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Influence of Real-Time Therapeutic Drug Monitoring on Carbapenems prescription amongst severely Burn Patients

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Services of:
1. Pharmacy
2. Intensive Care Medicine
3. Biomedicine
4. Infectious Diseases

CHUV

Infectious risk ↑
- o Loss of dermal barrier
- o Avascularity of the wound tissue
- o Immune deficits
- o Repeated surgeries, …

Modifications of drugs PKs
- o Patient (age, Cl_{creat}, burn, sepsis, …)
- o Time from burn (acute phase / hypermetabolic state)

Carbapenems
- o Beta-lactam ring
- o Broad-spectrum antibiotics
- o Stability against hydrolysis (most β-lactamases)
- o « Time-dependent » bactericidal effect
- o PD parameter of efficacy: **T > MIC**
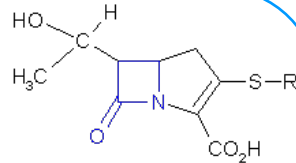
TDM
- o Plasma concentration measurement
- o Dosage individualization
- o ↑ therapeutic efficacy, ↓ toxicity
- o **Candidate drugs**? Long term therapy, significant inter-patient PK variability, low intra-patient PK variability, consistent concentration-efficacy/toxicity relationships, …

2. Method

Study period : 2001-2011
- ✓ Period 1: 2001- June 2007
- ✓ **Period 2: June 2007 - 2011**

« Real-Time » TDM

- a) **June 2007**: 1 day / week
- b) **January 2010**: 4 days / week

Carbapenems
- ✓ Imipenem/cilastin
- ✓ Meropenem

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1. Number of **doses**
2. Cumulative doses [grams]
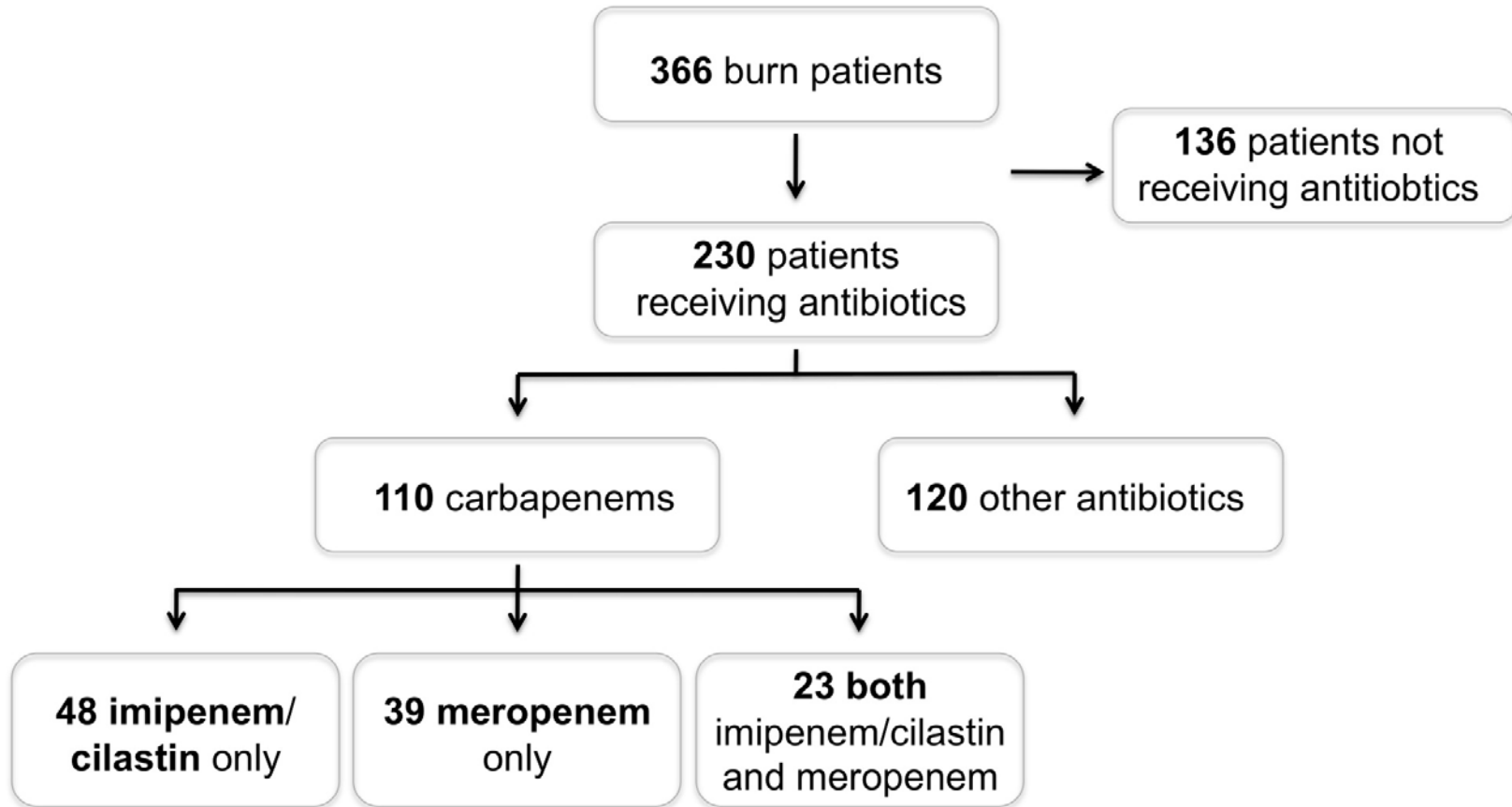3. Number of treatment **days**
4. Number of **cures**

