ONLINE SUPPLEMENTARY TEXT - 1

Glossary of Abbreviations

ACR	American College of Rheumatology
AE	Adverse Event
ANOVA	Analysis Of Variance
BMI	Body Mass Index
BOCF	Baseline-Observation-Carried-Forward
CI	Confidence Interval
ES	Effect Size
EMA	European Medicines Agency
HA	Hyaluronic Acid
ICOAP	Intermittent and Constant OsteoArthritis Pain
ITT	Intention-To-Treat
IVRS	Interactive Voice Response System
kD	kiloDaltons
MCII	Minimal Clinically Important Improvement
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligrams
ml	Milliliters
mm	Millimeters
MW	Molecular Weight
NASHA	Non-Animal Derived Hyaluronic Acid
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
OA	Osteoarthritis
OARSI	Osteoarthritis Research Society International
OMERACT	Outcome Measures in Rheumatology
PASS	Patient Acceptable Symptom State
PGA	Patient's Global Assessment
PP	Per-Protocol
SD	Standard Deviation
SE	Standard Error
VAS	Visual Analogue Scale
WOMAC	Western Ontario and McMaster Universities

ONLINE SUPPLEMENTARY TEXT - 2

Exact wording of the two questions for the assessment of Global Knee Pain and Patient's Global Assessment, translated into English.

Global knee pain (in addition to the standard questions of the WOMAC pain subscale):
"Please give a judgment on the intensity of global pain in the last48 hours in each of your knees, marking with "/" on each 100mm line".
The 0-100mm VAS was anchored at the two ends with "absent" to "unbearable pain".

Patient's global assessment
"Considering all the ways your knee osteoarthritis affects you, how would you rate your condition over the last week?"
The 0-100mm VAS was anchored at the two ends with "I am feeling as bad as possible" and "I am feeling very good".

ONLINE SUPPLEMENTARY TEXT - 3
Detailed description of the rescue medication use

During the whole study period, use of paracetamol was allowed as rescue medication. Patients were provided with boxes of paracetamol 500mg tablets at each clinic visit that were sufficient until the next one and were instructed to take up to 2 tablets every 8 hours (i.e. up to a maximum of 4g/day) if unbearable pain had not improved after at least 1-hour rest. Patients were advised not to exceed 4 consecutive days of paracetamol intake and were instructed to record the number of tablets taken on a patient daily diary. The number of returned paracetamol tablets was checked against the diary by the investigator and reported in Case Record Form (CRF) at each follow-up clinic visit.
In case of paracetamol failure or contraindication, non-steroidal anti-inflammatory drugs (NSAIDs) could be prescribed by the investigator for a limited and specified period as noted on the CRF and on the patient diary, where the number of doses was recorded as well.
Paracetamol or NSAIDs had in any case to be stopped 24 hours or two days, respectively, before each clinic visit, not to interfere with the efficacy assessments.

The number of patients reporting use of any symptomatic medication (paracetamol

and/or NSAIDs) was compared between treatment groups by means of a Chi-square test on both the Per-Protocol (PP) and Intention-To-Treat (ITT) populations. As far as the ITT population is concerned, dropout patients were conservatively classified as having accessed the rescue medication independently of their actual consumption (worst case approach).
The number of patients being prescribed NSAIDs was expected to be small and they were reported by descriptive statistics only in the PP population. Conversely, the daily mean consumption (dose) of paracetamol was derived from the number of 500mg tablets used per day, as reported in CRF and checked against the patient diary, referring to the whole study period by treatment group. Average daily consumption was compared in the PP population by means of two-way analysis of variance (ANOVA) with treatments and study center as factors.

During the study, the proportion of patients using the rescue medication was similar between groups: 166 out of 217 (77%) on GO-ON® and 154 out of 209 (74%) with Hyalgan® in the ITT population (p=0.50). Corresponding numbers in the PP population were 122/171 (71.4%) and 118/172 (68.6%), respectively (p=0.58). Only 6 patients in the GO-ON® group and 4 in the Hyalgan® group were prescribed NSAIDs as rescue medication. In the overall PP population the mean daily dose of paracetamol over the study period was low: 218±26mg (mean ± standard error) with GO-ON® and 223±24mg with Hyalgan® (median=118 vs 129mg, respectively), without differences between groups (p=0.60).