Background:
Ceftolozane (CLZ) is a novel cephalosporin and commercially available in combination with the beta-lactamase inhibitor tazobactam (TAZ) under the brand name Zerbaxa®. Zerbaxa® is a new option for the treatment of multidrug-resistant pseudomonas aeruginosa strains and extended-spectrum beta-lactamase (ESBL)-producing enterobacteria [1]. Cephalosporins show like all betalactams a time dependent antibacterial activity. In intensive care patients, the PK/PD target is usually to keep the plasma concentration of the cephalosporin above the pathogen's MIC throughout the whole dosing interval (100%T > MIC) [2]. For the beta-lactamase inhibitor tazobactam a time-dependent action is assumed as well [3].

According to the German prescribing information Zerbaxa® is administered as short infusion in sodium chloride 0.9% or glucose 5%. As shown by the simulation of the plasma concentrations over time (Figure 1), the pharmacokinetic target parameters are not reliably reached by short infusion. Especially the faster elimination of TAZ compared to CLZ leads to very low TAZ trough concentrations. In contrast, continuous administration may lead to the achievement of even stricter PK/PD targets (100% >4xMIC), which are often recommended for continuous application to prevent the development of resistance [4].

However, continuous application requires sufficient stability of both agents throughout the infusion. Although a literature search suggests sufficient stability of both substances [5], the German prescribing information for Zerbaxa® does not provide any specific information on prolonged storage at room temperature under exposure to light. The purpose of this investigation was to provide these stability data to the treating physicians.

Methods:

- Zerbaxa® was diluted with NaCl 0.9 % and glucose 5 % to obtain ceftolozan/tazobactam concentrations of 20/10 mg/ml and 10/5 mg/L (n=1 each).
- These CLZ/TAZ solutions were stored in polypropylene-tubes at room temperature (22° C) without protection from light for 24 h.
- CLZ and TAZ concentrations were determined at the start of the experiment and after 1, 4, 8 and 24 h using HPLC-UV.
- In addition, at these time point the solutions were visually examined and the pH values were determined.

Results:

- Ceftolozan and tazobactam were stable for 24 h (> 98.5 % of baseline) under real-life conditions (room temperature, light exposure and storage in polypropylene-tubes).
- Visual appearance and pH of the solutions did not change over time.

Conclusion:
Zerbaxa® is stable in sodium chloride 0.9% and glucose 5% at room temperature for at least 24 hours. This investigation, performed by the hospital pharmacy, provides the attending physician with the stability data needed for prolonged or continuous infusion.

Literature: