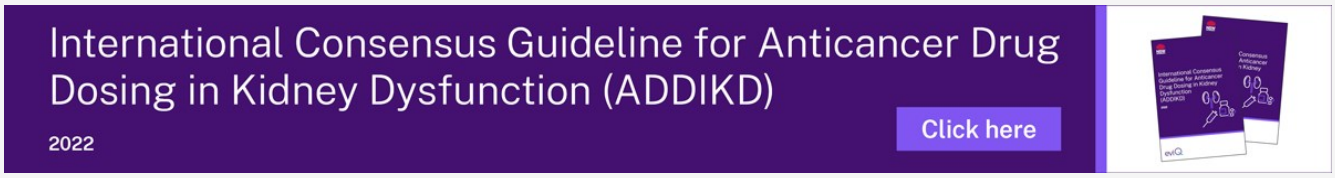
Lymphoma brentuximab vedotin

ID: 1665 v.5 **Endorsed**

Patients with lymphoma should be considered for inclusion into clinical trials. Link to ALLG website, ANZCTR website and Lymphoma Australia website.

Some indications in this protocol are based on limited evidence; please refer to the individual evidence sections for more information.

The anticancer drug(s) in this protocol may have been included in the ADDIKD guideline. Dose recommendations in kidney dysfunction have yet to be updated to align with the ADDIKD guideline. Recommendations will be updated once the individual protocol has been evaluated by the reference committee. For further information refer to the ADDIKD guideline. To assist with calculations, use the eviQ Estimated Glomerular Filtration Rate (eGFR) calculator.



Treatment schedule - Overview

Cycle 1 to 16

Drug	Dose	Route	Day
Brentuximab vedotin	1.8 mg/kg (Cap dose at 180 mg)	IV infusion	1

Frequency: 21 days

Cycles: 16 or until disease progression or unacceptable toxicity

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Drug status: **Brentuximab vedotin** (PBS authority)

Cost: ~ $12,630 per cycle

Treatment schedule - Detail

The supportive therapies (e.g. antiemetics, premedications, etc.), infusion times, diluents, volumes and routes of administration, if included, are listed as defaults. They may vary between institutions and can be substituted to reflect individual institutional policy.

*Antiemetics if included in the treatment schedule are based upon recommendations from national and international guidelines. These are **defaults only** and may be substituted to reflect individual institutional policy. Select here for recommended doses of alternative antiemetics.*

Cycle 1 to 16

Day 1		
Metoclopramide	10 mg (PO)	one tablet when necessary (maximum of 30 mg/24 hours, up to 5 days)
Brentuximab vedotin	1.8 mg/kg (IV infusion) (Cap dose at 180 mg)	in 150 mL sodium chloride 0.9% over 30 minutes

Frequency: 21 days

Cycles: 16 or until disease progression or unacceptable toxicity

Indications and patient population - Relapsed or refractory Hodgkin lymphoma

- Relapsed or refractory CD30+ Hodgkin lymphoma either following autologous stem cell transplant (ASCT) OR following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option.

Indications and patient population - High risk Hodgkin lymphoma post ASCT

- Patients with CD30+ Hodgkin lymphoma at higher risk of relapse or progression following ASCT.

Indications and patient population - Anaplastic large cell lymphoma

- Relapsed or refractory CD30+ systemic anaplastic large cell lymphoma in patients who have undergone appropriate prior front-line curative chemotherapy.

Indications and patient population - Cutaneous T-cell lymphoma

- Relapsed or refractory CD30+ cutaneous T-cell lymphoma (including mycoses fungoides, Sezary syndrome or primary cutaneous anaplastic large cell lymphoma).

Clinical information

Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Hypersensitivity/infusion related reaction	High risk with brentuximab vedotin. Patients who have experienced a prior infusion-related reaction should be given premedication (e.g. paracetamol, an antihistamine and a corticosteroid) for subsequent infusions. Read more about Hypersensitivity reaction
Emetogenicity LOW	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary. Read more about preventing anti-cancer therapy induced nausea and vomiting
Progressive multifocal leukoencephalopathy	Reactivation of the John Cunningham virus (JCV) in patients who have received brentuximab vedotin after receiving multiple chemotherapy regimens previously has resulted in progressive multifocal leukoencephalopathy (PML), a rare but potentially fatal opportunistic viral infection of the brain. Patients must be monitored for any new or worsening neurological symptoms. Brentuximab vedotin treatment may have to be withheld if PML is suspected or discontinued if diagnosis is confirmed. Read more about progressive multifocal leukoencephalopathy and the Therapeutic Goods Administration Medicines Safety update on progressive multifocal leukoencephalopathy from the Australian Government, Department of Health.

Pancreatitis	Pancreatitis is uncommon but has been reported. Unexplained abdominal pain should be promptly investigated to include measurement of serum amylase and lipase.
Pulmonary toxicity	Brentuximab vedotin has been associated with pulmonary toxicity. Patients should be monitored for pulmonary symptoms (e.g. cough, dyspnoea). If new or worsening pulmonary symptoms occur, a prompt diagnostic evaluation should be performed and patients should be treated appropriately. Read more about pulmonary toxicity associated with anti-cancer drugs.
Peripheral neuropathy	Assess prior to each treatment. If a patient experiences grade 2 or greater peripheral neuropathy, a dose reduction, delay, or omission of treatment may be required; review by medical officer before commencing treatment. Read more about peripheral neuropathy Link to chemotherapy-induced peripheral neuropathy screening tool
Skin toxicity	Severe cutaneous adverse reactions (SCARs) have been observed in patients receiving brentuximab vedotin. This includes rare cases of drug reaction with eosinophilia and systemic symptoms (DRESS) and sometimes fatal cases of Steven-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Monitor for rash, erythema and pruritus and discontinue treatment where clinically indicated.
Tumour lysis risk	Patients are at high risk of developing tumour lysis syndrome, prophylaxis is recommended. Read more about the prevention and management of tumour lysis syndrome.
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients
Antifungal prophylaxis	Read more about antifungal prophylaxis drugs and doses.
Antiviral prophylaxis	Read more about antiviral prophylaxis drugs and doses
Growth factor support	G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk. Access the PBS website
Irradiated blood components	The use of irradiated of blood components is recommended for patients receiving this treatment. Read more about the indications for the use of irradiated blood components
Blood tests	FBC, EUC, eGFR, LFTs and LDH at baseline, and prior to each cycle and as clinically indicated.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy
Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.
Fertility, pregnancy and lactation	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients. Read more about the effect of cancer treatment on fertility

Dose modifications

Evidence for dose modifications is limited, and the recommendations made on eviQ are intended as a guide only. They are generally conservative with an emphasis on safety. Any dose modification should be based on clinical judgement, and the individual patient's situation including but not limited to treatment intent (curative vs palliative), the anti-cancer regimen (single versus combination therapy versus chemotherapy versus immunotherapy), biology of the cancer (site, size, mutations, metastases), other treatment related side effects, additional co-morbidities, performance status and patient preferences.Suggested dose modifications are based on clinical trial findings, product information, published guidelines and reference committee consensus . The dose reduction applies to each individual dose and not to the total number of days or duration of treatment cycle unless stated otherwise. Non-haematological gradings are based on Common Terminology Criteria for Adverse Events (CTCAE) unless otherwise specified. Renal and hepatic dose modifications have been standardised where possible. For more information see dosing considerations & disclaimer .

The dose recommendations in kidney dysfunction (i.e.renal impairment) displayed may not reflect those in the ADDIKD guideline and have been included for historical reference only. Recommendations will be updated once the individual protocol has been evaluated by the reference committee, with this version of the protocol then being archived. Clinicians are expected to refer to the ADDIKD guideline prior to prescribing in kidney dysfunction.
International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD).

