

Study ART-ONE 75

The key points

Intra-articular single injection of hyaluronic acid in knee osteoarthritis: Multi-centre open prospective study (ART-ONE 75) with placebo post hoc comparison

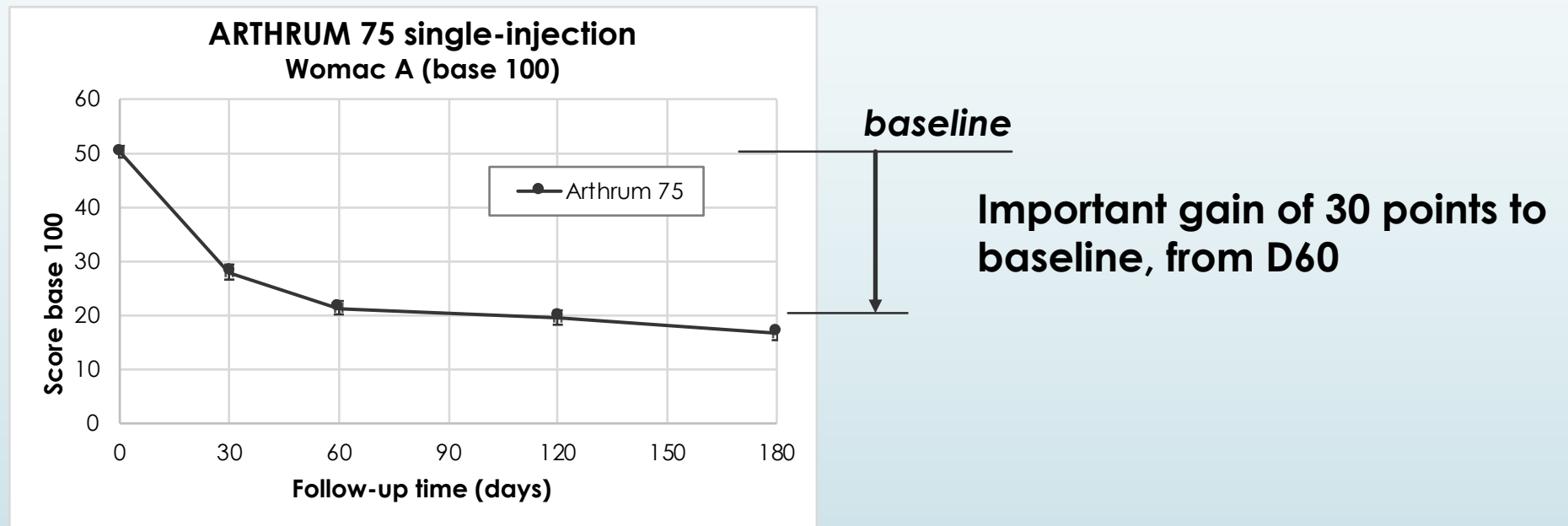
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Study ART-ONE 75 – The key points

- Two steps in the clinical research
 - Open study ART-ONE 75 performed in 2016
 - Post-hoc comparison versus injected placebo, completed in 2018
- Following, the study has been published in CTR (Current Therapeutic Research), an international journal of the Elsevier group

