

TITLE: Impact of Locally Applied Doxycycline-Eluting Drug (D-PLEX) on Incisional Infection Rate in Elective Colorectal Surgery: A Phase 3, Prospective, Randomized, Double-Blind, Multicenter and Multinational Clinical Trial.

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BACKGROUND: We aimed to assess the efficacy of D-PLEX in preventing surgical site infection (SSI) events by comparing the event rate in the standard of care (SOC) vs. D-PLEX+SOC (D-PLEX) treatment arms.

STUDY DESIGN: The primary endpoint was a composite of events that were assessed within 30 days post-surgery (incisional infections, reintervention at the incision site, all-cause mortality).

RESULTS: 977 patients were recruited (489 in SOC, 488 in D-PLEX). The primary outcome indicated a 23% relative reduction in D-PLEX (45/485, 9.3%) vs. SOC (59/489, 12.1%) which was not significant, $P=0.1520$. Pre-specified primary outcome analysis by incision length indicated a significant 54.3% reduction in the >20 cm subgroup in D-PLEX (17/212, 8%) vs. SOC (37/211, 17.5%); $P=0.0032$. The Odds ratio (OR) for the primary outcome in >20 cm vs. $>10 \leq 20$ cm was 2.50 in SOC (95% CI, 1.31-4.75; $P=0.0053$), and 0.83 in D-PLEX (95% CI, 0.41-1.68, $P=0.6018$). Post hoc analysis in increasing incision length subgroups (>10, >14, >20, >24 cm) revealed increasing primary events rate with increasing lengths in SOC (12.1%, 14.4%, 17.5%, 19.3% respectively) but similar rates across lengths in D-PLEX (9.3%, 10.4%, 8.0%, 8.2% respectively). Multivariate regression analysis assessing the impact of longer incision under various patient-related or procedural SSI risk factors indicated low odds for primary outcome events in the D-PLEX arm and high odds in the SOC arm.

CONCLUSIONS: In patients with SSI risk factors including incision length >20 cm, D-PLEX efficacy is significantly better than SOC.