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# Neoadjuvant Immunotherapy and De-Escalation of Surgery in Locally Advanced Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL)

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#### hstract

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare form of non-Hodgkin T cell lymphoma diagnosed in patients with a history of breast implants. Most patients develop a periprosthetic effusion at early stages of disease while less common presentations include a palpable mass, severe capsular contracture, lymphadenopathy, or cutaneous erythema. Due to the complex nature of this disease, a multidisciplinary approach is necessary for optimal management, particularly in locally advanced disease or inoperable patients. We present the successful use of neoadjuvant therapeutic protocols in two cases of locally advanced BIA-ALCL. The first case, a 52-year-old patient with a left breast mass-like stage III disease who underwent combined targeted immunotherapy and chemotherapy (BV-CHP). Following a complete radiological and metabolic response, the patient underwent bilateral implant removal, right total intact capsulectomy, left en bloc capsulectomy and skin resection from the left inframammary fold in continuity with the capsule. The second case, a 65-year-old patient with a right breast swelling and mass-like stage IIA disease who received targeted immunotherapy, Brentuximab vedotin (BV). Following a complete metabolic response, she underwent bilateral implant removal and en bloc capsulectomy. A literature review and the reported cases suggest the effectiveness of targeted immunotherapy as monotherapy or in combination with chemotherapy in locally advanced BIA-ALCL in disease downstaging, surgical de-escalation, reduction of significant post-operative complications and an acceptable tolerance profile. Although surgery is an essential part of treatment, timing and type of intervention should be carefully planned, especially when primary, radical resection is uncertain.

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Neoadjuvant Immunotherapy and De-Escalation of Surgery in Locally Advanced Breast Implant-Associated

Anaplastic Large Cell Lymphoma (BIA-ALCL)

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#### INTRODUCTION

Anaplastic large cell lymphomas (ALCL) are a group of mature CD30+ T-cell lymphomas characterized by the proliferation of large and pleomorphic cells with similar immunophenotypic features but a variety of clinical characteristics. ALCLs are divided into 4 distinct subtypes: Anaplastic Lymphoma Kinase (ALK) positive, ALKnegative, primary cutaneous (pALCL), and Breast-Implant associated (BIA-ALCL). BIA-ALCL is an uncommon CD30+ and ALK- lymphoma typically occurring in women 8-10 years following breast implantation for breast augmentation or reconstruction.<sup>2</sup> In 1997, Keech and Creech reported the first case of ALCL in proximity to a textured saline-filled breast implant 6 years following bilateral breast augmentation.<sup>3</sup> As of January 2011, the FDA declared a possible correlation between breast implants and ALCL and in May 2016 the WHO recognized BIA-ALCL first as a provisional and then in 2022 as a definitive T-cell lymphoma entity. The current lifetime risk of BIA-ALCL, according to the American Society of Plastic Surgeons (ASPS), is estimated to be 1:2,207-1:86,029 for patients with textured implants.<sup>4</sup> Although the molecular pathogenesis is poorly established, numerous hypotheses have been suggested including genetic predisposition, subclinical bacterial infection, and a chronic inflammatory response following long-term immune stimulation to breast implants. <sup>5</sup> The most common clinical presentation is a late onset of a periprosthetic effusion and may be associated with breast distortion, swelling and asymmetry. Less common presentations may be a palpable mass, severe capsular contracture, lymphadenopathy, or cutaneous erythema. Due to the complex nature of this disease, a multidisciplinary approach involving medical oncologists, hematopathologists, surgical oncologists, and plastic surgeons is recommended for the management of patients with BIA-ALCL, particularly in case of advanced disease or inoperable patients, with the aim of providing the best diagnostic work-up, treatment and surveillance strategies. The current National Comprehensive Cancer Network (NCCN) consensus guidelines indicate bilateral breast implant removal with en bloc surgical resection of the surrounding capsule in patients with diseased limited to the capsule.<sup>7</sup> According to FDA

regulations, the prophylactic explantation of textured implants is not recommended in asymptomatic BIA-ALCL patients; nevertheless, patients may discuss the benefits and drawback of implant removal with their health care providers to make an informed decision about their health. <sup>8</sup>

