Polyacrylamide Hydrogel for Knee Osteoarthritis: 5-Year Results from Two Prospective Studies

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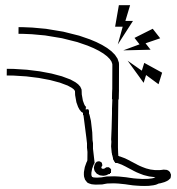
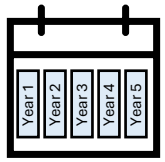
Background and purpose



There is a lack of available effective treatments for knee OA.
In particular, longer lasting therapies are needed.

The studies are a long-term extensions of clinical studies evaluating the efficacy and safety of a single 6 mL IA injection of 2.5% iPAAG* in knee OA



The purpose of these studies were to evaluate the long-term efficacy and safety of 2.5% iPAAG for up to 5 years after treatment.

*Arthrosamid®, Contura International A/S, Denmark.
iPAAG, Injectable Polyacrylamide Hydrogel.

What is 2.5% Polyacrylamide Hydrogel, iPAAG*

First in class treatment for knee OA

2.5% cross-linked polyacrylamide and 97.5% non-pyrogenic water.
Biocompatible, non-absorbable, non-biodegradable and stable

A soft, elastic synovial implant that biomechanically increases synovial elasticity in patients with knee OA, supporting improved mobility, range of motion, function and pain relief

Two studies with long term observation

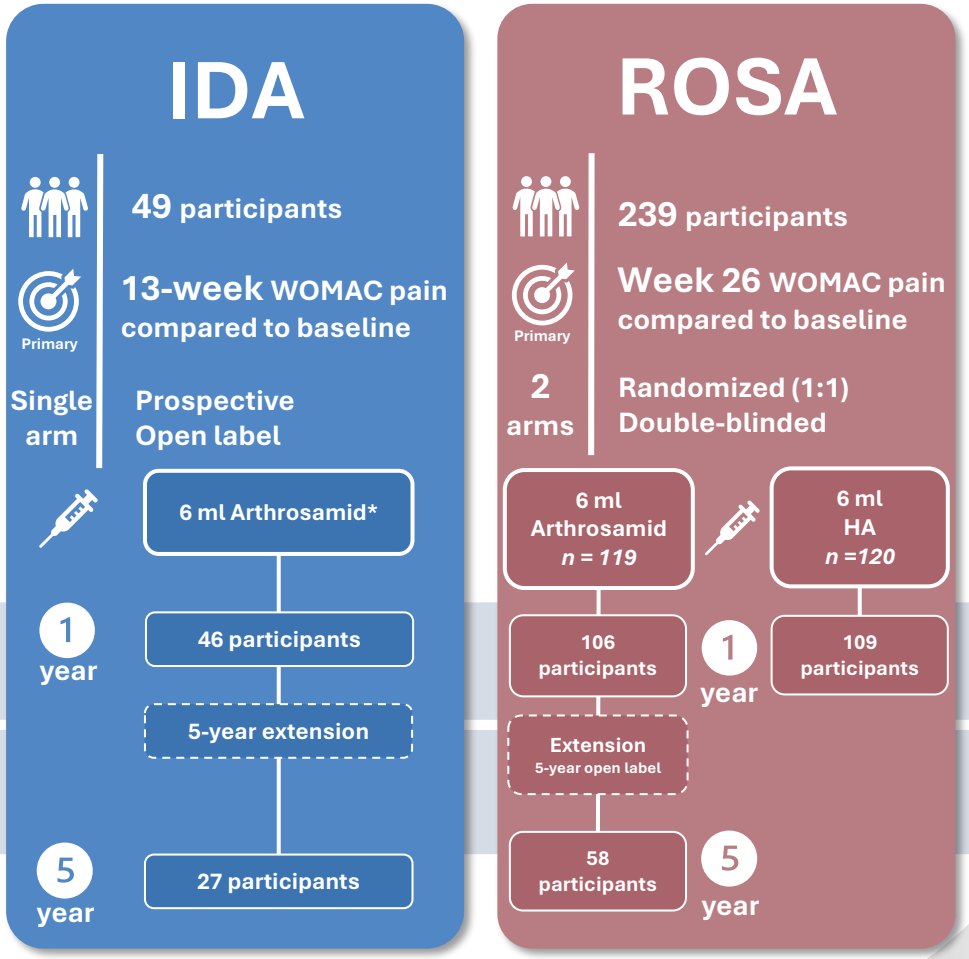
Long-term extensions of clinical trials conducted in Denmark, nicknamed IDA and ROSA.

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

1Y → 5Y

Initially 1-year studies; extended to 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.

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

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

*2.5% Injectable Polyacrylamide Hydrogel.

