

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

09 Jun 2026

### Pharmacokinetics and safety of high-dose intravenous daptomycin in infected hemodialysis patients

#### Protocol summary

##### Summary

Study rationale: central venous catheters are commonly used in conventional dialysis [16.5% (4768 patients) of the patients undergoing hemodialysis in France in 2010]. Their main complication is Catheter related Blood Stream Infection (CRBSI), which is associated with substantial morbidity and mortality. Staphylococcus sp, particularly Meticillin Resistant Staphylococcus Aureus (MRSA) is frequently associated with CRBSI. Treatment is based on catheter withdrawal and anti-Staphylococci parenteral antibiotic therapy. Vancomycin is the first line treatment but Daptomycin is an alternative treatment when Minimum Inhibitory Concentrations (MIC) of Vancomycin are  $\geq 2 \mu\text{g/ml}$ . However, removal of the catheter is an important issue among patients on hemodialysis, and the prevalence of MRSA and Coagulase Negative Staphylococci (CoNS) with elevated MIC to Vancomycin is increasing. Before setting up a clinical study to assess Daptomycin efficacy and safety in hemodialysis patients with infected catheter, pharmacokinetics parameters need to be collected. This is the aim of this pilot pharmacokinetics study in this specific population. In such context, Daptomycin is an interesting alternative as it is effective in MRSA and CoNS infections, is well tolerated and has shown to penetrate into bio films in vitro (Raad AAC 2007 ; Aslam AJIC 2008, Leite CM 2011) which could be of advantage when treating infected devices. A few studies showed satisfying pharmacokinetics parameters among non-infected patients with conventional hemodialysis where Daptomycin was administered at 6mg/kg/dialysis. Daptomycin has been shown to be a concentration-dependent antibiotic, and the AUC/minimum inhibitory concentration (MIC) ratio is the PK-PD parameter that is most closely linked with antibacterial activity (Bowker 2009; Dandekar 2003; Louie 2001; Safdar 2004). However, there is no single optimal AUC/MIC ratio associated with maximal effect throughout the literature (Bowker 2009; Dandekar 2003; Louie 2001; Safdar

2004). In some patients, Falcone (CID 2013) observed an increased Daptomycin clearance and lower exposition to drug in critically ill patients, correlated with infection severity and MRSA bacteremia. Recent data suggest that 10mg/kg/d among patient without renal impairment is a preferred dosing to avoid resistance and maximize the antibacterial effect: indeed it seems to be the dose associated with the best benefit/risk ratio (Soon IJAA 2013), with good bacteriostatic and bactericidal activity on strains with MIC  $< 2 \mu\text{g/mL}$ , and low toxicity risk. However, data are scarce on Daptomycin at 10mg/kg among patients with gram positive infections on hemodialysis. Since the literature is inconclusive on the definitive AUC/MIC threshold, we need an AUC distribution resulting from dosing schemes under chronic hemodialysis, as it is the PK target the most closely linked to effect. It is therefore important to better characterize Daptomycin PK in infected patients on hemodialysis. Hence, we evaluate the pharmacokinetics of Daptomycin at 10mg/kg after each of 3 consecutive dialysis sessions among patients with central catheter related blood stream infections on hemodialysis.

#### General information

##### Acronym

DaptoHD

##### IRCT registration information

IRCT registration number: **IRCT2016101730345N1**

Registration date: **2016-10-30, 1395/08/09**

Registration timing: **retrospective**

Last update:

Update count: **0**

##### Registration date

2016-10-30, 1395/08/09

##### Registrant information

##### Name

Guillaume Béraud

**Name of organization / entity**

CHU de Poitiers

**Country**

France

**Phone**

+33549443905

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**Recruitment status**

Recruitment complete

**Funding source**

None

**Expected recruitment start date**

2011-08-31, 1390/06/09

**Expected recruitment end date**

2015-01-31, 1393/11/11

**Actual recruitment start date**

empty

**Actual recruitment end date**

empty

**Trial completion date**

empty

**Scientific title**

Pharmacokinetics and safety of high-dose intravenous daptomycin in infected hemodialysis patients

**Public title**

Daptomycin at high dose for hemodialysis patient

**Purpose**

Treatment

**Inclusion/Exclusion criteria**

Inclusion: patients > 18 years, requiring conventional hemodialysis for chronic renal failure hospitalized at the University Hospital of Poitiers (CHU de Poitiers) and presenting a CRBSI. Exclusion: pregnant or breeding women, pneumonia, septic shock (which may affect pharmacokinetic parameters and therefore not represent the principal hemodialysis population); CPK >3ULN; known hypersensitivity to Daptomycin.

