D-PLEX$_{100}$, a Novel Doxycycline Formulation that Provides High, Local Concentrations of Antibiotic Activity for Approximately Four Weeks to Reduce Surgical Site Infections

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Objectives: 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. Even with the most robust adherence to currently accepted preventive measures, up to 60% of SSIs are deemed preventable. We developed a drug delivery system that addresses the major deficiencies of available local drug delivery systems including uncontrolled and large initial release of antibiotic, risk of dangerously high early systemic drug levels, and lack of prolonged drug release necessary to achieve therapeutic efficacy in SSI reduction.



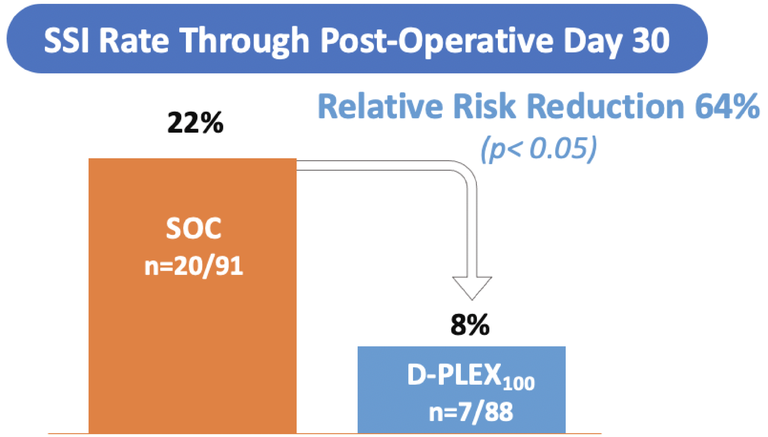
Fig. 1 Application of D-PLEX$_{100}$ during wound closure. Above is an illustrative rendering of the hydration process used prior to application.

Product Technology: D-PLEX$_{100}$ is a novel drug product which pairs the PLEX platform with the broad-spectrum antibiotic, doxycycline (DOX). By selectively matching chosen lipids with biodegradable polymers, the resulting Polymer-Lipid Encapsulation matriX (PLEX) fully integrates doxycycline and allows for a localized, zero-order kinetics release rate of doxycycline for a period determined by the chosen polymer-lipid composition.

The PLEX composition is confirmed via several methods, including differential scanning calorimetry, scanning electron microscopy, and X-ray diffraction. D-PLEX$_{100}$ is designed to provide local, prolonged, and high concentration anti-bacterial activity of DOX directly at the surgical site for a period of approximately four weeks (Figure 1). The localized, high concentrations of antimicrobial activity effectively treat many of the common pathogens associated with SSIs, including frequently encountered antimicrobial-resistant pathogens.

Methods: The product was evaluated in a single-blind Phase 2 clinical trial for patients undergoing elective colorectal surgery (Figure 2) (ClinicalTrials.gov identifier NCT03633123). D-PLEX$_{100}$ was applied to the wound surfaces immediately prior to closure. The length of incision guided the dose of D-PLEX$_{100}$ applied. Patients were assessed for SSIs at 30 days.

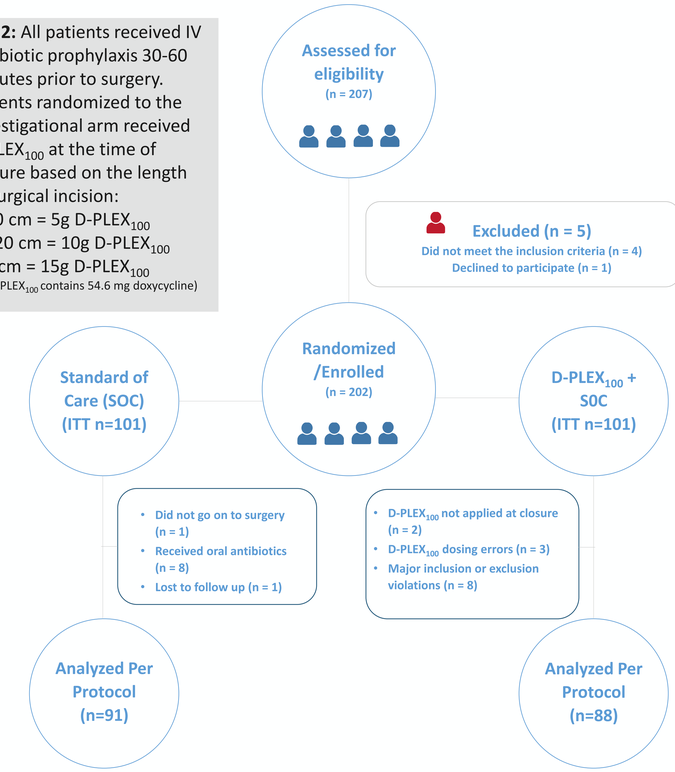
Fig. 3



Results: The SSI rate within 30 days post-index surgery revealed a 64% relative risk reduction in SSI rate in the D-PLEX$_{100}$ plus SOC group (N=7/88 [8%]) vs SOC alone (N=20/91 [22%]); p<0.05 (Figure 3). Measured systemic doxycycline levels were negligible compared to standard oral administration.

Conclusions: These data demonstrate that the addition of D-PLEX$_{100}$ to the SSI SOC prophylaxis regimen in elective colorectal surgery reduces the SSI rate. D-PLEX$_{100}$ may be a promising addition to established SSI bundles and is currently being evaluated in two Phase 3 clinical trials.

Fig. 2: All patients received IV antibiotic prophylaxis 30-60 minutes prior to surgery. Patients randomized to the investigational arm received D-PLEX$_{100}$ at the time of closure based on the length of surgical incision:
5-10 cm = 5g D-PLEX$_{100}$
11-20 cm = 10g D-PLEX$_{100}$
>20cm = 15g D-PLEX$_{100}$
(5g D-PLEX$_{100}$ contains 54.6 mg doxycycline)



References:
1. Anderson D, et al. Infect Control Hosp Epidemiol. 2014;35(6):605-627. doi:10.1086/676022
2. Lawson E, et al. JAMA Surg. 2013;148(9):849–858. doi:10.1001/jamasurg.2013.2925
3. Weiner-Lastinger L, et al. Infection Control & Hospital Epidemiology, 41(1), 1-18. doi:10.1017/ice.2019.296
4. Yamamoto T, et al. BMC Surg. 2015;15:128. Published 2015 Dec 18. doi:10.1186/s12893-015-0115-0
5. Ban K, et al. J Am Coll Surg. 2017 Jan;224(1):59-74. doi: 10.1016/j.jamcollsurg.2016.10.029. Epub 2016 Nov 30. PMID: 27915053.
6. Metsemakers WJ, et al. J Control Release. 2015 Jul 10;209:47-56. doi: 10.1016/j.jconrel.2015.04.022.
7. Kachel E, et al. J Card Surg. 2020 Oct;35(10):2695-2703. doi: 10.1111/jocs.14890. Epub 2020 Aug 2. PMID: 32743813.
8. Konstantinos A, et al. Acta Orthopaedica, 79:2, 302-307, DOI: 10.1080/17453670710015120
9. Emanual N, et al. European Cells and Materials Vol. 24. Suppl. 1, 2012 (page 42)
10. Emanual N, et al. European Cells and Materials Vol. 21. Suppl. 2, 2011 (page 17)
11. https://reference.medscape.com/drug/vibramycin-doryx-doxycycline-342548
12. Holmes NE, et al. Clinical Medicine Therapeutics. January 2009. doi:10.4137/CMT.S2035

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