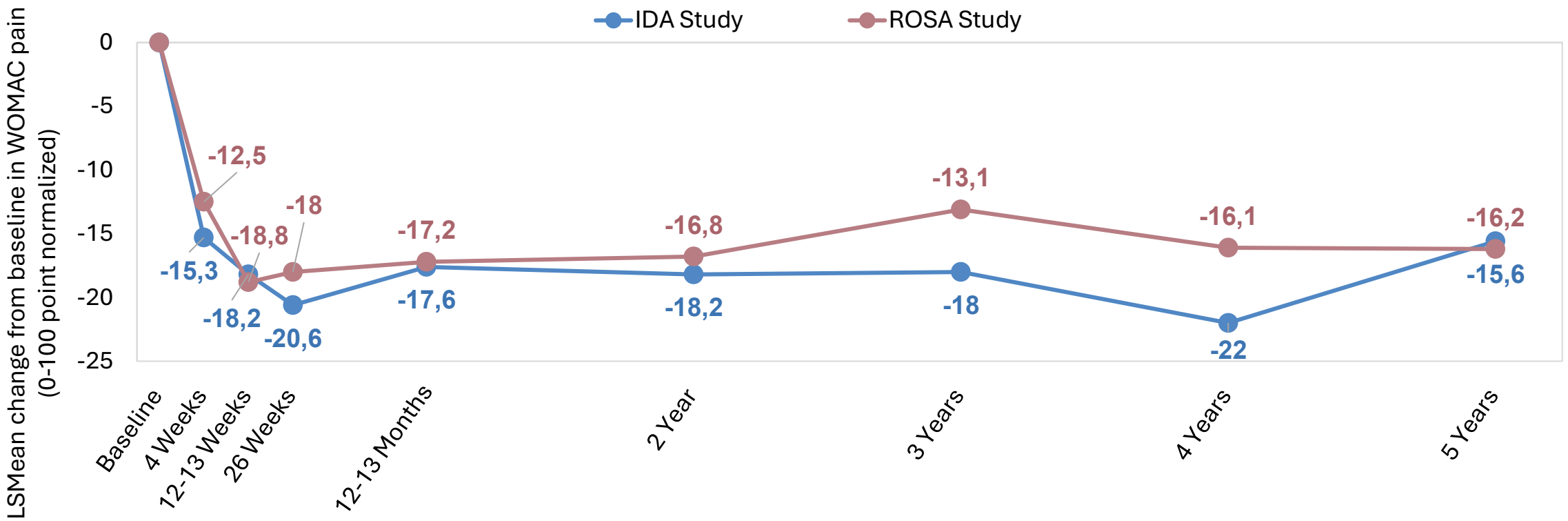
ANCOVA, Analysis of Covariance; BOCF, Baseline Observation Carried Forward; MMRM, Mixed-Effects Model for Repeated Measures; PGA, Patient Global Assessment; WOMAC, Western Ontario and McMaster Universities Arthritis Index.

Analyses of change from baseline

		Number of participants*		LSMean (95% CI)	p-value
		At baseline	At 5 years		
IDA	**WOMAC pain subscale**				
	Planned analysis	49	27	-14.6 (-21.4; -7.7)	0.0002
	Extension participants	35	27	-15.6 (-22.3; -8.9)	<0.0001
	Baseline carried forward	49	49	-9.1 (-14.1; -4.1)	0.0006
	WOMAC stiffness subscale	49	27	-19.6 (-29.9; -9.3)	0.0006
	WOMAC Phys. Function subscale	49	27	-12.5 (-19.8; -5.2)	0.0015
	Patient Global Assessment	49	27	-13.4 (-23.3; -3.5)	0.0100
ROSA	**WOMAC pain subscale**				
	Planned analysis	119	58	-16.2 (-20.0; -12.4)	<0.0001
	Extension participants	91	58	-18.3 (-22.1; -14.5)	<0.0001
	Baseline carried forward	119	119	-10.0 (-13.0; -7.0)	<0.0001
	WOMAC stiffness subscale	119	58	-12.7 (-18.7; -6.8)	<0.0001
	WOMAC Phys. Function subscale	119	58	-11.4 (-15.9; -7.0)	<0.0001
	Patient Global Assessment	119	58	-13.5 (-19.5; -7.4)	<0.0001

*Number of participants contributing to the analysis;
CI, Confidence Interval; LSMean, Least Squares Mean; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

Change from baseline WOMAC Pain Subscale



LSMean, Least Squares Mean; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

Safety Analysis – Adverse Events

Adverse events were reported in both cohorts.

- IDA: 87 events (11 serious)
- ROSA: 79 events (6 serious)

The majority of related non-serious events were transient and mild to moderate in severity.

None of the serious events were assessed as related to the treatment.

Limitations

- Lack of a control groups
- Relatively small sample sizes further reduced by participant attrition
- Incomplete data on concomitant therapies during the study period
- Timing of entry into the extension study may have introduced selection bias
- Participants who stayed in the extension study were more likely responders, while those who discontinued due to worsening symptoms, lack of improvement, or other reasons contributed to an evolving imbalance in the study population.

Conclusion

A single 6mL intra-articular injection of PAAG provides sustained, clinically meaningful symptom relief and is well tolerated over a 5-year period in patients with moderate-to-severe knee OA.