Seventy-Second Meeting of the

Obstetrics and Gynecology Devices Panel

Tuesday, August 29, 2006
Gaithersburg Hilton, Gaithersburg, MD

Mirabel Medical Systems, Inc. T-Scan™ 2000ED (P050003)
Draft Discussion Questions

1. The primary effectiveness endpoint of the pivotal study entailed using estimates of prevalence, sensitivity, and specificity to calculate the probability that a woman who is T-Scan positive has cancer relative to a randomly selected woman from the general target population. The success criterion was set at a level of 2 or greater. Using a sensitivity of 26.4%, a specificity of 94.7%, and a cancer prevalence of 0.15%, the sponsor obtained a "relative risk" or probability of 4.95 (95% CI 3.16; 7.14) thereby meeting the pre-defined endpoint for success. FDA, however, calculated the sensitivity of the device in different subgroups to range from 0% (U.S. cancer cases under the age of 40) to 25.5% (all women regardless of age or country of origin). FDA also calculated the prevalence of breast cancer in the target population to be significantly lower than the sponsor, in the range from 0.017% to 0.054%, depending on various assumptions. In addition, FDA found that the specificity varied significantly between study arms and for several covariates and subgroups within each arm of the study.

    a. Please discuss the clinical significance of the primary effectiveness measure and result obtained by the sponsor.

    b. As the values chosen for sensitivity, specificity, and prevalence may greatly affect the results of these calculations, including whether the primary endpoint is met, please comment on what you believe reflect the most accurate estimates for each of these parameters.

2. The T-Scan device is intended to be used in women aged 30-39 who are negative for both Clinical Breast Exam (CBE) and Family History. Due to the relatively low prevalence of disease in the intended population, FDA agreed to enriching the sensitivity arm with subjects outside these criteria to assist with patient accrual. In order to identify a cohort of biopsy positive women (i.e. the cohort needed to calculate sensitivity), the sensitivity arm included women who were undergoing a biopsy due to an earlier positive screening. In addition, the sample was enriched with women age 40-45 (382 pre-menopausal and 24 post-menopausal) to ensure a sufficient sample size. Of the evaluable cancer patients used to determine device sensitivity (FDA's per-protocol analysis), 61% (57/94) were over age 39, 81% (76/94) had an abnormal CBE, and 34% (30/88) had a positive family history. Only 5% (4/88) of cancer-positive subjects in the sensitivity arm were consistent with the indications for use statement.

Please discuss whether you believe the degree of enrichment of the sensitivity arm affects the interpretation of the final results of the study and their applicability to the intended target population and if so, how.

3. The pivotal study was conducted at multiple sites in the United States and Israel. As shown in the table below, the sponsor's per-protocol analysis (without post-menopausal women) showed no statistically significant difference in device sensitivity between countries while the FDA's per-protocol analysis (including post-menopausal women) did.

	Sponsor's Per Protocol Analysis	**FDA's Per-Protocol Analysis**
Sensitivity in U.S.	**11.5% (3/26)**	**10.3% (3/29)**
Sensitivity in Israel	**32.8% (20/61)**	**32.3% (21/65)**
Fisher's Exact Test	**p = 0.06**	**p = 0.0386** **95% exact CI = (3% - 40%)**

Please discuss the differences in clinical outcomes between the results for U.S. subjects and Israeli subjects and whether you believe the results from the two countries are poolable.

4. Eleven percent (11%) of patients (65/597) were excluded from the sensitivity arm due to technical difficulties with the device. Of the 37 cancers excluded from the sensitivity arm, 51% (19) were eliminated due to technical difficulties. All 19 of these cancer cases excluded due to technical difficulties were from U.S. sites. In contrast, only 0.7% (14/1946) of the patients were excluded for technical difficulties from the specificity arm.

   Please discuss whether these losses due to technical difficulties introduce significant bias into the study.

5. No device-related adverse events were reported during the course of the study. However, according to the sponsor's calculations, for every T-Scan positive patient who has cancer, additional mammograms will be conducted on 135 normal subjects. If the prevalence of disease in women 30-39 is lower than the sponsor's estimate of 0.15%, this number of additional mammograms may be significantly higher.

   Please discuss whether you believe there are any potential risks associated with these additional mammography exams in women age 30-39, taking into account that for any given woman, the T-Scan is intended to be used on a yearly basis.

6. The sponsor has proposed the following indication for use (IFU) for its device:

   The T-Scan 2000 ED is indicated for use as a complement to clinical breast examination (CBE) in asymptomatic women who are 30 to 39 years of age with a negative clinical breast exam and

a negative family history for breast cancer. The device detects electrical impedance changes in breast tissue that are associated with an increased risk of breast cancer. A positive T-Scan™ result provides physicians with additional information to guide a recommendation regarding further breast examination, e.g., mammography or ultrasound. The T-Scan evaluates women's risk of breast cancer at the time of the exam (current risk) and not lifetime risk.

Please comment on whether data provided in the PMA and discussed today provide a reasonable assurance of effectiveness and safety to support this proposed indication for use. If not, are there any simple modifications to this indication which the data clearly support?

7. Taking into account your responses to the previous questions, please discuss the overall risk/benefit profile for the T-Scan device for the intended patient population.

8. Please comment on the draft labeling provided by the sponsor.