

Obstetrics and Gynecology Devices Panel

Tuesday, May 22, 2001 – 2-5 p.m.

Uterine Fibroid Embolization (UFE)

Panel Discussion Questions

FDA is currently drafting an IDE/510(k) guidance document to help in the preparation of such submissions to the agency. Response to these discussion questions will help with the development of this guidance document.

1. Currently, the inclusion and exclusion criteria for UFE performed in FDA-approved clinical studies of UFE are (generally) as follows:

Inclusion Criteria

1. symptomatic uterine myoma
2. premenopausal; > 30-35 years of age
3. normal Pap smear, last 12 months
4. regular menstrual cycles
5. normal kidney function
6. use or non-use of hormonal contraception must be maintained uniformly from 3 months pre-treatment through study completion
7. willingness to consent and complete follow-up requirements of study

Exclusion Criteria

1. pregnancy or desire for pregnancy
2. gynecologic malignancy or pre-malignancy
3. adenomyosis
4. candidate for hysteroscopic or laparoscopic myomectomy
5. *any* drug treatment for uterine fibroids within three months pre-treatment
6. active pelvic infection or history of pelvic inflammatory disease
7. *any* acute or chronic infection
8. undiagnosed pelvic mass outside of the uterus
9. coagulopathy
10. history of pelvic irradiation
11. ASA score \geq IV
12. uterine arterio-venous fistula
13. allergy to IV contrast media

Please comment; are these the appropriate inclusion and exclusion criteria?

- Should hormone therapy (e.g. hormonal contraception) be an exclusion criterion for UAE studies? If patients on hormone therapy are included, should their data be pooled with data from patients not on any hormones, or should they be analyzed as a subset of study subjects?
- Exclusion criteria already include gynecologic malignancy or pre-malignancy. Should simple endometrial hyperplasia be considered a pre-malignant condition?
- Other comments?

2. As the primary study endpoint, FDA-approved studies currently use either a quality of life (QoL) instrument validated for uterine fibroids or a validated uterine bleeding scoring instrument coupled with a QoL instrument. Secondary endpoints include adverse events, fibroid and uterine size, time to return to normal activities, and comparisons to the non-randomized controls. Primarily, patients are serving as their own controls, with secondary comparisons to patients in non-randomized arms (either control subjects undergoing myomectomy or hysterectomy). Please comment on interpretation of these studies when completed.
3. FDA currently asks for a six-month follow up (premarket), with an additional six-month follow up (postmarket), for a total of a one-year follow up. Is this an appropriate follow up regime?
4. Preliminary results have shown that some subjects require re-treatment with UFE.
 - Should there be specific study requirements regarding re-treatment?
 - How should the clinical study design account for this? Should these subjects be handled as primary treatment failures?
 - Can these data provide additional information on the success of UFE re-treatment?
5. Labeling for New UFE Indication: What are the key elements that should be covered in the professional labeling of embolyzing agents that are cleared for UFE?
 - How should labeling handle the issue of women who desire a future pregnancy?
 - Should bleeding results be stratified by use and non-use of hormonal contraception?

Background Materials

- Fibroid registry protocol
- Fibroid registry case report form:
- Amato, P., Roberts, A.C., "Transient ovarian failure: a complication of uterine artery embolization," *Fertil Steril* 73:1241-1257, 1999.
- Goodwin, S.C., McLucas, B., Lee, M., Chen, G., Perrella, R., Vedantham, S., Muir, S., Lai, A., Sayre, J.W., DeLeon, M., "Uterine artery embolization for the treatment of uterine leiomyomata midterm results," *J Vasc Interv Radiol* 10:1159-1165, 1999.
- Hovsepian, D.M., "Uterine fibroid embolization: another paradigm shift for interventional radiology?" *J Vasc Interv Radiol* 10:1145-1147, 1999.
- Hurst, B.S., Stackhouse, D.J., Matthews, M.L., Marshburn, P.B., "Uterine artery embolization for symptomatic uterine myomas," *Fertil Steril* 74:855-869, 2000.
- *Management of Uterine Fibroids*. Summary, Evidence Report/Technology Assessment: Number 34. AHRQ Publication No. 01-E051, January 2001. Agency for Healthcare Research and Quality, Rockville, MD. <http://www.ahrq.gov/clinic/utsumm.htm>
- McLucas, B., Adler, L., Perrella, R., "Uterine fibroid embolization: nonsurgical treatment for symptomatic fibroids," *J Am Coll Surg*, 192(1):95-105, 2001.

- Spies, J., Niedzwiecki, G., Goodwin, S., et al. "Training standards for physicians performing uterine artery embolization for leiomyomata," *J Vasc Interv Radiol* 12:19-21, 2001.
- Spies, J.B., Roth, A.R., Gonslaves, S.M., Murphy-Skrzyniarz, S.M., "Ovarian Function after uterine artery embolization for leiomyomata: assessment with use of serum follicle stimulating hormone assay," *J Vasc Interv Radiol* 12:437-442, 2001.
- Spies, J.B., Scialli, A.R., Jha, R.C., Imaoka, I., Ascher, S.M., Fraga, V.M., Barth, K.H., "Initial results from uterine fibroid embolization for symptomatic leiomyomata," *J Vasc Interv Radiol* 10:1149-1157, 1999.
- Spies, J.B., Warren, E.H., Mathias, S.D., Walsh, S.M., Roth, A.R., Pentecost, M.J., "Uterine fibroid embolization: measurement of health-related quality of life before and after therapy," *J Vasc Interv Radiol* 10:1293-1303, 1999.
- Vahisht, A., Studd, J.W.W., Carey, A.H., McCall, J., Burn, P.R., Healy, J.C., Smith, J.R., "Fibroid embolization: a technique not without significant complications," *Br J Ob Gyn*, 107:1166-1170, 2000.
- Rosenthal, A.N., "Fibroid embolization: a technique not without significant complications," [letter] *Br J Ob Gyn*, 108:337-338, 2001.
- Vahisht, A., Studd, J., Carey, A., Burn, P., "Fatal Septicaemia after fibroid embolisation," *Lancet* 354: 307-308, 1999.
- Walker, W., Worthington-Kirsch, R.L., "Fatal Septicaemia after fibroid embolisation," [letter] *Lancet* 354: 1730, 1999

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