Lymphoma Pembrolizumab (flat dosing)

ID: 3671 v.4 **Endorsed**

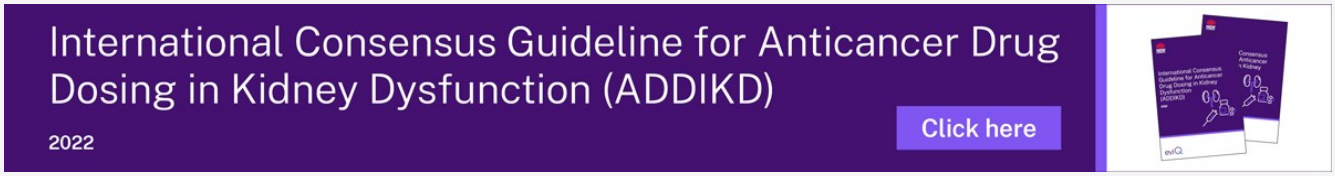
Treatment must be initiated and supervised by specialist physicians experienced in the treatment of cancer using immunological agents. Before commencing immunotherapy treatment in any patient, clinicians should have an understanding of the immune-related adverse events (irAEs) associated with immunotherapy treatment and their management.

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

This protocol is based on limited evidence; refer to the evidence section of this protocol for more information.

This protocol does not have a calculator.

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 and further cycles

Drug	Dose	Route	Day
Pembrolizumab	200 mg *	IV infusion	1

* Alternative dosing schedule of 400 mg every 42 days may be considered.[1, 2]

Frequency: 21 days

Cycles: 35 or until disease progression or unacceptable toxicity (maximum 24 months treatment)

Notes:
In the first few months after the start of immunotherapy, some patients can have a transient tumour flare (termed 'pseudo progression', an immune response). This may manifest as growth of existing lesions or the development of new lesions prior to later tumour regression. While this is rare (~5%), continuing treatment and performing a second scan 4 to 6 weeks later to confirm progression may be considered, particularly if the patient is believed to be deriving clinical benefit.

Radiation recall has been observed with PD1 inhibitors, consideration should be given to the timing when starting this treatment after a prolonged course of radiation therapy.

Drug status: **Pembrolizumab:** (PBS authority)

Cost: ~ $7,730 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 and further cycles

Day 1		
Pembrolizumab	200 mg (IV infusion)	in 50 mL sodium chloride 0.9% over 30 minutes

* Alternative dosing schedule of 400 mg every 42 days may be considered.[1, 2]

Frequency: 21 days

Cycles: 35 or until disease progression or unacceptable toxicity (maximum 24 months treatment)

Indications and patient population - Hodgkin lymphoma

Indications:

Monotherapy for relapsed or refractory classical Hodgkin lymphoma following:

- autologous stem cell transplant (ASCT), or
- at least two prior therapies when ASCT is not a treatment option.

Precautions:

If any of these conditions are present, clinical judgement should be used and individual cases discussed with an expert in the field as indicated:

- significant autoimmune disease (e.g. myasthenia gravis, inflammatory bowel disease, systemic lupus erythematosus, rheumatoid arthritis, autoimmune ocular disease)
- organ transplantation
- previous history of viral hepatitis
- HIV/acquired immune deficiency syndrome (AIDS)
- previous radiation to the lungs.

Indications and patient population - Primary mediastinal large B-cell lymphoma

Indications:

Relapsed or refractory primary mediastinal large B-cell lymphoma following:

- autologous stem cell transplant (ASCT), or
- at least one prior therapy when ASCT is not a treatment option, or
- two or more prior lines of therapy (one of which includes rituximab-based chemotherapy)

Precautions:

If any of these conditions are present, clinical judgement should be used and individual cases discussed with an expert in the field as indicated:

- significant autoimmune disease (e.g. myasthenia gravis, inflammatory bowel disease, systemic lupus erythematosus, rheumatoid arthritis, autoimmune ocular disease)
- organ transplantation
- previous history of viral hepatitis
- HIV/acquired immune deficiency syndrome (AIDS)
- previous radiation to the lungs.

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
Emetogenicity MINIMAL	No antiemetics should be routinely administered before treatment in patients without a history of nausea and vomiting. If patients experience nausea and/or vomiting, consider using the low antiemetic prophylaxis regimen. Read more about preventing anti-cancer therapy induced nausea and vomiting
Complications of allogeneic HSCT	Patients who received allogeneic haematopoietic stem cell transplant (HSCT) following discontinuation of pembrolizumab therapy experienced immune-mediated complications (some fatal) including graft versus host disease (GVHD) and severe sinusoidal obstructive syndrome (SOS; formerly called veno-occlusive disease) following reduced-intensity conditioning. Monitor closely for early signs/symptoms of transplant-related complications (e.g. hyper-acute GVHD, steroid-requiring febrile syndrome, SOS, and other immune-mediated adverse reactions) and manage promptly.
Immune-related adverse events (irAEs)	Immune-related adverse events (irAEs) can occur early and escalate quickly in patients receiving immune checkpoint inhibitors. irAEs can also occur after discontinuation of treatment. Fatalities have been reported. Management of irAEs is largely based on expert opinion and consensus guidelines. Examples of irAEs with high risk of mortality include: • cardiac toxicity: myocarditis • musculoskeletal toxicity: myositis • neurological toxicity: encephalitis, Guillain-Barré syndrome, myelitis, myasthenia gravis • pulmonary toxicity: pneumonitis • skin toxicity: Steven-Johnson syndrome, toxic epidermal necrolysis. Examples of irAEs in order of frequency include: • Common ◦ endocrinopathies: thyroid dysfunction ◦ gastrointestinal toxicity: diarrhoea ◦ musculoskeletal toxicity: arthralgia, myalgia ◦ skin toxicity: rash, erythema, pruritus • Less common ◦ endocrinopathies: hypophysitis, type I diabetes mellitus ◦ gastrointestinal toxicity: colitis ◦ musculoskeletal toxicity: inflammatory arthritis ◦ ocular toxicity: dry eye ◦ renal toxicity ◦ skin toxicity: vitiligo • Rare ◦ endocrinopathies: primary adrenal insufficiency ◦ gastrointestinal toxicity: pancreatitis ◦ haematological toxicity ◦ musculoskeletal toxicity: vasculitis ◦ ocular toxicity: uveitis, iritis. Proactive monitoring, patient self-monitoring and early reporting of adverse events is critical. Treatment interruptions/discontinuation, consultation with specialist and administration of corticosteroids and/or supportive care is required to minimise the risk of death. Read more about the management of immune-related adverse events (irAEs)

