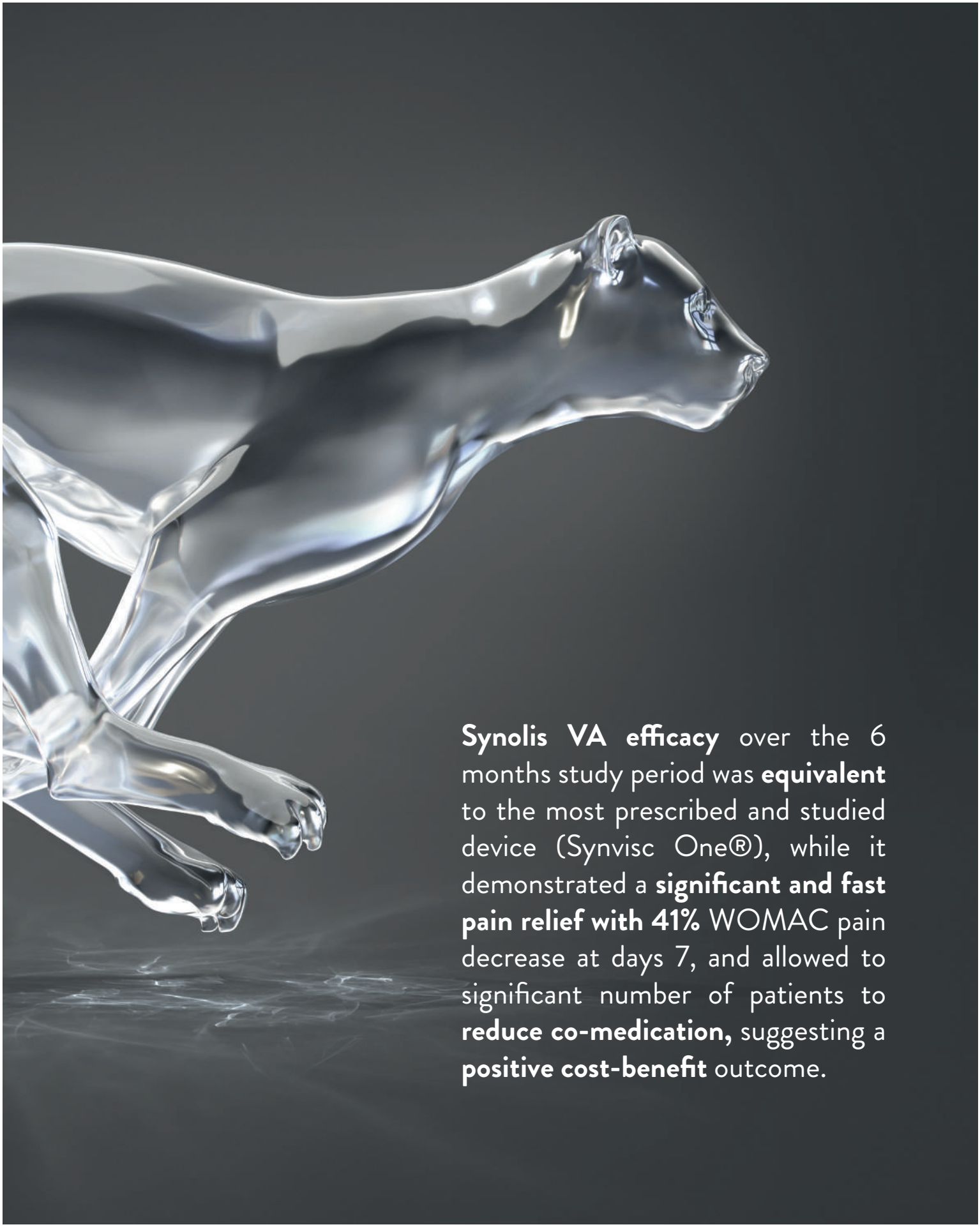

Synolis VA efficacy over the 6 months study period was **equivalent** to the most prescribed and studied device (Synvisc One®), while it demonstrated a **significant and fast pain relief with 41%** WOMAC pain decrease at days 7, and allowed to significant number of patients to **reduce co-medication,** suggesting a **positive cost-benefit** outcome.