The use of adjuvant chemotherapy or radiation therapy is considered for patients with local residual disease, positive margins, or surgically unresectable disease. Systemic therapies include BV, an anti-CD30 monoclonal antibody, anthracycline-based chemotherapeutic regimen CHOP (cyclophosphamide, adriamycin, vincristine, and prednisone) or CHOEP (cyclophosphamide, adriamycin, vincristine, etoposide and prednisone), or a combination of both are reserved for cases of residual or disseminated disease (Stage II-IV). There may, however, be a role for neoadjuvant therapy in advanced cases of BIA-ALCL. Italian Ministry of Health guidelines on the diagnosis and treatment of BIA-ALCL, recently published in November 2022, indicate the use of systemic chemotherapy, BV or a combination of both in the neoadjuvant setting in cases of stage IV disease. 10 Until now, few cases in literature have reported the use of neoadjuvant therapy for the treatment of locally advanced or disseminated disease. We present two clinical cases reporting the successful use of neoadjuvant therapeutic protocols in locally advanced BIA-ALCL. The first case reports a 52-year-old patient with a left breast mass-like stage III disease who underwent combined targeted immunotherapy and chemotherapy (BV-CHP). Following a complete radiological and metabolic response, the patient underwent bilateral implant removal, right total intact capsulectomy, left en bloc capsulectomy and skin resection from the left inframammary fold in continuity with the capsule. The second case reports a 65-year-old patient with a right breast swelling and mass-like stage IIA disease who received targeted immunotherapy with BV. Following a complete metabolic response and significant reduction in mass size, she underwent bilateral implant removal and en bloc capsulectomy. Both patients provided written informed consent for the publication and use of their images.

#### CASE REPORT 1

A-52-year-old woman underwent bilateral subglandular breast augmentation in 1998 with macrotextured silicone breast implants (Silimed 220cc). She did not undergo breast implant replacement since primary implantation. Physical examination showed bilateral inframammary fold scars consistent with her previous breast surgery. The left breast was slightly larger than the contralateral and a palpable breast mass in the lower-outer quadrant was felt fixed to the implant capsule. Previous surgical procedures included rhinoseptoplasty in 1989 and removal of a fibroadenoma of the left breast in 2006. Her past medical history included multiple thyroid nodules, sideropenic

anemia, and hiatal hernia. Daily pharmacological therapy included pantoprazole, levothyroxine, and sulfamethoxazole and trimethoprim for pneumocystis jirovecii pneumonia prophylaxis during the 4 months of chemotherapy administration. Our patient developed left breast heaviness and mastalgia as of December 2021. Breast and axillary cavity ultrasound as well as 3D mammography failed to document pathological findings. By February 2022, the patient noticed a palpable breast mass in the lower-outer quadrant of the left breast followed by cutaneous erythema of the lateral aspect of the left inframammary fold in March 2022 (Figure 1). She underwent breast MRI which did not show significant pathological findings. By June 2022, after failure of clinical improvement following an antibiotic and anti-inflammatory treatment, a second breast MRI noted multiple radial breast implant folds bilaterally and an area of altered mass-type enhancement approximately 5.0 cm x 4.0 cm x 4.2 cm located in the lower-outer quadrant of the left breast and appeared fixed to the lateral aspect of the left breast implant (Figure 2). No focal or diffuse areas with altered enhancement were noted in the right breast parenchyma. Multiple abnormal lymph nodes were observed in the left axilla, the largest of which measured 1.8 cm x 1.2 cm, while no lymph nodal abnormalities were present in the right axilla. Ultrasound-guided Tru-cut needle biopsy of the left periprosthetic mass documented morphologic and immunohistochemical features (CD30+, ALK-, CD3-, CD5-, PAX5-, LMP1, cytokeratin AE1/AE3-, S100-) compatible with a BIA-ALCL (Figure 3). Core biopsy from the left axillary lymph node documented fragments of a lymph node structure with rare CD30+ large cells suspicious but not conclusive for lymph node involvement of BIA-ALCL. One week later, whole body PET-CT scan documented a 5 x 4 x 2 cm metabolically active mass on the posterolateral aspect of the left breast, multiple active lymph nodes in the ipsilateral axilla, left internal mammary lymph node chain and left subpectoral lymph nodes (stage III, T4N2M0). Given the extent of surgery necessary to achieve complete excision of pathological tissue, neoadjuvant chemotherapy combined with targeted therapy was administered. From July to October 2022, she underwent a total of 6 cycles of neoadjuvant chemotherapy (doxorubicin, cyclophosphamide and prednisone) of which the 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> cycles were combined with BV. Immunotherapy was interrupted following the 4<sup>th</sup> cycle due to peripheral neuropathy. Following completion of 4 cycles of chemotherapy in September 2022, total body CT scan no longer documented pathological enhancement of the left breast periprosthetic mass as well as a significant reduction in size of the pathological axillary, subpectoral and internal mammary chain lymph nodes. After completion of 6 cycles of neoadjuvant chemotherapy, total body PET-CT scan in November 2022 showed a complete metabolic response and on December 1st, 2022, breast MRI demonstrated a total T response and a partial N response (Figure 4). On December 12th, 2022, the patient underwent bilateral implant removal, right total intact capsulectomy, left en bloc capsulectomy with a 6 cm x 0.7 cm cutaneous resection from the left inframammary

fold corresponding to the site of the previous erythema (Figure 5). Initial biopsy of axillary lymph node showed suspicious features, but not conclusive for lymph node involvement. Given the excellent response to neoadjuvant therapy (complete metabolic response on PET-CT), it was deemed acceptable to avoid the surgery to axilla and the risk of lymphedema. Close follow-up and interval ultrasound scans were offered, and alternative options were discussed with the patient. Pathological examination and immunohistochemistry of the breast capsule and skin resection showed no signs of residual disease (Figure 6). In view of an excellent pre-operative radiological response and absence of residual disease in the surgical specimen, no adjuvant radiotherapy or targeted therapy was recommended. Thus far, she has had a complete response and an unremarkable post-operative recovery without complications. (Figure 7). The patient has shown no evidence of disease reoccurrence after 12 months following surgery.

#### CASE REPORT 2

A 65-year-old woman presented with progressive right breast swelling and palpable mass in upper-inner quadrant (figure 8). Nine years earlier, she underwent bilateral mastopexy augmentation with silicone macrotextured implants, but denied previous breast problems. She had a history of chronic obstructive pulmonary disease, rosacea and pulmonary tuberculosis in childhood. She underwent hysterectomy and two Caesarean sections. Her regular medications included Formoterol and Salbutamol inhalers and Lymecycline. She was a long-term smoker and had a family history of cervical cancer, but no history of breast cancer or lymphoproliferative disease. Her physical examination revealed inverted-T incisions (Wise pattern) and swollen right breast with palpable 5 cm mass in parasternal area, which was firm and fixed to sternocostal junction and 3<sup>rd</sup> rib. Breast ultrasound confirmed large seroma, which was aspirated, and cytological features were suspicious, but inconclusive for BIA-ALCL. Subsequent MRI and CT revealed a 5x4x3 cm mass infiltrating underlying pectoralis muscle. The diagnosis of BIA-ALCL was confirmed on core biopsy from the chest wall mass, which showed large, atypical cells with strong expression of CD30, some staining with EMA and CD45, but negative for CD5, CD20, CD79a and epithelial markers. Further immunochemistry tests were positive for CD4, but negative for ALK1, PAX5, CD2, CD7 and CD8. A PET-CT confirmed FDG-avid (SUV max 7.2) mass infiltrating beyond the implant capsule (stage IIA – T4N0M0). The anticipated extent of surgical procedure at this stage involved excision of the mass en-bloc with capsulectomy and partial resection of ribs and sternum. In view of significant morbidity and high risk of surgery, the neoadjuvant therapy with BV was recommended to downstage the disease and ensure radical excision. The interval PET-CT after first 4 cycles of BV showed a Deauville 1 metabolic response with residual mass, therefore

further 4 cycles of BV were administered. Subsequent PET-CT confirmed complete metabolic response and significant reduction in size of the mass. Surgical procedure was performed at this point, involving bilateral enbloc capsulectomy and implants removal (Allergan CUI 410cc). Small peri-implant seroma was also aspirated intraoperatively. At surgery there was no evidence of pectoralis muscle infiltration with clear dissection plane around capsule, however multiple muscle biopsies were performed for histology. The surgical specimen, chest wall biopsies and immunochemistry tests of seroma did not reveal any residual disease. In view of complete pathological response, no further immunotherapy or radiotherapy was recommended. The patient made uneventful postoperative recovery; however she had myocardial infarction 2 months after surgery, which required coronary stenting and anticoagulation (Figure 9). The PET-CT performed 8 months after surgery confirmed complete metabolic remission as previously reported.<sup>22</sup> She is now 4 years post-surgery and remains well with no evidence of recurrence (figure 10).

