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BREAST IMPLANT ASSOCIATED-ANAPLASTIC LARGE CELL LYMPHOMA (BIA-ALCL)

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Superior Health Council

ADVISORY REPORT OF THE SUPERIOR HEALTH COUNCIL no. 9473

Breast Implant Associated-Anaplastic Large Cell Lymphoma (BIA-ALCL)

In this scientific advisory report on public health policy, the Superior Health Council of Belgium provides recommendations for the detection, registration and follow up of Breast Implant Associated-Anaplastic Large Cell Lymphoma of the Belgian population.

This report aims at providing information to health care providers and the public with specific recommendations on registration and follow up of BIA-ALCL cases.

This version was validated by the Board on November 2018[1]

I INTRODUCTION AND ISSUE

Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) is a rare type of non-Hodgkin lymphoma that can present as a delayed periprosthetic seroma or mass adjacent to the breast implant. All the information to date suggests that women with breast implants may have a very low but increased risk of developing this type of lymphoma. The current estimate is that there are approximately 600 reported cases of BIA-ALCL worldwide.

Given that there is an association between breast implants and ALCL, although of unknown aetiology, the Superior Health Council started a project with the Federal Agency of Medicines and Health Products (FAMHP). The aim was to have recommendations for the healthcare providers and information to the public regarding diagnosis, registration and clinical follow-up of BIA-ALCL cases.

Important to stress is that this advisory report solely depicts BIA-ALCL as a diagnosis. Other diagnosis resulting from similar symptoms are equally possible but are excluded from this advice.

[1] The Council reserves the right to make minor typographical amendments to this document at any time. On the other hand, amendments that alter its content are automatically included in an erratum. In this case, a new version of the advisory report is issued.

II CONCLUSION and RECOMMENDATIONS

II.1 Conclusions

BIA-ALCL is a rare type of non-Hodgkin type of lymphoma. The exact pathogenesis is still not well established and epidemiology is incomplete today by shortcomings in the reporting.
Therefore, a complete and up to date information of the medical community as well as a standardised way of reporting would be the way to improve the safety of the patients and a better knowledge of BIA-ALCL.

II.2 Other aspects

Because the risk of developing BIA-ALCL is low, societies and health authorities do not recommend additional screenings or prophylactic removal of implants.

Although BIA-ALCL has predominantly been reported in patients that were treated with textured breast implants, observed associations of BIA-ALCL with certain implant types should be approached with caution. Not only is the use of textured versus smooth implants variable around the world and over time, also implant history in individual patients is often unknown. With the prerequisite of having obtained a CE certificate and keeping in mind the very low absolute risk to develop BIA-ALCL, textured implants thus still have a reasonable assurance of safety and effectiveness and therefore remain available as an option for treatment until proven otherwise.

II.3 Recommendations

This working group would like to underline the importance of patient education. Although the absolute risk of BIA-ALCL is very small, informed consent in breast augmentation and reconstruction with implants should, amongst others, include a discussion of the risk of BIA-ALCL for all implants. Patients should be educated to detect signs that could be indicative for BIA-ALCL for aesthetic and reconstructive procedures.

When a patient presents herself with late onset (> 1 year post-implantation), persistent peri-implant seroma or masses adjacent to the breast implant, consider the possibility of BIA-ALCL. If you have a patient with confirmed BIA-ALCL, refer the individual's case to a multidisciplinary tumor board for evaluation.

Report all suspected and confirmed cases of BIA-ALCL to the FAMHP using the reporting template for BIA-ALCL cases. In cases where BIA-ALCL is confirmed through cytology and immunohistochemistry testing, the FAMHP may contact you for additional information. The FAMHP will keep the identities of the reporter and the patient confidential at all times.

Keywords and MeSH *descriptor terms*[2]

MeSH terms*	Keywords	Sleutelwoorden	Mots clés	Schlüsselwörter
Breast Implantation	Anaplastic large cell lymphoma	Anaplastisch grootcellig lymfoom	Lymphome anaplasique à grandes cellules	
Humans	BIA-ALCL	BIA-ALCL	LAGC-AIM	
Lymphoma,Large-Cell, Anaplastic/diagnosis	Breast implant lymphoma	Borstimplantaat-geassocieerd lymfoom	Lymphome associé à un implant mammaire	
Postoperative Complications	Report	Verslag	Rapport	

MeSH (Medical Subject Headings) is the NLM (National Library of Medicine) controlled vocabulary thesaurus used for indexing articles for PubMed http://www.ncbi.nlm.nih.gov/mesh.