Haematological toxicity	
ANC x 10^9/L (pre-treatment blood test)	
less than 1.0	Delay treatment until recovery and resume brentuximab vedotin at the same dose (and consider adding G-CSF for subsequent cycles)

Renal impairment	
Creatinine clearance (mL/min)	
less than 30	Patients with active disease and no other treatment options, consider use with caution after evaluating benefit-risk at a starting dose of 1.2 mg/kg

Hepatic impairment	
Hepatic dysfunction	
Use with caution in patients with hepatic impairment, due to potential increased exposure to MMAE (conjugated anti-microtubule agent) and increased toxicity.	
Mild (Child-Pugh A)	Recommend reducing starting dose to 1.2 mg/kg
Moderate (Child-Pugh B) to Severe (Child-Pugh C)	Patients with active disease and no other treatment options, consider use with caution after evaluating benefit-risk at a starting dose of 1.2 mg/kg

Peripheral neuropathy	
Grade 2 or Grade 3	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose of brentuximab vedotin to 1.2 mg/kg for subsequent cycles.
Grade 4	Omit brentuximab vedotin

Dermatological reactions	
Severe cutaneous adverse reactions (SCARs) e.g. Steven-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS)	Discontinue brentuximab vedotin

Interactions

Drug interactions in eviQ protocols are under review and being updated to align with current literature. Further site-wide updates and changes will occur in due course. References & Disclaimer

The drug interactions shown below are not an exhaustive list. For a more comprehensive list and for detailed information on specific drug interactions and clinical management, please refer to the specific drug product information and the following key resources:

- *MIMS - interactions tab (includes link to a CYP-450 table) (login required)*
- *Australian Medicines Handbook (AMH) – interactions tab (login required)*
- *Micromedex Drug Interactions (login required)*
- *Cancer Drug Interactions*
- *Cytochrome P450 Drug Interactions*

Brentuximab vedotin		
	Interaction	**Clinical management**
CYP3A4 and P-gp inhibitors (e.g. amiodarone, aprepitant, azole-antifungals, ritonavir, lapatinib, nilotinib, sorafenib, macrolides, ciclosporin, grapefruit juice etc.)	Increased toxicity of MMAE (conjugated anti-microtubule agent) possible due to reduced clearance	Avoid combination or monitor for MMAE toxicity and reduce the dose appropriately
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of MMAE possible due to increased clearance	Avoid combination or monitor for decreased clinical response to MMAE
Bleomycin	May have additive effect with brentuximab vedotin and is associated with pulmonary toxicity	Avoid combination as it is contraindicated

General		
	Interaction	**Clinical management**
Warfarin	Anti-cancer drugs may alter the anticoagulant effect of warfarin.	Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant.
Direct oral anticoagulants (DOACs) e.g. apixaban, rivaroxaban, dabigatran	Interaction with both CYP3A4 and P-gp inhibitors /inducers. DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding).	Apixaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. If treating VTE, avoid use with strong CYP3A4 and P-gp inducers. Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. Dabigatran: avoid combination with strong P-gp inducers and inhibitors. If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs.
Digoxin	Anti-cancer drugs can damage the lining of the intestine; affecting the absorption of digoxin.	Monitor digoxin serum levels; adjust digoxin dosage as appropriate.
Antiepileptics	Both altered antiepileptic and anti-cancer drug levels may occur, possibly leading to loss of efficacy or toxicity.	Where concurrent use of an enzyme-inducing antiepileptic cannot be avoided, monitor antiepileptic serum levels for toxicity, as well as seizure frequency for efficacy; adjust dosage as appropriate. Also monitor closely for efficacy of the anti-cancer therapy.
Antiplatelet agents and NSAIDs	Increased risk of bleeding due to treatment related thrombocytopenia.	Avoid or minimise combination. If combination deemed essential, (e.g. low dose aspirin for ischaemic heart disease) monitor for signs of bleeding.
Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)	Increased risk of serotonin syndrome with concurrent use of 5-HT3 receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.)	Avoid combination. If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia). For more information link to TGA Medicines Safety Update
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines.	Live vaccines (e.g. BCG, MMR, zoster and varicella) are contraindicated in patients on immunosuppressive therapy. Use with caution in patients on non-immunosuppressive therapy. For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook

Administration

eviQ provides safe and effective instructions on how to administer cancer treatments. However, eviQ does not provide every treatment delivery option, and is unable to provide a comprehensive list of cancer treatment agents and their required IV line giving set/filter. There may be alternative methods of treatment administration, and alternative supportive treatments that are also appropriate. Please refer to the individual

product information monographs via the TGA website for further information.

Day 1

Approximate treatment time: 60 minutes

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

Any toxicity grade 2 or greater may require dose reduction, delay or omission of treatment and review by medical officer before commencing treatment.

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

- weigh patient on each visit

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Brentuximab vedotin

Administer brentuximab vedotin (irritant):

- via IV infusion over 30 minutes
- flush with ~100 mL of sodium chloride 0.9%

Stop infusion at first sign of reaction:

- if symptoms are mild and resolve when infusion is stopped, consider recommencing infusion after review by medical officer with close monitoring.
- for severe reactions seek medical assistance immediately and do not restart infusion.
- premedication with paracetamol, an antihistamine and a corticosteroid should be considered for further doses for patients who have experienced a prior infusion related reaction.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Continue safe handling precautions until 7 days after completion of drug(s)

Discharge information

Antiemetics

- Antiemetics as prescribed.

Growth factor support

- Arrangements for administration if prescribed.

Prophylaxis medications

- Prophylaxis medications (if prescribed) i.e. tumour lysis prophylaxis, PJP prophylaxis, antifungals, antivirals.

Patient information

- Ensure patient receives patient information sheet.

Side effects

The side effects listed below are not a complete list of all possible side effects for this treatment. Side effects are categorised into the approximate onset of presentation and should only be used as a guide.

Immediate (onset hours to days)	
Extravasation, tissue or vein injury	The unintentional instillation or leakage of a drug or substance out of a blood vessel into surrounding tissue. This has the potential to cause damage to affected tissue. Read more about extravasation management
Flu-like symptoms	
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Abdominal pain	Dull ache, cramping or sharp pains are common with some anti-cancer drugs. These are caused by either increased or decreased gastrointestinal motility and can be associated with diarrhoea or constipation.
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Arthralgia and myalgia	Generalised joint pain or and/or stiffness and muscle aches, often worse upon waking or after long periods of inactivity. Can improve with movement. May be mild or severe, intermittent or constant and accompanied by inflammation. Read more about arthralgia and myalgia
Constipation	
Diarrhoea	Read more about treatment induced diarrhoea
Dizziness	Feeling faint or lightheaded, weak or unsteady. Advise patients to stand up slowly from sitting down or lying down positions and increase fluid intake if dehydrated.
Dyspnoea	
Fatigue	Read more about fatigue
Fever	
Headache	
Hepatotoxicity	Anti-cancer drugs administered either alone or in combination with other drugs and/or radiation may cause direct or indirect hepatotoxicity. Hepatic dysfunction can alter the metabolism of some drugs resulting in systemic toxicity.
Hyperglycaemia	High blood sugar, an excess of glucose in the blood stream.
Pancreatitis	Inflammation of the pancreas with impairment of function is associated with treatment.
Peripheral neuropathy	Typically symmetrical sensory neuropathy, affecting the fingers and toes, sometimes progressing to the hands and feet. It is associated with several classes of anti-cancer drugs. These include taxanes, platinum-based compounds, vinca alkaloids and some drugs used to treat multiple myeloma. Read more about peripheral neuropathy
Respiratory tract infection	
Severe cutaneous adverse reactions (SCARs)	Severe cutaneous adverse reactions (SCARs) have been reported with this treatment. SCARs are serious drug reactions involving the skin which may be life-threatening, or even fatal, and include conditions such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS). Onset may occur anytime between 1 to 6 weeks after drug exposure and the course of the illness can last from weeks to months. If SCARs occur, discontinue treatment immediately and seek specialist opinion to determine differential diagnosis so that appropriate supportive treatment can be administered.
Skin rash	Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction. Read more about skin rash

Late (onset weeks to months)	
Alopecia	Hair loss may occur from all parts of the body. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Progressive multifocal leukoencephalopathy (PML)	A rare opportunistic viral infection of the brain, usually leading to death or severe disability, can occur with monoclonal antibodies (e.g. rituximab, obinutuzumab, ofatumumab, brentuximab vedotin) and other targeted therapies (e.g. ibrutinib, ruxolitinib, idelalisib). Onset may occur up to months after the final dose. Read more about progressive multifocal leukoencephalopathy (PML)
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs

Evidence - Relapsed or refractory Hodgkin lymphoma

Brentuximab vedotin is an anti-CD30 antibody that is conjugated to an anti-microtubule agent, monomethyl aurostatin E (MMAE). This drug enables selective delivery of MMAE to CD30 expressing cells to cause apoptosis and cell cycle arrest.

