

# Outpatient treatment of febrile neutropenia in pediatric hemato-oncologic patients.

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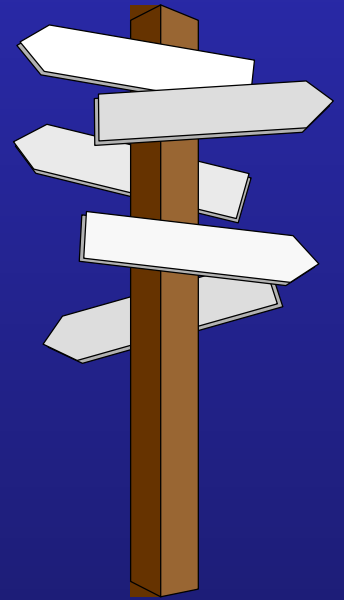


1. Febrile neutropenia (FEN) in cancer pts

2. Koester : Home Care Program ( Ped. Hemat/Oncology Unit, UHG)

3. Retrospective study (5/92- 9/95): Outpatient Intravenous Antibiotic Therapy for Pediatric Cancer patients

4. Prospective Study : Safety and Cost Effectiveness of Intravenous Antibiotic Treatment *at home* in Pediatric Cancer Patients with FEN



# 1. Febrile Neutropenia

- **Neutropenia:**

- absolute neutrophil count  $< 500/ \text{mm}^3$   
(granulocytes + bands + metamyelocytes)

- **Fever:**

- $> 38^\circ\text{C}$ , 2 times at 60 min interval or  $> 39^\circ\text{C}$

- Leading cause of **morbidity** and **mortality** in patients receiving myelosuppressive antineoplastic therapy!

- Effective empiric antibiotics ( $\leftrightarrow$  gram neg. strains):  
mortality dropped from 80 %  $\rightarrow$  10 à 40 %

- Shift gram neg  $\rightarrow$  gram pos bacteria (catheters)

# 1. Febrile Neutropenia

- High-risk febrile neutropenia :
  - neutropenia anticipated  $> 7$  days
  - defined site of infection ( $< 50\%$ )
  - clinical instability
- Low-risk febrile neutropenia :
  - neutropenia anticipated  $< 7$  days
  - no comorbidity
  - tumor under control

(Talcott et al. 1992)

# 1. Febrile Neutropenia



- Evaluation :

- History/ Physical examination
- Blood cultures
- Urinary analysis
- (Chest radiograph)
- Baseline chemistries

- Treatment :

- standard practice : inpatient treatment:  
empirical intravenous broad-spectrum  
antibiotics

# 1. Febrile Neutropenia: studies in adults



- Lower cost regimens: Treatment in hospital
  - monotherapy :safe and effective for low and high risk patients (Freifeld et al. 1995)
  - randomized study oral AB (ciprofloxacin + amoxy-clavu) ~ IV (ceftaz) -> eff in 70 % (Freifeld et al. 1999)

# 1. Febrile Neutropenia: studies in adults



- Outpatient treatment **low-risk patients**
  - Outpatient IV treatment: reduction in costs, sense of well-being at home -> several readmissions (Talcott et al. 1994)
  - Outpatient broad-spectrum oral AB ~ IV AB: IV regimen superior to oral (ciprof/clinda) -> renal toxicity, 6/83 pts readmitted (Rubenstein et al. 1993)
  - Inpatient ~outpatient oral treatment: 21 % readmissions (Malik et al. 1995)

# 1. Febrile Neutropenia: studies in children

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- Outpatient management of FEN children :
  - Outpt : 831 \$, Inpatient : 6465 \$ / course (Mustafa et al. 1996)
  - 40/45 episodes successfully treated with oral ciprofloxacin (Aquino et al. 1999)
  - after initial observation randomisation: oral cipro/ IV ceftaz -> equivalent , 14 % hospitalized (Mullen et al. 1999)
  - 72 hours in hospital (IV ceftriax+ amika) randomization: outpatient 4 d IV ~ 4d oral cefixime ->equivalent (Paganini et al. 2000)

# 1. Febrile Neutropenia: Outpatient Management

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## Advantages:

- reduced exposure to nosocomial bacterial and viral pathogens
- psychological benefits : improved quality of life for patient and family
- substantial costs savings
- better utilization of hospital beds

## Questions:

- safe?
- definition of low-risk patients?



