Ceftolozane/tazobactam: New treatment option for severe infections, but no proof of superiority

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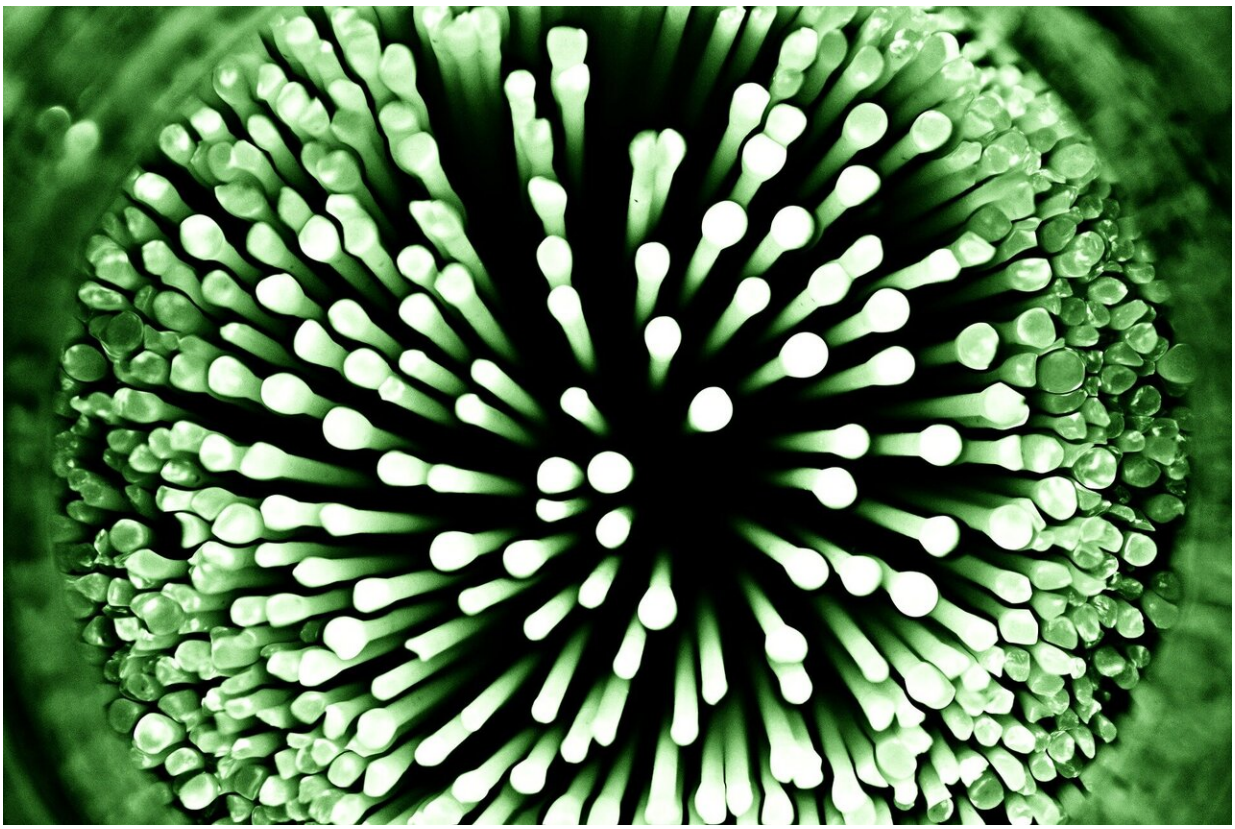

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The combination of ceftolozane with tazobactam broadens the range of antibiotic therapy in adults with severe infections of the lungs, the

urinary tract, the renal pelvis and the abdominal cavity. In view of the increasing resistance development in bacteria, this drug combination is therefore an important additional treatment option.

The German Institute for Quality and Efficiency in Health Care (IQWiG) has investigated in four early benefit assessments whether ceftolozane/tazobactam not only offers a broadening of the treatment options in severe infections of the different organs, but also an added benefit in comparison with individual antibiotic therapy, which takes the respective resistance situation into account.

The result: There are no informative studies for such a comparison, particularly, as the local and individual resistance situation was not sufficiently considered in the approval studies. In the overall consideration, there was therefore no proof of advantages or disadvantages of ceftolozane/tazobactam on the basis of the available data.

Comparison was too narrow and provided no hint of added benefit

To avoid the development of resistances, antibiotics should be used as specifically as possible, i. e. depending on the local pathogen spectrum and the individual pathogen sensitivity. The local resistance situation also has to be taken into account, as the spread of resistant germs can vary greatly from place to place.

The approval studies underlying the four drug manufacturer dossiers are principally high-quality randomized controlled trials (RCTs). However, they only compared the new drug combination in the therapeutic indications for lungs and abdominal cavity, and for urinary tract and renal pelvis only with one other antibiotic each—without showing

relevant differences between the intervention and the control groups. This very restricted comparison does not concur with the much broader treatment options specified as suitable therapy according to the appropriate comparator theapy. It can also not be inferred from the study data that the local resistance situation in the respective study centers and the individual resistance situation after pathogen detection were sufficiently taken into account.

"This is very regrettable," says Thomas Kaiser, Head of IQWIG's Drug Assessment Department, "because the development of new antibiotics is principally necessary and very welcome. However, to draw conclusions on the added benefit, we need studies that consider the local and individual resistance situation adequately. Unfortunately, this was not the case in the studies presented."

However, a comparison with further treatment options under consideration of the local pathogen spectrum, the resistance profile, the risk of infection with multi-resistant pathogens, and the pathogen sensitivity on the basis of an antibiogram offers promising opportunities for proof of an added value of new antibiotics.

Overall, no hint of an added benefit of ceftolozane/tazobactam could be derived in comparison with the appropriate comparator therapy; an added benefit is therefore not proven.

No advantage of ceftolozane/tazobactam can be inferred from in vitro data

The sensitivity or resistance of a pathogen for different antibiotics can be studied outside a concrete treatment situation, i. e. in the laboratory (in vitro). It is principally conceivable to derive an advantage of a new antibiotic on the basis of in vitro data if the new drug shows high

efficacy, whereas the drugs hitherto available in the therapeutic indication show (almost) no efficacy.

The in vitro data in the manufacturer dossier are incomplete, however, as not all available drugs were assessed. Furthermore, the analyses of these in vitro data show that several tested drugs are effective in the investigated pathogens and are a possible treatment option besides ceftolozane/tazobactam.

G-BA decides on the extent of added benefit

The dossier assessments are part of the early benefit assessment according to the Act on the Reform of the Market for Medicinal Products (AMNOG) supervised by the Federal Joint Committee (G-BA). After publication of the dossier assessments, the G-BA conducts commenting procedures and makes decisions on the extent of the added benefit.

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