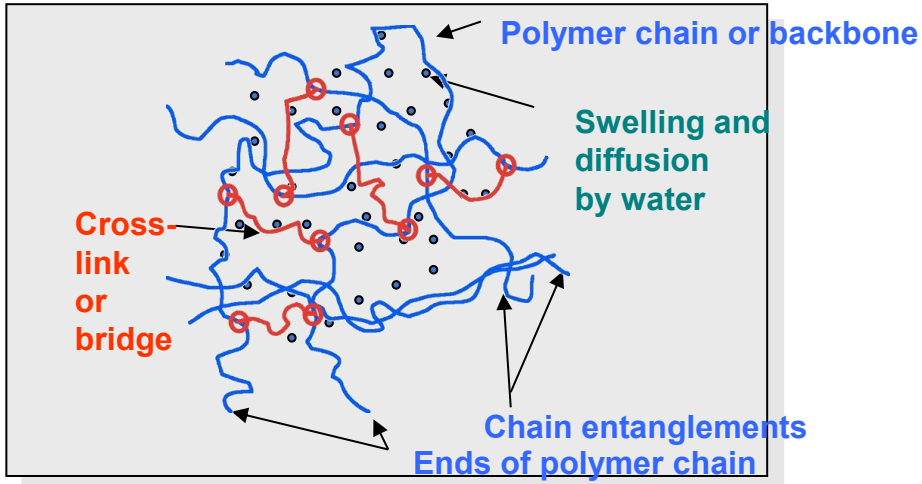


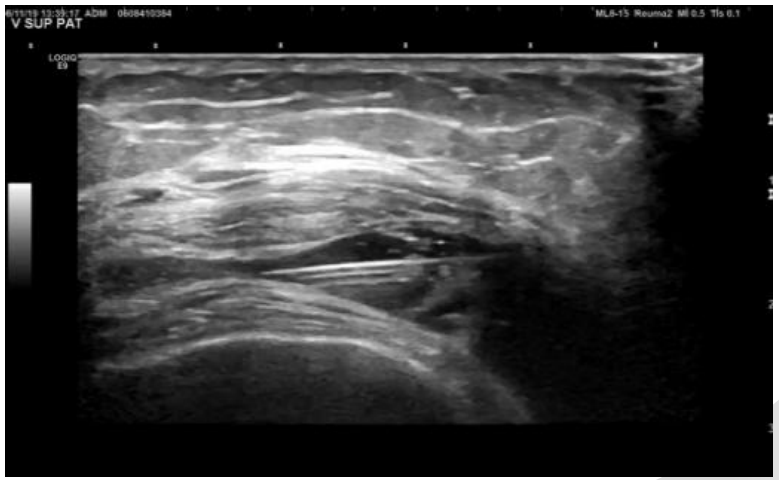
What is 2.5% Polyacrylamide Hydrogel, iPAAG*

2.5% cross-linked polyacrylamide and
97.5% non-pyrogenic water

Biocompatible,
Non-absorbable,
Non-biodegradable

Long term experience with
injection in various human tissues



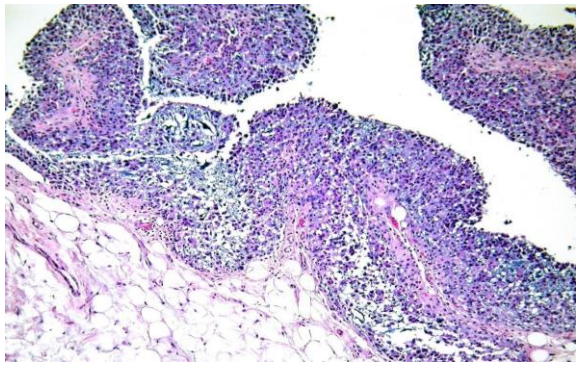


*Contura International A/S, Søborg, Denmark.

Integration of the Synovial Implant

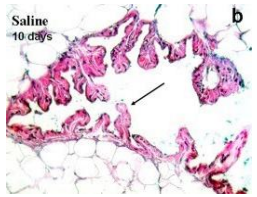
Consistent Histopathological Findings Across Species – Rabbits, Horses, Goats, Rats, and Humans

Hydrogel 10 days



At 10 days:

- The synovial membrane shows a 5- to 10-fold increase in size compared to the control.

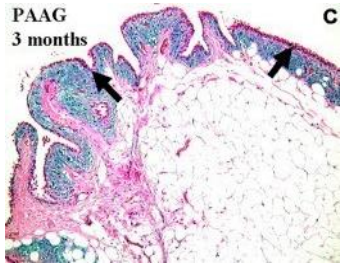


Saline
10 days

Saline-Injected Control

- The synovial lining consists of 1 to 4 cell layers.

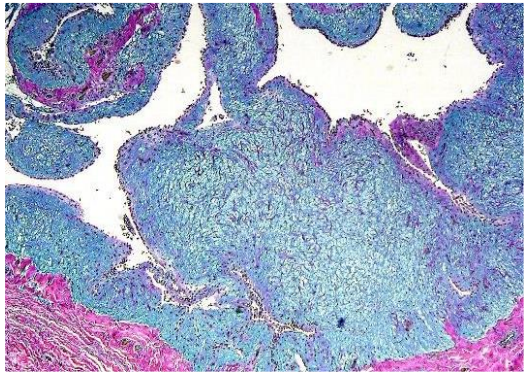
Hydrogel 3 months



At 3 months:

- Synovial lining of a 2-4 layer of cells restored.
- Blue rim of hydrogel integrated below.
- A fine network of thin connective tissue fibers anchors the hydrogel

Hydrogel 24 months



At 6, 12, and 24 Months:

- A stable situation is observed.
- The synovial layer remains 5–10 times thicker than the control.
- A fine network of thin connective tissue fibers persists.
- Only a minimal presence of mononuclear/inflammatory cells is observed.

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REGION

Mode of action: Synovial implant

Data

Mathematical simulations show that when 2.5% iPAAG is present in the synovial membrane, it helps reduce stress in the tissue.

In a study of synovial membrane elasticity in horses (OA bone chip model), treatment with 2.5% iPAAG restored the elasticity of the synovial membrane to the same level as healthy joints while placebo treated joints had a lower elasticity.

Mode of action: Synovial implant

Data

Mathematical simulations show that when 2.5% iPAAG is present in the synovial membrane, it helps reduce stress in the tissue.

In a study of synovial membrane elasticity in horses (OA bone chip model), treatment with 2.5% iPAAG restored the elasticity of the synovial membrane to the same level as healthy joints while placebo treated joints had a lower elasticity.

