JNI 21es Journées Nationales d'Infectiologie
Poitiers
et la région Nouvelle Aquitaine
Palais des Congrès du Futuroscope
du mercredi 9 septembre 2020
au vendredi 11 septembre 2020

SABATO – *S. aureus* Bacteremia Antibiotic Treatment Options

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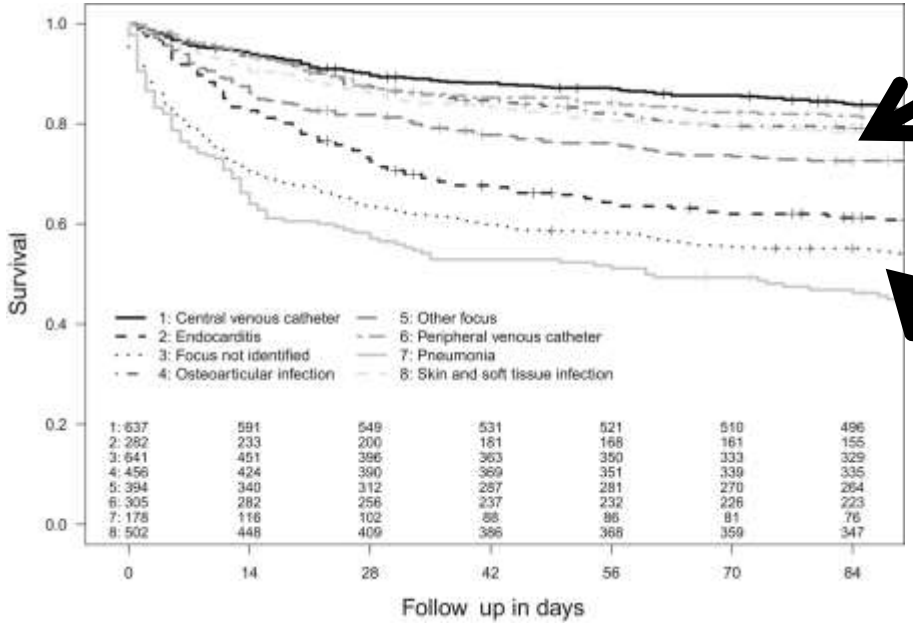
Déclaration d'intérêts de 2014 à 2019

- **Intérêts financiers : none**
- **Liens durables ou permanents : none**
- **Interventions ponctuelles : none**
- **Intérêts indirects : none**

S. aureus bacteraemia



CVC, skin/soft-tissue, osteoarticular

endocarditis, unknown focus, pneumonia

n=3395
Kaasch, *J Infect,* 2014

SABATO study

Standard therapy: >= 14 days intravenous therapy

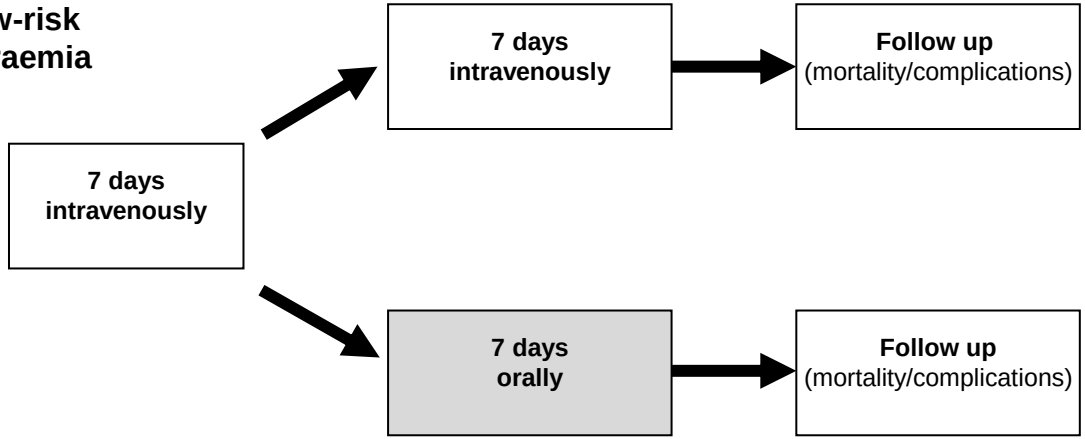
Is oral switch therapy after 7 days as safe as intravenous treatment?

