European Society of Sports Traumatology, Knee Surgery & Arthroscopy

ESSKA

ESSKA **ORBIT Consensus**

Use of injectable orthobiologics for the treatment of knee osteoarthritis

Part 1: blood-derived products (alias PRP)

Chairpersons: Laura de Girolamo, Lior Laver

This brochure is a summary of ESSKA Orthobiologics Consensus

Full text is available on **www.esska.org/page/projects**

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GRADING DESCRIPTION

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

PRESIDENTIAL FOREWORD

There is great variation across Europe when it comes to medical praxis. Agreeing a common approach to pathologies or procedures has always been a challenge. But some such agreement is important, if we are to ensure standards.

For years now, one of ESSKA's objectives has been to work on professional standards. Thus, ESSKA has developed a strict and painstaking methodology which employs our considerable European expertise. We call it ESSKA's European Consensus.

Our first European Consensus was presented in 2016-2018 on Meniscus (Degenerative lesions and Traumatic tears). More information is available on **www.esska.org**.

This year, at ESSKA 2022 Paris Congress, we are delighted to launch the **ESSKA ORBIT Consensus.**

We thank Laura de Girolamo and Lior Laver, the Project leaders, our Consensus Projects Advisor, Prof. Philippe Beaufils, as well as the members of the Steering, Rating, and Peer Review Groups for their efforts and dedication.

A special acknowledgement also for our staff, and particularly Mrs Anna Hansen Rak, without whom this would have been not possible.

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CHAIRPERSONS FOREWORD

The field of Orthobiologics has emerged in recent years as a result of the growing interest in biologic approaches for tissue healing for a variety of pathologies affecting bone, cartilage, tendons/ligaments and muscles, both as conservative injection treatment and in combination with surgical procedures.

The results of these treatments are inconclusive because of the lack of unanimous opinion by professionals in terms of patients' indications, administration protocols and even more in the choice of the available options/devices. Moreover, therapy developers and providers must address hurdles from regulatory issues, through reimbursement considerations and to commercial challenges before successful orthobiologic therapies are available to patients. All of this risks to devalue the potential and the use of these treatments, with a potential loss of valid care opportunities.

As Europe's largest association of musculoskeletal specialists, ESSKA felt it had a responsibility to advance the quality of care in the orthobiologics field in a fully transparent and scientific manner.

The ESSKA **OR**tho**Bi**ologics Initia**T**ive (**ORBIT**) aimed to generate and assemble a pan-European/International collaboration to create a common language and a uniform voice in the field of orthobiologics.

ORBIT has highlighted and prioritized the importance of adopting an evidence-based and systematic approach to evaluating the effectiveness of existing and emerging orthobiologic treatments.

While Orthobiologics can be used to treat a variety of conditions, osteoarthritis, and in particular knee osteoarthritis is the most commonly addressed pathology.

Therefore, the aim of this first ESSKA Consensus on the use of injectable orthobiologics is to integrate and promote the clearest message currently available from scientific work and expert opinion regarding the use of blood derived products for the treatment of knee OA. For the sake of simplicity PRP (Platelet Rich Plasma) has been used as the most common term to refer to this wide product category.

A consensus focusing on cell-based therapy for the treatment of knee OA will be available soon.

Laura de Girolamo
Chairperson

Lior Laver
Chairperson

PRP - RATIONALE/INDICATIONS

Does current clinical evidence support the use of PRP for knee OA?

Clinical evidence confirms the efficacy of PRP in the treatment of knee osteoarthritis (OA). Level I and II clinical studies, as well as additional prospective studies, support the safety and clinical benefit of PRP for knee OA, which was shown in comparison to both placebo (saline) and control treatments such as hyaluronic acid or corticosteroids (CS). The efficacy of PRP in the treatment of knee OA has been also supported by meta-analyses and confirms the findings of preclinical research.

The consensus group can therefore conclude that there is enough preclinical and clinical evidence to recommend/support the use of PRP in knee OA (see following questions addressing PRP specifications and indications). *Grade A*

For which degrees of knee OA is PRP best indicated?

Clinical evidence has shown the effectiveness of PRP in patients for both mild to moderate degrees of knee OA (KL $\leq$ 3). The consensus group concludes that PRP can be indicated mainly in mild and moderate cases of knee OA. *Grade A*

Can PRP be used in severe knee OA (KL4)?

