



MCRN / **arc** Paediatric
Rheumatology Clinical Studies
Group



Dear Colleagues,

Re: Feasibility questionnaire concerning collaboration with the Childhood Arthritis & Rheumatology Research Alliance (CARRA) in clinical trials

- **The TREAT Trial (Trial of Early Aggressive Itherapy of JIA)**

The MCRN/**arc** Paediatric Rheumatology Clinical Study Group (CSG) is interested in comment and feedback from BSPAR members regarding the possibility of developing collaborative links with the North American paediatric rheumatology research networks. These include the CARRA network (<http://www.carragroup.org/>) and the Pediatric Rheumatology Collaborative Study Group (PRCSG) (<http://prcsg.org/>).

For those of you not familiar with CARRA, they are multi-centre network of paediatric rheumatology research centres across North America who have joined together to answer critical clinical research questions. They are committed to advancing the health and quality of life of children living with rheumatic disease and arthritis. They also work collaboratively with the PRCSG which is the other major North American paediatric rheumatology network. PRCSG is a consortium of North American academic clinical paediatric rheumatology centres whose chief aim is to conduct high quality industry sponsored clinical trials of therapeutic agents to advance the state-of-the-art in healthcare for children with rheumatic conditions. Both of these research networks have been working in collaboration with PRINTO (<http://www.printo.it/>) and together have made a significant contribution to our evidence base for the treatment of children with rheumatic diseases.

Currently both CARRA and PRCSG are very interested in exploring the possibility of including the UK Paediatric Rheumatology community in clinical trials they are running. This would be with the support of the CSG and the MCRN / CLRN network. There are a large number of administrative and logistical obstacles to do this (partly due to regulatory / funding issues) so both they and the CSG would like to gauge support / interest / feasibility before proceeding.

This process is primarily in function of future trials that are / may be developed. However in order to get the ball rolling, there is a current proposal to participate in the so called "TREAT Trial in JIA" which is currently being run by Drs Carrol Wallace and Dan Lovell in the US by CARRA. Funding would cover per / patient and drug costs although the CSG would need to look to find additional funding where possible for start up costs. Summary details attached (appendix), and can be found at: <http://clinicaltrials.gov/ct2/show/record/NCT00443430?term=NCT00443430&rank=1>

We would therefore invite all BSPAR members to comment on any of the following questions.

We would ask **each unit** to respond specifically regarding unit-background details, participation and the specifics of the TREAT Trial to the following brief questionnaire.

Please return to Laura Pilkington (laura.pilkington@liv.ac.uk) copying it to me (m.w.beresford@liverpool.ac.uk)

Please reply as soon as possible, preferably by the 20th June 2008.

Many thanks

M.W. Beresford

Chair,
On behalf of the MCRN/**arc** Paediatric Rheumatology CSG

MCRN/arc Paediatric Rheumatology CSG
Feasibility questionnaire concerning collaboration with North American clinical trials and the TREAT Trial

Name: _____ Job title: _____ Unit / Hospital:

Please write as much comment as possible

Collaboration with North America

In principle are you interested in participating in clinical trials supported by the CSG done in collaboration with the North American Paediatric Rheumatology research networks (e.g. CARRA, PRCSSG etc.):

- Yes / No
- Concerns / comments:

Infrastructure support

CARRA would like to have some information about the types /amount of infrastructure support available at local centres. Can you outline briefly the following - Number of (or FTE):

- Paediatric rheumatologists: _____
- Paediatricians with interest paediatric rheumatologist: _____
- Adult rheumatologists with seeing paediatric patients: _____
- Nurse specialists: _____ ; Research nurses: _____; AHPs with research experience: _____
- Have you established working rapport with a:
 - Comprehensive Local Research Network: Yes / No
 - MCRN Local Research Network: Yes / No
 - What study/ies have you been working on together:

- Other infrastructure clinical research support do you have available / comment:

- What studies / trials has your unit actively been recruiting to in the last 5 years (approx recruited numbers):

JIA activity

In your unit, can you give as close as possible estimates of the:

- Number new JIA patients / year: _____ Number of patients on Methotrexate: _____
- Number JIA patients on anti-TNFs: _____ Number new patients / year on anti-TNF: _____

Specifics: The TREAT Trial

Looking at the study outline (appendix attached). This is an established protocol that is has been approved and is recruiting so cannot be changed at this point:

- How many patients would you have each year realistically who could be considered eligible: _____
- Would you like to participate in this trial: Yes / No
- If not this trial, would you be interested in a trial using biologic therapy in the first 6 months from diagnosis: Yes / No
- Please comment in as much detail as possible on what would encourage you to participate / not participate:

