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ORIGINAL ARTICLE

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

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BACKGROUND

- Patients with infective endocarditis on the left side of the heart are typically treated with intravenous antibiotic agents for up to 6 weeks. Whether a shift from intravenous to oral antibiotics once the patient is in stable condition would result in efficacy and safety similar to those with continued intravenous treatment is unknown.

Methods

- The Partial Oral Treatment of Endocarditis (POET) trial was a nationwide investigator-initiated, multicenter, randomized, unblinded, noninferiority trial performed at cardiac centers in Denmark.
- From July 15, 2011, to August 30, 2017, a total of 1954 patients who were referred to a cardiac center because of suspected endocarditis were screened for inclusion; 400 patients (20%) with endocarditis on the left side of the heart who fulfilled the modified Duke criteria for definite endocarditis were enrolled

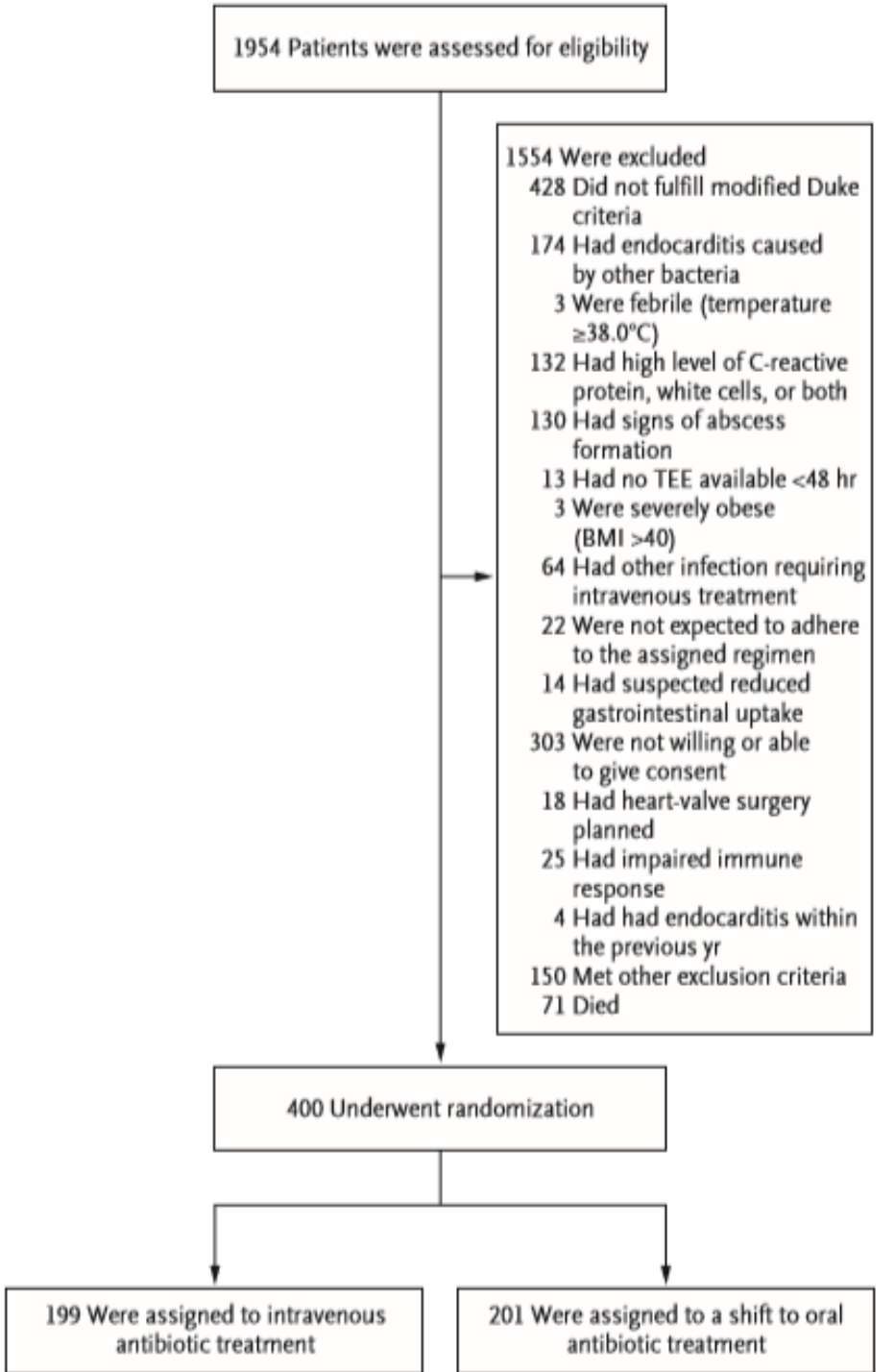

1954 Patients were assessed for eligibility
1554 Were excluded
428 Did not fulfill modified Duke criteria
174 Had endocarditis caused by other bacteria
3 Were febrile (temperature ≥38.0°C)
132 Had high level of C-reactive protein, white cells, or both
130 Had signs of abscess formation
13 Had no TEE available <48 hr
3 Were severely obese (BMI >40)
64 Had other infection requiring intravenous treatment
22 Were not expected to adhere to the assigned regimen
14 Had suspected reduced gastrointestinal uptake
303 Were not willing or able to give consent
18 Had heart-valve surgery planned
25 Had impaired immune response
4 Had had endocarditis within the previous yr