Baseline investigations	Consider ECG and troponin at baseline. There is no clear evidence regarding the efficacy/value of baseline ECG or troponin in patients receiving immune checkpoint inhibitor therapy. Some cancer specialists obtain baseline testing, and others continue this through the initial period of therapy. Consider urinalysis at baseline, particularly in patients with additional risk factors for developing immune-related acute kidney injury.
Blood tests	FBC, EUC, eGFR, LFTs, serum cortisol, TFTs and BSL at baseline. Repeat FBC, EUC, eGFR, LFTs and BSL prior to each cycle and serum cortisol and TFTs alternate cycles. Check lipase and amylase if symptomatic of pancreatitis. In the absence of suspicion of immune-related adverse events less frequent monitoring may be applicable, according to institutional guidelines. Evidence for the frequency of routine blood testing with immunotherapies varies within published studies and guidelines. Read more about immunotherapy blood test monitoring recommendations.
Hepatitis and HIV	Hepatitis screening is recommended in all patients who are to receive immune checkpoint inhibitors. Immunotherapy is associated with inflammatory adverse reactions resulting from increased or excessive immune activity and patients are at risk of developing autoimmune hepatitis. It should be used with caution in patients who have a history of chronic hepatic infections (hepatitis B and C), detectable human immunodeficiency virus (HIV) viral load or acquired immune deficiency syndrome (AIDS).
Vaccinations	The safety of having vaccinations during treatment is unknown. Patients in the clinical trials were typically allowed to receive inactivated and recombinant vaccines but not live vaccines. Read more about COVID-19 vaccines and cancer.
Effects of cancer treatment on fertility	Studies to evaluate the effects of immune checkpoint inhibitor therapy on fertility have not been performed. Therefore, the effect on male and female fertility is unknown. Limited evidence supports that immune checkpoint inhibitor-related hypogonadism due to orchitis and hypophysitis can impact fertility. Immune checkpoint inhibitors can cause fetal harm when given to pregnant women. A pregnancy test should be considered 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. There is very limited evidence to provide guidance regarding contraception timelines. Some studies have demonstrated PD-1 receptor occupancy for greater than 9 months after anti-PD-1 therapy (Brahmer et al., 2010). As a result, some cancer specialists advise using contraception for at least six months or even as long as two years after treatment finishes. Read more about the effect of cancer treatment on fertility Link to Brahmer et al., 2010

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).

- dose reduction is not recommended
- no dose adjustment is required in the elderly, mild or moderate renal impairment or mild hepatic impairment. Pembrolizumab has not been studied in patients with severe renal impairment or moderate to severe hepatic impairment.

Management of immune-related adverse events (irAEs)

Link to Management of immune-related adverse events (irAEs)

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*

Pembrolizumab

No formal pharmacokinetic drug interaction studies have been conducted with pembrolizumab. Since pembrolizumab is cleared from the circulation through catabolism, no metabolic drug-drug interactions are expected.

	Interaction	Clinical management
Immunosuppressants (inc. corticosteroids)	Reduced efficacy of both immunosuppressants and pembrolizumab possible due to pharmacodynamic interaction	It is recommended that patients requiring corticosteroids **prior** to treatment receive the lowest possible dose (preferably no greater than 10 mg prednisolone or equivalent steroid per day). **Once started** on pembrolizumab the use of corticosteroids to treat immune related adverse events (irAEs) does not appear to impact the clinical response to pembrolizumab. In patients requiring ongoing corticosteroids **post management** of an irAE, the dose should be as low as possible. Monitor for signs of organ rejection in transplant recipients.
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely

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

Handling of monoclonal antibodies and waste management

Safe administration

Immunotherapy patient assessment prior to each treatment.

Any toxicity may require delay of treatment and review by medical officer before commencing treatment.

Prime IV line(s) with sodium chloride 0.9%.

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Administer antiemetics if required

Treatment - Time out

Pembrolizumab

Administer pembrolizumab:

- a low protein binding 0.2 micron to 5 micron in-line or add-on filter must be used
- attach a second IV line via a luer lock connector as close as possible to the site of injection
  - this may be required in case of a hypersensitivity reaction.
- via IV infusion over 30 minutes
- observe for infusion-related reactions
- flush with 50 mL of sodium chloride 0.9%
- do not co-administer other drugs through the same infusion line.

