Allergan Breast Implants: Benefits and Risks

FDA Medical Devices Advisory Committee
General and Plastic Surgery Devices Panel
March 25, 2019

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Vice President, Clinical Development
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\(^5,6\)

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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

- 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

- 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

<table>
<thead>
<tr>
<th>Study Arm</th>
<th>Enrolled / Response</th>
<th>Total N=53,262</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Silicone N=39,153</td>
<td>Saline N=14,109</td>
</tr>
<tr>
<td>BIFS</td>
<td>Number enrolled</td>
<td>2000</td>
</tr>
<tr>
<td></td>
<td>Year 1 office visit follow-up</td>
<td>67.2%</td>
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<tr>
<td></td>
<td>Year 4 office visit follow-up</td>
<td>29.8%</td>
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<tr>
<td></td>
<td>Year 5 questionnaire follow-up</td>
<td>83.6%</td>
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<td></td>
<td>Year 6 questionnaire follow-up</td>
<td>79.9%</td>
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<tr>
<td></td>
<td>Year 7 questionnaire follow-up</td>
<td>78.8%</td>
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<tr>
<td>410</td>
<td>Number enrolled</td>
<td>421</td>
</tr>
<tr>
<td></td>
<td>Year 1 office visit (interim data) follow-up</td>
<td>35%</td>
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<tr>
<td></td>
<td>Year 1 questionnaire follow-up</td>
<td>71.4%</td>
</tr>
<tr>
<td>NBIR</td>
<td>Number enrolled</td>
<td>36,732</td>
</tr>
</tbody>
</table>

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

- 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
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\(^2\)

2. Oishi N et al. Blood 2018
BIA-ALCL Incidence Rates in Textured Implants: Literature*

1. USA 1:30,000 to 1:50,000
2. Netherlands 1:25,000
3. Italy 1:28,000
4. Australia 1:2,800 to 1:86,000
5. Few cases reported in Asia

1. Doren et al. 2017
2. Campanale 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*

- **Worldwide BIOCELL Rate (Postmarket Surveillance)**
  1:32,000

- **410 CA/CARE Study¹**
  1:3000

- **US BIOCELL Rate (Postmarket Surveillance)**
  1:16,000

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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

- Enhanced 14-point aseptic technique¹
  - Changing gloves
  - Antiseptic solutions
  - Minimal touch
- Zero BIA-ALCL cases
  - 42,000 BIOCELL implants²
  - 11.7 years mean follow-up
- Continue to communicate the importance of enhanced aseptic surgical technique

¹ Deva 2013; ² Adams WP et al. 2017
Evidence Suggests BIA-ALCL Treatments are Effective

- 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

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.