Activity Score) (Ann. Rheum. Dis 916,1990). The US Food and Drug Administration has also developed several different labels for drugs in RA including improvement in signs and symptoms, function and quality of life, stabilisation in radiographic progression and complete clinical response and remission.

Methotrexate remains the most most widely studied and popular therapy to treat RA. Leflunomide, the oral pyrimidine inhibitor, was recently approved for RA. One randomised trial of 359 pts compared leflunomide (20 mg/day) to sulfasalazine (2 gr/day) and to placebo (Lancet 353:259,1999). At week 24, 29% of the placebo patients met ACR 20% response criteria compared to 55% in the lef group and 56% in the ssa group. There was less radiographic progression in the lef and ssa group as compared to placebo. In a study of 482 pts leflunomide (20 mg/day) was compared to methotrexate (7.5 to 15.0 mg/wk) and to placebo (Arch. Intern. Med.159:2542,1999). Of those patients who completed 52 weeks of therapy, 41% of patients on lef met an ACR 20% criteria compared to 35% on MTX and 19% on placebo. There was significantly more radiographic progression as measured by Sharp score in those receiving placebo as compared to either MTX or lef (Arthritis Rheum. 43:495, 2000). Leflunomide has received the signs and symptoms claim and the radiographic label.

Infliximab, the chimeric monoclonal antibody, that down regulates TNF activity is the first biologic that reported efficacy in RA. In the pivotal study, 428 patients who had active RA were maintained on chronic MTX therapy and were randomised to receive placebo or one of four dosing regimens of infliximab (Lancet 354, 1932, 2000, NEJM 343:1594, 2000). Patients were dosed with infliximab either every 4 or 8 weeks at doses of either 3.0 or 10.0 mg/kg or placebo. At week 52, there was sustained clinical response with ACR 20% being noted in 52% of the infliximab groups as compared to 17% in the placebo group. At wk 52 a reduction in the rate of radiographic progression was observed with all doses and dosing regimens of infliximab as compared to placebo plus MTX. Infliximab has received the signs and symptoms claim and the radiographic label. Etanercept, the p75 TNF receptor, has been extensively studied in trials in North America. One study of 234 patients with active RA evaluated 25 mg or 10 mg of etanercept injected twice per week versus placebo for 6 months (Ann Intern Med. 130:478, 1999). At month 6, 59% of the 25-mg group and 11% of the placebo achieved an ACR 20% response. In a 24-week double-blind study, 89 patients on chronic MTX patients were randomised to receive either etanercept 25 mg twice a week or placebo (NEJM 340:253,1999). At week 24, 71% of those patients receiving etanercept plus MTX and 27% of those receiving placebo plus MTX met ACR 20% response criteria. In another trial 632 patients with early RA (less than 3 years) were randomised to receive either MTX or etanercept (NEJM 343:1586, 2000). Patients were treated for one year with either etanercept 25 mg twice a week, etanercept 10 mg twice a week or MTX at a dose that was rapidly escalated to a dose of 20 mg/wk. There was a more rapid effect with etanercept as compared to MTX in the first several months of treatment but both drugs lead to significant improvements in ACR response criteria and a reduction in radiographic progression. Etanercept has received the signs and symptoms claim and the radiographic label

Fibromyalgia is a central nervous system disorder – Friday 15 June, 10.00-11.45/ Forum Hall

SP0062 FIBROMYALGIA: EVIDENCE FOR A CENTRAL NERVOUS SYSTEM DISORDER

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This presentation reviews evidence from several studies in our laboratory regarding central factors associated with abnormal pain sensitivity in fibromyalgia (FM). We have found that, compared to healthy controls, clinic patients with FM and community residents who meet criteria for FM but have not consulted a physician (FM non-patients) display significantly lower pain thresholds in response to pressure stimulation and exhibit significantly higher cerebrospinal fluid (CSF) levels of substance P. In addition, during exposure to suprathreshold levels of pressure stimulation, controls and FM patients differ in changes in brain regional cerebral blood flow (rCBF). That is, controls show significant rCBF increases in the contralateral thalamus, somatosensory cortex, and the anterior cingulate cortex, whereas patients with FM show significant and bilateral increases in rCBF in these brain structures. Finally, patients with FM show greater cardiovascular responses to stress than controls. Moreover, stress produces greater increases in thermal pain unpleasantness ratings among FM patients compared to controls. Together, these findings indicate that FM patients show abnormal central processing of nociceptive stimuli that tends to be exacerbated by stress. We plan to determine whether the effects of stress on pain unpleasantness in FM (a) are associated with abnormal rCBF changes in the anterior cingulate cortex; and (2) may be mediated by abnormal cortisol release or cytokine production.

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SP0063 GENETIC FACTORS IN FIBROMYALGIA

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