

# The rate of response to viscosupplementation is depending on the choice of the Patient Reported Outcomes (PROs) in patients with knee osteoarthritis

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# Disclosure of interest

- ✓ Aptissen
- ✓ Genevrier
- ✓ Labrha
- ✓ Sanofi

# Background



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5-7 October 2017

✓ Meta- analyses on viscosupplementation for treating knee OA are controversial whereas, **most of patients are satisfied with treatment.**

We assume that **patients' opinion** is the most relevant mean for assessing effectiveness of a treatment aimed to alleviate pain and improve joint function.

✓ **Several Patient-Reported-Outcomes (PROs)** are being developed for more relevant assessment of pain and disability in knee OA.

# Patient Acceptable Symptom State

- ✧ **Clinically relevant cut-off** to assess the **individual clinical status of a patient, at a given time**, by classifying him (her) as being in “an acceptable state” (score  $\leq$  PASS threshold) or not (score  $>$  the PASS).
- ✧ **PASS** can be defined as the « **highest level of symptoms beyond which patients consider themselves well** ».

# Patient Acceptable Symptom State

- ★ **PASS** introduces the concept of **wellbeing or remission**.
- ★ **PASS** is subject to variations related to the country or method of collection.
- ✓ **PASS Womac pain  $\leq 4/10$** , varying from 2.6 in France to 5.3 in Italy.
- ✓ **PASS Womac function  $\leq 5/10$**  ranging from 2.9 in Spain to 5.3 in Italy.
- ✓ **PASS Patient Global assessment  $\leq 4/10$**

Bellamy N, et al. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol. 1988; 15[12]:1833-40.

Golightly YM, et al. Patient-reported outcomes to initiate a provider-patient dialog for the management of hip and knee osteoarthritis. Semin Arthritis Rheum. 2015;45[2]:123-31.

# Hypothesis



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Assuming that the caregivers objective is that patients are satisfied with the treatment, we hypothesized that a **state-attainment criterion**, such as the PASS, has to be preferred to a **responder criterion**, such as pain decrease, to assess the individual clinical status of a patient **at a given time, as it is done in daily practice.**

# Objectives



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1. To assess, in daily practice conditions, the percentage of patients with knee OA, who **reached the PASS threshold** (PASS +), 6 months after viscosupplementation for knee OA
  
2. To study the **relationship between patient's satisfaction (yes/no) and several validated PROs**, including
  - ✓ **PASS pain**
  - ✓ **PASS function**
  - ✓ **PASS global assessment of pain**
  - ✓ **Changes over time of WOMAC score..**

# Patients & methods



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- ✓ **Design:** Post-hoc analysis of a 6 month open-label clinical trial.



## Research Article

Volume 5 Issue 3 – March 2017  
DOI: 10.19080/OROAJ.2017.05.555664

Ortho & Rheum Open Access

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## Safety and Efficacy of Single Intra-Articular Injection of a Cross-Linked Hyaluronic Acid/Mannitol Formulation [Happycross®] in knee Osteoarthritis Results of a Prospective Observational Study in Daily Practice Conditions



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**Submission:** March 16, 2017; **Published:** March 24, 2017

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# Patients & methods



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- ✓ **53 consecutive patients with symptomatic knee OA were treated with a single injection of HANOX-M-XL (HAPPYCROSS; Labrha, France), a cross-linked HA (1.6 mg/g ) combined with mannitol (35 mg/g).**
- ✓ **All were prospectively followed using a standardized procedure including the following PROs at baseline and month 6:**
  - ❖ **WOMAC pain (normalized 0-10)**
  - ❖ **WOMAC function (normalized 0-10)**
  - ❖ **Patient's global assessment of pain : PGAP (0-10)**
  - ❖ **Patient's self-assessment of satisfaction (0-3)**

# Patients & methods



✓ **PASS was obtained at month 6 from:**

- ❖ WOMAC pain
- ❖ WOMAC function
- ❖ PGAP

Patients were considered as **RESPONDERS** if they fulfilled the PASS criteria\* for **PAIN (4/10), Function (5/10) or PGAP (4/10)**

✓ **Decrease over time in WOMAC pain, WOMAC function and PGAP.** Patients were considered as **RESPONDERS** if they experienced a **≥50% decrease** over time.