#### **DISCUSSION**

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is an uncommon and emerging form of Peripheral T-cell lymphoma diagnosed in patients with a history of textured breast implants. Etiology of this condition is still poorly understood, however current evidence indicates possible transformation and clonal expansion of deregulated immune cells as a response to chronic exposure to inflammatory cytokines in a genetically susceptible individual.<sup>8, 11</sup> The majority of patients present at early stages of the disease with periimplant effusion and breast swelling. In the systematic review by Lebenfinger et al, 66% of patients were seen initially with seroma, 8% with a mass, 7% with mass and seroma, while 18% with other symptoms such as capsular contracture, axillary lymphadenopathy and skin lesions. 12 One of our cases presented with skin rush, mass and lymphadenopathy whereas the other with mass and seroma. Surgical resection remains the standard of care for patients with BIA-ALCL and includes explantation, total intact capsulectomy and en bloc resection of all associated masses and involved lymph nodes. The technical aspects of this procedure were described by Tevis et al <sup>13</sup>, who recommended en bloc resection of breast implants with surrounding capsules, utilizing existing scars. Some patients may require skin excision in case of local involvement or close proximity of the mass, which may be incorporated in planned Wise-pattern mastopexy to reduce redundant skin after explantation but may occasionally require separate incision. Tumescence of posterior part of the capsule during total capsulectomy can be useful in case of subpectoral implants, where the capsule is usually densely adherent to the periosteum and ribs and inadvertent injury can lead to pneumothorax. 13,14 Every effort should be made to remove entire capsule and avoid

spillage of malignant effusion into the cavity. To mitigate this risk, an ultrasound-guided aspiration of the seroma just before surgery may be considered. The oncological radicality of surgery is essential for successful long-term outcome as evidenced in several publications.8,14,24 Clemens et al reported improved overall survival (OS) (p<0.001) and event-free survival (EFS) in patients treated with complete surgical excision compared to other therapeutic interventions. Only 5% of patients treated with complete excision had further events, which underlines importance of achieving clear margins, regardless of adjuvant therapy regimens. However, the stage of BIA-ALCL at diagnosis had significant effect on event-free survival. The rate of events was 2.6-fold higher for stage II and was 2.7-fold higher for stage III disease compared to stage I disease in this case series. 15 Moreover, the size of the tumor and local invasion adversely affect the prognosis, as indicated by event rate of 14.3% for stage T4 compared to 0% for stages T1/T2, even if complete resection was achieved. 8,15 In a recent systematic review including 178 BIA-ALCL cases, Naga et al found that presentation with mass as opposed to a seroma was significantly associated with recurrence and mortality (odds ratio of 19.4). 16 Management of locally advanced or surgically unresectable BIA-ALCL poses significant challenge and requires a multidisciplinary approach. Early experience with use of systemic chemotherapy and regimens including cyclophosphamide, doxorubicin, vincristine and prednisolone, showed variable response. In a study of 87 BIA-ALCL cases published by Clemens et al<sup>15</sup>, over 50% patients received chemotherapy and approximately one third of these patients experienced progression of the disease or did not achieve response. Eleven patients were treated with systemic chemotherapy and never underwent complete surgical excision, and six of these patients died as a result of the disease. The authors concluded that systemic chemotherapy alone was insufficient to control the disease. Retrospective review of 39 patients with locally advanced BIA-ALCL (stage IIB-IV) by Collins et al showed much lower rates of definitive surgery (59%), higher mortality (20.8%) and lower rates of complete remission (71.8%) in this group compared to early-stage BIA-ALCL. Very rapid disease progression (hyperprogression) was observed in five patients (12.8%) who had only limited surgery, indicating possible detrimental effect of incomplete BIA-ALCL excision. 16 Poor outcomes of locally advanced BIA-ALCL prompted interest in neoadjuvant systemic therapies in order to downstage the disease and enable complete surgical excision. Recently published National Cancer Centre Network (NCCN) guidelines<sup>7</sup> recommend adjuvant chemotherapy in advanced BIA-ALCL (stage II-IV) with either CHOP, CHOEP or CHP + BV regimens. Efficacy of immunochemotherapy in treatment of CD30+ peripheral T-cell lymphomas was also demonstrated in ECHELON II trial, which exhibited statistically superior progression-free survival (PFS) and overall survival (OS) compared to standard anthracycline-based chemotherapy.<sup>18</sup> Single-agent immunotherapy with BV as CD30 targeting antibody-drug conjugate is also an