The primary evidence supporting the use of brentuximab vedotin in relapsed/refractory Hodgkin lymphoma is provided by the pivotal single-arm multicentre phase II trial (trial SG035-0003). This study enrolled 102 patients who had CD30-positive Hodgkin lymphoma who relapsed post autologous stem cell transplant (ASCT), 71% of whom had primary refractory disease. This was initially reported in 2012[1] with long term data subsequently reported in 2016.[2] All patients received brentuximab vedotin (1.8 mg/kg IV every 3 weeks for up to 16 doses).

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trials	Younes et al. 2012	**Yes**	Yes	-
Phase II trials	Chen et al. 2016	**Yes**	Yes	-
Guidelines	**Date published/revised**	**Supports Use**	**Is the dose and regimen consistent with the protocol?**	**Comments**
NCCN	v.2 2015/2023	**Yes**	N/A	-
BCCA	Jun 2014/Jan 2023	**Yes**	Yes	-
CCO	Mar 2015/Dec 2021	**Yes**	Yes	-

Efficacy

As per the long term follow-up data[2], at a median follow-up of 35.1 months, the median OS and PFS were 40.5 and 9.3 months respectively. The estimated 5-year OS and PFS rates were 41% and 22%, respectively.

34/102 (33%) achieved CR on study.

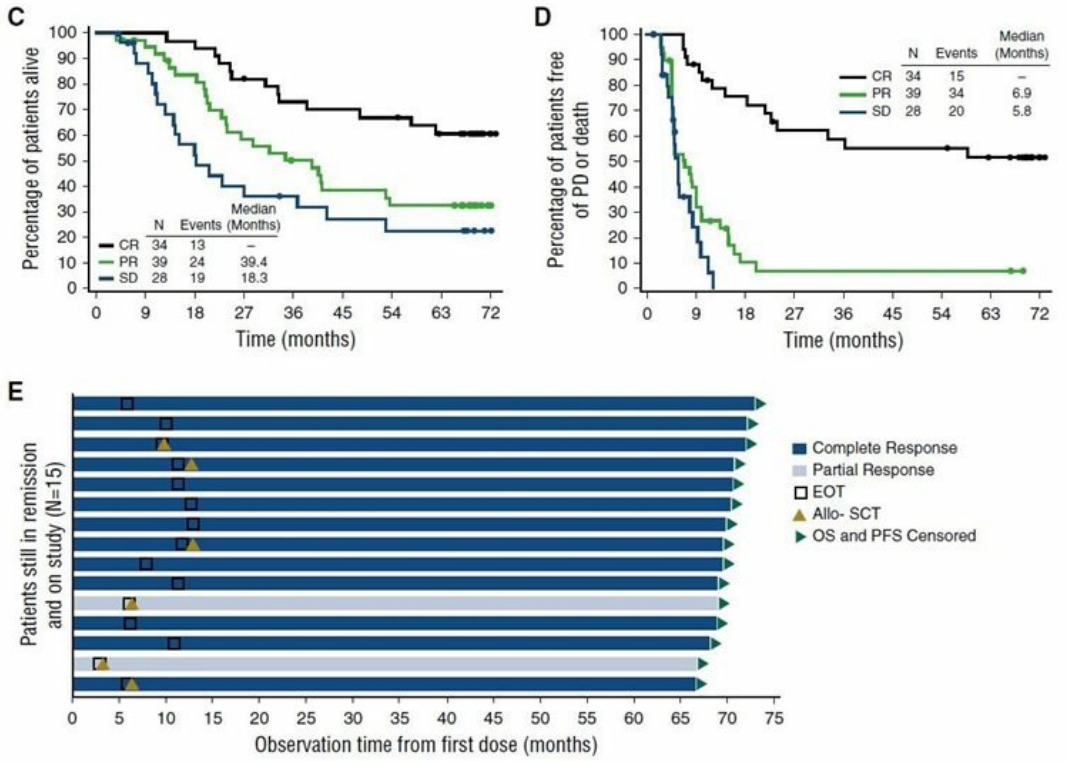
In those achieving CR, median response duration was not reached, while the 5 year OS was 64% and PFS 52%. Of the 13/34 patients achieving CR who then remained in CR at study close, 4 had undergone allogeneic transplant, while 9 had received no further therapy. A number of patients who relapsed after discontinuing brentuximab vedotin in remission were rechallenged with brentuximab vedotin.[3] Of 21 retreated patients, there was a 60% second objective response rate (CR 30%).

Note that there is evidence that some patients can respond to retreatment with brentuximab after having previously discontinued brentuximab therapy.[3]

Table 2. Key Response Results

Parameter	No. of Patients (N = 102)	%
Objective response	76	75
Complete remission	35	34
Partial remission	41	40
Stable disease	22	22
Progressive disease	3	3
Not evaluable	1	1
Duration of objective response, months		
Median	6.7	
95% CI	3.6 to 14.8	
Duration of response for patients with complete remission, months (n = 35)		
Median	20.5	
95% CI	10.8 to NE	
Progression-free survival, months		
Median	5.6	
95% CI	5.0 to 9.0	
Overall survival, months		
Median	22.4	
95% CI	21.7 to NE	

Abbreviation: NE, not estimable.



Toxicity

The most clinically relevant adverse event was peripheral neuropathy (PN) in 42% of patients, the majority (36%) of which was grade 1 or 2. Neuropathy typically developed after prolonged drug exposure (median onset of grade 2 and grade 3 PN was 27.3 weeks and 38.0 weeks, respectively). The majority of PN (80%) was reversible upon dose reduction/discontinuation. Other common toxicities are as outlined in the table below. 55% of patients experienced grade 3 adverse events. Twenty of 102 patients had adverse events that led to treatment discontinuation. No drug-related deaths occurred.[1]

Table 3. Drug-Related Adverse Events Reported by ≥ 10% of Patients and Grade 3 or 4 Incidence of These Events Regardless of Relationship to Brentuximab Vedotin

Adverse Event	Events Related to Brentuximab Vedotin (any grade)		Any Grade 3 Events		Any Grade 4 Events	
	No. of Patients	%	No. of Patients	%	No. of Patients	%
Peripheral sensory neuropathy	43	42	8	8	0	0
Nausea	36	35	0	0	0	0
Fatigue	35	34	2	2	0	0
Neutropenia	19	19	14	14	6	6
Diarrhea	18	18	1	1	0	0
Pyrexia	14	14	2	2	0	0
Vomiting	13	13	0	0	0	0
Arthralgia	12	12	0	0	0	0
Pruritus	12	12	0	0	0	0
Myalgia	11	11	0	0	0	0
Peripheral motor neuropathy	11	11	1	1	0	0
Alopecia	10	10	0	0	0	0

