HOW AND WHEN TO TREAT CLINICALLY ISOLATED SYNDROME (CIS)?

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Clinically isolated syndrome (CIS) suggestive of multiple sclerosis (MS) is the first clinical episode in patients who will potentially develop MS. To determine whether early treatment following a CIS, can delay the second clinical event and a diagnosis of clinically definite MS (CDMS), five placebo-controlled clinical trials with conventional disease modifying therapies (DMT) were conducted..

In the CHAMPS (Controlled High-Risk Subjects AVONEX Multiple Sclerosis Prevention Study) study, weekly injections of 30 mcg interferon (IFN)-beta 1a im resulted in a significant reduction of the cumulative probability of the development of CDMS (35% vs. 50% for placebo; p=0.002). In the ETOMS (Early Treatment Of Multiple Sclerosis) trial, the rate of conversion to CDMS was reduced from 45% to 34% (p=0.047) for once-weekly treatment with 22 mcg IFN-beta 1a sc. In the BENEFIT (BETAFERON in Newly Emerging Multiple Sclerosis for Initial Treatment) study, treatment with IFN-beta 1b 250 mcg sc every other day delayed time to CDMS by 363 days (HR: 0.50; p<0.0001) and decreased the risk for CDMS by 50%. In the PreCISe (early glatiramer acetate treatment in delaying conversion to clinically definite multiple sclerosis in subjects Presenting with a Clinically Isolated Syndrome trial) glatiramer acetate (GA) 20 mg/d reduced conversion to CDMS by 45% (p=0.0005) with the time to conversion significantly prolonged from 336 days to 722 days. Finally, recently, another study with IFN-beta 1a sc was performed in CIS. In this Rebif FLEXible dosing in early multiple sclerosis (REFLEX) study, patients were randomly assigned to receive IFN-beta 1a sc 44 mcg three times a week, once weekly, or placebo. The two year rate of conversion to CDMS was lower for both doses of IFN-beta 1a sc (three times a week 63%, p<0.0001; once weekly 76%, p=0.008) compared to placebo (86%). Thus, all these trials with IFN-beta and GA have shown a consistent reduction in the cumulative probability of developing CDMS in CIS patients receiving early treatment. Additionally, they demonstrated that IFN-beta and GA decreased the number of lesions detected on brain MRI. However, up to now extension studies and follow up data, which demonstrated persisting benefits in relapse activity, have not shown an effect in preventing early disability. Therefore, having all above-mentioned in mind, along with the poor adherence rates and side effects, DMT should be offered to selected CIS patients at high risk of developing MS.