AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

American College of Rheumatology (ACR)
Juvenile Idiopathic Arthritis Guideline

Project Plan – August 2019

PARTICIPANTS

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ORGANIZATIONAL LEADERSHIP AND SUPPORT

This project of the American College of Rheumatology (ACR) has the broad objective of developing an evidence-based clinical practice guideline for the management of juvenile idiopathic arthritis (JIA) in topic areas not already covered by the ACR-Arthritis Foundation 2019 JIA and uveitis guidelines.

BACKGROUND

Juvenile idiopathic arthritis (JIA) is a collection of chronic idiopathic autoimmune non-infectious arthritides. By definition, disease onset is prior to 16 years of age and includes joint inflammation that is present for 6 weeks or more after the exclusion of other forms of arthritis. JIA affects approximately 1 in 1,000 children; approximately 50% of children have oligoarticular disease (involves 4 or fewer joints), 40% have polyarticular (involves 5 or more joints), and ~10% have systemic symptoms along with arthritis (i.e., systemic arthritis).

The cardinal clinical features are persistent swelling and pain of the joints. Morning stiffness may be present and typically improves throughout the day with joint use. Linear growth delay can occur in children with JIA, and untreated arthritis can lead to severe joint deformities and disability. Uveitis is the most common extra-articular manifestation and can lead to ocular complications and permanent vision loss. Regular screening by ophthalmology for early detection and timely treatment is crucial.

Treatment depends on the severity of disease and associated manifestations, including presence of systemic features and/or extra articular manifestations. Biologic therapies have significantly changed the approach to treatment for JIA, and new data continue to accumulate regarding their effectiveness. Given these and other new data, updated recommendations for the treatment of JIA patients are needed to help clinicians optimize the care of these patients.

OBJECTIVES

The objective of this project is to develop recommendations for the pharmacologic and non-pharmacologic treatments for treatment juvenile idiopathic arthritis (JIA), covering topics that were not covered in the ACR-Arthritis Foundation 2019 JIA and uveitis guidelines.

Specifically, we aim to:

1. Develop recommendations for the use of glucocorticoids, non-biologic, and biologic disease-modifying anti-rheumatic drugs (DMARDs) for the treatment of children with *oligoarticular JIA arthritis*, taking into consideration both safety and efficacy issues.

2. Develop recommendations for the use of glucocorticoids, non-biologic, and biologic disease-modifying anti-rheumatic drugs (DMARDs) for the treatment of children with *TMJ arthritis*, taking into consideration both safety and efficacy issues.
3. Develop recommendations for the use of non-biologic and biologic disease-modifying anti-rheumatic drugs (DMARDs) for the treatment for children with *systemic JIA*, taking into consideration both safety and efficacy issues.
4. Develop screening guidelines for the use of conventional and biologic DMARDs for the treatment of children with JIA.
5. Develop guidance for the use of immunizations for children with JIA.
6. Develop guidance for the use of imaging for children with JIA.

METHODS

Identification of Studies

Literature search strategies, based on PICO questions (Population/patients, Intervention, Comparator, and Outcomes; *see Appendix A*) will be developed by the Core Team and a research librarian, after input into the PICO questions was received from the entire guideline development team. The search strategies will be peer reviewed by another medical librarian using Peer Review of Electronic Search Strategies (PRESS) (1). Searches will be performed in OVID Medline (1946 +), Embase (1974 +), the Cochrane Library, and PubMed (mid-1960s +).

The search strategies will be developed using the controlled vocabulary or thesauri language for each database: Medical Subject Headings (MeSH) for OVID Medline, PubMed and Cochrane Library; and Emtree terms for Embase. Text words will also be used in OVID Medline, PubMed, and Embase, and keyword/title/abstract words in the Cochrane Library.

Search Limits

Only English language articles will be retrieved.

Grey Literature

The websites of appropriate agencies, such as the Agency for Healthcare Research and Quality (AHRQ), will be searched for peer-reviewed reports not indexed by electronic databases.

Literature Search Update

Literature searches will be updated just before the voting panel meeting to ensure completeness.

Inclusion/Exclusion Criteria

See PICO questions (*Appendix A*), which outline the defined patient population, interventions, comparators and outcomes.

Management of Studies and Data

References and abstracts will be imported into bibliographic management software (Reference Manager) (2), duplicates removed, and exported to Distiller SR, a web-based systematic review manager (3). Screening and data abstraction forms will be created in Distiller SR. Search results will be divided among reviewers, and two reviewers will screen each title/abstract, with disagreements at the title/abstract screening stage defaulting to inclusion for full manuscript review. Following the same dual review process, disagreements at the full manuscript screening stage will be discussed and adjudicated by the literature review leadership, if necessary.