drug conjugate composed of an anti-CD30 chimeric antibody conjugated to monomethyl auristatin E, the microtubule-disrupting agent. The primary mechanism of action is a targeted delivery of monomethyl auristatin E to CD30-expressing tumor cells. Additional proposed mechanisms that may contribute to the clinical activity of brentuximab vedotin include antibody-dependent cellular phagocytosis and immunogenic cell death. However, the data on treatment of BIA-ALCL in neoadjuvant settings is limited and based mainly on case reports (Table 1). Therapeutic decisions are extrapolated from experience with systemic and refractory ALCL, due to lack of prospective studies and rarity of BIA-ALCL. Coombs et al. reported on two cases of locally advanced BIA-ALCL (stage III) treated with neoadjuvant therapy (CHOEP and BV) with excellent clinical and pathological response. Both patients presented with large tumors and underwent extensive surgical procedures, including chest wall reconstructions, due to hypermetabolic activity on interval PET-CT and concerns about possible residual disease, however final results confirmed complete pathological response.<sup>24</sup> Stack et al.<sup>20</sup> described complete clinical and radiological response to monotherapy with BV in a case of unresectable ALCL. The patient received also palliative radiation therapy and remained in remission at 20 months after therapy. Combination of BV and vincristine was successfully used in neoadjuvant settings by Caputo et al<sup>23</sup> in case of massive, fungating mass-like BIA-ALCL, infiltrating pectoralis muscle (stage IIA). The patient underwent radical excision followed by adjuvant BV and COMP chemotherapy and remained in complete remission for 12 months. Excellent response to neoadjuvant chemotherapy (CHOEP) in stage IV BIA-ALCL was also reported by Thibodeau et al.21 Despite significant complications (pulmonary embolism and pancytopenia), the patient completed 5 cycles of CHOEP with complete resolution of hypermetabolic areas on PET-CT and no residual disease in surgical specimen. All above case reports are consistent with our experience with neoadjuvant therapy in two cases of advanced BIA-ALCL. The limited sample size of this study and the paucity of literature regarding neoadjuvant therapeutic regimens underline the need for larger-scale studies to validate current findings. Although the results of the present case reports as well as those reported in literature are promising, surgical management remains the standard care of locally advanced BIA-ALCL and should always be performed in accordance with the most recent guidelines in the best interest of the patient. Similarly to the patients reported in this study, suitable candidates for neoadjuvant therapeutic regimens include locally-advanced cases of BIA-ALCL with surgically unresectable disease due to extension in the chest wall, patients with lymph node involvement, and those suitable to undergo chemoimmunotherapy or immunotherapy alone. The potential benefits of administering neoadjuvant therapeutic

regimens may promote surgical de-escalation, in terms of a reduction in the extent of surgical intervention and

interesting therapeutic option, particularly for non-responders to standard chemotherapy. 19,20 BV is an antibody-

change of its timing. It is, however, important to underline that neoadjuvant therapies do not indicate avoidance surgery and must be performed in accordance with current guidelines. Therefore, tumor downstaging signifies a reduction in surgical extent as well as potential side effects associated to surgery.

In order to assess a long-term outcomes of immunotherapy in locally-advanced BIA-ALCL, the patients should be closely monitored according to NCCN guidelines: clinical and radiological follow-up very 3-6 months for the first 2 years and subsequently annual review until 5 years post therapy. The interval PET-CT provided important information about response and determined the duration of treatment and timing of surgical intervention. Complete surgical excision and complete pathological response were achieved in both our patients after PET-CT confirmed resolution of metabolically active disease. Both patients received BV, which proved to be very effective as single-agent or combined therapy. Several authors reported that BV is a potential alternative to cytotoxic chemotherapy and is characterized by excellent response rates and favorable tolerability profile.20,23,24

#### CONCLUSION

The optimal management of patient with advanced BIA-ALCL and possible chest wall invasion remains unclear. Although surgery is an essential part of treatment, the extent and timing of surgical intervention should be carefully planned and warrants multidisciplinary discussion, especially when primary, radical resection is uncertain. We believe that in such cases, neoadjuvant therapy should be strongly considered. Monitoring of the response to neoadjuvant therapy is essential and may necessitate modification of treatment plan.

Our experience supports the concept of neoadjuvant therapy in management of locally advanced BIA-ALCL, which can offer downstaging of the disease, de-escalation of surgery and reducing the risk of significant complications. Based on emerging evidence, targeted immunotherapy with BV as monotherapy or in combination with chemotherapy, seems to be a preferred induction therapy in such cases, offering good response rates and acceptable tolerance profile. Further genomic research and clinical data from larger, controlled studies may provide further evidence on patients selection and optimal management of locally advanced BIA-ALCL.