Hypothesis

iPAAG restores synovial elasticity

leading to improved joint function and long-lasting pain relief

Experience with iPAAG: Off label use 2010-2017

Clinical Orthopedics
Advanced Research Journal

Research Article Overgaard A, et al. Clin Ortho Adv Res J: COARJ-100001

Safety of Intra-Articular Polyacrylamide Hydrogel for the Treatment of Knee Osteoarthritis Symptoms: A Retrospective Case Series

N=91, 2x3 ml of IPAAG at baseline

Overgaard 2019 Clin Ortho Adv Res J,

Soreness	3	7.3%
Burning sensation	1	2.4%
Sensation of distension	15	36.6%
Skin or joint pricking sensation	3	7.3%
Numbness	1	2.4%
Cold sensation	1	2.4%
Heat sensation	1	2.4%
Reduced range of motion	4	9.8%
Stiffness	2	4.9%
Total	41	100%

Table 2: Patient reported events

Overgaard 2019 Clin Ortho Adv Res J,

Experience with iPAAG: Off label use 2010-2017

Poster 11

Demographics

61 Participants

24 Women

37 Men

89 Knees

As some participants had treatment in both knees

At time of injection

Mean **age**

64 years

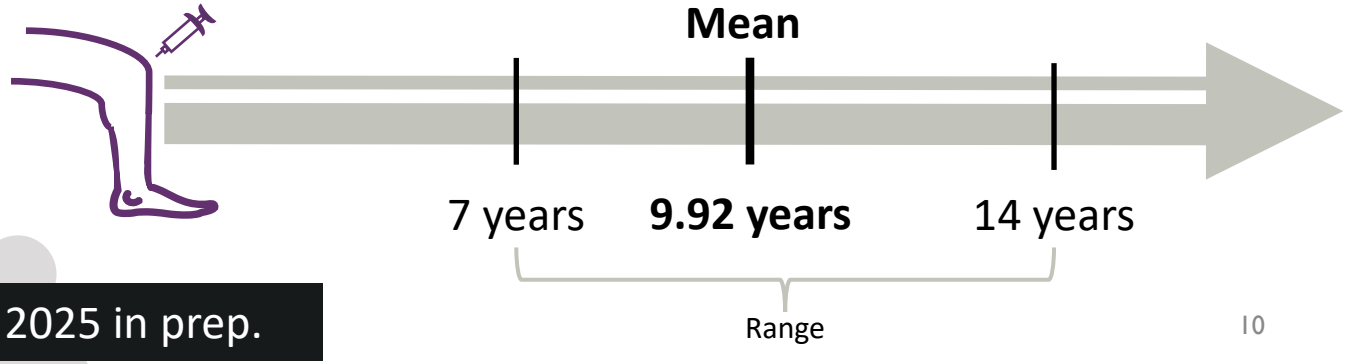
(range 34-81 years)

Mean **BMI**

27 kg/m^2

(range 19-43 kg/m^2)

Observation time



BMI, Body Mass Index.

Bliddal et al 2025 in prep.

Long Term Safety-Study

Results

Poster 11

No significant adverse events associated with iPAAG were reported by patients or identified in the reviewed medical records.

Specifically, there were no indications of allergic reactions, infections, or systemic complications attributable to the injection.

Of the **89** Knees

50 (56.2%) Did not require knee replacement in the follow-up period

39 (43.8%) Knee replacements were performed after a mean time lapse of 3.4 years (range 0.2 – 7.6)

No unusual findings that could be related to iPAAG treatment were noted in the knee replacements

Post-surgical abnormal events were noted in **2** cases

- Prolonged knee bleeding
- Infection that required revision and prolonged antibiotics

Neither case was considered related to the prior iPAAG-treatment

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Experience with iPAAG

ROSA: RCT , one injection of

6 ml of 2.5% Polyacrylamide Hydrogel, iPAAG,

6 ml of Synvisc-one

Polyacrylamide gel *versus* hyaluronic acid for the treatment of knee osteoarthritis: a randomised controlled study

H. Bliddal[1], J. Beier[2], A. Hartkopp[3], P.G. Conaghan[4], M. Henriksen[1]

[1]The Parker Institute, Bispebjerg Frederiksberg Hospital, University of Copenhagen, Denmark; [2]Reumatolog Odense, Odense, Denmark; [3]A2 Rheumatology and Sports Medicine, Holte, Denmark; [4]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds and NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom.

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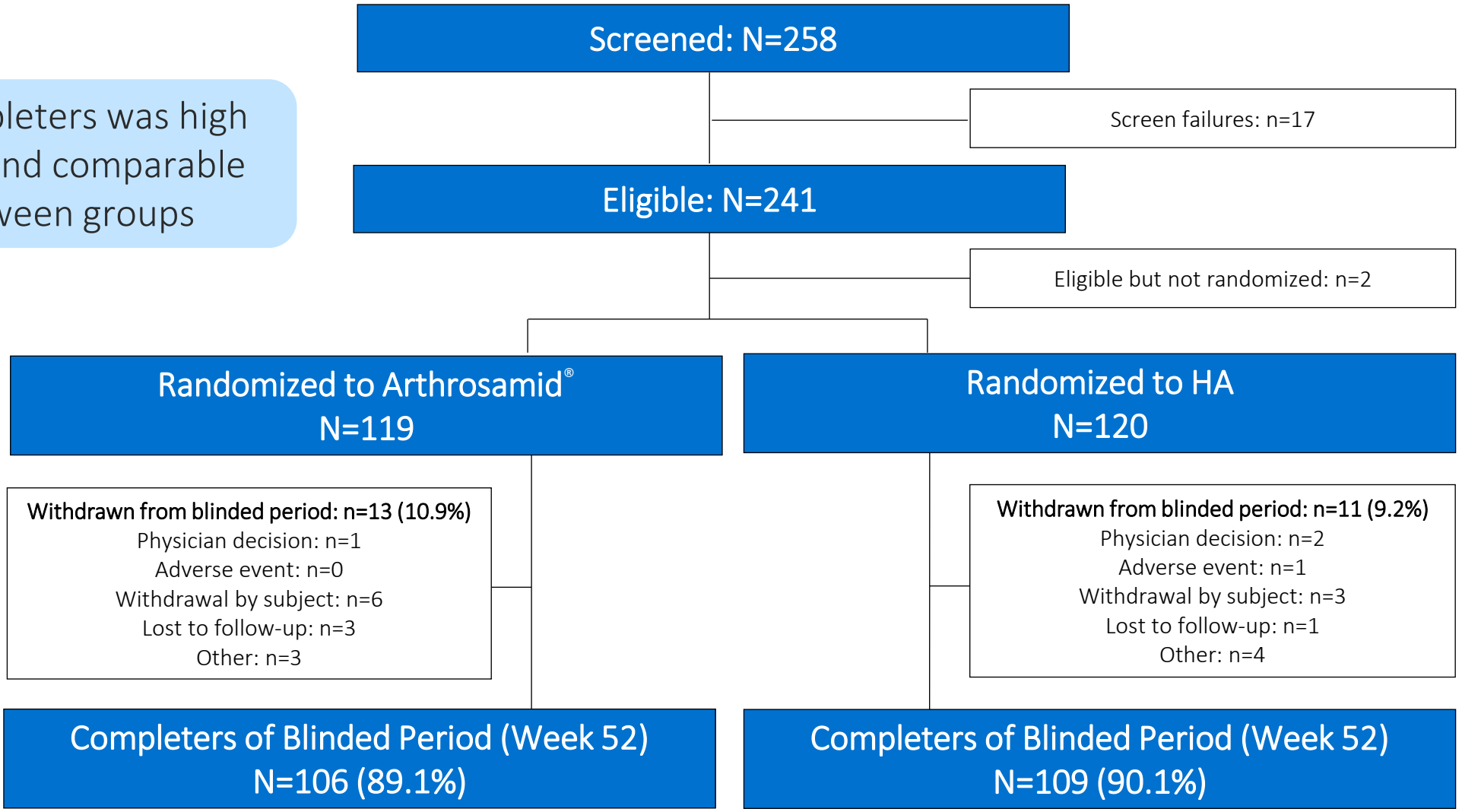
ROSA: RCT of iPAAG vs Synvisc-one

% completers was high (90%) and comparable between groups



Inclusion Criteria

- Male or female, aged ≥ 18 years
- Clinical diagnosis of knee OA according to American College of Rheumatology criteria
- Definite radiographic OA in the most symptomatic knee (target knee) at mild to severe stage (Kellgren-Lawrence 2-4)
- If participant is using analgesics for knee OA the dose should have been stable for the past four weeks
- Score of 2 or more (0-4 scale) on WOMAC question A1 (pain while walking on flat surface)
- BMI <35 kg/m^2
- For females of reproductive potential: use of adequate contraception must be used throughout the trial

Exclusion Criteria

- Previous intra-articular injection of 2.5% iPAAG in the target knee
- Previous intra-articular injection with hyaluronic acid or derivatives in target knee in the previous 6 months
- Intra-articular injection of any substance other than hyaluronic acid (e.g. corticosteroids) in the target knee within the last 3 month; Treatment with systemic steroids
- Significant valgus/varus deformity of the knee, ligamentous laxity or meniscal instability; Diseases in target knee other than OA;
- History of surgery in the target knee within the past 6 months; Planned surgery on any lower extremity
- Symptomatic osteoarthritis of the hips, spine or ankle, that interferes with the evaluation of the target knee; Inflammatory or other disease/condition which may affect the knee joint; History of sepsis in any joint or any clinical concern for an infectious process in the target knee; Infected or severely inflamed knees
- Any other contraindication to intra-articular injection; Any other condition that in the opinion of the investigator puts a potential participant at risk or otherwise precludes participation in the investigation

BMI, Body Mass Index; OA, Osteoarthritis; PAAG, Polyacrylamide Hydrogel; WOMAC, Western Ontario and McMaster Universities Arthritis Index.

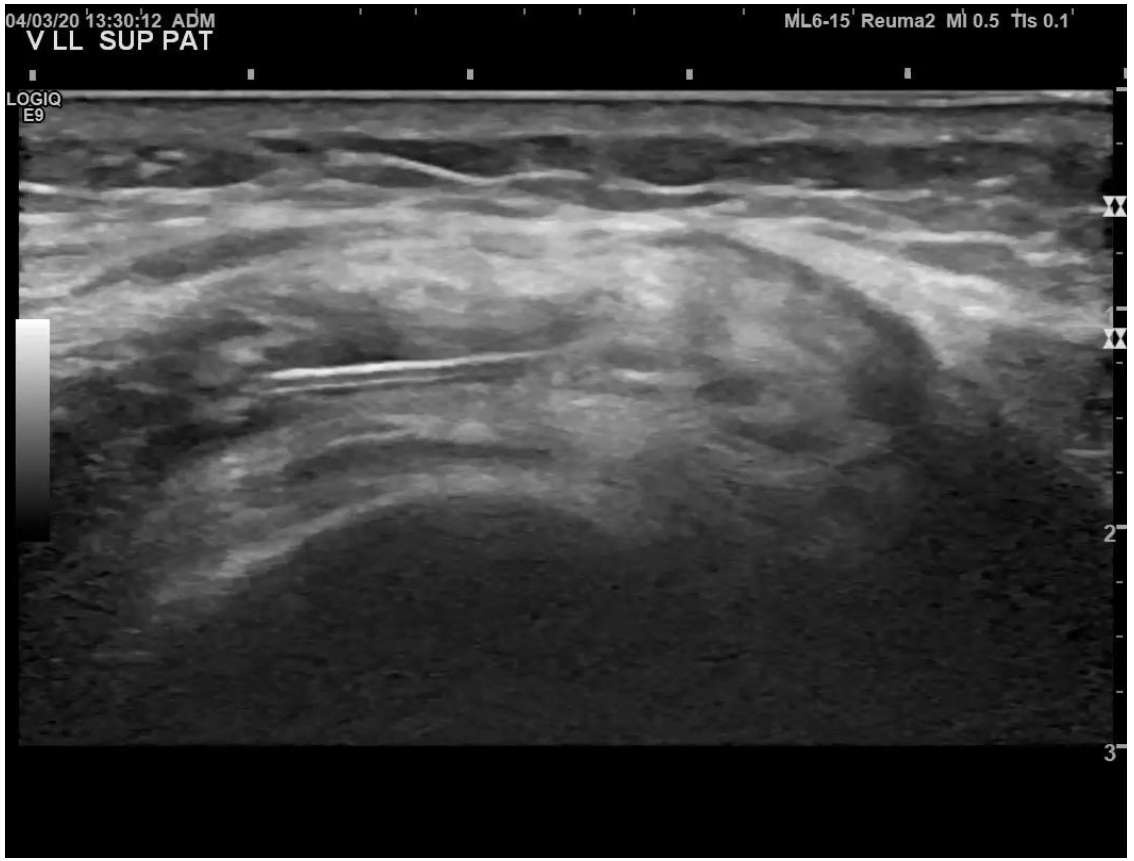
Baseline Characteristics for ROSA Study

	Arthrosamid® (N=119)	HA (N=120)
Age, years, mean ± SD (range)	67.2 ± 9.5 (42–90)	66.6 ± 9.2 (31-85)
Females, n (%)	58 (48.7%)	68 (56.7%)
Race, white, n (%)	118 (99.2%)	119 (99.2%)
Body Mass Index, kg/m^2, mean ± SD (range)	27.6 ± 3.6 (20.4–35.0)	27.3 ± 3.9 (20.0–34.9)
Baseline WOMAC Pain, mean ± SD (range)	45.1 ± 13.4 (10–75)	46.5 ± 13.3 (15–75)
Baseline WOMAC Stiffness, mean ± SD (range)	52.7 ± 20.8 (0–88)	51.1 ± 20.9 (0–88)
Baseline WOMAC Physical Function, mean ± SD (range)	44.4 ± 15.1 (3–76)	43.5 ± 16.2 (4–82)