Mild or moderate infusion-related reaction:

- decrease the rate of infusion and monitor closely
- give any further doses with close monitoring
- premedication with paracetamol and an antihistamine should be considered for further doses.

Severe infusion reaction:

- stop infusion immediately
- medical officer review
- permanently discontinue pembrolizumab.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Discharge Information

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.

The most common side effects with this treatment are immune-related adverse events (irAEs). irAEs can escalate quickly and close monitoring of the patient is required. Symptoms should improve promptly after the introduction of immunosuppressive therapy. If this does not occur review the diagnosis and seek further specialist advice. Refer to the Management of immune related adverse events document for further information.

Immune related adverse events	
Cardiotoxicity	Cardiotoxicity is a rare but serious side effect, which may manifest as asymptomatic reduction in left ventricular ejection fraction (LVEF), arrhythmia, cardiomyopathy, myocarditis, pericarditis, cardiac fibrosis, hypertension, cardiac ischaemia, congestive heart failure (CHF) and cardiac arrest. Read more about Management of immune related adverse events.
Gastrointestinal toxicity	Colitis, diarrhoea or more bowel movements than usual; blood or mucous in stools; dark, tarry, sticky stools; abdominal pain or tenderness. Read more about Management of immune related adverse events
Haematological toxicity	Autoimmune haemolytic anaemia (AIHA), acquired thrombotic thrombocytopenic purpura (TTP), aplastic anaemia (AA), immune thrombocytopenia (ITP), acquired haemophilia (AH), haemolytic uremic syndrome (HUS) and lymphopenia are rare but potentially serious immune-related adverse events associated with immunotherapy treatment. Read more about Management of immune related adverse events.
Hepatotoxicity	Transaminase and total bilirubin elevation, jaundice, severe nausea or vomiting, pain on the right side of the abdomen, drowsiness, dark urine, bleeding or bruising more easily than normal, anorexia. Read more about Management of immune related adverse events.
Musculoskeletal toxicity	Inflammatory arthritis, temporal arteritis, arthralgia, myalgia, synovitis, vasculitis, polymyalgia-like syndrome and myositis. Read more about Management of immune related adverse events.
Neurological toxicity	Aseptic meningitis, myasthenia gravis, Guillain-Barre syndrome, encephalitis, meningeal symptoms, optic neuritis, neuropathy and acute inflammatory demyelinating polyneuropathy are infrequent but potentially serious immune-related adverse events associated with immunotherapy treatment. Read more about Management of immune related adverse events.
Ocular toxicity	Eye pain, blurred vision, Uveitis/iritis, episcleritis, blepharitis, optic neuritis, tear duct stenosis, conjunctivitis, hyperlacrimation, watery or dry eyes and photophobia. Read more about Management of immune related adverse events.
Other endocrinopathies	Type 1 diabetes mellitus, hypophysitis, hypopituitarism and adrenal insufficiency are infrequent but potentially serious immune-related adverse events associated with immunotherapy treatment. Read more about Management of immune related adverse events
Pulmonary toxicity	Radiographic changes, dyspnoea, new or worsening cough, hypoxia, tachycardia, chest pain or fever. Read more about Management of immune related adverse events.
Renal toxicity	Increase in serum creatinine, oliguria, haematuria, peripheral oedema and anorexia. Read more about Management of immune related adverse events.
Skin toxicity	Rash including full thickness, pruritus, skin blisters, ulceration and necrosis. Radiation recall can occur at site of previous radiation therapy. Symptoms include vesiculation, desquamation and ulceration of the skin. Read more about Management of immune related adverse events
Thyroid toxicity	Thyroid toxicity is common with immune checkpoint inhibitors. Hypothyroidism is most frequent however hyperthyroidism can also occur. Read more about Management of immune related adverse events

Non-immune related adverse events	
Fatigue	Read more about fatigue
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting

Evidence - Hodgkin lymphoma

The rationale for pembrolizumab, a humanised IgG4/k monoAb that blocks binding between PD-1 and its ligands, is due to the fact that malignant Reed-Sternberg cells in classical Hodgkin lymphoma frequently have 9p24.1 alterations, resulting in over-expression of PD-L1 and PD-L2.

The primary evidence supporting this protocol is provided by a single-arm, open-label phase II multicentre study (KEYNOTE-087) involving a total of 210 patients in three cohorts.[3] Which demonstrated strong anti-tumour activity with pembrolizumab in patients with relapsed/refractory Hodgkin lymphoma. This led to the approval of pembrolizumab for use in this population.

A subsequent phase III study KEYNOTE-204 which compared the use of pembrolizumab vs brentuximab vedotin in a total of 304 patients provided further robust evidence. This study is a multicentre, randomised, open-label study comparing the use of Pembrolizumab vs brentuximab vedotin in a total of 304 patients. Patients with relapsed or refractory classical Hodgkin lymphoma who were ineligible for or had relapsed after autologous stem cell transplant were included and randomly assigned 1:1 to receive pembrolizumab or brentuximab vedotin.[4]

Pembrolizumab 200 mg was administered intravenously, every 3 weeks and brentuximab vedotin 1.8 mg/kg was administered intravenously every 3 weeks. Treatment was administered for up to 35 cycles or until disease progression, unacceptable toxicity or investigator decision. The median duration of treatment was 305 days for Pembrolizumab and 146.5 days from brentuximab vedotin. This study showed an improved progression-free survival (PFS) compared with brentuximab vedotin.[4]

Pembrolizumab has also been studied in patients with classical Hodgkin lymphoma who were ineligible for or had relapsed after autologous stem cell transplant and experienced progression with or did not respond to brentuximab vedotin in the KEYNOTE-013 study.[5]

Efficacy

After a median follow-up of 8 months, the overall response rate (ORR) across all cohorts was 69% (CI 62.3-75.2). The complete response rate (CRR) overall was 22.4% (CI 16.9-28.6). Progressive disease (PD) occurred in 14.3% (CI 9.9-19.8).[3] Patients attaining a complete response (CR) could consider stopping pembrolizumab after a minimum of 6 months of treatment with ≥ 2 doses received after documented CR.[3]

Updated patient-reported outcomes out to 24 weeks were published in 2019.[6] There was an improvement in health-related quality of life at each time point across all three cohorts (as measured by The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 global health status/quality of life score and EuroQoL Five Dimensions Questionnaire).

Two-year follow-up of KEYNOTE-087 was presented at the American Society of Haematology (ASH) meeting in 2018.[7] Median follow-up was 27.6 months, and 5 of the 210 patients were still receiving pembrolizumab therapy. The ORR was 71.9% (95% CI, 65.3-77.9) and CRR 27.6% (95% CI, 21.7-34.2), response rate by cohort is seen in table below.[7] Median duration of response was 16.5 months, median PFS was 13.7 months and median OS was not reached. OS at 2 years was 90.9% and PFS was 31.3%.

In the KEYNOTE-204 study, the median time from randomisation to data cut-off was 25.7 months. The median PFS was 13.2 months (95% CI 10.9-19.4) for pembrolizumab and 8.3 months (95% CI 5.7-8.8) for brentuximab vedotin (HR 0.65 [95% CI 0.48-0.88]; p=0.0027. With an objective response seen in 65.6% of patients treated with pembrolizumab and 54.2% treated with brentuximab vedotin.[4]

In KEYNOTE-013, after greater than 4 years median follow up the CR rate was 19% with median duration of response and median overall survival not reached. The 36 month overall survival was 81%.[5]

Table 1. Objective response as assessed by blinded independent central review by International Working Group 2007 criteria

	Pembrolizumab group (n=151)	Brentuximab group (n=153)
Proportion of patients with objective response	99 (65·6% [57·4–73·1])	83 (54·2% [46·0–62·3])
Best overall response		
Complete response	37 (25%)	37 (24%)
Partial response	62 (41%)	46 (30%)
Stable disease	21 (14%)	36 (24%)
Progressive disease	26 (17%)	28 (18%)
Not evaluable	1 (1%)	1 (1%)
No assessment	4 (3%)	5 (3%)

Data are n (% [95% CI]) or n (%).

Table 2: Objective response as assessed by blinded independent central review by International Working Group 2007 criteria

Figure 1. Progression-free survival by blinded independent central review per International Working Group 2007 criteria. (A) including (B) excluding; clinical and imaging data following autologous or allogeneic haematopoietic stem-cell transplantation

