Name of sponsor/company: Heinrich-Heine-Universität Düsseldorf, Universitätsstr.1, 40225 Düsseldorf, Germany **Name of finished product**: - **Name of active ingredient**: Trimethoprim/sulfamethoxazole Clindamycin Linezolid Flucloxacillin Cloxacillin Cefazolin Vancomycin Daptomycin	Individual study table referring to part of the dossier Volume: Page:	(For National Authority Use only)

Title of study:
Early oral switch therapy in low-risk *Staphylococcus aureus* bloodstream infection
Acronym: SABATO (*Staphylococcus aureus* Bacteremia Antibiotic Treatment Options)

Versions of study protocol:
Current version of the trial protocol:
Amendment IV: Version V01-F, 18JUL2019, Study Protocol Version V08-F_18JUL2019
Amendment III: Version V01-F, 20MAR2018, Study Protocol Version V07-F_20MAR2018

Previous versions (Germany, Spain, The Netherlands):
Amendment II: Version V01_0, 20JUL 2016, Study Protocol Version V05_0 of 20JUL2016
Amendment I: Version v01-01-F, 03 December 2014, Study Protocol Version v03-04-F of 03 December 2014

Previous Versions in France (contain minor country specific modifications):
Amendment II: Version V01_0, 20JUL 2016, Study Protocol Version V05-F-France of 20JUL2016
Amendment I: Version v01-01-F, 03 December 2014, Study Protocol Version v03-04-F of 03 December 2014

Registration numbers:
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EudraCT: 2013-000577-77
ISRCTN: NCT01792804, DRKS00004741
Protocol Identification: Uni-Koeln-1400

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Publication (reference):
Kaasch AJ, Rommerskirchen A, Hellmich M, Fätkenheuer G, Prinz-Langenohl R, Rieg S, Kern WV, Seifert H; SABATO trial group. Protocol update for the SABATO trial: a randomized controlled trial to assess early oral switch therapy in low-risk *Staphylococcus aureus* bloodstream infection. Trials. 2020 Feb 12;21(1):175. doi: 10.1186/s13063-020-4102-0.
Kaasch AJ, Fätkenheuer G, Prinz-Langenohl R, Paulus U, Hellmich M, Weiß V, Jung N, Rieg S, Kern WV, Seifert H; SABATO trial group. Early oral switch therapy in low-risk *Staphylococcus aureus* bloodstream infection (SABATO): study protocol for a randomized controlled trial. Trials. 2015 Oct 9;16:450. doi: 10.1186/s13063-015-0973-x.

Studies period (years): 6 years date of first enrollment: 20 Dec 2013 date of last completed: 26 Apr 2020	**Phase of development**: Phase 3

Objectives: The primary objective of this trial is to demonstrate that in patients with low-risk *Staphylococcus aureus* bloodstream infection (SAB) a switch from intravenous to oral antimicrobial therapy (oral switch therapy, OST) is non-inferior to a conventional course of intravenous therapy (intravenous standard therapy, IST). This will be achieved by comparing the rate of SAB-related complications (relapsing SAB, deep-seated infection with *S. aureus*, or mortality attributable to SAB) within 90 days. Low-risk SAB manifests itself typically in patients with comorbidities. Therefore, survival is largely determined by the underlying disease and was not chosen as a primary endpoint. However, death related to SAB is included in the primary endpoint. Death unrelated to SAB will be carefully evaluated and compared.
The secondary objective is to measure the potential benefit for the patient. This is achieved by evaluating the length of hospital stay after the first positive blood culture and complications of intravenous therapy. A considerable number of patients on OST are expected to be discharged earlier from hospital, since hospital stay due to intravenous therapy is no longer required. This will reduce the risks associated with hospitalization and i.v. therapy (catheter-related infection, venous thrombosis, and septic thrombophlebitis) and is likely to improve patients' quality of life.

Methodology: The study is a Phase III, multicentre, open-label, randomized, controlled, non-inferiority trial to test whether a switch form intravenous to oral antimicrobial therapy (oral switch therapy, OST) is non-inferior to a conventional course of intravenous therapy (intravenous standard therapy, IST) in patients with SAB. The clinical trial will be carried out as a multicentre open trial at trial sites in Germany, the Netherlands, France, and Spain.