**Age**

From 18 years old

**Gender**

Both

**Phase**

0

**Groups that have been masked**

No information

**Sample size**

Target sample size: 10

**Randomization (investigator's opinion)**

N/A

**Randomization description****Blinding (investigator's opinion)**

Not blinded

**Blinding description****Placebo**

Not used

**Assignment**

Single

**Other design features**

Pharmacokinetics

**Secondary Ids**

empty

**Ethics committees****1****Ethics committee****Name of ethics committee**

CPP Ouest III

**Street address**

CHU de Poitiers

**City**

Poitiers

**Postal code**

86000

**Approval date**

2011-02-01, 1389/11/12

**Ethics committee reference number**

n° 13.10.33

**Health conditions studied****1****Description of health condition studied**

Catheter related blood stream infection

**ICD-10 code**

T80-211

**ICD-10 code description**

Catheter-related bloodstream infection (CRBSI)

**Primary outcomes****1****Description**

Pharmacokinetics of Daptomycin at 10 mg/kg after dialysis in conventional hemodialysis in patients with central catheter related infections

**Timepoint**

1 week

**Method of measurement**

Cmax, Cmin, AUC

**Secondary outcomes****1****Description**

To evaluate clinical parameters (physical examination, vital signs and temperature) in order to monitor infection evolution and side effects in relation to Daptomycin treatment.

**Timepoint**

2 weeks

**Method of measurement**

Cinical examination

## Intervention groups

1

### Description

Patient on hemodialysis (regimen 2/2/3) with suspected CRBSI will be treated with Daptomycin at 10mg/kg immediately after dialysis (2 minutes intravenous infusion). Area under curve for 48h (AUC48h), AUC72h, Cmax, C0.5h (30 min after infusion) and Cmin will be determined. Pharmacokinetics parameters will be documented during the first 3 Daptomycin injections with blood sampling at 2 min, 1h, 2h, 4h, 12h, 24h, 44h (immediately before the next dialysis) and at 48h (immediately after completion of dialysis and before the next dose) after each injection. A 72h point will be added if the interval between two subsequent hemodialysis sessions and therefore also the Daptomycin injection interval of Daptomycin is 72 h. Treatment will be adapted according to microbiological results. Treatment duration is determined by the investigator according to medical need and microbiology. Catheter removal will be determined by the investigator according to infection severity, microbiology when available (systematic removal in case of Candida or Pseudomonas aeruginosa infections), and possibilities to create another vascular access if needed (hemodialysis catheters being vital for these patients, a conservative approach can be used as described by ERA-EDTA guidelines in 2007 and the Infectious Diseases Society of America in 2009). If the catheter is left in place, antiseptic lock (taurolidin) will be used at the end of each hemodialysis session.

### Category

Treatment - Drugs

## Recruitment centers

1

### Recruitment center

#### Name of recruitment center

CHU de Poitiers

#### Full name of responsible person

Guillaume Béraud

#### Street address

2, rue de la Milétrie

#### City

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## Sponsors / Funding sources

1

### Sponsor

#### Name of organization / entity

CHU de Poitiers

#### Full name of responsible person

Frank Bridoux

#### Street address

2, rue de la Milétrie

#### City

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#### Grant name

#### Grant code / Reference number

#### Is the source of funding the same sponsor organization/entity?

Yes

#### Title of funding source

CHU de Poitiers

#### Proportion provided by this source

100

#### Public or private sector

empty

#### Domestic or foreign origin

empty

#### Category of foreign source of funding

empty

#### Country of origin

#### Type of organization providing the funding

empty

## Person responsible for general inquiries

### Contact

#### Name of organization / entity

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#### Full name of responsible person

Guillaume Béraud

#### Position

MD, PhD

#### Other areas of specialty/work

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**Province****Sharing plan****Deidentified Individual Participant Data Set (IPD)***empty***Study Protocol***empty***Statistical Analysis Plan***empty***Informed Consent Form***empty***Clinical Study Report***empty***Analytic Code***empty***Data Dictionary***empty*