[2] The Council wishes to clarify that the MeSH terms and keywords are used for referencing purposes as well as to provide an easy definition of the scope of the advisory report. For more information, see the section entitled "methodology".

III METHODOLOGY

After analysing the request, the Board of the SHC and the Chair of the area Cosmetics identified the necessary fields of expertise. An *ad hoc* working group was then set up which included experts in Aesthetic Techniques, Aesthetic Surgery and Vigilance. The experts of this working group provided a general and an *ad hoc* declaration of interests and the Committee on Deontology assessed the potential risk of conflicts of interest.

This advisory report is based on a review of the scientific literature published in both scientific journals and reports from national and international organisations competent in this field (peer-reviewed), as well as on the opinion of the experts.

Once the advisory report was endorsed by the working group and peer reviewed by international experts, it was ultimately validated by the Board.

IV ELABORATION AND ARGUMENTATION

List of abbreviations used

AJCC	American Joint Committee on Cancer
ALCL	Anaplastic large cell lymphoma
ALK	Anaplastic Lymphoma Kinase
ANSM	Agency Nationale de Sécurité du Médicament
ASPS	American Society of Plastic Surgeons
BIA-ALCL	Breast Implant Associated-Anaplastic Large Cell Lymphoma
FAMHP	Federal Agency for Medicines and Health Products
MHRA	Medicines and Healthcare products Regulatory
NCCN	National Comprehensive Cancer Network
SHC	Superior Health Council
TGA	Therapeutic Goods Administration
TNM	Tumor, lymph Node, Metastasis
US FDA	US Food and Drug Administration
WHO	World Health Organisation

1 Breast Implant Associated-Anaplastic Large Cell Lymphoma (BIA-ALCL)

1.1 Introduction

Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) is a rare type of non-Hodgkin lymphoma of T-cell origin that most commonly presents as a delayed periprosthetic seroma or mass(es) adjacent to the breast implant. In accordance with the criteria defined in the WHO classification, diagnosis is made by the finding of abnormal cells in the aspirate or biopsy, accompanied by the hallmark uniform over-expression of CD30, a T cell clonal expansion, and negative staining for Anaplastic Lymphoma Kinase (ALK) (WHO criteria).

The first case was reported in 1997 and since then the rate of diagnosis of BIA-ALCL is rising. To date, around 600 known cases of BIA-ALCL have been registered. All evidence suggests that patients with breast implants may have a very low but increased risk of developing ALCL adjacent to the breast implants. In line with this observation, the World Health Organization

classified BIA-ALCL as a distinct entity in 2016. In the US, the National Comprehensive Cancer Network (NCCN) established consensus oncology guidelines for the diagnosis and management of BIA-ALCL in 2016.

Given the association between breast implants and ALCL, the Superior Health Council started a project with the FAMHP. The aim was to have recommendations for the healthcare providers regarding diagnosis, registration and clinical follow-up of BIA-ALCL cases.

1.2 Pathogenesis

The aetiology of the disease remains unclear. Several theories have been proposed for lymphomagenesis such as the presence of a subclinical biofilm on the implant surface, capsular contracture, chronic innate immunity response to texture particulate, repeated capsular trauma, genetic predisposition or an autoimmune aetiology. All authors agree to consider BIA-ALCL being caused by a multifactorial chronic inflammatory stimulus leading to T cell dysplasia in a potentially genetically susceptible patient. The initiation of a chronic inflammatory response in the fibrous capsule and draining lymph nodes with lymphocyte infiltration, along with the production of specific cytokines, likely causes indirect stimulation of malignant clones. Removal of the implant and accompanying tumour may switch off the T cell expansion trigger, thus explaining the good prognosis of BIA-ALCL in the majority of patients.

From all data available it is generally accepted that BIA-ALCL is predominantly seen in patients having textured (rough surface) breast implants. To date, there are no confirmed cases of BIA-ALCL with only a smooth implant clinical history, but this association can neither be definitely excluded. One working theory to explain this predominance is that, when compared to smooth implants, concavities present from the texturing process predispose to subclinical infection and/or chronic inflammatory stimulation from the textured surface itself ultimately resulting in lymphoma.