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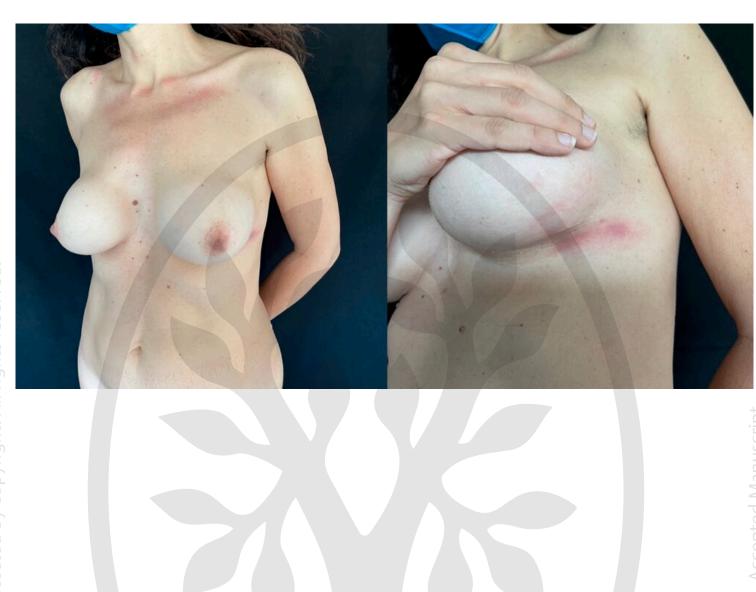
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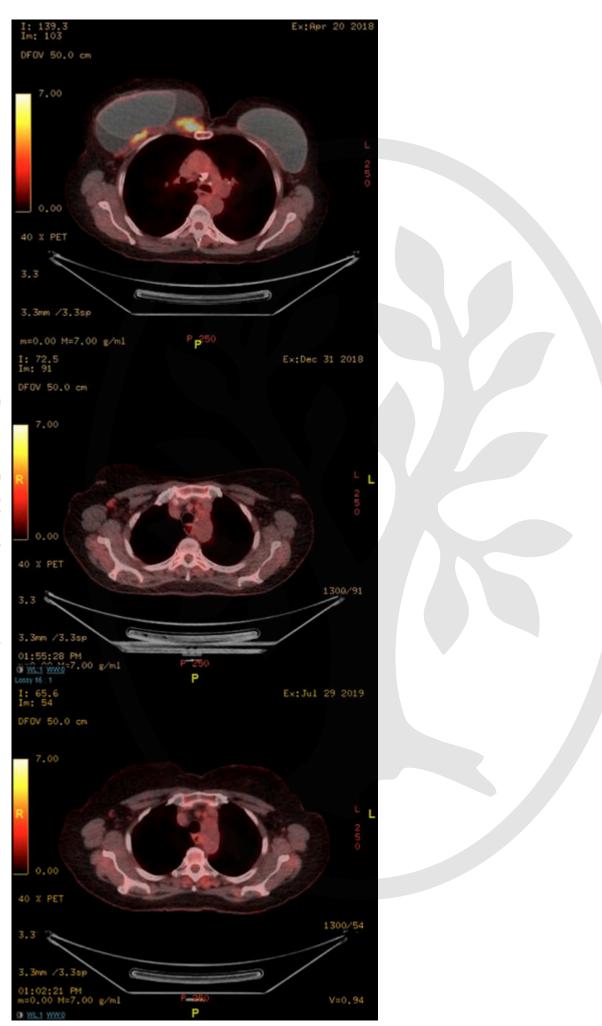
Table 1. Literature Review on neoadjuvant therapy in locally advanced BIA-ALCL.

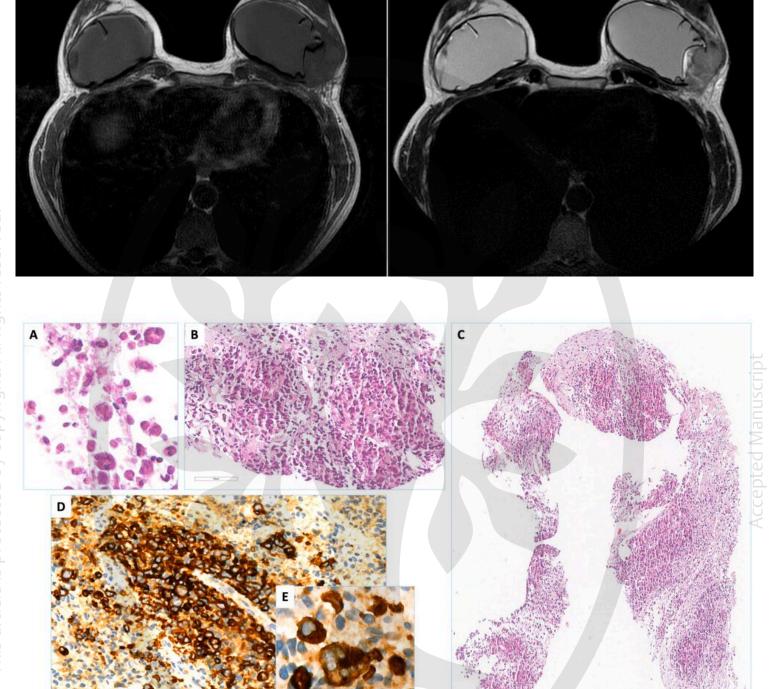
Author	Yea r	Stag e	Neoadjuvan t therapy	Surgery	Patholo gical	Adjuvant therapy	Outcome	
	-		culcrupy		respons	cherupy		
					e			
Thibodea u et al. (21)	2019	IV	CHOEP 5 cycles	Bilateral explantation + en bloc capsulectomies. Wire-guided excision of left axillary and lateral breast masses.	Complet	No	Complete remission at 8 months post therapy	
Allchin et	2020	IIA	BV	Bilateral	Complet	No	Complete	
al. (22)			8 cycles	explantation + right en bloc capsulectomy + chest wall biopsies.	e		remission at 18 months post-surgery	
Caputo et al. (23)	2021	IIA	BV + Vincristine	Excision of fungating, necrotic tumor en bloc with implant and pectoralis muscle.  Dermal substitute for coverage and subsequent skin grafting.	Partial / Complet e excision + skin grafting	Yes - BV + COMP 5 cycles	Complete remission for 12 months/ Died of cardiovascula r disease	

