

**INTRODUCTION** The Gonarthrosis arthropathy is the most prevalent disease worldwide and the most common cause of disability for wandering in the elderly (WHO, 2013). Different molecular weight of hyaluronic acid (HA) has been shown to both stimulate and inhibit inflammatory responses depending on cell type and disease model (1). Pharmacologic therapies are orally administered drugs but if this therapies are ineffective, intraarticular (IA) injection (viscosupplements) is the nonoperative modality preferred in moderate osteoarthritis grade.

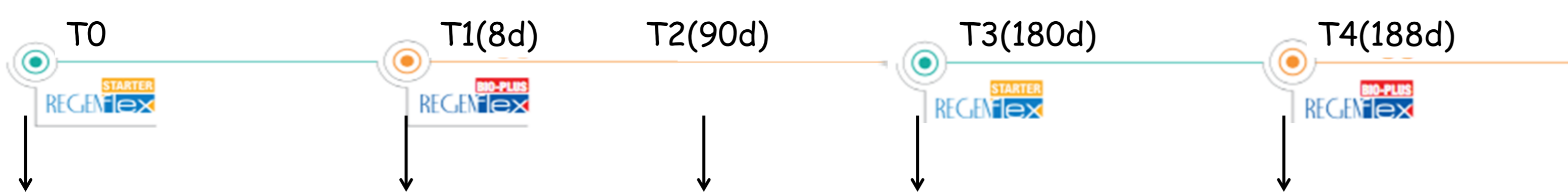
**Primary outcome** : Modulation of cytokine biomarker expression pattern.

**Secondary outcomes** : Pain reduction during 50 ft (15 m) walk test, Amelioration of clinic conditions and Quality of life, Reduction of paracetamol dosage.



**MATERIAL AND METHODS** Eligible gonarthrosis (GA) patients from both "dry" knee and articular fluid knee groups (14 and 15, respectively) were treated with HA [(Regenflex Starter - 32mg/2ml highly-purified HA, with molecular weight between 800-1.200 kDa (T0=0d) and Regenflex Bioplus - 75mg/3ml mg 1 M, 2 M and 500 thousand Da, after 8 days (T1=8d)]. Study design consisted of 40 weeks of follow up (T2=90d), HA was administered intra-articularly after 180 and 188 days (T3=180d and T4=188d, respectively). Clinical assessment of knee function: visual assessment scale (VAS 0-10) for pain intensity, Range of Motion (ROM) and HHS questionnaire. Blood and synovial fluid were collected. Cytokines were determined through the 27-plex panel of Pro™Human Cytokine27-plex Assay (Bio-Rad Labs).

### Experimental design



Samplings: Plasma/Synovial liquids

### Inclusion criteria:

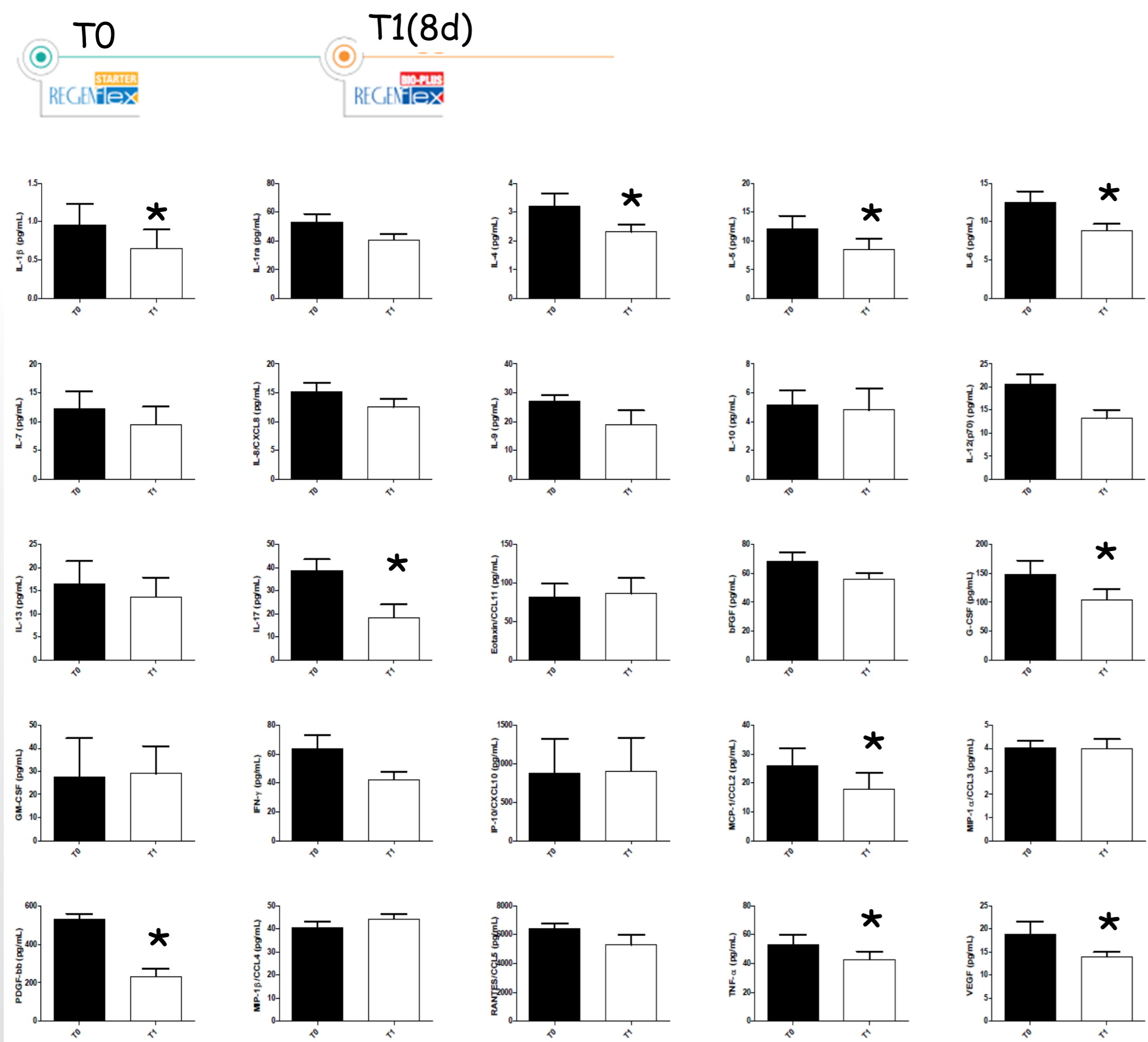
baseline knee pain score <150 mm; 50-80 years; corticosteroids prior to study; index knee Kellgren-Lawrence Grade II or III.