✓ **Correlations between Patients satisfaction (YES/NO) and PRO's were studied.** A Mann-Whitney or a chi-square was used to assess the association of quantitative or qualitative factors and PASS. Multivariate logistic regression analysis was used to identify predictors of PASS + and included sex, age, BMI, WOMAC pain and function at baseline and other factors with  $P < 0.20$  on uni-variate analysis.  $P < 0.05$  was considered statistically significant.



# Patients characteristics at baseline



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5-7 october 2017

Items	Mean	SD	Range
Age	62.6	12.3	39-87
Height cm	164.9	7.2	150-179
Weight kg	74.9	15.2	40-107
BMI kg/m <sup>2</sup>	27.5	5.2	17.8-40.2
Disease duration months	54	36.5	3-180
WOMAC pain (0-10)	4.5	1.2	2.6-7.2
WOMAC function (0-10)	3.9	1.2	1.6-6.3
WOMAC Total (0-10)	3.9	1.2	1.1-6.5
PGAP (0-10)	6.0	1.1	4-8

❖ **PGAP score was significantly higher than WOMAC pain or function scores.**

Patients characteristics at baseline (N=53)

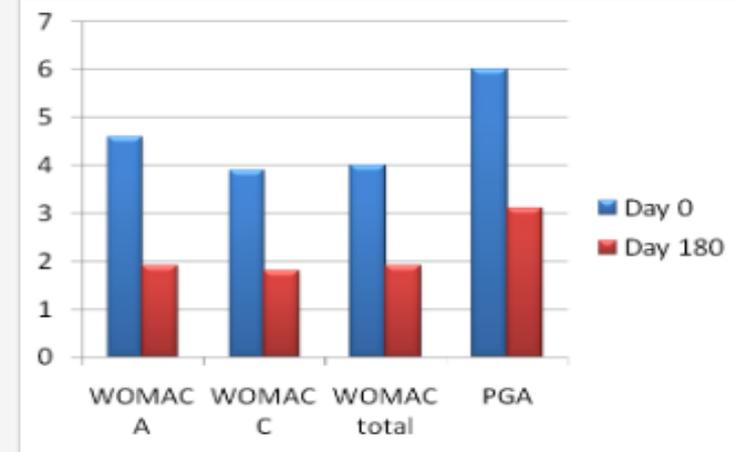
BMI: Body Mass Index; WOMAC: Western Ontario & McMaster Universities Osteoarthritis Index ; PGAP: Patient's Global Assessment of Pain

# Results



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- ❖ Throughout the 6 month follow-up, **WOMAC pain, function and total scores decreased dramatically by 58%, 51.2% and 52.5% respectively** (all  $P < 0.0001$ ) and **PGAP decreased by 48.6%** ( $P < 0.0001$ ).
- ❖ Improvement was unrelated to age, gender, X-ray grade, joint space narrowing location, presence or absence of joint effusion and disease duration (all  $P > 0.05$ ).



**WOMAC:** Western Ontario & McMaster Universities Osteoarthritis Index normalized on a 11 point rating numeric scale (0-10)

**WOMAC A:** WOMAC pain sub-score normalized on a 11 point rating numeric scale (0-10)

**WOMAC C:** WOMAC function sub-score normalized on a 11 point rating numeric scale (0-10);

**PGA:** Patient global assessment of pain on a 11 point rating numeric scale (0-10);

**Figure 1:** Decrease over time of WOMAC A, WOMAC C, WOMAC total and PGA in 53 patients with knee OA treated with a single injection of HANOX-M-XL.

- ❖ **A higher BMI was associated with a lower rate of PASS +** ( $P = 0.1$ ).
- ❖ **The difference was more significant between obese (BMI > 30 kg/m<sup>2</sup>) and non-obese subjects** ( $P = 0.03$ ).