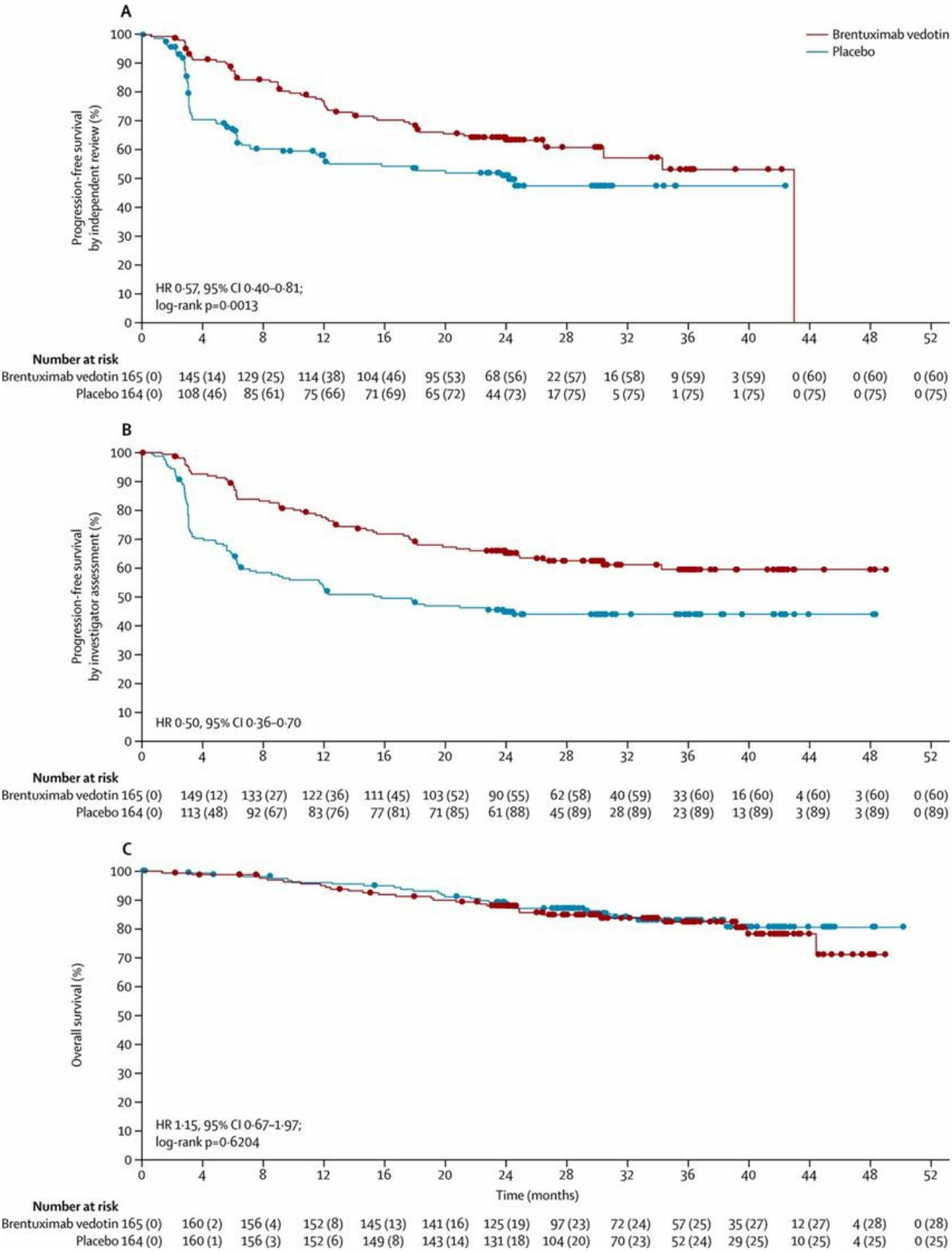
Evidence - High risk Hodgkin lymphoma post ASCT

The AETHERA study investigated the role of brentuximab vedotin (BV) administered as consolidation following autologous stem cell transplantation in patients considered at high risk of relapse or progression.[4] In this randomised, double-blind, placebo-controlled Phase III trial, patients were eligible if they had failed to achieve a complete response to front-line therapy, relapsed following an initial remission duration of less than 12 months, or had extranodal disease at the time of commencement of pre-transplant salvage therapy. 165 patients were randomised to receive brentuximab vedotin, with 164 patients in the placebo arm. Brentuximab was administered in the same dosing schedule as the SG035-0003 study above.

Efficacy

After a median of 30 months follow-up, progression-free survival (PFS) was significantly improved in patients in the BV arm [HR=0.57, 95% CI 0.40-0.81, p=0.0013]. Median PFS was 42.9 months in the BV arm versus 24.1 months in the placebo group. Overall survival was not seen to be different between the two arms. Benefit appeared to be maintained across most subgroups analysed.

Progression free and overall survival analyses [4]



A subsequent brief report was published updating outcomes to a median follow-up of 5 years.[5] Longer PFS continued to be demonstrated in the BV arm (Median not reached versus 15.8 months for placebo). Significantly fewer BV treated patients required subsequent anti-lymphoma treatment (54% v 32%, p<0.001), with 87% of patients requiring treatment in the placebo arm receiving BV at disease progression.

Toxicity

32% of patients in the BV arm required dose modifications versus 3% in the placebo arm. Peripheral neuropathy was again the most commonly reported adverse event (AE), with 56% of patients experiencing any grade, and 10% ≥ Grade 3. Neutropenia was the most commonly reported severe AE, with 29% experiencing ≥ Grade 3 toxicity (35% any grade). [6]

Infections and Pulmonary Toxicity* during the AETHERA Trial

	BV (n = 167)		Placebo (n = 160)	
	All	Grade ≥ 3†	All	Grade ≥ 3†
Any infections and infestations	100 (60)	15 (9)	80 (50)	15 (9)
Any opportunistic infections	20 (12)	4 (2)	6 (4)	3 (2)
Herpes zoster	12 (7)	2 (1)	4 (3)	2 (1)
Herpes simplex	7 (4)	0	1 (1)	0
Bronchopulmonary aspergillosis	0	0	2 (1)	1 (1)
Hepatic candidiasis	1 (1)	1 (1)	0	0
PCP‡	1 (1)	1 (1)	0	0
Any pulmonary toxicity event	8 (5)	8 (5)	5 (3)	4 (3)
Pneumonitis	4 (2)	4 (2)	1 (1)	0
Acute respiratory distress syndrome	2 (1)	4 (2)	1 (1)	2 (1)
Lung infiltration	1 (1)	0	2 (1)	0
Pulmonary toxicity	2 (1)	2 (1)	0	0
Idiopathic pneumonia syndrome	0	0	1 (1)	2 (1)
Radiation pneumonitis	1 (1)	0	0	0

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In the 5 year follow-up, 90% of patients who experience peripheral neuropathy reported resolution or improvement, with 73% having complete resolution. Median time to resolution was 37.6 weeks. There was no difference in incidence of secondary malignancies between the two groups.[5]

Evidence - Anaplastic large cell lymphoma

Brentuximab vedotin is an anti-CD30 antibody that is conjugated to an anti-microtubule agent, monomethyl aurostatin E (MMAE). This drug enables selective delivery of MMAE to CD30 expressing cells to cause apoptosis and cell cycle arrest.

The primary evidence supporting the use of brentuximab vedotin in this setting is a pivotal phase 2 study of 58 patients with relapsed/refractory anaplastic large cell lymphoma (ALCL). This study was initially reported in 2012[7] and updated in 2017[8]. The regimen was identical to that for Hodgkin lymphoma as above.