Patients are randomly allocated to treatment arms (1:1) not earlier than one day before starting study drug. This is achieved by a central 24-7 Internet randomization service ALEA (stratified by study center, permuted blocks of varying length). Authorized local study staff may login to a secure website, randomize a patient and receive an email with attached pdf giving all the details on the allocated treatment. The randomization service is set up and maintained by IMSB, University of Cologne.

Number of patients (planned and analyzed):
Original sample size: 430 patients
recalculated sample size: 215 patients

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Patients screened: 5330
Intention-to-treat analysis 1: 213 patients
Intention-to-treat analysis 2: 206 patients
Per-protocol analysis: 165 patients
Safety analysis: 210 patients

Diagnosis and main criteria for inclusion:
Low-risk *Staphylococcus aureus* bloodstream infection
Principal inclusion criteria:
- blood culture positive for *S. aureus* not considered to represent contamination
- 5-7 days of adequate intravenous antimicrobial therapy

Principal exclusion criteria:
- polymicrobial bloodstream infection
- signs and symptoms of complicated SAB (deep-seated infection, hematogenous dissemination, septic shock, prolonged bacteremia)
- severe comorbidity

Test product, dose and mode of administration, batch number:
Protocol-approved orally administered antimicrobial – Oral switch therapy (OST)
First choice (MRSA and MSSA): trimethoprim-sulfamethoxazole 160/800mg q12h
Second choice (MSSA): clindamycin 600 mg q8h
Second choice (MRSA): linezolid 600 mg q12h

Duration of treatment:
7-9 days

Reference therapy, dose and mode of administration, batch number:
Protocol-approved intravenously administered antimicrobial – Intravenous standard therapy (IST)
First choice (MSSA): flucloxacillin 2g q6h
[Spain/France: cloxacillin (2g q6h)] or cefazolin 2g q8h
Second choice (MSSA): vancomycin 1g q12h
First choice (MRSA): vancomycin 1g q12h
Second choice (MRSA): daptomycin 6 mg/kg q24h

Criteria for evaluation:
Efficacy:
Primary variable
All data were obtained at the study visits or telephone contacts and are based on the assessment of the study physician, patient interviews, laboratory reports, and chart data. After discharge, patients were encouraged to report to the study center any changes in health (e.g. adverse events). Study site staff followed-up on reported issues.
The primary endpoint, SAB-related complication, defined as relapsing SAB, deep-seated infection with S. aureus (clinically suspected or microbiologically confirmed), or death related to SAB, is derived from laboratory and clinical reports. Patients with either condition are classified as “failure”. To ensure a high quality of data, late complications were assessed by the principal investigator. SAB-related complications are classified as either “microbiologically documented” or “clinically suspected”. All cases of SAB-related complication were carefully evaluated for plausibility by the masked Clinical Review Committee (CRC) on the basis of clinical symptoms, vital signs, laboratory parameters, the assessment of the study physician, patient interviews and chart data. The CRC was provided with further information by the principal investigator as needed.

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To qualify for a “microbiologically documented” relapsing SAB or deep-seated infection, the *S. aureus* isolate needs to exhibit the same characteristics as the original infecting isolate (based on antimicrobial susceptibility and genotyping tests as appropriate). Furthermore, the isolated strain needs to be judged not to represent a contaminant by the local investigator.
Relapsing SAB is defined as positive blood culture for *S. aureus* within the intervention or follow-up period. During the follow-up phase blood cultures were taken according to standard of care at the local site, when a bloodstream infection was clinically suspected. Since every blood culture carries the risk of contamination, study sites were encouraged to draw at least two blood cultures, when clinically indicated.
Proven catheter-related *S. aureus* bloodstream infections during the follow-up period are not considered relapsing SAB, since they are highly likely to result from a new infection. Catheter-related blood-stream infection is considered “proven”, when:
- The same *S. aureus* isolate is present in the positive blood culture and in the catheter tip culture, or
- The same *S. aureus* isolate is present in the positive blood culture and in pus or skin swab from the catheter exit site, or
- Two initial bloodcultures positive for *S. aureus* exhibit a positive differential time to positivity and there is no other plausible source of infection.

Deep-seated infection is any deep-seated focus of *S. aureus* infection resulting from hematogenous dissemination. In case of a “microbiologically documented deep-seated infection”, diagnosis requires either a positive culture from the respective site, or a blood culture positive with *S. aureus* plus imaging studies showing the presumed focus. In case of a “clinically suspected deep-seated infection”, there are no microbiological results available or there is a plausible reason for a negative result. The classification of deep-seated infection was finally judged by the CRC based on all available evidence.
Deep-seated foci consist of, but are not limited to:
- Infective endocarditis, judged by modified Duke criteria
- Vertebral and non-vertebral osteomyelitis
- Suppurative arthritis
- Spinal empyema
- Muscle abscess (e.g. psoas abscess)
- Meningitis, brain abscess
- Lung abscess
- Visceral abscess (kidney, liver, spleen, etc.)

