Title

Randomized Double-Blinded Placebo-Controlled Trial to Assess the Effect of Retapamulin for Nasal Decolonization of Mupirocin-Resistant Methicillin-Resistant Staphylococcus aureus Nasal Carriers

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POSTER ABSTRACTS

301. Randomized Double-Blinded Placebo-Controlled Trial to Assess the Effect of Retapamulin for Nasal Decolonization of Mupirocin-Resistant Methicillin-Resistant *Staphylococcus aureus* Nasal Carriers

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Background. Mupirocin is commonly used for nasal clearance of methicillin-resistant *Staphylococcus aureus* (MRSA) in carriers during high risk situations such as pre-operatively, during ICU stays, and to prevent recurrent disease. Low level (LL) and high level (HL) mupirocin resistance have been reported and may warrant evaluation of alternative therapies.

Methods. We conducted a double-blinded randomized controlled trial (RCT) of retapamulin versus placebo for patients with confirmed nasal mupirocin-resistant methicillin-resistant *S aureus* (Mup-R MRSA). Subjects were identified from MRSA samples tested for Mup-R from the UC Irvine Medical Center microbiology laboratory and from samples from participants who completed a separate clinical trial (Project CLEAR) from September 2012 to August 2015. Randomization was stratified by LL versus HL Mup-R. Subjects used a 5-day twice daily course of assigned product (D1-5) followed by nasal sampling one week later (D12). If still positive, subjects were given another 5-day course of the assigned product. Primary outcome was MRSA nasal carriage at 6 weeks following the initial course (D47). Secondary outcome was MRSA nasal carriage at D12. Unadjusted trial results were based upon Fisher's exact tests. Adjusted results used logistic regression models that selected from a priori variables (recent hospitalization, recent ICU stay, bathing frequency, skin infection, steroid use, and college education) to minimize Akaike's Information Criterion.

Results. A total of 4394 MRSA isolates were screened to find 294 (6.7%) patients with Mup-R isolates. Of these, 95 were contacted and 53 were randomized (Table 1). Three dropped out prior to any follow up visit, leaving 25 subjects per group to complete both visits with high adherence. Reduction in MRSA nasal carriage was found at Day 12, but not Day 47 (Table 2). Case counts by HL and LL Mup-R are found in Table 3. No change in estimated effects was seen in adjusted models. No adverse events were reported.

	Retapamulin (n=27)	Placebo (n=26)	Overall (n=53)
Age (years)	60.3 (16.9)	59.0 (16.2)	59.7 (16.4)
Female	17 (63%)	11 (42%)	28 (53%)
White	24 (89%)	23 (88%)	47 (89%)
Hispanic	5 (19%)	4(15%)	9 (17%)
High school graduate	23 (85%)	20 (77%)	43 (81%)
Nursing home resident	2 (7%)	2 (8%)	4 (8%)

* Mean (sd) for continuous characteristics and N (%) for discrete characteristics

Table 1: Baseline Patient Characteristics by Treatment Arm

Table 2: Primary and Secondary Efficacy Endpoint Analyses

Efficacy Endpoint	Observed Proportion of MRSA		Risk Difference[1] (R – P; 95% CI)	Odds Ratio[2] (R : P; 95% CI)	P-value[3]
	Retapamulin (R) (N=25)	Placebo (P) (N=25)			
Primary Endpoint					
MRSA status at D47	0.68	0.84	-0.16 (–0.43, 0.11)	0.41 (0.08, 1.86)	0.320
Secondary Endpoint					
MRSA status at D12	0.32	0.76	-0.44 (–0.73, -0.15)	0.16 (.04, 0.60)	0.004

1: Confidence interval for risk difference is based upon the asymptotic normal approximation
2: Confidence interval for the odds ratio is based upon the inversion of Fisher's exact test
3: P-value for difference based on Fisher's Exact Test

Table 3: Analysis of MRSA-micro results at Visit 1 and Visit 2

Outcome	Retapamulin (N=25)	Placebo (N=25)	P-value [1]
Enrollment (D0)			
- LL Mup-R	10 (40%)	10 (40%)	
- HL Mup-R	15 (60%)	15 (60%)	
Visit 1 (D12)			**0.018**
- LL Mup-R	2 (8%)	7 (28%)	
- HL Mup-R	5 (20%)	10 (40%)	
- MRSA not Mup-R	1 (4%)	2 (8%)	
- MRSA negative	17 (68%)	6 (24%)	
Visit 2 (D47)			0.590
- LL Mup-R	5 (20%)	7 (28%)	
- HL Mup-R	10 (40%)	11 (44%)	
- MRSA not Mup-R	2 (8%)	3 (12%)	
- MRSA negative	8 (32%)	4 (16%)	

1: P-value for test of difference by treatment group based upon Chi-squared test with continuity correction.

Conclusion. This RCT found that nasal retapamulin significantly reduced Mup-R nasal MRSA 1 week following a 5-day application, but reductions were not sustained at 6 weeks. Retapamulin may be a viable alternative to mupirocin for temporary risk periods such as surgery and ICU stays, but long-lived benefit may require alternative agents or longer therapeutic duration.

Disclosures. **R. Singh**, Sage Products: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product. 3M: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product. Clorox: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product; **A. Gombosev**, Sage Products: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product. Molnlycke: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product. 3M: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product. Clorox: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product; **T. Dutciuc**, Sage Products: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product. 3M: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product. Clorox: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product; **M. K. Hayden**, Sage Products: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product. Molnlycke: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product; **D. Kim**, Sage Products: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product. 3M: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product. Clorox: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product; **L. Miller**, Sage Products: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product. 3M: Conducting studies in healthcare facilities that are receiving contributed product, Conducting studies in healthcare facilities that are receiving contributed product. Clorox: Conducting studies

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