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trials	Pro et al. 2012	**Yes**	Yes	-
Phase II trials	Pro et al. 2017	**Yes**	Yes	-
Guidelines	**Date published/revised**	**Supports Use**	**Is the dose and regimen consistent with the protocol?**	**Comments**
NCCN	Peripheral T-cell Lymphomas V.1 2023	**Yes**	Yes	-
BCCA	Jun 2014/Jan 2023	**Yes**	Yes	-
CCO	Mar 2015/Dec 2021	**Yes**	Yes	-

Efficacy

Of 58 patients enrolled, 16/58 (28%) were ALK+ve, while 42/58 (72%) were ALK-ve. 36/58 (62%) were primary refractory to frontline therapy, including 13 (22%) who had no previously demonstrated response. At a median follow-up of 71.4 months, the estimated 5-yr overall survival (OS) and progression-free survival (PFS) were 60% and 39%, respectively. The duration of median OS was not reached, while median PFS was 20 months.[8]

16 of 38 patients achieving CR (42%) underwent consolidative stem cell transplant. 11 of these patients (69%) remained alive and progression free. Outcomes were similar between autologous and allogeneic transplants (PFS 75% versus 63%, respectively). However, of the 8 allogeneic transplants, 6 had previously undergone autologous transplantation. Of the 22 CR patients who did not receive SCT (58%), 12 (54%) were alive without progressive disease.[8]

Note that, as with Hodgkin lymphoma, there is evidence that some patients can respond to re-treatment with brentuximab after

having previously discontinued brentuximab therapy.[3]

Table 1. Overall response and durability results per investigator

Results	n = 58	95% CI
Objective response (%)	86	74.6-93.9*
CR (%)	66	51.9-77.5*
Partial response (%)	21	
Stable disease (%)	7	
Progressive disease (%)	3	
Not evaluable (%)†	3	
Median duration of objective response (months)	25.6	11.8-NE‡
Median duration of response in patients with CR (months)	Not reached	20.0-NE‡
Median PFS (months)	20.0	9.4-NE‡
Median OS (months)	Not reached	21.3-NE‡

NE, not estimable.
*Two-sided 95% exact CI computed using the F distribution method.[18]
†Defined as patients determined to have systemic ALCL by local assessment, but not by central pathology review; scored as nonresponder per protocol.
‡Computed using the method of Brookmeyer and Crowley.[19]

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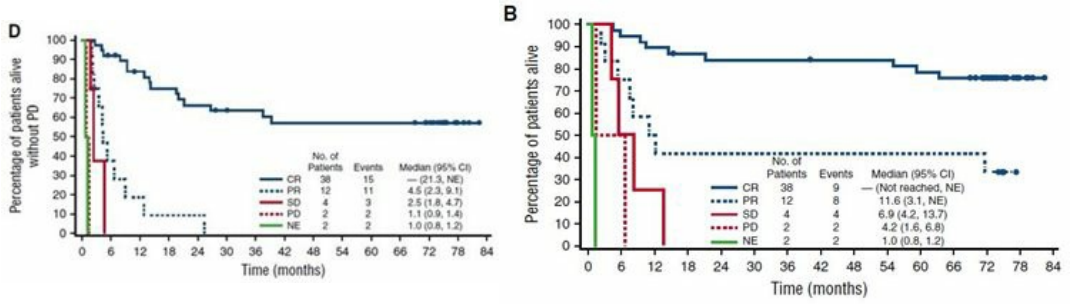

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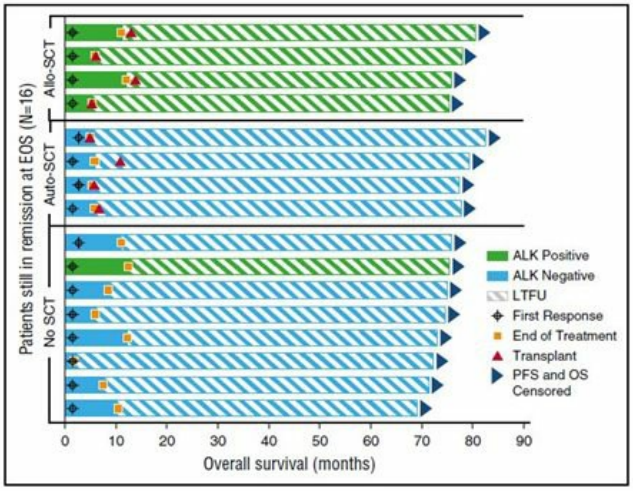

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Toxicity

Toxicity was similar to that seen with Hodgkin lymphoma as above.

Table 3. Most Common Adverse Events (> 10%)

Adverse Event*	All Grades (N = 58)		Grade 3 (N = 58)		Grade 4 (N = 58)	
	No. of Patients	%	No. of Patients	%	No. of Patients	%
Peripheral sensory neuropathy	24	41	7	12	0	0
Nausea	23	40	1	2	0	0
Fatigue	22	38	2	3	1	2
Pyrexia	20	34	1	2	0	0
Diarrhea	17	29	2	3	0	0
Rash	14	24	0	0	0	0
Constipation	13	22	1	2	0	0
Neutropenia	12	21	7	12	5	9
Headache	11	19	1	2	0	0
Pruritus	11	19	0	0	0	0
Cough	10	17	0	0	0	0
Dyspnea	10	17	1	2	0	0
Upper respiratory tract infection	10	17	0	0	0	0
Vomiting	10	17	2	3	0	0
Decreased appetite	9	16	1	2	0	0
Dizziness	9	16	0	0	0	0
Insomnia	9	16	0	0	0	0
Myalgia	9	16	1	2	0	0
Alopecia	8	14	0	0	0	0
Chills	8	14	0	0	0	0
Muscle spasms	8	14	1	2	0	0
Thrombocytopenia	8	14	5	9	3	5
Weight decreased	8	14	2	3	0	0
Edema peripheral	7	12	0	0	0	0
Pain in extremity	7	12	1	2	1	2

*Terms according to Medical Dictionary for Regulatory Activities, Version 13.0.

Evidence - Cutaneous T-cell lymphoma

Brentuximab vedotin is an anti-CD30 antibody that is conjugated to an anti-microtubule agent, monomethyl aurostatin E (MMAE). This drug enables selective delivery of MMAE to CD30 expressing cells to cause apoptosis and cell cycle arrest.

The evidence supporting this protocol is provided by a phase III multicentre international randomised trial involving 131 patients comparing Brentuximab with physician's choice of therapy in patients with relapsed refractory CD30-positive mycosis fungoides or primary cutaneous anaplastic large-cell lymphoma.[9]

Between 2012 and 2015, 66 patients were randomised to receive brentuximab vedotin (BV) 1.8mg/kg every 3 weeks for up to 16 cycles, and 65 patients were randomised to receive physician's choice (oral methotrexate 5–50 mg once per week or oral bexarotene 300 mg/m^2 once per day) for up to 48 weeks. The primary end point was the proportion obtaining an objective global response of at least 4 months.

Efficacy

After a median follow up of 22.9 months, the primary endpoint (objective global response of at least 4 months) was achieved in 56.3% of the BV arm versus 12.5% in the best supportive arm, which is an improvement of 43.8% (95% CI 29.1–58.4; p<0.0001).

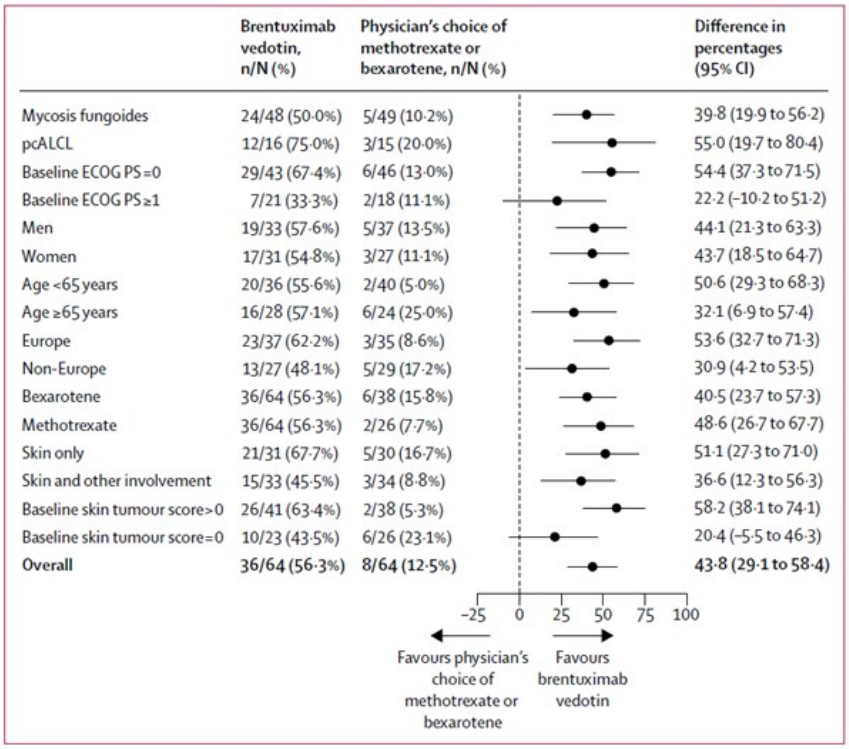

Figure 2: **Proportion of patients achieving an objective global response lasting at least 4 months**
pcALCL=primary cutaneous anaplastic large-cell lymphoma. ECOG PS=Eastern Cooperative Oncology Group performance status.