In the light of the possible genetic predisposition to a specific antigen local immune response through activated T cells, research is currently being conducted to identify potential mutation(s) in BIA-ALCL patients.

No difference between silicone and saline filled implants or between reconstructive and cosmetic patients have been identified.

1.3 Epidemiology

Determining the precise incidence and prevalence of BIA-ALCL is challenging due to significant limitation in worldwide reporting. Lack of global breast implant sales data and implant use (primary versus revision, uni/bilateral use). Although increasing awareness and recognition of BIA-ALCL has resulted in an increase in the number of reported cases, it remains uncommon.

Several researchers tried to quantify the risk of BIA-ALCL, however for most of the figures these are derived using a number of assumptions and estimations. Moreover, it is believed that BIA-ALCL is currently underdiagnosed. Not all cases have been properly diagnosed and most likely not all diagnosed cases have been reported. Given the nature of in situ BIA-ALCL, it is possible that cases with persistent periprosthetic effusion have been misdiagnosed as subclinical infections and treated by removal of the implants without testing the fluid for CD 30 positivity. This statement is supported by the observation that due to the increased awareness of BIA-ALCL, more cases are being reported as more cases with late seromas are being investigated.

In the first epidemiological study on BIA-ALCL published in 2008, De Jong et al. reported the incidence of BIA-ALCL to be 0.1-0.3 per 100 000 women undergoing breast implantation. The associated odds ratio was 18.2 with a wide 95% confidence interval 2.1 – 156.8 secondary to the low absolute risk which, however, appeared higher than sporadic ALCL. In 2011, the FDA reported a higher incidence of 0.6 – 1.2 per 100 000 based on 60 reported cases of implant associated ALCL among the roughly 5-10 million women with breast implants. In 2016, Doren et al. estimated the incidence at 2.03 per million per year and the lifetime prevalence at 33 per 1 million women with textured implants. In 2018, the same research group who published the first epidemiological study reported an updated study. This large nationwide epidemiological study indicated that the odds ratio for women with breast implants to develop breast ALCL as compared to those without implants was > 400 which can be regarded as an attributable risk. The research group further concluded that the life time absolute risk could be determined at 1:7000.

The most recent data available indicate that health authority governments all over the world have in total registered around 600 cases of BIA-ALCL. A major drawback is that reporting of these BIA-ALCL cases is still not uniform nor mandatory in all regions.

1.3.1 Belgium

Healthcare providers are expected to report BIA-ALCL cases to the FAMHP. In 2015 the agency had no reported cases of BIA-ALCL. After a retrospective study which was done in collaboration with the Belgian Cancer Registry, 2 cases could have been identified. Following this, the agency issued a letter requesting healthcare providers to be aware of the potential link between ALCL and breast implants. In that letter, healthcare providers were reminded to report all cases of BIA-ALCL to the authority upon diagnosis. Today the agency has 9 confirmed cases of BIA-ALCL.

1.3.2 Europe

A number of healthcare governments have published rates on BIA-ALCL. The Italian Ministry of Health recently published a review of 22 cases of BIA-ALCL with a subsequent incidence rate of 2.8 per 100000 implanted patients. The Medicines and Healthcare products Regulatory Agency (MHRA - United Kingdom) reported on their website that as of November 2017 they have received 48 reports of ALCL in patients with breast implants, of these 40 met the WHO diagnostic criteria. MHRA further stated to have received 3 cases of patient death for ALCL in women with breast implants of which 1 was confirmed to meet the diagnostic criteria of BIA-ALCL. Agency Nationale de Sécurité du Médicament et des produits de santé (ANSM - France), recently reported having registered 50 cases.

Upon request of the European Commission, all European competent authorities on medical devices should at a regular interval submit information on BIA-ALCL cases that were reported to them. A European Commission Vigilance Medical Device Expert Group task force has been established. This task force is in charge of collecting and analysing all available data on BIA-ALCL. During the last discussion a total of 180 confirmed cases were presented for Europe.

1.3.3 World wide

The most recent update of the US Food and Drug Administration (US FDA) mentions that they had received a total of 414 medical device reports (MDRs) of BIA-ALCL, including the death of nine patients. However, the FDA cautioned that the MDR system may contain incomplete inaccurate, untimely, unverified, biased, under-reported or duplicate reporting of events.

