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Efficacy of remission-induction regimen (cyclophosphamide versus infliximab) for severe extrathoracic sarcoidosis

EFIR ES STUDY

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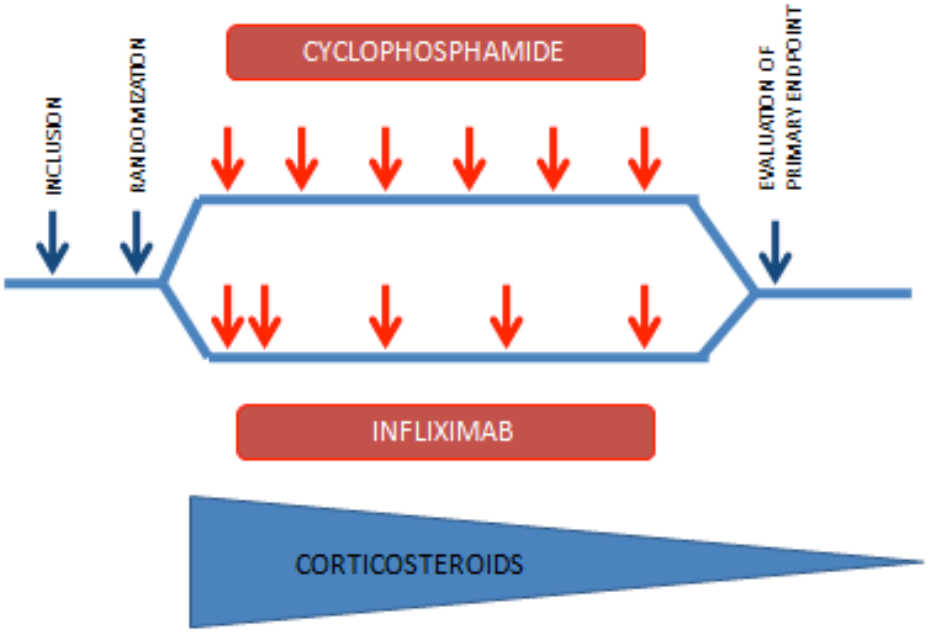
SUMMARY

Full title	Efficacy of remission-induction regimen (cyclophosphamide versus infliximab) for severe extrathoracic sarcoidosis.
Acronym	EFIR ES
Coordinating Investigator	Docteur Fleur COHEN AUBART Service de Médecine Interne Groupe Hospitalier Pitié-Salpêtriere, 75013 Paris, France
Sponsor	Assistance Publique – Hôpitaux de Paris
Primary objective and assessment criterion	To evaluate the efficacy of infliximab and cyclophosphamide to induce remission in sarcoidosis with extrathoracic localization and serious organ involvement or relapse with at least one first-line immunosuppressive drug
Secondary objectives and assessment criteria	To assess the incidence of side effects in the two groups, in particular infection rate, liver toxicity, anaphylaxy To compare the cumulative dose of corticosteroids in the two groups To compare the mortality in the two groups To compare the global and organ related ePOST score in the two groups To compare the time to relapse To compare the quality of life, Health status and Fatigue (FAS) in the two groups To compare hospitalizations (number and duration) To compare working stop duration
Experimental design	Multicenter randomized, controlled, parallel group trial
Population involved	Patients with severe extrathoracic sarcoidosis
Inclusion criteria	Clinical and radiological presentation concordant with sarcoidosis Presence of non caseating granuloma At least one extrathoracic localization, including hypercalcemia Presence of serious organ involvement or relapse/apparition of a new localization with more than 10 mg/d of steroids and one first-line immunosuppressive drug Signed Informed consent Age superior or equal to 18 years Affiliated to National French social security system
Non-inclusion criteria	• Previous use of cyclophosphamide or infliximab for more than 3 months • Pregnancy or breast feeding or women in age of pregnancy without efficient contraception • Patients with multiple sclerosis, • Patients with prior history of urothelial cancer, • Patients with prior history of any cancer in the 5 years before inclusion (except for cutaneous basocellular cancers),

	• Patients with a history of hypersensitivity to infliximab to other murine proteins, or to any of the excipients • Patients with tuberculosis or other severe infections such as sepsis, abscesses, and opportunistic infections • Patients with moderate or severe heart failure (NYHA class III/IV) Patients with: • hypersensitivity to cyclophosphamide or any of its metabolites • bone marrow aplasia or bone marrow hypoplasia, significant anaemia, leucopenia, or thrombocytopenia prior to treatment • urinary tract infection • acute urothelial toxicity from cytotoxic chemotherapy or radiation therapy • urinary outflow obstruction • Hypersensitivity to methotrexate or any of the excipients • Significantly impaired hepatic function • Significantly impaired renal function : creatinin level < 30ml/min and no extrarenal epuration. • Alcoholism • Concurrent vaccination with live vaccines during therapy •Inability to understand information about the protocol •Persons deprived of their liberty by judicial or administrative decision •Adult subject under legal protection or unable to consent.
Treatment being tested	Control group: *cyclophosphamide* Experimental group: *infliximab/low dose methotrexate*.
Benchmark treatment	Intravenous cyclophosphamide at 0.7 g/m2 (maximal dose of 1g), every 4 weeks Infliximab 5 mg/kg D1-D15 and every 6 weeks, in association with low dose methotrexate (10 mg/week) Corticosteroids tapering regimen until 0.1 mg/kg/day
Number of subjects chosen	*76*
Number of centres	*10*
Research period	3 years
Statistical analysis	Primary end point will be compared by chisquared test with alpha risk of 0.05 and power of 0.8
Funding source	PHRC
Data Safety Monitoring Board anticipated	Yes



Description of the sequence and duration of all trial periods :
1. Screening, inclusion and randomization (30 months)
2. Treatment period (6 months for one patient)
3. Observational follow-up : 5 years, including fertility