Phases

1. A search for randomized controlled trials and observational studies about interventions aimed at treatment of JIA and prevention of JIA flares and complications will be performed to determine existing studies covering outcomes of interest.
2. Additionally, recently published systematic reviews covering outcomes of interest will also be sought and used for reference cross-checking.
3. Chosen studies will be quality-assessed using the Cochrane Risk of Bias Tool, the Cochrane Effective Practice and Organization of Care Risk of Bias Tool, the Newcastle-Ottawa Scale (4), or a similar tool.
4. Subsequently, identified studies will be assessed using the RevMan (5) and GRADE Pro tools (6).

GRADE Methodology

GRADE methodology will be used in this project to grade available evidence and facilitate development of recommendations. The certainty in the evidence (also known as 'quality' of evidence) will be graded as high, moderate, low or very low. The recommendations will have a strength, strong or conditional, and a direction, as in favor or against the intervention. The strength of recommendations will not depend solely on the certainty in the evidence, but also on patient preferences and values, and the weight between benefits and harms. A series of articles that describe the GRADE methodology can be found on the GRADE working group's website: www.gradeworkinggroup.org.

Analysis and Synthesis

The literature review team will analyze and synthesize data from included studies that address the PICO questions. An evidence profile, including a GRADE Summary of Findings table, will be prepared for each PICO question using Review Manager (RevMan) (5) and GRADEprofiler (GRADEpro) software (6). The Summary of Findings table contains the benefits and harms for each outcome across studies, the assumed and corresponding risk for comparators and interventions (95% CI), the absolute risk and relative effect (95% CI), the number of participants/number of studies, and the certainty in the evidence for each critical and important outcome (i.e., high, moderate, low or very low).

The evidence profile documents the overall certainty in the evidence for each critical and important outcome across studies and summarizes the rationale of the GRADE criteria for downgrading (risk of bias, inconsistency, indirectness, imprecision and publication bias), or upgrading the certainty in a body of evidence (large magnitude of effect, dose-response gradient, and all plausible confounding that would reduce a demonstrated effect).

Development of Recommendation Statements

PICO questions will be revised into drafted recommendation statements. Using the GRADE Evidence Profiles and Summaries of Findings tables, the voting panel, consisting of 12 pediatric rheumatologists and two patient representatives, will consider the drafted recommendation statements in two stages. The first assessment will be done individually, and the results will be anonymous; this vote will only be used to determine where consensus might or might not already exist and develop the voting panel meeting agenda. At the face-to-face voting panel meeting, chaired by the principal investigators, the panelists will discuss the evidence in the context of their clinical experience and expertise to arrive at consensus on the final recommendations. The voting panel meeting discussions will be supported by the literature review leader, the GRADE expert, and selected members of the literature review team, who will attend the meeting to provide details about the evidence, as requested. Voting panel discussions and decisions will be informed by a separately convened patient panel, which will meet in the days before the voting panel meeting, to provide unique patient perspectives on the drafted recommendations based on their experiences and the available literature.

PLANNED APPENDICES (AT MINIMUM)

A. Final literature search strategies
B. GRADE evidence profiles and summary of findings tables for each PICO question

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AUTHORSHIP

Authorship of the guideline will include: principal investigator, Dr. Karen Onel, as the lead author; a literature review leader to be determined; Drs. Daniel Horton, Susan Shenoi and Daniel Lovell, content experts; and Dr. Carlos A. Cuello Garcia, GRADE expert. Members of the literature review team and voting panel will also be authors. The PI will determine final authorship, dependent on the efforts made by individuals throughout the guideline development process, using international authorship standards as guidance.

DISCLOSURES/CONFLICTS OF INTEREST

The ACR's disclosure and COI policies for guideline development will be followed for this project. These can be found in the ACR Guideline Manual on this page of the ACR web site, under Policies & Procedures. *See Appendix B for participant disclosures.*

REFERENCES

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4. Wells GA, Shea B, O'Connell D, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2010. Available: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
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APPENDIX A – PICO Questions

Oligoarticular JIA

POPULATION:

This group includes children with Oligoarticular JIA (< 5 joints involved). This includes children from different ILAR JIA categories but excludes children with systemic arthritis or axial arthritis. These guidelines are not intended to be applicable to children with JIA and other active extra-articular manifestations (e.g., psoriasis, uveitis, IBD) that may influence treatment decisions. Treatment groups currently considered are 1) low disease activity (LDA) versus moderate/high disease activity as determined by JADAS and 2) presence or absence of risk factors (presence of risk factors defined as one or more of the following: + RF, + anti-CCP, + HLA-B27, radiographic evidence of joint damage). Initial therapy is disease activity irrespective. The questions are intended to address typical patients.

