

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



✓ 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

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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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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



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✓ **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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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 ²	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

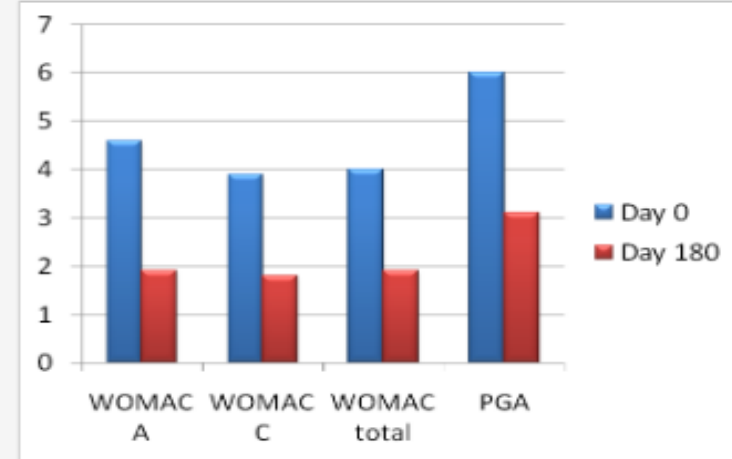
Results



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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 ($BMI>30 \text{ kg/m}^2$) 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
	Satisfaction	79	21
	PASS + Function	100	0
	PASS + pain	83	17
	PASS + PGAP	79	21
	WOMAC pain decrease > 50%	73.6	26.4
	PGAP < 3	66	44

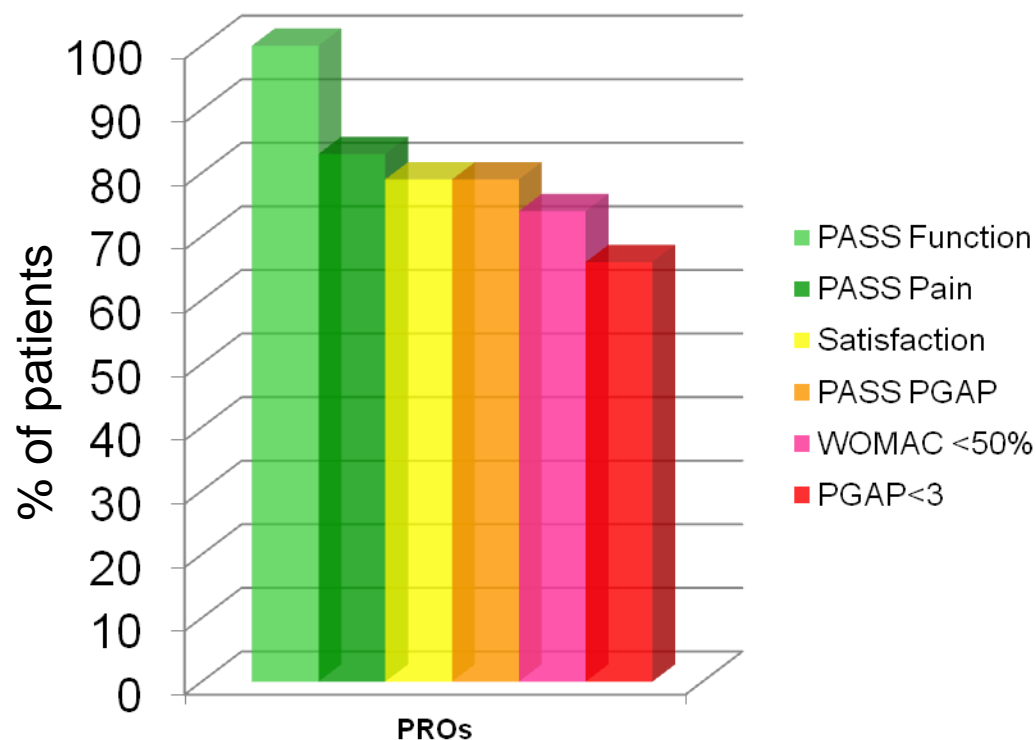
PGAP: Patient global assessment of pain on a 11 point rating numeric scale (0-10)

