



ASCRS 2020

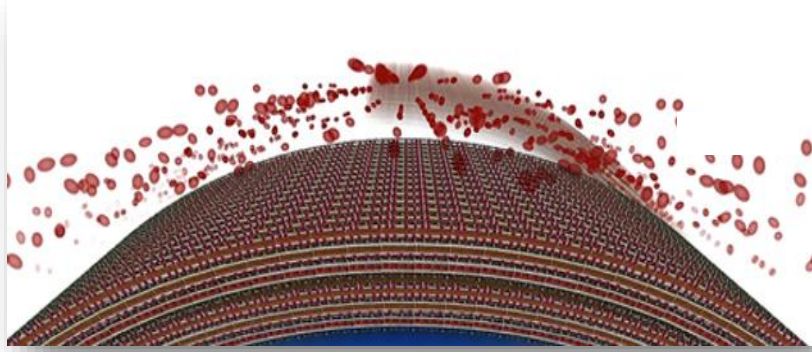
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PROLONGED DRUG DELIVERY

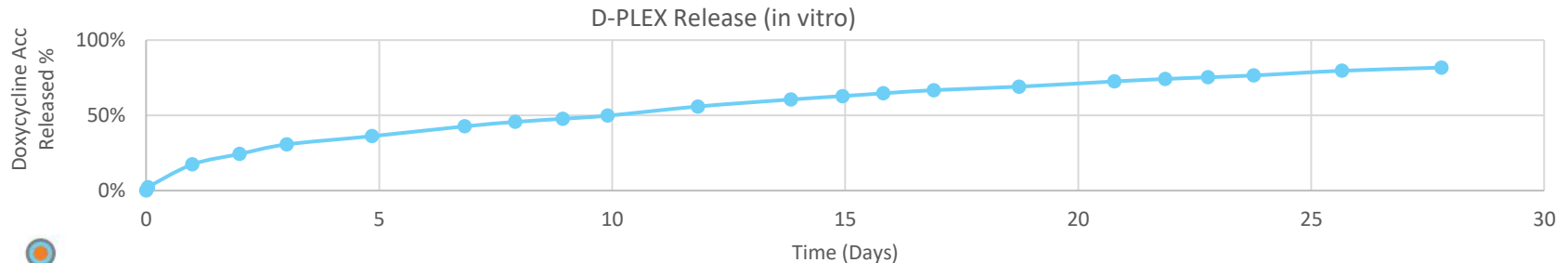


D-PLEX₁₀₀ – Localized drug delivery system that is optimized for the management of surgical site infections (SSIs)



D-PLEX for prophylaxis of SSIs:

- ✓ **Active Ingredient:** Doxycycline (broad spectrum antibiotic)
- ✓ **Release Duration:** Prolonged Effect - 4 weeks
- ✓ **Release profile:** No Burst > Constant & Linear Release
- ✓ **Release rate:** Overcome Resistant Bacteria & Biofilm



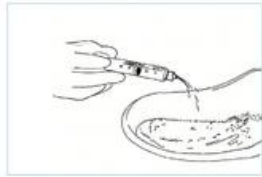
D-PLEX₁₀₀ - administration is adaptable to different applications; No training required



