Background Information

Systemic Juvenile Idiopathic Arthritis

What is systemic juvenile idiopathic arthritis?

Systemic juvenile idiopathic arthritis (sJIA) is a subtype of juvenile idiopathic arthritis (JIA), a group of conditions characterised by chronic arthritis in children. Other subtypes include oligoarticular JIA and polyarticular JIA.

JIA affects approximately 100 in every 100,000 children[i] of which sJIA accounts for 10 to 20 percent.[ii] In Europe and North America the incidence of disease is the same in both sexes, unlike the female predominance seen in other subtypes of JIA.[i] sJIA differs from the other types of JIA by having severe systemic symptoms such as a spiking fever, in addition to the arthritis. Despite conventional therapies, a significant number of children are often left with serious and life-long complications such as growth defects and osteoporosis.[i]

Characteristics of sJIA

sJIA begins in children aged 16 years or younger with a peak age of onset between 18 months and two years, although persistence of the disease into adulthood does occur.[i] The arthritis is accompanied by a characteristic fever, skin rash, anaemia, enlargement of the liver and/or spleen and inflammation of the lining of the heart and/or lungs.[i]

The impact of sJIA

sJIA presents a huge daily burden for the children and families affected. One-half to two-thirds of patients develop chronic and persistent arthritis and approximately half of these children are left with significant disability.[ii]

The disease can disturb emotional development and psychological support for the child and their family is often required.[i] Extra support may be needed at school to ensure educational progress and help the child to integrate with their peers. Previous studies have indicated that these children are more socially isolated and have higher rates of unemployment later in life.[i]

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Long-term prognosis

The severity and outcomes of sJIA are unpredictable. Some children may be free of disease within two to four years, whereas others experience a relapsing course with both systemic and arthritic symptoms.[i] Patients with severe disease often have to endure active arthritis well into adult life despite treatment with existing therapies.[i] In two large European studies, 23 to 30 percent of children had systemic symptoms 10 to 15 years after the initial onset of sJIA.[i]

Serious, life-threatening complications occur much more frequently in sJIA than in other types of rheumatic disease and the overall mortality rate is estimated to be between two to four percent.[iii] One severe, life-threatening complication is macrophage activation syndrome (MAS), a systemic inflammatory reaction caused by the excessive activation and multiplication of particular immune system cells.[ii]

The treatment challenge

sJIA has the worst long-term prognosis compared to other types of JIA, yet current medical treatment is considered unsatisfactory.[i] Mild forms of disease are usually treated with non-steroidal anti-inflammatory drugs. High dose corticosteroids are often necessary to control systemic symptoms, but do not improve the long-term prognosis and their use is accompanied by severe side effects.[i]

Treatment with traditional arthritis medications such as methotrexate (MTX) is of little benefit and only 30 percent of children respond to anti-tumour necrosis factor (anti-TNF) therapy.[i]

IL-6: The hidden key?

A large body of evidence demonstrates the critical role of interleukin-6 (IL-6) in sJIA and explains why this messenger substance is a promising target for future therapies.

Studies have shown that patients with sJIA have significantly higher levels of IL-6 in their blood and joints compared to other types of JIA or adult rheumatoid arthritis (RA).[ii] IL-6 contributes to all the major features of sJIA including joint inflammation, joint damage, fever, anaemia, growth impairment and osteoporosis.[ii]

Genetic research suggests that a mutation in the IL-6 gene could be responsible for its increased production in sJIA.[ii] Secretion of IL-1, another pro-inflammatory messenger, is also high in sJIA and clinical trials of biologic drugs that block either IL-1 or IL-6 have seen good results.[i]

RoACTEMRA: A new treatment for sJIA

A new biologic drug, developed by Roche in collaboration with Chugai, provides a promising new treatment option for children with sJIA. RoACTEMRA (tocilizumab, ACTEMRA outside the EU) is the first fully humanised monoclonal antibody that targets the IL-6 receptor.

In April 2011, the US Food and Drug Administration (FDA) approved RoACTEMRA for the treatment of sJIA in patients two years of age and older, as a mono or combination therapy with MTX.

Evidence for sJIA treatment

52 week data from the global Phase III TENDER study demonstrated that RoACTEMRA is highly effective and generally well tolerated in patients with sJIA.[iv] Significantly more patients achieved JIA ACR30 (a 30% improvement in disease activity) and were fever-free at week 52 compared to placebo. The study also showed that the mean number of joints with active arthritis, or with limitation of movement were reduced at week 52[4].

References

[i] Woo, P. Systemic juvenile rheumatoid arthritis: diagnosis, management, and outcome. *Nature Clinical Practice: Rheumatology*. 2006. 2:1

[ii] De Benedetti F. Inflammatory cytokines in the pathogenesis and treatment of systemic juvenile idiopathic arthritis – Basic science for the clinician. *Pediatric Rheumatology Online Journal* 2005. Vol 3:2

[iii] Cassidy JT, *et al.* Juvenile rheumatoid arthritis. Cassidy JT, Petty RE, eds. Textbook of Pediatric Rheumatology. 2001:218–322

[iv] De Benedetti f. Efficacy and Safety of Tocilizumab (TCZ) in Patients (pts) with Systemic Juvenile Idiopathic Arthritis (sJIA): TENDER 52-Week Data. EULAR 2011