Did you like *Terminator 3* better than *Terminator 2*? “Rise of machines” with HeartMate 3?

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A newer installment in a movie series is not always better liked than the previous, especially if it is following a great one. People tend to expect far more staff in the new story. For example, many people may not have preferred *Terminator 3* to *Terminator 2*.

The HeartMate II (HM-II) is the control device, or the “old version,” against which the newer left ventricular assist devices (LVADs) have been tested: the HVAD (HeartWare, Framingham, Mass) in the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation),¹ ENDURANCE (A Clinical Trial to Evaluate the HeartWare Ventricular Assist System),² and ENDURANCE2 trials, as well as the HeartMate 3 (HM3) in the MOMENTUM3 (Mechanical Circulatory Support Therapy With HeartMate 3) trial.³ Postapproval studies of bridge to transplant (n = 169)/destination therapy (n = 247) application of the HM-II LVAD showed a 1-year survival rate of 85/74%. Rates of adverse event (AEs) were 1.44/0.93 (/patient-year) for bleeding; 0.35/0.22 for device-related infection; 0.08/0.08 for stroke; and 0.18/0.16 for right heart failure.^{4,5} Of importance, a concern for the increasing incidence of pump thrombosis was raised in 2014,⁶ and this was again highlighted in comparison with the HVAD in the ENDURANCE trial.² In addition, gastrointestinal bleeding, acquired von Willebrand disease, and development of aortic insufficiency are recognized as the continuous-flow-LVAD-induced diseases.⁷

These “high” rates of AEs had halted the initial enthusiasm for application of continuous-flow-LVAD in less sick patients in the REVIVE-IT (Randomized Evaluation of VAD InterVention before Inotropic Therapy) trial, a prospective, randomized, controlled trial that compared the HM-II with optimal medical management (OMM) in Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) 4-7 patients.⁸ The ROADMAP (Randomized Olmesartan and Diabetes Microalbuminuria Prevention) trial, a prospective, nonrandomized observational trial of inotrope-nondependent patients treated with

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Central Message

The HeartMate-II is a good machine although not perfect. The HeartMate 3 CE Mark trial showed occurrence of the left ventricular assist device–related complications. For the HeartMate 3 to raise the role of the machines, it has to overwhelm the HeartMate-II performance in the MOMENTUM3 (Mechanical Circulatory Support Therapy With HeartMate 3).

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either HM-II or with OMM, showed that, on the basis of as-treated analysis, 12-month survival was greater for HM-II versus OMM (80% ± 4% vs 63% ± 5%; $P = .022$); however, intention-to-treat analysis showed no significant difference in survival, and the AEs were greater in the HM-II patients.⁹

One-year updates of the CE Mark study of the HM3, a prospective single-arm observational study, enrolling a total of 50 bridge to transplant or destination therapy patients in Europe, were presented at the 2016 Meeting of the International Society for Heart & Lung Transplantation.¹⁰ One-year survival rate was 81% ± 6%. AEs occurred in 44% for bleeding that required a blood transfusion; 12% for gastrointestinal bleeding; 16% for driveline infection; 18% for stroke (10% ischemic and 8% hemorrhagic); and 10% for right heart failure. There was no pump malfunction or thrombosis. The ongoing MOMENTUM3 trial will provide more definitive information. The enrollment is expected to end in the middle of 2016.

Although we do recognize that the HM-II is far from perfect, we do agree that it is a fairly good machine. Now remember, people expect more in the newer version. For the HM3 to raise the role of the “machines,” it would need to surpass the performance of the HM-II by

substantially improving survival and decreasing AEs/cost/readmission rate, not only demonstrating the noninferiority (the primary end point of the MOMENTUM3). Also important, the CE Mark trial of another important development of the LVAD technology, MVAD (HeartWare), is on hold. A lot is on the shoulders of the HM3, and we surely hope it is the game-changer. Although I didn't like T3 better than T2, I liked iPhone 3 than 2 and like my iPhone 6 far better!

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