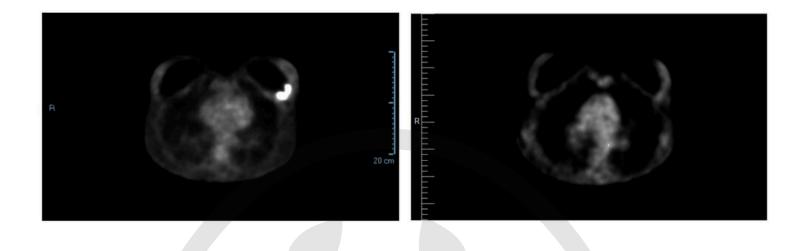
C 1	2021	TTT	CHOED	T 1		N.T.	C 1.
Coombs et al. (24)	2021	III	CHOEP 4 cycles	Initial open biopsy for diagnosis.	Complet e	No	Complete remission at 4
				Definitive			years post-
				procedure after			surgery
				neoadjuvant therapy			
				<ul> <li>left anterior</li> </ul>			
				capsulectomy,			
				partial breast			
				excision, anterior			
				chest wall resection			
				(including 3 <sup>rd</sup> -5 <sup>th</sup>			
				rib) +			
				reconstruction with			
				Prolene mesh and			
				methacrylate.			
		III	BV	Incisional biopsy of	Complet	No	Complete
			8 cycles	right chest wall	e		remission at 3
	/			mass. Definitive			years post-
				surgery after			surgery
				completion of			
				neoadjuvant			
				immunotherapy –			
				chest wall mass			
				resection (including			
				$3^{\text{rd}} - 5^{\text{th}} \text{ rib}) +$			
				reconstruction with			
			V	pedicled latissimus			
				dorsi flap + Prolene			
				mesh and			
				methacrylate.			
				Postoperative hematoma and			
				1			
Premji et	2022	III	CHP + BV	requiring drainage.  Resection of right	Partial /	Yes –	Complete
al. (25)	2022	111	6 cycles	chest wall tumor	Complet	Radiotherap	remission at 1
ai. (23)			o cycles	(including 3 <sup>rd</sup> – 5 <sup>th</sup>	e	_	year post
				rib), partial	excision	y Auto-SCT	auto-SCT
				sternectomy,	+ chest	BV (12	uuto oci
				thymectomy, en	wall	cycles)	
				bloc removal of the	reconstr		
				implant +	uction		
				reconstruction with			
				mesh/bone cement			
				and serratus			
				advancement flap.			[
				Postoperative chest			
				wall incision			
				necrosis requiring			
				debridement,			
				washout and tissue			
				transfer.			

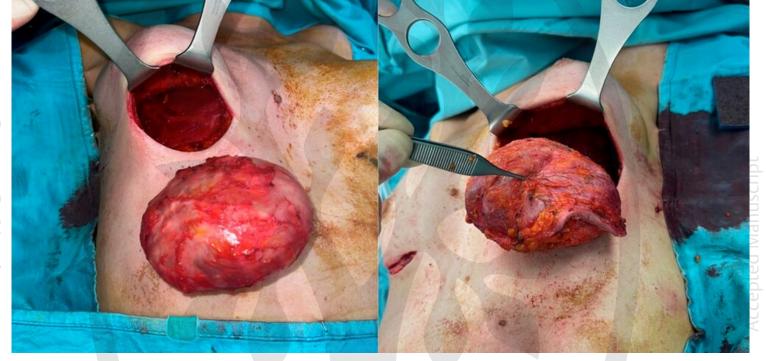
Abbreviations: Auto-SCT, autologous stem cells transplant; CHOEP, cyclophosphamide, doxorubicin, vincristine, etoposide, prednisolone; CHP, cyclophosphamide, doxorubicin, prednisone; COMP, cyclophosphamide, liposomal doxorubicin, vincristine, prednisone, rituximab.

