

EFFICACY AND SAFETY OF THE COMBINATION OF PRP + NON-CROSSLINKED HYALURONIC ACID VERSUS HYALURONIC ACID, IN MONO-INJECTION, IN SYMPTOMATIC KNEE OSTEOARTHRITIS. RANDOMIZED CONTROLLED PHASE III TRIAL, SINGLE BLIND

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Background: Despite the recent results of meta-analyses of randomized controlled trials (RCTs), the place of PRP and hyaluronic acid in the symptomatic treatment of knee osteoarthritis (KOA) remains uncertain in the latest international recommendations. Very few studies are available on the potential synergistic effect of their combination in mild to moderate forms of KOA⁽¹⁾.

Objectives: Randomized, controlled, multicenter, non-inferiority trial (clinical trial NCT03328728), single-blinded (investigator) to compare the efficacy and safety of the combination of PRP and non-crosslinked hyaluronic acid (PRP-HA, Cellular Matrix A-CP-HA, Regen Lab) as a single injection versus Hyal G-F 20 (HA), with follow-up at 1, 3 and 6 months, on an intention-to-treat (ITT) basis.

Methods: Patients aged 40-80 years with symptomatic femorotibial KOA (WOMAC A1 (pain on walking) or WOMAC Function > 50/100) and a Kellgren and Lawrence (KL) radiographic stage II or III were randomized into two groups: PRP-HA vs. HA, as a radio- or ultrasound-guided single injection at M0. Patients should not have received injectable treatments (corticosteroids, HA or PRP) for 3 months, nor per os NSAIDs for at least 1 month. A 6-month follow-up of the impact of the KOA was performed at M1, M3 and M6. The primary endpoint was the difference in the WOMAC score for pain on walking between M0 and M6 between the 2 groups. Secondary endpoints were collected and compared at M1, M3, and M6 (WOMAC Pain, Function, and Total; SF-36 score) as well as the percentage of patients responding at M6 according to the OMERACT-OARSI criteria, according to the Patient Acceptable Symptomatic State (PASS), and the Minimal Clinical Important Improvement (MCII) of the WOMAC pain. The factors of good response (PASS and MCII responders) at M6 were investigated in univariate and multivariate analysis. Tolerance was assessed by comparing adverse events over 6 months in both groups.

Results: 156 patients were included in three French teaching hospitals between 2018 and 2021 with the following characteristics: age 59.6±9.2 years, BMI 28.1±5.8 kg/m², 37.8% grade II KL and 62.2% grade III KL. The two groups were homogeneous at inclusion except in terms of analgesic consumption (PRP-HA vs. HA, 30% vs. 45%, p=0.042) and KL III radiographic stage (70% vs. 53%, p=0.04). The symptomatic improvement (WOMAC pain, function and WOMAC Total) was significant in both groups at M1, M3 and M6. The difference in WOMAC pain on walking at M6 was significant for the non-inferiority test (-6.34 [-12.51; -0.18], p=0.044) and for the superiority test (-6.34 [-12.45; -0.22], p=0.042) in favor of PRP-HA. At M6, there was a non-significant difference in terms of OMERACT-OARSI responders in favor of the PRP-HA combination (58% vs. 48%, p=0.261) but significant in terms of MCII responders (78.8% vs. 61.3%, p=0.036) and PASS responders (50.6% vs. 33.3%, p=0.035). PASS response was associated in univariate analysis with pain and total WOMAC at inclusion (p<0.001) as well as with allocated treatment (p=0.03). In multivariate analysis, only allocated treatment was associated with a good response at M6 for both PASS (PRP+HA, OR=2.05 [1.02-3.92]; p=0.05) and MCII (PRP+HA, OR=2.21 [1.09-4.44]; p=0.02). There was no difference in patient satisfaction at M1, M3 and M6, nor in the occurrence of adverse events.

Conclusion: In this non-inferiority RCT in symptomatic knee osteoarthritis, the combination of PRP-non-crosslinked HA in mono-injection was at least equivalent to Hyal G-F 20 for symptomatic benefit (WOMAC) at 6 months, with a good safety profile. The proportion of patients achieving PASS and MCII of WOMAC pain was higher in the PRP-HA group.

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Disclosure of Interests: Thomas Delgado: None declared, Rosanna Ferreira Lopez: None declared, Philippe Adam Speakers bureau: RegenLab, Consultant of: RegenLab, Yves-Marie Pers: None declared, Leila Benguella: None declared, Catherine Cyteval: None declared, Valerie de Fourmestraux Speakers bureau: RegenLab, Employee of: RegenLab, Sandrine Lombion Paid instructor for: RegenLab, Consultant of: RegenLab, Paul Ornetti Speakers bureau: RegenLab, Consultant of: RegenLab, Grant/research support from: RegenLab.

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