Long-Term Outcomes of Partial Oral Treatment of Endocarditis

TO THE EDITOR: In the Partial Oral Treatment of Endocarditis (POET) trial, we found that in patients who had infective endocarditis on the left side of the heart and whose condition had stabilized, a change from initial intravenous antibiotic treatment to two-drug oral antibiotic treatment was noninferior to continued conventional intravenous antibiotic treatment, as assessed 6 months after the end of treatment (the primary trial outcome).1,2 It is unknown whether a switch from intravenous to oral antibiotics affects the long-term outcome. Here, we report the outcomes of the POET trial after a median follow-up of 3.5 years.

In the trial, after at least 10 days of initial intravenous treatment, adult patients in stabilized condition who had endocarditis on the left side of the heart caused by streptococcus, Enterococcus faecalis, Staphylococcus aureus, or coagulase-negative staphylococci were randomly assigned to receive continued intravenous antibiotic treatment (199 patients) or to switch to oral antibiotic treatment (201 patients). Patients who received oral treatment were eligible for outpatient treatment, and 80% of these patients were treated as outpatients, in part or completely, after randomization.2 The trial was approved by the local ethics committee.

In this extended follow-up, we assessed the same primary outcome as in the original trial: a composite of all-cause mortality, unplanned (at randomization) cardiac surgery, embolic events, or relapse of bacteremia with the primary pathogen, from the time of randomization until the end of follow-up (see the protocol and statistical analysis plan, available with the full text of this letter at NEJM.org). Patients were followed from randomization until December 10, 2018, or until death. A clinical-event committee, whose members were unaware of the treatment assignments, adjudicated the prespecified clinical outcomes.

None of the patients were lost to follow-up. We performed a post hoc exploratory analysis of the longer-term follow-up. After a median follow-up of 3.5 years (interquartile range, 2.3 to 5.1), the primary composite outcome had occurred in 76 patients in the intravenously treated group (38.2%) and in 53 patients in the orally treated group (26.4%) (hazard ratio, 0.64, 95% confidence interval [CI], 0.45 to 0.91) (Fig. 1; and Table S1 in the Supplementary Appendix, available at NEJM.org). No significant between-group differences in outcomes were observed with respect to unplanned cardiac surgery, embolic events, or — of particular interest — relapse of infection.

A total of 87 patients (21.8%) died, including 54 in the intravenously treated group (27.1%) and 33 in the orally treated group (16.4%) (hazard ratio, 0.57, 95% CI, 0.37 to 0.87) (Table S2 in the Supplementary Appendix). Mortality 5 years after endocarditis is reported to range from 30% to 40%;3–5; thus, the baseline risk profile of the patients included in the trial was probably similar to the general profile in patients with endocarditis. In conclusion, in patients in stabilized condition who had infective endocarditis on the left side of the heart, a change from intravenous antibiotic treatment to early oral antibiotic treatment was not associated with delayed treatment failure.

Figure 1. Cumulative Incidence Plot 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.
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Supported by grants from the Danish Heart Foundation, the Svend Andersens Foundation, the Capital Regions Research Council, the Hartmann's Foundation, and the Novo Nordisk Foundation.

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

This letter was published on March 17, 2019, at NEJM.org.


DOI: 10.1056/NEJMc1902096
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