INTERVENTIONS:

Nonsteroidal anti-inflammatory drugs (NSAIDs)	Any at therapeutic dosing [ibuprofen, naproxen, tolmentin, indomethacin, meloxicam, nabumetone, diclofenac, piroxicam, etodolac, celecoxib]
Conventional disease modifying anti-rheumatic drugs (DMARDs)	Methotrexate, Sulfasalazine, Hydroxychloroquine, Leflunomide

Biologic DMARDs	Tumor necrosis factor alpha inhibitors (TNFi): Adalimumab, Etanercept, Infliximab, Golimumab, Certolizumab pegol Other Biologic Response Modifiers (OBRM): Abatacept, Tocilizumab, Rituximab, Tofacitinib, Secukinumab
Glucocorticoids	Oral: Any Intraarticular: Triamcinolone Acetonide, Triamcinolone Hexacetonide, Methylprednisolone Acetate
Non-medical interventions	Physical Therapy (PT) Occupational Therapy (OT) Dietary changes Herbal supplements

OUTCOMES:

Critical Outcomes:

- Quality of life (QOL) (e.g., PedsQL, CHQ, PROMIS)
- Disease activity (including active joint count, patient/parent global, MD global, ESR/CRP) as measured by the individual variables and/or composite disease activity measure (e.g., Pediatric ACR response, JADAS)
- ACR provisional criteria for clinical inactive disease
- Functional ability (e.g., CHAQ/PROMIS)
- Joint damage requiring surgical intervention
- Significant limb length discrepancy

- Significant or life-threatening adverse events (e.g., hospitalization, infection, malignancy)

Important Outcomes:

- Arthritis-related pain
- Preservation of normal growth and development
- Fatigue
- Joint damage
- Significant medication side effects leading to medication discontinuation

Risk Factors:

- Signs of joint damage
- Presence of RF or CCP antibodies
- Severe functional impairment

NSAIDS

1. In patients with oligoarticular JIA, should a trial of consistent NSAIDs be recommended and should there be any preferred NSAID treatment?

Glucocorticoids

2. In patients with oligoarticular JIA, should adding intraarticular glucocorticoids to initial therapy be recommended?
3. In patients with oligoarticular JIA, should adding oral steroids to initial therapy be recommended?
4. In patients with oligoarticular JIA, should a specific steroid type be recommended for intraarticular injection?

Non-biologic DMARDs

5. In patients with oligoarticular JIA, should DMARD therapies be recommended, and should there be any preferred order of treatment: methotrexate (subcutaneous and oral), leflunomide, sulfasalazine, and/or hydroxychloroquine?

Biologics

6. In patients with oligoarticular JIA, should biologic therapies be recommended, and should there be any preferred order of treatment: anti-TNF treatment, biologic treatments with other mechanisms of action?

Non-medical treatments

7. In patients with oligoarticular JIA, should dietary or herbal interventions be recommended, in addition to whatever other therapeutic options are given, versus not recommending them?

PT/OT (REGARDLESS OF CONCURRENT MEDICATION USE)

8. In patients with oligoarticular JIA, regardless of disease activity and risk factors, should PT/OT versus no PT/OT (regardless of concomitant medical therapy) be recommended?

Risk factors and disease activity

9. In patients with oligoarticular JIA, should *risk factors* alter the treatment paradigm?
10. In patients with oligoarticular JIA, should *disease activity measures* alter the treatment paradigm?

TMJ

POPULATION:

This group is intended to include patients with predominant TMJ arthritis who may include patients from any of the ILAR JIA categories. Patients may or may not have active peripheral joint disease in addition to active TMJ arthritis to be included in these recommendations, but it is anticipated that patients with peripheral Oligoarticular JIA would otherwise be treated using the Oligoarticular JIA recommendations included in this update.

DEFINITIONS:

Active TMJ arthritis is disease considered active by the examining clinician based upon clinical exam findings, patient-reported symptoms of inflammatory jaw pain, and prior or current MRI findings consistent with active TMJ inflammatory disease.