### Exclusion criteria:

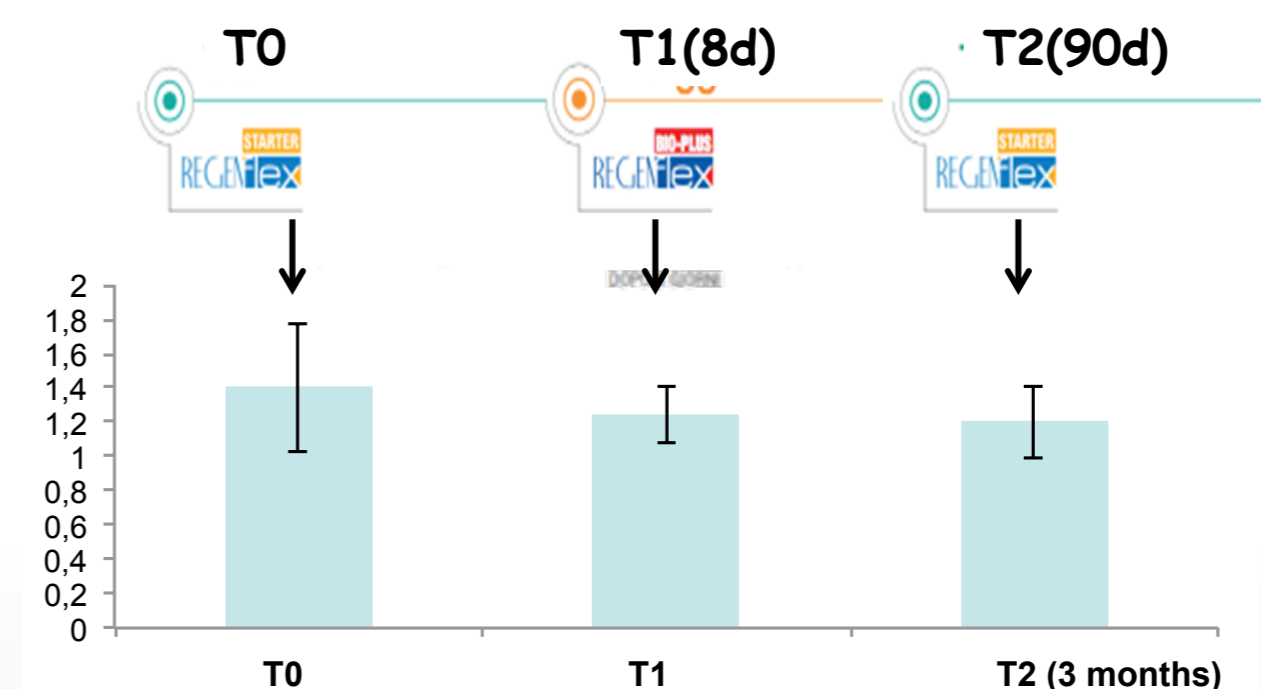
joint infection; inflammatory joint disease, osteonecrosis; recent intra-articular HA injections and knee trauma or surgery; full-thickness cartilage loss.

## RESULTS

### Pro-inflammatory and anti-inflammatory cytokines



### Crosslinked C-telopeptide type II collagen (CTX-II)



Worse scale quality of life was observed in GA patients with "dry" knee, mostly due to higher joint stiffness. Viscosupplementation treatment improved VAS scores. Patients received Regenflex Starter injections improve knee injury symptoms. The comparison between plasma cytokine levels at baseline (T=0) vs Regenflex Starter HA injection (T=1) showed that several inflammatory cytokines, chemokines and growth factors, such as IL-1beta, IL-6, IL-8, MCP-1, and PDGFbb, significantly decreased.

**CONCLUSIONS** Clinical data indicate that viscosupplementation with highly-purified HA with between 800-1.200 kDa promotes pain reduction and knee function improvement within articular fluid and "dry" knee joints. Of particular interest is the drastic down regulation of several plasma inflammatory cytokines induced by Regenflex Starter HA, data particularly useful for clinical assessment and therapeutic efficacy.

**REFERENCES** 1. Cooper C. et al., Arthritis Care & Research 2017 doi: 10.1002/acr.23204.

### AKNOLEDGMENTS

Regenyal Laboratories Srl for providing hyaluronic acid 800-1.200 kDa. Dr. Eugenio Grassi for technical assistance.