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BIA-ALCL IN PRACTICE

Over the last two decades, rare reports in the medical literature of anaplastic large cell lymphoma (ALCL) occurring in patients with breast implants has led the medical community to recognise a new and rare type of ALCL, called Breast Implant-Associated ALCL (BIA-ALCL).

Allergan is working with the medical community and regulatory agencies to further understand BIA-ALCL. It is anticipated that increased awareness will facilitate earlier detection which in turn may allow for earlier intervention and better patient outcomes.

MAJOR REGULATORY AGENCIES DO NOT RECOMMEND ANY CHANGES TO CURRENT BEST PRACTICE[1–3]

THE NUMBER OF REPORTS OF BIA-ALCL REMAINS VERY LOW

Lymphoma is a cancer of the lymphoid tissue that is classified as either Hodgkin lymphoma (HL) or non-Hodgkin lymphoma (NHL). Anaplastic large cell lymphoma (ALCL) is a rare form of NHL.

BIA-ALCL is a rare sub-type of ALCL that is distinct from both spontaneously occurring ALCL and breast cancer. It is not specific to aesthetic or reconstructive procedures.[1,4–10]

The number of reports of BIA-ALCL remains very low compared to the total number of breast implants sold worldwide: less than 200 cases reported in the literature since 1997[11,12] vs. up to 10 million implants sold during the same period.[1,2]

BREAST CANCER:	123.8 new cases per 100,000 women per year in the US[13]
NHL:	19.7 new cases per 100,000 men and women per year in the US[14]
ALCL:	0.2 new cases per 100,000 women per year in the US[1]
ALCL (IN THE BREAST):	3 new cases per 100,000,000 women per year in the US[1]
BIA-ALCL:	ALCL in women with breast implants is a subset of ALCL (breast) cases
BREAST IMPLANTS:	5 to 10 million women worldwide[1]

The medical community's understanding of BIA-ALCL is still evolving. Given its recent recognition as a clinical entity and the fact that it is a rare cancer infrequently encountered by physicians, detailed data on reported cases are sometimes inconsistent and incomplete. The exact cause of BIA-ALCL is not known and it is not yet possible to determine if it is specific to any manufacturer or breast implant type.[1,15–18]

Investigators at MD Anderson recently identified and analysed cases of BIA-ALCL reported in clinical literature over the past 20 years (1997 to November 2014) and followed up with the reporting investigators and institutions to establish as detailed a picture of every case as possible.[12]

OF THE 128 CASES IDENTIFIED:

- 50.4% were associated with 'unknown' implants.*
- 38.2% of the 128 case reports were with Allergan implants (including Inamed and McGhan).
- 10.4% were associated with five other manufacturers, including Mentor and Silimed.

Note – percentages obtained from personal communication with Dr Clemens and do not equal 100%.

*'Unknown' includes cases where no manufacturer was identified, or where multiple manufacturers' implants were used, so a clear association cannot be established.
Allergan has always labelled their devices with the company name (including Inamed and McGhan), facilitating identification at explantation.

MAJOR REGULATORY AGENCIES DO NOT RECOMMEND ANY CHANGES TO CURRENT BEST PRACTICE

In response to the case reports, major regulatory agencies including the US FDA, the French National Association of Health and Medicines (ANSM) and the UK MHRA have published recommendations for healthcare professionals in the diagnosis, treatment, monitoring, and reporting of BIA-ALCL; they do not recommend any changes to current best practice.[1–3]

> "If you are contacted by concerned women about this issue, reassure them that ALCL is a rare form of cancer, which can be treated if detected in the early stages… No change to current best practice is needed."[2]
>
> MHRA, July 2014

> "The FDA does not recommend prophylactic breast implant removal in patients without symptoms or other abnormality."[1]
>
> FDA, January 2011

> "Suggesting preventive explantation due to the risk of ALCL is not recommended in women with breast implants."[3]
>
> ANSM, 2015

RECOMMENDATIONS FOR THE DIAGNOSIS, TREATMENT AND MONITORING OF BIA-ALCL

Diagnosis: Patients typically present with effusion around the implant or in continuity with the implant capsule.