INTERVENTIONS:

Nonsteroidal anti-inflammatory drugs (NSAIDs)	Any at therapeutic dosing [ibuprofen, naproxen, tolmentin, indomethacin, meloxicam, nabumetone, diclofenac, piroxicam, etodolac, celecoxib]
Glucocorticoids	Oral: Any Intraarticular: Triamcinolone Acetonide, Triamcinolone Hexacetonide, Methylprednisolone acetate

Biologic DMARDs	Tumor necrosis factor-alpha inhibitors (TNFi): Adalimumab, Etanercept, Infliximab, Golimumab, Certolizumab pegol Other Biologic Response Modifiers (OBRM): Abatacept, Tocilizumab, Rituximab, Tofacitinib, Secukinumab
Non-biological disease modifying anti-rheumatic drugs (DMARDs)	Methotrexate, Sulfasalazine, Hydroxychloroquine, leflunomide
Non-medical interventions	Physical therapy (PT), including devices such as mouth guards Dietary changes Herbal supplements

OUTCOMES:

Critical Outcomes:

- Quality of life (QOL) (e.g., PedsQL, CHQ, PROMIS)
- Disease activity components (e.g., active joint count, patient/parent global, MD global, ESR/CRP) as measured by the individual variables and/or composite disease activity measure (e.g., Pediatric ACR response, JADAS)
- ACR provisional criteria for clinical inactive disease
- Functional ability (e.g., CHAQ/PROMIS)
- Joint damage *requiring surgical intervention*
- Significant or life-threatening adverse events (e.g., hospitalization, infection, malignancy)
- Resolution of MRI findings consistent with active TMJ arthritis

Important Outcomes:

- Arthritis-related pain
- Preservation of normal growth and development
- Fatigue
- Joint damage
- Significant medication side effects leading to medication discontinuation

ACTIVE TMJ ARTHRITIS

NSAIDS

11. In patients with active TMJ arthritis, should a trial of consistent NSAIDs be recommended and should there be any preferred NSAID treatment?

Glucocorticoids

12. In patients with active TMJ arthritis, should adding intraarticular glucocorticoids to initial therapy be recommended?
13. In patients with active TMJ arthritis, should adding oral glucocorticoids to initial therapy be recommended?
14. In patients with active TMJ arthritis, should a specific steroid type be recommended for intraarticular injection?

Non-biologic DMARDs

15. In patients with active TMJ arthritis, should DMARD therapies be recommended, and should there be any preferred order of treatment: methotrexate (subcutaneous and oral), leflunomide, sulfasalazine, and/or hydroxychloroquine?

Biologics

16. In patients with active TMJ arthritis, should biologic therapies be recommended, and should there be any preferred order of treatment: anti-TNF treatment, biologic treatments with other mechanisms of action?

Non-medical treatments

17. In patients with active TMJ arthritis, should dietary or herbal interventions be recommended, in addition to whatever other therapeutic options are given, versus not recommending them?

PT (REGARDLESS OF CONCURRENT MEDICATION USE)

18. In patients with active TMJ arthritis, regardless of disease activity and risk factors, should PT versus no PT (regardless of concomitant medical therapy) be recommended?

Risk factors and disease activity

19. In patients with active TMJ arthritis, should risk factors alter the treatment paradigm?

Systemic JIA (sJIA) with and without Macrophage Activation Syndrome (MAS)

POPULATION:

Broad population includes systemic JIA with or without MAS, both overt and subclinical. These guidelines are not intended to be applicable to children with other categories of JIA and other active extra-articular manifestations (e.g., psoriasis, uveitis, IBD) that may influence treatment decisions.

Patients divided into 3 treatment groups: 1) sJIA and no MAS; 2) sJIA and subclinical MAS; 3) sJIA and MAS.

- Disease activity is measured using PhGAS. PhGAS < 3 intended to define a low risk group of patients that may not need biologics or glucocorticoids (e.g., NSAID monotherapy).

- Subclinical MAS is defined as: elevated inflammatory marker (CRP), disproportionately low platelet, elevated ferritin, hepatosplenomegaly, +/- coagulopathy.
- MAS is defined using Ravelli criteria; however, it is notable that these are classification criteria and sensitivity is < 80%, and therefore, physician judgement is the most important element.
- Improvement is defined as ≥ mpACR 50 at 2 weeks (resolution of fever and down trending ESR/CRP indicative of improvement in systemic inflammatory component and decreasing joint count reflecting arthritis).

