Bucharest 2-4 October 2025

ESSKA ORBIT Consensus Project: The Use of Injectable Orthobiologics For Knee Osteoarthritis

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ESSKA Consensus-Part 1 - Blood-derived Products -PRP

- PRP (Platelet Rich Plasma)- generically =autologous blood-derived product: platelet concentration by minimal blood manipulation
- Orthobiologics -biologic tissue healing- MSK conditions.
- Results -not consistent- great variability
- **Risks: to devalue potential + use of these treatments!**
- Consensus goal: general recommendations- PRP use in KOA.

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ORBIT CONSENSUS

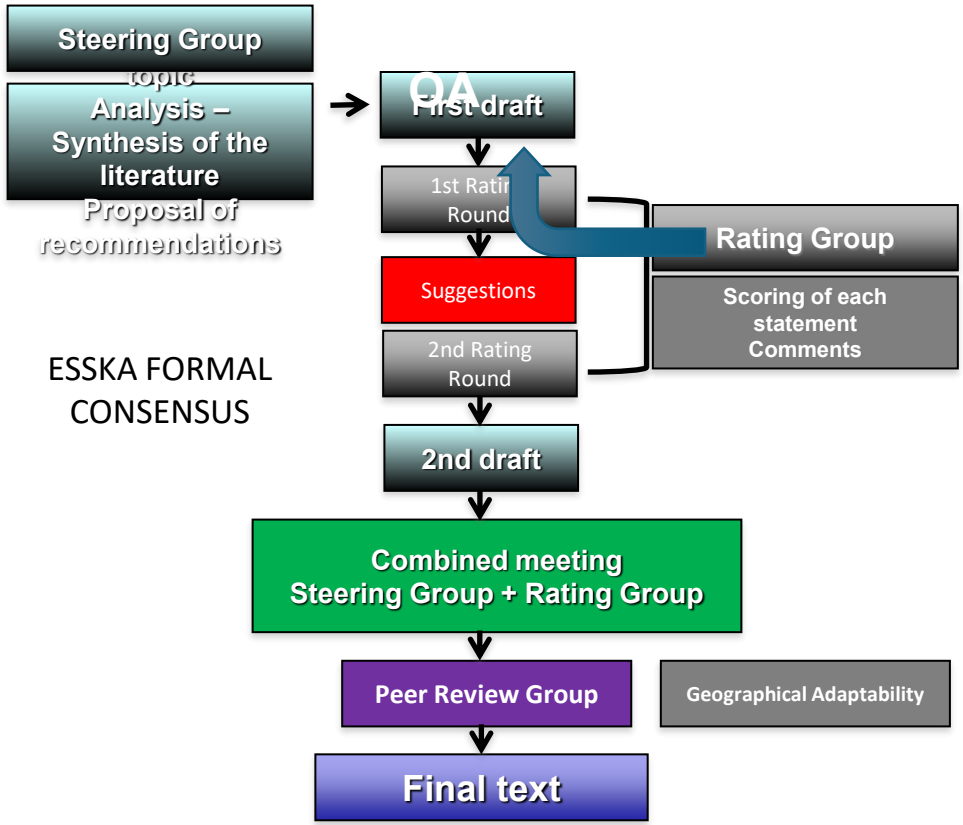
GRADING DESCRIPTION

- Grade A: high scientific level
- Grade B: scientific presumption
- Grade C: low scientific level
- Grade D: expert opinion

Agreement score: 1=minimum

- 9=maximum

MA = Meta-Analyses SR = Systematic Reviews
RCT = Randomized Controlled Trials



Section 1: PRP Rational/Indications-Q 1-14

Section 2: PRP Preparation/Characterization-Q 15-18

Section 3: PRP Protocol-Q 19-28

S1-Q1: Does current clinical evidence support the use of PRP for knee OA?

Clinical evidence -**confirms the efficacy of PRP** in knee OA.

Level I+ II : support **safety + clinical benefit** of PRP in KOA, in comparison: placebo (saline)/control: HA or CS. The **efficacy** of PRP in KOA- supported by **meta-analyses** and confirms findings of **preclinical research.**

Consensus: enough preclinical and clinical evidence to support the use of **PRP** in knee OA.