## 2. Koester : Home Care Project (1990)

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- **Koester** : Dutch word for to 'cherish'
- Childrens Oncology Unit for Specific Home Care and Rehabilitation
- **Objectives** : Improvement of life quality for children with cancer (and for their families) by providing high quality medical treatment at home -> limiting the number of days of stay in the hospital
- **Home care** : given in collaboration with general practitioner/pediatrician and with district nurses

## **2. Koester : Home Care Project**

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**Koester is functioning as a 'bridge' between 'hospital' and 'home', necessary to provide the feelings of 'safety' to patient and family**

**• Multidisciplinary team : Ped. Hemat/Oncol.**

**Dept**

- nurses (2.5 full time equivalents)**
- doctors**
- psychologists**
- social workers**

**Nurses and doctors : 24-hr on call coverage**

**Nurses :**

Marie-Jeanne De Clercq  
Annemie  
Kristien Mattheeuws

**Doctors:**

Yves Benoit  
Geneviève Laureys  
Catharina Dhooge  
Els Vandecruys

**Psychologists :**

Nathalie Nolf  
Elke Van der Beken  
Patricia De Vos

**Social workers:**

Jeannot Symoens  
Koen Van Haver



**MULTIDISCIPLINAIR TEAM !**

## 2. Koester : Home Care Project



### •Activities

- palliative care : treatment of pain, hydration, psychosocial support, transfusions
- postpalliative care : visits to parents at regular intervals

## **2. Koester : Home Care Project**

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### **Activities:**

- **Curative care :**
  - catheter care
  - antibiotic treatment
  - gastric tube feeding
  - start of growth factors...
- Educational sessions of district nurses
- Individual instruction of pediatrician/district nurses  
(patient home/local hospital/office physician)

## **2. Koester : Home Care Project**



**Example of organisation: antibiotic treatment:**

**University Hospital Gent:**

- PHO doctor contacts Koester nurse
- PHO doctor contacts family physician
- Koester nurse contacts family for explanation
- Koester nurse asks for information (which district nurse?)
- Koester nurse contacts district nurse for explanation to fix a date for instruction locally

## 2. Koester : Home Care Project

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**Example of organisation: antibiotic treatment at home patient/regional hospital/office physician:**

\* 1st day after discharge of patient : care given by Koester nurse, instructions and demonstration to district nurse/physician

\* 2nd day: care is given by district nurse in presence of Koester nurse

\* next days care given by district nurse

**second course : one phone call is sufficient!**

GETUNNELDE  
HICKMAN® - BROVIAC®  
CATHETER

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OUTPATIENT PARENTERAL ANTIBIOTIC  
THERAPY (OPAT)  
IN FEBRILE NEUTROPENIA

LEVER

Code: 000000 000 0000

*Elia*

### **3. Retrospective Study: Outpatient intravenous antibiotic therapy for Pediatric Cancer Patients (May 92 - September 95)**

- Ceftriaxone plus amikacine once-daily schedule compared favorably with multidose regimen in cancer patients with FEN (inpatients) (EORTC study, 1993)
- UH-Gent : Children with cancer and bad prognosis: quality of life is **most important -> being home!**
- -> infectious complications generally necessitating hospitalisation were treated at home if central venous access, if motivated parents.



BEHANDELING EN BEGELEIDING THUIS !

### **3. Retrospective Study: Outpatient intravenous antibiotic therapy for Pediatric Cancer patients (May 92 - September 95)**

- Estimation of cost savings for health insurances
- indeed patients were treated at home with intravenous antibiotics therapy instead of occupying a hospital bed
- Ultimate goal : reimbursement of costs possible? (Koester project depends on private funding. Supplies distributed by Koester, transport costs etc..)



Who is going to pay the bill?

### 3. Retrospective Study: Outpatient **Intravenous antibiotic therapy for Pediatric Cancer Pts**

**Results : Period May1992 - September 1995**

- **number of patients treated at home : 26**
- **episodes of fever : 36**
  - **number of days of home treatment : 375**  
**- mean: 10 days/episode**

(patient with staph.coag neg and prothesis received antibiotics for a long period)

### 3. Retrospective Study: Outpatient intravenous antibiotic therapy for Pediatric Cancer Pts

Daily costs hospital: 630 \$

#### Health insurances:

- occupation hospital bed: 400 \$
- others (med, mat ): 160 \$

#### Parents:

- not reimbursed : 35 \$
- transport : 35 \$

(US estimation 1000 \$/d)

Daily costs home : 200 \$

#### Health insurances:

- Antibiotics : 100 \$
- others (district nurse, family doctor : 25 \$

#### Parents:

- medic/mat/gen.pract: 35 \$

#### Koester :

- Transport, material, working hours : 40 \$

### 3. Retrospective Study: Outpatient intravenous antibiotic therapy for Pediatric Cancer Pts

Results : 375 days of IV antibiotic treatment at home resulted in :

Cost savings for **health insurances** :  $435 \text{ \$/d} \times 375 \text{ d} = 163\,125 \text{ \$} \sim 4\,500\,000 \text{ BF}$

(occupation hospital bed: if not occupied : **lower revenues for UHG**)

Expenses for **Koester** : 15 000 \$

**Higher** expenses for **parents** if antibiotics not ordered in hospital

## 4. Prospective Study: Outpatient intravenous antibiotic therapy for Pediatric Cancer patients:

Economic factors are exerting pressure on the health care system to deliver more cost-effective health care !

