5PSQ-051 IMMUNE RELATED ADVERSE EVENTS IN CANCER PATIENTS TREATED WITH CONTROL POINT INHIBITORS

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Background and importance Despite the clinical benefits of therapy with control point inhibitors in several malignancies, this inhibition is closely linked to a series of immune related adverse events (irAEs). The early detection and management of these is of vital importance.

Aim and objectives To identify and describe irAEs with programmed cell death protein 1 (PD-1) inhibitors and programmed death ligand 1 (PD-L1) inhibitors in clinical practice.

Material and methods A retrospective, descriptive, observational study was conducted in a 400 bed hospital in patients treated with immunotherapy (IT) from 1 January 2016 to 30 October 2018. Variables were age, gender, type of tumour, stage, IT, irAEs and grade, cycles until irAE appearance, irAE treatment and IT suspension. The electronic medical history was reviewed in OrionClinic and IT treatment in Farmis-Oncofarm. The causality of irAEs was ascertained on the basis of the European Society for Medical Oncology (ESMO) algorithms. Statistical analysis was performed with SPSS V.15.

Results A total of 127 patients were treated with an average age of 65 years (range 36–88) and 75% were women: 76% of patients had non-microcytic lung cancer, 7% head-neck, 6% bladder, 5% breast, 4% renal, 2% melanoma and colorectal cancer. In 67% of patients, stage IV tumours were found, in 27% stage III, in 4% stage II and in 2% stage I. Nivolumab was prescribed in 54% of patients, pembrolizumab in 26%, atezolizumab in 13% and durvalumab in 7%. Fifty-two irAEs were identified. The average number of cycles until irAE appearance was 3.25 (range 1–57). The main irAEs were cutaneous (37%), gastrointestinal (23%), pneumonitis (14%) and endocrinological (8%); 64% grade I, 25% grade II, 12% grade III and no grade IV. Treatment was given for 66% of irAEs: oral corticoids (52%), topical corticoids (17%), antihistamines (12%) and hormone replacement therapy (5%). IT was resumed in 83% of patients. By the end of the study period, 31% of patients remained on therapy. Non-continuity was due to progression (55%), irAEs (10%) and other reasons (4%).

Conclusion and relevance The most frequent irAEs in patients receiving IT were cutaneous and gastrointestinal, mostly transitory and grades I–II. They were mostly resolved with corticotherapy and antihistamines. Management of irAEs was presented on the basis of clinical experience; cooperation of patients, caregivers and healthcare professionals is required to watch over their safety to obtain the maximum efficacy with the lowest irAEs possible.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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5PSQ-052 EARLY RESULTS FROM THE EFFECTIVENESS AND SAFETY EVALUATION OF BIOSIMILAR RITUXIMAB AND BRAND RITUXIMAB IN GLOMERULAR INFLAMMATORY DISEASE

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Background and importance Biosimilar drugs should have proven clinical efficacy comparable with the referring brand to obtain authorisation from medicine regulatory agencies. Nevertheless, the effectiveness and safety of off-label uses are not always proved.

Aim and objectives The endpoint of this study was to evaluate the early effectiveness and safety of biosimilar rituximab compared with the referring brand for an off-label use: glomerular inflammatory renal disease.

Material and methods This was an observational retrospective study in patients with glomerular inflammatory disease treated with rituximab (1 g single dose or 1 g two doses). Patients receiving rituximab for the first time between March 2018 and March 2019 were included. Information on patient demographics, underlying disease and associated treatment was collected from the patient medical records. Laboratory data including creatinine, proteinuria, leucocyte and lymphocyte count were collected before (0–60 previous days) and after (0–60 days after) administration of rituximab.

Results Six patients (mean age 59 years (26–74); 50% women) with baseline $6.52 \pm 2.00 \times 10^9/L$ leucocyte count, $2.28 \pm 1.10 \times 10^9/L$ lymphocyte count, 1.63 ± 1.04 mg/dL creatinine and 6.84 ± 3.36 g/24 hours proteinuria were treated with biosimilar rituximab. Thirteen patients (mean age 58 years (25–81); 30% women) with baseline $9.80 \pm 4.62 \times 10^9/L$ leucocyte count, $1.92 \pm 1.13 \times 10^9/L$ lymphocyte count, 1.61 ± 0.85 mg/dL creatinine and 5.81 ± 4.55 g/24 hours proteinuria were treated with brand rituximab. After rituximab administration, these values were $6.13 \pm 1.94 \times 10^9/L$ leucocyte count, $1.30 \pm 0.59 \times 10^9/L$ lymphocyte count, 1.16 ± 1.19 mg/dL creatinine, 3.29 ± 0.58 g/24 hours and proteinuria for the biosimilar group, and $8.77 \pm 3.78 \times 10^9/L$ leucocyte count, $1.67 \pm 1.13 \times 10^9/L$ lymphocyte count, 1.56 ± 1.19 mg/dL creatinine and 3.36 ± 2.20 g/24 hours proteinuria for the brand group. After rituximab administration, CD19+ lymphocytes become negative in both groups (5/5 for the biosimilar group; 6/6 for the brand group). There were two total remissions, one partial remission and three non-responses with the biosimilar rituximab, and one total remission, five partial remissions and seven non-responses with the brand rituximab. Biosimilar rituximab was well tolerated in 6/6 patients and no infections developed. Brand rituximab was well tolerated in 11/13 patients and 4/13 patients showed an infectious episode. No significant differences were observed for the treatment response between the two groups.