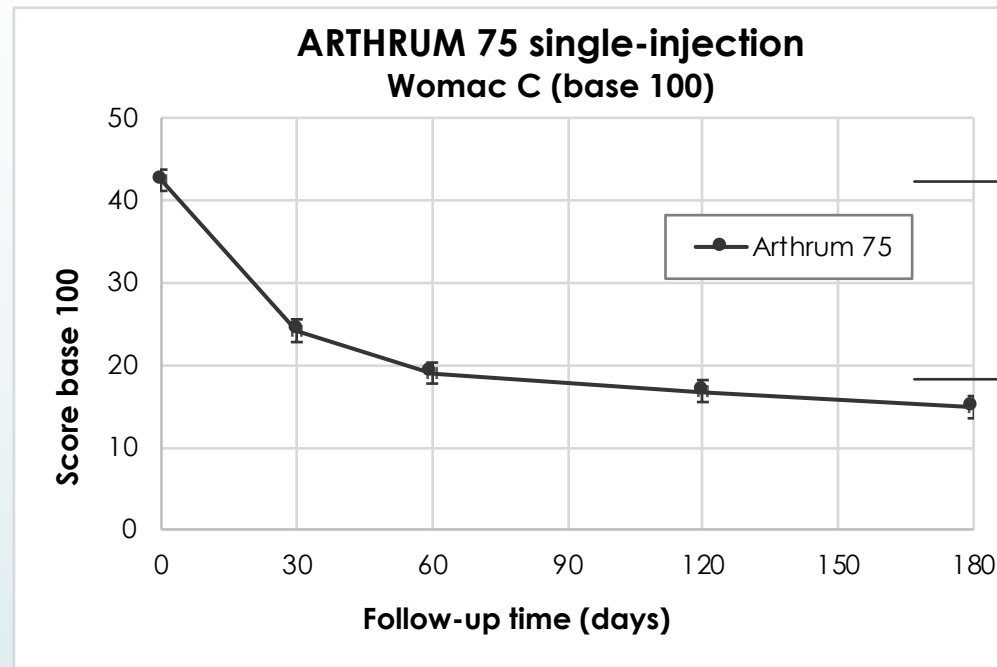
Study ART-ONE 75 – The key points

- Clinical results of the open study :
 - Analyzed population : 214 patients (ITT, real world)
 - Average patient profile representative of knee OA : age 62,9 years – BMI 27,2 kg/m² – KL I-III (45,6% grade III)
 - Main criterion WOMAC A (pain sub-score) at D60



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- ▶ Secondary criterion WOMAC C (function sub-score)



baseline

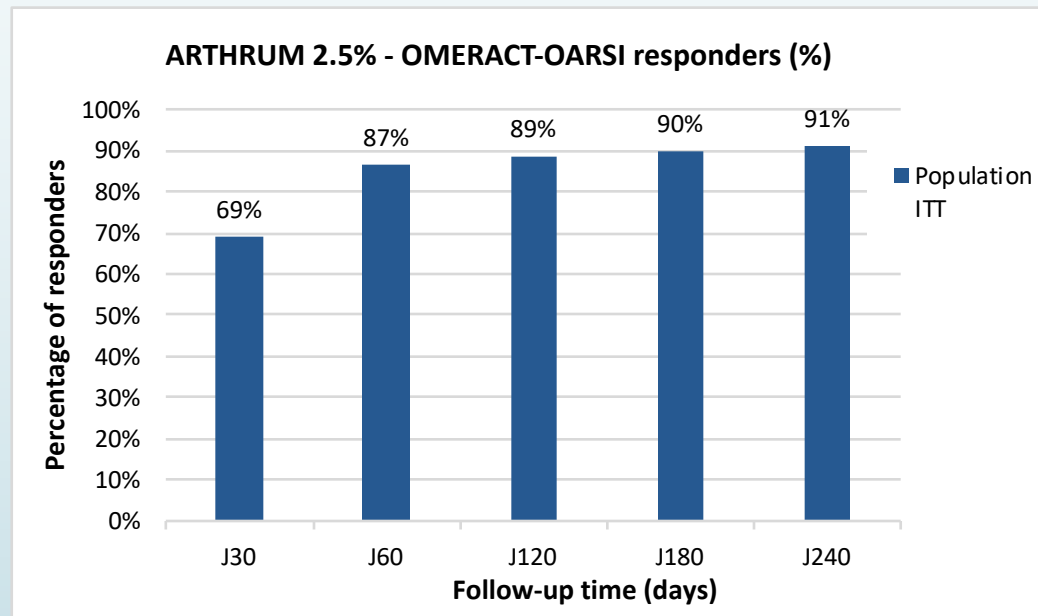
Important gain of 25 points to baseline, from D60