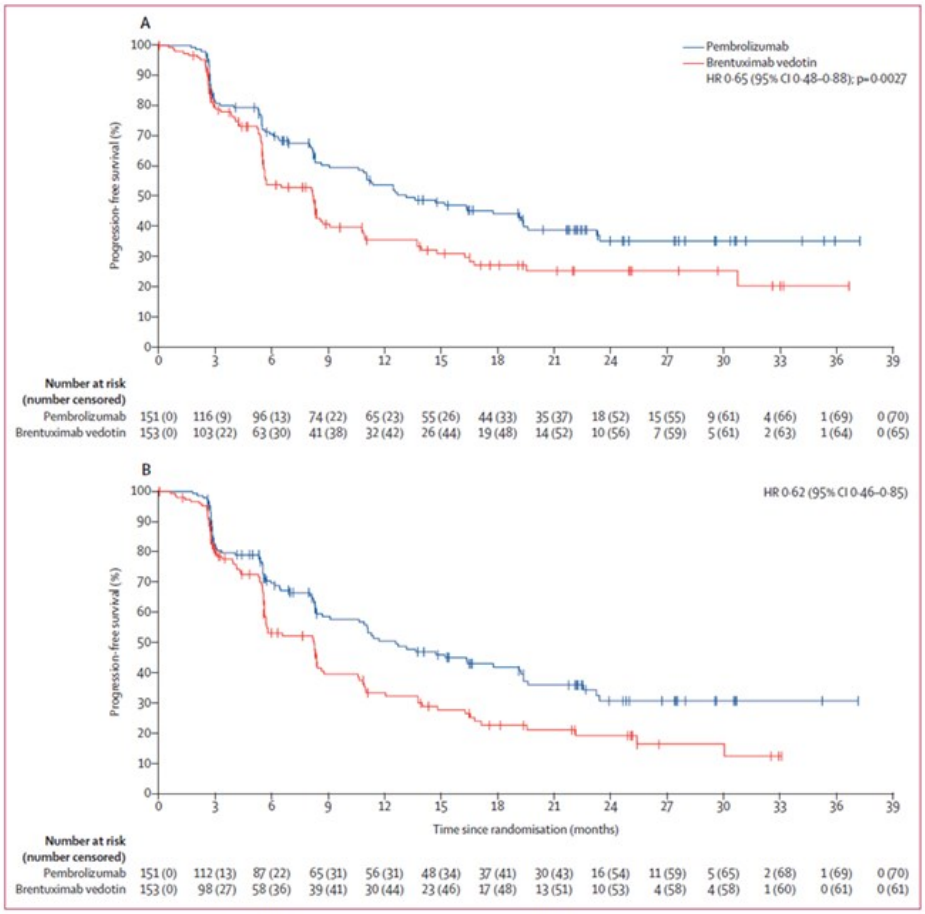


Figure 2: Progression-free survival by blinded independent central review per International Working Group 2007 criteria
Progression-free survival including (A) or excluding (B) clinical and imaging data following autologous HSCT or allogeneic HSCT. HSCT=haematopoietic stem-cell transplantation. HR=hazard ratio. HRs based on Cox regression model with Efron's method of tie-handling, with treatment as a covariate stratified by previous autologous HSCT (yes *vs* no) and classical Hodgkin lymphoma status after front-line therapy (primary refractory *vs* relapsed <12 months after completion of front-line therapy *vs* relapsed ≥12 months after completion of front-line therapy). One-sided p value based on log-rank test stratified by the same parameters as the HR.

Toxicity

The most common grade 3-5 treatment-related adverse events were pneumonitis in 4% of patients treated with pembrolizumab, neutropenia in 2%. Immune-mediated adverse events occurred in 33% of patients treated with pembrolizumab most commonly hypothyroidism; with grade 3-5 immune-mediated adverse events occurring in 7% of patients. One treatment-related death due to pneumonia occurred in the pembrolizumab group.[4]

Evidence - Primary mediastinal large B-cell lymphoma

Primary mediastinal large B-cell lymphoma (PMBCL) is a subtype of diffuse large B-cell lymphoma (DLBCL), however, it is molecularly different from DLBCL and shares many common features with the classical Hodgkin lymphoma (cHL) subtype, nodular sclerosing Hodgkin lymphoma (nsHL).

Most patients with newly diagnosed PMBCL are cured from standard frontline therapy such as DA-R-EPOCH with an overall survival (OS) rate of 97%.[8] For patients with relapsed/refractory PMBCL (rrPMBCL), however, prognosis is poor with limited treatment options because conventional chemotherapy is often ineffective in this setting.[9] CD30 expression is observed in over 80% of PMBCL, although it is weaker and more heterogeneous than that observed in classical Hodgkin Lymphoma.[10] The anti-CD30 immunodrug conjugate brentuximab does not seem to have significant activity[9] and a phase II trial in patients with rrPMBCL was terminated prematurely due to an unexpectedly low ORR.[10] Historically, patients with rrPMBCL have been treated with salvage regimens commonly used for DLBCL such as DHAP, mini-BEAM, often followed by transplant, with a 2-year OS of only 15%.[11] Outcomes are especially poor for patients who are ineligible for or relapse after second-line autologous stem cell transplantation.[9]

Pembrolizumab is a humanized anti-PD-1 monoclonal antibody that blocks the interaction of PD-1 and its ligands PD-L1 and PD-L2. Pembrolizumab has shown efficacy in cHL and is approved for the treatment of rrHL.[3] The rationale for pembrolizumab in the treatment of rrPMBCL, is that PMBCL, like cHL, frequently exhibits 9p24.1 alterations (including chromosome amplification) and overexpresses PD-1 ligands.[10, 12]

KEYNOTE-013 was a multicentre, international phase Ib study of pembrolizumab in patients with rrPMBCL, followed by a phase II trial (KEYNOTE-170).[9] For KEYNOTE-013, eligible patients included those with rrPMBCL who had either relapsed after, or were ineligible for autologous stem cell transplant (ASCT).[13] The first 10 patients received intravenous (IV) pembrolizumab at a dose of 10 mg/kg every 2 weeks for the trial's duration; however, after a study amendment, the subsequent 11 patients received an equivalent regimen with a fixed dose of pembrolizumab 200 mg every 3 weeks. Treatment continued up to 2 years until disease progression or unacceptable toxicity. Treatment response was assessed by PET CT at 6 and 12 weeks, and then every 9 weeks thereafter. For both KEYNOTE-013 and KEYNOTE-170, responses were assessed by a central review using International Working Group (IWG) 2007 Criteria and Lugano Criteria.[14] Primary endpoints of KEYNOTE-013 were safety and objective response rate (ORR) by investigator assessment. Secondary endpoints included complete response (CR), duration of response, and time to subsequent lymphoma therapy.

The preliminary efficacy and safety findings in the KEYNOTE-013 trial indicated pembrolizumab has the potential to provide clinical benefit in patients with rrPMBCL and led to the development of the phase II trial (KEYNOTE-170). Together these trials established the clinical benefit and safety of pembrolizumab in this patient population, with almost half of all patients in both studies having an objective and durable response.[9] KEYNOTE-170 was a multicentre, international phase II trial of pembrolizumab (MK- 3475) in 53 patients with rrPMBCL or relapsed/refractory Richter syndrome (rrRS). Eligible participants in the rrPMBCL cohort were those who had either failed ASCT or have failed two or more prior lines of therapy and were ineligible for ASCT.[13] Patients were also required to have an ECOG performance status of 0 or 1 and adequate organ function, and were excluded if they had active central nervous system (CNS) involvement or any autoimmune disease with systemic treatment in the past 2 years. Baseline patient characteristics were similar between the 2 studies.[9] Patients were treated with pembrolizumab 200 mg intravenously (IV) every 3 weeks for a maximum of 35 administrations (approximately 2 years) or until disease progression or unacceptable toxicity. Response was assessed by PET CT every 12 weeks. The primary endpoint was the ORR. Secondary endpoints included CR, ORR by investigator assessment, duration of response, OS, and safety/tolerability.

