Response to: What Is Missing From the 2022 Practice Recommendation Updates From the World Consensus Conference on BIA-ALCL?

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We thank Mr Nigel Mercer for his reflections and overall positive support of our recent paper and understand these comments represent his personal viewpoints and not the opinions of the Plastic, Reconstructive and Aesthetic Surgery Expert Advisory Group, Medicines and Healthcare products Regulatory Agency, or Sure Insurance ltd (Santa Monica, CA). It is important for us to clarify several points that Mr Mercer has raised in his letter. Mr Mercer comments that we "make reference to 1300 plus cases of breast implant associated anaplastic large cell lymphoma (BIA-ALCL) being mostly related to highly textured, salt loss implants. Without relating incidence to sales data, the relative risks between implants remains unclear to both the profession and the public." We want to bring to Mr Mercer's attention that the United States FDA reports that when manufacture history was known, approximately 91% of world cases involved prior exposure to an Allergan Biocell macrotextured device (Allergan, Irvine, CA).[1] In addition, the incidence of BIA-ALCL increases with higher texture grade.[2] Utilizing sales data, Silimed (Silimed Corporation, Rio De Janeiro, Brazil) polyurethane implants and Allergan Biocell implants confer the highest risk of developing BIA-ALCL (odds ratio of 23.4 and 16.52, respectively, compared with Siltex).[3] In the only prospective level 2 evidence on BIA-ALCL risk, the Allergan Biocell Continuing Access and Reconstruction (CARE) trial demonstrated 8 cases of BIA-ALCL out of 17,656 patients, a risk of 1 in 2207 (95% confidence interval, 1120-5112).[4] In a more recent study, Cordeiro shows an even higher risk of BIA-ALCL with Allergan Biocell breast implants, with 1:355 women.[5] In summary, there is an extensive body of evidence conclusively showing an increased risk of BIA-ALCL associated with specific manufacturers and a significant difference across numerous studies of the occurrence of BIA-ALCL being manufacturer and texture specific. It is critical to note that neither Nagor (Cumbernauld, UK) nor Polytech (Dieburg, Germany) have released annualized sales data to an independent reviewer for an accurate risk calculation. Surely Mr Mercer joins us in calling for manufacturers to release these critical data for independent review. Simply dividing a few ALCL cases by all-time world aggregated sales data is wholly inaccurate and misleading, particularly when the national markets of some of these implants have no established BIA-ALCL registries to capture cases. Consider that prior to Allergan releasing sales data to several academic institutions for review, best calculations of Biocell risk up to that point was 1:500,000 patients. Accurate disease risk calculations directly led to the US FDA device recall of Biocell, which quickly precipitated a worldwide ban. Considering this precedence, manufacturers such as Polytech may understandably be hesitant to supply this level of transparency, but it is in the best interest of patient safety and critical to the integrity of our profession. If manufacturers do not supply these data, we are unable to calculate their implant specific risk and cannot infer or compare risks across devices.

In Mr Mercer's letter, the terms incidence/risk and prevalence seem to be employed interchangeably. In particular, a BIA-ALCL risk of 1:16,500 implants is reported, but this estimate seems to be calculated simply by dividing the number of BIA-ALCL cases by the number of breast implants and tissue expanders sold in the UK. Because there is no specific time frame, this cannot be considered an incidence but more likely a "prevalence." Therefore this is neither an incidence nor a risk and is completely dependent on the accurate reporting of disease within that population.

Accurate numbers of BIA-ALCL cases (the numerator) optimally come from either mandatory/opt-out national breast implant registries or long-term post-market approval studies. Consider, Medicines and Healthcare products Regulatory Agency and Health Canada report BIA-ALCL prevalence based on calculations per implant sold within that country, which is potentially biased by several facts, such as

- in the UK, not all brands of implant are sold;
- not all implants sold in the UK have been implanted into patients;
- an unknown number of implants sold have been explanted;
- an unknown number of implants sold have been replaced;
- not all implants sold in the UK have been implanted into British patients,
- and conversely some patients have been implanted abroad;
- not considering contralateral symmetrization, 25% of the population at risk (post-oncologic) may undergo a single implant positioning with a prevalence in UK of 1:16,550, while the remaining 75% (aesthetic) usually receive 2 implants, with a twofold prevalence (not a risk) of 1:8250. Moreover, we know that in 97% of cases, BIA-ALCL occurs on only in 1 of the 2 implanted devices.

For an appropriate case tracking, the health care system of the country where diagnoses are issued should consider all patients, independent of where the surgery was performed. Due to possible underestimation, we recommend calculating occurrence per active population at risk, as calculated by de Boer et al, Doren et al, and Santanelli di Pompeo et al, because the per-sold-implant calculation does not appropriately reflect the magnitude of the BIA-ALCL impact on patients and consequently on health care systems.[6–8]

Finally, Mr Mercer comments that "We, therefore, cannot assume that any implant is safe, perhaps including smooth implants, where the reported incidence of Breast Implant Illness (BII) is greater with smooth implants." Although BII

is beyond the scope from our paper, there exists no formalized risk calculation of BII in the literature, and therefore any attempt to stratify risk across implant type, fill, surface characteristic, or manufacturer is not based on data or outcomes. Therefore, we urge caution and patience before making speculative or sweeping generalizations in particular to BII, which is only recently recognized as an entity by government authorities and patient advocacy groups. To be clear, no BIA-ALCL cases have been reported in case reports, case series, or registries worldwide with a clinical history of only smooth-surface devices.[9,10] Mr Mercer raises an industry-promoted misconception about BIA-ALCL cases that "clustering" represents surgeons with poor technique, which gives patients lymphoma. We acknowledge clustering of cases in the United States, Australia and New Zealand, United Kingdom, Netherlands, France, Italy, and Poland with widespread geographic variation in global risk estimates. Importantly, these differences in clustering and subsequent risk profiles are the result of increased awareness, improved surveillance, access to care, and long-term follow-up rather than epidemiologic, technique, or pathologic phenomena.[11] Attempts to link surgeon technique to ALCL has no credible data support, and more importantly surgeon-shaming threatens to undermine the reporting of future ALCL cases required to build robust outcomes databases for scientific investigation. In summary, we appreciate Dr Mercer's close reading of our manuscript while fostering healthy academic discourse. Let us all agree to improve open and transparent BIA-ALCL research.

Disclosures

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