Rationale

Benefits	Risks
Early discharge Fewer complications of intravenous therapy - thrombophlebitis - line infection - fluid overload	Oral therapy might be less effective

Study Design

Patients with low-risk
***S. aureus* bacteraemia**



Early challenges

- **Conceptual**
  - What are low-risk patients?
  - What is a relevant endpoint?
  - Which drugs?
- **Practical**
  - What is a desirable and feasible sample size?
  - How much monitoring is needed?
- **Administrative**
  - How to organize an international study?

What are low-risk patients?

SABATO IV → oral

Inclusion

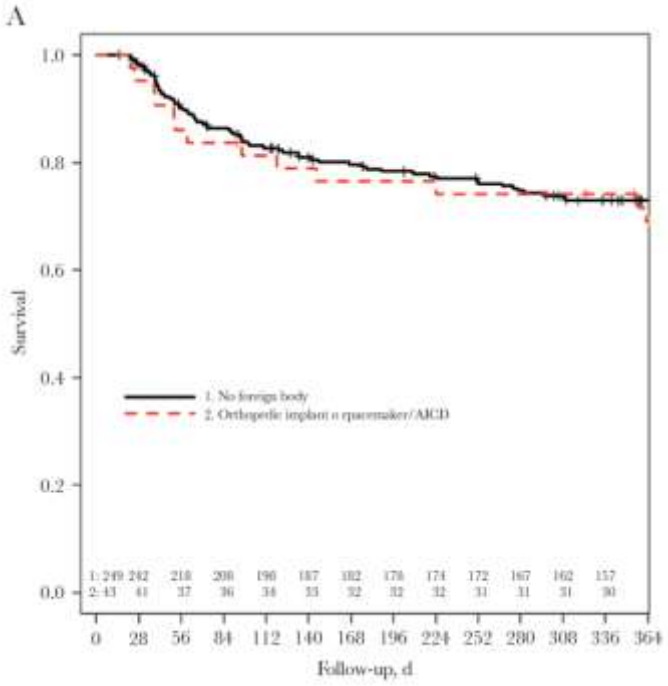
- 5-7 days of adequate intravenous treatment
- uncomplicated SAB (absence of deep focus)
- intravascular catheter removed within 4 days
- negative blood culture at 24-96h

Exclusion

- severe immunodeficiency (e.g. neutropenia)
- some permanent foreign bodies (e.g. prosthetic valve)
- end-stage renal disease, severe liver disease in some cases

Low-risk patients

- orthopaedic implant?
- pacemaker?



n=1288 (n=292)
Kaasch, *OFID,* 2020

Endpoints

Primary

- **"SAB-related complications" (recurrent SAB, deep-seated *S. aureus* infection or attributable mortality) within 90 days**

Secondary

- **Length of hospital stay**
- **14, 30 and 90-day survival**
- **Complications of intravenous therapy**

