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Clinical Commissioning Policy:

Vemurafenib plus rituximab for patients with relapsed or refractory classic hairy cell leukaemia (HCL) (Adults) [2318]

Summary

Vemurafenib plus rituximab is not recommended to be available as a routinely commissioned treatment option for adult patients with classic hairy cell leukaemia (HCL) who are either a) refractory to first-line treatment with a purine analogue (PA) therapy; or b) refractory to, or relapse following, treatment with a second-line purine analogue (PA) therapy with or without rituximab; or c) for patients who are unsuitable for PA therapy at any time.

The policy is restricted to certain age groups as there is insufficient evidence to confirm safety and/or it is not recommended through the licence authorisation process to be used in those age groups not included in the policy.

Committee discussion

Clinical Panel considered the evidence base and the recommendation was made to progress the policy. Please see Clinical Panel reports for full details of Clinical Panel's discussion.

The Clinical Priorities Advisory Group committee papers can be accessed here.

What we have decided

NHS England has carefully reviewed the evidence to treat adult patients with classic HCL who are either a) refractory to first-line treatment with a PA therapy; or b), refractory to, or relapse following, treatment with a second-line PA therapy with or without rituximab; or c) for patients who are unsuitable for PA therapy at any stage, with vemurafenib plus rituximab. NHS England recognises that the published evidence identifies that, at present, there is sufficient evidence to commission this treatment. However, following the relative prioritisation process undertaken in May 2024, NHS England has concluded that, balanced against other relative priorities that were also considered during this process, Vemurafenib plus rituximab for patients with relapsed or refractory classic hairy cell leukaemia (HCL) will not be funded at this time within the resources available.

The evidence review can be accessed here.

Links and updates to other policies

Not applicable

Plain language summary

About classic hairy cell leukaemia (HCL)

Hairy cell leukaemia (HCL) is a very rare type of leukaemia (blood cancer). In patients with HCL there is an excess number of lymphocytes (a type of white blood cell) in the blood. These lymphocytes are abnormal and cannot help to defend the body against infection. Classic HCL is characterised by a mutation called BRAF V600E which is present in all leukaemic cells. This differentiates classic HCL from hairy cell leukaemia variant (HCL-V), which does not harbour BRAF mutations. Classic HCL predominantly affects middle-aged individuals and is more common in males than females. Symptoms of classic HCL can include: weight loss, weakness and frequent infections. However, approximately 25% of patients have no symptoms at the time of diagnosis and are identified based on the findings of routine blood tests. The majority of patients with classic HCL will require treatment soon after diagnosis.

About current treatment

The first-line treatment for patients with classic hairy cell leukaemia are cytotoxic drugs called purine nucleoside analogue (PA) therapy. A single PA therapy (either cladribine or pentostatin) is the current standard care. The standard length of treatment with cladribine monotherapy for classic HCL is 5 days (given by subcutaneous injection just under the skin). Pentostatin is administered intravenously (IV) every 14 days until a maximum response (e.g. normalisation of blood counts) has been achieved; a further 2 doses should then be given. On average ten doses are required. With treatment, classic hairy cell leukaemia can generally be kept under control for many years. The median time after first-line treatment before relapse (cancer returns) is around 11 years (Cancer Research UK, 2022).

However, there is a significant minority of patients who do not respond or become resistant (refractory) to PA therapy. Additionally, some patients will relapse sooner than others following first-line treatment with PA therapy. For patients who are refractory to first-line PA therapy, or who relapse within 2 years following PA therapy, standard second-line treatment is generally with an alternative PA therapy in combination with rituximab. Patients who relapse within 2-5 years following PA therapy, can be retreated with the initial PA therapy plus rituximab. Patients who relapse beyond 5 years from the end of initial treatment with PA therapy can be re-treated with the same, or an alternative, single agent PA therapy, plus or minus rituximab.

About vemurafenib plus rituximab

The proposed intervention is for vemurafenib plus rituximab in adult patients with classic hairy cell leukaemia who are either a) refractory to first-line treatment with a purine analogue (PA) therapy; or b) refractory to, or relapse following, treatment with a second-line purine analogue (PA) therapy with or without rituximab; or c) for patients who are unsuitable for PA therapy at any stage. For the purposes of this policy, refractory disease is defined as a failure to achieve at least a partial response (PR) 3-6 months from the end of treatment with cladribine or pentostatin. A PR is defined by the international consensus guidelines as requiring near normalisation of the peripheral blood count with a minimum of 50% improvement in organomegaly and bone marrow biopsy infiltration with HCL (Grever et al. *Blood* 2017). Relapsed disease is defined as the return of the cancer following a period of remission.

Vemurafenib is a BRAF-inhibitor which targets the BRAF V600E mutation that drives the increase in classic hairy cell leukaemia. Vemurafenib is a film-coated tablet which is taken by mouth (orally). Vemurafenib is proposed along with rituximab as vemurafenib-resistant leukaemic cells retain strong CD20 expression. As an anti-CD20 monoclonal antibody, the aim of concurrent treatment with rituximab is to target these cells. Rituximab is administered as an intravenous infusion. This will be a fixed length of treatment for a maximum duration of 8 weeks of treatment with vemurafenib and 18 weeks (8 doses) for the concurrent and sequential administration of rituximab.

The use of vemurafenib for the proposed indication is off label. The use of rituximab for the proposed indication is also off-label.

Epidemiology and needs assessment

Classic HCL has an annual incidence of 0.3 per 100,000 individuals in England. This equates to approximately 210 new cases of HCL diagnosed in England every year (Cancer Research, 2021). According to clinical consensus, 3-4% of all patients diagnosed with classic HCL are refractory to, or relapse following, systemic purine nucleoside analogue (PA) therapy plus or minus rituximab. Younger patients under the age of 40 years are more likely to have shorter remissions following PA therapy than patients aged over 40 years (Rosenberg et al. 2014). A further 3% of patients are estimated to be unsuitable for PA therapy. This equates to approximately 15 patients per year in England who would be suitable for treatment with vemurafenib plus rituximab.

Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Definitions

Chemotherapy	A cancer treatment where medicine is used to kill cancer cells. The most common types of chemotherapy are either given into a vein (intravenous) or as chemotherapy tablets (oral chemotherapy).
Mutation	A change or alternation to genetic material. Mutations can result in altered function of the gene which can be harmful or beneficial. In cancer the mutations are usually harmful.
Proliferation	The growth or spread of cells.
Radiotherapy	A cancer treatment where radiation is used to kill cancer cells.
Refractory	Refractory disease is defined as a failure to achieve at least a partial response (PR) 3-6 months from the end of treatment with cladribine or pentostatin. A PR is defined by the international consensus guidelines as requiring near normalisation of the peripheral blood count with a minimum of 50% improvement in organomegaly and bone marrow biopsy infiltration with HCL (Grever et al. *Blood* 2017).
Relapsed	When cancer returns after a period of remission.

References

Cancer Research UK What is hairy cell leukaemia? 2022. Available at: https://about-cancer.cancerresearchuk.org/about-cancer/hairy-cell-leukaemia/about (Accessed: 24 July 2023)

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