

Jewel AF Only Study (P980050/S1) Panel Questions

1. Safety Results

A. Evaluating Device Safety

0264 '00 DEC -8 A9:54

Complication-Free Survival - As summarized in the table below, Medtronic's reported 3- and 6-month Complication Free Survival results were lower when compared to adverse event results from previous ICD studies:

Table 1. Complication Free Survival Results

GROUP	ICD MODEL	COMPLICATION-FREE SURVIVAL	
		3 MONTHS	6 MONTHS
Study	Model 7250 (Jewel AF Only)	90%	87%
Control	Model 7250 (VT/AT Patients)	92%	88%
Control	Model 7219D	93%	92%

Cerebrovascular Accidents - Medtronic reported that 4 patients (3%) had a cerebrovascular accident (CVA) during the course of the study. Although these 4 CVAs have already been accounted for in the safety analysis as part of the overall complication rate of the Jewel AF, the risk of CVA (possibly as a result of frequent cardioversions) raises an important issue when evaluating the safety of atrial shock therapy.

Q: Please discuss the clinical significance of the Complication-Free Survival results and the occurrence of CVAs in assessing the safety of the Jewel AF for the new indication of treating patients with atrial tachyarrhythmias.

B. Control Group - In their investigational plan, Medtronic prospectively specified ICD Model 7219D as the safety control. The sponsor, however, anticipated that there would be differences between the AF Only and VT/VF patient populations because of differences in the underlying disease of the 2 patient groups. It appears from the demographic co-morbidity data that the Model 7219D patient population was in many ways sicker than the Jewel AF Only group. To address this, Medtronic performed a risk factor analysis intended to take into account baseline differences in cardiac health.

Q: Given this choice of controls, do the clinical results of the Jewel AF Only study demonstrate device safety for the intended patient population?

2. Effectiveness Results

- A. Atrial Tachyarrhythmia Termination Therapies - As reported in the clinical study, Medtronic met their prospectively specified effectiveness hypothesis for atrial shock therapy (91%; lower bound of $82\% \geq 75\%$). Additional effectiveness results are summarized below:

Table 2. Effectiveness of ATP and HFB in Terminating Atrial Tachyarrhythmias

ARRHYTHMIA AND TREATMENT	EPISODES	PERCENT
AT episodes treated with ATP or HFB	1212 / 2896	42%
AT episodes treated with ATP	1049 / 2720	39%
AF episodes treated with HFB	286 / 1570	18%
AT episodes treated with HFB	163 / 1394	12%

- B. Atrial Tachyarrhythmia Prevention Therapies - The study also examined the effect of atrial prevention therapies on frequency of atrial tachyarrhythmias using a crossover study design. Medtronic reported that the reduction in AT/AF frequency when atrial prevention therapies were programmed ON vs. OFF was not statistically significantly different from 0.

Q: Based on these effectiveness results, please discuss whether you believe the potential benefits of Atrial Tachyarrhythmia Termination and Prevention Therapies outweigh the risks of implanting the Jewel AF in the intended patient population.

3. Model 9465 Patient Activator

The Patient Activator is used by patients in the ambulatory setting to initiate physician programmed atrial defibrillation therapy. Medtronic reported 93% (85% lower bound) effectiveness for atrial shock therapy when self-administered using the Patient Activator. The sponsor also reported 13 adverse events (in 12 patients) relating to the Patient Activator: 9 patients were "unable to activate manual shock therapy" and 3 patients "experienced shock without prior warning tone". None of these adverse events were determined to be device failures.

Medtronic reported that over the course of the study, there was continued use over time of the Patient Activator which suggests that in a significant portion of patients, manually enabled shocks are acceptable and the degree of acceptability increases over time. The clinical results also suggest that the device was relatively easy to use from a human factors perspective.

Q: Do you think that the Model 9464 Patient Activator is safe and effective? Do you have any comments regarding its clinical use?

4. Risk/Benefit Assessment

Q: Given the proposed new Indications for Use for the Jewel AF and the likelihood that the patients will be healthier than the ICD patient population, please discuss whether you believe that the potential benefits of implanting the Jewel AF in patients with atrial tachyarrhythmias outweigh the possible risks associated with the implantation and therapies of the device.

5. Product Labeling

- A. Failure to Implant / Device Explants - Of the 2 enrolled patients who were not implanted with the Jewel AF, FDA believes that the patient with "no atrial capture during the implant procedure" should be considered an intention-to-treat failure. Likewise, of the 10 reported device explanations, FDA believes that 6 of the reported reasons suggest that device therapy in these patients was either ineffective or poorly tolerated and should also be considered intention-to-treat failures.
- B. Patients Having RF Ablation - Medtronic reported that 13 patients (9%) had an ablation procedure (an alternative therapy) after being implanted with the Jewel AF. FDA is concerned that the Jewel AF may not provide adequate AF prevention and/or treatment therapy for this patient population, or that the therapies (particularly atrial shock therapy) may be poorly tolerated in some patients.

Q: Please provide your clinical impression of these potential intention-to-treat failures and discuss how this clinical information should be presented in the Jewel AF's Instructions for Use labeling.

C. Indications for Use

The Jewel AF System is intended to provide pacing, cardioversion and defibrillation for treatment of patients with:

- symptomatic, drug-refractory atrial tachyarrhythmias and/or
- life threatening ventricular tachyarrhythmias

Q: Please provide your clinical impression of Medtronic's proposed Indications for Use and comment on whether it is clinically appropriate for the Jewel AF's indicated patient population.