SUPPLEMENTAL MATERIAL

Contents

1. Treatment protocol

Group A received induction treatment with oral cyclophosphamide 2 mg/kg/d (age >65 1.5 mg/kg/d) for 6 months. Group B received induction treatment with MMF 1000 mg twice daily for 6 months. Both treatment groups received prednisolone in a tapering regime during induction treatment. All patients received initially prednisolone 1 mg/kg/d (max 60 mg) until six weeks after start of treatment. Thereafter, prednisolone was tapered with 10 mg every two weeks until a daily dose of 30 mg/d, subsequently with 5 mg every two week until 15 mg daily and with 2.5 mg every four weeks until discontinuation of prednisolone. With this regimen, by 6 months prednisolone should be 10 mg daily and should be discontinued by 9,5 months after study entry.

All patients were switched to maintenance therapy with azathioprine 1.5 mg/kg/d after six months, provided that the patient was in stable remission for at least three months. If not, switch of therapy could be postponed to a maximum of nine months after start of therapy. When remission was not attained within 6 months, therapy was considered to have failed. Azathioprine maintenance therapy was tapered after 12 months and completely withdrawn 2 years after study entry.

If the following events occurred, dosages had to be adjusted as it follows: leukocytopenia ($<4{,}0 \times 10^9$/L) prompted for a 25% reduction of cyclophosphamide, MMF and azathioprine; if the leukocyte count dropped below 3.0×10^9/L, medication had to be stopped temporarily until leukocyte counts normalized, and treatment had to be resumed with at least 25% decrease.

The treatment protocol was stopped after 4 years of follow-up, or if remission was not achieved within 6 months, a relapse developed, the patient experienced unacceptable side-effects or withdrawal of informed consent.

Concomitant medication

Both groups received additional therapy, entailing prophylaxis against Pneumocystis pneumonia (co-trimoxazole for 6 months), osteoporosis prophylaxis, candida prophylaxis (until prednisolone dose reached ≤15 mg/day), and prophylaxis of dyspeptic symptoms (as required).

2. Supplemental table 1. Inclusion sites.

Inclusion site	**Number of included patients**
University Medical Center Groningen	47
Maastricht University Medical Center	20
Medisch Centrum Leeuwarden	11
Scheper Ziekenhuis Emmen	2
Ziekenhuis St Jansdal Hardenberg	2
Isala Zwolle	1
Erasmus MC	1

3. Supplemental table 2. Malignancies during study follow-up.

Malignancy during study	Time after study entry diagnosed	Previous treatment	Outcome, last information (date)
Randomization: CYC			
Pancreas carcinoma	4 months	Diagnosis: CYC and CS induction, AZA maintenance	Died
Esophagus carcinoma	2 months	Diagnosis: CYC and CS, 1 relapse: CYC and CS	Treatment: surgery, recovered without sequelae (6-10-2016)
Bladder carcinoma	33 months	Diagnosis: CYC and CS	Recovered without sequelae (July 2016)
Randomization: MMF			
Lung carcinoma	12 months	Diagnosis: CYC and CS; First relapse: CYC and CS	Died
Squamous cell carcinoma	49 months	Diagnosis: CYC and CS; First relapse: CYC and CS	Recovered without sequelae
Melanoma	6 months	Unknown	Alive 9 years after inclusion