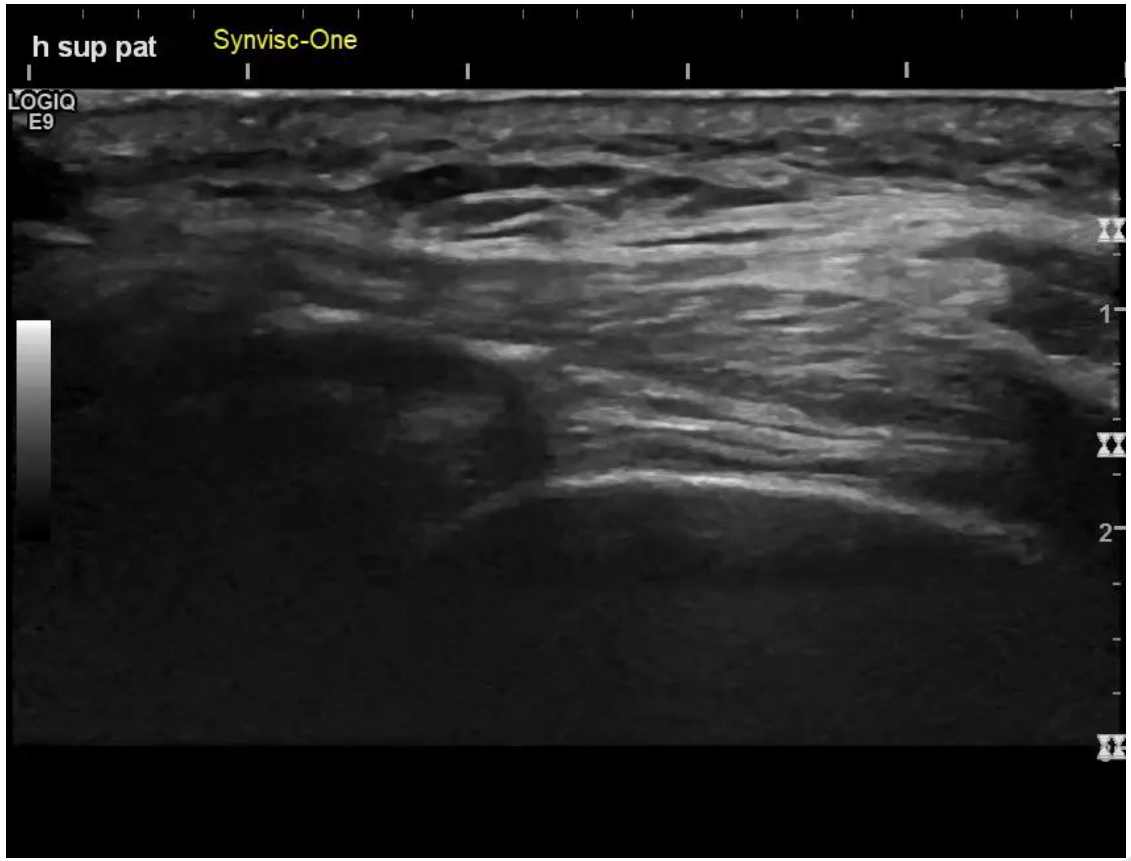
Demographic and baseline characteristics similar between groups with an average age at treatment of approximately 67 years (range 31–90 years)

HA: hyaluronic acid; SD: standard deviation; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

Videos of injection



iPAAG



Synvisc-One

ROSA Primary Endpoint: Analysis of Change from Baseline to Week 26 in WOMAC Pain Subscale (FAS)

	N	LS Mean (95% CI)	Treatment difference (95% CI)	Non-inferiority* (yes/no)	P-value
HA	117	-14.8 (-18.0; -11.7)			
Arthrosamid®	115	-18.5 (-21.7; -15.4)	3.7 (-0.8; 8.1)	Yes	NA

N: Number of subjects contributing to the analysis
The analysis is performed on change from baseline in the transformed WOMAC pain subscale (0–100) using a mixed model for repeated measures including fixed, categorical effects of treatment, week, treatment-by-week interaction and site, as well as the baseline value and baseline-by-week interaction as covariates
* If the lower bound of the 95 % CI is >-9 the objective of non-inferiority has been met
* If the lower bound of the 95 % CI is > 0 superiority is declared, and the p-value for the test of superiority was presented

Primary analysis on the change from baseline to week 26 in WOMAC pain subscale demonstrated noninferiority, with a treatment difference of 3.7 (95% CI: -0.8; 8.1) in favour of Arthrosamid® compared to HA

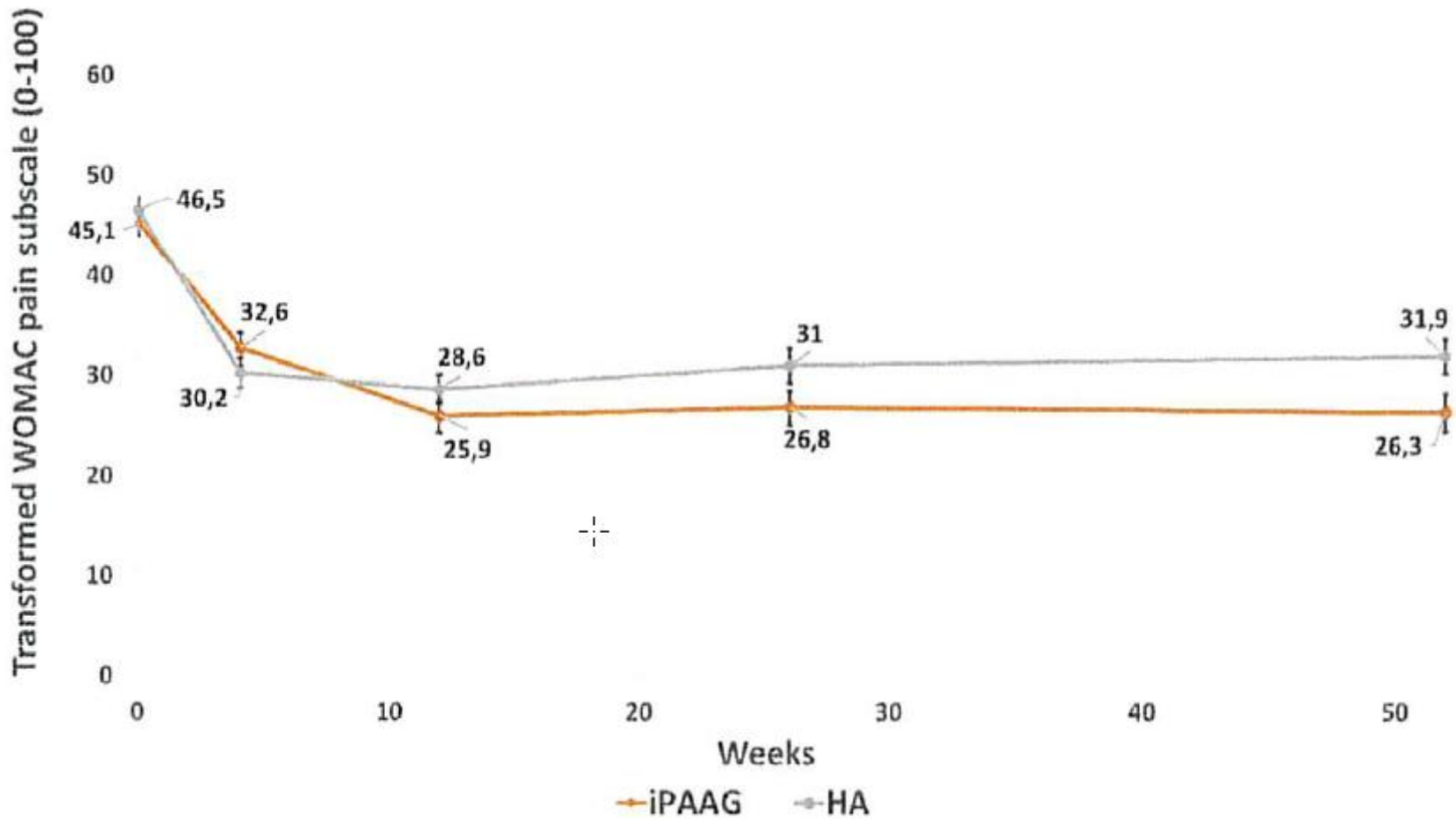


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Table IV. Adverse device effects in the safety analysis set*.