Grade A - Agreement 8.0

Literature summary Best evidence: 5 MA, 1 SR, 4 RCTs

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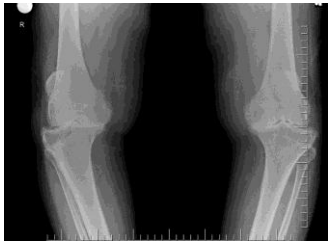


How severe knee OA?

S1-Q2: For which degrees of knee OA is PRP best indicated?

CE -PRP **effective mild - moderate** degrees of KOA-**KL ≤ 3**.

Consensus : **PRP can be indicated mainly in mild and moderate** cases of knee OA.

Grade A - Agreement 8.1

Literature Review Best evidence: 6 RCTs

S1-Q3: Can PRP be used in severe knee OA –KL4 ?

Consensus : PRP -selected severe KOA KL4. Ex: pts decline/not suitable for surgery. Lower results to be expected; physicians -**cautious expectations** when discussing/suggesting.

Grade C – Agreement: 8.1

Literature Review Best evidence: 6 RCTs

S1-Q6: For what age is PRP recommended?

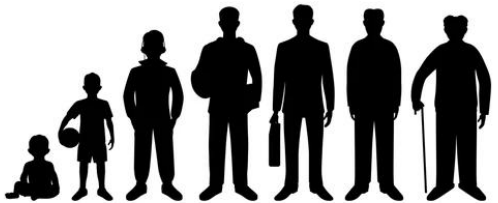
Majority of studies: mean **age 55 - 65** y.

Consensus : specific age- cannot be recommended; there is evidence of reduced response in older patients.

Consensus: **other factors should be considered-decision- not based only on chronologic age.**

Grade D – **Agreement: 8.4**

Literature Review Best evidence: 3 MA, 2 RCTs



S1-Q7: Could PRP be used during the inflammatory phase- joint effusion is present (following effusion aspiration)?

CE – lacking in **inflammatory phase/ effusion aspiration** prior to PRP injection.

Pre-clinical/ clinical studies -anti-inflammatory properties in PRP- support rationale for its use during the inflammatory phase.

Effusion aspiration- likely **beneficial: pain** + **functional limitations**.

Consensus: **effusion aspiration- avoid PRP dilution** following injection.

Grade D – Agreement: 7.9

Literature Review Best evidence: 3 RCTs, 4 Controlled lab studies

S1-Q8: Is a repeated cycle of PRP inj recommended following a previous successful PRP treatment for knee OA symptoms re-emergence?

CE- limited; this strategy may have clinical benefit.

Evidence: decrease in PRP effects of PRP over time.

Consensus: **additional cycle- considered if symptoms re-emergence**

Grade D – Agreement: 8.4

Literature Review Best evidence: 3RCTs, 1 Prospective randomized study

S1-Q9: there is rationale for PRP in asymptomatic early knee OA? - Prevention

Currently- **not enough clinical studies –** cannot be stated that PRP in asymptomatic OA prevents its progression.

Preclinical studies suggest a chondroprotective role of PRP; there is **no sufficient clinical evidence on the chondroprotective effect of PRP** in patients with asymptomatic early stages of OA.

Consensus: **does not advocate the use of PRP in asymptomatic early knee OA**

Grade D – Agreement: 8.7

Literature Review Best evidence: 3 SR, 2 in vitro studies

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PRP ADVANTAGES COMPARING:

S1-O10-CS

CS- anti-inflammatory agents+ short pain relief. **CS- affects chondrocytes +accelerated cartilage degeneration**, especially in multiple/repeated injections.

PRP-a **longer effect + safer profile+ less complications**.

Consensus: **PRP** a **safer, non-chondro-toxic** + **more effective** treatment, with **longer term clinical improvements** compared to CS.

Grade A – Agreement: 8.7

Literature Review Best evidence: 6 MA, 2 SR, 1 RCT

S1-O11:HA

High level studies + >MA: > **favoring PRP- clinical improvement + longer-lasting effect.**

Consensus: supports **PRP use over HA for KOA** due to overall clinical improvement and expected longer-lasting effects, whilst acknowledging that there are different formulations-some bias in MA conclusions.

Grade B – Agreement: 8.1

Literature Review Best evidence: 10 MA

S1-Q12: Does PRP induce disease-modifying effects in KOA?