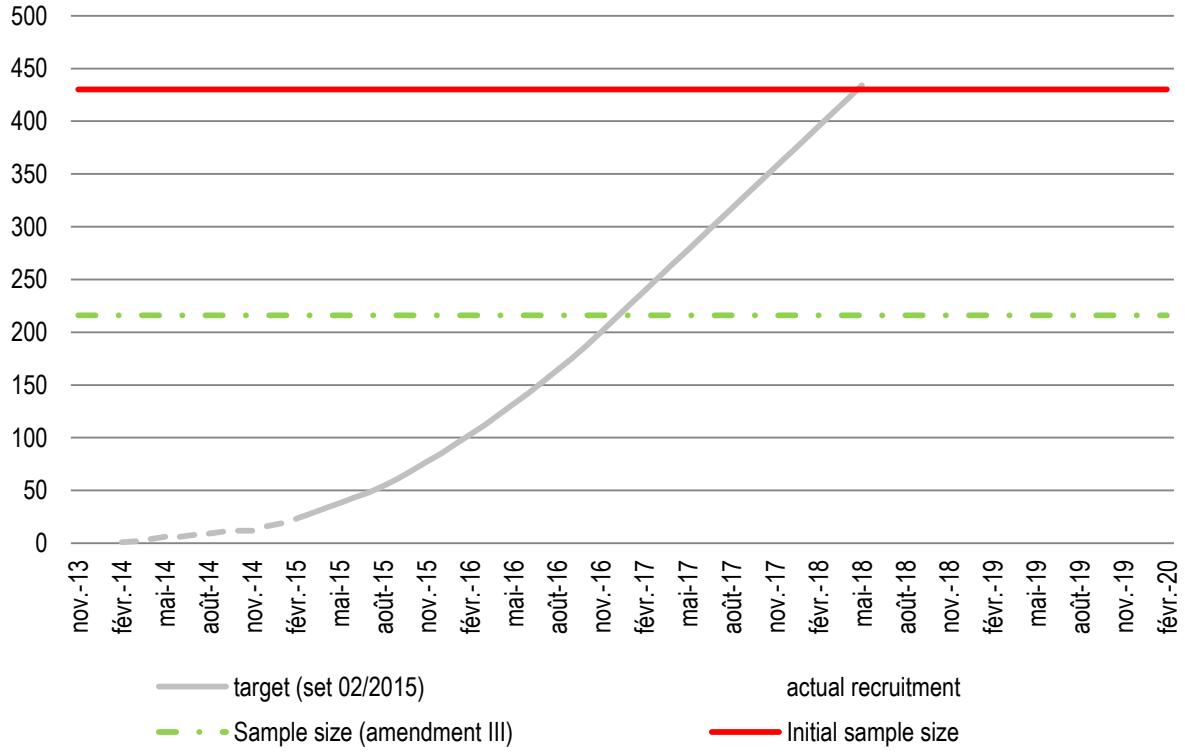
Safety

- ***Clostridium difficile* associated diarrhoea (CDAD)**
- **(severe) adverse events**