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Number of **TDM requests**

3. Results

a) Study flow chart

b) Burn population with carbapenems (n = 110)

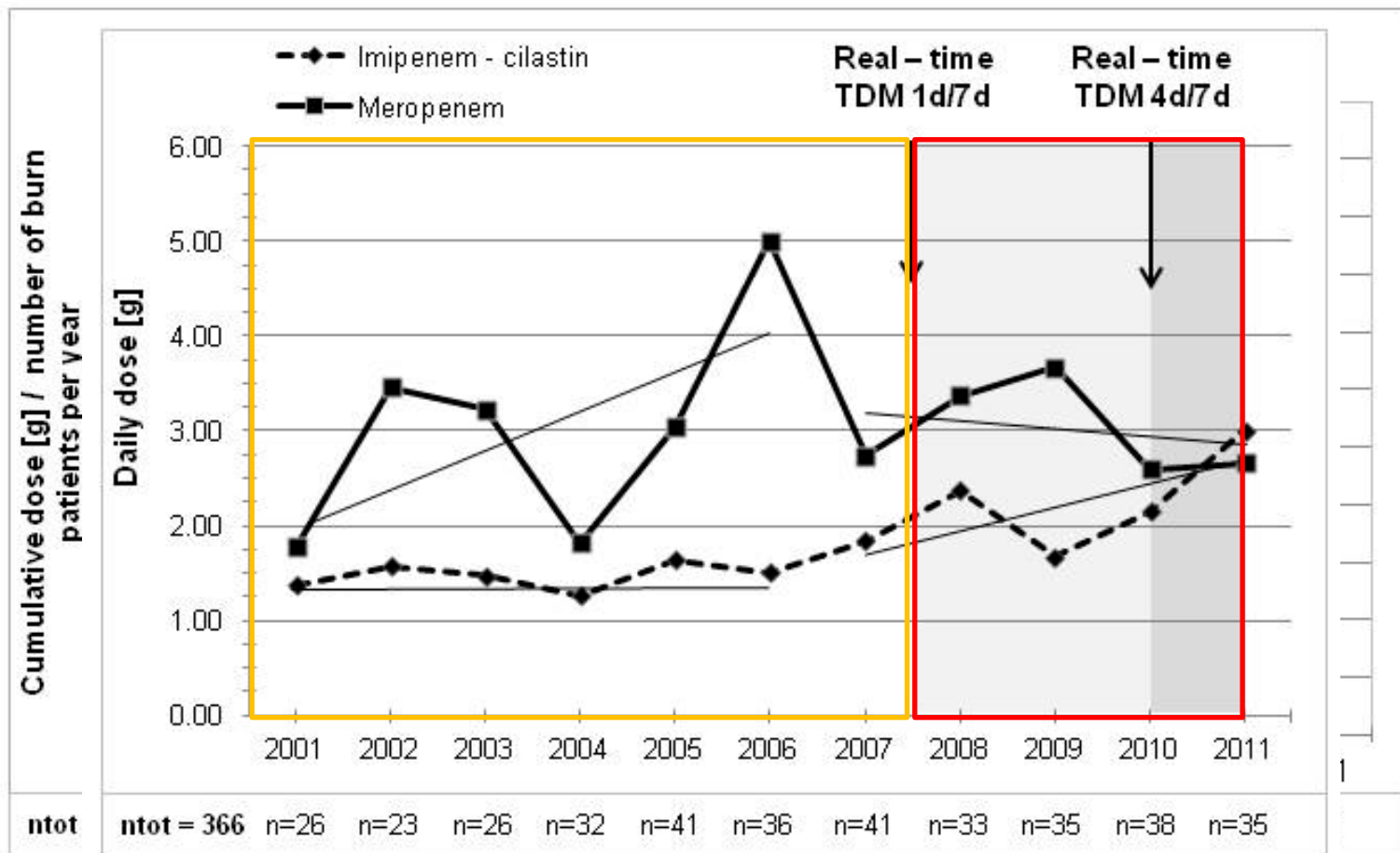|	2001 - 2011	Period 1 TDM on request	Period 2 Real-time TDM[1]	P-value
	(n = 110)	(n = 63)	(n = 47)	
Demographics				
Age, yrs (median [p25;p75])	45.50 [29.00;59.00]	42.00 [28.00;58.00]	50.00 [34.00;61.00]	0.18
Male (n, %)	62 (56.4)	37 (58.7)	25 (53.2)	0.70
Burn characteristics				
TBSA (median [p25;p75])	30.00 [19.75;46.25]	30.00 [20.00;45.00]	28.00 [17.00;50.00]	0.92
< 20% (n, %)	27 (24.5)	13 (20.6)	14 (29.8)	0.37
20-40% (n, %)	48 (43.6)	32 (50.8)	16 (34.0)	0.08
41-60% (n, %)	23 (20.9)	13 (20.6)	10 (21.3)	1.00
> 60%	12 (10.9)	5 (7.9)	7 (14.9)	0.35
Inhalation (n, %)	56 (50.9)	35 (62.5)	21 (37.5)	0.33
Ryan Score (mean ± SD)	1.06 ± 0.67	1.06 ± 0.64	1.06 ± 0.70	1.00
Outcome				
Length of stay (median [p25;p75])	32.00 [18.75;53.25]	31.00 [18.00;51.00]	33.00 [20.00;66.00]	0.47
Burn ICU mortality (n, %)	12 (10.9)	5 (7.9)	7 (14.9)	0.35

