Background The role of gold salts in the present therapy of rheumatoid arthritis (RA) remains controversial.

Objectives To analyse the clinical efficacy (according to ACR response criteria) of a therapeutic protocol, that includes sodium aurothiomalate as first option DMARD in patients with recent onset RA.

Methods All patients with RA (ACR diagnostic criteria) for less than two years disease duration and no previous DMARD therapy, attending our Rheumatology Units during 1998–99, have been included in a therapeutic protocol, in which the first administered DMARD was sodium aurothiomalate at a dose of 50 mg/week. According to the ACR response at 6 months (no improvement, ACR-20 or ACR-50) patients were treated with methotrexate (MTX) alone, aurothiomalate plus MTX or aurothiomalate alone, respectively. Low dose of steroids (< 10 mg/d of prednisone) were allowed and intraarticular therapy with triamcinolone hexacetonide was performed in large joint with persistent synovitis.

Results Forty seven (7M/40F) patients were included (age: 54 ± 16 years; disease duration: 10 ± 7 months; RF+: 40(85%)). The percentages of ACR responders at 6 and 12 months were as shown at the Table 1. Twenty-four per cent of patients discontinued gold salts due to adverse events or inefficacy at 12 months. Aurothiomalate was continued in 61% of patients as monotherapy and in 15% of patients in combination with MTX.

Abstract FRI0026 Table 1

	Remission	ACR-20	ACR-50	No improve
6 months	11%	61%	50%	28%
12 months	27%	52%	30%	21%

Conclusion Gold salts still have an important role in RA treatment. The use of aurothiomalate should be taken into account in the present therapeutic strategies of patients with early RA.

FRI0027 5-AMINOLEVULINIC ACID INDUCED PROTOPORPHYRIN IX FORMATION IN ARTHRITIC SYNOVIAL TISSUES: AN APPROACH FOR SYNOVIAL PHOTODYNAMIC THERAPY IN ARTHRITIS

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Background

Objectives To determine the optimal conditions for synovial accumulation of protoporphyrin IX (PpIX) and light induced synovial cytotoxicity in arthritis *in vitro* and *in vivo*.

Methods *In vitro* studies: Synovial biopsies from patients with osteoarthritis (OA, n = 9), rheumatoid arthritis (RA, n = 3) and synovial tissues from mice with antigen-induced arthritis (AIA, n = 9) were incubated with different concentrations of 5-aminolevulinic acid hexyl-ester (h-ALA), a protoporphyrin IX (PpIX) precursor. Tissue PpIX content was determined by microspectrofluorometry. Following photoexcitation, the synovial tissues were evaluated by Sytox-Green fluorescence for cell death.

Animal studies: h-ALA was injected intra-articularly into knee joints of mice with AIA (n = 40). Following photodynamic

therapy (PDT) *in vivo*, joint inflammation was assessed by technetium scintigraphy and histology.

Results In human biopsies, the highest fluorescence intensity was observed after incubation with 0.5–1 mM h-ALA. Kinetic studies showed that PpIX accumulation in human tissues reached a peak at 3 h in OA and increased linearly up to 6 h in RA. Murine tissues showed highest fluorescence intensity at a concentration of 4 mM *in vitro* and 8 mM *in vivo*. By fluorescence microscopy, PpIX was localised to the synovial lining layer, endothelial cells and macrophages. Irradiation of pre-incubated tissues *in vitro* led to significant cell death. PDT *in vivo* in AIA led to a statistically significant reduction of histological parameters of joint damage in irradiated joints.

Conclusion Our findings suggest that PDT based on PpIX accumulation in the synovial membrane may be a rational basis for photodynamic synovectomy in arthritic diseases.

FRI0028 SUPPRESSION OF EXPERIMENTAL ARTHRITIS BY TREATMENT WITH A NOVEL DMARD, SMP-114

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Background A more promising therapeutic approach to rheumatoid arthritis would be to maintain joint function. Our studies have been performed with the above goal in mind and showed that some azole compounds meet these requirements. SMP-114, a novel isoxazole derivative, was selected from them and characterised as a compound with antiarthritic activity and without any cyclooxygenase inhibitory activity.

Objectives The objective of these studies was to evaluate the effect of SMP-114 on joint oedema, bone resorption and ankylosis in experimental models of rheumatoid arthritis.

Methods Adjuvant arthritis was induced in Lewis rats by a single injection of *Mycobacterium butyricum* in the plantar surface of right hindpaw on day 0, and animals were treated therapeutically (days 10–24 or days 17–21) with SMP-114. Anti-inflammatory activity was determined by measurements of paw swelling. The protective effect on joint integrity was determined by measuring radiographic and histological changes. Collagen-induced arthritis was induced in DBA/1J mice. Animals were immunised intradermally at the base of the tail with type II collagen (day 0 and day 21). SMP-114 was administered orally (days 0–49). Efficacy was assessed clinically, histologically and radiographically.

Results Treatment (days 10–24) of adjuvant arthritis with SMP-114 significantly reduced paw oedema with a minimum effective dose of 10 mg/kg. This was accompanied by a more extensive reduction in bone and cartilage destruction around the metatarsal-phalangeal joint, as assessed by histologic and radiographic examinations. SMP-114 was also able to significantly ameliorate full-blown adjuvant arthritis. When daily administration of SMP-114 began on day 17, well into the chronic destructive phase, the agent produced a dose-response effect on paw oedema, with a minimum effective dose of less than 2.5 mg/kg. The compound (range 20–80 mg/kg) demonstrated a capacity for ameliorating joint inflammation (paw oedema) and protecting joint structure coincident with a decrease in the number of osteoclasts in articular lesions in mice with collagen-induced arthritis. SMP-114 also showed anti-fibroblastic effect and, as a result, reduced a frequency of development of ankylosis in these models. This profile