## Percentage of patients fulfilling the response criteria at month 6.

Percentage of patients fulfilling the response criteria	Patient Reported Outcomes	Yes	No
	<b>Satisfaction</b>	<b>79</b>	<b>21</b>
	PASS + Function	100	0
	PASS + pain	83	17
	PASS + PGAP	79	21
	WOMAC pain decrease >50%	73.6	26.4
	PGAP <3	66	44

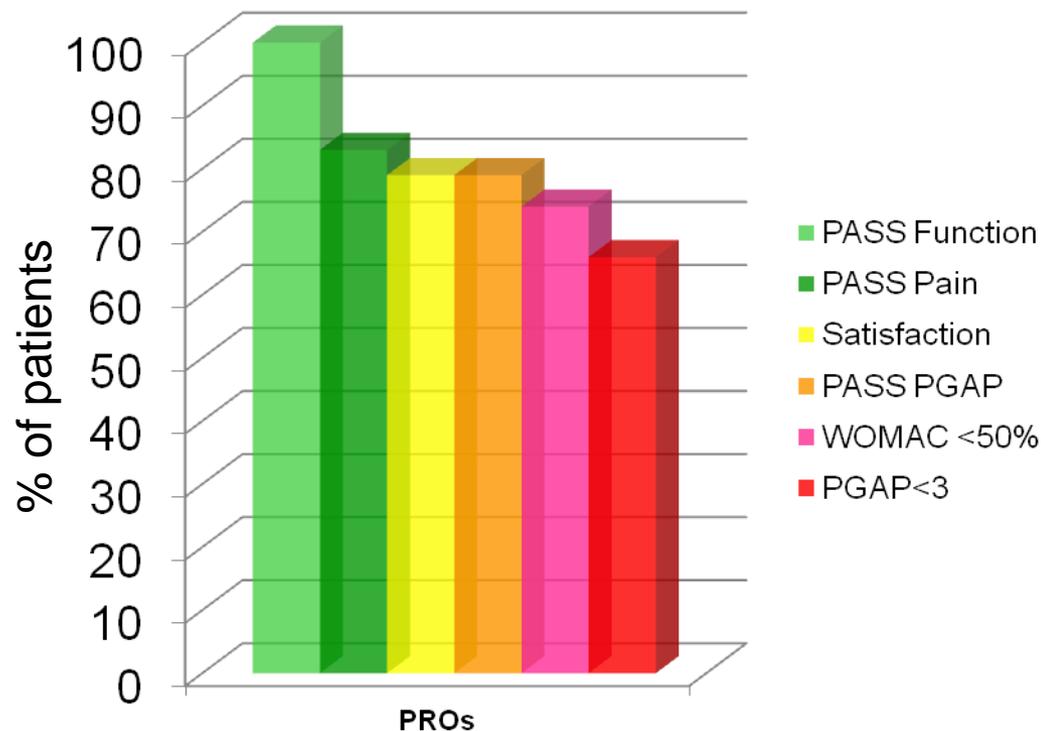
PGAP: Patient global assessment of pain on a 11 point rating numeric scale (0-10)