Catheter-related infections, superficial skin-and soft tissue infections such as thrombophlebitis, or superficial wound infections do not qualify as “deep-seated”, since they are likely to result from a new infection.
There is a possibility that late complications of SAB may be overlooked. By educating the patient about signs and symptoms of potential late complications, we expect that a diagnostic work-up was performed in nearly all suspected cases. In the case of a suspected complication, the patient’s current care-providers were contacted by the principal investigator for relevant clinical information and lab reports.
Detailed patient data are listed in a table for patients who reached the primary endpoint.

Secondary variables
The length of hospital stay is defined as the number of days a patient spends in the hospital from date of the first positive blood culture to discharge. If the date of the first positive blood culture is prior to the date of admission to the hospital, the date of admission is used instead. When a patient is transferred to another hospital, days spent at the other hospital are included. Note: In-hospital days due to re-admissions are not counted.
Survival will be assessed during the hospital stay and at the follow-up telephone interviews. Death will be attributed to SAB when at least one of the following conditions is present:
- positive blood culture for *S. aureus* drawn within 72h before death
- persistent focus of deep-seated *S. aureus* infection at time of death

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- persistent signs and symptoms of systemic infection at time of death as judged by study physician
- post-mortem analysis proving *S. aureus* related complication as cause of death

All other causes are classified as unrelated to SAB.
The survival time is defined as the number of days a patient survives from the date of the first positive blood culture to (i) death, or (ii) end of the study, or (iii) loss of contact or withdrawal from the study.
Complications of i.v. therapy will be assessed from chart data, assessment of the study physician and from the patient interview. Complications may include, but are not limited to:
- local complications, such as: infiltration, extravasation, hematoma, phlebitis, thrombosis, thrombophlebitis, or infection at catheter insertion site
- systemic complications, such as: embolism, systemic infection, circulatory overload, allergic reaction
- in vancomycin therapy: “red man syndrome” due to inappropriately fast i.v. administration
- any other complication felt to be due to intravenous therapy by the principle investigator

Safety:
In patients that report diarrhea during the intervention or follow-up phase, testing for *Clostridium difficile* associated diarrhea (CDAD) is not mandatory and will be performed according to the standard of care at the respective trial site. Furthermore, AEs and SAEs are collected until EOS.

Statistical methods
Analysis populations
All analyses are done on three study populations:
The primary analysis set is derived from the per-protocol (PP) population. This dataset includes all study subjects who were essentially treated according to protocol and reached a defined endpoint in the trial (SAB-unrelated deaths will be excluded). The evaluability of study subjects will be assessed in a blind manner by the CRC. Details of the selection criteria and evaluation criteria are laid down in the CRC manual.
The secondary analysis set is derived from the intention-to-treat (ITT) population. This dataset includes all randomized study subjects, analyzed as assigned, with indeterminate and missing outcomes counted as failures. For time-to-event outcomes these cases are censored. Following current recommendations, CPMP/EWP/558/95 rev 2 and CPMP/EWP/482/99, the primary analysis is based on the per-protocol set; the analysis of the full analysis set (intention-to-treat, all randomized patients) will be of equal importance and should lead to similar conclusions for a robust interpretation.
The ITT population will be analysed as (ITT-1) any patient randomized, (ITT-2) only patients that were randomized AND received study drug without patients in whom a major inclusion criterion was violated.
The tertiary analysis set is for safety purposes (safety population). This dataset includes all study subjects who received any study drug as treated. Specifically, patients who ever received an oral antibiotic are compared to patients who never received an oral antibiotic.

Major protocol violations / Withdrawals
A premature withdrawal occurs when an enrolled patient ceases participation in the study prior to the completion of the protocol (e.g. withdrawn consent). All patients prematurely discontinuing from the study, regardless of cause, should receive a final evaluation at the time of withdrawal, preferably by a study visit. Premature withdrawal is considered a protocol violation and patients may be classified as non-evaluable (to be decided upon by the masked CRC). All data collected until this point of time will be stored according to AMG §40, 2a, 3. Patients will not be replaced. If possible, EOS and EOT data should be collected from each patient (this is relevant for the ITT analysis)
In case a patient is withdrawn from the study before the first dose of study drug (e.g. due to withdrawn informed consent, or a late positive follow-up blood culture), baseline information will be collected, but follow-up visits are not performed. These patients will be included in ITT-1.

