3PC-016 STABILITY OF COMPOUNDED NIVOLUMAB SOLUTION AFTER PNEUMATIC SYSTEM TRANSPORTATION

^{1,2}L Camuffo*, ³F Selmin, ⁵F Vasilie, ¹M Rivano, ¹M Piccoli, ¹G Mangoni, ¹L Cancanelli, ⁴M Fazio, ³F Cilurzo, ³P Minghetti. ¹University of Milan, School in Hospital Pharmacy, Milan, Italy; ²Humanitas Research Hospital, Pharmacy, Rozzano, Italy; ³University of Milan, Department of Pharmaceutical Sciences, Milan, Italy; ⁴San Raffaele Hospital, Pharmacy, Milan, Italy; ⁵University of Milan, Department of Chemistry, Milan, Italy

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Background and importance Pneumatic delivery is not recommended for medicinal products that could undergo physical alteration of the active ingredient, such as protein denaturation (Peak, 2003). A review of the literature reveals that the solution air-liquid interface and number of travel cycles can be risk determining factors for compounded stability of monoclonal antibodies after pneumatic delivery (Vieillard *et al*, 2012; Vieillard *et al*, 2013; Vieillard *et al*, 2014). In our hospital, all compounded monoclonal antibodies are delivered via a pneumatic system to the oncologic day hospital unit from the pharmacy compounding department.

Aim and objectives To investigate the stability of nivolumab compounded solution after pneumatic delivery, and the effect of residual air inside the infusion bag.

Material and methods The following nivolumab samples, diluted to 2.4 mg/mL in a prefilled 0.9% sodium chloride polyolefin infusion bag, were prepared: sample nivolumab, not undergoing pneumatic delivery, sample PNA, with residual air, and sample PN, without residual air, both undergoing single travel inside the pneumatic delivery system. On the day of preparation, all samples were analysed for pH, osmolality, turbidity, dynamic light scattering (DLS), size exclusion chromatography-high performance liquid chromatography (SEC-HPLC) and nuclear magnetic resonance (NMR).

Results All samples were clear, without particulate or precipitates, and turbidity free at 350 nm. pH values shifted from 5.77 to 5.92. Osmolality values ranged from 286 and 296 mOsm/kg. DLS revealed a monodisperse peak at about 11 nm, with similar shape and intensity. SEC-HPLC did not reveal any peak retention time variations, and NMR did not reveal any modifications regarding peak shape or intensity.

Conclusion and relevance No difference in physical or chemical stability was found between compounded nivolumab solutions not undergoing and undergoing single travel inside the pneumatic system. The presence of the air-liquid interface inside the solution bag was not risk determining for solution stability. The pneumatic delivery system at our hospital can be used for delivery of compounded nivolumab solution to the oncologic day hospital.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

3PC-017 INCREASING PHARMACY PRODUCTIVITY BY EXPANDING THE ROLE OF THE INTRAVENOUS COMPOUNDING ROBOT IN A COMPREHENSIVE CANCER CENTRE

¹M Capilli*, ²M Federici, ³T Comandone, ¹G Maffei, ⁴F Foglio, ⁴L Omini, ⁴F Enrico. ¹University of Turin, Drug Science and Technology-School of Specialisation in Hospital Pharmacy, Turin, Italy; ²Loccioni, Angeli Di Rosora, Ancona, Italy; ³University of Turin, Drug Science and Technology, Turin, Italy; ⁴Fpo Irccs Candiolo, Hospital Pharmacy, Candiolo, Italy

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Background and importance In a comprehensive cancer centre, injectable anticancer drugs are compounded in the pharmacy based preparation unit with the compounding robot APOTECACHemo to guarantee a high level of quality and safety. In 2018, the oncology pharmacy implemented workflow improvements to manage the growing workload due to the centralisation of the activities of a hospital's satellite pharmacy.

Aim and objectives The aim of the study was to analyse the pharmacy workflow and impact of the robotic system on turnaround time to meet increasing pharmacy productivity.

Material and methods Data were collected from the hospital information system and the workflow management software APOTECAManager, and examined over a 2 year period (2017–2018). The total annual throughput in terms of doses prepared and patients treated were determined. Productivity, number of active ingredients processed, average usage time per day and dosage accuracy (ie, per cent discrepancy between compounded and prescribed dose) were calculated for the robotic system. Medication turnaround time (MTAT) for outpatients, defined as total time from the release of a medication order by the prescriber to administration of the medication to the patient, was measured over 3 months.

Results Overall, the annual doses prepared and patients treated increased by 18% (from 18 574 doses/year in 2017 to 22 754 doses/year in 2018) and by 10% (from 1421 patients/year in 2017 to 16 604 patients/year in 2018), respectively. The robot was used to compound 47% of the overall doses prepared in 2017 (8677 doses/year) compared with 57% in 2018 (13 047 doses/year). The average usage time of the robot increased by 58% (from 2.09 hours/day in 2017 to 5.01 hours/day in 2018), while the number of active ingredients processed rose from 20 in 2017 to 30 in 2018. Overall, 95.0% of doses prepared with the robot showed an error <2.0%. The average MTAT for outpatients was lowered by 24.7% (from 2.8 hours in 2017 to 2.1 hours in 2018).

Conclusion and relevance The study revealed that the oncology pharmacy was able to meet escalating demands of ready to administer anticancer drugs by satellite hospitals, by making more use of the robotic system without increasing pharmacy staff. The pharmacy workflow changes enabled reduced MTAT and better order processing efficacy, thereby providing improved patient care.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

3PC-018 MITOMYCIN C STABILITY ACCORDING TO PH AND TEMPERATURE CONDITIONS

G Miralles Andreu*, I Truyols García, M Pomares Bernabeu, L Soriano Irigaray, L Peral Ballester, A Navarro Ruiz. Hospital General Universitario De Elche, Hospital Pharmacy Department, Elche, Spain

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Background and importance Mitomycin C is used in different regimens for the treatment of bladder, anus and lung cancer. According to the data sheet, reconstitution of the vial should be carried out with water for preparation of injectables or with 20% dextrose. Despite this, sodium chloride solutions are commonly used for its administration. However, it is known that the stability of mitomycin C molecule is affected by the pH of the preparation as degradation increases with pH values <7. Sodium chloride solutions have an approximate

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

¹M Rivano*, ²F Selmin, ¹L Camuffo, ¹L Cancanelli, ¹G Mangoni, ¹MA Piccoli, ³G Longobardo, ²F Cilurzo, ²P Minghetti. ¹University of Milan, School of Hospital Pharmacy, Milan, Italy; ²University of Milan, Department of Pharmaceutical Sciences, Milan, Italy; ³Ircs San Raffaele, Pharmacy, Milan, Italy

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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

YE Nisse*, J Vigneron, N Sobalak, B Demoré. Chru Nancy, Pharmacy, Vandoeuvre-Lès-Nancy, France

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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