Preclinical studies (animal models) **suggest** some disease modifying effects:+ changes on: cartilage tissue + synovial membrane.

Consensus: current clinical evidence on disease modifying effects of PRP in knee OA in humans is **insufficient**.

Grade C – Agreement: 8.3

Literature Review Best evidence: 8 RCTs, 1 SR

- *Boffa A, Salerno M, Merli G, de Girolamo L, Laver L, Magalon J, Sánchez M, Tischer T, Filardo G,ESSKA Orthobiologic Initiative - KSSTA 2021*

CARTILAGE (61%)	**Attenuation of damage progression** **Improvement in histology and immunohistochemistry**
SYNOVIUM (75%)	**Decrease of inflammation**
BIOMARKERS (92%)	**Positive changes in OA inflammation biomarkers**

Overall low quality of the studies and no evidence on the best PRP formulation, injective interval, and synergistic effect with other injectables

S2-PRP-Preparation&caracterisation

Q15: Which PRP is preferred for KOA: Leukocyte-Rich or Leukocyte-Poor PRP?

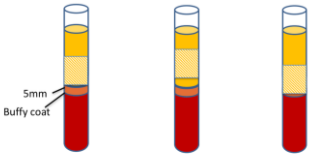
MA +network MA: compared effectiveness of LP-PRP vs LR-PRP for KOA- **inconclusive results**.

Consensus : effectiveness of PRP – **multifactorial;** dependence on leucocytes alone- might be overestimated.

Consensus: **not support one type of PRP over the other;** considers both LP-PRP + LR-PRP- valid options in KOA.

Grade B – Agreement: 8.1

Literature Review Best evidence: 5 MA, 2 RCTs



Cell type	Leukocyte-poor PRP	Pure PRP	Leukocyte-rich PRP
Platelet	++	+	+++
Leukocyte	±	–	++

S2-Q16: What is the recommended platelet number/concentration for PRP injections in KOA?

PRP effect : complex & multifactorial; >> **growth factors** released- important role; **pro**-/ **anti-inflammatory cytokines** released -platelet activation.

Platelets = central player in PRP products.

Consensus: **PRP characterization - complex** + **many variables;** optimal platelet ranges- cannot be defined.

Standardization is needed!

Grade C – Agreement: 8.2

Literature Review Best evidence: 4 RCTs, 1 Systematic review, 3 case series

S2- PRP preparations/products for a knee OA: what should we measure in PRP/quality control?

PRP preparations & products vary.
PRP products - vary in content + induce inconsistent preparations.

Consensus : recording -improve **understanding of PRP efficacy** in KOA. Recommended as **quality control measures in clinical research setups.**

Grade D – Agreement: 8.0
Literature Review Best evidence: 10 Expert opinion publications

Platelet-rich plasma for the treatment of knee osteoarthritis: an expert opinion and proposal for a novel classification and coding system

Elizaveta Kon , Berardo Di Matteo , Diego Delgado , Brian J Cole , Andrea Dorotei , Jason L Dragoo , Giuseppe Filardo , Lisa A Fortier , Alberto Giuffrida , Chris H Jo , Jeremy Magalon , Gerard A Malanga , Allan Mishra , Norimasa Nakamura , Scott A Rodeo , Steve Samspon & Mikel Sánchez

PRP code: e.g. 14-10-10

N_1: basal platelet concentration in blood: 0=0-100,000 platelets/μl, 1=100,000-200,000, 3 …. ,

N_2: platelet concentration in PRP: 0=0-100,000 platelets/μl, 1=100,000-200,000, 3 …. ,

N_3: red blood cells in PRP 0=No presence/trace, 1=Presence (>1x10^6/μl)

N_4: white blood cells in PRP 0=less than baseline, 1=1.01 to 2x baseline, 3 …, 5=>5x baseline

N_5: external activation 0=No (endogenous), 1=Yes

N_6: calcium activation 0=No, 1=Yes

Expert Opinion on Biological Therapy 2020

S2-Q18: What is the recommended volume of PRP to inject into a knee for the treatment of KOA?

PRP volume-may play a role; **no evidence** for optimal volume to be injected; volumes range from **2 to 12 ml**.

Consensus: no recommendation on the volume; suggests- **knee size could be taken into consideration**.