INTERVENTIONS:

Nonsteroidal anti-inflammatory drugs (NSAIDs)	Any at therapeutic dosing [ibuprofen, naproxen, tolmentin, indomethacin, meloxicam, nabumetone, diclofenac, piroxicam, etodolac, celecoxib]
Non-biologic disease modifying anti-rheumatic drugs (DMARDs)	Methotrexate, Calcineurin inhibitor
Biologic DMARDs	IL-1 inhibitors: Canakinumab, Anakinra, Rilonacept IL-6 inhibitors: Tocilizumab, Sarilumab IL-18 inhibitors: Tadekenig alpha JAK inhibitors: Tofacitinib, Baracitinib Interferon gamma inhibitors: Emapalumab B cell inhibitors: Rituximab Costimulator blockers: Abatacept

Glucocorticoids	Oral Intravenous
Medications *not* addressed	Sarilumab, TNF inhibitors
Non-medical interventions	Physical Therapy (PT) Occupational Therapy (OT) Dietary changes Herbal supplements

OUTCOMES:

Critical outcomes

- Achievement of inactive disease
- Avoiding emergence of MAS
- Resolution of subclinical MAS
- Prevention of re-emergence/progression to overt MAS
- Resolution of overt MAS
- Mortality
- ICU admission
- Hospital admission
- Prediction of persistent systemic disease activity at 6 months

- Response to treatment/inactive disease
- Sustained response to medication (no development of tolerance/antibodies)
- Growth
- Ability to taper/discontinue steroids
- Prevention of exacerbation
- Minimizing side effects/medication toxicity (steroids)
- Predict ability to wean treatment without disease flare
- Proportion of durable inactive disease off therapy

Important outcomes

- Minimizing side effects/medication toxicity (other)
- Duration of hospitalization
- Non-response to NSAIDs
- Non-response to treatment
- Partial response to treatment
- Patient preference / quality of life
- Adherence

Initial and subsequent therapy for sJIA and no MAS:

Treatment naïve, newly diagnosed sJIA patients with no MAS:

20. In patients with treatment naïve, newly diagnosed sJIA without MAS, should non-DMARD treatment (NSAIDS, glucocorticoids) be used as initial therapy?
21. In patients with treatment naïve, newly diagnosed sJIA without MAS, should DMARD treatment (methotrexate, calcineurin inhibitor) be used as initial therapy and is there a preferred order?

22. In patients with treatment naïve, newly diagnosed sJIA without MAS, should biologic treatment (anakinra, canakinumab, tocilizumab or others) be used as initial therapy and is there a preferred order?

sJIA patients with no MAS who do not respond to initial therapy:

23. In patients with sJIA without MAS who do not respond to initial therapy with non-biologic treatments (NSAIDs, glucocorticoids, DMARDs), should non-biologic treatments be combined or biologic treatment started?

Initial and subsequent therapy for SJIA and subclinical MAS:

24. In patients with sJIA, does the presence of subclinical MAS alter the treatment paradigm?

Initial and subsequent therapy for sJIA and overt MAS:

25. In patients with sJIA and overt MAS, Is biologic therapy superior to calcineurin inhibitors in achievement of inactive disease and resolution of MAS?
26. For non-response or partial response to biologic therapy, is addition of calcineurin inhibitor superior to etoposide or IVIG or plasmapheresis at achievement of inactive disease, resolution of MAS?

Other

27. In sJIA patients who cannot achieve inactive disease despite treatment with both IL-1 and IL-6 agents and/or are chronically steroid dependent, is chronic stable steroid treatment superior to non-steroid treatments (cytoxan or abatacept or rituximab or IVIG or mesenchymal stem cell transplant or bone marrow transplant) at achievement of inactive disease, achievement of partial response, growth, ability to taper/discontinue steroids, and minimize side effects/medication toxicity?
28. In sJIA patients with inactive disease treated with oral steroids, is taper to discontinuation of steroids superior to continuing long-term stable dose steroids for preventing disease flare and minimizing side effects/medication toxicity?
29. In sJIA patients in clinical remission of biologic monotherapy, is tapering by decreasing dose superior to tapering dosing interval at preventing disease exacerbation, preventing development of anti-drug antibodies and minimizing medication toxicity?

Specific medication screening irrespective of disease subtype

NSAID monitoring

30. Is there a recommended laboratory screening schedule (complete blood count, comprehensive metabolic panel and urinalysis) for patients receiving chronic daily NSAIDs?

Methotrexate monitoring

31. Is there a recommended laboratory screening schedule (complete blood count, comprehensive metabolic panel) for patients being treated with methotrexate (po or sq)?
32. After methotrexate (po or sq) is initiated, is there a recommended medication change secondary to elevated liver function tests and decreased neutrophil or platelet count?

