Allergan Breast Implants: Benefits and Risks

FDA Medical Devices Advisory Committee
General and Plastic Surgery Devices Panel
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Stephanie Manson Brown, MD
Vice President, Clinical Development

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Requested Presentation Topics

1. Breast Implants
2. Post-market Monitoring
3. Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL)
4. Breast Implant Illness (BII)

Breast Implants are Important to the Millions of Women Who Have Them Implanted

- Supported by clinical evidence
- More than 500,000 person-years from clinical studies
- Large body of published literature

Two Implant Surface Options to Meet Individual Patient Needs

- Smooth implants
  - Round shape
  - 90% use in US
- Textured implants
  - Anatomical and round shape
  - 10% use in US
- Rates reversed outside US

Key Benefits of Breast Implants

- Psychosocial improvements[1,2,3]
  - Quality of life
  - Sexual well-being
- Restoration of physical form[1,2]
  - Congenital abnormalities
  - Loss of volume
- Reconstruction post-mastectomy[1,2]

1. Penaud and De Mortillet 2013
2. Von Soest et al. 2009
3. Alderman et al. 2000

Benefits and Risks are Important to Discuss with Every Patient

- Textured implant benefits include
  - Anatomical shape[1]
  - Increased tissue adherence and implant stabilization[1]
  - Lower capsular contracture rate relative to smooth[1,2,3,4]
- Textured implant risks include
  - Rare occurrence of BIA-ALCL, with excellent prognosis if identified early and appropriately treated[5,6]

1. Calobrace, et al. 2018; 2. Barnsley et al. 2006; 3. Seify, et al. 2005 4. Brown, et al. 2005; 5. American Society of Plastic Surgeons: BIA-ALCL Physician Resources; 6. UT-Southwestern: The Truth about Breast Implant-Related Cancer Risk

Literature Supports Textured Implant Use

- Aesthetic preference
- Primary cancer reconstruction[1]
- Compromised soft tissue[1]
- Congenital abnormalities[2]
- Previous capsular contracture[1]

- Discussion of benefits and risks is critical for every patient

1. Calobrace, et al. 2018
2. Mandrekas AD 2010

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Comprehensive Postmarket Monitoring of Breast Implants

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- Postmarket surveillance
- National Breast Implant Registry
- Post-approval study
- Additional post-approval commitments
  - Completion of continued access studies through 5 years
  - Focus group studies of patient labeling
  - Ongoing analyses of all returned devices

Post-Market Surveillance, National Breast Implant Registry and Post-Approval Study

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- Post-market surveillance
  - Medical assessment of AE reports from patients, surgeons and literature
  - Evaluation of safety trends
- National Breast Implant Registry
  - Collects baseline implant data
  - Improves time to identification of events
  - Evaluates signals across registries
- Post-approval study
  - BIFS arm: round implant data
  - 410 arm: anatomically-shaped implant data
  - NBIR arm: reoperations data

Long-Term Post-Approval Study Ongoing

Study Arm		Enrolled / Response Total N=53,262	
		Silicone N=39,153	Saline N=14,109
BIFS	Number enrolled	2000	257
	Year 1 office visit follow-up	67.2%	Not Scheduled
	Year 4 office visit follow-up	29.8%	Not Scheduled
	Year 5 questionnaire follow-up	83.6%	86.4%
	Year 6 questionnaire follow-up	79.9%	80.9%
	Year 7 questionnaire follow-up	78.8%	78.1%
410	Number enrolled	421	N/A
	Year 1 office visit (interim data) follow-up	35%	N/A
	Year 1 questionnaire follow-up	71.4%	
NBIR	Number enrolled	36,732	13,852

Interim data; not all patients have reached one year

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BIA-ALCL Can Have an Excellent Prognosis when Appropriately Identified and Treated

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- Uncommon, slow growing T-cell lymphoma
- Typically presents with fluid around the implant[1,2,3]
- Median time to onset ~8 Years (range 2–25y)[3]
- Etiology not fully understood
- Higher implant surface area may be a risk factor[4]