The Australian Therapeutic Goods Administration (TGA) reported that a total of 72 cases have been recorded in Australia so far, including 3 deaths in Australia. The TGA estimated the risk of developing BIA-ALCL to be between 1 in 1000 and 1 in 10 000 women with breast implants.

5 Canadian cases of confirmed WHO defined BIA ALCL were reported to Health Canada by the manufacturers in the last 10 years, none of the cases reported a fatal outcome. Based on the cases reported, the rate of WHO defined BIA-ALCL cases per implant sold over the past 10 years in Canada was calculated as 0.0013% or 1 case in 77190 implants sold. The rate per textured implant is estimated at 0.0041% or 1 case per 24177 textured implants sold.

Additionally, only a few cases have been reported in Latin America (3 in Mexico, 3 in Chile and 1 case in Argentina), Africa and Asia. The unequal spread of cases may represent a lack of awareness of the potential link and/or lack of reporting in some regions.

1.4 BIA-ALCL diagnosis

The majority of patients (60 to 90%) describe a rapid swelling of the breast at an average of 8 to 10 years after implantation of breast prostheses. Every late onset (≥ 1 year) periprosthetic effusion after breast augmentation or reconstruction using implants should be considered as potential BIA-ALCL until proven otherwise. Other described symptoms included the presence of a capsular mass, breast enlargement, skin rash, capsular contracture and lymphadenopathy.

The initial workup of an enlarged breast must include an ultrasound evaluation for a fluid collection, breast masses and enlarged regional lymph nodes. Ultrasound has been reported to have the highest sensitivity (84%) in detecting effusion in cases of BIA-ALCL and has the added benefit of being readily available for image-guided aspiration of the fluid for diagnosis. When ultrasound is inconclusive, a magnetic resonance imaging is recommended. PET/CT may be useful to determine disease extension in confirmed cases.

BIA-ALCL is a monoclonal T cell expansion of large anaplastic cells with uniform expression of CD30 protein, a cell membrane protein that serves as lymphoma tumour marker. A specific cytology work-up for the aspirated periprosthetic fluid and representative samples of the capsule as well as lymph nodes in case of lymph nodes involvement includes immunohistochemistry and/or flow cytometry for T-cell markers and CD30. Anaplastic Lymphoma Kinase staining will be negative in BIA-ALCL as opposed to the systemic more aggressive ALCL.

1.5 Registration of BIA-ALCL cases

The relative low number of cases requires accurate reporting by the public for optimal data collection of this rare malignancy.

In general, healthcare providers are expected to report confirmed cases of BIA-ALCL both to the manufacturer of the implant as well as to the appropriate national regulatory authority.

1.5.1 Belgium

In Belgium, incidents with medical devices are being submitted to the FAMHP by healthcare providers and patients, manufacturers, and distributors. In the current way of working, cases of BIA-ALCL should be reporting using the general template to report an incident with a medical device trough this website:
https://www.famhp.be/en/human_use/health_products/medical_devices_accessories/materiovigilance/how_notify

There are however a number of drawbacks using this method for reporting BIA-ALCL cases. This report is very general and does not capture specific details on diagnosis, treatment modalities and oncologic outcomes. This observed shortcoming is probably related to the fact that reporting of cases is most commonly performed at the time of diagnosis but not after completed treatment or long-term follow up. Further the report lacks information on pathologic findings. As this information is not readily available for review in the current template, this advisory group sought for a more elegant solution for reporting BIA-ALCL cases to the authority.

The new template that is proposed captures the most relevant information (patient age & gender, breast implant exposure {date implanted, implant indication [reconstructive / aesthetic], brand name, type of implant [saline vs silicone filled] and type of implant surface [smooth or textured] }, history of subsequent revision surgeries, clinical presentation & date of diagnosis, pathological markers {CD30 & ALK}, tumour staging, treatment the patient received as well as clinical outcome). By keeping its content fairly limited we are hoping to restrict the administrative burden for healthcare providers the best way possible (annex 1).