Sulfasalazine monitoring

33. Is there a recommended laboratory screening schedule (complete blood count, comprehensive metabolic panel) for patients being treated with sulfasalazine?
34. After sulfasalazine is initiated, is there a recommended medication change in response to elevated liver function tests and decreased neutrophil or platelet count?

Leflunomide monitoring

35. Should patients receiving leflunomide have serum creatinine, urinalysis, complete blood cell count, and liver enzymes before and during treatment, per manufacturer's recommendations?
36. After leflunomide is initiated, should medication dosage be altered according to the package insert secondary to elevated liver function tests?

Hydroxychloroquine monitoring

37. Should patients receiving treatment with hydroxychloroquine have annual screening tests with automated visual fields, if age appropriate, plus spectral-domain optical coherence tomography (SD OCT) versus starting annual screening 5 years after treatment onset?
38. Is there a recommended laboratory screening schedule (complete blood count, comprehensive metabolic panel) for patients being treated with hydroxychloroquine?

TNF inhibitor monitoring

39. Is there a recommended laboratory screening schedule (complete blood count, comprehensive metabolic panel and urinalysis) for patients receiving TNF inhibitor treatment?

Abatacept monitoring

40. Is there a recommended laboratory screening schedule (complete blood count, comprehensive metabolic panel and urinalysis) for patients receiving abatacept treatment?

Tocilizumab monitoring

41. Should patients receiving tocilizumab have serum creatinine, urinalysis, complete blood cell count, and liver enzymes before and during treatment, per manufacturer's recommendations?
42. After tocilizumab is initiated, should medication dosage be altered according to the package insert secondary to elevated liver function tests, neutropenia and/or thrombocytopenia?

Anakinra monitoring

43. Is there a recommended laboratory screening schedule (complete blood count, comprehensive metabolic panel and urinalysis) for patients receiving anakinra treatment?

Canakinumab monitoring

44. Is there a recommended laboratory screening schedule (complete blood count, comprehensive metabolic panel and urinalysis) for patients receiving canakinumab treatment?

Infection screening

45. Should all children have infection titers (measles, varicella, hepatitis B, hepatitis C) checked prior to starting immunosuppressive medication?
46. Should children with no evidence of immunity to important infections have a booster immunization prior to starting immunosuppressive medication?

TB Surveillance

47. Should screening for TB be done prior to starting biologic DMARD therapy and then annually in children?
48. In children receiving biologic DMARD therapy, is there a preferred method of TB screening?

Vaccination

Definitions:

- Immunosuppression is defined by use of DMARDs, biologics, and/or corticosteroids.
- Inactivated vaccines include tetanus/diphtheria/acellular pertussis (Tdap), pneumococcal vaccines (conjugate PCV-13 or polysaccharide PPV-23), meningococcal vaccines (MenACWY or MenB), human papillomavirus (HPV), and inactivated influenza vaccine.
- Live attenuated vaccines include the varicella vaccine, MMR vaccine, live attenuated influenza vaccine, and rotavirus vaccine.

49. In JIA patients *not on immunosuppression*, do inactivated or live attenuated vaccines result in flare of disease?
50. In JIA patients *not on immunosuppression*, are patients able to develop protective antibodies against infections targeted by the vaccine?
51. In JIA patients *on immunosuppression*, do inactivated vaccines result in flare of disease?

52. In JIA patients *on immunosuppression*, are patients able to develop protective antibodies against infections targeted by the vaccine?
53. In JIA patients *on immunosuppression*, can treatment with live attenuated vaccines be given safely (initial dose, booster dose)?
54. Can live attenuated vaccines be used safely in the households of children with JIA *on immunosuppression*?

Imaging modalities

Inflammation and damage detection

55. In children with Juvenile Idiopathic arthritis, is any specific imaging technique recommended to best detect inflammation and damage, make a diagnosis, predict structural damage, flare or treatment response?

Imaging and intraarticular injections

56. In children with Juvenile Idiopathic arthritis who require intraarticular corticosteroid injections, should injections be done with imaging guidance?

APPENDIX B – Participant Disclosures

In order for the College to most effectively further its mission and to otherwise maintain its excellent reputation in the medical community and with the public, it is important that confidence in the College's integrity be maintained. The cornerstone of the ACR's Disclosure Policy is disclosure of actual and potential conflicts so that they can be evaluated by the College in order to avoid undue influence of potential conflicts. The purpose of the ACR's Disclosure Policy is identification of relationships which may pose actual or potential conflicts. These actual or potential conflicts can then be evaluated by the College so that adjustments can be made that will avoid any undue influence. This policy is based on the principle that, in many cases, full disclosure of the actual or potentially conflicting relationship will of itself suffice to protect the integrity of the College and its interests.