- Any patient presenting with late peri-implant seroma (>1 year) should be considered for a breast ultrasound to rule out mass and have the seroma fluid sent for culture, cytology, flow cytometry, and cell block.[10,19]
- Any tissue samples should be sent for immunohistochemical analysis, including CD30 and anaplastic lymphoma kinase (ALK), to a haematopathologist experienced in diagnosing ALCL.[10,19]
- A diagnosis should be established in consultation with a centre of excellence with appropriate expertise, given the rarity of the disease.[19]

TREATMENT AND MONITORING: CONFIRMED BIA-ALCL

- Surgical removal of the affected implant and total capsulectomy (complete resection of capsule including posterior wall), ideally in consultation with a surgical oncologist, should occur; this is generally considered sufficient to eradicate capsule-confined BIA-ALCL without the need for additional chemotherapy or radiation treatment.[10]
- Develop an individualised treatment plan in coordination with the patient's multi-disciplinary care team. Because of the small number of cases worldwide, there is no defined consensus treatment regimen.[1]
- Following implant removal and total capsulectomy, surveillance includes clinical follow-up every 6 months for 5 years with annual ultrasounds and/or PET CT for 2 years.[10]

RECOMMENDATIONS FOR WOMEN WITH BREAST IMPLANTS:

- Patients should continue to follow current best practices for medical care and follow-up, in consultation with their healthcare provider.[20]
- Women should regularly perform breast self-examination and consult their healthcare provider if they notice pain, swelling or any changes in or around the breast implant.[2,3,20,21]
- There is no reason to contact the healthcare provider if they have no symptoms.[20]

A NUMBER OF INITIATIVES ARE WORKING TOWARDS A BETTER UNDERSTANDING OF BIA-ALCL

As a leading manufacturer of breast implants, Allergan has been, and remains committed to, understanding more about the health impacts and longer term risks of BIA-ALCL. The company has supported a number of initiatives to increase the understanding and awareness of BIA-ALCL with clinicians, regulatory agencies, professional associations and patients to help the global community address this issue directly.

INTERNAL RESEARCH:

- Since 2011, Allergan has established a multi-disciplinary team with the objective of further understanding the issue.
- Allergan has ongoing non-clinical projects evaluating immune cell activation, capsule formation, and biofilm formation.[8]
- Allergan is conducting in-vitro testing to investigate theories related to root causes of BIA-ALCL.
- Allergan R&D is assessing bacterial colonisation and biofilm formation on various textured surfaces.

EXTERNAL COLLABORATIONS:

- To better understand the aetiology, diagnosis and appropriate treatment of BIA-ALCL, Allergan has supported several expert panels:
  - In 2010, Allergan supported the establishment of an independent expert panel from the American Plastic Surgery societies (ASPS and ASAPS) and their Educational Foundations (PSEF and ASERF).
  - In 2011, and again in 2014, Allergan gave an independent research grant to the RAND Corporation to fund scientific advisory panels on BIA-ALCL to perform systematic literature reviews and update recommendations for evaluation, treatment, and follow-up of women presenting with BIA-ALCL.[6,10,15,21]
- Independent research since 2012 at the world-renowned cancer centre of excellence, MD Anderson, through an unrestricted research grant.

REGULATORY ACTIVITIES:

- Allergan reports all cases, confirmed or suspected, to regulatory agencies according to the requirements of each country.
- Annually, summaries of these case reports are provided to various regulatory agencies around the world.
- Allergan has been in direct communication with the FDA and other global regulatory agencies regarding the cumulative data and research associated with BIA-ALCL.
- Allergan is a key stakeholder in the development of a US National Breast Implant Registry. When established, this registry could be a useful tool in identifying potential factors associated with long term adverse events that may occur with breast implants.

BIA-ALCL IN PRACTICE

The medical community recognises a new and rare sub-type of ALCL called Breast Implant-Associated ALCL (BIA-ALCL).

The number of reports of BIA-ALCL remains very low compared to the total number of breast implants sold worldwide.[1,2,11,12]

Major regulatory agencies do not recommend any changes to current best practice.[1–3]

As a leading manufacturer of breast implants, Allergan continues to support a number of initiatives to improve the understanding of BIA-ALCL with clinicians, regulatory agencies, professional associations and patients. If you have a suspected case of BIA-ALCL associated with an Allergan product, please report the case to Allergan in one of the following ways:

Product Support:

Phone: +44 (0)1628 497456

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ALLERGAN TEXTURED IMPLANTS HAVE BEEN AVAILABLE SINCE THE LATE 1980S. TEXTURE IS DESIGNED TO HELP REDUCE BREAST IMPLANT COMPLICATIONS BY IMPROVING TISSUE ADHERENCE, WHICH IS PARTICULARLY IMPORTANT WITH SHAPED IMPLANTS. PHYSICIANS SHOULD BALANCE THE KNOWN BENEFITS OF TEXTURED IMPLANTS WITH THE KNOWN POTENTIAL COMPLICATIONS WHEN COUNSELLING PATIENTS.

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