

# Prevention of anastomotic leak in rectal cancer surgery with local antibiotic decontamination: a prospective, randomized, double-blind, placebo-controlled single center trial

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## ABSTRACT

**Purpose:** Anastomotic leak (AL) is a septic complication of rectal cancer surgery caused by bacteria. We aimed to study the efficacy of topical antibiotic decontamination on the incidence of AL in rectal cancer surgery.

**Methods:** A prospective, randomized, double-blind, placebo-controlled trial was conducted (LMU Munich). Patients received either placebo or decontamination with polymyxin B, tobramycin, **vancomycin (125mg)**, and amphotericin B 4 times/day starting 1 day before surgery to POD7. In patients with a protective ileostomy, a transanal Foley catheter was placed to deliver medication directly to the anastomosis.

**Results:** The trial was stopped early for ethical reasons after the first interim analysis with 80 patients. In the placebo group (n=40), 8 patients (20%) developed AL compared to only 2 (5%) in the treatment group (p=0.0425, 4-fold reduction). Total infectious complications were 38% vs 18% (p=0.045). Hospital stay was shortened from 28.9 to 21.9 days (p=0.0206). Treatment costs were reduced by 37% (€5,551 saved/patient).

**Conclusion:** Local decontamination with polymyxin B, tobramycin, vancomycin, and amphotericin B is safe and effective in preventing anastomotic leak in rectal cancer surgery.

## 1. Introduction

Colorectal anastomotic leak (AL) following low anterior resection (LAR) remains a frequent and serious complication (incidence 10-30%, mortality up to 30%). Despite surgical advances, AL rates have not significantly changed over the past 30 years. Bacteria, specifically *Enterococcus faecalis* and *Pseudomonas aeruginosa*, play a key role in collagen degradation and tissue destruction. This study investigated whether local antibiotic decontamination expanding the SDD regimen with **vancomycin** could effectively prevent AL.

## 2. Patients and Methods

80 patients undergoing anterior or low anterior rectal resection for UICC I-IV adenocarcinoma were randomized to treatment (n=40) or placebo (n=40). The treatment medication contained Polymyxin B (100mg), Tobramycin (80mg), **Vancomycin (125mg)**, and Amphotericin B (500mg), given 4 times/day (q6h) until postoperative day 7 (31 doses total). Placebo received subclinical lactulose (305mg). Patients with a protective loop ileostomy (90%) received medication dissolved in 20 ml distilled water via a transanal Foley catheter directly to the anastomotic site. Integrity of every anastomosis was verified by rigid rectoscopy before discharge.

## 3. Results and Key Clinical Endpoints

| Clinical Parameter                 | Placebo (n=40) | Decontamination (n=40) | p value                    |
|------------------------------------|----------------|------------------------|----------------------------|
| Anastomotic Leak (AL) %            | 8 (20.0%)      | 2 (5.0%)               | p = 0.0425 * (4-fold drop) |
| AL in Patients with Ileostomy      | 8/36 (22.2%)   | 2/36 (5.6%)            | p = 0.041 *                |
| Infectious Complications (inc. AL) | 15 (38.0%)     | 7 (18.0%)              | p = 0.045 *                |
| Postoperative Hospital Stay (days) | 28.85 ± 17.22  | 21.92 ± 11.72          | p = 0.0206 **              |
| Endoscopies per Patient            | 17.5 ± 24.8    | 4.5 ± 6.2              | p = 0.049 *                |

|                                 |          |         |                     |
|---------------------------------|----------|---------|---------------------|
| Mean Treatment Cost (€/patient) | € 14,985 | € 9,308 | -37% (Saved €5,551) |
|---------------------------------|----------|---------|---------------------|

#### 4. Discussion Highlights: The Crucial Role of Vancomycin

In the discussion, the authors specifically address why this study achieved a 4-fold AL reduction compared to the Dutch SELECT and Finnish MOBILE trials (2019):

- 1. **Why MOBILE failed:** Single-dose pre-op antibiotics fail to protect during the critical POD 1-7 collagen remodeling period.
- 2. **Why SELECT was insufficient:** Standard SDD lacks **Vancomycin**. Eliminating G- bacilli leads to *Enterococcus faecalis* overgrowth. *E. faecalis* directly degrades collagen via GeLE, activates host MMP-9, and hijacks plasminogen to cause hyperfibrinolysis.
- 3. **Vancomycin's Targeted Mechanism:** Adding non-absorbable Vancomycin provides potent double-coverage against G+ cocci, directly shutting down bacterial collagenolysis and preserving anastomotic tensile strength.
- 4. **PK/PD & Safety:** Topical vancomycin is not absorbed into circulation, eliminating nephrotoxicity, while achieving >2000 µg/mL locally. 20 years of surveillance showed zero VRE outbreaks.

#### 5. Conclusion

Perioperative local decontamination with polymyxin B, tobramycin, and **vancomycin** effectively reduces anastomotic leakage by 4-fold and overall treatment costs by 37% in rectal cancer surgery.