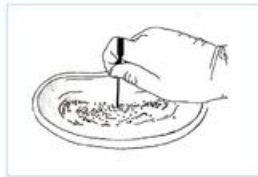
PLEX candidate



1) Pour



2) Hydrate



3) Mix



D-PLEX₁₀₀ in Soft tissue –
during abdominal surgery



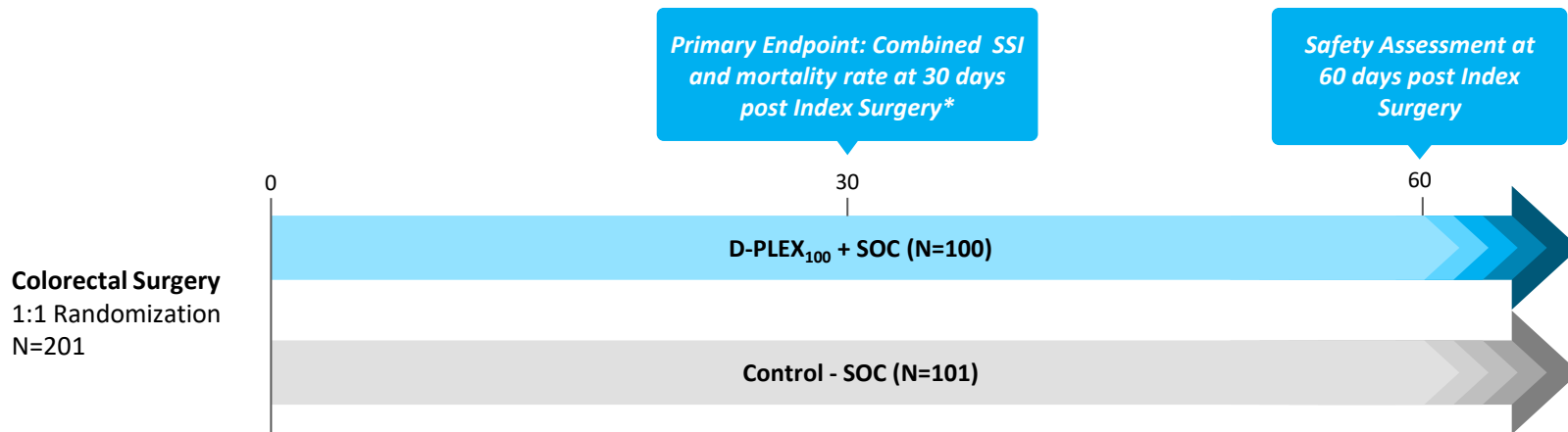
D-PLEX₁₀₀ in bone
– during open heart surgery



D-PLEX₁₀₀ Phase 2 Study Design in Abdominal Surgeries (soft tissues)



- Prospective, multicenter, randomized, controlled, two arm, single blind, study
- Assess safety and efficacy of D-PLEX administered prophylactically to prevention incisional infection



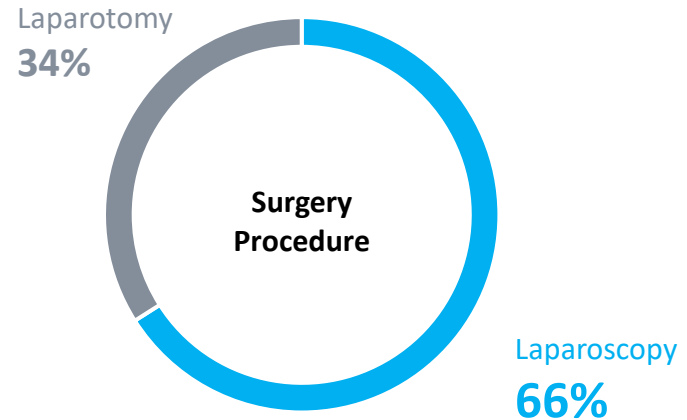
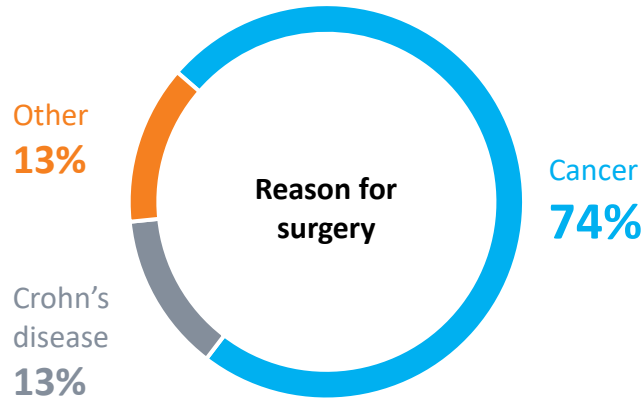
* As confirmed by a blinded and independent adjudication committee





Demographics and Baseline Data Summary Statistics

- **Elective abdominal colon surgery involving resection** and ileocolonic, ileorectal, colocolonic or colorectal anastomosis or with a stoma. In laparoscopic or open surgery, an abdominal wall incision ≥ 5 cm.
- Baseline demographic (Age, BMI, etc.) and surgical characteristics were balanced between the groups