The minimal clinically important difference is 7.5 points for WOMAC A and 6.7 points for WOMAC C, from Angst 2001

In the real world, these improvements to baseline are well matching with patient's feeling

Study ART-ONE 75 – The key points

- ▶ Functional handicap widely improved from patient :
 - ▶ Rate of high handicap patients 40% at inclusion → <10% from D60
 - ▶ Rate of low/zero handicap patients 10% at inclusion → >65% from D60
- ▶ Excellent tolerance
- ▶ OMERACT-OARSI responders (%)



Important rate of responders over 85% from D60 to D240

Study ART-ONE 75 – The key points

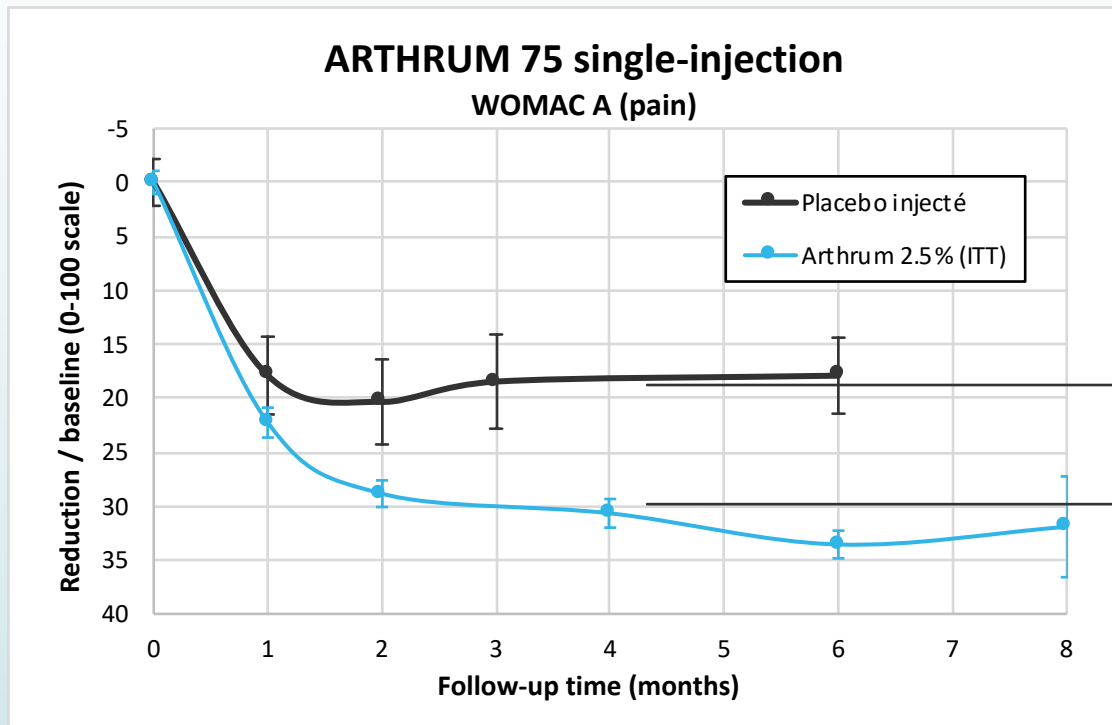
- ▶ Interest of the post-hoc comparison versus injected placebo :
 - ▶ Baseline comparison is not enough...
 - ▶ To present the results in the same terms as done with a controlled randomized trial :
 - ▶ Score Difference
 - ▶ Effect Size
 - ▶ Confidence Interval
 - ▶ Statistical proof (p-value)

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- ▶ Which placebo has been selected ?
 - ▶ Published trials for single-injections versus injected saline solution, using WOMAC A and C have been considered as the base
 - ▶ The weighted mean scores between the placebo arms from Chevalier 2010, Strand 2012 and Hangody 2017 trials
 - ▶ Average patient profile : age 60,7 years – BMI 29,2 kg/m² – KL I-III (48% grade III), *just perfect for KL (p = 0.65)*
 - ▶ This analysis has been accepted by the CTR reviewers