Further in the aim to improve our prospective tracking of Belgian BIA-ALCL, we tried to understand how we could best catch all cases. One of the reasons why not all BIA-ALCL cases are being reported to the FAMHP is probably related to the involvement of multiple specialties in diagnosis and management for these patients. We therefore suggest to already report data to the FAMHP once you have a suspicion your patient has BIA-ALCL using the very same template. As not all information will be present at the time of reporting, the healthcare provider who suspects the patient to have developed BIA-ALCL only fills in the data he/she has knowledge of. Healthcare provider from multiple specialities can submit a case capturing data from their point of interest. As soon as a suspected case is being reported, the agency will follow-up the case until diagnosis of BIA-ALCL has been confirmed or rejected. Once a case has been confirmed, additional information such as the immunohistochemical and histopathological results will be further requested in order to gather additional information to better characterize ALCL in women with breast implants. Reporting of suspected cases which are later rejected is not effortless as these cases might provide valuable information on potential differential diagnoses.

1.5.2 Europe

BIA-ALCL remains uncommon and as such it will not be possible to draw any evidence-based conclusions based solely on national data. It is imperative that international regulators work closely together to characterize and quantify the risk. The Vigilance Medical Device Expert Group of the European Commission has a mission of developing common policies in the field of vigilance by establishing close cooperation among institutions of the member states. In 2015, the Vigilance Medical Device Expert Group established a BIA-ALCL task force to examine the possible correlation between ALCL and breast implants. A European database was created that uniformly collects data on all reported BIA-ALCL cases by the different member states. The database is managed and updated by each competent authority, which gives a real-time picture of BIA-ALCL cases in Europe.

The FAMHP as a member of the task force regularly updates the European database like any other member state. The FAMHP provides only the information that is relevant to draw evidence-based conclusions to this European database. Information that is certainly not provided by the FAMHP, if they are in FAMHP possession, include but are not limited to reporter names, contact details, patient codes and patient initials/names. As the chair of the task force, the European Commission organises teleconferences to discuss the updates of European BIA-ALCL along with the evolutions described in medical literature.

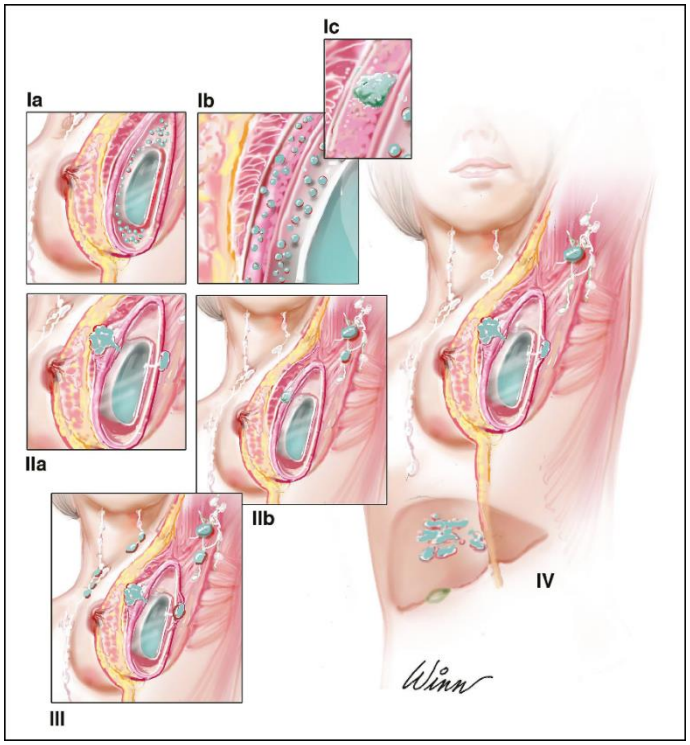
1.5.3 World wide

BIA-ALCL is not a European but a global emerging risk. Regulatory bodies outside Europe are also working extensively to gather information on BIA-ALCL. The European Commission often invites members from the US FDA, Health Canada, TGA, DKMA (Japan) and Anvisa (Brazil) to join the discussion and to provide a regular update on state of play in the different jurisdictions.

Worthwhile to mention is also that the Plastic Surgery Foundation, based in the United States of America, in collaboration with the American Society of Plastic Surgeons (ASPS) and the US FDA have created a BIA-ALCL specific database for collecting and following up cases of BIA-ALCL in various countries worldwide. (www.thepsf.org/PROFILE) This PROFILE registry also provides up to date information on BIA-ALCL. As of October 2018, the PROFILE registry has received 252 unique cases of BIA-ALCL in the US.