	HA n (%) E	iPAAG n (%) E
Safety analysis set** n (%)	118 (100.0)	121 (100.0)
Any adverse device effects (ADEs)	9 (7.6) 13	35 (28.9) 41
Musculoskeletal and connective tissue disorders		
Arthralgia	7 (5.9) 8	19 (15.7) 21
Joint swelling	3 (2.5) 4	13 (10.7) 13
Synovitis		1 (0.8) 1
General disorders and administration site conditions		
Injection site pain		1 (0.8) 1
Peripheral swelling		1 (0.8) 1
Skin and subcutaneous tissue disorders		
Pruritus generalised		1 (0.8) 1
Rash	1 (0.8) 1	
Gastrointestinal disorders		
Constipation		1 (0.8) 1
Nervous system disorders		
Restless leg syndrome		1 (0.8) 1
Respiratory, thoracic and mediastinal disorders		
Cough		1 (0.8) 1

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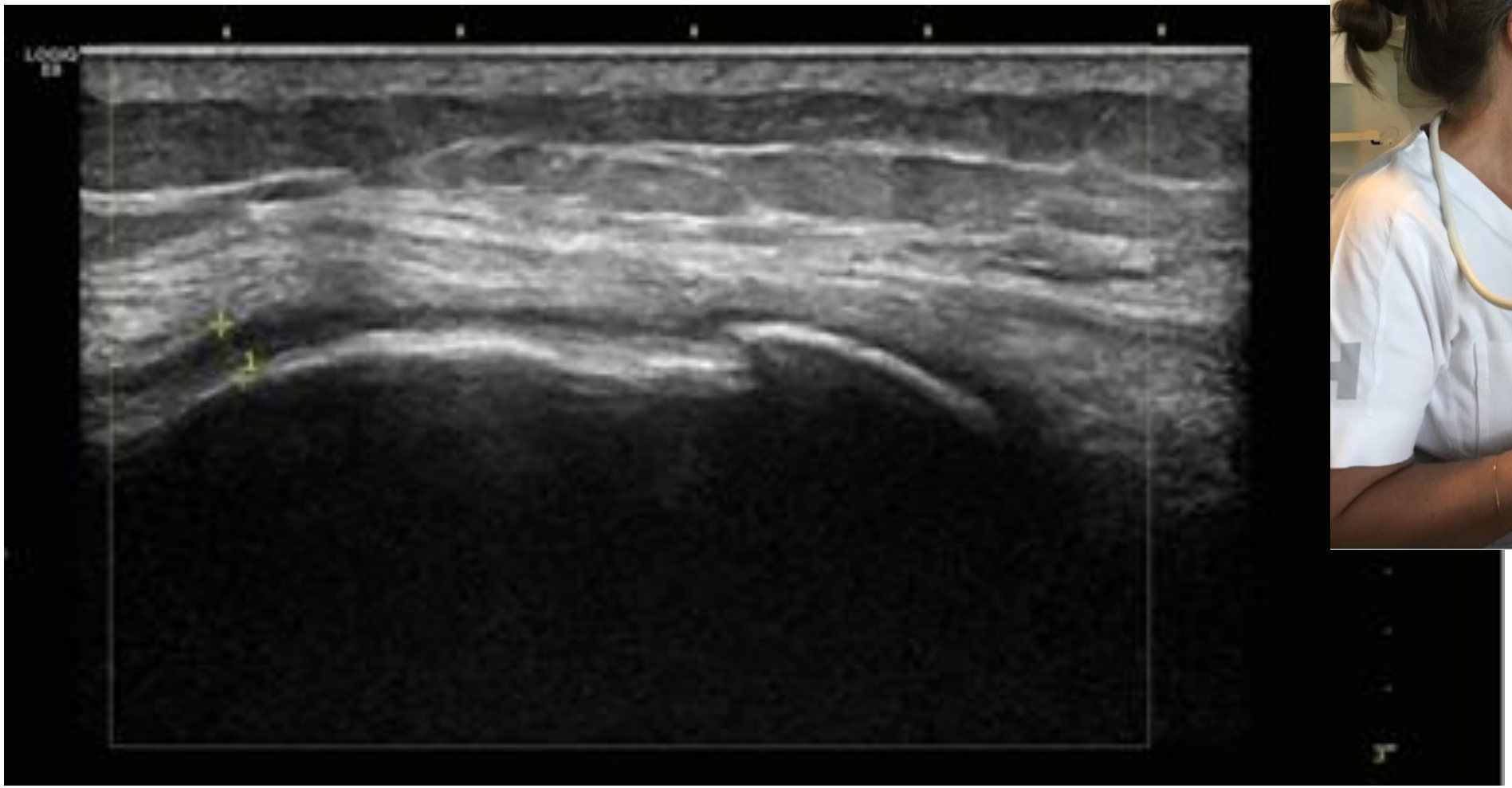
Ultrasound results from ROSA



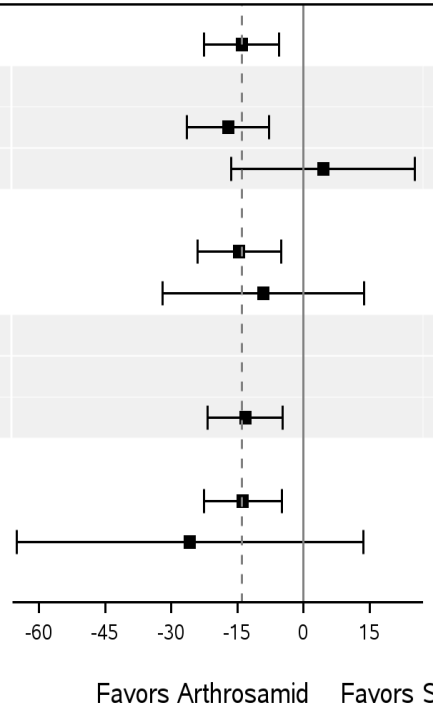
Evaluation of US signs of synovitis: medial, lateral, effusion, Doppler

Ellegaard et al 2025, in prep

Ultrasound results from ROSA

Evaluation of US signs of synovitis: medial, lateral, effusion, Doppler

Subgroup	No. of patients (Arthr./Synv.)	Arthrosamid Mean (SE)	Synvisc-One Mean (SE)	Contrasts within subgroups Mean diff. (95% CI)	Contrasts between subgroups Mean diff. (95% CI)	P Value for interaction
Overall	55/56	-32.9 (3.05)	-18.8 (3.03)	-14.0 (-23 to -5.5)		
Medial Synovitis					-21.5 (-44.3 to 1.22)	0.0633
Yes	46/44	-34.1 (3.27)	-16.9 (3.35)	-17.1 (-26 to -7.9)		
No	9 /9	-26.9 (7.41)	-31.3 (7.40)	4.40 (-16 to 25.2)		
Lateral Synovitis					-5.48 (-30.2 to 19.2)	0.6606
Yes	47/46	-34.3 (3.35)	-19.8 (3.39)	-14.6 (-24 to -5.1)		
No	8 /8	-25.6 (8.12)	-16.5 (8.16)	-9.10 (-32 to 13.7)		
Doppler Activity					not est.	
Yes	0 /1	not est.	24.75 (22.5)	not est.		
No	55/55	-32.8 (3.02)	-19.6 (3.02)	-13.2 (-22 to -4.8)		
Effusion					12.01 (-28.3 to 52.3)	0.5559
Yes	51/54	-33.1 (3.19)	-19.4 (3.10)	-13.8 (-23 to -4.9)		
No	4 /2	-29.4 (11.4)	-3.61 (16.2)	-25.8 (-65 to 13.5)		