150 Met other exclusion criteria
71 Died
400 Underwent randomization
199 Were assigned to intravenous antibiotic treatment
201 Were assigned to a shift to oral antibiotic treatment

Table 1. Characteristics of the Patients at Baseline.*

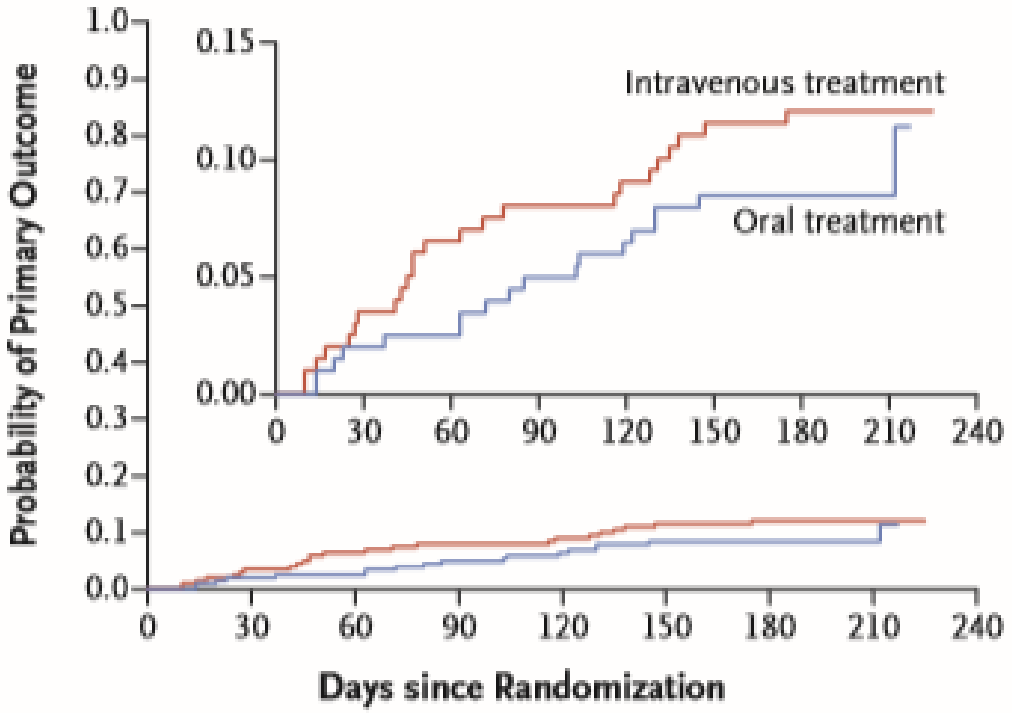
Characteristic	Intravenous Treatment (N=199)	Oral Treatment (N=201)
Mean age — yr	67.3±12.0	67.6±12.6
Female sex — no. (%)	50 (25.1)	42 (20.9)
Body temperature — °C	36.9±0.45	37.0±0.44
Coexisting condition or risk factor — no. (%)		
Diabetes	36 (18.1)	31 (15.4)
Renal failure	25 (12.6)	21 (10.4)
Dialysis	13 (6.5)	15 (7.5)
COPD	17 (8.5)	9 (4.5)
Liver disease	7 (3.5)	6 (3.0)
Cancer	14 (7.0)	18 (9.0)
Intravenous drug use	3 (1.5)	2 (1.0)
Pathogen — no. (%)†		
Streptococcus	104 (52.3)	92 (45.8)
Enterococcus faecalis	46 (23.1)	51 (25.4)
Staphylococcus aureus‡	40 (20.1)	47 (23.4)
Coagulase-negative staphylococci	10 (5.0)	13 (6.5)
Laboratory results at randomization		
Hemoglobin — mmol/liter	6.3±1.1	6.5±1.0
Leukocytes — $\times 10^{-9}$/liter	7.6±3.6	7.2±2.6
C-reactive protein — mg/liter	24.3±18.4	19.9±16.7
Creatinine — μmol/liter	124±112	141±164
Preexisting prosthesis, implant, or cardiac disease — no. (%)		
Prosthetic heart valve	53 (26.6)	54 (26.9)
Pacemaker	15 (7.5)	20 (10.0)
Other known valve disease	82 (41.2)	90 (44.8)
Cardiac involvement at randomization — no. (%)§		
Mitral-valve endocarditis	65 (32.7)	72 (35.8)
Aortic-valve endocarditis	109 (54.8)	109 (54.2)
Mitral-valve and aortic-valve endocarditis	23 (11.6)	20 (10.0)
Endocarditis in other locations§	2 (1.0)	0
Pacemaker endocarditis	6 (3.0)	8 (4.0)
Vegetation size >9 mm	7 (3.5)	11 (5.5)
Moderate or severe valve regurgitation	19 (9.5)	23 (11.4)
Valve surgery during current disease course	75 (37.7)	77 (38.3)