Trial of Early Aggressive Drug Therapy in Juvenile Idiopathic Arthritis	
Official Title †	Trial of Early Aggressive Therapy in Juvenile Idiopathic Arthritis (TREAT in JIA)
Brief Summary	The purpose of this study is to compare two aggressive drug regimens for children with poly-juvenile idiopathic arthritis (JIA).
Detailed Description	<p>JIA is a type of arthritis with no definite cause and an onset prior to 16 years of age. JIA causes joint destruction, pain, and permanent disability. There are multiple types of JIA; collectively, they represent one of the most common chronic diseases in children and the most prevalent pediatric rheumatic illness. Poly-JIA, one type of JIA, affects at least five joints in the body within the first 6 months of disease. Long-term remission of poly-JIA is uncommon, and most children must remain on multiple combinations of medications for many years. The usual treatment for poly-JIA is based upon the gradual addition of medications that might be more effective in treating this disease. There is a need to find uniformly effective treatments for children with poly-JIA. Based on previous adult arthritis studies, there appears to be an early window of opportunity in the disease progression during which aggressive therapy has a profound beneficial long-term effect. The purpose of this study is to compare the effectiveness of two aggressive drug regimens in treating children with poly-JIA. Specifically, the study will determine whether aggressive therapy started in the first 6 months of disease onset can result in inactive disease and clinical remission while on these medications.</p> <ul style="list-style-type: none"> • All participants will receive weekly methotrexate shots while in the study (0.5mg/kg/wk) [plus at least 5mg folic acid / wk]. In addition, participants will be randomly assigned to one of two groups: • Group 1 participants will receive placebo etanercept shots for up to 12 months and daily placebo prednisolone liquid for 4 months. • Group 2 participants will receive etanercept shots [0.8mg/kg/wk, max 50mg] for up to 12 months and daily prednisolone liquid for 4 months. • [Starting dose of prednisolone is 0.5mg/kg/day (max 30mg); from 2 wks, steroids weaned as follows: week 2 - 0.4 mg/kg/d; week 3 - 0.3 mg/kg/d; week 4 - 0.2 mg/kg/d; week 5 - 0.15 mg/kg/d; week 6 through week 15 - 0.1 mg/kg/d; week 16 - 0.05 mg/kg/d; week 17 no prednisolone. Doses rounded to nearest 0.3mg (0.1mL)] <p>The study will last up to 12 months and include two parts.</p> <ul style="list-style-type: none"> • Part A will last 1 to 6 months, depending on response to assigned treatments. • If participants are still experiencing active arthritis at 6 months, they will be offered open-label treatment with etanercept and prednisolone. If participants experience <u>inactive disease</u> any time prior to 6 months, they will enter Part B of the study. • During Part B, which will last up to 6 months, participants will remain on the same treatment regimen that they were provided in Part A. If participants experience inactive disease followed by a flare of disease any time during the

	<p>study, they will stop participating.</p> <p>[Subjects who do not achieve at least an ACR Pediatric 70 response by 4 months or do not achieve ID by 6 months will enter the Part B of the trial and will receive ETN / Pred (this may be a re-treatment with prednisone for some subjects). Up to 2 intra-articular steroid joint injections (IAS) are allowed before or within 2 weeks after the baseline visit. The subject must still have at least 5 active joints at baseline in addition to those injected to enroll in this study. Up to <u>two</u> IAS injections will be allowed in the Part B. If only 1 or 2 joints are active at 6 months, subjects can continue to receive blinded drug and receive up to 2 IA injections. At month 7, if the subject is still not in ID, the subject will be offered ETN/Pred.]</p> <p>During the study, there will be 11 study visits for all participants. Study visits will include a physical exam, including joint evaluations; blood and urine collection; and questionnaires regarding function, quality of life, medication compliance, other medications used, infections, and adverse symptoms. Blood will be collected for translational studies.</p>		
Primary Outcome	Proportion of participants who attain inactive disease by 6 months [Time Frame: 6 months after initiation of study intervention] [Designated as safety issue: No]		
Secondary Outcome Measure †	Safety profiles, including the number of treatment-emergent, serious, or unexpected adverse events and other important medical events [Time Frame: Over 12 months maximum study participation per subject] [Designated as safety issue: Yes]		
Start Date †	June 2007	Completion	December 2009
Eligibility Criteria †	<p>Inclusion Criteria:</p> <ul style="list-style-type: none"> • Diagnosis of active poly-JIA as determined by International League of Associations for Rheumatology (ILAR) criteria • Onset of signs and symptoms of poly-JIA for 6 months or less prior to study screening • Willing to use acceptable forms of contraception for the duration of the study and for 3 months after the study • Parent or guardian willing to provide informed consent • Able to attend all study visits <p>Exclusion Criteria:</p> <ul style="list-style-type: none"> • Received or currently receiving biologic disease-modifying antirheumatic drugs (DMARDs) or prednisone for any duration for treatment of poly-JIA, with the following exceptions: <ol style="list-style-type: none"> 1. Methotrexate duration must be less than or equal to 6 weeks at a dose of less than or equal to 0.5 mg/kg/week (40 mg max), 2. Steroid use has been less than or equal to 4 weeks and the subject is off of steroids for at least 1 week prior to enrollment • Received intramuscular, intra-articular, or soft-tissue injections of corticosteroids for treatment of poly-JIA before receiving the first dose of study medication. Up to 2 joint injections with intra-articular steroids (IAS) will be allowed up to 2 weeks after the baseline visit • History of or active cancer of any type • Active gastrointestinal disease (e.g., inflammatory bowel disease) • Chronic or acute kidney or liver disorder • Significant blood clotting defect • AST (SGOT), ALT (SGPT), or BUN levels more than two times the upper level of normal, creatinine levels more than 1.5 mg/dl, or any other laboratory abnormality considered to be clinically significant within 28 days prior to baseline • Chronic condition (e.g., diabetes, epilepsy) that is either not stable or poorly controlled and may interfere with study participation • Received any investigational medication within 30 days prior to the first dose of study medication or scheduled to receive an investigational drug (other than the study medications) during the course of the study 		

	<ul style="list-style-type: none"> • Chronic or active infection or any major episode of infection requiring hospitalization or treatment with intravenous antibiotics within 30 days prior to study screening or oral antibiotics within 14 days prior to study screening • HIV infected • Known past or current hepatitis infection • Received a live virus vaccine within 1 month prior to baseline • Purified protein derivative (PPD) positive (positive tuberculosis [TB] test) • Pregnancy • Any medical condition that would make study participation difficult or inadvisable in the opinion of the investigator • History of or current psychiatric illness that would interfere with study participation • History of alcohol or drug abuse within the 6 months prior to study entry that would interfere with study participation • Inability to comply with study requirements for any reason
Gender / Age	Both / 4 Years to 16 Years
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