Grade D – Agreement: 8.7

Literature Review Best evidence: 1 MA, 1 RCT, 1 Prospective study, 1 Consensus/Expert opinion

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ANY SYNERGY WITH:

Q 27-HA

Pre-clinical+ clinical : potential benefits; **evidence** of clear benefits- **still lacking**.

Consensus: **more data is required** before recommending PRP+HA vs PRP alone for knee OA.

Grade C – Agreement: 7.8

Literature Review Best evidence: 3 MA, 1 systematic review, 1 RCT

Q 28-CBT

Pre-clinical +clinical- potential benefits of PRP+CBT: no evidence.

Consensus: d**oes not suggest the combination** of PRP+CBT vs PRP or CBT alone for knee OA.

Grade B – Agreement: 8.0

Literature Review Best evidence: 5RCTs, 1 Prospective study, 4 Controlled lab

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PRP-PROTOCOL

INJECTION NO/CYCLE

Literature -**not conclusive-** optimal PRP **inj no**/cycle in KOA; most articles= protocols with **>1 injection -** better clinical improvement- early OA.

Consensus- factors: inj vol, platelets%- largely differ btw available PRP products -may influence the effect of each injection.

Consensus: **recommends a range of 2-4 injections.**

Grade B – **Agreement**: **8.0**

Literature Review Best evidence: 15 RCTs

INJECTION INTERVAL

Literature - not conclusive; intervals range from 1wk to 4wk.

Main period of released growth factor activity- within first 3 w from injection, Consensus: **interval ranges of 1-3 weeks –** appropriate.

Grade B – **Agreement: 8.0**

Literature Review Best evidence: 11 RCTs

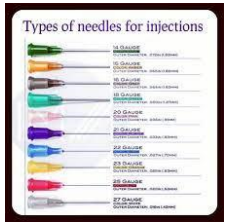
S3-Q21: Do syringe and needle size matter for blood harvesting and injecting PRP?

CE- needle size not a factor influencing platelet integrity.

Consensus: needle size **should not matter neither for injection of PRP nor for blood collection**.

Grade C – Agreement 7.9

Literature Review Best evidence: 1 prospective clinical study, 1 Observational study



Caution should be applied to **flow rate** during blood aspiration when using large size syringes in a manual technique to avoid blood hemolysis.

Grade D – Agreement 7.9

Literature Review Best evidence: 1 prospective clinical study, 1 Observational study

S3-Q22: Are NSAID allowed around PRP use?

CE-inconclusive-NSAIDs around PRP inj; potential effects of NSAIDs on platelets+ in vivo growth factors release-warrants caution.

Consensus: **avoid use of NSAIDs for 2 weeks prior to PRP administration.**

Grade C – Agreement: 8.1

Literature Review Best evidence: 1 RCT, 2 Clinical studies, 3 in-vitro studies, 2 SR

Pain management after PRP inj- **NSAIDs may affect GFR release,** even after the injection, Consensus: **avoid NSAIDS for the first week post-injection;** if necessary, use non anti-inflammatory pain medications (i.e paracetamol, dipyrone, tramadol).

.**Grade C – Agreement: 8.3**

Literature Review Best evidence: 1 RCT, 2 Clinical studies, 3 in-vitro studies

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S3-Q24: Is Antibiotics administration recommended around PRP use?

CE **does not support antibiotics** use around PRP use.

Consensus: **does not recommend the use of antibiotics** around PRP administration.

Grade D - Mean score: 8.6

Literature Review Best evidence: 1 Systematic review

- **PRP – Evidence of antimicrobial effect**

A Platelet-Rich Plasma-Derived Biologic Clears *Staphylococcus aureus* Biofilms While Mitigating Cartilage Degeneration and Joint Inflammation in a Clinically Relevant Large Animal Infectious Arthritis Model

Jessica M. Gilbertie[1,2], Thomas P. Schaer[3†], Julie B. Engiles[3,4], Gabriela S. Seiler[5], Bennett L. Deddens[5], Alicia G. Schubert[1], Megan E. Jacob[2,6], Darko Stefanovski[3], Gordon Ruthel[4], Noreen J. Hickok[7], Devorah M. Stowe[6], Alexa Frink[1] and Lauren V. Schnabel[1,2*†]*

Platelet-rich plasma lysate displays antibiofilm properties and restores antimicrobial activity against synovial fluid biofilms in vitro

Jessica M. Gilbertie[1,2,3], Thomas P. Schaer[3], Alicia G. Schubert[1], Megan E. Jacob[2,4], Stefano Menegatti[2,5], R. Ashton Lavoie[5], Lauren V. Schnabel[1,2]

S3-Q25: Is fasting recommended before PRP use? Any other patients' behavior could affect the treatment?