Based on the positive results of the interim data from the KEYNOTE-170 trial,[15] in June 2018, pembrolizumab was granted accelerated approval by the United States Food and Drug Administration for use in rrPMBCL patients who have progressed after two or more lines of prior therapy. The full trial data was published in 2019.[9]

Other references related to the use and rationale for pembrolizumab are noted in the reference section below.

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trials	Armand et al. 2019[9]	**Yes**	Yes	Interim data published by Zinzani et al. 2017[15]
Phase Ib trials	Zinzani et al. 2016[13]	**Yes**	N/A	-
Guidelines	**Date published/revised**	**Supports Use**	**Is the dose and regimen consistent**	**Comments**

			with the protocol?	
NCCN	March 2023	**Yes**	Yes	-
BCCA	February 2023	**Yes**	Yes	-
CCO	March 2023	**Yes**	Yes	

Efficacy

Twenty-one patients were treated in the phase 1b multi-cohort trial assessing the safety and efficacy of pembrolizumab in patients with rrPMBCL (KEYNOTE-013).[9] The median age of participants was 30 years, 72% female, with 61% of participants receiving a median of 3 prior lines of therapy and 33% having had prior ASCT.

Using the International Working Group 2007 criteria for response, the ORR was 48% (7 complete responses (CR), 33%, and 14% partial responses (PR)) amongst 21 patients. 24% had stable disease (SD), while 19% had progressive disease (PD). Median time to response was 2.7 months. The estimated progression-free survival (PFS) rate at 12 months was 47%, and median OS was 31.4 months.[9]

A follow-up of KEYNOTE-013 with investigator data and an additional 26 months follow-up for the PMBCL cohort was published in 2022. 21 patients with PMBCL were included in the study. In these patients, the ORR was 48% (6 patients with CR and 4 with PR). The median duration of response for responders with PMBCL was not reached with a median follow-up time of 10.8 months.[16]

The phase II study (KEYNOTE-170) showed a total of 53 patients with a median age of 33 years, 55% female, who were heavily pre-treated, receiving a median of three prior lines of therapy.[9] The ORR was 45% , with 13% achieving a CR (according to the IWG 2007 criteria) and 28% achieving a PR. 9% had SD with 23% showing progressive disease and 23% had no assessment (i.e., discontinued or died prior to the 24-week imaging assessment). 11 patients (21%) had CR with assessment by Lugano criteria. 75% of 40 evaluable patients had an overall reduction from baseline in target lesion size. Median time to response was 2.8 months. Pembrolizumab was well-tolerated with a 1-year OS of 62%[15] and the estimated PFS rate at 12 months was 38%. After a median follow-up time of 12.5 months, the median duration of response was not reached. No patient with complete response (in either study, as determined by central review) experienced progression, including 2 patients with complete response for at least 1 year off therapy.

A follow-up of KEYNOTE-170 presented at ASH in 2021. After a median duration of follow-up of 48.7 months, the ORR was 41.5%, with 20.8% achieving CR and 20.8% achieving PR. The median PFS was 4.3 months and the median OS was 22.3 months. The 48-month OS rate was 45.3%.[17]

Overall these results showed that almost half of patients in both studies had an objective response. The responses also appeared to be durable, particularly in the patients who achieved complete response.

Toxicity

Overall, the results from the phase IB study (KEYNOTE-013) and the phase II study (KEYNOTE-170) showed that pembrolizumab was generally well-tolerated.[9] 15 patients (71%) in the KEYNOTE-013 study and 30 patients (57%) in the KEYNOTE-170 study experienced treatment-related adverse events (TRAEs) of any grade.[15] Grade 3 or 4 events occurred in 5 patients (24%) and 12 patients (23%) in KEYNOTE-013 and KEYNOTE-170 respectively – the most common being neutropenia which occurred in 13-14% and caused one patient in each study to discontinue treatment. There were no treatment-related deaths. Other grade 3/4 TRAEs included myositis in 1 patient and pneumonitis in 1 patient.[9]

In the 4 year follow-up presented by Zinzani et al. at ASH 2022, in KEYNOTE-170 grade 3-4 TRAEs occurred in 22.6% of patients.[17]

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History

Version 4

Date	Summary of changes
14/04/2022	Protocol updated based on the consensus gained at the immunotherapy reference committee meeting held on 4th of March 2022. The following changes have been made across all immune checkpoint inhibitor protocols:

Date	Summary of changes
	• Indications and patient populations- previous radiation to the lungs added to precautions. • Clinical information- general irAEs, hepatitis and HIV, and fertility blocks updated. Individual irAE-related blocks removed. New block (baseline investigations) added. • Patient information- pregnancy and breastfeeding block in general advice section updated. Version number increased to V.4.
19/09/2023	Reviewed electronically by the Haematology Reference Committee with the following changes made: • Addition of note under treatment schedule about alternate dosing. • Update of evidence for both indications to include updated trial data. Review in 2 years.

