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The role of IA injection in the OARSI guidelines for the non-surgical management of OA

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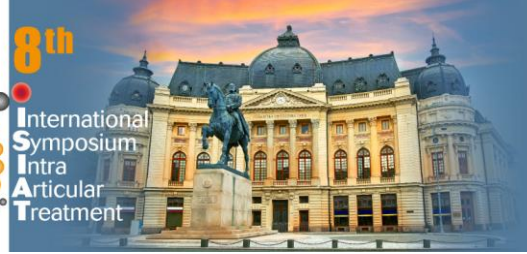
Disclosures

- Nothing to disclose

Patient-centered Recommendations

- Three OA phenotypes
  - Knee
  - Hip
  - Polyarticular
- "Precision Medicine": Five comorbidity groups
  - None
  - Gastrointestinal
  - Cardiovascular
  - Frailty
  - Widespread pain disorder (e.g. fibromyalgia) and/or depression

- Bannuru et al 2019 Osteoarthritis & Cartilage 27:1578-89



GRADE Methodology

- Strict, **objective criteria** for risk of bias, inconsistency, indirectness, and imprecision were determined *a priori*
- **Two Critical Outcomes** were selected to accurately reflect overall Quality of Evidence
- **Transparently displayed** percentage gradients from Voting Sessions

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Outcomes of interest

Supplementary Table 3: Outcomes of Interest

Outcome Name	Outcome Type*	Acceptable Measures, Definitions	GRADE Designation
Pain	Primary: Continuous	WOMAC Pain, NRS Pain, VAS Pain, KOOS Pain, HOOS Pain, AIMS Pain, BPI, any other validated scale	CRITICAL
Function (Subjective)	Primary: Continuous	WOMAC Function, Lequesne Index, KOOS-ADL, HOOS-ADL, AIMS Function, any other validated scale	CRITICAL
Function (Objective)	Primary: Continuous	6 minute walk test, time to ascend/descend stairs, Timed Get Up and Go Test	IMPORTANT
Quality of Life	Primary: Continuous	SF-36, SF-12, EQ-5D, KOOS-QoL, HOOS-QoL, HAQ, any other validated scale	IMPORTANT
Structural Progression	Primary: Continuous	JSN (mm), JSW (mm), cartilage thickness (mm), cartilage volume (mm^3)	IMPORTANT
Withdrawals due to Adverse Events	Primary: Dichotomous	N withdrawing from study due to one or more Adverse Event(s)	IMPORTANT
Total Adverse Events	Primary: Dichotomous	N experiencing one or more Adverse Event(s)	IMPORTANT
Serious Adverse Events	Primary: Dichotomous	N experiencing one or more Serious Adverse Event(s)	IMPORTANT
Treatment-specified Harms	Primary: Dichotomous	N experiencing one or more Adverse Event(s) specific to the intervention of interest	IMPORTANT

Recommendation Levels

Level	% in favor	% against	% Conditional/strong
Level 1A	75-100	0-25	>50 strong
Level 1B	75-100	0-25	>50 conditional
Level 2	60-74	26-40	*conditional by default*
Level 3	41-59	41-59	*conditional by default*
Level 4B	26-40	60-74	*conditional by default*
Level 4A	0-25	75-100	>50 conditional
Level 5	0-25	75-100	>50 strong

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Definitions- Treatments

- **Core Treatment:** Treatment that is recommended for use in a majority of patients at any point during the course of treatment, as appropriate

- **Primary Treatment (Level 1A):** First selection of treatment(s) if Core Treatment(s) alone are insufficient

- **Secondary Treatment (Level 1B or Level 2):** Next selection of treatment(s) if Primary Treatment(s) are insufficient

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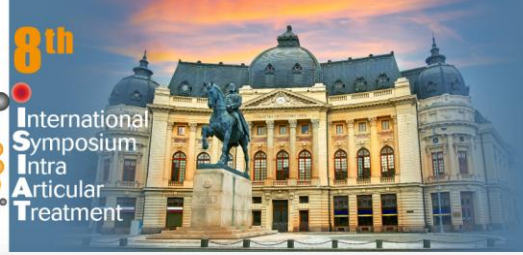

