Testimony for

FDA Panel on Trans-vaginal Mesh for the Anterior Wall

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Introduction

- Patients benefit from having treatment options
- Trans-vaginal mesh procedures for anterior prolapse are a reasonable choice for some patients
- Safety concerns must be balanced by increased benefit
- Polypropylene mesh does not cause:
  - Cancer
  - Autoimmune disease

Surgery is a Benefit/Risk Proposition

- Prolapse is a quality of life issue
  - The impact varies among women
  - Treatment goals also vary
- Surgical benefits and risks vary by:
  - Procedure
  - Patient
  - Surgeon
- Treatment options maximize patient's opportunity to personally balance benefit and risk

Focus of the Panel

- FDA Announcement:
  - “Serious complications associated with surgical mesh for transvaginal repair of POP are not rare.”[1]
- Systematic Review of trans-vaginal mesh[2]:
  - Anterior compartment: better anatomical outcomes
  - Posterior compartment: higher complications
- RCTs:
  - Anatomical benefit and possible symptomatic benefit in anterior compartment

1. www.fda.gov/downloads/medicaldevices/safety/alertsandnotices/ucm262760.pdf
2. Schimpf MO, et al.. Obstet Gynecol. 2016 Jul;128(1):81-91.
3. Maher C, et al. Neurourol Urodyn 2008;27(1):3-12.

Patient Characteristics Favoring Trans-vaginal Mesh Procedure

- Failed native tissue repairs
- Injury to the pelvic floor musculature
- Connective tissue or neurologic disorders
- Medical or surgical issues compromising abdominal access
- Medical advantage for regional anaesthesia

Optimizing the Evidence for Trans-vaginal Mesh in POP Repairs

Evidence Gaps:

- RCTs assessing newer products
- Performance in different populations
- Treatment of mesh complications
- External validity
  - Spectrum of surgical experience
  - Real world performance

FDA Benefit-Risk Framework

Decision Factor	Evidence	Uncertainties	Conclusions
Analysis of Condition			
Current treatment options			
Benefit			
Risk			
Risk Management			
Benefit-risk Summary Assessment			

http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM329758.pdf

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FDA Benefit-Risk Framework
Trans-vaginal Mesh for Anterior Wall POP

Decision Factor	Evidence	Uncertainties	Conclusions
Analysis of Condition	common negative QOL	subpopulations	
Current treatment options	13% reoperation at 5yrs[1] 17% reoperation at 10 yrs[2]	risks for recurrence[1]	
Benefit			
Risk			
Risk Management			
Benefit-risk Summary Assessment			

1.Clark AL, et al. Am J Obstet Gynecol. 2003 Nov;189(5):1261-7.
2.Denman MA, et al. Am J Obstet Gynecol. 2008 May198(5):555

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Current treatment options	13% reoperation at 5yrs 17% reoperation at 10 yrs	risks for recurrence	
Benefit	durability	subpopulations surgeon experience	
Risk	mesh complications	subpopulations surgeon experience	
Risk Management			
Benefit-risk Summary Assessment			

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Current treatment options	13% reoperation at 5yrs 17% reoperation at 10 yrs	risks for recurrence	
Benefit	durability	subpopulations surgeon experience	
Risk	mesh complications	subpopulations surgeon experience	
Risk Management	inadequate	best management	
Benefit-risk Summary Assessment			

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Assessing Benefit

- Patient relief from symptoms
  - Patient centered outcomes = validated condition specific quality of life metrics[1,2]
    - Prolapse symptoms
    - Urinary symptoms
    - Bowel function
    - Sexual function
  - Patient reported outcomes = direct patient responses

- Anatomical correction
  - Objective
  - Longitudinal outcome

1. Barber MD, et al. Am J Obstet Gynecol. 2005 Jul; 193(1):103-13.
2. Rogers RG, et al. Int Urogynecol J Pelvic Floor Dysfunct. 2003 Aug;14(3):164-8; discussion 168.

Assessing Risk

- Surgical Complications
  - Related to pelvic floor surgery[1]
  - Related to mesh surgery[2]

- Reoperation
  - Recurrent prolapse
  - Mesh complications

1.Clavien PA, et al. Ann Surg. 2009;250:187–96.
2. Gutman RE, et al. Am J Obstet Gynecol. 2013 Jan;208(1):81.e1-9.

Methodological Considerations

- Long term assessment (5-10yrs)[1]
- Sub-population analysis
  - Parameters associated with recurrent prolapse[2]
    - Prior prolapse failure
    - Pelvic floor muscle injury
    - Stage of prolapse
    - Obesity
  - Parameters associated with mesh complications[3]
    - Smoking
    - Vaginal atrophy
    - Concurrent hysterectomy
- Blinding[4]
- Trials vs. Registries

1. Nygaard I, et al. JAMA. 2013 May 15;309(19):2016-24.
2. Veggeldt TF, et al. Int J Urogyn, 2015;26(11):1559-73.
3. Cundiff et al. Am J Obstet Gynecol. 2008 Dec;199(6):688.e1-5. Epub 2008 Oct 31.
4. Brubaker L, et al.Am J Obstet Gynecol. 2014 Nov;211(5):554.e1-7.

AUGS Quality Improvement Registry (AQUIRE)

- Conditions
  - Stress Urinary Incontinence
  - Pelvic Organ Prolapse
  - Surgical complications
- Treatments
  - Spectrum of nonsurgical & surgical
- Surgeons
  - Spectrum of experience
- Patients
  - Patient reported outcomes
  - Assessment of subpopulations
- Longitudinal

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- **Assesses Benefits & Risks**
- **Real world performance**
- **Patient reported outcomes**
- **Allows analysis of subpopulations**
- **Feasible long-term evaluations**
- **Flexible framework for nested trials**

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Educational Considerations

- Patients
  - Shared-decision making tools
- Surgeons
  - Lifelong learning
  - Skill development and volume to support competency
    - Alternative surgical treatments
    - Management of complications
  - Monitoring of quality through registry

Thank You


ANY
QUESTIONS
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