Version 3

Date	Summary of changes
22/10/2021	Protocol reviewed by Haematology reference committee. Indication and evidence for PMBCL updated. Version number increased to V.3, for review in 2 years.

Version 2

Date	Summary of changes
18/11/2020	Protocol updated to align with ID 1993 Management of immune-related adverse events (irAEs) clinical resource which has been electronically reviewed and approved by the eviQ immunotherapy reference committee. The following changes have been made across all immune checkpoint inhibitor protocols: • Treatment schedule - additional note added: transient tumour flare and radiation recall. • Clinical information- cardiotoxicity, haematological toxicity, musculoskeletal toxicity and ocular toxicity added; rheumatological toxicity removed; immunotherapy clinical information changed to alphabetical order. • Side effects- haematological added; rheumatological replaced with musculoskeletal; immunotherapy side effects changed to alphabetical order. Arthralgia and myalgia non-irAE side effect removed to align with other immune checkpoint inhibitor protocols. Version number increased to V.2.

Version 1

Date	Summary of changes
15/11/2019	New multi-indication protocol developed and presented at the Haematology Reference Committee meeting in September. Protocol combined ID 3419 Hodgkin lymphoma pembrolizumab and new indication primary mediastinal large B-cell lymphoma. Approved and published on eviQ. Review in 1 year.

As ID 3671 Pembrolizumab replaces the ID 3419 Hodgkin lymphoma pembrolizumab protocol, this History section is included below for consistency in documentation.

ID 3419 Hodgkin lymphoma pembrolizumab version 1	
Date	**Summary of changes**
21/06/2018	New protocol developed and presented at the May Haematology Reference Committee meeting. Discussion continued over email and protocol approved for publication with a second yearly review period.

First approved: 13 September 2019
Last reviewed: 19 September 2023
Review due: 31 December 2025

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/3671
26 Nov 2023

Patient information - Lymphoma - Pembrolizumab

Patient's name:

Your treatment

It is important to understand that pembrolizumab is not a traditional chemotherapy drug and has a different way of working. It is an immunotherapy treatment (also called anticancer drug) that works with your immune system to detect and destroy cancer cells. Immunotherapy can potentially affect any organ of the body.

The treatment schedule below explains how the immunotherapy drug for this treatment is given.

Pembrolizumab

This treatment cycle is repeated every 21 days. It can also be repeated every 42 days at a higher dose. Your doctor will advise you of the number of treatments you will have.

Day	Treatment	How it is given	How long it takes
1	**Pembrolizumab** (*pem-broe-LIZ-ue-mab*)	By a drip into a vein	About 30 to 60 minutes

Prior to your treatment tell your doctor if you are taking any other medicines (e.g. corticosteroids, immunosuppressive therapy), have or ever had chronic liver infections e.g. hepatitis B (HBV) or C (HCV), human immunodeficiency virus (HIV) or an organ transplant.

When to get help

It is important that you tell your doctor or nurse immediately if you develop any of the symptoms listed below in the side effects section. If you can't contact your doctor or nurse, go to your nearest hospital Emergency Department for help.

Emergency contact details

Ask your doctor or nurse from your treating team who to contact if you have a problem

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
- 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

Treatment delays

There may 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. Your doctor will explain if you need any delays to your treatment and the reason why.

Blood tests and monitoring

You will need to have a blood test before you start treatment and regularly throughout your treatment. 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

- **Steroids:** you may be given some steroid tablets to help reduce immune-related side effects. Your doctor or nurse will tell you how and when to take the steroids. You may need to monitor your blood sugar levels closely while you are taking steroids. If you have diabetes, your diabetic medication may need to be adjusted because of the effects of steroids. Speak to your diabetes advisor.

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.

Immunotherapy may cause serious immune reactions against your own body. These are called immune-related adverse events. They may occur during your treatment, or after your treatment has ended. Immunotherapy can affect many parts of your body. Some side effects can cause severe or life threatening conditions, so even mild side effects must be reported immediately. Do not try to treat these symptoms yourself without talking to your doctor or nurse first.You will be given an information pack at the start of your treatment. This contains an alert card which you should carry with you at all times. Bring this alert card with you to hospital, especially if you are unwell or attending the emergency department.

Immune related side effects	
Heart problems	• You may get: ◦ chest pain or tightness ◦ shortness of breath ◦ swelling of your ankles ◦ an abnormal heartbeat. • Heart problems are uncommon but potentially fatal. If heart problems were to occur, symptoms usually start within the first 3 months of treatment, but can happen at any time even after the treatment has finished. • Tell your doctor if you have a history of heart problems or high blood pressure. • Before or during treatment, you may be asked to have a test to see how well your heart is working. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.**