* Plus–minus values are means ±SD. To convert the values for creatinine to milligrams per deciliter, divide by 88.4. There were no significant differences between the groups except for the C-reactive protein level, which was slightly higher in the intravenously treated group. COPD denotes chronic obstructive pulmonary disease.
† Patients could have had an infection with more than one pathogen.
‡ No patients had an infection with a methicillin-resistant strain of *S. aureus*.
§ One patient had an infected ventricular septal defect, and one patient had an infected myxoma in the left atrium.

Table 2. Distribution of the Four Components of the Primary Composite Outcome.*

Component	Intravenous Treatment (N=199)	Oral Treatment (N=201)	Difference	Hazard Ratio (95% CI)
	number (percent)		*percentage points (95% CI)*	
All-cause mortality	13 (6.5)	7 (3.5)	3.0 (−1.4 to 7.7)	0.53 (0.21 to 1.32)
Unplanned cardiac surgery	6 (3.0)	6 (3.0)	0 (−3.3 to 3.4)	0.99 (0.32 to 3.07)
Embolic event	3 (1.5)	3 (1.5)	0 (−2.4 to 2.4)	0.97 (0.20 to 4.82)
Relapse of the positive blood culture†	5 (2.5)	5 (2.5)	0 (−3.1 to 3.1)	0.97 (0.28 to 3.33)

* Six patients, three in each group, had two outcomes.
† For details about relapse of the positive blood culture, see the Supplementary Appendix.



No. at Risk

Intravenous treatment	199	192	186	183	181	176	174	28	0
Oral treatment	201	197	196	191	188	184	183	36	0

Figure 2. Kaplan–Meier Plot of the Probability of the Primary Composite Outcome.

The primary composite outcome was all-cause mortality, unplanned cardiac surgery, embolic events, or relapse of bacteremia with the primary pathogen, from randomization until 6 months after antibiotic treatment was completed. The oral treatment group shifted from intravenously administered antibiotics to orally administered antibiotics at a median of 17 days after the start of treatment. The inset shows the same data on an enlarged y axis.

CONCLUSION:

- In patients with endocarditis on the left side of the heart who were in stable condition, changing to oral antibiotic treatment was non inferior to continued intravenous antibiotic treatment.