Macrophage activation syndrome (MAS) in systemic juvenile idiopathic arthritis (sJIA)

MAS is a well-recognised and potentially life-threatening complication of sJIA with an estimated incidence in patients with sJIA of between 7% and 13%[1,2] and a reported mortality rate of 8% to 22%.[1,3]

MAS is thought to be triggered by infections or changes in medications, but MAS can occur without clear reasons or aetiology.[1]

Diagnosis

There are currently no universally accepted definitive diagnostic criteria although preliminary criteria have been published.[4]

The differential diagnosis of MAS is broad because of the variable and multi-system abnormalities of the disorder and the non-specific nature of the most prominent clinical features, which include fever, hepatosplenomegaly and cytopenia. As a result, achieving a rapid clinical diagnosis is often difficult. Other features of MAS include neurologic abnormalities, and laboratory abnormalities including hypofibrinogenaemia. Successful treatment of MAS has been reported with ciclosporin and glucocorticoids.

The severity and life-threatening nature of this complication, coupled with the frequent difficulties in achieving a rapid diagnosis, necessitate appropriate vigilance and careful management of patients with active sJIA.

RoActemra® (tocilizumab) indication in sJIA

RoActemra is indicated for the treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 2 years of age and older who have responded inadequately to previous therapy with non-steroidal anti-inflammatory drugs (NSAIDs) and systemic corticosteroids. RoActemra can be given as monotherapy (in case of intolerance to methotrexate [MTX] or where treatment with MTX is inappropriate) or in combination with MTX.[5]

IL-6 inhibition and MAS

Some of the laboratory features associated with RoActemra administration, related to IL-6 inhibition, are similar to some of the laboratory features associated with the diagnosis of MAS (such as a decline in leukocyte count, neutrophil count, platelet count, serum fibrinogen and erythrocyte sedimentation rate, all of which occur most notably within the week following RoActemra administration).[1,5]

However, the following characteristics: central nervous system dysfunction, haemorrhage, and hepatosplenomegaly, if present, are useful in establishing the diagnosis of MAS in the context of IL-6 inhibition. In addition, ferritin levels frequently decrease with RoActemra administration,[6,7] but often increase with MAS[1,4] and, therefore, may be a useful differential laboratory parameter.

Clinical experience and the clinical status of the patient, coupled with the timing of the laboratory specimens in relation to RoActemra administration, must guide interpretation of these laboratory data and their potential significance in making a diagnosis of MAS.

Incidence of MAS in RoActemra-treated patients

In clinical trials, RoActemra has not been studied in patients during an episode of active MAS.[5]

In a 12 week controlled study, no patient in any treatment group experienced MAS while on assigned treatment. However, during open-label treatment with RoActemra, 3% (3 out of 112) of patients developed MAS. All 3 patients had RoActemra interrupted (2 patients) or discontinued (1 patient). One patient who withdrew from TCZ treatment died of probable MAS 14 months after the last TCZ dose while receiving another biologic for persistent active disease. Based on a limited number of cases, the incidence of MAS does not appear to be elevated in the RoActemra sJIA clinical development experience; however no definitive conclusions can be made.[8]

References

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If you have any further questions relating to RoActemra please contact Roche Medical Information on +44 (0)800 3281629 or email: medinfo.uk@roche.com.

Full prescribing information can be found in the RoActemra Summary of Product Characteristics (SmPC) via the electronic Medicines Compendium (eMC) website: www.medicines.org.uk.

Suspected adverse reactions associated with the use of RoActemra should be reported to: Medicines Authority Post-licensing Directorate 203. Level 3. Rue D'Argens, Gzira GZR 1368, or at: http://www.medicinesauthority.gov.mt/adrportal. Suspected adverse events should also be reported to Roche by phone on +44 (0)1707 367554, fax on +44 (0)1707 367582 or e-mail at welwyn.uk_dsc@roche.com.

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