iPAAG had better results than synvisc-one in knees with synovitis

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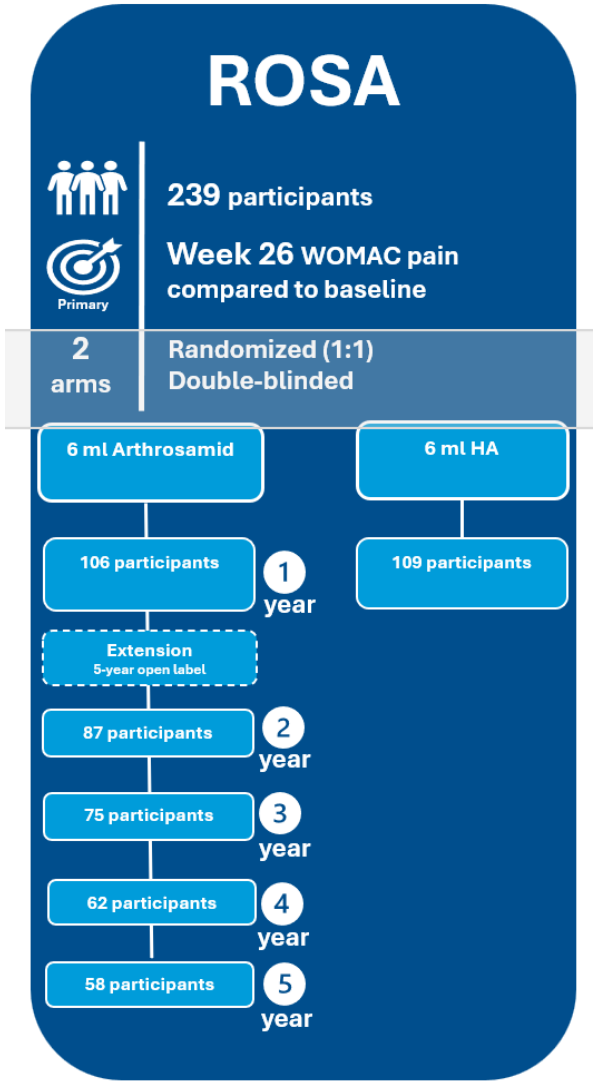
ROSA (iPAAG) Long term

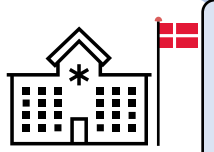


Endpoints:

- WOMAC pain, stiffness and physical function subscales
- PGA
- OMERACT-OARSI response
- EuroQoL-5D-5L questionnaire

iPAAG Long term, 2-5 years

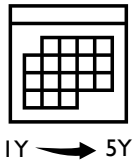
ROSA (iPAAG) Long term



Long-Term Extension of Randomised Clinical Trial, Conducted in Denmark

119 participants received an intra-articular injection of 6 mL 2.5% iPAAG from which 91 entered the extension study.

Participants continued analgesics (except 48 hours prior to visits) and non-pharmacologic therapy



Originally a 1-year study; extended to 5 years follow-up

58 participants completed the 5-year follow-up

Topical therapies and intra-articular corticosteroids were not allowed.

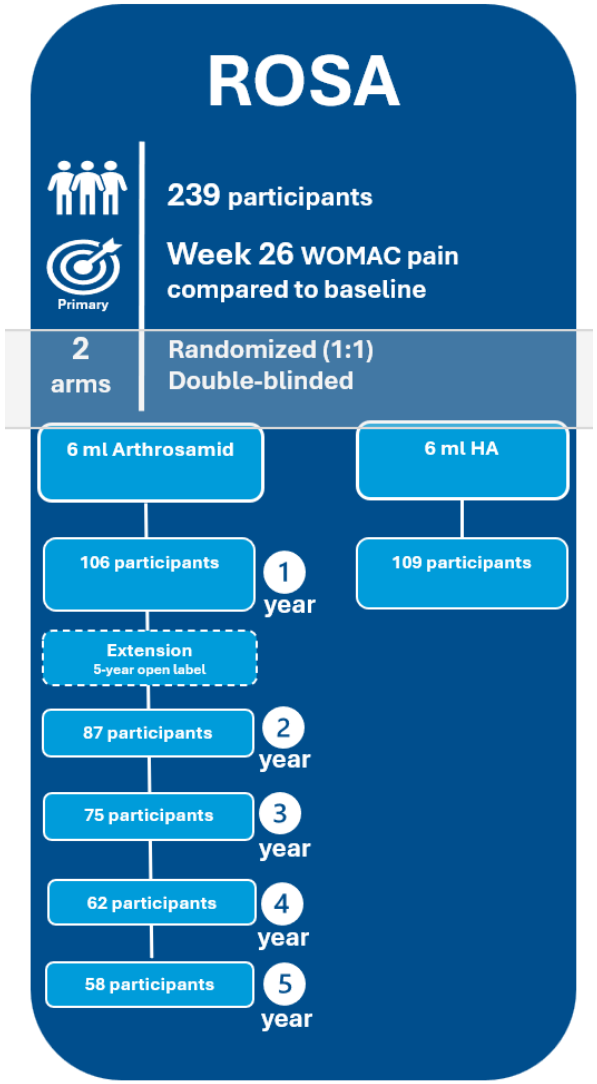
Changes from baseline in the WOMAC pain, stiffness and function subscales and PGA of disease impact were analysed using a MMRM with a restricted maximum likelihood-based approach.

2 sensitivity analyses were performed on the WOMAC pain subscale data:

- A second MMRM analysis was performed only using data from the participants in the extension phase
- An ANCOVA model was used where missing year 5 values were replaced by the respective BOCF.

ANOVA, Analysis of Variance; BOCF, Baseline Observation Carried Forward; iPAAG, Injectable Polyacrylamide Hydrogel; MMRM, Mixed-Effects Model for Repeated Measures; PGA, Patient Global Assessment; WOMAC, Western Ontario and McMaster Universities Arthritis Index.