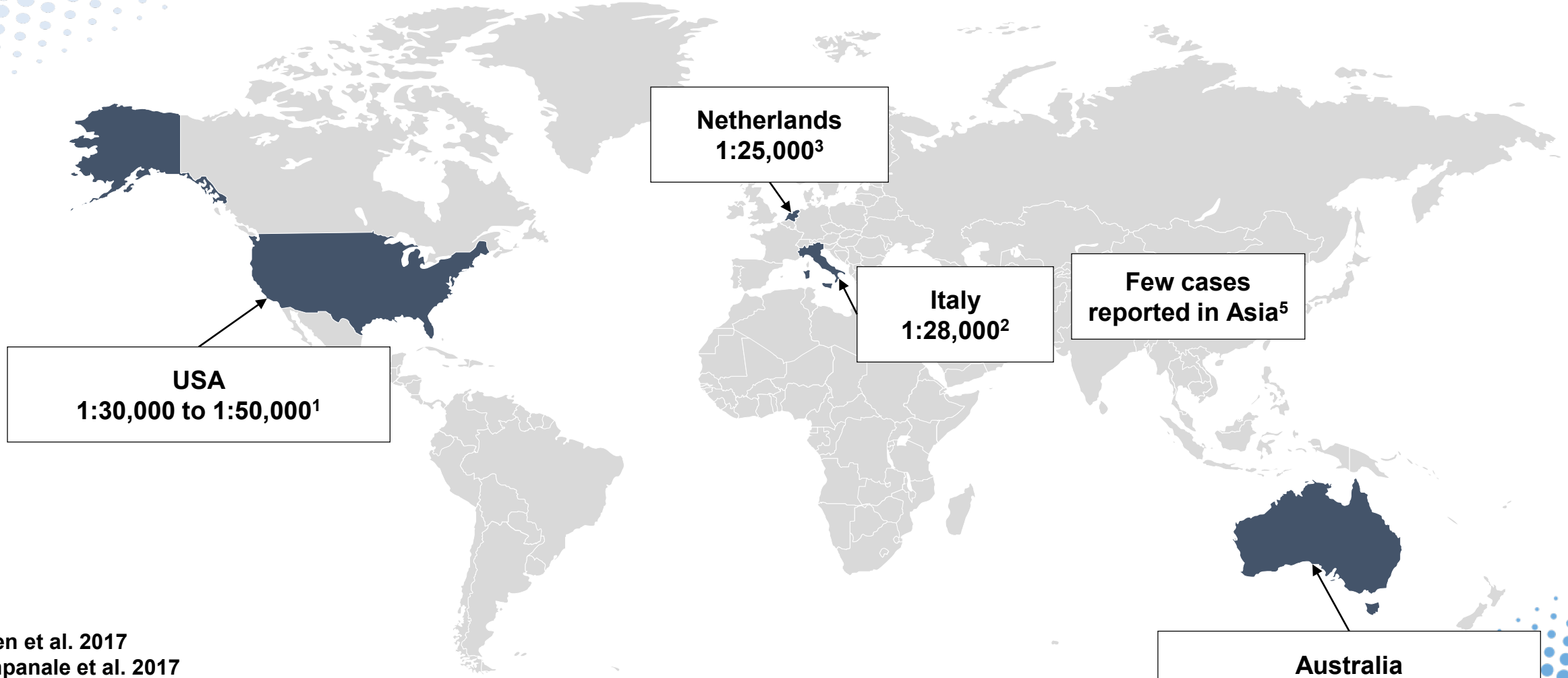
1. American Society of Plastic Surgeons: BIA-ALCL Physician Resources
2. UT-Southwestern: The Truth about Breast Implant-Related Cancer Risk
3. Clemens MW. et al. 2016
4. Loch-Wilkinson A et al. 2017

Leading Hypothesis Centers Around Biofilm

- Three likely contributing factors
  - **Procedure:** Introduction of bacteria[1]
  - **Product:** Surface area contributes to bacterial accumulation[1]
  - **Patient:** Genetic predisposition[2]