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Primary analysis
The primary endpoint SAB-related complications (relapsing SAB, deep-seated infection with *S. aureus*, or mortality attributable to SAB) within 90 days is evaluated regarding non-inferiority of oral vs. intravenous antimicrobial therapy by Zhao's test (test 1) of non-null hypothesis on proportions stratified by study center at one-sided level 5% and with a non-inferiority margin of 10%. Thus, the hypotheses in terms of the proportion p of patients with SAB-related complications to be decided upon are
(A: null hypothesis) H_0: $p_{OST} > p_{IST} + 0.10$ vs
(A: alternative hypothesis) H_a: $p_{OST} \leq p_{IST} + 0.10$
If this null hypothesis can be rejected (fixed sequence of hypotheses, thus no alpha-inflation), the above test (A) is repeated at one-sided level 2.5%.
If this null hypothesis can also be rejected (fixed sequence of hypotheses, thus no alpha-inflation), the non-inferiority margin of 5% is applied, i.e.
(B: null hypothesis) H_0: $p_{OST} > p_{IST} + 0.05$ vs
(B: alternative hypothesis) H_a: $p_{OST} \leq p_{IST} + 0.05$
If this null hypothesis can also be rejected (fixed sequence of hypotheses, thus no alpha-inflation), the above test (B) is repeated at one-sided level 2.5%.
Corresponding test-based confidence intervals are calculated to aid interpretation.

Secondary analyses
Secondary endpoints are evaluated by descriptive methods (by treatment group), including generalised linear modelling, methods for rates, proportions, and the time to event.
Time to event endpoints such as length of hospital stay or 14, 30 and 90-day survival are analysed with the Kaplan-Meier method. The log-rank test is used to compare survival curves between the two treatment groups. The analysis of length of hospital stay is as follows: (i) Patients who died in hospital or were discharged are counted as events (no censoring); (ii) patients who died in hospital are censored, patients discharged are counted as events; (iii) patients who died in hospital are counted as events, patients discharged are censored ("reverse" Kaplan-Meier method). In addition to Kaplan-Meier curves, descriptive measures such as median and interquartile are reported, too.
Complications of intravenous therapy are counted by treatment group and evaluated with methods for rates or proportions.

Safety
AE/SAEs are MedDRA coded and listed / summarized by treatment group, system organ class, preferred term, severity and relationship. Further safety variables (esp. laboratory data) are listed / summarised by treatment group using valid count and either percentage (qualitative data) or mean, standard deviation and (0, 25, 50, 75, 100) percentiles (quantitative data).
Clostridium difficile associated diarrhea (CDAD) will be counted by treatment group and analysed with methods for rates or proportions.

Subgroup analyses
Subgroup analyses (of primary and secondary endpoints) are performed by sex (male-female ratio 3:2), country (not study center since there are too many (32)) and antibiotic susceptibility status (MSSA/MRSA), respectively. Further subgroup analysis are conducted for (1) different foci of infection, (2) patients with comorbidities (pacemaker, prosthetic joints, moderate or severe liver disease, end-stage renal failure, immune suppression (at least one of the following: corticoid therapy, neutropenia, current antineoplastic therapy, immunosuppressive therapy, organ or marrow transplant)), (3) Charlson Comorbidity Index (<3 vs. >=3), (4) performance of diagnostic echocardiography (TEE/TTE), and (5) age groups (<65y vs. >= 65y). At least 10 patients in each subgroup are necessary for analysis. The infective focus is grouped in "central venous catheter" (central venous catheter, Shaldon catheter, Hickman/Broviac catheter, PICC line, and port system),

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"peripheral catheter" (peripheral venous catheter and arterial catheter), "skin and soft-tissue" (skin and soft tissue infection (without surgical wound) and surgical wound), "other", and "focus not identified".