Bowel and stomach inflammation	• You may get: ◦ bowel motions (stools, poo) that are more frequent or more liquid (diarrhoea) ◦ blood or mucous in your stool ◦ dark, tarry, or sticky bowel motions ◦ bloating, cramping, pain or tenderness in your stomach area. • Inform your doctor or nurse immediately if you get diarrhoea • Take your anti-diarrhoeal or steroid medication as directed by your doctor. • Drink plenty of fluids (unless you are on a fluid restriction). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled despite taking anti-diarrhoea medicine, severe stomach pains and bloating, and/or if you feel dizzy or light-headed.**
Blood problems	• Blood problems are infrequent but can be serious. • You may feel dizzy, light-headed, tired, weak and appear more pale than usual. • You may get: • dark, tarry bowel motions (stools, poo) • blood in your urine or not urinating as often • dark-coloured urine • yellowing of the whites of your eyes, and/or your skin • pinpoint red spots on your skin • unexplained bleeding • major bruising • a fever • shortness of breath • a severe headache • confusion • faster heartbeat than normal • **Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if it has been longer than 12 hours since you have emptied your bladder or if you get any of the symptoms listed above.**
Liver damage	• You may get: ◦ fatigue ◦ severe nausea and vomiting ◦ weight loss ◦ bruising or bleeding more easily ◦ pain or tenderness on the right side of your stomach area ◦ dark coloured urine ◦ yellowing of the whites of your eyes and/or your skin ◦ itchy skin ◦ drowsiness • You will have regular blood tests to check how well your liver is working. • Take your steroid medication as directed by your doctor. • **Tell your doctor or nurse as soon as possible if you notice that your urine is a dark colour, the whites of your eyes or skin look yellow, if you have unexplained bruising or bleeding or if you have severe stomach pain.**
Muscle and joint problems	• You may get: • muscle or joint stiffness, especially after a period of rest • muscle weakness • pain in your muscles or joints • joint swelling • tiredness • headaches • Take your pain relief or steroid medication as directed by your doctor. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above.**

Nervous system problems	• Nervous system changes are rare, but can be serious. • You may get: ◦ headaches ◦ fever ◦ stiff neck ◦ confusion or difficulty concentrating ◦ dizziness or drowsiness ◦ loss of consciousness ◦ muscle weakness or pain ◦ numbness or tingling in your hands or feet ◦ jerky movements. • Take your steroid medication as directed by your doctor. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.**
Eye problems	• You may get: ◦ eye pain ◦ itchy eyes ◦ red or swollen eyes ◦ blurred or change in vision ◦ change in colour vision ◦ watery or gritty eyes ◦ dry eyes ◦ sensitivity to light. • Protect your eyes from the weather (sun and wind) by wearing sunglasses. • Use your eye drops or take your steroid medication as directed by your doctor. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above.**
Hormone problems	• Hormone changes are infrequent, but can be serious. • You may get: ◦ headaches ◦ tiredness, dizziness or fainting ◦ abnormal heartbeat (faster than usual) ◦ a feeling of being hot or cold more easily ◦ excessive sweating ◦ weight changes ◦ a deepened voice ◦ irregular or absent periods ◦ nausea and vomiting ◦ thirsty and need to urinate more often than normal ◦ high blood sugar levels ◦ pain in your stomach area ◦ muscle pain or weakness ◦ difficulty sleeping ◦ agitated more easily ◦ changes in your mood or behaviour, such as decreased sex drive or irritability. • Take your hormone or steroid medication as directed by your doctor. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you feel confused, weak, dizzy, or faint, or get sudden pain in your lower back or legs.**

Lung problems	• You may get: ◦ shortness of breath ◦ difficulty breathing ◦ faster heartbeat than normal ◦ chest pain ◦ new or worsening cough ◦ fever. • Your doctor will monitor how well your lungs are working during your treatment. • Take your steroid medication as directed by your doctor. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.**
Kidney damage	• This treatment can cause changes to how your kidneys work. • You may get: ◦ a feeling of needing to urinate less often than normal ◦ blood in your urine ◦ swollen hands and feet ◦ loss of appetite. • You will have regular blood tests to check how well your kidneys are working. • You may need to drink more fluids while you are having treatment. Your doctor or nurse will tell you if you need to do this. • Take your steroid medication as directed by your doctor. • **Tell your doctor or nurse as soon as possible if you notice that your urine changes colour or you don't need to empty your bladder as often.**
Skin rash	• You may get ◦ a red rash ◦ a bumpy rash ◦ dry and itchy skin ◦ skin peeling or blisters. ◦ if you have had previous radiation therapy to an area this effect may be worse • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Avoid scratching your skin. • Avoid wearing tight fitting clothing • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • Take your antihistamine medication or apply your steroid cream as directed by your doctor. • **Tell your doctor or nurse as soon as possible if you notice any changes to the rash like pain or pus forming.**

Thyroid problems	Thyroid problems are common with this treatment. The most common problem is an underactive thyroid gland (hypothyroidism), occasionally you may get an overactive thyroid gland (hyperthyroidism). • If you have an **underactive** thyroid, you may get: ◦ fatigue and low energy levels ◦ depression ◦ slow heart rate ◦ unexplained weight gain ◦ intolerance to cold temperatures ◦ fatigued and aching muscles ◦ dry, coarse skin ◦ puffy face ◦ hair loss ◦ constipation ◦ problems with concentration ◦ changes in your periods • If you have an **overactive** thyroid, you may get ◦ abnormal heartbeat (faster than usual) ◦ a feeling of being hot or cold more easily ◦ excessive sweating ◦ difficulty sleeping ◦ anxiety, nervousness or agitated more easily ◦ diarrhoea ◦ changes in your periods • You will have regular blood tests to check how well your thyroid is working. • Take your hormone or steroid medication as directed by your doctor. • Tell your doctor or nurse if you get any of the symptoms listed above.

Non-immune related side effects	
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.**
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • 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. • Anti-sickness medication is usually not needed but may help in some people. • 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.**

General advice for people having cancer treatment

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 treatments.
- 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.
- Don't have **any** vaccinations without talking to the doctor who is managing your cancer treatment.
- People you live with should be fully vaccinated, 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.
- 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 more 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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