Participants	Role	Primary Employer	Sources of Personal Income (salary information from primary employer is not required):	Intellectual Property	Research Grants/Contracts	Investments to Include Medical Industry and Nonmedical Industry	Organizational Benefit	Activities with Other Organizations	Family or Other Relations
Karen Onel	Core Team - PI	Hospital for Special Surgery	Sack Law Office	N/A	N/A	N/A	N/A	N/A	N/A
Daniel B. Horton	Core Team - Content Expert	Rutgers University	N/A	N/A	NIAMS/NIH; CARRA-Arthritis Foundation; New Jersey Health Foundation	N/A	CARRA-AF	N/A	N/A
Daniel Lovell	Core Team - Content Expert	Cincinnati Children's Hospital	Astra-Zeneca Pharm; Wyeth Pharm; Amgen; Abbott; Pfizer; Hoffman-La Roche; Novartis; UCB; Takeda; Janssen; GSK; Boehringer Ingelheim; Celgene; Novartis; Roche; Bristol Myers Squibb; AbbVie; Forest Research	N/A	NIH; BMS IM101-240 Registry; Roche WA29231 LTE CTA; Janssen CNTO 148JIA3003 CTA; Roche WA28029 (Arthur) CTA; AbbView Consult Contract; Eli Lilly MSA Consult Contract; GSK Consult Contract; Janssen Steering Committee; Novartis Secukinumab Consult Contract; Pfizer 1165 Steering Committee Consult Contract; Pfizer TOFA Consult Contract; Roche WA29231 Coordinating Center	N/A	N/A	N/A	N/A
Susan Shenoi	Core Team - Content Expert	Seattle Childrens Hospital	Novartis	N/A	N/A	N/A	N/A	ABP	N/A
Carlos A. Cuello-Garcia	Core Team - GRADE Expert	McMaster University	American College of Physicians	N/A	Hamilton Academic Health Sciences Organization (HAHSO) Innovation Grant	N/A	N/A	The Journal of Pediatrics; World Allergy Journal; MacGRADE	N/A
Marisa Klein Gitelman	BOD Liaison	Ann & Robert H. Lurie Children's Hospital of Chicago	UpToDate	N/A	BMS; British Columbian Telethon Small Grants; CARRA; ALR; LFA/Canadian Institutes of Health Research; NIAMS; YCB; LFA; Pfizer; Abbvie	N/A	N/A	Arthritis Foundation	N/A
Amit Shah	Lit Review Team	American College of Rheumatology	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Ann Marie Szymanski	Lit Review Team	National Institutes of Health	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Ashley Cooper	Lit Review Team	Children's Mercy Hospital	N/A	N/A	Sobi; NIH; DCRI; NIH; CARRA-Arthritis Foundation	N/A	N/A	AAP; AAPOS	N/A
Barbara Edelheit	Lit Review Team	Ct. Children's, Hartford CT	Crico Risk Management Firm	N/A	N/A	N/A	N/A	N/A	N/A
Elaine Ramsey Flanagan	Lit Review Team	Children's healthcare of Atlanta, Emory University	Piedmont Hospital Columbus	N/A	Childhood Arthritis and Rheumatology Research Alliance	Vanguard	N/A	N/A	Brother works for Roche, carries Actemra
Fatima Barbar-Smiley	Lit Review Team	Nationwide Children's Hospital; The Ohio State University	N/A	N/A	Alliance; NIH/National Institute of Arthritis and Musculoskeletal and Skin Diseases	N/A	N/A	Pediatric Rheumatology Collaborative Study Group (PRCOIN); Childhood Arthritis and Rheumatology Research Alliance; American Academy of Pediatrics	N/A
Keila Veiga	Lit Review Team	Hospital for Special Surgery	Best Doctors	N/A	N/A	N/A	N/A	N/A	N/A
Kimberly Hays	Lit Review Team	Penn State Milton Hershey Medical Center; MUSC	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Marat Turgunbaev	Lit Review Team	American College of Rheumatology	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Miriah Gillispie-Taylor	Lit Review Team	Atrium Health/Levine Children's Hospital	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Melissa Mannion	Lit Review Team	University of Alabama at Birmingham	N/A	N/A	CARRA; PR-COIN	N/A	N/A	Arthritis Foundation	N/A