Median progression-free survival (PFS) (EMA criteria) was 16.7 months versus 3.5 months (HR 0.270, 95% CI 0.169–0.430; p<0.0001; adjusted p<0.0001). Median duration of response for the 43 responders to BV was 15.1 months (95% CI 9.7–25.5) versus 18.3 months (3.5–18.4) for the 13 responders to physician's choice treatment.

Patient-reported symptoms (Skindex-29), showed significantly greater symptom reduction in the brentuximab vedotin group, compared with the physician's choice group, with a mean maximum reduction of –27.96 (SD 26.877) versus –8.62 (17.013; p<0.0001).

A final analysis has been presented in abstract form at ICML15.[10] At a median follow-up of 45.9 months, the benefit in median PFS was maintained (16.7 v 3.5 months, p<0.001). Similar numbers of patients had received subsequent therapy in each group (78% v 75%), but median time to next therapy remained significantly longer in the BV treated group (14.2 v 5.6 months, p<0.001).

Toxicity

The median duration of treatment was 269 days of BV versus 114 days of bexarotene and 77 days of methotrexate. The most frequent reasons for treatment discontinuation were completion of 16 cycles in the brentuximab vedotin group (23 [35%] of 66 patients). Adverse events led to discontinuation in 16 (24%) patients in the BV group versus five (8%) in the physician's choice group.

Peripheral neuropathy was identified in 44 (67%) of 66 patients in the brentuximab vedotin group (n=17 grade 1, n=21 grade 2, n=6 grade 3) and four (6%) of 62 patients in the physician's choice group (n=1 grade 1, n=3 grade 2). This led to 9/66 patients in the BV arm discontinuing BV therapy (compared to none discontinuing for this indication in the physicians choice arm).

In the updated analysis, 86% of patients with peripheral neuropathy had resolution or improvement, with no patients having persistent neuropathy ≥ Grade 3.[10]

	Brentuximab vedotin (n=66)			Methotrexate (n=25)			Bexarotene (n=37)		
	Any grade	Grade 3	Grade 4	Any grade	Grade 3	Grade 4	Any grade	Grade 3	Grade 4
Peripheral sensory neuropathy SMQ	30 (45%)*	3 (5%)	0	1 (4%)	0	0	0	0	0
Nausea	24 (36%)	1 (2%)	0	4 (16%)	0	0	4 (11%)	0	0
Diarrhoea	19 (29%)	2 (3%)	0	1 (4%)	0	0	3 (8%)	0	0
Fatigue	19 (29%)	3 (5%)	0	5 (20%)	1 (4%)	0	12 (32%)	0	0
Vomiting	11 (17%)	1 (2%)	0	2 (8%)	0	0	1 (3%)	0	0
Alopecia	10 (15%)	0	0	1 (4%)	0	0	1 (3%)	0	0
Pruritus	11 (17%)	1 (2%)	0	2 (8%)	0	0	6 (16%)	2 (5%)	0
Pyrexia	11 (17%)	0	0	7 (28%)	1 (4%)	0	4 (11%)	0	0
Decreased appetite	10 (15%)	0	0	1 (4%)	0	0	2 (5%)	0	0
Asthenia	7 (11%)	1 (2%)	0	3 (12%)	0	0	2 (5%)	0	1 (3%)
Dyspnoea	7 (11%)	0	0	0	0	0	0	0	0
Maculopapular rash	7 (11%)	1 (2%)	0	1 (4%)	0	0	2 (5%)	0	0
Peripheral oedema	7 (11%)	0	0	4 (16%)	0	0	2 (5%)	0	0
Pruritus (generalised)	7 (11%)	1 (2%)	0	0	0	0	1 (3%)	0	0
Arthralgia	8 (12%)	0	0	2 (8%)	0	0	2 (5%)	0	0
Myalgia	8 (12%)	0	0	0	0	0	2 (5%)	0	0
Headache	5 (8%)	0	0	1 (4%)	0	0	5 (14%)	0	0
Anaemia	3 (5%)	0	0	0	0	0	6 (16%)	3 (8%)	0
Skin infection	2 (3%)	2 (3%)	0	3 (12%)	1 (4%)	0	4 (11%)	0	0
Hypertriglyceridaemia	1 (2%)	0	0	0	0	0	11 (30%)	5 (14%)	3 (8%)

Shown are commonly reported (≥10% of patients) treatment-emergent adverse events in the safety population. SMQ=standardised Medical Dictionary for Regulatory Activities query. *Overall, events reported by investigators as peripheral neuropathy or peripheral sensory neuropathy (including events additional to those reported in ≥10% of patients) were reported as grade 1 in 17 patients, grade 2 in 21 patients, and grade 3 in six patients.

Table 3: **Treatment-emergent adverse events**

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10 Horwitz S.M., J. Scarisbrick, H.M. Prince, et al 2019. Final Data from the Phase 3 ALCANZA Study: Brentuximab Vedotin (BV) vs Physicians Choice (PC) in Patients with CD3-Positive Cutaneous T-cell Lymphoma. Hematological Oncology 37 (S2): 286-288

History

Version 5

Date	Summary of changes
27/03/2020	Protocol reviewed by Haematology Reference Committee: • New indications added to include high risk Hodgkin lymphoma post ASCT • New evidence added for high risk Hodgkin lymphoma post ASCT • New evidence added for cutaneous T-cell lymphoma • Version number changed to v.5
22/10/2021	Protocol reviewed by Haematology Reference Committee. Clinical information & side effects updated. Review in 2 years.
31/08/2022	Brentuximab vedotin extravasation category updated to align with extravasation clinical resources update.
28/04/2023	Reviewed by Haematology Reference Committee, pancreatitis added to side effects, update and reformatting of administration instructions. Review in 4 years.
31/08/2023	Updated to align with product information - skin toxicity and dermatological reaction dose modification added; side effects updated.

Version 4

Date	Summary of changes
13/09/2019	Protocol reviewed at Haematology Reference Committee meeting: • Reformatted as per eviQ multi-indication protocol standard • New indications updated to include Cutaneous T-cell lymphoma • Hepatic dose modifications clarified • New evidence added for Cutaneous T-cell lymphoma • Peripheral neuropathy checklist added in Administration section • Version number changed to v.4
10/10/2019	Clinical information updated with PBS expanded indications for G-CSF.

Version 3

Date	Summary of changes
26/02/2016	Approved and published on eviQ
31/05/2017	Transferred to new eviQ website. Version number change to v.2.
25/05/2018	Protocol reviewed at Haematology Reference Committee meeting: • Title changed from Hodgkin lymphoma to Lymphoma • New indications updated to include anaplastic large cell lymphoma. • Hepatic dose modifications clarified • Existing evidence for Hodgkin lymphoma updated and new evidence added for anaplastic large cell lymphoma. • Version number changed to v.3.

First approved: 26 February 2016
Last reviewed: 28 April 2023
Review due: 30 June 2027

The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/p/1665
22 Nov 2023

Patient information - Lymphoma - Brentuximab vedotin

Patient's name:

Your treatment

The treatment schedule below explains how the drug for this treatment is given. It may be given to treat non-Hodgkin lymphoma or Hodgkin lymphoma.