Summary – Conclusions:

Efficacy results: In the PP analysis of the primary endpoint (SAB-related complications), OST was non-inferior to IST regarding the hierarchical analysis A (for alpha=5% and delta=10%: 90%-confidence interval from -0.0867 to 0.0295, one-sided p<0.001; and for alpha=2.5% and delta=10%: 95%-confidence interval from -0.0960 to 0.0388, one-sided p<0.001), and B (for alpha=5% and delta=5%: 90% confidence interval -0.0867 to 0.0295, one-sided p=0.010; and for alpha=2.5% and delta=5%: 95% confidence interval -0.0960 to 0.0388, one-sided p=0.010). The mean treatment-control difference is -0.0286, favoring OST. See appendix 1 chapter 2.2.2.

In the ITT-1 analysis of the primary endpoint (SAB-related complications), OST was non-inferior to IST regarding the hierarchical analysis A (for alpha=5% and delta=10%: 90%-confidence interval from -0.0666 to 0.0797, one-sided p=0.013; and for alpha=2.5% and delta=10%: 95%-confidence interval from -0.0777 to 0.0907, one-sided p=0.013). Hypothesis B could not be rejected (for alpha=5% and delta=5%: 90% confidence interval -0.0666 to 0.0797, one-sided p=0.207). The mean treatment-control difference is 0.0065 favoring IST. See appendix 1 chapter 3.2.2.

In the ITT-2 analysis of the primary endpoint (SAB-related complications), OST was non-inferior to IST regarding the hierarchical analysis A (for alpha=5% and delta=10%: 90%-confidence interval from -0.0822 to 0.0602, one-sided p=0.002; and for alpha=2.5% and delta=10%: 95%-confidence interval from -0.0931 to 0.0710, one-sided p=0.002). Hypothesis B could not be rejected (for alpha=5% and delta=5%: 90% confidence interval -0.0822 to 0.0602, one-sided p=0.088). The mean treatment-control difference is -0.0110, favoring OST. See appendix 1 chapter 4.2.2.

SAB-related complications within 90 days are a composite endpoint (PP: 4/77 (IST) vs. 3/83 (OST); ITT-1: 13/105 vs. 14/108; ITT-2: 11/101 vs. 11/105). The individual components attributable mortality (PP: 0/79 vs. 1/86; ITT-1: 0/104 vs. 2/108; ITT-2: 0/100 vs. 2/105), deep-seated focus (PP: 4/4 vs. 3/3; ITT-1: 8/13 vs. 5/14; ITT-2: 8/11 vs. 4/11), and relapse of bacteremia (PP: 2/4 vs. 2/3; ITT-1: 4/13 vs. 3/14; ITT-2: 4/11 vs. 3/11). See appendix 1, chapters 2.1.2, 3.1.2, 4.1.2.

Secondary analyses

Length of hospital stay
In the PP analysis, the median length of stay (patients who died in hospital or were discharged are counted as event) was 15 days (95%CI: 15 to 16 days) (IST) vs. 11 days (95%CI: 10 to 13 days) (OST) (p=0.020, Wilcoxon test). See chapter 2.3.1.

In the ITT-1 analysis, the median length of stay (patients who died in hospital or were discharged are counted as event) was 16 days (95%CI: 15 to 16 days) (IST) vs. 12 days (95%CI: 11 to 14 days) (OST) (p=0.055, Wilcoxon test). See chapter 3.3.1.

In the ITT-2 analysis, the median length of stay (patients who died in hospital or were discharged are counted as event) was 16 days (95%CI: 15 to 16 days) (IST) vs. 11 days (95%CI: 11 to 14 days) (OST) (p=0.030, Wilcoxon test). See chapter 4.3.1.

Name of sponsor/company: Heinrich-Heine-Universität Düsseldorf, Universitätsstr.1, 40225 Düsseldorf, Germany	Individual study table referring to part of the dossier Volume: Page:	(For National Authority Use only)
Name of finished product: -		
Name of active ingredient: Trimethoprim/sulfamethoxazole Clindamycin Linezolid Flucloxacillin Cloxacillin Cefazolin Vancomycin Daptomycin		

<u>90-day Survival</u>
In the PP analysis, 0.948 (IST) vs. 0.929 (OST), p=0.616 (log-rank test). See chapter 2.4.8.
In the ITT-1 analysis, 0.890 (IST) vs. 0.836 (OST), p=0.261 (log-rank test). See chapter 3.4.8.
In the ITT-2 analysis, 0.888 (IST) vs. 0.843 (OST), p=0.355 (log-rank test). See chapter 4.4.8.

