VOTING FOR A PROTOCOL TO RECOMMEND TO HTA FOR A FUTURE RCT FOR JIA

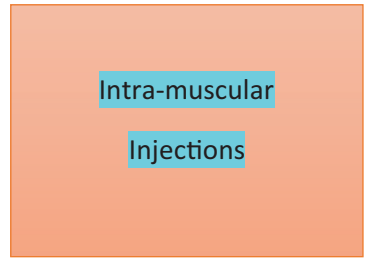
Possible Final Protocols Choice

The HTA brief is that control arm in a future full trial of corticosteroids in JIA will be the most commonly used "treatment as usual". These first 3 protocols assume that our feasibility study will find that intra-articular corticosteroid injections will be most common route.

The treatment for uncomplicated oligo-articular JIA is well established as being by intra-articular steroid injection. Patients with oligo-articular JIA with their first disease presentation will therefore be excluded from the initial trial of steroids in induction of remission.

PART A PROTOCOLS 1-6 CHOOSE ONLY 1 PROTOCOL

PROTOCOL 1: Intra-Articular Corticosteroid Injections (IACI) versus Intra-muscular Depot Injection



Versus

Control Arm 1

The most commonly used steroids in the initial treatment of JIA are intra-articular corticosteroid injections and this route will therefore be used as the control arm of the study.

Treatment 1

Patients will receive a single dose of IM depot medrone/ methylprednisolone up to a maximum of 150 mg IM

Inclusion Criteria

- Polyarticular JIA, or a polyarticular course.
- Patients with Systemic Onset JIA and Enthesitis Related Arthritis (ERA) and psoriatic arthritis are included with the provisos in the exclusion criteria.
- Extended oligo-articular JIA.
- Flaring Oligo-articular JIA with at least 6 months since the first injection will also be included (Note that a flare does not imply that the I/A route did not work the first time if we put in a time scale since the first injections).

Exclusion Criteria

- New onset oligoarticular arthritis.
- Patients with active systemic JIA with systemic features or a ferritin above 1000.
- Patients with ERA with predominantly active enthesitis.
- Patients with active infection.
- Patients with active uveitis as the main indication for steroid treatment.

*Note

This protocol will have the widest inclusion criteria by subtype.

PROTOCOL 2: IV methylprednisolone versus IACI excluding oligo JIA completely

Control Arm 2

The most commonly used steroids in the initial treatment of JIA are intra-articular corticosteroid injections and this route will therefore be used as the control arm of the study. Dosing will be up to a maximum of *10 joints* with a maximum of *40 mg* of triamcinolone hexacetonide per joint will be used.

Treatment Arm 2

Intravenous methylprednisolone 20-30 mg/kg to a maximum of 1 gm given on 3 consecutive days with gastric protection.

Inclusion Criteria

- Patients with polyarticular JIA or a poly joint course will be included, patients with SOJIA, psoriatic arthritis and ERA are included with the provisos in the exclusion criteria.
- Extended oligo-articular JIA.

Exclusion Criteria

- Patients with Oligo-JIA.
- Patients with active systemic JIA with systemic features or a ferritin above 1000.
- Patients with active infection.
- Patients with active uveitis as the main indication for steroid treatment.

*NOTE

The issue is the age of the patients to be included where I have not suggested a minimum age despite the IV route. If we wanted to include all oligos on this one we could maybe amend the regime to a single IV dose.

PROTOCOL 3: Oral prednisolone versus IA excluding oligo JIA completely

Versus

Control Arm

The most commonly used steroids in the initial treatment of JIA are intra-articular injections and this route will therefore be used as the control arm of the study.

Treatment Arm 3

Oral prednisone 2 mg/kg to a maximum of 40- 60 mg given with gastric protection.

Duration of treatment example: High dose for 1-2 weeks.
1/2 dose for 1-2 weeks, 1/4 dose for 1-2 weeks, then discontinue.

Inclusion Criteria 3

- Patients with polyarticular JIA or a poly joint course will be included, patients with SOJIA, psoriatic arthritis and ERA are included with the provisos in the exclusion criteria.

- Extended oligo-articular JIA.

Exclusion Criteria 3

- Patients with Oligo-JIA.
- Patients with active systemic JIA with systemic features or a ferritin above 1000/ with macrophage activation syndrome.
- Patients with predominantly active enthesitis.
- Patients with active infection.
- Patients with active uveitis as the main indication for steroid treatment.