ROSA (iPAAG)-Study



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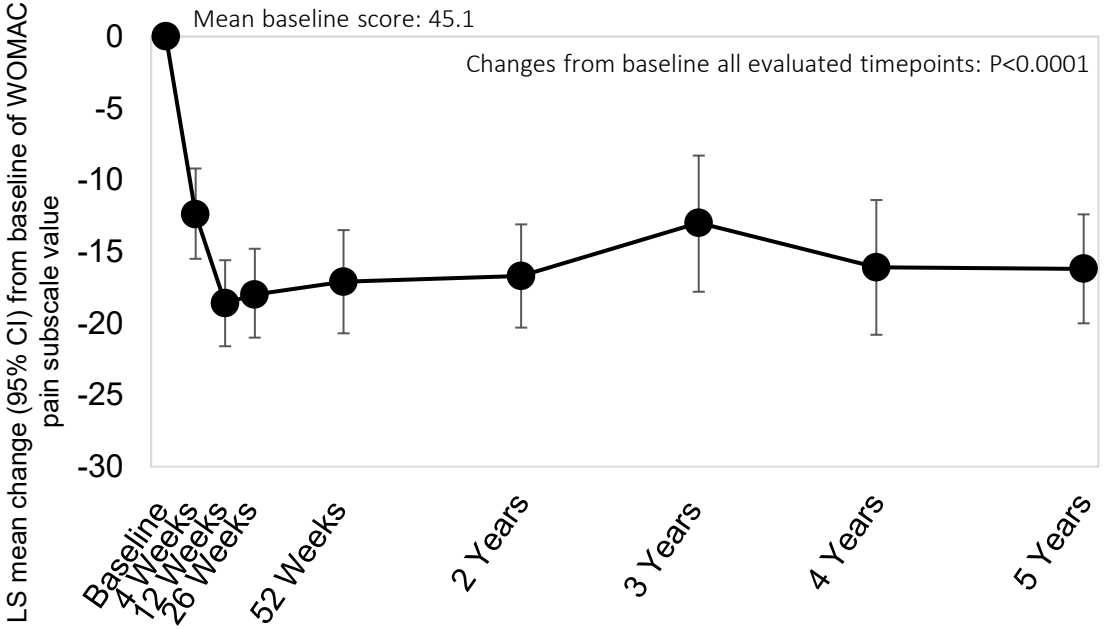
Demographic and baseline characteristics

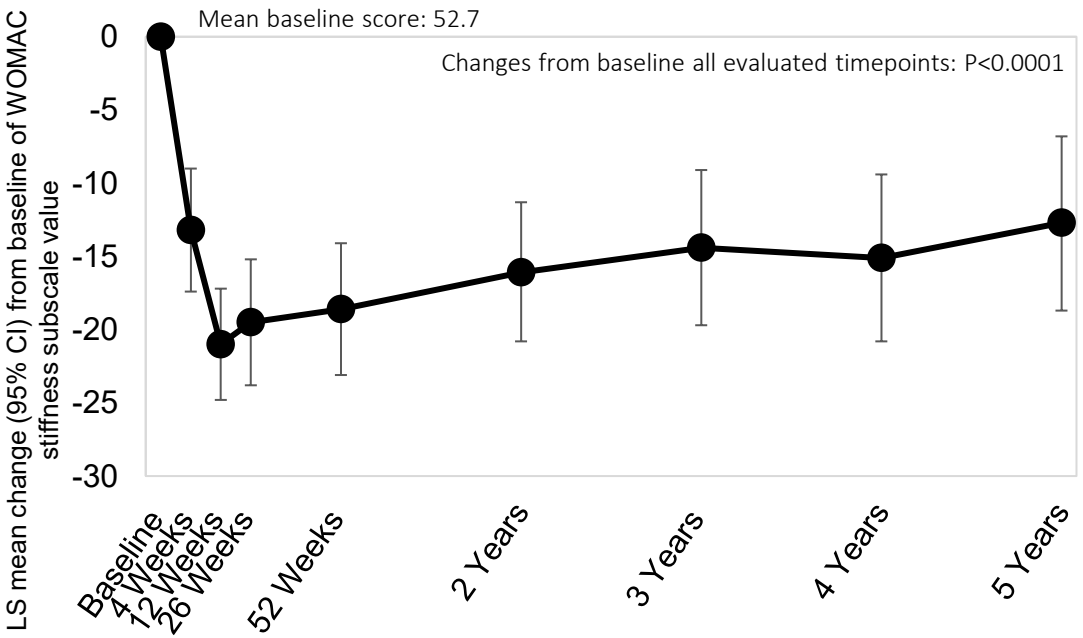
	Total	Included in extension	Not included in extension	Completers
ITT analysis set (N,%)	119 (100.0)	91 (100.0)	28 (100.0)	58 (100.0)
Age (years)				
Mean (SD)	67.2 (9.5)	67.5 (9.0)	66.1 (10.9)	67.2 (7.3)
Median	67.0	67.0	68.5	67.0
Min - Max	42 - 90	42 - 90	46 - 88	46 – 82
Sex (N,%)				
Female	58 (48.7)	44 (48.4)	14 (50.0)	27 (46.6)
Male	61 (51.3)	47 (51.6)	14 (50.0)	31 (53.4)
Race (N,%)				
White	118 (99.2)	90 (98.9)	28 (100.0)	57 (98.3)
Other	1 (0.8)	1 (1.1)		1 (1.7)
Height (cm)				
Mean (SD)	172.9 (9.4)	172.7 (9.4)	173.6 (9.7)	173.3 (9.0)
Median	173.0	172.0	173.0	173.0
Min - Max	155 - 201	155 – 201	156 - 198	156 - 190
Weight (kg)				
Mean (SD)	82.6 (13.5)	81.7 (12.7)	85.6 (15.5)	81.5 (12.8)
Median	81.0	80.0	85.0	82.5
Min - Max	53 - 129	53 - 123	57 - 129	55 - 123
BMI (kg/m²)				
Mean (SD)	27.58 (3.60)	27.37 (3.58)	28.26 (3.64)	27.12 (3.52)
Median	27.20	27.10	27.70	26.55
Min - Max	20.4 - 35.0	20.4 - 35.0	22.0 - 34.6	20.4 - 34.8
Baseline WOMAC pain				
Mean (SD)	45.1 (13.4)	44.1 (12.6)	48.4 (15.5)	42.8 (13.7)
Median	45.0	45.0	45.0	42.5
Min - Max	10 - 75	10 - 70	25 - 75	10 - 70

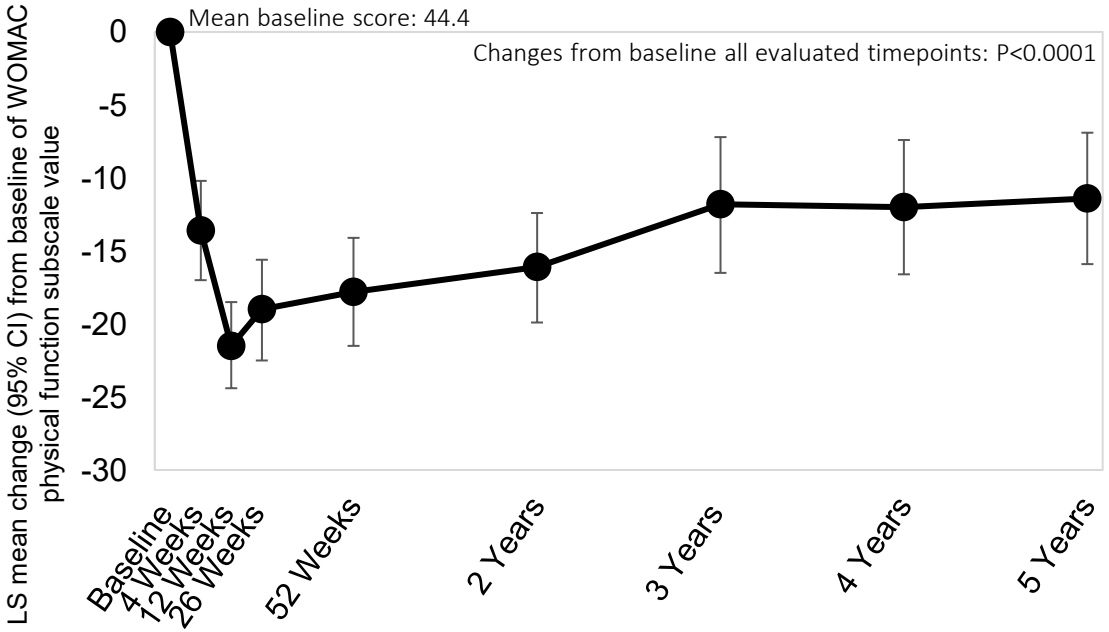
ROSA (iPAAG) – Changes from Baseline to Year 5 in WOMAC Subscales