1. Hu H et al. Plastic Reconstructive Surgery 2016
2. Oishi N et al. Blood 2018

BIA-ALCL Incidence Rates in Textured Implants: Literature*



1. Doren et al. 2017
2. Campanale et al. 2017
3. De Boer, et al. 2017
4. Magnusson M et al. 2019
5. Collett 2019

*Textured implants used for denominator in determining incidence

BIA-ALCL Incidence Rates in BIOCELL Textured Implants: Post-Market*

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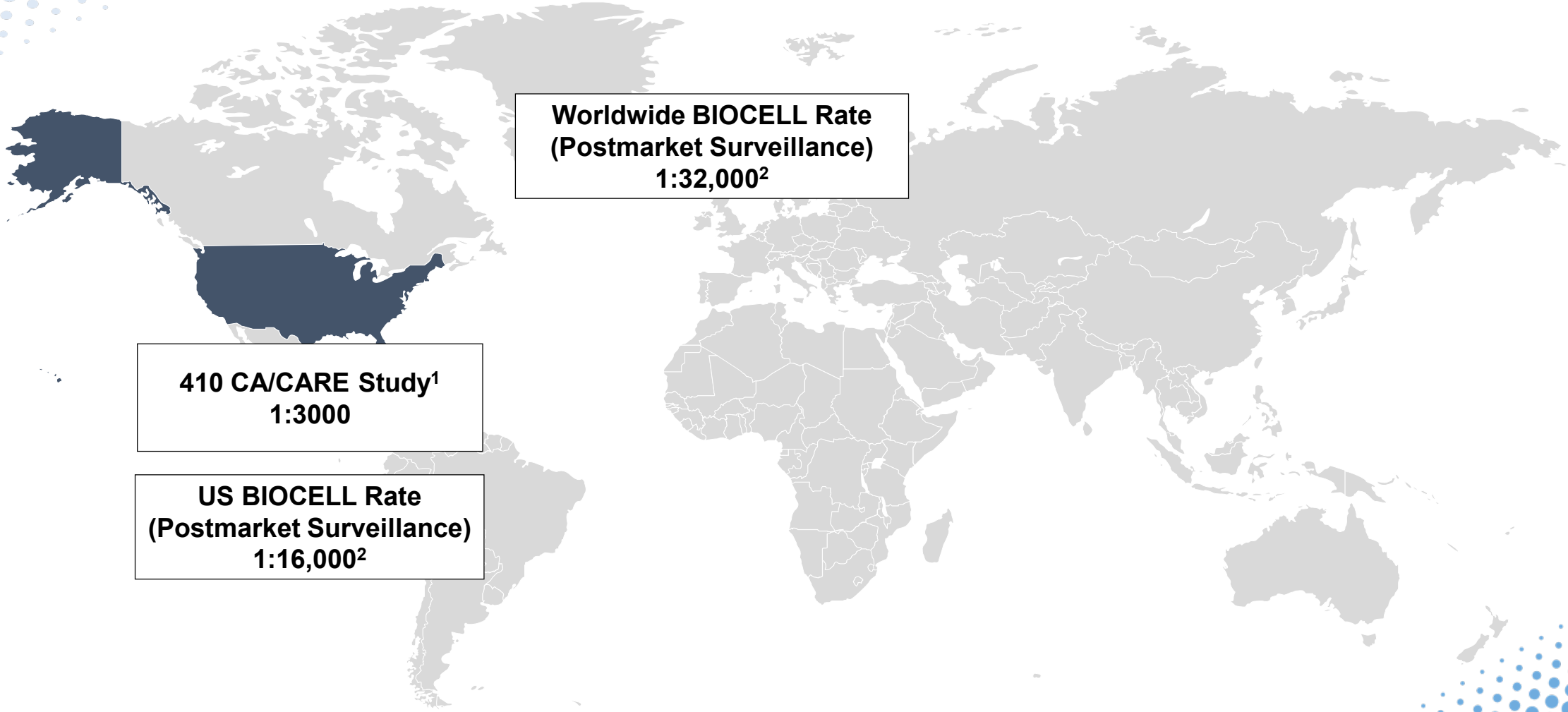

1. McGuire P et al. 2017
2. Data on File

*Textured implants used for denominator in determining incidence

Evidence Suggests BIA-ALCL Mitigation Can Be Effective

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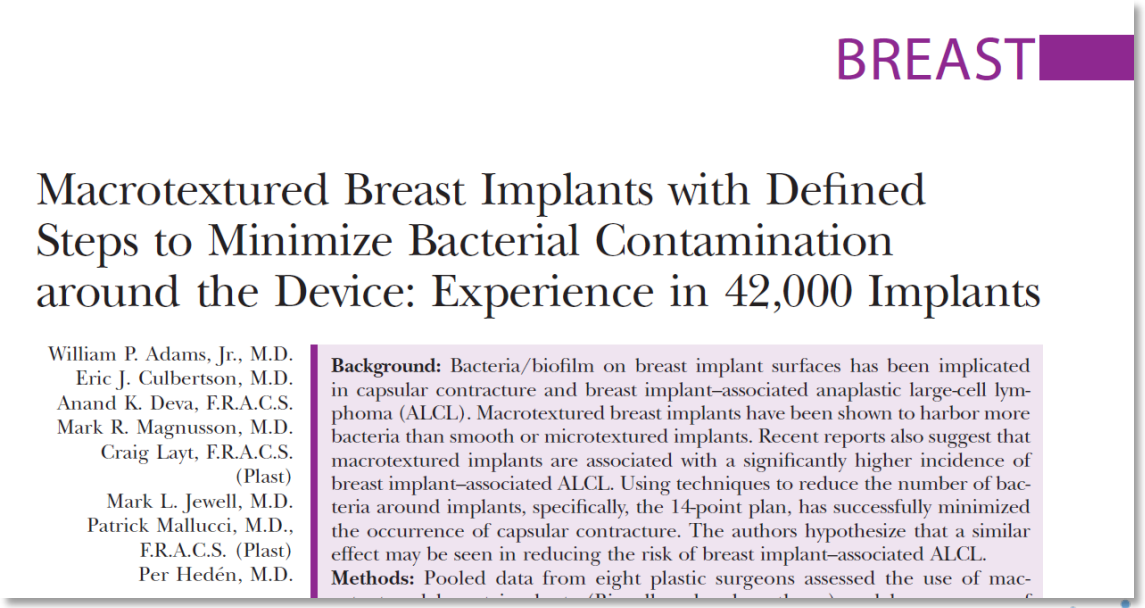
- Enhanced 14-point aseptic technique[1]
  - Changing gloves
  - Antiseptic solutions
  - Minimal touch
- Zero BIA-ALCL cases
  - 42,000 BIOCELL implants[2]
  - 11.7 years mean follow-up
- Continue to communicate the importance of enhanced aseptic surgical technique