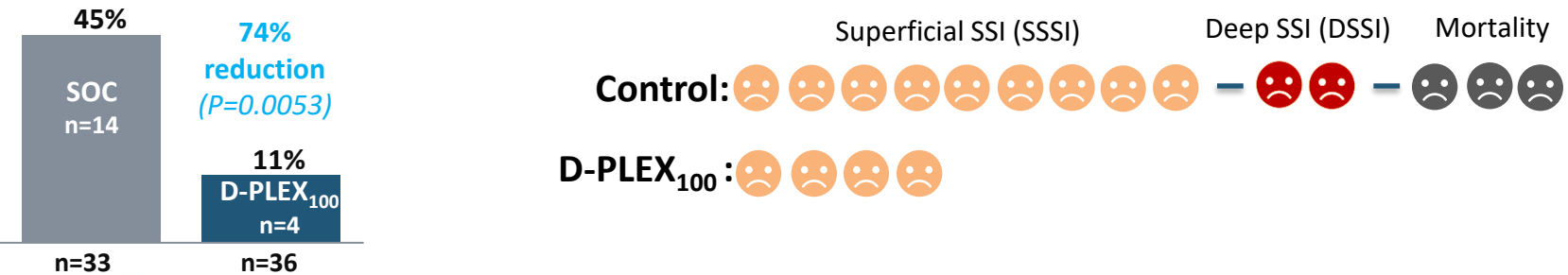


D-PLEX₁₀₀ Effective in Reduction of SSI & Mortality in Soft Tissue Colorectal Surgical Model within 30 days (primary end-point, ITT population)

Laparoscopy & Open Laparotomy



Open Laparotomy

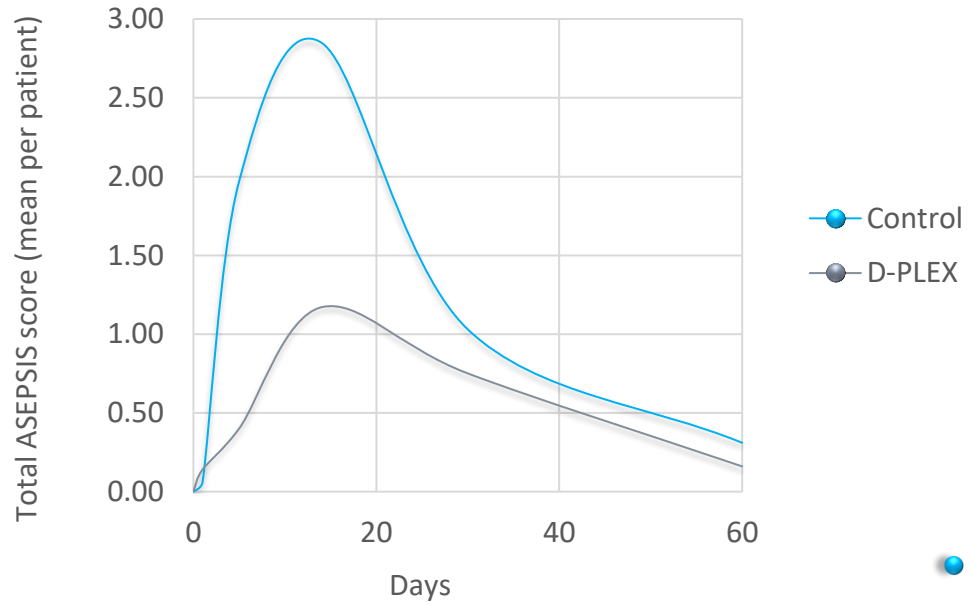


Reduction Consistent with Validated Assessment of Surgical Site Complications (ASEPSIS Score. PP population)

Surgical Site Complications (SSC)

ASEPSIS score assessment:

- Separation of deep tissues
- Antibiotic treatment
- Isolation of bacteria
- Stay as inpatient > 14 days
- Drainage of pus
- Serous exudate
- Purulent exudate
- Erythema



D-PLEX₁₀₀ Effective Against: Gram-positive, Gram-negative Bacteria & MDR

The number of bacteria was reduced in both Gram-positive or Gram-negative isolates

Bacteria isolated:

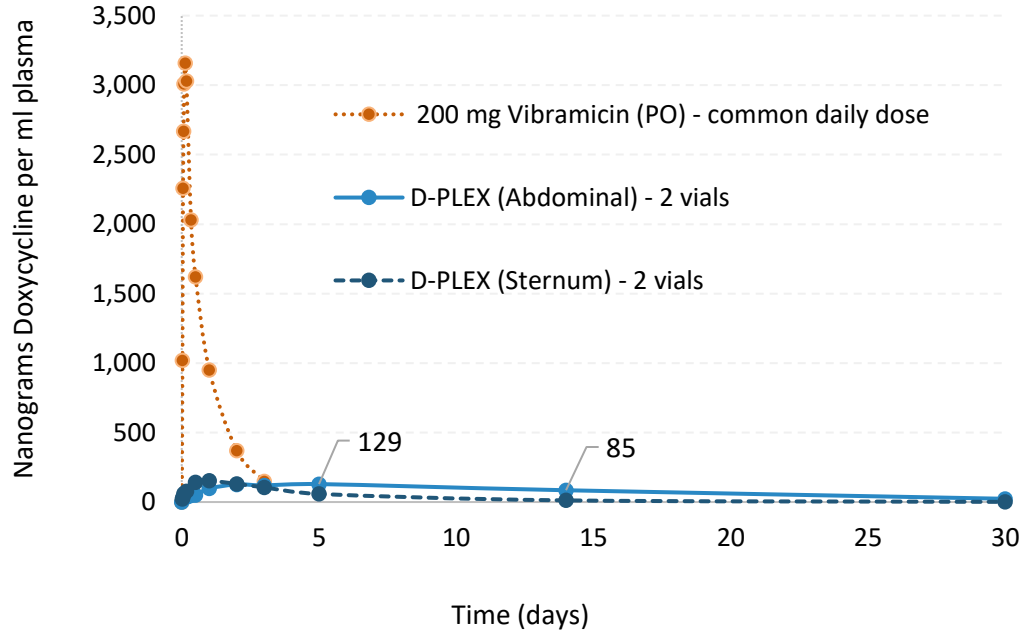
- *Staphylococcus epidermidis*
- *Pseudomonas aeruginosa*
- *Klebsiella pneumoniae*
- *Escherichia coli*
- *Enterococcus faecalis*
- *Serratia marcescens*
- *Enterobacter cloacae* complex
- *Staphylococcus aureus* (MRSA)

Most frequent isolated bacterial strains		Control	D-PLEX
Escherichia coli	Gram negative	11	2
Pseudomonas aeruginosa	Gram negative	2	2
Enterococcus faecalis	Gram positive	4	3
Staphylococcus epidermidis	Gram positive	4	1

D-PLEX demonstrated efficacy against multidrug resistance bacteria (MDR) strains, with more than 70% of the infected bacteria resistant to more than one antibiotics



D-PLEX₁₀₀ Local Administration Anchored at Site, Nearly Undetectable Systemic Exposure, Reduces Prolonged Systemic Risks



D-PLEX₁₀₀ PK Characteristics

- ✓ No burst release
- ✓ Prolong, constant release over 4 weeks
- ✓ Similar release profile, regardless the tissue; bone and soft tissues

Same Rate of Serious Treatment Emergent Adverse Events (TEAE)

- D-PLEX did not to impact wound healing impairment vs the Control arm (4% in both arms)
- There were no TEAEs determined to be related to D-PLEX

Subjects with **Serious** Treatment Emergent Adverse Events

	D-PLEX (N=99)	CONTROL (N=100)
Anastomotic haemorrhage	1 (1.0%)	0 (0.0%)
Anastomotic leak	2 (2.0%)	3 (3.0%)
Injury	0 (0.0%)	1 (1.0%)
Procedural complication	1 (1.0%)	0 (0.0%)
Ureteric injury	1 (1.0%)	0 (0.0%)
Stoma site haemorrhage	1 (1.0%)	1 (1.0%)
Overall	5 (5.0%)	5 (5.0%)



Conclusions

- D-PLEX₁₀₀ technology is novel and the first to demonstrate:
 - ✓ Prolonged & consistent high local concentration, broad spectrum antibiotic for prophylaxis of SSIs
 - ✓ More than 10 fold lower (C_{max}) peak systemic exposure
- D-PLEX₁₀₀ Demonstrated significant reduction in SSI + Mortality in soft tissue surgical model
 - ✓ 59% reduction in ITT, 69% reduction in PP, and 74% reduction in laparotomy populations
- Safety equal to control arm for overall adverse events and no negative impact on soft tissue wound healing
- Overall, prolonged, constant local exposure effective against wide range of bacteria including gram-positive, gram-negative, and multi-drug resistant (MDR)