PROTOCOL 4: Oral prednisolone versus IV methylprednisolone excluding oligo JIA completely

Versus

Control arm 4

The control arm for this study will be a short steroid regime of oral prednisone 2 mg/kg to a maximum of 40- 60 mg given with gastric protection given for *5* days.

Treatment arm 4

Intravenous methylprednisolone 20-30 mg/kg to a maximum of 1 gm given on 1-3 consecutive days with gastric protection.

Inclusion Criteria 4

- Patients with polyarticular JIA or a poly joint course will be included, patients with SOJIA, psoriatic arthritis and ERA are included with the provisos in the exclusion criteria.
- Extended oligo-articular JIA.

Exclusion Criteria 4

- Patients with Oligo-JIA.
- Patients with active systemic JIA with systemic features or a ferritin above 1000/ macrophage activation syndrome.
- Patients with active infection.
- Patients with active uveitis as the main indication for steroid treatment.

PROTOCOL 5: Essentially active joints randomised to oral prednisone versus IM depot -medrone including oligo JIA flares

Control Arm 5

The control arm for this study will be a short steroid regime of oral prednisone 2 mg/kg to a maximum of 40- 60 mg given with gastric protection given for *5* days.

Treatment Arm 5

Patients will receive a single dose of IM depot medrone/ methylprednisolone up to a maximum of 150 mg IM (or per kg).

Inclusion Criteria 5

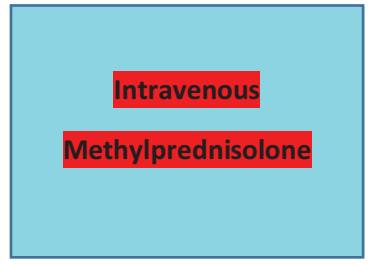
- Patients with polyarticular JIA or a poly joint course will be included, patients with SOJIA, psoriatic arthritis and ERA are included with the provisos in the exclusion criteria.
- Extended oligo-articular JIA.

Exclusion Criteria

- Patients with Oligo-JIA.
- Patients with active systemic JIA with systemic features or a ferritin above 1000/ macrophage activation syndrome.
- Patients with active infection.
- Patients with active uveitis as the main indication for steroid treatment.

PROTOCOL 6: IM depot medrone versus IV methyl prednisone including oligo JIA flares

Versus



Control Arm 6

Patients will receive a single dose of IM depot medrone/ methylprednisolone up to a maximum of 150 mg IM (or per kg).

Treatment Arm 6

Intravenous methylprednisolone 20-30 mg/kg to a maximum of 1 gm given on 1-3 consecutive days with gastric protection.

Inclusion Criteria 6

- Patients with polyarticular JIA or a poly joint course.
- Patients with SOJIA and ERA are included with the provisos in the exclusion criteria.
- Patients with flaring oligo-articular JIA can be included.

Exclusion Criteria 6

- Patients with Oligo-JIA.
- Patients with active systemic JIA with systemic features or a ferritin above 1000/ macrophage activation syndrome.
- Patients with active infection.
- Patients with active uveitis as the main indication for steroid treatment.

PART B PROTOCOLS 7 & 8 CHOOSE ONLY 1 PROTOCOL

PROTOCOL 7: A Staged Steroid Protocol Approach

In this protocol essentially entry is through failed intra-articular steroids and is therefore open to all subtypes

INCLUSION: All patients that have failed intra-articular steroid treatments for all subtypes.

Randomise to one of the following routes: IV, IM or Oral

Intra-muscular Injections

or

Oral Prednisolone

or

Intravenous Methylprednisolone

PROTOCOL 8: An Adaptive Design with all routes are compared with IACI and the least effective removed from further study at interim analysis

This protocol has intra-articular steroids as the control group

INCLUSION 1: Does the patient have Oligo JIA with active joints in the first flare? Is the patient able to have intra-articular steroid injections in a timely way (within 2 weeks)?

If YES then treat with IACI

Intra-articular Injections

If the patient flares then treat as for the polyarticular inclusion 2

INCLUSION 2: Does that patient have polyarticular course JIA (including systemic onset without systemic features, ERA or Psoriatic Arthritis, extending Oligo JIA and flaring but still persistent oligoarticular with active joints of more? YES?

Randomise to one of the following: IV or oral, or IM with comparator arm being IACI

Intravenous Methylprednisolone

or

Oral Prednisolone

or

Intra-muscular Injections

VERSUS

Intra-articular Injections

Randomise to one of the following: IV or oral, or IM with comparator arm being IACI