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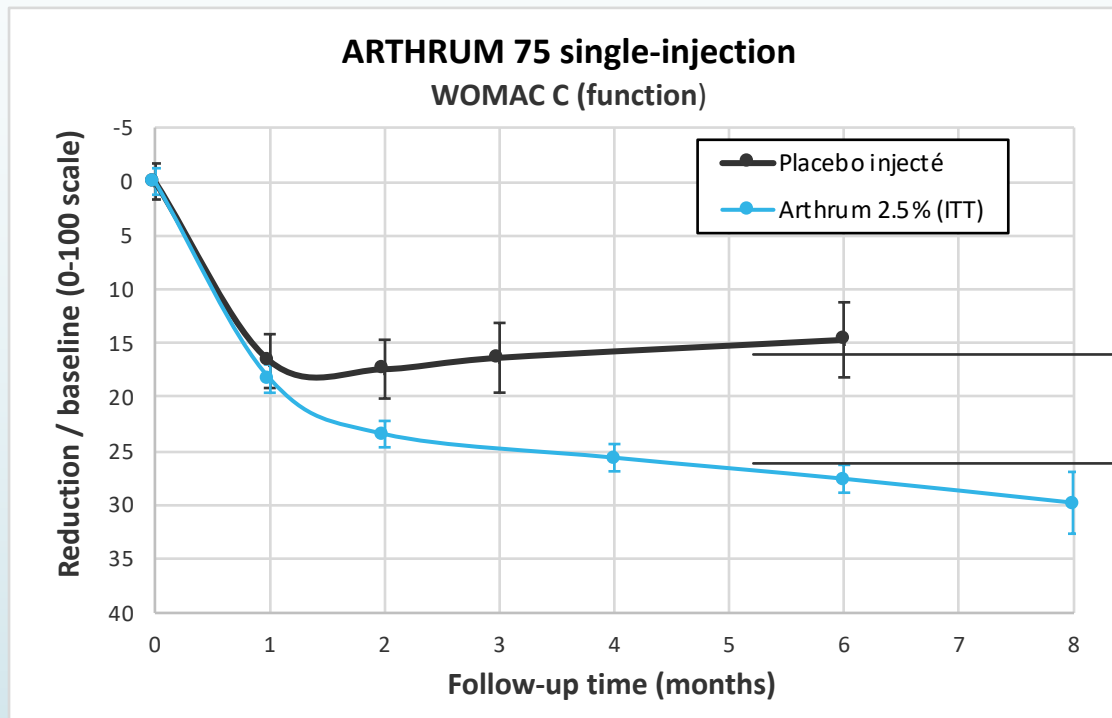
- Injected placebo post-hoc comparison result
 - WOMAC A (pain sub-score) criterion



Gain 9 to 15 points compared to the injected placebo, significant from D60

Study ART-ONE 75 – The key points

- ▶ Injected placebo post-hoc comparison result
 - ▶ WOMAC C (function sub-score) criterion



Gain 8 to 12 points compared to the injected placebo, significant from D90

Study ART-ONE 75 – The key points

- ▶ Injected placebo post-hoc comparison result
 - ▶ Criterion WOMAC A index (pain sub-score)
 - ▶ Effect Size at D60 **0.33** [0.15 ; 0.51] p < 0.001
 - ▶ Effect Size at D90 **0.52** [0.34 ; 0.70] p < 0.001
 - ▶ Effect Size at D180 **0.65** [0.45 ; 0.85] p < 0.001
 - ▶ Criterion WOMAC C index (function sub-score)
 - ▶ Effect Size at D90 **0.34** [0.13 ; 0.55] p = 0.001
 - ▶ Effect Size at D180 **0.48** [0.27 ; 0.69] p < 0.001
- ▶ Effect Size results* obtained with ARTHRUM 75, confirm its efficacy

(*) **0.2 = small, 0.5 = medium, 0.8 = large**