SABATO – S. aureus Bacteremia Antibiotic Treatment Options

Prof. Achim Kaasch, Medical Faculty, Otto-von-Guericke University, Magdeburg
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: \(\geq 14\) days intravenous therapy

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

- Early discharge
- Fewer complications of intravenous therapy
  - thrombophlebitis
  - line infection
  - fluid overload

## Risks

- Oral therapy might be less effective
Study Design

Patients with low-risk *S. aureus* bacteraemia

- 7 days intravenously
- Follow up (mortality/complications)

- 7 days orally
- Follow up (mortality/complications)
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?

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% $\rightarrow$ 430 subjects
Recruitment

- Target (set 02/2015)
- Actual recruitment
- Sample size (amendment III)
- Initial sample size
Recruitment

<table>
<thead>
<tr>
<th>country</th>
<th>sites</th>
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<tbody>
<tr>
<td>D</td>
<td>12</td>
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<td>ES</td>
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<td>NL</td>
<td>5</td>
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<td>15</td>
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- **ES & NL**
- **France**

- target (set 02/2015)
- target (set 07/2019)
- actual recruitment
- Sample size (amendment III)
- Initial sample size
Screening vs. Enrolment

• Screened: 5,331
• Recruited: 215

→ Ratio 1 : 24.7
# Choice of drugs

<table>
<thead>
<tr>
<th>Choice of therapy</th>
<th>First choice</th>
<th>Alternative</th>
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<tbody>
<tr>
<td><strong>oral therapy</strong></td>
<td></td>
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<tr>
<td>MSSA</td>
<td>trimethoprim/ Sulfamethoxazole (160/800mg q12h)</td>
<td>clindamycin (600 mg q8h)</td>
</tr>
<tr>
<td>MRSA</td>
<td>as above</td>
<td>linezolid (600 mg q12h)</td>
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<tr>
<td><strong>intravenous therapy</strong></td>
<td></td>
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<tr>
<td>MSSA</td>
<td>cloxacillin (2g q6h)</td>
<td>vancomycin (1g q12h)</td>
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<tr>
<td></td>
<td>cefazolin (2g q8h)</td>
<td></td>
</tr>
<tr>
<td>MRSA</td>
<td>vancomycin (1g q12h)</td>
<td>daptomycin (6-10 mg/kg q24h)</td>
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How to organize?

Sponsor
University of Cologne/ HH-University Düsseldorf

Princ. Coord. Inv.
A. Kaasch

Scientific Advisory Committee

Steering Committee

Data Monitoring Committee

Data Review Committee

36 study centers

CTU Cologne/Düsseldorf
- Quality control
- Data management
- Administrative PM
- Safety Management

International trial units
- Barcelona
- Utrecht/Amsterdam
- Paris

IMSIE Cologne
- Statistics
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. Arastéh, 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