PRP treatment could be considered in selected severe knee OA cases (KL4), for example in patients who decline or are not suitable for surgery due to comorbidities, although lower results could be expected and physicians should provide cautious expectations when discussing or suggesting this biological approach. *Grade C*

Are there advantages of PRP use in comparison to corticosteroids for treating knee OA?

While corticosteroids are strong anti-inflammatory agents and can provide short term relief in knee OA, they have been shown to have detrimental effects on chondrocytes and can lead to accelerated cartilage degeneration, especially with multiple/repeated injections. PRP injections have been shown to have a longer effect in comparison to the shorter term effect of CS injections. They also seem to provide a safer use profile with less potential related complications. The consensus group considers PRP injections to be a safer, non-chondro-toxic and more effective treatment option, with longer term clinical improvements compared to CS injections. *Grade A*

Is PRP a clinically better injectable option than hyaluronic acid for the treatment of knee OA?

Several high level studies as well as multiple meta-analyses exist comparing the effectiveness of PRP compared to HA for knee OA, with the majority favoring PRP in terms of overall clinical improvement and a longer-lasting effect.

Based on current available evidence, the consensus group supports the use of PRP over HA for knee OA due to overall clinical improvement and expected longer-lasting effects, whilst acknowledging that there are different formulations of the products that may introduce some bias in the conclusions of meta-analyses. *Grade B*

Does PRP induce disease-modifying effects in knee OA?

Preclinical studies (animal models) suggest some disease modifying effects, with positive changes on cartilage tissue and on the synovial membrane. Although few clinical studies have suggested disease modifying potential of PRP on degenerative cartilage, current clinical evidence regarding the disease modifying effects of PRP in knee OA in humans is insufficient. *Grade C*

PRP - PREPARATION/CHARACTERIZATION

Which PRP is preferred for knee OA: LR-PRP or LP-PRP?

Several meta-analyses and network meta-analyses have compared the effectiveness of LP-PRP compared to LR-PRP for knee OA with overall inconclusive results.

The consensus group acknowledges that the effectiveness of PRP is likely multifactorial and therefore the dependence on the presence of leukocytes alone might be overestimated as other factors may also have a contribution. Therefore, the consensus group currently does not support one type of PRP over the other and considers both LP-PRP and LR-PRP valid options for the management of knee OA when PRP is considered. *Grade B*

What is the recommended platelet number/ concentration range for PRP injections in knee OA?

The effect of PRP is complex and multifactorial, with the numerous growth factors released playing an important role, as well as pro- and anti-inflammatory cytokines released following platelet activation. However, a clear correlation between the number of platelets in the PRP and clinical response has not been well established. There is no doubt that platelets are the central player in PRP products, however the consensus group concludes that the optimal characterization of PRP for knee OA is complex and includes many variables, and therefore currently optimal platelet ranges for the treatment of knee OA cannot be defined. *Grade C*

How many injections of PRP are recommended for the treatment of knee OA?

While the literature is not conclusive with regards to the optimal number of injections per PRP treatment cycle for knee OA, the majority of articles reports that protocols with >1 injection provide better clinical improvement, at least with early OA.

The consensus group realizes that factors such as injection volume and platelet concentration may largely differ between available PRP products and may influence the effect of an injection.

The consensus group recommends a range of 2-4 injections. *Grade B*

When using a treatment protocol with more than one injection for knee OA, what is the recommended interval between each injection of PRP?

While the literature is not conclusive on the optimal interval between injections when using a multiple PRP injection protocol (>1 injection per treatment cycle) for knee OA, intervals ranging from 1-week to 4-week have been reported.

As the main period of released growth factor activity takes place within the first 3 weeks from injection, the consensus group suggests interval ranges of 1-3 weeks may be more appropriate. *Grade B*

PRP - PROTOCOL

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

Currently no high-level clinical studies exist regarding the effect of local anesthetics on PRP, however, In vitro studies have shown that local anesthetics interfere with platelets integrity and functionality as well as diminish the positive effects of PRP on cell proliferation. Therefore, the consensus group currently does not recommend the use of intra-articular local anesthetics when injecting PRP.

The consensus group does, however, agree that local anesthetics can be administered subcutaneously, without penetrating the capsule. *Grade D*

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