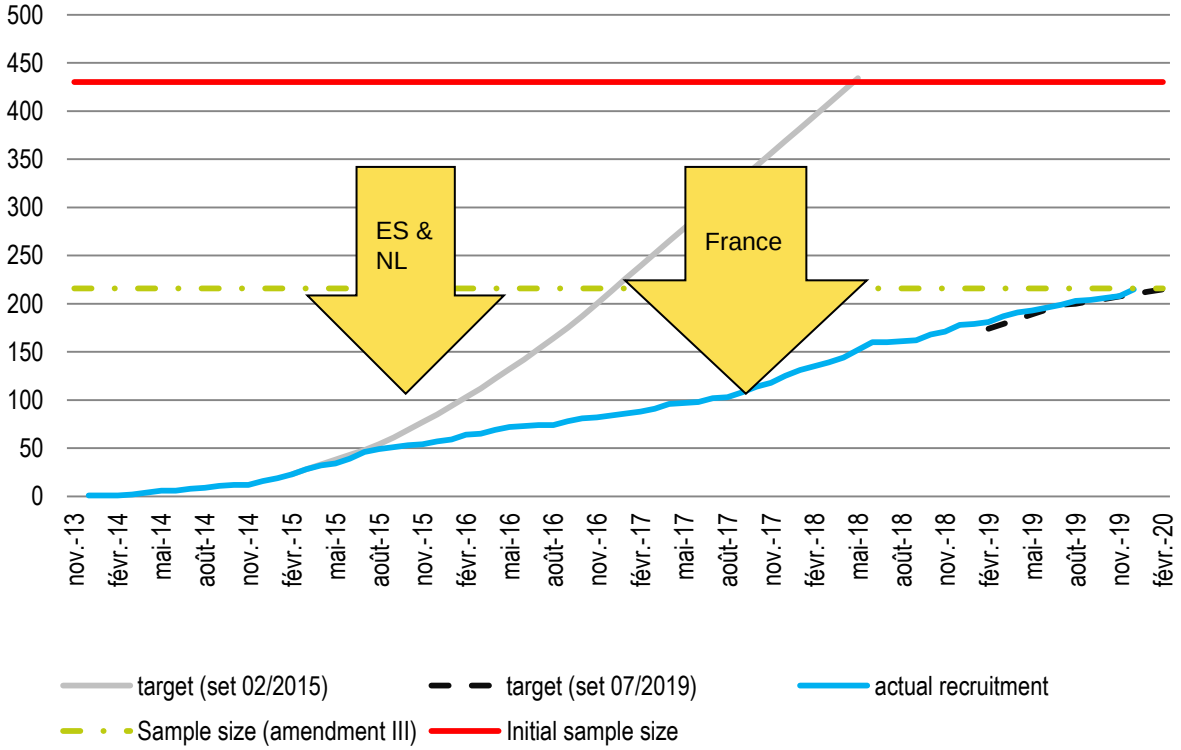
Desirable sample size

- Expected effect size (complications in 1-5%)
- Non-inferiority margin (5%, 10%, 15%, 20%)
- 5% → 430 subjects

Recruitment



Recruitment



country	sites
D	12
ES	4
NL	5
F	15

Screening vs. Enrolment

- **Screened: 5.331**
- **Recruited: 215**

→ Ratio 1 : 24.7

Choice of drugs

	First choice	Alternative
oral therapy		
MSSA	trimethoprim/ Sulfamethoxazole (160/800mg q12h)	clindamycin (600 mg q8h)
MRSA	as above	linezolid (600 mg q12h)
intravenous therapy		
MSSA	cloxacillin (2g q6h) cefazolin (2g q8h)	vancomycin (1g q12h)
MRSA	vancomycin (1g q12h)	daptomycin (6-10 mg/kg q24h)

How to organize?

Sponsor

University of Cologne/ HH-University Düsseldorf

Princ. Coord. Inv.

A. Kaasch

CTU Cologne/Düsseldorf

- Quality control
- Data management
- Administrative PM
- Safety Management

Scientific Advisory Committee

Steering Committee

International trial units

- Barcelona
- Utrecht/Amsterdam
- Paris

Data Monitoring Committee

Data Review Committee

IMSIE Cologne

- Statistics

36 study centers

Problems on the way…

- international regulatory aspects
- change of sponsor
- adjustment of sample size
- language barrier (legal contracts)
- COVID19

Current status

- Recruitment closed
- Final meeting of adjudication committee pending
- Final analysis pending

Credits

Thanks to all persons involved in the study, particularly:

- Administrative: A. Rommerskirchen, M. Noret, R. Prinz-Langenohl
- Study site leaders: G. Fätkenheuer, N. Jung, M. Hellmich (Köln), W.V. Kern, Siegbert Rieg (Köln), K. Arasteh, H. Stocker (Berlin), K. Kösters (Krefeld), T. Welte (Hannover), M. Pletz (Jena), S. Lemmen (Aachen), J. Rupp (Lübeck), S. Reuter (Leverkusen), B. Salzberger, F. Hanses (Regensburg), C. Stephan (Frankfurt), J. Kluytmans (Breda), M. Bonten (Utrecht), A. Soriano, L. Morata (Barcelona), J. Rodríguez-Baño, E. Lopez, J. Cisneros (Sevilla), M. Riera (Palma), J. Gaillat, E. Rouveix-Nordon, F. Mechai, B. Fantin, R. Lepeule, J. Molina (Paris), E. Forestier (Chambéry), T. Guimard (La Roche sur Yon), D. Boutoille (Nantes), L. Hocqeloux (Orléans), J. Tallarmin (Quimper), P. Tattevin (Rennes), F. Lucht (St. Etienne), J. Stahl (Grenoble), B. Sinha (Groningen), A. Vlek (Utrecht)
- All study site staff
- All panel and board members