1.6 Follow up and treatment

A careful staging evaluation should dictate the appropriate treatment plan. Recently, a TNM classification has been proposed (table 1). This staging differs from the commonly used Ann Arbor staging by describing local infiltration depth that implicates on local treatment options. A BIA-ALCL specific treatment management using the TNM staging system has been proposed by Clemens et al. The staging recognises a very low risk group with localized seroma-restricted disease and a separate higher risk group with infiltration beyond the fibrous capsule into breast tissue or a breast mass who will benefit from more aggressive systemic treatment. The majority of cases at diagnosis are seroma-restricted stage, i.e. confined to the space around the prosthesis.



Determination of clinical and pathologic BIA-ALCL staging is essential for treatment strategies. This figure represents a BIA-ALCL tumor, lymph node, metastasis (TNM) staging system modeled after the American Joint Committee on Cancer (AJCC) TNM staging system for solid tumors. Adapted from original illustration by Dave Arten, MA, CMI, in Clemens et al.

Table 1.
BIA-ALCL Tumor, Lymph Node, and Metastasis (TNM) Staging and Stages. Adapted from Clemens et al.[5]

Staging				
Tumor size	**T1**	**T2**	**T3**	**T4**
T	Confined to effusion	Early capsule invasion	Mass aggregate, confined to capsule	Tumor locally invasive out of capsule
Lymph Nodes	NO	N1	N2	
N	No lymph node involvement	One regional lymph node	Multiple regional lymph nodes	
Metastasis	MO	M1		
M	No distant spread	Other organs/distant sites		
Stages				
Stage IA: T1N0M0		Stage IIA: T4N0M0		Stage III: TanyN2M0, T4N1M0
Stage IB: T2N0M0		Stage IIB: T1-3N1M0		Stage IV: TanyNanyM1
Stage IC: T3N0M0				

From: NCCN Consensus Guidelines for the Diagnosis and Management of Breast Implant-Associated Anaplastic Large Cell Lymphoma
Aesthet Surg J. 2017;37(3):285-289. doi:10.1093/asj/sjw259

A complete surgical excision of the implant and the capsule with negative margins is the recommended approach for treatment of BIA-ALCL in the majority of patients. There is no indication for a radical mastectomy, sentinel lymph node biopsy, and full axillary dissection is only reserved for multi-node metastasis. Chemo- or radiotherapy is only recommended in advanced cases with distant extension or metastases after advice of a (hemato-)oncologist. Interestingly, 2 cases have been described in literature assessing the use of Brentuximab Vedotin, a monocloncal anti-CD30 antibody conjugated to the anti-microtubule agent monomethyl auristatin E and both have shown promising results in these advanced cases.

The prognosis of the disease mostly depends on the extent of the disease at the time of diagnosis. Up till now, all relapses after any kind of therapy occur within the first 3 years. If complete excision with no residual disease is achieved, clinical follow-up should be done every 3 to 6 months during 2 years by clinical examination echogram and in suspicious cases only by positron tomographic exam (PET-CT) and thereafter as clinically indicated.

Only a very small number of deaths, 16 total to date, have been reported worldwide and each of these cases were characterized by a delay in diagnosis and limited or no surgical resection. This highlights the importance of timely diagnosis and the fact that complete surgical excision is essential for the management of patient with BIA-ALCL.

The risk of developing recurrent, or a new primary, BIA-ALCL tumour upon replacement remains uncertain. Replacement by smooth prosthesis or autologous tissue is recommended, replacement by textured prostheses may best be avoided even though define proof to underpin this notion is lacking thus far.

1.7 Conclusion

BIA-ALCL is a uncommon disease with an excellent prognosis when diagnosed at an early stage and treated by complete surgical excision. The most important adverse prognostic indicator is being the presence of a solid mass or lymph node involvement which is indicative of the necessity of adjuvant chemotherapy. Due to the rarity of the disease, it is imperative to collect all information on BIA-ALCL cases to be able to study both epidemiology as well as

proper diagnosis and clinical management. Within this aim a close collaboration between the associations, experts in the clinical and scientific communities and governmental institutions should be pursued.

Serous fluid collections around a prosthesis are relatively common and are benign in most patients. The recommendation of this expert group is to consider the possibility of BIA-ALCL in every patient presenting herself with late onset (> 1 year post-implantation) persistent peri-implant seroma or mass(es) adjacent to the breast implant.

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VI COMPOSITION OF THE WORKING GROUP

The composition of the Committee and that of the Board as well as the list of experts appointed by Royal Decree are available on the following website: About us.

