# Oral Levofloxacin for the Management of Low-Risk Fever and Neutropenia in Children with Cancer

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## Background

- Fever and neutropenia (FN) is a common complication in children treated for cancer
- Empiric therapy should be broad spectrum to cover likely pathogens and is traditionally administered intravenously (IV) (e.g. ceftriaxone, piperacillin-tazobactam)
- Low-risk FN defined as patients deemed to have low risk of serious complications as determined by their clinical picture, comorbidities, and cancer type
- Current guidelines recommend children with low-risk FN be treated with oral antibiotics
- In May 2015, BC Children's Hospital (BCCH) updated their FN guideline: oral levofloxacin as antibiotic of choice for low-risk FN

## Objectives

- **Primary:** To describe the proportion of patients with low-risk FN who received treatment with oral levofloxacin
- **Secondary:**
  - To characterize patients treated with oral levofloxacin vs. parenteral antibiotics
  - To compare:
    - Rate of treatment success
    - Duration of hospitalization
    - Duration of fever
    - Time to resolution of bacteremia and/or other signs of infection
  - To describe and quantify the rate of adverse events secondary to oral levofloxacin and parenteral antibiotics

## Methods

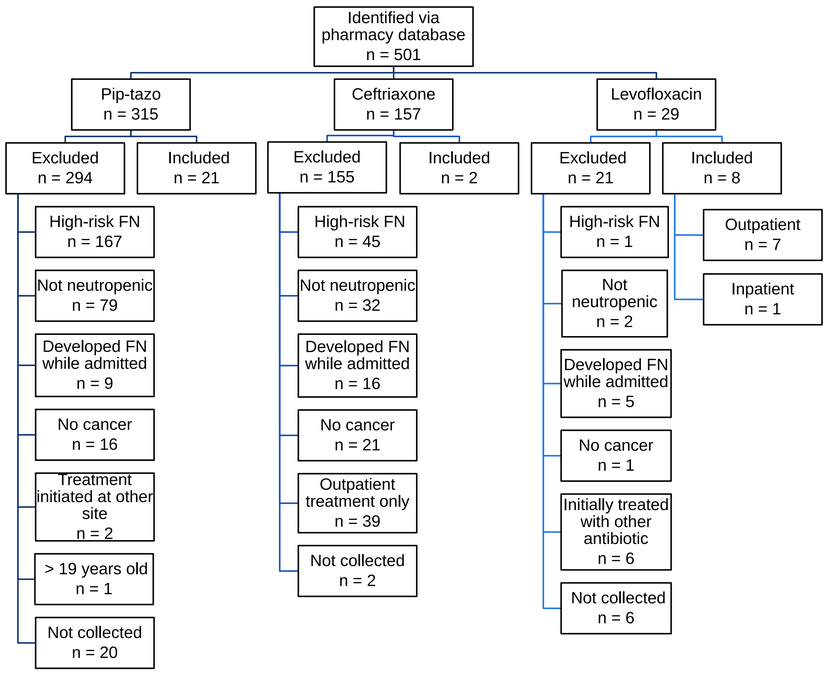
- Clinical research ethics board approved
- **Design:** Retrospective cohort
- **Population:** Children (age 0 to 19 years) admitted to or treated in the emergency department of BCCH with low-risk FN after chemotherapy or radiation between May 2015 and August 2019
- **Statistics:** Descriptive statistics
- **Adverse Events (AE):** All events with a Naranjo score of > 0 ("doubtful") were reported

**Definitions:**

- **Fever:** A single oral temperature of ≥ 38.5°C or two temperatures > 38°C taken one hour apart
- **Neutropenia:** Absolute Neutrophil Count (ANC) < 0.5x $10^9$/L
- **Treatment success:** Resolution of fever and neutropenia with no readmission due to new fever infection within 7 days of discharge or new febrile episode during same period of neutropenia, and no modification of antibiotic therapy (excluding step-down)