WOMAC: Western Ontario & McMaster Universities Osteoarthritis Index

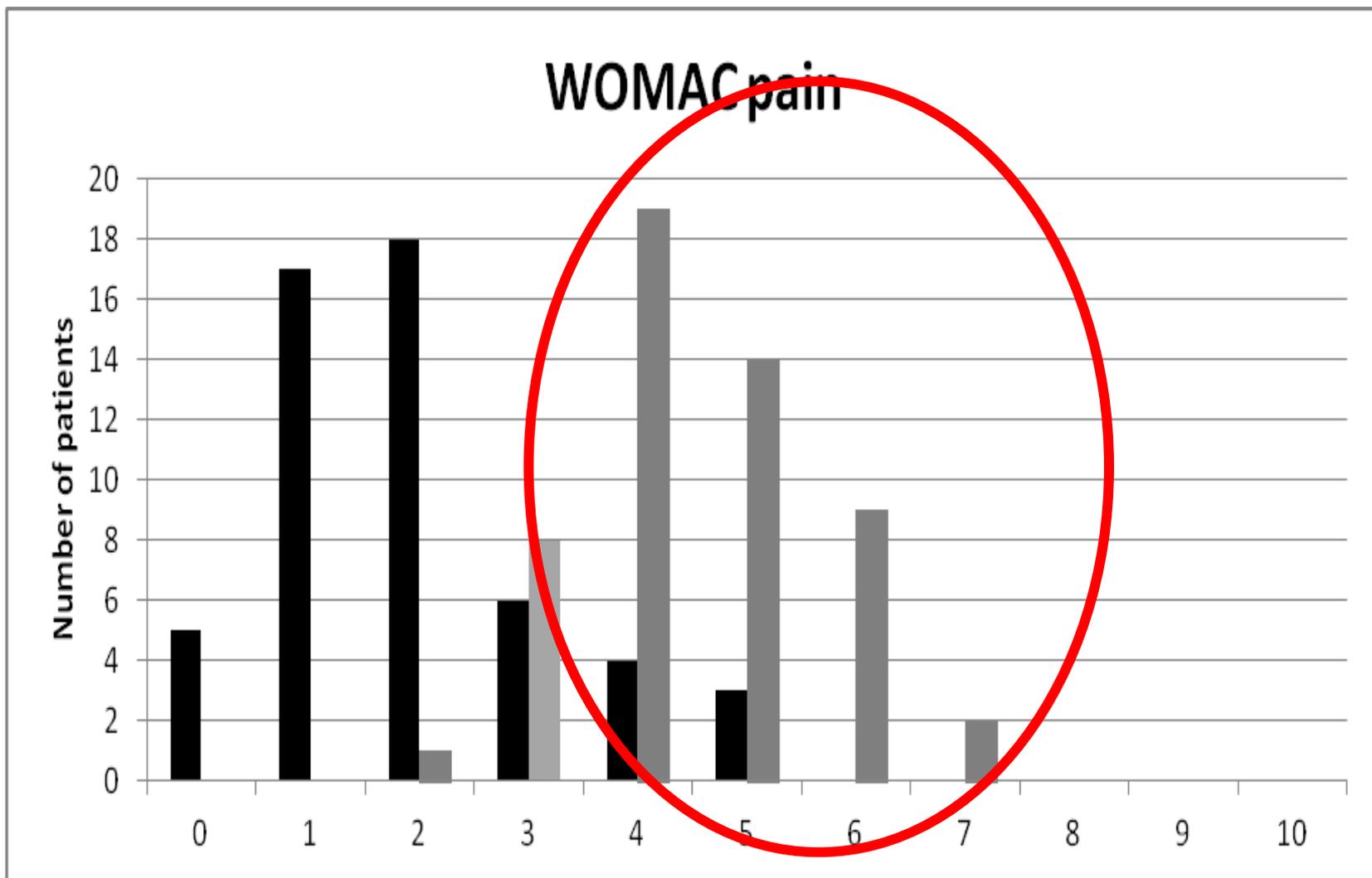
PASS + pain: WOMAC pain sub-score  $\leq 4$  normalized on a 11 point rating numeric scale (0-10);

PASS + function: WOMAC function sub-score  $\leq 5$  normalized on a 11 point rating numeric scale (0-10);

PASS + PGAP: Patient global assessment of pain  $\leq 4$  on a 11 point rating numeric scale (0-10);



Number of patients ranked according WOMAC A (0-10) values before  and 6 months after  viscosupplementation



# Conclusion



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**Six months after a single injection of Hanox-M-XL for symptomatic knee OA, the overall percentage of responders was 80% but varied according to PROs.**

- ❖ **PASS** was better related to patients perception of pain and satisfaction than the decrease of WOMAC score.
- ❖ **“PASS PGAP”** was more correlated with patients satisfaction than PASS pain.
- ❖ **“PGAP”** score , which was higher than all WOMAC sub-scores, appears to be the more relevant PRO.

# Conclusion



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The effectiveness of **VS** appears to be better when a state-attainment criterion, **which represents the patient's perception at a given time** such as PASS, than when the decrease of **WOMAC** score is used.

Health authorities and guideline developers should take this in consideration whilst decision making and be cautious in not to recommend and lose therapeutic options that may benefit a significant number of patients in a chronic and debilitating pathology in which few effective and safe treatments are available.

# Getting Better or Getting Well? The Patient Acceptable Symptom State (PASS) Better Predicts Patient's Satisfaction than the Decrease of Pain, in Knee Osteoarthritis Subjects Treated with Viscosupplementation

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DOI: 10.1177/1947603517723072  
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Many thanks to Miss Vesna YENGO for Statistical analysis