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SYNOLIS VA

FAST PAIN RELIEF

Long term efficacy and safety evaluation of an intra-articular injection of a non-crosslinked sodium hyaluronate (2%) combined with sorbitol (4%) vs 0.8 % hylan G-F20 in the treatment of symptomatic knee osteoarthritis: A double blind, controlled, randomized, parallel-group non-inferiority study

Bernard Cortet (1), Sandrine Lombion (2) Bernina Naissant (3), Eduard Vidovic (3) and Olivier Bruyère (4)

1) Department of Rheumatology and ULR 4490, University-Hospital of Lille, Lille, France
2) SLC consulting
3) Aptissen SA
4) WHO Collaborating Centre for Public Health Aspects of Musculo-Skeletal Health and Ageing & Division of Public Health, Epidemiology and Health Economics, University of Liège, Belgium

Poster 5617

Introduction

Viscosupplementation (VS) or intra-articular injections of hyaluronic (IA-HA) acid is a symptomatic treatment of osteoarthritis reducing pain and restoring mobility in the affected synovial joint1,2.

Hyaluronic acid (HA) is a natural polysaccharide present in a physiological state in the synovial fluid with beneficial effect within the synovial fluid including lubrification, shock absorption, anti-inflammatory effect, chondroprotective properties, proteoglycan synthesis, and subchondral protection3.

The difference between the variety of viscosupplement care their intrinsic properties like the molecular weight , rheological properties. Surprisingly, but few comparative clinical trials on different HA compounds have been conducted.

Objectives: The primary objective of the study was to demonstrate at 24 weeks the non-inferiority of Synolis VA® , a linear hyaluronate (2%) with sorbitol 4% , (Group HA1) compared with SYNVISC ONE ® 48 mg Hylane GF-20 (Group HA2) in terms of efficacy (pain relief) for patients with knee OA patients (Kellgren and Lawrence radiologic stage II or III) for whom pain killers failed.

Methods

Design: This was a prospective, multicenter, phase IIIb, comparative, randomized, double-blinded study (i.e. one independent physician evaluator and one physician injector)

Inclusion criteria: Women and men aged 40 to 85 years, with Kellgren-Lawrence grade II to III uni- or bilateral tibiofemoral OA according to the ACR criteria, and WOMAC A pain on VAS of at least 40 mm

Treatment used over a period of 168 days in two parallel groups :
Group HA1 **:** Synolis VA® 80mg HA - 160 mg sorbitol, Aptissen SA, Switzerland
Group HA2: Synvisc one® 48 mg Hylan GF-20, Genzyme Biosurgery, USA

Statistics: The primary endpoint was the change from baseline in WOMAC Pain at Day 168 (+/-15 Days). The lower margin of non-inferiority was pre-specified at -8 mm. The per protocol (PP) set was used for the main analysis.

Results

Population distribution and baseline characteristics:

Data set: Out of 201 randomised patients (ITT population) 197 (98 % of randomised patients) presented no protocol violations (94 in group HA1 and 103 in the group HA2)

Demographic and baseline characteristics:
Both groups were homogenous at baseline and OA characteristics:

- Gender: 66% Women – 34 % Men
- Age (year; mean): 65
- BMI (kg/m2; mean): 27,4
- Kellgren and Lawrence scale :
- 30,5% Grade 2 - 69,5% Grade 3
- History pathology (mean) : 5 y.
- Average VAS Pain at inclusion (1-100) : 62.5

Primary endpoint

In both groups of treatment, a significant decrease from D0 has been observed at D168 in the PP population and ITT population (ITT data not shown).