Conclusion and relevance Biosimilar rituximab showed an effectiveness and safety profile similar to brand rituximab. Nevertheless, the small sample limits the statistical power and suggests a larger study is required to confirm these results, which we are currently working on.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

5PSQ-053 OFF-LABEL USE OF RITUXIMAB IN SYSTEMIC AUTOIMMUNE DISEASES

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Background and importance A large number of patients with systemic autoimmune diseases (SAD) do not respond or relapse to firstline therapies. Current guidelines recommend the off-label use of rituximab for many severe refractory SAD even though most of the available data rely on observational studies and case reports

Aim and objectives The aim of this study was to analyse the efficacy and safety of the off-label use of rituximab for patients with severe refractory SAD in a tertiary hospital

Material and methods Off-label use of rituximab between January 2016 and December 2018 was reviewed. Clinical data were collected retrospectively. Therapeutic response was evaluated after 12 months of rituximab initiation based on clinical judgement: complete response was defined as no disease activity, partial response as a significant improvement (>50% of initial disease activity) and no response if there was no improvement or worsening of symptoms

Results A total of 52 applications were analysed. There were 28 men (54%) and 24 women (46%) with a mean age of 54.41 years (SD 15.31). The indications for rituximab included systemic lupus erythematosus (SLE) (17.3%), glomerulonephritis (15.4%), inflammatory myopathy (9.6%), cryoglobulinaemia (7.7%), polyneuropathy (7.7%) and other SAD. As for previous therapies, 42 patients (82.4%) received corticosteroids and 37 (71.2%) received at least one immunosuppressive drug.

From all patients with an assessable treatment (n=47), 70.2% achieved an improvement in disease after 12 months: 34% (n=16) a complete response and 36% (n=17) a partial response. The most favourable results were found in the treatment of SLE, glomerulonephritis, cryoglobulinaemia, multiple sclerosis and optic neuromyelitis in which >80% of patients obtained a complete or partial response.

Adverse events were reported in 22 patients (42.3%): the most frequent were infections (n=7) followed by infusion related reactions (n=3). No serious or death related adverse events were reported

Conclusion and relevance Rituximab had acceptable tolerance and reduced disease activity in some severe refractory SAD. Future controlled trials are needed to confirm the potential use of rituximab in patients with SAD. In the meantime, it is necessary to closely follow-up these patients.

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5PSQ-054 EXAMINATION OF A NEW METHOD FOR ANALYSING IDENTITY AND CONCENTRATION OF DRUGS IN READY TO USE PREPARATIONS: PROOF OF CONCEPT OF THE DRUGLOG SYSTEM

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Background and importance The increasing awareness of drug therapy safety and at the same time immense skills shortages pose new challenges for hospital pharmacies. The number of ready to use preparations has increased, especially in high risk fields such as oncological and paediatric medicine. For immediate quality control, in accordance with the German and European Pharmacopoeia, there is a need for analytical methods which (1) do not require large volumes for testing and (2) are safe and fast in processing with accurate results. Pharmacolog (Upsala, Sweden) promotes the UV/Vis spectrometer DrugLog with these features.

Aim and objectives The aim of examining DrugLog was to test the reliability and precision of the method as well as the process for optimisation during quality control. As part of this, sample extraction without further processing in terms of everyday usability and safety, especially in the analysis of cytostatic drugs, was examined.

Material and methods The drugs norepinephrine, midazolam, atropine and cytarabine were tested during the first step. Standard curves of each drug were created in the system. Samples of ready to use preparations were analysed without further processing with 0.5 mL sample volumes each in micro UV single use cuvettes with a lid. For preparations of cytarabine cuvettes, Luer-Lock closures were used. The content as well as the identity of drugs were determined simultaneously in the instrument. The method of the DrugLog system was compared with the established methods.

Results All tested substances were analysed reliable with the new method. The cytostatic drug cytarabine was analysed without cytotoxic contamination of staff or equipment. Measurement of atropine was possible with the DrugLog system at a minimum concentration of 0.05 mg/mL even with low UV absorption. The total time required for the analyses was reduced by 50–75% compared with the established UV-Vis analysis, depending on the drug analysed.

Conclusion and relevance DrugLog simplified processing, provided maximum work safety when dealing with cytotoxic drugs and provided stable results for the tested drugs. Each drug required a separate calibration. For substances without UV activity or very similar spectra, the methodology has limitations. Future investigations are planned, in particular for application in paediatric settings.

REFERENCES AND/OR ACKNOWLEDGEMENTS

German and European Pharmacopoeia.

No conflict of interest.