“M/R CVC use is not associated with long term increased staphylococcal resistance to tetracyclines and rifampin; however, it represents a crucial strategy to significantly decrease CRBSI in critically ill cancer patients.”
UNMATCHED EVIDENCE

In vitro studies show that our M+R catheters maintain an effective zone of inhibition for up to 21 days—longer than any other catheters. Over two decades of evidence, including more than 21 peer-reviewed studies and meta-analyses, prove M+R’s ability to prevent bloodstream infections.

Meta-analyses Comparing Antimicrobial CVCs

<table>
<thead>
<tr>
<th>CVCs (n/N)</th>
<th>OR</th>
<th>OR (95%CI)</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard Compares</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silver iontophoretic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monnet et al (2005)</td>
<td>1/262 0/252</td>
<td>D.14 (0.00–7.09)</td>
<td>262</td>
</tr>
<tr>
<td>Cornal et al (2005)</td>
<td>1/103 4/103</td>
<td>3.40 (0.58–19.97)</td>
<td>NA</td>
</tr>
<tr>
<td>Total (FEM)</td>
<td>2/365 4/355</td>
<td>1.98 (0.45–9.95)</td>
<td>NA</td>
</tr>
<tr>
<td>Test for heterogeneity: Q=21.1 (4 df), p&lt;0.01, I²=0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second generation CSS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rapp et al (2005)</td>
<td>3/103 1/104</td>
<td>D.39 (0.05–2.87)</td>
<td>199</td>
</tr>
<tr>
<td>D’Andrea et al (2005)</td>
<td>3/84 1/84</td>
<td>D.45 (0.13–1.61)</td>
<td>24</td>
</tr>
<tr>
<td>Total (FEM)</td>
<td>7/582 4/582</td>
<td>0.47 (0.20–1.10)</td>
<td>154</td>
</tr>
<tr>
<td>Test for heterogeneity: Q=10.1 (2 df), p&lt;0.01, I²=0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minocycline–rifampicin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rand et al (1997)</td>
<td>1/126 0/130</td>
<td>0.14 (0.00–0.65)</td>
<td>19</td>
</tr>
<tr>
<td>Markel et al (1999)</td>
<td>2/39 0/38</td>
<td>0.14 (0.01–2.20)</td>
<td>20</td>
</tr>
<tr>
<td>Chatzinikolaou et al (2003)</td>
<td>1/19 0/19</td>
<td>0.13 (0.00–6.61)</td>
<td>64</td>
</tr>
<tr>
<td>Less et al (2004)</td>
<td>11/180 0/187</td>
<td>0.52 (0.20–1.37)</td>
<td>34</td>
</tr>
<tr>
<td>Hanna et al (2004)</td>
<td>14/174 3/182</td>
<td>0.25 (0.09–0.65)</td>
<td>16</td>
</tr>
<tr>
<td>Total (FEM)</td>
<td>32/993 9/993</td>
<td>0.29 (0.16–0.52)</td>
<td>21</td>
</tr>
<tr>
<td>Test for heterogeneity: Q=2.93 (4 df), p&lt;0.01, I²=0%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CRBSI in trials comparing antimicrobial CVCs with standard CVCs

Within each subgroup, the studies are ordered by increasing mean catheter indwell duration. The vertical line represents the null hypothesis of no difference between test and control groups. Odds ratios (ORs) and 95% CIs are shown. Black diamonds indicate the pooled ORs (95% CIs). Results of the Peto fixed-effects model (FEM) are quoted unless substantial heterogeneity is present, in which case the results of the DerSimonian-Laird random-effects model (REM) are stated. NNT=number needed to treat (the expected number of people who need to receive the antimicrobial rather than the standard CVC for one additional person to avoid CRBSI). NA=not applicable (if the estimated OR is ≥1.0).

"In our pooled analyses, neither silver-alloy-coated, silver-iontophoretic, nor silver-impregnated CVCs showed any significant reduction in colonisation or CRBSI by comparison with standard CVCs."6

First Trial of Second Generation AGB+® and Spectrum, Partially Funded by CDC

Process Process with Ch-SS+ (AGB+) Process with M+R (Spectrum)

3.38 2.77 1.47 INFECTIONS PER 1,000 CATHETER DAYS

ANALYSIS OF TYPES OF INFECTION INFECTIONS PER 1,000 CATHETER DAYS

1.35 .55 .68 .55 .68 .31

Gram Positive Gram Negative Fungal
THE RIGHT COMBINATION

Minocycline+rifampin is proven to be the most synergistic combination of antibiotics in reducing infections through two distinct pathways, and has the ability to penetrate the biofilm that forms on all indwelling catheters.

**Zones of Inhibition**

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Antimicrobial Durability of Minocycline+Rifampin vs. Second Generation Chlorhexidine/Silver Sulfadiazine and Silver/Platinum/Carbon</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
</tbody>
</table>

**Baseline**

- Spectrum polyurethane 24 mm
- Uncoated polyurethane 0 mm
- Edwards Vantex™ Oligon™ 14 mm
- ARROWg’aard Blue PLUS® 15 mm

**9 Day Durability**

- Spectrum polyurethane 25 mm
- Uncoated polyurethane 0 mm
- Edwards Vantex™ Oligon™ 0 mm
- ARROWg’aard Blue PLUS® 8 mm

**“Coated catheters [that can maintain an in vitro zone of inhibition] of ≥ 15 mm were highly predictive of in vivo efficacy.”**

3, citing 4

Arrowg’aard Blue PLUS and AGB+ are registered trademarks of Teleflex Incorporated. Vantex and Oligon are trademarks of Edwards Lifesciences Corporation.
1. Raad I, MD, Department of Infectious Disease, M.D. Anderson Cancer Center, University of Texas School of Medicine, Houston, Texas.
11. Ramos ER, Jiang Y, Hachem R, et al. The risk of emerging resistance associated with prolonged use of antibiotic coated catheters: a seven year experience and > 0.5 million catheter days. Poster presented at: Society for Healthcare Epidemiology of America (SHEA) 18th Annual Scientific Meeting, April 5-8, 2008; Orlando, FL.

Dr. Raad is the co-inventor of the synergistic pairing of the antibiotics minocycline and rifampin that are impregnated within the catheter material of the Cook Spectrum® catheter. His institution receives a royalty payment based upon Cook’s license to use this patented technology.
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