WOMAC: Western Ontario & McMaster Universities Osteoarthritis Index

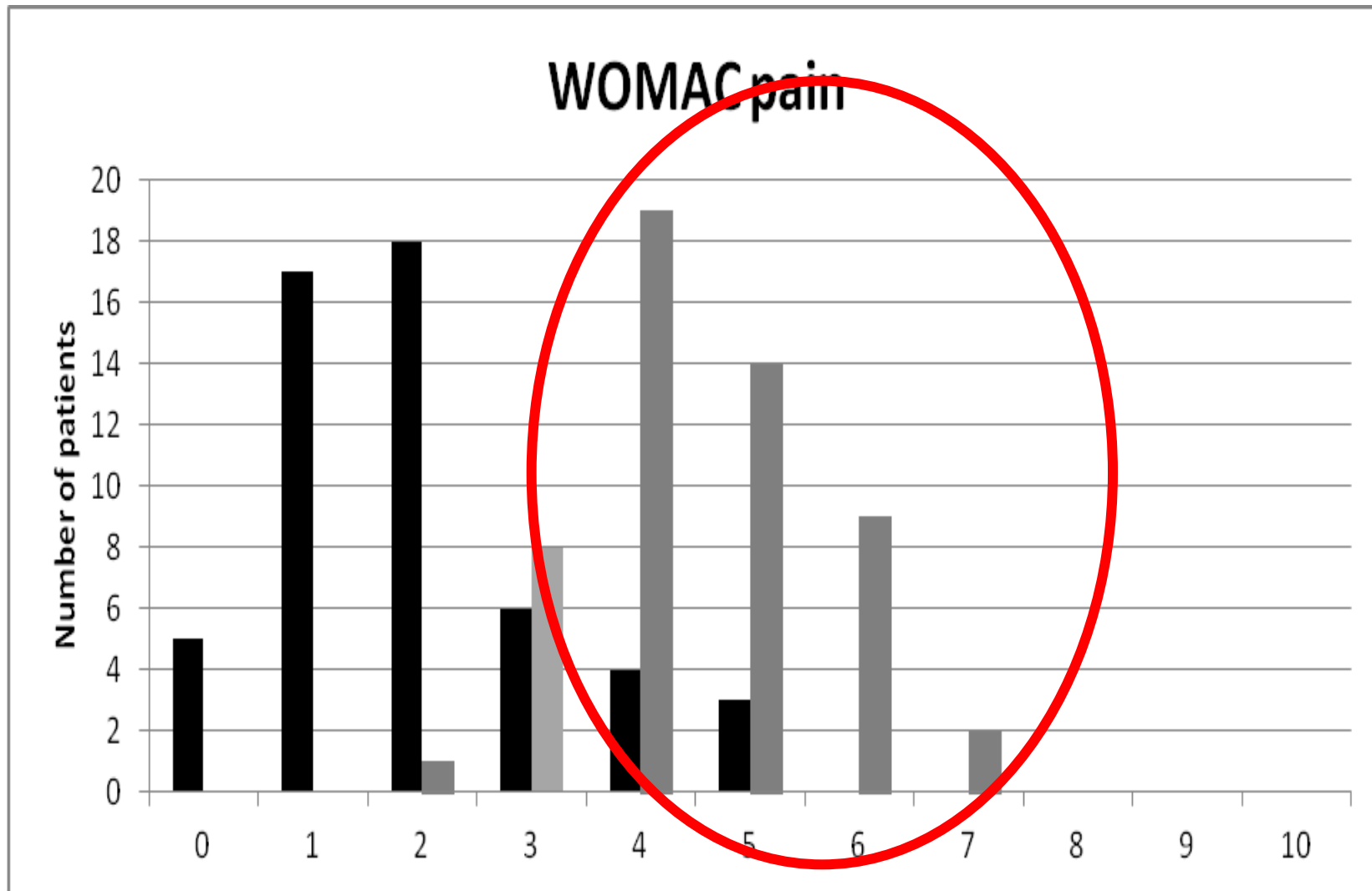
PASS + pain: WOMAC pain sub-score ≤ 4 normalized on a 11 point rating numeric scale (0-10);

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

PASS + PGAP: Patient global assessment of pain ≤ 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



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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