Table 1. Continued

| Patient | Genotype (PR) | Phenotype (PR) FC to DRV | Drugs taken with darunavir/ritonavir | Active drugs in OBR | Viral load drop (log copies/mL) at week 4 | Weeks on darunavir/ritonavir | Viral load <50 copies/mL
<table>
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<tbody>
<tr>
<td>19</td>
<td>L10I, I54V, L63P, L90M, I93L</td>
<td>NA</td>
<td>tenofovir, emtricitabine</td>
<td>none</td>
<td>1.81</td>
<td>4</td>
<td>yes</td>
</tr>
</tbody>
</table>

FC, fold change; when >10 this is interpreted as resistance to DRV; NA, data not available; PR, protease; OBR, optimized background regimen.

*Indicates if patients achieve and maintain a viral load <50 copies/mL during follow-up.

**DRV/ritonavir resistance mutations are underlined.**

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**Transparency declarations**

None to declare.

**References**


**Use of very old and very new antibiotics in intensive care units in Germany**

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Sir,

The increasing problem of multidrug-resistant Gram-positive and Gram-negative bacteria causing severe infections has led to a re-evaluation of old drugs and the application of newly developed reserve antibiotics.

Polymyxins and chloramphenicol were discovered in 1947. Both drugs were gradually withdrawn from clinical practice in Europe and the USA because of reports about toxicity. However, the emergence of Pseudomonas aeruginosa and Acinetobacter baumannii strains that are resistant to almost all available antibiotics has led to a revival of polymyxins given parenterally. Chloramphenicol is still prescribed to a majority of the populations in developing countries because of its low cost of production and its broad spectrum. Fosfomycin, which was discovered in 1969, is effective against numerous Gram-positive and Gram-negative bacteria and acts synergistically against methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE) and multiresistant P. aeruginosa strains. Quinupristin/dalfopristin, linezolid and tigecycline are considered to be new antibiotics with a spectrum that also covers multiresistant pathogens; they were approved by the FDA in...
Quinupristin/dalfopristin is effective against Gram-positive bacteria including MRSA and vancomycin-resistant Enterococcus faecium, linezolid is effective against Gram-positive bacteria including MRSA and VRE and tigecycline is effective against Gram-positive and Gram-negative bacteria including MRSA, VRE and extended-spectrum β-lactamase producers.3

Although in recent years data on antibiotic use have become available from surveillance systems such as European Surveillance of Antimicrobial Consumption (ESAC), there are no multicentre data on the consumption of reserve antibiotics.4 The aim of our study was to provide such data for intensive care units (ICUs), which are known high-risk areas for resistant pathogens.

Data from 44 ICUs in Germany participating in the project Surveillance of Antimicrobial Use and Resistance in ICUs (SARI) were analysed from 2001 through 2006.5 Consumption was measured as antimicrobial usage density (AD) and expressed as defined daily doses (DDD) and normalized per 1000 patient-days (pd), one DDD being the standard adult daily dose of an antimicrobial agent for 1 day of treatment defined by the WHO (by DDD index 2006). SARI collects data on 13 pathogens including MRSA, VRE, imipenem-resistant P. aeruginosa and Escherichia coli resistant to third-generation cephalosporins. Isolates documented were non-duplicate.

Figure 1. Yearly use of new antimicrobials (tigecycline, linezolid and quinupristin/dalfopristin) and old antimicrobials (amphenicols, polymyxins and fosfomycin), and resistance rates of MRSA, vancomycin-resistant *E. faecium*, imipenem-resistant *P. aeruginosa* and *E. coli* resistant to third-generation cephalosporins in SARI-ICUs from 2001 to 2006.

1999, 2000 and 2005, respectively. Quinupristin/dalfopristin is effective against Gram-positive bacteria including MRSA and vancomycin-resistant *Enterococcus faecium*, linezolid is effective against Gram-positive bacteria including MRSA and VRE and tigecycline is effective against Gram-positive and Gram-negative bacteria including MRSA, VRE and extended-spectrum β-lactamase producers.3

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Consumption of old antibiotics, i.e. amphenicols, polymyxins (parenteral or for inhalation) and fosfomycin, proved to be fairly stable over a period of 6 years and constituted 0.5% of total antibiotic use (without sulbactam) in 2001 and 0.6% in 2006. Maximum use was 1.1% in 2002.

Use of new antibiotics, i.e. quinupristin/dalfopristin, linezolid and tigecycline, increased steadily from 0.1% in 2001 to 1.1% in 2003 and 2.0% in 2005. In 2006 it accounted for 2.9% of total antibiotic consumption. Quinupristin/dalfopristin was rarely used, in contrast to linezolid, where consumption continuously grew to a total of 2.6% of total antibiotic use in 2006.

Antibiotic use data and resistance data of selected pathogens are given in Figure 1. MRSA resistance rates fluctuated without a clear trend between 26.4% in 2001 and 23.2% in 2006 (*P* = 0.106, Cochran-Armitage trend test, two-sided). The same was true for imipenem-resistant *P. aeruginosa* (24.1% in 2001 and 22.5 in 2006, *P* = 0.422). In contrast, *E. coli* resistant to third-generation cephalosporins increased continuously from 1.1% in 2001 to 5.6% in 2006 (*P* < 0.001). Vancomycin-resistant
E. faecium showed a sharp peak in resistance in 2004/2005 of 5.2%/5.6%, but decreased again to 1.8% in 2006 (P = 0.037).

Linezolid consumption steadily increased from 2001 to 2006, although MRSA resistance did not. The rise was not curtailed by the drop of vancomycin-resistant E. faecium rates in 2006. The preceding increase of vancomycin resistance in E. faecium in 2004/2005 was due to an outbreak that affected only two SARI-ICUs in the South West of Germany.

Old antibiotics such as fosfomycin, with a consumption of 6.6 DDD/1000 pd in 2006, accounted for <1% of total antibiotic consumption. Use did not increase over time.

Although there are reports on multi- or even pan-resistance evolving in P. aeruginosa, A. baumannii and K. pneumoniae, and a revival of polymyxins applied parenterally or by inhalation, they were not used in 2006 in 41 German ICUs.6

However, it has to be taken into account that in SARI no data are available on multiresistance. Furthermore, these data might only reflect the situation in German ICUs. ICUs might differ in other European regions with a different resistance situation.

This study reports data on use of linezolid, quinupristin/dalfopristin, tigecycline, polymyxins, amphenicols and fosfomycin and provides benchmarking data on these reserve antimicrobials for use in ICUs.

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We would like to thank all the SARI-ICUs that provided data for this study.

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Transparency declarations

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References


