NEJM BALANCE Trial 2024

Antibiotic Treatment for 7 versus 14 Days in Patients with Bloodstream Infections

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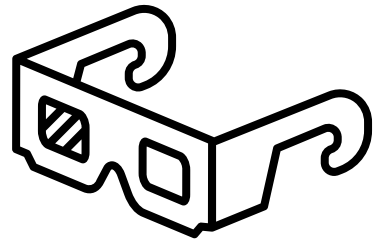
Bloodstream infections:
antibiotic treatment 7 days vs 14 days

Conclusion: antibiotic treatment for 7 days was noninferior to treatment for 14 days.

Let’s dive into it!



INTRO

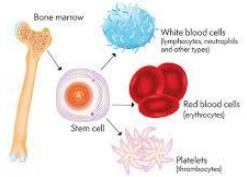
- Bloodstream infections are very common, ~ >600,000 cases in North America alone.
  - 90,000 deaths
- Duration: median 14 days

- Bacteremia Antibiotic Length Actually Needed for Clinical Effectiveness (BALANCE) randomized clinical trial

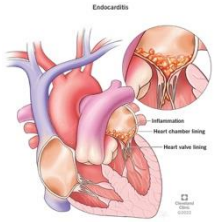
Methods

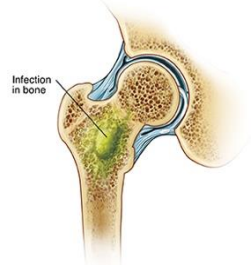
- Multi-center, non inferiority trial – 74 hospital sites in 7 countries
- Exclusion:
  - Immunocompromised

Neutrophils <500



  - ”Complicated bacteremia”





  - Positive culture with common contaminants:
    - Coagulase-negative staph
  - **Staphylococcus Aureus or Staph lugdunensis**
  - Fungemia

Methods – randomization & outcomes

- Stratification according to hospital site and admission to ICU or hospital ward.
- 1:1 ratio = 7 days vs 14 d
- Primary outcome: death from any cause at 90 days
- Secondary outcome: death in the hospital/ICU, relapse bacteremia with same organism, allergy to abx, c diff infection, length of stay, number of ICU-free days

Results

Table 1. Characteristics of the Patients, Infections, and Pathogens at Baseline (Primary Intention-to-Treat Analysis).*

Characteristic	Overall (N=3608)	7-Day Group (N=1814)	14-Day Group (N=1794)
Male sex — no. (%)	1922 (53.3)	974 (53.7)	948 (52.8)
Median age (IQR) — yr	70 (59–80)	70 (58–80)	70 (59–80)
Median SOFA score on day 0 (IQR)†	4 (2–8)	4 (2–8)	5 (2–8)
Enrolled in ICU — no. (%)	1986 (55.0)	997 (55.0)	989 (55.1)
Enrolled in hospital ward — no. (%)	1622 (45.0)	817 (45.0)	805 (44.9)
Receiving mechanical ventilation — no. (%)	766 (21.2)	374 (20.6)	392 (21.9)

Results

Characteristic	Overall (N = 3608)	7-Day Group (N = 1814)	14-Day Group (N = 1794)
Source of acquisition of bacteremia — no. (%)			
Community	2722 (75.4)	1380 (76.1)	1342 (74.8)
Hospital ward	483 (13.4)	231 (12.7)	252 (14.0)
ICU	403 (11.2)	203 (11.2)	200 (11.1)
Source of bacteremia — no. (%)			
Urinary tract	1523 (42.2)	757 (41.7)	766 (42.7)
Intraabdominal or hepatobiliary	679 (18.8)	337 (18.6)	342 (19.1)
Lung	469 (13.0)	229 (12.6)	240 (13.4)
Vascular catheter	229 (6.3)	116 (6.4)	113 (6.3)
Skin, soft tissue, or both	187 (5.2)	104 (5.7)	83 (4.6)
Other	67 (1.9)	37 (2.0)	30 (1.7)
Undefined or unknown	454 (12.6)	234 (12.9)	220 (12.3)

