

Title:

Incisional microenvironments and reduction in SSIs in patients treated with a local doxycycline-eluting formulation

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Background: Despite significant advances in infection control guidelines and practices, surgical site infections (SSIs) remain a substantial cause of morbidity, prolonged hospitalization, and mortality among patients undergoing both elective and emergent surgeries. D-PLEX₁₀₀ is a novel, drug-eluting polymer-lipid matrix that supplies a high, local concentration of doxycycline for approximately four weeks with minimal systemic drug exposure. The objective of this analysis was to evaluate SSI reduction and identify the causative pathogens found within the postoperative soft tissue infection to determine variations in the surgical wound microenvironment following administration of D-PLEX₁₀₀.

Patients and methods: Patients undergoing elective colorectal surgery were randomized 1:1 to D-PLEX₁₀₀ plus Standard of Care (SOC) or SOC alone (ClinicalTrials.gov identifier NCT03633123). All patients received prophylactic IV antibiotics 30-60 minutes prior to surgery. Patients randomized to the investigational arm received D-PLEX₁₀₀ at the time of closure based on the length of surgical incision (5-10 cm = 5g D-PLEX₁₀₀ (5g D-PLEX₁₀₀ contains 54.6 mg doxycycline), 11-20 cm = 10g D-PLEX₁₀₀, >20cm = 15g D-PLEX₁₀₀). The SSI rate within 30 days post-index surgery was evaluated. Pre- and post-treatment bacterial colonization analysis was assessed by rectal swab, and organisms were identified and isolated from adjudicated incisional SSIs. Systemic doxycycline plasma concentrations were assessed at various post-operative time points.

Results: There was a 64% reduction in SSI rate in the D-PLEX₁₀₀ plus SOC group (N=7/88 [7.9%]) vs SOC alone (N=20/91 [21.9%]); p<0.05. Causative organisms from SSI wounds were similar between study arms. There was no significant difference in colonization with multi-drug resistant organisms (MDROs) between groups based on rectal swabs. The maximum systemic doxycycline exposure (mean C_{max}) was 183ng/ml in patients treated with 15g D-PLEX₁₀₀ (maximum dose), significantly lower than the 5,100ng/ml found after a standard 200mg doxycycline oral dose.

Conclusions: These data demonstrated that the addition of D-PLEX₁₀₀ to the SSI SOC prophylaxis regimen in elective colorectal surgery provided a 64% reduction in SSIs and importantly this was achieved without affecting the incidence of postoperative colonization by MDROs. As such, D-PLEX₁₀₀ may be a promising addition to established colorectal SSI bundles for reducing SSIs without the risks associated with systemic antibiotic exposure.