

Non-Voting Panel Questions

Study Population

1. The sponsor planned to enroll a study population that includes subjects with an increased risk of disc reherniation (i.e. large annular defects defined as between 4-6 mm tall and 6-12 mm wide post-discectomy) that would potentially benefit from a permanent implant to prevent reherniation compared to discectomy alone. After review of the data summarized in Section 3.1 of FDA's Executive Summary, it appears that patients were enrolled consecutively across multiple sites, and the enrolled study population appeared to differ from prior literature reports regarding the incidence of "at risk" disc herniations types as identified by Caragee (2003). For example, the Barricaid study had a much lower number of "fragment-fissure" type annular defects which are associated with a low rate of recurrent lumbar disc herniation in the enrollment population. Additionally, the majority of study subjects appeared to receive anulotomies (box and cruciate shape) during the discectomy procedure, prior to randomization, which suggests surgical resection of disc annulus may have gone beyond the extent required for performing a limited discectomy as defined by the sponsor. Based on the observations regarding the study population described above and in Section 3.1 of FDA's Executive Summary, please comment on the following:
 - a. Please discuss the patient characteristics, herniation types, and size and types of annular defects that would likely benefit from an annular closure device and if that population was adequately investigated in this study.
 - b. Please comment on the differences noted between the limited discectomy procedures reported in the literature compared to the treatment received by those enrolled in the Barricaid study. Then, please discuss whether the differences had an effect on the clinical outcomes, especially with respect to reherniation rates and subsequent surgical interventions in the control group.

Endplate Lesions

2. The sponsor reported 40% of control patients with an end-plate lesion (EPL), compared to 88% of Barricaid patients. Furthermore, the control patients with EPLs have lesions that are smaller, appear to reach stability sooner, and present features more in line with Schmorl's nodes. In contrast, the EPLs of the Barricaid patients are larger than those of the control, progress in size faster, have radiographically distinct features (e.g., lytic features and a location in proximity to the mesh), and show signs of mesh subsidence into the lesion. However, based on the secondary analyses performed by the sponsor, there does not appear to be a correlation between the presence of EPLs and measured clinical study outcomes. Based on the observations regarding EPLs highlighted in Section 3.2 of FDA's Executive Summary, please address the following:
 - a. Please comment on any present and future clinical impact or relevance of the EPLs.

- b. Please comment on any additional analyses (e.g., which assessments at what time points), that should be conducted to evaluate the clinical significance of the EPLs.

Study Endpoints

3. As summarized in Section 3.3 of FDA's Executive Summary, the co-primary endpoints developed *a priori* included a measure of radiographic reherniation rate designed to capture all disc reherniations (symptomatic and asymptomatic) in order to measure device effectiveness at 24 months. Radiographic endpoints to evaluate device integrity (i.e. migration, disassembly) were also included to evaluate the device function, though positive clinical outcomes occurred regardless of device integrity. In addition, the sponsor reported results from an alternative primary endpoint developed *post-hoc* that focused on symptomatic reherniations at 24 months. Please discuss the following:
 - a. Please discuss all appropriate endpoint(s) (both safety and effectiveness) for an anular closure device, and the control population, the time point(s) at which the endpoint(s) should be evaluated and whether these should be the same.
 - b. Please provide the specific criteria that should be included in a definition of symptomatic recurrent lumbar disc herniation for the anular closure device and the control.
 - c. While both a secondary discectomy and a secondary procedure that results in a supplemental fixation/fusion are typically counted as failures, should they be given equal weight in discussing risks accrued from implanting a device?

Voting Panel Questions

The Barricaid is intended to be implanted following a limited discectomy, to prevent reherniation and the recurrence of pain or dysfunction. The Barricaid is indicated for patients with radiculopathy (with or without back pain), a posterior or posterolateral herniation, characterized by radiographic confirmation of neural compression using MRI, and a large annular defect (e.g., between 4-6 mm tall and between 6-12 mm wide) post discectomy, at one level between L4 and S1.

1. Is there a reasonable assurance that the Barricaid is safe for the indication for use in patients who meet the criteria specified in the proposed indications?
2. Is there a reasonable assurance that the Barricaid is effective for use in patients who meet the criteria specified in the proposed indications?
3. Do the benefits of the Barricaid outweigh the risks for use in patients who meet the criteria specified in the proposed indications?