5PSQ-066 ADEQUACY TO PROTOCOL OF USE OF TOCILIZUMAB FOR MANAGEMENT OF COVD-19 DISEASE

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Background and Importance The severe affectation by the COVID-19 virus is caused by an inflammatory response triggered in the individual. The use of immunosuppressive agents such as tocilizumab may be effective due to cytokine storm blockade. Since it is about off-label use, experts recommend developing management protocols from hospitals.

Aim and Objectives To determine the efficacy of tocilizumab in severe COVID-19 disease and the adequacy to a protocol of use.

Material and Methods A retrospective, observational and descriptive study over a 12-month period was conducted. All COVID-19 patients who received tocilizumab were included.

For the protocol development, following criteria were included: 1)Interstitial pneumonia with respiratory insufficiency and high-flow oxygen; 2)Absence of response to 3 boluses of corticosteroids; 3)Interleukin-6>40UI/L. In the absence of interleukin-6, patients had to meet at least 3 criteria: C-reactive protein(CRP)> 10 mg/dl; D-Dimer>1µg/ml; Ferritine>1000ng/ml; cytopenia of at least 1 series. To evaluate response, CRP was monitored.

Collected data were age, gender, administration date, vaccination against COVID-19, administered dose, CRP, exitus.

Data were collected from an electronic prescription programme Farmatools® and the computerised medical history, MambrinoXXI®.

Results A total of 32 patients were analysed, of which 90.6% adhered to the protocol for use. Of those who were not adhered 9,4% due to severity of sudden illness.

The mean value of the initial CRP was 5.96mg/dl reducing to 1.14mg/dl after the tocilizumab administration. In 81.3% of patients there was a reduction.

Refering to dose based on weigh, 60% of the patients received the 600mg dose, the remaining 40% receive the dose of 400mg.

Of the total of patients, 43.75% had not been vaccinated against COVID-19, 37.5% of patients treated the final result was exitus, all of them vaccinated.

Conclusion and Relevance A high percentage of patients meet the protocol criteria. The reason why Patients accomplished the protocol was a rapid evolution of the disease.

A high percentage of treated patients were not vaccinated. In general, the vaccine protects from severe disease.

The role of the hospital pharmacist is important in the development of protocols, especially in these cases of off-label uses for a correct treatment approach avoiding indiscriminate use.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of Interest No conflict of interest

5PSQ-067 TRACKING THE OVERAL IN USE AND STRESS STABILITY OF ROMIPLISTIM (N-PLATE®) BY THE EVALUATION OF A SELECTED SET OF CRITICAL QUALITY ATTRIBUTES

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Background and Importance Romiplostim (N-Plate®) is a Fc-fusion protein in which a TPO agonist peptide is associated with the Fc domain of a human antibody. It contains of two identical subunits each consisting of an Fc domain of human immunoglobulin IgG1 linked to a peptide containing two human TPO receptor binding domains. This drug is indicated in the treatment of immune thrombocytopenic purpura (ITP). As proteinaceous based-medicine, romiplostim is indicated to have low stability, thus the studies on the effects of possible in-use mishandling and in stress conditions are welcomed to get knowledge upon its stability and degradation.

Aim and Objectives To evaluate the impact of in use mishandling and forced degradation on romiplostim chemical structure by evaluation of several Critical Quality Attributes (CQAs).

Material and Methods Vials of romiplostim (N-plate, 0.5 mg/mL) were reconstituted as it is indicated by the manufacturer and submitted to several stress stimuli: exposition at 80 °C (2h), smooth shaking (12h), room light and temperature (excursion aprox. 20-24 °C) exposition (24h), accelerated light exposition (24h) and 1 freeze/thaw cycle. The CQAs evaluated were: (A) primary structure, by peptide mapping-RP/UHPLC-(Orbitrap)MS/MS; (B) tertiary structure by Intrinsic tryptophan fluorescence spectroscopy; (C) aggregation by SE-HPLC/DAD; and functional activity (as the capacity to bind to its therapeutic target) by ELISA.

Results Changes in the primary and tertiary structure and the formation of aggregates were detected after romiplostim samples were submitted to high temperature and to room conditions. These changes detected were accompanied by a loss of functionality. Similar effects were caused when stressed by accelerated light exposition. The smooth shake and freeze/thaw cycle stimuli did not affect the CQAs studied.

Conclusion and Relevance This study proves that romiplostim must be reconstituted and administrated avoiding long-time light exposure and elevated temperatures as they can induce the activation of several degradation pathways which cause loss of functionality and aggregation, and thus, losing the original safety, quality and efficacy of the drug.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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