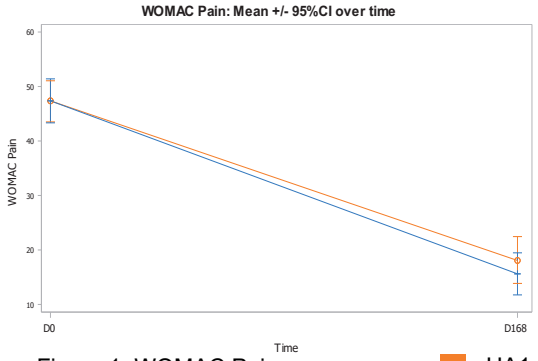
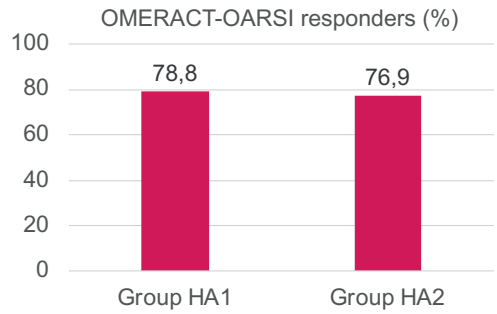


Figure 1: WOMAC Pain score from D168-D0 – PP population

The OMERACT-OARSI responders at D168



Secondary endpoints

Both groups showed a significant score improvement in all WOMAC parameters, with no difference between treatment groups from baseline to D168 (P <0.001), in the PP and the ITT datasets (table 2).

Outcome	HA1 n=85	HA2 n=92	Difference	P
WOMAC A change from baseline (mm)				
Mean (SE)	-29.716 (2.052)	-31.325 (2.972)	1.610 (2.846)	0.572
95% CI	(-33.766, -25.666)	(-35.218, -27.433)	(-4.008, 7.227)	
Outcome	HA1 n=85	HA2 n=92	Difference	P
WOMAC B change from baseline (mm)				
Mean (SE)	-27.20 (2.16)	-30.71 (2.07)	3.51 (2.99)	0.2411
95% CI	(-31.44, -22.96)	(-34.78, -26.64)	(-2.37, 9.39)	
Outcome	HA1 n=82	HA2 n=89	Difference	P
WOMAC C change from baseline (mm)				
Mean (SE)	-23.55 (2.01)	-27.08 (1.94)	3.52 (2.80)	0.2089
95% CI	(-27.52, -19.59)	(-30.89, -23.26)	(-1.98, 9.03)	
Outcome	HA1 n=82	HA2 n=89	Difference	P
WOMAC Total change from baseline (mm)				
Mean (SE)	-24.59 (1.98)	-28.20 (1.91)	3.61 (2.76)	0.1909
95% CI	(-28.5, -20.69)	(-31.96, -24.45)	(-1.81, 9.03)	

TABLE 2: Primary and secondary efficacy criteria at D7 (ITT population) and 6 months (PP population) post injection.

Conclusion

The statistical test applied with an upper limit of the 95% CI being at 7.227, below 8 did allow to conclude that group HA1 is non-inferior group HA2 on this parameter in this population. The same test applied on the mITT population did show a non-inferiority with an upper limit of the 95% CI being at 7.8. No safety issues were reported in any of the groups.

References: 1. Balazs EA. Viscosupplement for treatment of osteoarthritis: from initial discovery to current status and results.Surg Technol Int. 2004;12:278-89.
2. Balazs EA, Gibbs DA. Rheology of hyaluronic acid. Biopolymers. 1968 Jun;6(6):777-91.
3. Altman R, Manjoo A, Fierlinger A, Niazi F, Nicholls M. The mechanism of action for hyaluronic acid treatment in theosteoarthritic knee: a systematic review. BMC Musculoskeletal Disorders. 2015;16:321. doi:10.1186/s12891-015-0775-z.

NC-01-54EN