Nadine Saad	Lit Review Team	Hospital for Special Surgery	Best Doctor's	N/A	N/A	N/A	N/A	N/A	N/A
Rebecca Trachtman	Lit Review Team	Icahn School of Medicine at Mount Sanai	N/A	N/A	Childhood Arthritis & Rheumatology Research Alliance (CARRA)	N/A	N/A	N/A	N/A
Rosemary Peterson	Lit Review Team	Children's Hospital of Philadelphia	NEJM Resident 360 Rotation Prep	N/A	5 T32 HD 60550-9	N/A	N/A	N/A	N/A
Brian Feldman	Voting Panel	The Hospital for Sick Children	Agility Clinical ; OPTUM; Pfizer; BMS	Haemophilia Joint Health Scale	Cure JM; CIHR; Novartis	N/A	The Arthritis Society	The Arthritis Society	N/A
C. Egla Rabinovich	Voting Panel	Duke University	Hall, Render, Killiam, Health & Lyman, LLP	N/A	AbbVie; CARRA; UCB Pharma, Inc.; Janssen Research & Development, LLC.; Sanofi; SOBI	N/A	N/A	American Board of Pediatrics	N/A
Harry L Gewanter	Voting Panel	Self employed; Children's Hospital of Richmond at VCU	CSRO; Social Security; Children's Hospital of Richmond Pension; Surveys; Children's Hospital of Richmond at VCU	Various firms via Mutual Funds	CSRO; Medical Home Plus, Inc; Arthritis Foundation; Virginia Society of Rheumatologists; disAbility Law Center of Virginia	N/A	N/A	N/A	N/A
Jaime Guzman	Voting Panel	BC Children's Hospital	BC Children's Hospital Research	N/A	Canadian Institutes of Health Research; The Athritis Society Canada	N/A	N/A	Arthritis Society Canada	N/A
Mara L Becker	Voting Panel	Duke University; Duke Clinical Research Institute; FDA	N/A	N/A	NICHD; NCATS	N/A	N/A	American Board of Pediatrics; CARRA; Pediatric Dermatology Research Alliance	N/A
Melissa Tesher	Voting Panel	University of Chicago	American Academy of Pediatrics	N/A	Donor (Lake Shore Recycling); CARRA	N/A	N/A	CARRA; AAP	N/A
Michael Ombrello	Voting Panel	National Institutes of Health	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Peter Nigrovic	Voting Panel	Brigham and Women's Hospital; Boston Children's Hospital	CARRA Steering Committee; UpToDate; AAP; ANRF; Novartis; Sobi; Simcere	N/A	NIH (3); Lupus Research Alliance; RRF; Boston Children's Hospital-Broad Institute Collaboration Grant, Novarits; Pfizer; NIH R01 AR069569; NIH 3U54AR057319-16S1; NIH P30 AR070549; NIH P30 AR072577; Amgen/Bristol-Meyers-Squibb/Crescendo/Sanofi/Regeneron; ***(Pending) NIH R01 AR075906; (Pending) Bristol-Meyers-Squibb***	N/A	N/A	CARRA; ANRF	N/A
Polly Ferguson	Voting Panel	University of Iowa	Wolters Kluwer; NIH-study sections, Board of Scientific Counselors; American Board of Pediatrics	N/A	NIH; CARRA	N/A	N/A	Amereican Board of Pediatrics; ACR/ARP	N/A
Rayfel Schneider	Voting Panel	The Hospital for Sick Children, Toronto	Novartis; Novimmune; SOBI	N/A	Novimmune S.A.; Swedish Orphan Biovitrum AB; Pfizer; Hoffman-La Roche Limited	N/A	N/A	N/A	N/A
Sheila T. Angeles-Han	Voting Panel	Cincinnati Children's Hospital Medical Center	N/A	N/A	CARRA; NIH; PCORI	N/A	N/A	N/A	N/A
Tzielan Lee	Voting Panel	Stanford University School of Medicine	ACR REF	N/A	N/A	N/A	N/A	Lupus Foundation of Northern California	N/A
Yukiko Kimura	Voting Panel	Hackensack Meridan Health	UpToDate	N/A	PCORI; Genentech; ***Novartis (anticipated)***; Rheumatology Research Foundation	N/A	N/A	CARRA	N/A
Jennifer Horonjeff	Voting Panel/Patient Rep	Savvy Cooperative (Self employed)	Hankensack University; HHS	N/A	N/A	N/A	N/A	Savvy Cooperative; Arthritis Foundation	N/A
Katherine Murphy	Voting Panel/Patient Rep	Louisiana Office of Public Health	CARRA	N/A	CARRA	N/A	N/A	N/A	N/A