Data –fasting direct impact on therapeutic effects of PRP- **lacking**.

There is evidence on effect of various foods, high-fat and high-cholesterol diets on platelet **behavior-no+ function+activation,** Consensus: **recommends patients to avoid high-fat foods for at least 24 hours prior to blood harvest**.

Grade D – Agreement: 8.0

Eliminating alcohol –at least **48 hours prior PRP preparation** allow platelets to **re-establish their normal factor content and aggregation** properties and therefore the Consensus group considers it as a **safe suggestion**.

Grade D – Agreement: 7.5

S3-Q26: Can Corticosteroid –CS- injections prior to PRP improve the results in KOA?

Consensus: **avoid PRP in close proximity to CS**.

In pts- recent CS injections Consensus: **suggests a minimum interval of 6 weeks from a recent CS injection.**

Grade D – Agreement: 8.3

Literature Review Best evidence: 1 Meta-analysis, 1 Systematic review,

1 RCT, 1 Prospective, 2 Pilot studies

S3-Q23: Should intra-articular local anesthetics be used when injecting PRP?

Currently -no high-level clinical studies - effect of local anesthetics on PRP

In vitro studies: **local anesthetics interfere with platelets integrity and functionality + diminish the positive effects of PRP on cell proliferation.**

Consensus: **not recommend the use of intra-articular local anesthetics when injecting PRP.**

Consensus agree-local anesthetics can be administered subcutaneously, **without penetrating the capsule.**

Grade D - Agreement: 8.7

Literature Review Best evidence: 3 in-vitro studies

CONSENSUS

Rather a « framework » than strict guidelines

Guidance

- Strengths+ limitations- one managed-RAND-see KSSTA!
- Is a consensus the only factor which may influence the decision of the surgeon and the patient ?

Conclusions

PRP = a valid treatment for KOA –> KL 1-3

PRP could be considered as a 1st line injectable treatment option

PRP –clinical superiority over other available injectable treatment: CS,HA

Attn: great variability in PRP!

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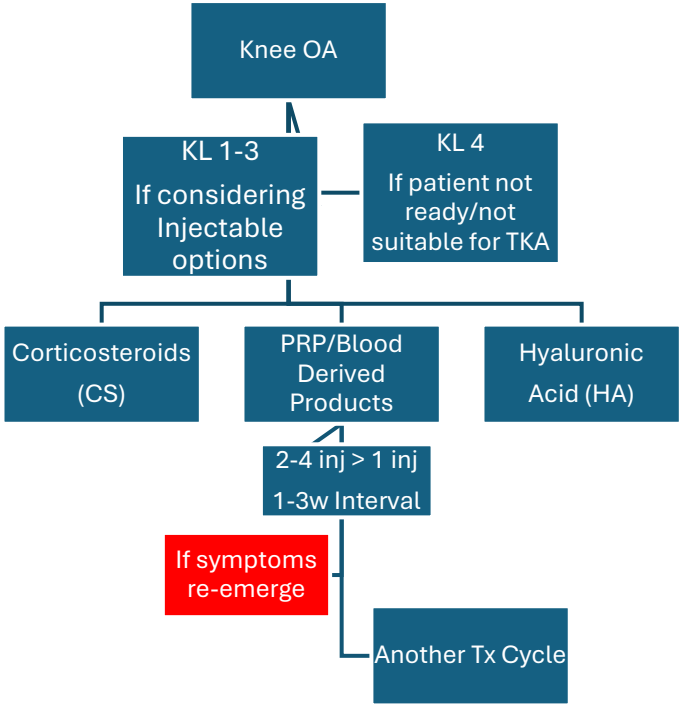
THANK YOU!



- The use of injectable orthobiologics for knee osteoarthritis: A formal ESSKA-ORBIT consensus. Part **2-Cell-based therapy** ORBIT CONSENSUS-Part II-CBT-KSSTA/09.2025