# STORAGE OF NIVOLUMAB PEMBROLIZUMAB AND DARATUMUMAB FOR 14 DAYS AFTER COMPOUNDING IN THE HOSPITAL PHARMACY: A MICROBIOLOGICAL STABILITY STUDY

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## BACKGROUND AND IMPORTANCE

Viable microorganisms and/or endotoxins administered parenterally via contaminated preparations, may lead to nosocomial infections, SIRS/sepsis and increased mortality of patients. The pharmacist has the responsibility to ensure that the product is stable in the final administrated

## AIM AND OBJECTIVES

To verify if monoclonal antibodies as nivolumab, pembrolizumab and daratumumab are promoters or inhibitors for microbial growth. Moreover, the microbiological stability of dilutions at clinically relevant concentrations were verified over a 14-day period.

## MATERIALS AND METHODS

Samples, reconstituted according to summary of product characteristics (SPC) in 1 ml syringes, were injected into standardized suspension of P. aeruginosa, S. aureus and C. albicans [1]. At different time points (i.e. 0, 1, 3, 5, 24, 48 and 144 h) an aliquot of 0.01 mL, containing about 100 CFU, was transferred to the trypticase soy agar plate and sabouraud dextrose agar+chloramphenicol plate. After 24 h incubation at 37 ° C, samples were assayed. Moreover, a total of 24 syringes were stored for 1, 3, 6, 7, 10 and 14 days before being incubated to determine the microbiological stability according to EP method.

## RESULTS

The results show that 144 hours after inoculation no colony-forming units were detected for the C. albicans and S. aurerus strains. The only microorganism that survived after 5 days was P. aeruginosa.

| CONTROL / DRUG | *C. albicans* (CFU Log/ml) | | | | | | |
|---|---|---|---|---|---|---|---|
| **ore** | **0** | **1** | **3** | **5** | **24** | **48** | **144** |
| 0,9 % NaCl | 2,30 | 2,70 | 2,00 | 3,00 | 3,04 | 2,78 | 0 |
| Nivolumab | 2,48 | 2,00 | 2,30 | 2,00 | 3,15 | 2,30 | 0 |
| Pembrolizumab | 2,78 | 2,00 | 2,60 | 2,48 | 2,90 | 2,00 | 0 |
| Daratumumab | 2,85 | 2,30 | 2,30 | 2,48 | 2,48 | 2,00 | 0 |

| CONTROL / DRUG | *S. aureus* (CFU Log/ml) | | | | | | |
|---|---|---|---|---|---|---|---|
| **ore** | **0** | **1** | **3** | **5** | **24** | **48** | **144** |
| 0,9 % Na Cl | 3,90 | 3,60 | 4,08 | 4,26 | 4,08 | 4,02 | 0 |
| Nivolumab | 4,00 | 3,70 | 3,30 | 3,73 | 3,71 | 3,18 | 0 |
| Pembrolizumab | 4,00 | 3,98 | 3,60 | 3,66 | 3,66 | 3,62 | 0 |
| Daratumumab | 3,90 | 3,78 | 3,88 | 3,57 | 3,57 | 3,49 | 0 |

| CONTROL / DRUG | *P. aeruginosa* (CFU Log/ml) | | | | | | |
|---|---|---|---|---|---|---|---|
| **ore** | **0** | **1** | **3** | **5** | **24** | **48** | **144** |
| 0,9 % Na Cl | 3,30 | 3,30 | 3,30 | 3,48 | 3,32 | 3,11 | 3,51 |
| Nivolumab | 3,63 | 3,26 | 3,00 | 3,46 | 3,41 | 3,45 | 3,43 |
| Pembrolizumab | 3,60 | 3,40 | 3,18 | 3,26 | 3,45 | 3,28 | 3,26 |
| Daratumumab | 3,30 | 3,08 | 3,26 | 3,48 | 3,23 | 3,08 | 3,08 |

Comparing the control with the samples analysed, no significant growths or reductions in microorganisms were observed. The samples were all clear after 14 days of incubation.

## CONCLUSION AND RELEVANCE

Compared to the control, no significant growths or reductions of microorganisms are observed thus indicating that the monoclonal antibodies investigated cannot be used by the strains as substrates for their survival. It can also be deduced that these monoclonal antibodies have no bactericidal or bacteriostatic action. In these use condition these monoclonal antibodies were microbiologically stable for 14 days.

In conclusion, when data on “in-use” stability” are available for a period of 14 days, a new model of patient management in Day Hospital and drug preparation in Hospital Pharmacy could be organized.

References

1. I Sarakbi, M Federici, I Krämer, Viability of microorganisms in novel chemical and biopharmaceutical anticancer drug solutions, European Journal of Parenteral & Pharmaceutical Sciences 2015;20(1): 5-12