All experts joined the working group ***in a private capacity***. Their general declarations of interests as well as those of the members of the Committee and the Board can be viewed on the SHC website (site: conflicts of interest).

The following experts were involved in drawing up and/or endorsing this advisory report. The working group was chaired by **Albert DE MEY**; the scientific secretary Veerle MERTENS.

BEELE Hilde	Medicine, dermatology	UZ Gent
BORIES Yvon	Hospital hygiene	AZ Sint Niklaas
DECALUWE Kelly	Materiovigilance entity	FAMHP
DE CUYPER Christa	Medicine, dermatology	AZ Sint-Jan, Brugge
DE MEY Albert	Medicine, Plastic surgery	ULB
DIERICKX Christine	Medicine, dermatology	
GOOSSENS An	Dermatology, contact allergy centrum	UZ Leuven
HAUSDORFER Susanne	Medicine, dermatology	
MONSTREY Stanislas	Plastic surgery	UZ Gent
NIZET Jean-Luc	Plastic surgery	CHU Liège
ROGIERS Vera	Toxicology, Cosmetics	VUB
SNAUWAERT Johan	Medicine, dermatology	UPDVB
VANHOOTEGHEM Olivier	Surgical dermatology	CHU UCL Namur
VERHAEGHE Evelien	Medicine, dermatologie	UZ Gent

The following administrations and/or ministerial cabinets were heard:

AYOUT Mehdi	FPS Public Health
DRIESMANS Christophe	FAMHP
MEUNIER Joëlle	FPS Public Health
PASTEELS Karine	FPS Public Health
ROISIN Thierry	FAMHP
WATERBLEY Patrick	FPS Public Health

The following firms/associations/etc. were heard:

BOECKX John	BESKO
DELGOFFE Daniel	UNEB
GYS-BEHETS Francine	BESKO
HEBRANT Jean	Belgian Society of Aesthetic Medicine

This advisory report was peer reviewed by the following international experts

CLEMENS Mark	Plastic Surgery	MD Anderson Cancer Center, University of Texas, USA
CAMPANALE Antonella	Medical devices, vigilance sytems and inspection	Ministry of Health, DG of medical devices and pharmaceutical services, Italy
DE JONG Daphne	Hemopathology (specialized in lymphoma research and diagnosis)	Division of Pathology, VU University Medical Center, Amsterdam, Netherlands
HAMDI Moustapha	Plastic Surgery	UZ Brussels, Royal Belgian Society of Plastic Surgery, Belgium

VII APPENDIXES

Appendix 1: BIA-ALCL specific reporting template (alcl@fagg.be)

CASE REFERENCE	EXAMPLE
DATE OF BIRTH	*1-janv-80*
PATIENT INITIALS	*KD*
SEX	*F*
IMPLANT DETAILS OF IMPLANT PRESENT AT TIME OF DIAGNOSIS (SILICONE / SALINE, SMOOTH / TEXTURED, NAME MF, REFERENCES, …)	*Silicone, Textured, Reference, unknown*
IMPLANT INDICATION (RECONSTRUCTIVE / AESTHETIC)	*Reconstructive*
IMPLANTATION DATE	*1-janv-00*
IMPLANT PLACEMENT (SUBGLANDULAR / SUBFASCIAL / SUBPECTORAL / SUBMUSCULAR)	*Subpectoral*
INCISION TYPES (INFRAMAMMARY /PERIAREOLAR / TRANSAXILLARY / TRANSUMBILICAL / TRANSABDOMINAL)	*Inframammary*
EXPLANT DATE	*1-janv-00*
PREVIOUS IMPLANTS YES / NO (IF KNOWN, PLEASE PROVIDE MORE INFO ON PREVIOUS IMPLANT)	*Yes (details unknown)*
BREAST IMPACTED (R/L/BILATERAL)	*Left*
SYMPTOMS (DESCRIPTION + TIME INDICATION)	*Seroma (2011)*
BIA-ALCL DIAGNOSIS (DESCRIPTION + TIME INDICATION)	*CD30+ / ALK- (2012)*
BIA-ALCL STAGE	*T1N1M0*
BIA-ALCL TREATMENT	*Implant removal + total capsulectomy + chemotherapy*
FOLLOW-UP	*Remission*
NAME AND FUNCTION CASE SUBMITTER	*Dr. X, Plastic Surgeon*
COMMENTS	*Patient has familial history of autoimmune disease*

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