EFFECTIVENESS AND SAFETY OF OFF-LABEL USE OF TOCILIZUMAB IN AUTOIMMUNE DISEASES: A MULTICENTER STUDY IN INTERNAL MEDICINE DEPARTMENTS

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Background: Tocilizumab (TCZ) is a recombinant humanized anti-interleukin-6 receptor monoclonal antibody. There is increasing evidence of TCZ efficacy in refractory auto-immune diseases.

Objectives: To describe off-label use, efficacy and tolerance of TCZ use in Internal Medicine Departments.

Methods: This is a retrospective, descriptive and multicenter study from 9 departments of Internal Medicine. Data were reported using a standardized case report file in January 2019.

Results: Fifty one patients were included (19 men, 32 women). Mean age was 55.6 ± 17 years (range 23 - 80). TCZ was used in:

- 12 connective tissue diseases (23.5%): relapsing polychondritis (n=6), systemic sclerosis (n=3), anti-synthetase syndrome (n=1), and unclassified connective tissue disease (n=3).
- 10 vasculitis (19%): Takayasu arteritis (n=7), Cogan disease (n=1), panarteritis nodosa (n=1), unclassified vasculitis (n=1).
- 10 ophthalmologic conditions (19%): non infectious posterior uveitis (n=8), sympathetic ophthal mia (n=1), Basedow orbitopathy (n=1).
- 8 adult-onset Still’s diseases (16%).
- 5 cases of polymyalgia rheumatica (10%)..
- 3 miscellaneous diseases (6%): idiopathic AA amyloidosis, multicentric non HHV8 Castelmann disease, Erdheim Chester disease (1 case each).

Mean disease duration was 7.5 ± 6.4 years. In 44 cases (86%) TCZ was administered for refractory disease to corticosteroids and immunosuppressive drugs. Previous therapies included corticosteroids (83%), methotrexate (66%), TNF inhibitor drug (44%), azathioprine (20.8%), mycophenolate (12%), cyclophosphamide (8%), rituximab (16%), hydroxychloroquine (6%), anakinra in 2 patients and intereron, dapsone, etoposide, leflunomide, abatacept, salazopyrin or intra-venous immunoglobulin in 1 patient each.

TCZ was initiated as first-line therapy (15.5%), second-line therapy (17.5%), third-line therapy (31%), fourth-line therapy (19%), fifth-line therapy (14%), sixth-line therapy (12%) or as seventh line therapy in one case. TCZ was associated with methotrexate in 3 cases (6%). Treatment route was intravenous (96%).

At the end of the follow up, 41 patients (80%) were still using TCZ, with a mean follow up period of 22 ± 23 months (range 1-90). In these patients, daily corticosteroid use significantly decrease from 16.5 ± 18 mg to 5.7 ± 13.7 mg (p<0.005, using paired T test). Considering the 28 patients using TCZ since more than 6 months, short term efficacy was 93% (2 cases of loss of efficacy).

TCZ was interrupted in 10 patients (19%), because of treatment failure (n=2), loss of efficacy (n=2) or side effect (n=6). Side effects were infection (2 pneumonia, zona, sinus infection), pruritus (n=1), urticaria (n=1), dyslipidemia (n=1), high blood pressure (n=2), infusion-related reaction (n=1), bullous dermatitis (n=1), acute renal failure (n=1), angioedema (n=1), mouth ulcers (n=1).

Conclusion: TCZ is used in various autoimmune diseases. TCZ allowed a significant corticosteroids reduction and short term efficacy was 93% in patients using TCZ for more than 6 months. Nevertheless TCZ was interrupted in 19% of the patients. TCZ use will probably be more common in the future to treat refractory autoimmune diseases.

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