Table 2: Recommended Treatments, by Level, for Knee Osteoarthritis

Recommendation level	Strength	Treatment Type	No Comorbidities	Gastrointestinal	Cardiovascular	Frailty	Widespread pain/Depression
CORE	**Strong**	Arthritis Education; Structured Land-Based Exercise Programs (Type 1- strengthening and/or cardio and/or balance training/neuromuscular exercise OR Type 2- Mind-body Exercise including Tai Chi or Yoga) with or without Dietary Weight Management					
Level 1A **High Consensus** *≥75% "in favor"*	**Strong**	***Pharmacologic***	Topical NSAIDs	Topical NSAIDs		Topical NSAIDs	*refer to Level 1B*
		Non-Pharmacologic	*refer to Level 1B*	*refer to Level 1B*		*refer to Level 1B*	*refer to Level 1B*
Level 1B **High Consensus** *≥75% "in favor" & >50% "conditional" Recommendation*	**Conditional**	***Pharmacologic***	• Non-selective NSAIDs • Non-selective NSAID + PPI • COX-2 Inhibitors IACS	COX-2 Inhibitors IACS, IAHA	IACS, IAHA	IACS, IAHA	• Non-selective NSAIDs • Non-selective NSAID + PPI • COX-2 Inhibitors
		Non-Pharmacologic	Aquatic Exercise, Gait Aids, Self-Management Programs	Aquatic Exercise, Gait Aids, Self-Management Programs		Aquatic Exercise, Gait Aids, Self-Management Programs	Aquatic Exercise, Cognitive Behavioral Therapy (with or without Exercise), Self-Management Programs, Gait Aids
Level 2 **Low Consensus** *60%-74% "in favor"*	**Conditional**	***Pharmacologic***	IAHA	Non-selective NSAID + PPI	*see below*	*see below*	Duloxetine, IACS, IAHA, Topical NSAIDs
		Non-Pharmacologic	Cognitive Behavioral Therapy with Exercise	Cognitive Behavioral Therapy with Exercise		Cognitive Behavioral Therapy with Exercise	*none recommended*
Good Clinical Practice Statements	**Conditional**	***Various***	*Intra-articular treatment*	*Intra-articular treatment, NSAID risk mitigation*		*Intra-articular treatment, NSAID risk mitigation*	*Pain management program, Intra-articular treatment*

Intra-articular treatment: Intra-articular corticosteroids (IACS) are conditionally recommended for acute (1-2 weeks) and short-term (4-6 weeks) pain relief; Intra-articular Hyaluronic Acid (IAHA) is conditionally recommended for longer term treatment effect, as it was associated with significant functional improvement at 26 weeks and demonstrated a favorable safety profile.

Hip OA Recommendations

- IACS
  - Conditional “in favor” – no comorbidities, GI/CV and frailty
  - Conditional “against” – widespread pain/depression

- IAHA
  - Conditional “against” – in all phenotypes

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Polyarticular OA Recommendations

- IACS
  - Conditional “against” – in all phenotypes
- IAHA
  - Conditional “against” – in all phenotypes

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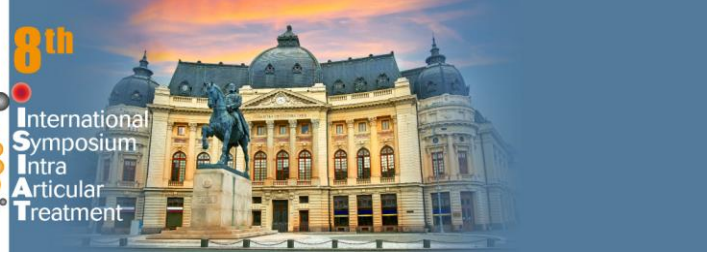