<u>Complications of intravenous therapy</u>
In the PP analysis, 0.169 (IST) vs. 0.072 (OST), p=0.100. See chapter 2.5.1.
In the ITT-1 analysis, 0.210 (IST) vs. 0.185 (OST), p=0.731. See chapter 3.5.1.
In the ITT-2 analysis, 0.198 (IST) vs. 0.171 (OST), p=0.720. See chapter 4.5.1.

<u>*Clostridium difficile* associated diarrhea</u>
In the PP analysis, 0.014 (IST) vs. 0.024 (OST), p=1.000. See chapter 2.6.1.
In the ITT-1 analysis, 0.114 (IST) vs. 0.130 (OST), p=0.835. See chapter 3.6.1.
In the ITT-2 analysis, 0.099 (IST) vs. 0.114 (OST), p=0.823. See chapter 4.6.1.

<u>Safety results</u>
Frequency of serious adverse events (SAE) per study arm:
In the PP analysis, 26 events in 18 patients (IST) vs. 35 events in 20 patients (OST). See chapter 2.7.
In the ITT-1 analysis, 40 events in 27 patients (IST) vs. 60 events in 36 patients (OST). See chapter 3.7.
In the ITT-2 analysis, 40 events in 27 patients (IST) vs. 58 events in 34 patients (OST). See chapter 4.7.

Frequency of adverse events (AE) per study arm:
In the PP analysis, 40 events in 29 patients (IST) vs. 58 events in 33 patients (OST). See chapter 2.7.
In the ITT-1 analysis, 61 events in 42 patients (IST) vs. 89 events in 52 patients (OST). See chapter 3.7.
In the ITT-2 analysis, 61 events in 42 patients (IST) vs. 87 events in 50 patients (OST). See chapter 4.7.

The study was interrupted from 25 June 2018 to 18 July 2018 (Spain and Germany; until 13 August 2018 in France). The Data Monitoring Committee recommended the temporary stop of enrollment on 25 June 2018 and requested more data. Enrollment was suspended and additional data was provided. On 18 July 2018 the DMC recommended the continuation of the trial as planned.

There were major changes in the trial design during the study. In Amendment I, inclusion criteria were adapted to enhance recruitment to the trial. In Amendment III, the sample size was reduced to 215 patients as recommended by the Scientific Advisory Committee and the Trial Steering Committee.

Conclusion:
The trial has reached its objective. It has been shown that OST is non-inferior to IST using a 5% non-inferiority margin at one-sided significance level 2.5% in PP. In ITT-1/-2 non-inferiority could still be demonstrated at margin 10% at one-sided significance level 2.5%; the 5% margin could not be excluded by the 95% confidence interval. The length of hospital stay was 4-5 days shorter in OST (p=0.02 in PP, Wilcoxon test). The 90-day overall survival was lower in OST (2-6 percentage points difference) but did not reach statistical significance. The difference was mainly due to death unrelated to SAB. Adverse events and serious adverse events were more frequently reported in the OST group.

Date of Report: 07.09.2021

Univ.-Prof. Achim J. Kaasch, Principal Coordinating Investigator, 08.06.2022
Medical Faculty, Otto-von-Guericke University Magdeburg

Approved

Prof. Dr. rer.-medic. Martin Hellmich, Statistician, 08.06.2022
Medical Faculty, University of Cologne, Germany

APPENDIX

1. TFL (attached, AE and SAE listings in chapter 2.7, 3.7, and 4.7)
2. TFL subgroup: male
3. TFL subgroup: female
4. TFL subgroup: age greater than or equal to 65
5. TFL subgroup: age lower than 65
6. TFL subgroup: CCI greater than or equal to 3
7. TFL subgroup: CCI lower than 3
8. TFL subgroup: german study centers
9. TFL subgroup: spain study centers
10. TFL subgroup: french study centers
11. TFL subgroup: dutch study centers
12. TFL subgroup: MSSA
13. TFL subgroup: MRSA
14. TFL subgroup: central venous catheter
15. TFL subgroup: peripheral catheter
16. TFL subgroup: skin and soft tissue
17. TFL subgroup: other focus
18. TFL subgroup: focus unidentified
19. TFL subgroup: with comorbidities
20. TFL subgroup: without comorbidieties
21. TFL subgroup: with echocardiography
22. TFL subgroup: without echocardiography

HISTORY

07.09.2021 Update of TFL document (category „missing values“ of endpoints added in report)
08.06.2022 Update of TFL document (incidence rates for AE, Kaplan-Meier for overall survival)