	N	LS Mean (95% CI)	p-value
WOMAC pain subscale			
population	58	-16.2 (-20.0; 12.4)	<0.0001
Extension participants	58	-18.3 (-22.1; 14.5)	<0.0001
BOCF	119	-10.0 (-13.0; -7.0)	<0.0001
WOMAC stiffness subscale			
population	58	-12.7 (-18.7; -6.8)	<0.0001
Extension participants	58	-14.9 (-20.8; -8.9)	<0.0001
BOCF	119	-8.5 (-12.2; -4.8)	<0.0001
WOMAC phys. function subscale			
population	58	-11.4 (-15.9; -7.0)	<0.0001
Extension participants	58	-13.8 (-18.2; -9.5)	<0.0001
BOCF	119	-8.6 (-11.6; -5.7)	<0.0001

Results – Changes from Baseline to Year 5 in WOMAC Subscales (ITT) for ROSA (iPAAG) – Study







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Summary for ROSA (iPAAG)-Study

Treatment was well tolerated. No serious adverse events assessed as related to iPAAG

Treatment with iPAAG remains safe and appears effective for its intended use 5 years after injection.

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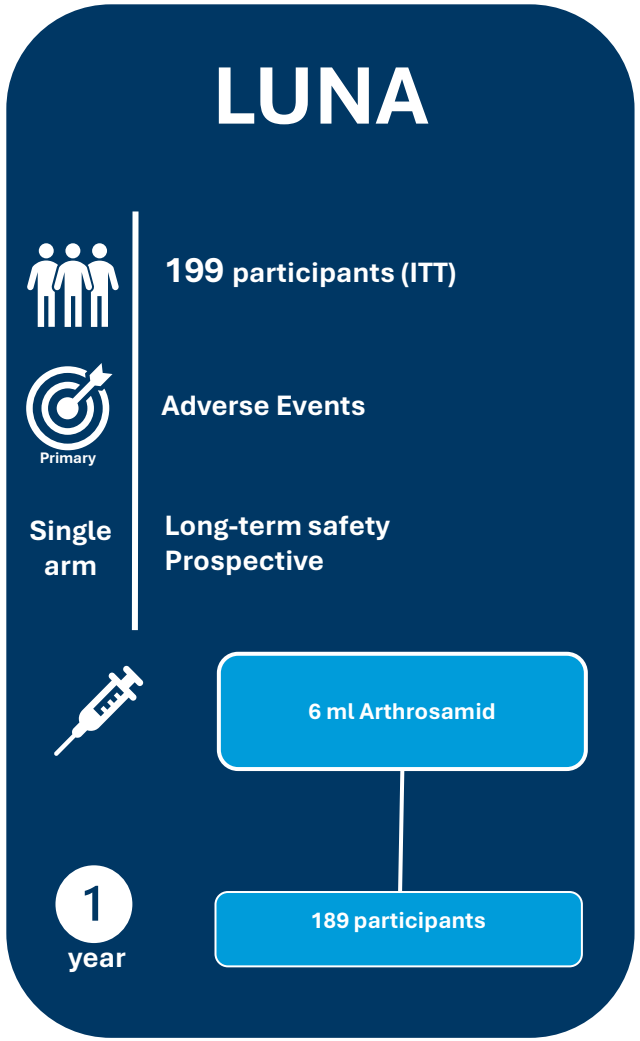
Prospective international cohort (LUNA, iPAAG)

Poster 10



- Prospective, observational, open-label, multi-centre.
- Adults (≥18 years) with knee OA.
- Sample Size: 199 subjects across 9 centres in Europe.
- Duration: 5 years with assessments at 6, 12, 24, 36, 48, and 60 months.
- Endpoints:
  Primary - AEs;
  Secondary - WOMAC subscales, PGA scores.
- Statistical Analysis: MMRM for effectiveness, AE categorization.

Prospective international cohort (LUNA, iPAAG)

Poster 10

- Mean Age: 62.8 years
- Mean BMI: 29.4
- % female: 53.3%

Baseline characteristics of all 199 patients

- Baseline Mean WOMAC Pain (0-100): 46.0
- Baseline Mean WOMAC Stiffness (0-100): 50.6
- Baseline Mean WOMAC Phys. Function (0-100): 47.4
- Baseline Mean PGA (0-10): 6.6

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Prospective international cohort (LUNA, iPAAG)

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	% of subjects	Number of events
Adverse events (AEs)	48.7	163
Serious AEs	2.5	6
Non-serious AEs	48.2	157
Adverse device effects (ADE)	9.0	28
Serious ADEs	0	0
AEs leading to withdrawal from study	1.0	2
Fatal AEs	0	0
Severity *Mild* *Moderate* *Severe*	 29.6 21.1 4.5	 99 54 10

LUNA safety overview

Most commonly reported AEs	% of subjects	Number of events
Arthralgia	11.1	24
COVID-19	6.0	12
Osteoarthritis	4.5	11
Injection site pain	4.5	10

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Prospective international cohort (LUNA, iPAAG)

Reported ADEs	Number of subjects	% of total population	Number of events
Injection site pain	9	4.5%	10
Arthralgia	5	2.5%	6
Erectile dysfunction	2	1.0%	2
Inflammation	1	0.5%	1
Injection site swelling	1	0.5%	1
Pain	1	0.5%	1
Haemarthrosis	1	0.5%	1
Joint effusion	1	0.5%	1
Joint stiffness	1	0.5%	1
Musculoskeletal stiffness	1	0.5%	1
Hypoaesthesia	1	0.5%	1
Presyncope	1	0.5%	1
Procedural pain	1	0.5%	1
Total	**18**	**9.0%**	**28**

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Adverse Device Effects

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Changes from Baseline to Year 1 in WOMAC Subscales

	Number of participants		LSMean (95% CI)	p-value
	At baseline	At 1 years		
WOMAC pain subscale	199	189	-17.0 (-19-6; -14.4)	<0.0001
WOMAC stiffness subscale	199	189	-18.5 (-21.7; -15.4)	<0.0001
WOMAC Phys. Function subscale	199	189	-18.8 (-20.6; -15.3)	<0.0001

Prospective international cohort (LUNA, iPAAG)

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Summary for LUNA-Study

Treatment was well tolerated. No serious adverse events assessed as related to iPAAG

Efficacy outcomes demonstrated sustained symptom relief over 12 months, supporting its use as a well-tolerated, non-surgical treatment option for knee OA.

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Conclusion
2.5% Polyacrylamide Hydrogel, iPAAG

- iPAAG acts as an implant in the synovial membrane
- The effect of iPAAG is better in knees with signs of inflammation
- In open-labelled studies effect is maintained as long as 5 years
- Safety of iPAAG has been demonstrated by long-term observation
    - after the injection up to 10 years
    - with later knee replacement

Thank you

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