Treatments that were Strongly Recommended Against

Treatment	Rationale	Applicable Joints & Comorbidities
Dextrose Prolotherapy	*Low quality evidence*	Knee OA- all phenotypes Hip OA- all phenotypes Polyarticular OA- all phenotypes
IA Stem Cells	*Low quality evidence, no safety data provided, potential safety concerns, uncertainty regarding specific stem cell formulations utilized*	Knee OA- all phenotypes Hip OA- all phenotypes Polyarticular OA- all phenotypes
IL-1 Receptor Antagonists	*No efficacy*	Knee OA- all phenotypes Hip OA- all phenotypes Polyarticular OA- all phenotypes
PRP	*Low quality evidence*	Knee OA- all phenotypes Hip OA- all phenotypes Polyarticular OA- all phenotypes
TNF-α Inhibitors	*No data*	Knee OA- all phenotypes Hip OA- all phenotypes Polyarticular OA- all phenotypes
FX006 strongly not recommended over IACS	*Traditional IACS were recommended over FX006, but the use of traditional IACS was controversial in hip and polyarticular OA, therefore the use of FX006 was strongly not recommended.*	Hip OA- all phenotypes Polyarticular OA- all phenotypes

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8th International Symposium Intra Articular Treatment

Treatment Algorithm

Initial Assessment:

1. **Identify location of OA**
2. **Diagnose comorbidities**
3. Assess clinical status
   a. Pain, function, stiffness
   b. Effusion, instability, malalignment
4. Assess emotional & environmental status
   a. Social network
   b. Health beliefs & expectations
   c. Mood
   d. Sleep quality
   e. Occupational factors

→ **Select one or more Core Treatment(s)**

After initial assessment, proceed to patient-centered pathways

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Treatment Algorithm

Review and/or Select one or more Core Treatment(s)

Primary Options:
Select a Level 1A treatment. IF no Level 1A treatment, select a Level 1B treatment . Refer to Good Clinical Practice Statements as appropriate.

Re-assess as needed

Acceptable State:
Maintain current treatment regimen as needed

Review and/or Select one or more Core Treatment(s)

Secondary Options:
Select a Level 1B or Level 2 treatment from. Refer to Good Clinical Practice Statements as appropriate.

Re-assess as needed

Review and/or Select one or more Core Treatment(s)

Reassessment of diagnosis and pragmatic discussion. Consider referral to pain clinic or orthopedic consultation

Re-assess regularly

PATIENT-CENTERED

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Treatment Algorithm- Case

Initial Assessment:

1. **Knee OA**
2. **Hypertension, Overweight**
3. Assess clinical status
   a. Pain, function, stiffness
   b. Effusion, instability, malalignment
4. Assess emotional & environmental status
   a. Social network
   b. Health beliefs & expectations
   c. Mood
   d. Sleep quality
   e. Occupational factors

Structured Land-based Exercise & Dietary Weight Management Initiated

After initial assessment, proceed to patient-centered pathways

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Treatment Algorithm- Case

Maintain Diet & Structured Exercise

Primary Options:
Try Topical NSAIDs

Re-assess as needed

Review Diet & Structured Exercise

Secondary Options:
Try IACS
Try Aerobic Exercise

Re-assess as needed

Switch to Mind-body Exercise & Maintain Diet

Reassessment of diagnosis and pragmatic discussion. Consider referral to pain clinic or orthopedic consultation

Re-assess regularly

PATIENT-CENTERED

If NSAIDs are used in this patient: Lowest possible dose of NSAID for **short treatment duration** (1-4 weeks) along with **gastric protection** with a PPI. Some data suggest that Naproxen has a more favorable cardiovascular safety profile than other NSAIDs

Limitations & Strengths

- 2019 guidelines (>6 yrs old)
- More data on several IA therapies including stem cells and PRP has been accumulated since then
- Need for an update

Summary

- IACS
  - Recommended for Knee OA in all phenotypes
  - Recommended for hip OA – no comorbidities, GI/CV and frailty

- IAHA
  - Recommended for Knee OA in all phenotypes

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