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

Martin Michaud, Thomas Sene, Pascal Chazerain, Olivier Lidove, Geoffrey Urbanski, Frederique Retornaz, Boris Bienvenu, Laurent Chiche, Florian Catros, Laurent Sailler, Laurent Alric, Jean Thomas Giraud, Léo Caudrelier, Slim Lassoued, Sophie Ancellin, Francis Gaches

[1]Joseph Ducuing Hospital, Internal Medicine, Toulouse, France , [2]Croix Saint Simon Hospital, Paris, France , [3]Angers University Hospital, Internal Medicine, Toulouse, France , [4]Hopital Européen, Internal Medicine, Marseille, France [5]Saint Joseph Hospital, Internal Medicine, Marseille, France , [6]Toulouse University hospital, Internal Medicine, Toulouse, France , [7]Tarbes Hospital, Internal Medicine, Tarbes, France , [8]Cahors Hospital, Internal Medicine, Cahors, France

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 ophtalmia (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 (10%), hydroxychloroquine (6%), anakinra in 2 patients and interferon, dapsone, etoposide, leflunomide, abatacept, salazopyrin or intra-venous immunoglobulin in 1 patient each.

TCZ was initiated as first-ligne 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 (=6). Side effects were infection (2 pneumonias, 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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