pH of 5.4. There are no published data to support how pH affects mitomycin C stability in 0.9% sodium chloride solutions (NSS).

Aim and objectives To study the stability of mitomycin C in NSS under different pH conditions and storage temperatures.

Material and methods A stability study was carried out in eight NSS with a commonly used mitomycin C concentration of 0.12 mg/mL. Solutions were prepared in duplicate for each pH: 4.5, 5.5, 6 and 7. The pH was adjusted with sodium hydroxide or phosphoric acid. Four solutions were stored at room temperature and four at 5°C. Mitomycin C concentration was assessed at 0, 30, 60, 120 and 300 min and 24 hours by high performance liquid chromatography. The areas obtained were compared with the initial area (time 0 min) to calculate the remaining mitomycin C percentage. A 10% level of degradation is assumed as the limit in terms of stability.

Results Remaining mitomycin C percentages were calculated. Analysing the results at room temperature, the remaining mitomycin C percentages were 98.5% at 30 min; 97.2% at 60 min; 92.7% at 120 min; 89.3% at 300 min; and 88.4% at 1 hour at pH=7. Remaining percentages were 99.2%, 98.6%, 97.6%, 95.8% and 87.4%, respectively, at pH=6. Percentages were 98.9%, 98.2%, 96.6%, 93.5% and 87.3%, respectively, at pH=5.5. Percentages for pH=4.5 were 98.0%, 96.7%, 88.1%, 85.4% and 83.2%, respectively. The concentration of all solutions remained above 90% of the initial concentration after 1 hour, regardless of the pH value, in contrast with the values at 24 hours.

Analysing the concentrations at 5°C, the remaining mitomycin C percentages were 99.2%, 98.4%, 97.3%, 94.9% and 90.0% at pH=7. Remaining percentages were 99.5%, 99.2%, 98.6%, 97.4% and 94.0%, respectively, at pH=6. Percentages were 99.8%, 99.6%, 99.2%, 98.4% and 95.3%, respectively, at pH=5.5. Percentages for pH=4.5 were 99.8%, 99.7%, 99.3%, 98.5% and 93.1%, respectively, for each time studied. All solutions stored in the fridge were stable over the 24 hours of the study.

Conclusion and relevance We demonstrated that the stability of mitomycin C solutions decreased over time and with lower pH values in NSS. Furthermore, room temperature significantly affected mitomycin C stability. However, degradation was greatly reduced at 5°C, regardless of pH. This proves that mitomycin C solutions in NSS can be stored in the fridge for 24 hours.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

3PC-019 IN USE PHYSICOCHEMICAL AND MICROBIOLOGICAL STABILITY OF DILUTED SOLUTIONS OF THE MONOCLONAL ANTIBODY NIVOLUMAB

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10.1136/ejhp-pharm-2020-eahpconf.66

Background and importance Nivolumab, a fully human IgG4 anti-PD-1 monoclonal antibody, is available as a concentrated solution for intravenous (IV) injection and diluted in 0.9% saline. These solutions are reported to be physically and chemically stable for 24 hours at 2–8°C and a maximum of 8

hours at 20–25°C. As the ‘real world’ use after dilution in IV infusion bags may exceed the manufacturer’s recommendations, ‘in use’ studies assessing their stability is important as the formulation components are diluted and may not be able to protect the protein against degradation or denaturation.

Aim and objectives The aim of the study was to assess physicochemical and microbiological in use stability of diluted solutions of nivolumab stored at 2–8°C.

Material and methods Four polyolefin bags of nivolumab were compounded under aseptic conditions at a concentration of 2 mg/mL with 0.9% saline solution and stored at 2–8°C over a 7 day period. At selected time points, different methods were used to evaluate stability: pH, osmolality, turbidimetry, dynamic light scattering (DLS), size exclusion chromatography-high performance liquid chromatography (SEC-HPLC) and gel electrophoresis. Microbiological assays were also performed after 30 days.

Results Diluted nivolumab solutions remained clear and colourless with no visible particles during the test period. Physicochemical analyses demonstrated that all samples were not affected in terms of formation of subvisible particles or changes in pH or osmolality. Results of SEC-HPLC analyses revealed no change in high molecular weight, soluble aggregate or low molecular weight fragmented product. Moreover, the relative ratio remained constant over time. These results were also confirmed by gel electrophoresis under both non-reducing and reducing conditions as no change in band distribution was detected. Finally, no bacterial or fungal contamination was observed in any of the samples tested after 30 days of storage.

Conclusion and relevance These analyses demonstrated that nivolumab under the dilution conditions required for IV infusion can be stored for 7 days at 2–8°C with no evidence of physical or chemical alteration. When further data are available on how quality and potency may vary over time under different environmental factors, these results may support the possibility of compounding ‘dose banding’ batches in order to improve the patient’s management, pharmacy workload and reduce costs.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

3PC-020 PHYSICOCHEMICAL STABILITY OF 25 MG/ML PEMETREXED DIARGININE IN PARTIALLY USED VIALS AND 3 AND 12 MG/ML DILUTED IN DEXTROSE 5% IN POLYOLEFIN BAG

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10.1136/ejhp-pharm-2020-eahpconf.67

Background and importance A new pemetrexed salt, pemetrexed diarginine (PDA), was recently marketed by Mylan. The product is a ready to dilute 25 mg/mL solution. The manufacturer indicates 24 hour stability after dilution in dextrose 5% (D5W).

Aim and objectives To study the stability of: (1) PDA in D5W polyolefin bag at 3 and 12 mg/mL protected from light (PFL) at 2–8°C and at 25°C; (2) PDA vial at 25 mg/mL partially used and perforated with a plastic spike PFL at 2–8°C and at 25°C; (3) PDA in D5W polyolefin bag at 3 and 12 mg/mL, not PFL at room temperature; (4) PDA vial at 25 mg/mL