c) The evolution of the prescription

Figure 1: Imipenem (dashed line) and meropenem (full line) prescription from 2001 to June 2007 **(period 1)** and overly period 2 (2001 (grey) **period 2** and period 2 (July 2007 and 2011). of antibiotic used each year with the total number of patients admitted to the Burn ICU during the corresponding year.

	Period 1	Period 2	P-value
	TDM on request	Real-time TDM	
Imipenem	(n = 53)	(n = 18)	
Course per year (mean ± SD)	10.29 ± 5.50	4.20 ± 2.28	0.04
Daily dose (grams) (median [p25;p75])	1.60 [1.23; 1.77]	1.81 [1.54; 2.44]	0.01
Meropenem	(n = 24)	(n =38)	
Course per year (mean ± SD)	4.43 ± 2.57	10.80 ± 5.72	0.02
Daily dose (grams) (median [p25;p75])	2.29 [2.00; 3.92]	2.61 [2.00; 3.95]	0.77

Figure 3: Correlation between the number of TDM requests and the daily dosage of imipenem / cilastin
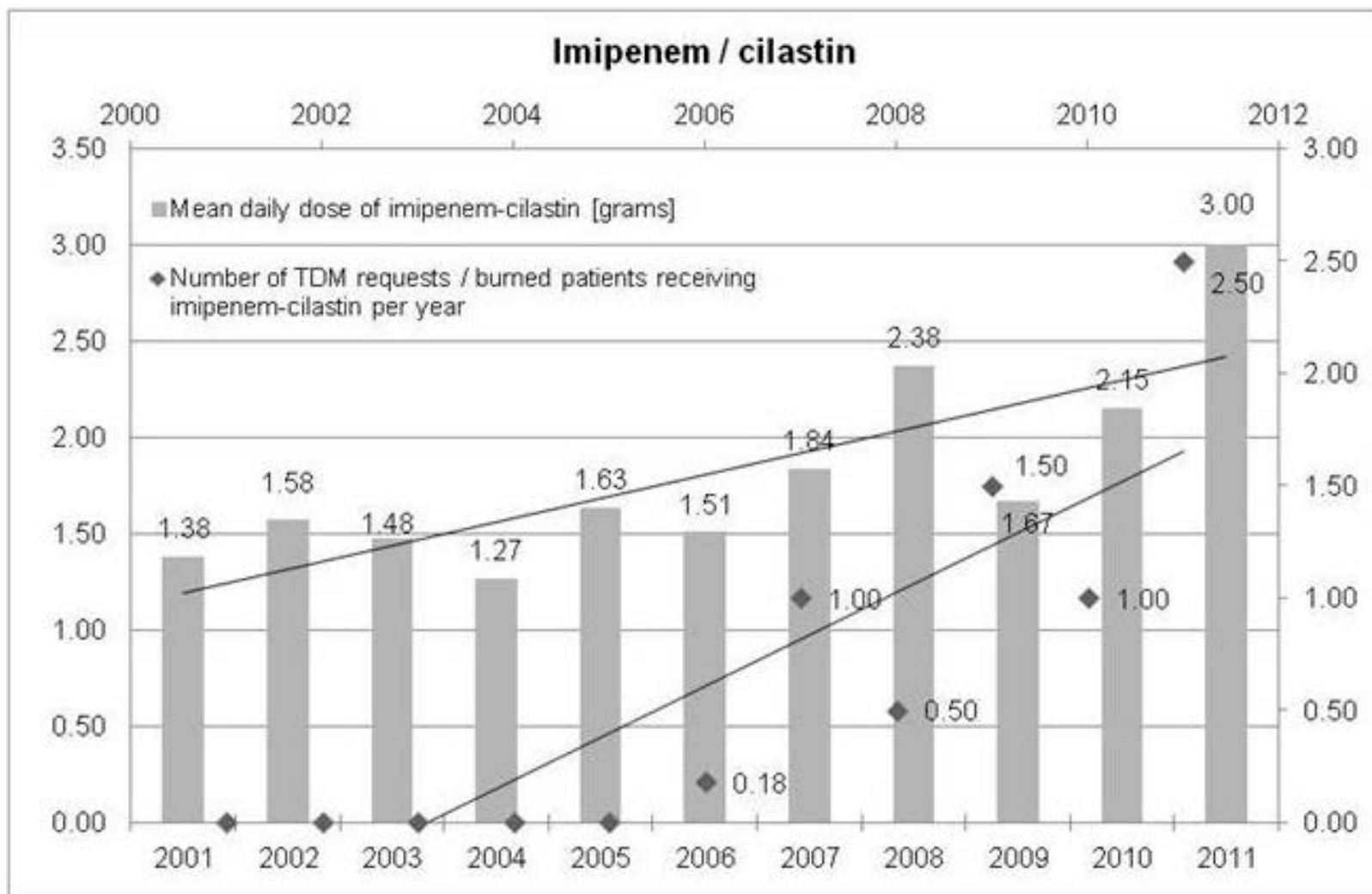
4. Conclusion

Real-time availability of **TDM** → **significative changes** in carbapenems prescription.

Consumption
- ✓ **Imipenem/cilastin**: ↓ from 10.3 cures/year (**period 1**) → 4.2 cures/year (**period 2**)
- ✓ **Meropenem**: ↑ from 4.4 cures/year (**period 1**) → 10.8 cures/year (**period 2**)

Daily doses
- ✓ **Imipenem/cilastin**: ↑ from 1.6g (**period 1**) → 1.8g. (**period 2**)
- ✓ **Meropenem**: peak of 5.0g. (2006) → 2.7g (2011)

Clinicians were justified in :
- Maintaining meropenem dosage
- Increasing the dosage of imipenem/cilastin

Further prospective studies are required to determine if these changes will impact treatment efficacy and safety.