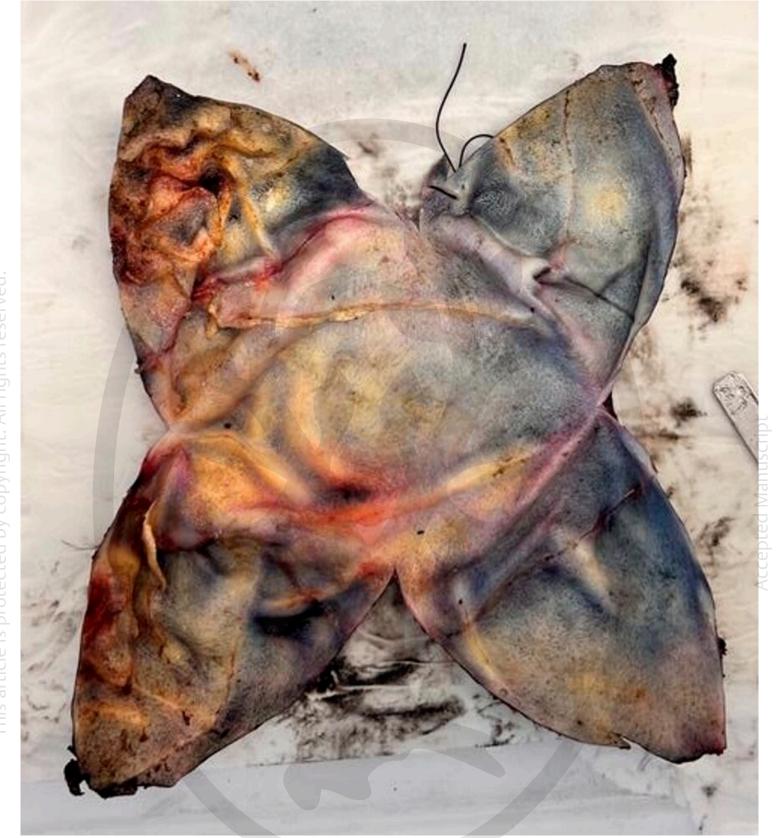




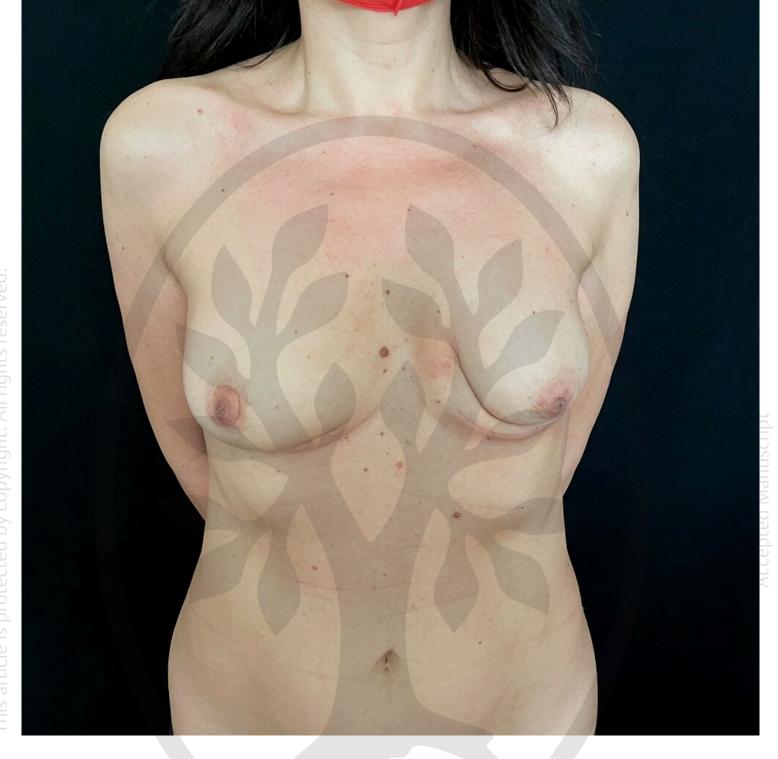








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