Brentuximab vedotin			
This treatment cycle is repeated every 21 days. Your doctor will advise you of the number of treatments you will have.			
Day	**Treatment**	**How it is given**	**How long it takes**
1	**Brentuximab vedotin** (*bren-TUX-i-mab ve-DOE-tin*)	By a drip into a vein	About 30 minutes

When to get help

Anticancer drugs (drugs used to treat cancer) can sometimes cause serious problems. It is important to get medical help immediately if you become unwell.

IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:	**Emergency contact details** Ask your doctor or nurse from your treating team who to contact if you have a problem
• a temperature of 38°C or higher • chills, sweats, shivers or shakes • shortness of breath • uncontrolled vomiting or diarrhoea • pain, tingling or discomfort in your chest or arms • you become unwell.	Daytime: Night/weekend: Other instructions:

During your treatment immediately tell the doctor or nurse looking after you if you get any of the following problems:

- leaking from the area where the drugs are being given
- pain, stinging, swelling or redness in the area where the drugs are being given or at any injection sites
- a skin rash, itching, feeling short of breath, wheezing, fever, shivers, or feeling dizzy or unwell in any way (allergic reaction).

Other information about your treatment

Changes to your dose or treatment delays

Sometimes a treatment may be started at a lower dose or the dose needs to be changed during treatment. There may also be times when your treatment is delayed. This can happen if your doctor thinks you are likely to have severe side effects, if you get severe side effects, if your blood counts are affected and causing delays in treatment, or if you are finding it hard to cope with the

treatment. This is called a dose reduction, dose change or treatment delay. Your doctor will explain if you need any changes or delays to your treatment and the reason why.

Blood tests and monitoring

Anti-cancer drugs can reduce the number of blood cells in your body. You will need to have regular blood tests to check that your blood cell count has returned to normal. If your blood count is low, your treatment may be delayed until it has returned to normal. Your doctor or nurse will tell you when to have these blood tests.

Central venous access devices (CVADs)

This treatment may involve having chemotherapy through a central venous access device (CVAD). Your doctor or nurse will explain this to you. For more information, see the eviQ patient information sheets on CVADs.

Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.
- **Prophylaxis medication:** you may need to take some medications to prevent infection and to help prevent or reduce some of the side effects of the chemotherapy. Your doctor or nurse will tell you how and when to take these medications.
- **G-CSF:** you may be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. This helps to boost your white blood cell count. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover. Your doctor will decide if you need this medication. Follow this link to read more information on how to give this injection.

Side effects

Cancer treatments can cause damage to normal cells in your body, which can cause side effects. Everyone gets different side effects, and some people will have more problems than others.

The table below shows some of the side effects you may get with this treatment. You are unlikely to get all of those listed and you may also get some side effects that have not been listed.

Tell your doctor or nurse about any side effects that worry you. Follow the instructions below and those given to you by your doctor or nurse.

Immediate (onset hours to days)	
Pain or swelling at injection site (extravasation)	• This treatment can cause serious injury if it leaks from the area where it is going into the vein. • This can cause pain, stinging, swelling or redness at or near the site where the drug enters the vein. • If not treated correctly, you may get blistering and ulceration. • **Tell your doctor or nurse immediately if you get any of the symptoms listed above during or after treatment.**
Flu-like symptoms	• You may get: ◦ a fever ◦ chills or sweats ◦ muscle and joint pain ◦ a cough ◦ headaches. • Tell your doctor or nurse if you get any of the symptoms listed above. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have a temperature of 38°C or higher.**
Allergic reaction	• Allergic reactions are uncommon but can be life threatening. • **If you feel unwell during the infusion or shortly after it, or:** ◦ **get a fever, shivers or shakes** ◦ **feel dizzy, faint, confused or anxious** ◦ **start wheezing or have difficulty breathing** ◦ **have a rash, itch or redness of the face** **<u>While you are in hospital:</u> Tell your doctor or nurse immediately.** **<u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.**
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**

Early (onset days to weeks)

Infection risk (neutropenia)	• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening. • Wash your hands often. • Keep a thermometer at home and take your temperature regularly, and if you feel unwell. • Do your mouth care regularly. • Inspect your central line site (if you have one) daily for any redness, pus or swelling. • Limit contact with people who are sick. • Learn how to recognise the signs of infection. • Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **a temperature of 38°C or higher** ◦ **chills, shivers, sweats or shakes** ◦ **a sore throat or cough** ◦ **uncontrolled diarrhoea** ◦ **shortness of breath** ◦ **a fast heartbeat** ◦ **become unwell even without a temperature.**
Low platelets (thrombocytopenia)	• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**
Stomach pain	• You may get: ◦ dull aches ◦ cramping or pain ◦ bloating or flatulence (gas). • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have stomach pain that you are unable to control.**
Appetite loss (anorexia)	• You may not feel like eating. • Try to avoid drinking fluids at meal times. • Try to eat small meals or snacks regularly throughout the day. • Try to eat food that is high in protein and calories. • If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.
Joint and muscle pain and stiffness	• You may get muscle, joint or general body pain and stiffness. • Applying a heat pack to affected areas may help. • Talk to your doctor or nurse about other ways to manage these symptoms. You may need medication to help with any pain.

Constipation	• You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass.
	• You may also get:
	  ◦ bloating, cramping or pain
	  ◦ a loss of appetite
	  ◦ nausea or vomiting.
	• Drink plenty of fluids (unless you are fluid restricted).
	• Eat plenty of fibre-containing foods such as fruit, vegetables and bran.
	• Take laxatives as directed by your doctor.
	• Try some gentle exercise daily.
	• **Tell your doctor or nurse if you have not opened your bowels for more than 3 days.**

Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**
Dizziness or feeling light-headed	• You may feel dizzy or light-headed. • These symptoms may be caused by your treatment, or other problems like dehydration. • If you are feeling dehydrated, drink plenty of fluids (unless you are fluid restricted) as this can be a cause of dizziness. • If you are feeling dizzy, try lying down until the dizziness passes. • When you want to get up from a sitting or lying down position, get up slowly to let your body adjust to the new position. • Tell your doctor or nurse if you get any of the symptoms listed above.
Shortness of breath	• You may have a cough. • You may feel short of breath. • **Tell your doctor or nurse immediately if you feel you have a cough or feel short of breath.**
Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Fever	• You may feel warm. • Tell your doctor or nurse if you get this symptom.
Headache	• You can take paracetamol if you have a headache. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.**

Liver problems	• You may get: ◦ yellowing of your skin or eyes ◦ itchy skin ◦ pain or tenderness in your stomach ◦ nausea and vomiting ◦ loss of appetite • You will have regular blood tests to check how well your liver is working. • **Tell your doctor or nurse as soon as possible if you notice that your urine is a dark colour, the whites of your eyes look yellow, or if you have stomach pain.**
High blood sugar level (hyperglycaemia)	• You may feel thirsty and need to urinate more often than normal. • You may get repeated infections, especially thrush. • If you are a diabetic you will need to have your blood sugar levels checked more often. You may also need to have your diabetes medication increased. • **Tell your doctor or nurse if you get any of the signs or symptoms listed above.**
Inflamed pancreas (pancreatitis)	• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get:** ◦ **abdominal (stomach) pain** ◦ **a swollen stomach** ◦ **nausea or vomiting** ◦ **fever or chills** ◦ **a fast heartbeat.**
Nerve damage (peripheral neuropathy)	• You may notice a change in the sensations in your hands and feet, including: ◦ tingling or pins and needles ◦ numbness or loss of feeling ◦ pain. • You may find it difficult to do everyday activities, such as doing up buttons or picking up small objects. • Test water temperature with your elbow when bathing to avoid burns. • Use rubber gloves, pot holders and oven mitts in the kitchen. • Wear rubber shoes or boots when working in the garden or garage. • Keep rooms well lit and uncluttered. • Ask your doctor or nurse for eviQ patient information – Nerve problems during cancer treatment. • Tell your doctor or nurse if you get any of the symptoms listed above.
Chest infection	• You can develop a chest infection whilst receiving this treatment. • **Tell your doctor or nurse as soon as possible if you get any of the following symptoms:** ◦ **shortness of breath** ◦ **difficulty breathing** ◦ **wheezing** ◦ **coughing up mucus**