### Objectives : Evaluation of

**Safety and cost effectiveness** of intravenous antibiotic treatment *at home* compared to treatment *in the hospital* for pediatric cancer patients with febrile neutropenia.

**Psychosocial benefits** for patient and family

## 4. Prospective Study:

### **Treatment of FEN (unknown origin) Ped. Hem/Oncol Dept, UHG**

1. Piperacillin+ netromycin
2. Fever 24-48 hr later: change : ceftaz +amikacin
3. Fever 24-48 hr later: + vancomycin
4. Persisting fever: + fluconazole
5. Persisting fever: Amfotericin-B

### **Prospective Study: once-daily antibiotic treatment**

1. Ceftriaxone + amikacin
2. Fever 24-48 hr later : + teicoplanin

## 4. Prospective Study:

Safety? Change of regimen as effective?

Costs?

- direct costs related to medical care: antibiotics, physician/nurse visits, laboratory tests...

- direct costs: transport to hospital

- indirect costs: absence at work

-> for parents, health insurances, Koester

Psychosocial benefits?



Rocophine  
2g

TARGEMID 400

## 4. Prospective Study:

Methods: Pt : \* hospitalised for minimum 48 hours  
discharged if no fever for 24 hr,  
clin. stable

\* D 2 in the hospital is compared <->  
with next days at home

Safety: readmissions?

Cost evaluation : through hospital billings, records of  
all expenses (booklets for parents, Koester, local care)

Psychosocial benefits? questionnaire

## 4. Prospective Study :Patients eligibility

### Inclusion criteria

- age over 1 year
- central venous access
- good socioeconomic environment (teleph)
- written informed consent of parents
- no exclusion criteria related to diagnosis

### Exclusion criteria

- age < 1 year
- No central venous access
- Pts with ANLL, relapses of ALL, patients post BMT

## 4. Prospective Study:

### Antibiotics :

- Treatment starts in hospital: Ceftriaxone 100 mg/kg/d (first day: x 2) + Amikacin (15 mg/kg/d)
- If persisting fever after 36-48 hr or signs of gram pos infection : + teicoplanin : 10 mg/kg/day (first day x 2)
- Patient discharged if no fever for 24-hr and clinically well
- Home treatment until recovery of gran  $> 500/ \text{mm}^3$  (blood counts 2 times / week)

### Data analysis:

- Independent health economist
- Pharmacist of University Hospital Gent

## 4. Prospective Study:

### **Part A: Variability of daily costs?**

#### retrospective analysis of 11 patient files:

- median inpatient length of stay : 8 days ( 5 to 12)
- average total per diem cost : 20 929 BF to 24 441 BF
- > **no significant variation d 2 to d 12**
- > **d 2: good reference day**

### **Part B : Feasibility ?**

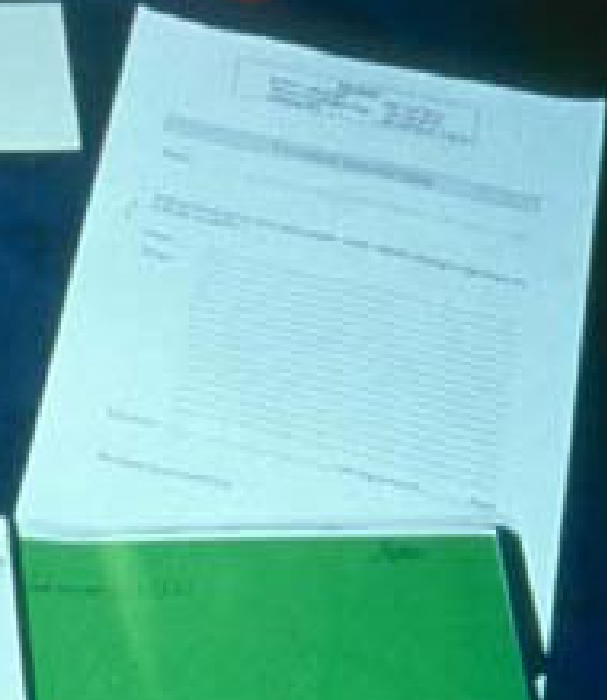
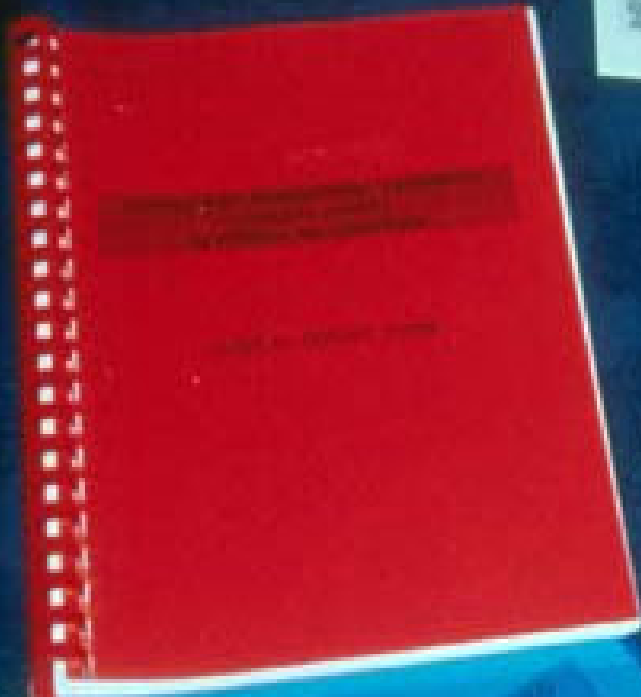
5 patients were treated at home:

- booklets were tested : Are all costs recorded?
- Practical problems?
- Questionnaires? Clear?
  - > **minor changes**

## 4. Prospective Study :

### **Part C: 30 episodes of FEN**

- Start of study : June 1998
- Second or more episodes for same patient :  
    less compliance in completing data
- > extension of study to **30 patients**
- End of study : January 2000



## 4. Prospective Study:

### **Part C: Comparison of inpatient versus outpatient treatment of febrile neutropenia in pediatric cancer patients**

**Study : start June 1998, closed January 2000 :**

- 30 patients, 45 FEN episodes**
- Collection of data finished**
- Analysis ongoing, results expected for January 2001**
- Preliminary data**

## Part C: Prospective study : Results

### **Patient characteristics :**

**Mean Age: 8y9 m ( 1y6 m to 16y10 m )**

**Sex : 15 F, 15 M**

**Eligibility: ~ 70 % of patients**

**Diagnosis (not representative for patient population):**

**-> more patients with higher stage tumors**

**-> low percentage of ALL patients**

## 4. Prospective Study:

### **Patient characteristics : 30 patients : Disease**

- SR-ALL: 5
- preB-ly: 1
- T-lymphoma: 1
- VHR-ALL: 3
- mature B-ly: 2
- Neuroblastoma st 4: 2  
st 3: 1
- Wilms tumor st 3: 1  
st 4: 1
- Rhabdomyosarcoma stage 4: 2
- Teratocarc st 4: 1
- Brain tumor: 6
- Osteosarcoma : 1
- Hepatoblastoma : 1
- Ewing sarcoma : 1
- Post-BMT (> 3 m): 1

## Part C: Prospective study : Results

### **Antibiotic treatment:**

Amikacin/ceftriaxone: 36

Amikacin/ceftriaxone/teicoplanin: 5

Ceftriaxone only: 1

**Other treatment:** growth factors: 4?

**Inpatient treatment days:** mean : 3.4 (weekend!)

**Outpatient treatment days:** mean : 3.6

**No readmissions for fever**

**Hemocultures:** positive in 4 cases : Staph. Aureus, Staph.coag.neg (2 x) , E. Coli (Kaplinsky et al. 1994 : 2/41 low risk patients)

## Part C: Prospective study : Results :

### **FEN episodes in hospital during same period:**

**\* not eligible:** ALL in induction, AML, Hodgkin, patients with no central venous catheter, patients < 1y, BMT patients , ALL pts in relapse, patients with comorbidity (hypotension/extreme diarrhea)

**\* eligible and treated in the hospital:** anxious parent, recovery NF within 3 days, others?

**degree of neutropenia at admission**

**\* 5 patient files: 52 / mm<sup>3</sup> ( 17 to 115/mm<sup>3</sup>)**

## Part C: Prospective study : Results

**Safety:** OK, no readmissions in this group -> good selection of eligibility

**Costs:** Results of analysis pending

**Psychosocial benefits:** Results of questionnaire awaited,

children and parents were very enthusiastic (second episode: too much paper work again), no apparent problems with responsibility for the parents

## Conclusions :

Outpatient parenteral antibiotic treatment for low-risk febrile neutropenic children with cancer :

- if well organised home therapy program
- good definition of eligible patients
- > is safe and efficacious
- > reduces risk of hospital acquired infections
- > provides cost-effective use of health care money
- > but most important is a **positive experience** for the children and their families