## Results

### Figure 1. Included patients




### Table 1. Patient characteristics (N=31)

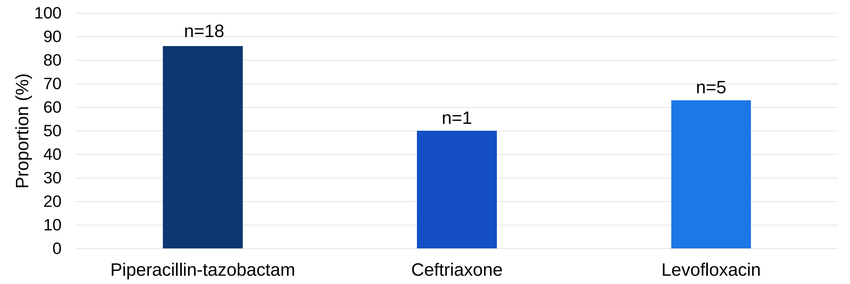
| | Pip-tazo (n=21) | Ceftriaxone (n=2) | Levofloxacin (n=8) |
|---|---|---|---|
| Age, years [mean (SD)] | 7.9 (5.6) | 7.0 (0) | 7.4 (3.9) |
| Oncology diagnosis, n (%) | | | |
| ALL | 16 (76) | 1 (50) | 4 (50) |
| Hodgkins lymphoma | 0 | 1 (50) | 1 (25) |
| Brain tumour | 3 (14) | 0 | 0 |
| Other solid tumour | 2 (10) | 0 | 3 (38) |
| ANC on admission, $10^9$/L [mean (SD)] | 0.33 (0.2) | 0.44 (0.1) | 0.44 (0.2) |
| Temperature on admission, °C [mean (SD)] | 38.8 (0.6) | 39.2 (0.6) | 38.5 (0.2) |
| Site of infection, n (%) | | | |
| Bacteremia | 3 (14) | 0 | 0 |
| Respiratory tract | 3 (14) | 1 (50) | 2 (25) |
| Unknown | 15 (71) | 1 (50) | 6 (75) |
| Bacteria identified on culture, n (%) | 3 (14) | 0 | 0 |
| CoNS | 2 (10) | 0 | 0 |
| MSSA | 1 (5) | 0 | 0 |
| Positive for respiratory virus, n (%) | 3 (14) | 0 | 2 (25) |

ALL = Acute lymphoblastic leukemia
CoNS = Coagulase-negative *Staphylococcus*
MSSA = Methicillin-sensitive *Staphylococcus aureus*

### Table 2. Initial therapy (N=31)

| | Pip-tazo (n=21) | Ceftriaxone (n=2) | Levofloxacin (n=8) |
|---|---|---|---|
| Proportion of total patients (%) | 68 | 6 | 26 |
| Unable to tolerate oral antibiotics, n (%) | 3 (14) | 0 | 0 |
| Dose, mg/kg/day [median (range)] | 300 (224-314) | 90 (80-100) | 10 (8.6-10.5) |
| Duration of initial therapy, days [mean (SD)] | 4.9 (1.8) | 2.5 (2.1) | 5.5 (3.4) |
| Modification of initial therapy, n (%) | 5 (24) | 2 (100) | 2 (25) |
| Condition improved (step-down) | 2 (10) | 1 (50) | 0 |
| Condition worsened | 0 | 1 (50) | 0 |
| Condition not improving | 0 | 0 | 1 (13) |
| Adverse effect | 1 (5) | 0 | 0 |
| Unknown | 1 (5) | 0 | 1 (13) |
| Targeted therapy for known bacteria | 1 (5) | 0 | 0 |

### Figure 2. Rate of treatment success




### Table 3. Duration of illness

| | Pip-tazo (n=21) | Ceftriaxone (n=2) | Levofloxacin (n=8) |
|---|---|---|---|
| Total duration of fever, days [median (range)] | 3 (1-13) | 7.5 (1-14) | 3.5 (1-13) |
| Total duration of hospitalization, days [median (range)] | 11 (2-161) | 13.5 (9-18) | 0 (0-15) |

### Table 4. Adverse events

| | Pip-tazo (n=21) | Ceftriaxone (n=2) | Levofloxacin (n=8) |
|---|---|---|---|
| Possible, n (%) | 6 (29) | 0 | 0 |
| Acute kidney injury, n (Naranjo score) | 2 (3) | 0 | 0 |
| Vomiting, n (Naranjo score) | 2 (1) | 0 | 0 |
| Diarrhea, n (Naranjo score) | 1 (3) | 0 | 0 |
| Skin rash, n (Naranjo score) | 1 (3) | 0 | 0 |
| Probable, n (%) | 1 (5) | 0 | 0 |
| *Clostridium difficile*-associated diarrhea, n (Naranjo score) | 1 (5) | 0 | 0 |

## Conclusions

- The majority of patients admitted to BCCH for low-risk febrile neutropenia received IV empiric therapy
- Patients in the piperacillin-tazobactam group appear to have higher rates of treatment success; however, other treatment groups are underrepresented in this sample