Severe skin reaction	• One of the drugs you are receiving may cause severe skin reactions.
	• This can start as a mild skin rash and develop into more serious and concerning skin problems.
	• Before the rash appears, you may feel generally unwell and may experience some of the following symptoms:
	  ◦ a fever
	  ◦ aches
	  ◦ fatigue
	  ◦ cough
	  ◦ blocked or runny nose
	  ◦ sore throat
	  ◦ sore eyes.
	• The skin rash may be painful and itchy and sometimes small blisters can form.
	• You may also notice mouth ulcers, pain in the mouth or throat, or difficulty eating or swallowing.
	• **Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if you get any of the above symptoms.**

Skin rash	• You may get a red, bumpy rash and dry, itchy skin. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • **Talk to your doctor or nurse about other ways to manage your skin rash.**

Late (onset weeks to months)	
Hair loss (alopecia)	• Your hair may start to fall out from your head and body. • Hair loss usually starts 2 to 3 weeks after your first treatment. • You may become completely bald and your scalp might feel tender. • Use a gentle shampoo and a soft brush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat, scarf or wig. • Protect your scalp from the sun with a hat or sunscreen of SPF 50 or higher. • Moisturise your scalp to prevent itching. • Ask your doctor or nurse about the Look Good Feel Better program
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
Changes in the way your brain works [progressive multifocal leukoencephalopathy (PML)]	• This treatment can affect your central nervous system. This can be very serious. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following symptoms:** ◦ **trouble with your speech or vision** ◦ **confusion or memory loss** ◦ **changes in your personality** ◦ **weakness in your arms and legs** ◦ **poor balance or coordination** ◦ **fits (seizures).**
Lung problems	• Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment. • You may get: ◦ shortness of breath ◦ fever ◦ dry cough ◦ wheezing ◦ fast heartbeat ◦ chest pain. • Your doctor will monitor how well your lungs are working during your treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.**

General advice for patients having cancer treatment

Chemotherapy safety

- Learn how to keep you and your family safe while you are having anticancer drugs.
- See our patient information sheet - Chemotherapy safety at home.

Blood clot risk

- Cancer and anticancer drugs can increase the risk of a blood clot (thrombosis).
- Tell your doctor if you have a family history of blood clots.
- A blood clot can cause pain, redness, swelling in your arms or legs, shortness of breath or chest pain.
- If you have any of these symptoms go to your nearest hospital Emergency Department.

Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.
- Don’t stop or start any medications during treatment without talking to your doctor and pharmacist first.

- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.
- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.
- People you live with should be fully vaccinated, including having live vaccines according to the current vaccination schedule. Extra care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the rotavirus vaccine.

Other medical and dental treatment

- If you go to hospital or any other medical appointment (including dental appointments), always tell the person treating you that you are receiving anticancer drugs.
- Before you have any dental treatment, talk to your doctor.

Diet and food safety

- While you are receiving this treatment, it is important that you try to maintain a healthy diet.
- Grapefruit and grapefruit juice can interact with your medication and should be avoided while you are on this treatment.
- Speak to your doctor or nurse about whether drinking alcohol is safe with your treatment.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.
- There are some foods that may cause infection in high risk individuals and should be avoided. For further information on foods to avoid and food hygiene please ask for a copy of the Listeria and food brochure.

Fertility

- Some cancer treatments can reduce your fertility. This can make it difficult or impossible to get pregnant or father a child.
- Talk to your doctor or nurse before you start any treatment. Depending on your situation there may be fertility sparing options available to you and/or your partner, discuss these with your doctor or nurse.

Pregnancy and breastfeeding

- Some cancer treatments can be dangerous to unborn babies. Talk to your doctor or nurse if you think there is any chance that you could be pregnant.
- Do not try to get pregnant or father a child during this treatment. Contraception should be used during treatment and after stopping treatment. Ask your doctor or nurse about what type of contraception you should use.
- If you are planning pregnancy/fatherhood after completing this treatment, talk to your doctor. Some doctors advise waiting between 6 months and 2 years after treatment.
- Do not breastfeed if you are on this treatment, as anti-cancer medications can also pass into breast milk.

Sex life and sexuality

- The desire to have sex may decrease as a result of this treatment or its side effects.
- Your emotions and the way you feel about yourself may also be affected by this treatment.
- It may help to discuss your concerns with your partner and doctor or nurse.

Quitting smoking

- It is never too late to quit smoking. Quitting smoking is one of the best things you can do to help your treatment work better.
- There are many effective tools to improve your chances of quitting.
- Talk to your treating team for more information and referral to a smoking cessation support service.

Staying active

- Research shows that exercise, no matter how small, has many benefits for people during and after cancer treatment.
- Talk to your doctor before starting an exercise program. Your doctor can advise whether you need a modified exercise program.

For more information about cancer treatment, side effects and side effect management see our Patient and carers section.

Where to get more information

Telephone support

- Call Cancer Council on 13 11 20 for cancer information and support
- Call the Leukaemia Foundation on 1800 620 420 (Mon to Fri 9am – 5pm)

- Call the Lymphoma Nurse Support Line on 1800 953 081 (Mon to Fri 9am - 5pm)
- Call the Myeloma Australia Support Line on 1800 693 566 (Mon to Fri 9am - 5pm)

Haematology, transplant and cellular therapy information

- Arrow bone marrow transplant foundation – arrow.org.au
- Australasian Menopause Society – menopause.org.au
- Chris O'Brien Lifehouse - Total Body Irradiation - mylifehouse.org.au/departments/radiation-oncology/total-body-irradiation/
- Healthy Male Andrology Australia – healthymale.org.au/
- International Myeloma Foundation – myeloma.org
- Leukaemia Foundation – leukaemia.org.au
- Lymphoma Australia – lymphoma.org.au
- Myeloma Australia – myeloma.org.au
- NSW Agency for Clinical Innovation, Blood & Marrow Transplant Network – https://aci.health.nsw.gov.au/networks/bmtct
- NSW Agency for Clinical Innovation - aci.health.nsw.gov.au/projects/immune-effector-cell-service
- NCCN Guidelines for Patients Immunotherapy Side Effects: CAR T-Cell Therapy - nccn.org/patientresources/patient-resources/guidelines-for-patients
- Talk Blood Cancer – cmlsupport.org.uk/organisation-type/social-media-groups

General cancer information and support

- Australian Rare Cancer (ARC) Portal – arcportal.org.au/
- Beyondblue – beyondblue.org.au
- Cancer Australia – canceraustralia.gov.au
- Cancer Council Australia – cancer.org.au
- Cancer Voices Australia – cancervoicesaustralia.org
- CanTeen – canteen.org.au
- Carers Australia – carersaustralia.com.au
- Carer Help - carerhelp.com.au
- eviQ Cancer Treatments Online – eviQ.org.au
- Food Standards Australia New Zealand: Listeria & Food Safety – foodstandards.gov.au/publications/pages/listeriabrochuretext.aspx
- LGBTQI+ People and Cancer - cancercouncil.com.au/cancer-information/lgbtqi
- Look Good Feel Better – lgfb.org.au
- Patient Information - patients.cancer.nsw.gov.au
- Radiation Oncology Targeting Cancer - targetingcancer.com.au
- Redkite – redkite.org.au
- Return Unwanted Medicines – returnmed.com.au
- Staying active during cancer treatment – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/staying-active

Quit smoking information and support

Quitting smoking is helpful even after you have been diagnosed with cancer. The following resources provide useful information and support to help you quit smoking. Talk to your treating team about any other questions you may have.

- Call Quitline on 13 QUIT (13 78 48)
- iCanQuit – iCanQuit.com.au
- Patient Information - patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/quitting-smoking
- Quitnow – quitnow.gov.au

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