Results

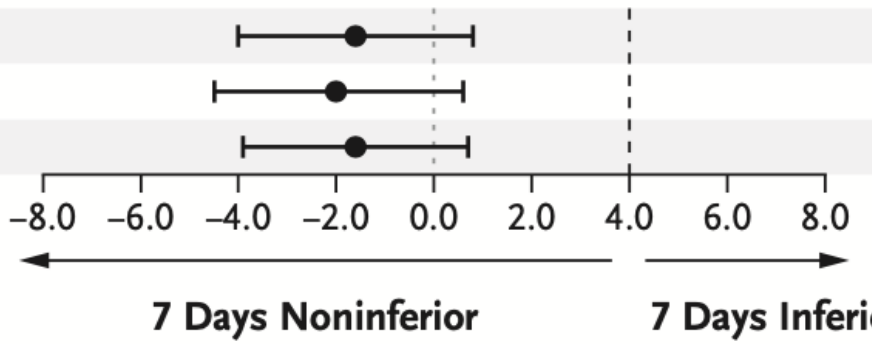
Characteristic	Overall (N = 3608)	7-Day Group (N = 1814)	14-Day Group (N = 1794)
Coexisting conditions — no. (%)			
Diabetes mellitus	1148 (31.8)	596 (32.9)	552 (30.8)
Solid-organ cancer	782 (21.7)	400 (22.1)	382 (21.3)
Obesity	655 (18.2)	331 (18.2)	324 (18.1)
Arrhythmia	540 (15.0)	264 (14.6)	276 (15.4)
Glucocorticoid use or immunosuppression‡	440 (12.2)	230 (12.7)	210 (11.7)
Chronic obstructive pulmonary disease	393 (10.9)	198 (10.9)	195 (10.9)
Renal insufficiency	425 (11.8)	217 (12.0)	208 (11.6)
Coronary artery disease	393 (10.9)	193 (10.6)	200 (11.1)
Congestive heart failure	386 (10.7)	205 (11.3)	181 (10.1)
Liver disease	227 (6.3)	117 (6.4)	110 (6.1)
Peripheral vascular disease	223 (6.2)	107 (5.9)	116 (6.5)
Dialysis dependency	127 (3.5)	60 (3.3)	67 (3.7)
Leukemia or lymphoma	101 (2.8)	49 (2.7)	52 (2.9)

Results

Characteristic	Overall (N=3608)	7-Day Group (N=1814)	14-Day Group (N=1794)
Most commonly isolated pathogens in blood cultures — no. (%)‖			
Escherichia coli	1582 (43.8)	805 (44.4)	777 (43.3)
Klebsiella species	552 (15.3)	273 (15.0)	279 (15.6)
Enterococcus species	250 (6.9)	119 (6.6)	131 (7.3)
Coagulase-negative staphylococci	174 (4.8)	81 (4.5)	93 (5.2)
Pseudomonas species	170 (4.7)	80 (4.4)	90 (5.0)
Streptococcus pneumoniae	164 (4.5)	86 (4.7)	78 (4.3)
Enterobacter species	157 (4.4)	80 (4.4)	77 (4.3)
Proteus species	133 (3.7)	58 (3.2)	75 (4.2)
Serratia species	86 (2.4)	38 (2.1)	48 (2.7)
S. pyogenes	74 (2.1)	39 (2.1)	35 (2.0)
S. agalactiae	75 (2.1)	40 (2.2)	35 (2.0)
Number and type of organisms — no. (%)			
Monomicrobial, gram-negative	2562 (71.0)	1299 (71.6)	1263 (70.4)
Monomicrobial, gram-positive	625 (17.3)	323 (17.8)	302 (16.8)
Polymicrobial	421 (11.7)	192 (10.6)	229 (12.8)

Results

Analysis	7 Days	14 Days	Risk Difference (95% CI)
	no. of events/total no.		*percentage points*
Intention-to-treat	261/1802	286/1779	−1.6 (−4.0 to 0.8)
Per-protocol	178/1370	222/1483	−2.0 (−4.5 to 0.6)
Modified intention-to-treat	247/1788	272/1765	−1.6 (−3.9 to 0.7)



Death by 90 days (the primary outcome) occurred in 261 patients (14.5%) in the 7-day group and in 286 patients (16.1%) in the 14-day group.

Percentages of patients with antimicrobial-related adverse outcomes, C. difficile infections, and secondary infection or colonization with antibiotic-resistant organisms were similar in the two groups

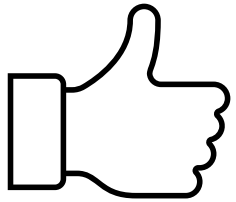
Results

- Since recruitment for the BALANCE trial began, three well-conducted, smaller, randomized, clinical trials have compared 7 days and 14 days of treatment in patients with bloodstream infection. All three trials showed noninferiority of the shorter, 7-day, duration of treatment.
  - Enrolled fewer patients
  - Larger noninferiority margins (10% points)
  - Very few ICU patients included

Takeaways – Did this trial change my way of practice?

- **YES**

- We can extrapolate results to bacteremia with Pseudomonas, some gram positives (streptococci spp),
- We can also extrapolate results to severe illness (patients in ICU)



- **Questions?**

What’s you go-to site to find quick answers?

- Up-to-date
- OCCAM

- You have a patient with bacteremia? What medicine sites say.
- Up to date
- OCCAM

What's you go-to site to find quick answers?

- OCCAM Uncomplicated Gram Negative bacteremia guidelines
- Up-to-date:
  - PsA: immunocompetent 7 to 10 days with good source control
  - Uncomplicated enterobacteriace – 7 days
  - Strep pneumo bacteremia w/o pneumonia 8 – 10 days
  - Group C and Group G strep bacteremia : 14 days
  - GAS : 14 days
  - Enterococcus: 5 to 7 d