BREAST

Macrotextured Breast Implants with Defined Steps to Minimize Bacterial Contamination around the Device: Experience in 42,000 Implants

William P. Adams, Jr., M.D.
Eric J. Culbertson, M.D.
Anand K. Deva, F.R.A.C.S.
Mark R. Magnusson, M.D.
Craig Layt, F.R.A.C.S. (Plast)
Mark L. Jewell, M.D.
Patrick Mallucci, M.D., F.R.A.C.S. (Plast)
Per Hedén, M.D.

Background: Bacteria/biofilm on breast implant surfaces has been implicated in capsular contracture and breast implant–associated anaplastic large-cell lymphoma (ALCL). Macrotextured breast implants have been shown to harbor more bacteria than smooth or microtextured implants. Recent reports also suggest that macrotextured implants are associated with a significantly higher incidence of breast implant–associated ALCL. Using techniques to reduce the number of bacteria around implants, specifically, the 14-point plan, has successfully minimized the occurrence of capsular contracture. The authors hypothesize that a similar effect may be seen in reducing the risk of breast implant–associated ALCL.
Methods: Pooled data from eight plastic surgeons assessed the use of mac-

1. Deva 2013; 2. Adams WP et al. 2017

Evidence Suggests BIA-ALCL Treatments are Effective

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- Early identification and appropriate treatment are critical for optimal patient outcomes[1,2]
- Implant removal with surgical capsulectomy alone is effective for the majority of patients
- Addition of novel treatment in advanced disease is effective
  - Complete remission has been achieved with brentuximab[3]

1. American Society of Plastic Surgeons: BIA-ALCL Physician Resources
2. UT-Southwestern: The Truth about Breast Implant-Related Cancer Risk
3. Clemens MW et al. ASRM 2018

Allergan Remains Committed to Improved Awareness Through Education, Insurance Support, Financial Assistance

- Education
  - Educational activities for surgeons and primary care providers
  - Working with international medical societies to increase awareness
  - Global scientific roundtables, online seminars, consensus statements, and journal supplements
  - Patient materials including website and brochures
- Insurance access support
  - Assist surgeons in obtaining coverage for patients
- Financial assistance
  - Seroma evaluation
  - Surgical treatment following BIA-ALCL diagnosis

Allergan Remains Committed to Improved Awareness Through Research

- Independent research
  - Immunology
  - Cause of BIA-ALCL
  - Genetic associations
- Internal research
  - Infection control
    - Antiseptic solution efficacy
    - Impact of textured surface area on bacterial contamination
  - Lower surface area textured implant development

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Breast Implant Illness

- Over 80 signs and symptoms reported[1]
  - Cognitive issues
  - Fatigue
  - Muscle pain[2]
- No established case definition
- Variable time to onset[3]
- Difficult to quantify, yet important to understand

1. Magnusson M et al. 2019.
2. FDA Statement: Scott Gottlieb, M.D. and Jeff Shuren, M.D., March 15 2019
3. Jewell M et al. 2019

Breast Implant Illness – Next Steps

- Key challenges in understanding breast implant illness
  - No established case definition
  - Symptoms present in patients without breast implants
  - No standardized assessment tools
- Ongoing activities
  - Actively monitoring data in post-approval study
    - Investigating links between implants and symptoms
  - Regularly communicate with FDA
    - Post-market surveillance
    - Medical assessment of every reported event

Breast Implant Illness – Recommendations

- Close collaboration between
  - Patient groups
  - Industry
  - Regulators
  - Experts
- Improved symptom to disease mapping
- Independent epidemiologic review of signs and symptoms data from large post-approval studies

Conclusion

- Breast implants are backed by significant long-term clinical experience and comprehensive post-market monitoring
- Evidence supports
  - Breast implants, including BIOCELL textured implants, provide important benefits
  - Incidence of BIA-ALCL is low and when treated appropriately, prognosis is excellent
- We continue to listen to patients and evaluate signs and symptoms from each patient case individually
- Evidence supports that benefits of breast implants outweigh their risks
- We are committed to working with FDA and other parties to get the best outcomes for patients