

Can cyclophosphamide be used as a first line therapy in IgG4-RD without oral glucocorticoids?

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Objective:

Glucocorticoids (GC) are considered “gold standard” for IgG4-RD treatment, but they have multiple toxicities. Rituximab is effective and safe strategy, but extremely costly, so searching for alternative drugs is essential.

Methods:

Real-practice single center open study. From our IgG4-RD cohort we chose patients that were treated with cyclophosphamide (CyP) only without middle doses of oral GC and/or rituximab. Diagnosis of IgG4-RD was based on comprehensive diagnostic criteria. CyP was administered first in intensive manner: 1000 mg IV every 14 days (5-6 infusions) with 500 mg IV methylprednisone premedication. Then CyP was administered 200 mg per week intramuscularly (supportive phase). Oral GC dose was 2,5-5 mg daily. 17 patients with active IgG4-RD for whom at least 1 follow-up point during first 12 months of treatment was available were included in the present study.

Results:

The mean age was 47.8 years (range 23-76), median duration of the disease before treatment administration was 36 months (range 3-228). The mean number of organs involved was 1.8 (range 1-4): orbit 14, salivary glands 7, lymph nodes 3, lungs 3, retroperitoneum 2, kidneys 1. Thirteen (76.5%) had elevated serum IgG4 levels >135 mg/dl at baseline (median 290 mg/dl, range 27 -5060 mg/dl). Four patients had prior treatment (GC – 2, mycophenolate mofetil – 1, polychemotherapy- 1) which was not effective. The mean duration of follow-up after first CyP infusion was 13 months (range 3-122). Dramatic or notable clinical improvement within 6 months was observed in 9 patients (52.9%) and in majority of them the effect was notable within first 1,5-3 months, 3 patients (17.6%) had light clinical improvement and 5 patients (29.4%) had no improvement. As for post-CyP imaging studies among patients with clinical improvement 7/12 (58%) demonstrated reduction of the tumor size, in 3 it was stable. Three patients had relapses: 1 patient after 12 months of treatment, 1 patient after 4 months due to discontinuation of CyP, 1 patient within 3 years from the start of treatment having been off any drugs for 1 year. Serum IgG4 level had a tendency to decrease, but the difference wasn't statistically significant. CyP was well tolerated and there were no serious side effects, only 1 case required discontinuation of the treatment.

Conclusions:

Further investigations are needed, but it seems that CyP can be used in IgG4-RD treatment, in some cases as a first line therapy without administration large doses of oral GC.