
Purpose: To test the hypothesis that a combination of systemically administered host-modulating therapy (HMT) and locally administered topical antimicrobial therapy (TAT), as adjuncts to scaling and root planing (SRP), would provide significantly improved clinical benefits in the treatment of untreated moderate to severe chronic periodontitis (CP) compared to SRP alone.

Materials and Methods: A group of 180 systemically healthy adult human subjects (age range: 18-75 years) with untreated moderate to severe chronic periodontitis were enrolled in a six-month randomized multicenter, placebo controlled, examiner-masked clinical study to compare the effectiveness of combination therapy which included systemically delivered host-modulating therapy (HMT)- low dose(20 mg) doxycycline hyclate, locally delivered topical antimicrobial therapy (TAT)- doxycycline hyclate gel, and SRP versus SRP + placebo to treat periodontal disease. Subjects were screened for the presence of at least eight qualifying tooth sites on a minimum of three teeth in at least 2 quadrants with untreated periodontal breakdown: each site had to have positive bleeding upon probing and a GI greater than 1; 6 of the eight teeth required probing depths greater than 5 mm; and 2 of the 8 sites needed probing depths greater than 7 mm and clinical attachment loss of 5 mm. A tooth site with probing depths of 4-6 mm was defined as moderate while a tooth site with probing depths greater than 6 mm was defined as severe. At baseline, all participating subjects were clinically assessed (full-mouth probing, BOP, and GI) and received full-mouth SRP. Ensuing, subjects were randomly assigned to either a test group (combination therapy) or a control group (placebo group.) Participants were directed to immediately commence with the assigned regimen and maintain the regimen for a 6-month duration. Subjects returned at the 3-month period and the 6-month period for clinical re-evaluations and assessments of drug/placebo compliance. The primary efficacy outcome was intended to be probing depth reductions while secondary efficacy outcome were changes in clinical attachment loss (CAL), bleeding upon probing (BOP), and the gingival index (GI).

Findings: At 3-month and 6-month re-assessments, the test group attained clinical improvements more rapidly and consistently demonstrated greater reductions in probing depths, greater gains in clinical attachment levels, and greater decreases in number of sites with positive bleeding upon probing compared to the control group. Tooth sites with either moderate or severe probing depths adhered to this pattern of clinical improvements. The positive trends in clinical improvements can be seen in the case of the primary efficacy outcome: reductions in probing depths. In sites with moderate probing depths (4-6 mm), the test group showed reductions in probing depths of 1.5 mm versus 0.9 mm for controls by 3 months, and 1.7 mm versus 1.2 mm, respectively, by six months. In sites with severe probing depths (greater than 7 mm), the test group showed reductions in probing depths of 2.1 mm versus 1.4 mm for controls at 3 months, and 2.4 mm versus 1.7 mm, respectively, at 6 months. Similar improvements were seen in the
case of CAL, BOP, and GI. Thus, the test group showed statistically significant clinical improvements compared to SRP alone.

**Conclusion**: The combined regimen of systemically delivered host modulating agents (HMT), locally delivered host modulating agents (TAT), and SRP proved to be clinically superior to SRP alone. The investigators speculate that the HMT and TAT work synergistically to arrest the activity of MMPs and tissue inflammation at both the local and systemic levels. Therefore, this study supports the concept that host modulators play a critical role in disrupting the progression of periodontal breakdown.