reference no: 2269
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Clinical Commissioning Policy:

Neoadjuvant vismodegib for locally advanced basal cell carcinoma (BCC) prior to curative treatment for lesions likely to result in functional sequelae or significant aesthetic sequelae (Adults) [URN 2269]

Summary

Neoadjuvant vismodegib is recommended to be available as a routinely commissioned treatment option for locally advanced basal cell carcinoma (BCC) prior to curative treatment for lesions likely to result functional sequelae or significant aesthetic sequelae within the criteria set out in this document. Patients must be suitable or potentially suitable for curative treatment at baseline.

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 agreed with the policy and recommended this proceeds as a routine commissioning 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: Clinical commissioning policy: Neoadjuvant vismodegib for locally advanced basal cell carcinoma (BCC) prior to curative treatment for lesions likely to result in functional sequelae or significant aesthetic sequelae (adults)

What we have decided

NHS England has carefully reviewed the evidence to treat locally advanced BCC for lesions likely to result in functional sequelae or significant aesthetic sequelae with neoadjuvant vismodegib. We have concluded that there is enough evidence to make the treatment available at this time.

The evidence review which informs this commissioning position can be accessed here: Clinical commissioning policy: Neoadjuvant vismodegib for locally advanced basal cell carcinoma (BCC) prior to curative treatment for lesions likely to result in functional sequelae or significant aesthetic sequelae (adults)

Links and updates to other policies

This document relates to: 210504P NHS England Clinical Commissioning Policy: Vismodegib for adults with either Gorlin syndrome or non-Gorlin syndrome related multiple basal cell carcinomas. (Adults)

Plain language summary

About locally advanced basal cell carcinoma

Basal cell carcinomas (BCCs) are slow-growing, malignant skin tumours which develop in the top layer of skin (epidermis). The majority of BCCs affect chronically sun-exposed areas such as the face, head and neck. Basal cell carcinoma is more common in the Caucasian population, particularly amongst older people.

The majority of cases of BCC are cured fairly straightforwardly with topical creams, cryotherapy (using cold temperatures to remove the cancer), surgical removal or radiotherapy. However, in some cases, either where the BCC has been left to enlarge for a long time without treatment, or in cases of recurrence following first-line treatment, the BCC can go on to cause progressive destruction of surrounding tissue structures. This is termed locally advanced BCC and is more difficult to treat.

About current treatment

The current standard treatment for patients with locally advanced BCC is surgery or radiotherapy. Most BCCs affect the face and a common site for locally advanced BCC is the eyelid. If the locally advanced BCC extends to involve the tissues and muscles of the orbit, then the only curative surgery is orbital exenteration (removal of the eye and surrounding soft tissues.) The resulting defect requires major reconstructive surgery, and the patient is often left with severe facial disfigurement. Other types of radical curative surgery for locally advanced BCC include rhinectomy (amputation of the nose) and removal of the ear. Radiotherapy to the face, particularly around the eye, can cause a painful eye and eventual visual loss. Additionally, radiotherapy is not always possible for patients with locally advanced BCC, either due to the patient having had previous radiotherapy at the same site, or for technical reasons. However, locally advanced BCC's can occasionally affect areas other than the head and neck, such as the trunk or perianal region. Radical curative treatment in these areas may involve extensive surgery or radiotherapy, which may result in, for example, loss of function of an affected limb or the removal of the rectum and affected bowel.

Locally advanced BCC most commonly affects the elderly population, many of whom will have significant comorbidities and may be unable to undergo extensive curative treatment in the form of radical surgery and/or radical radiotherapy. For these patients, the only option is best supportive care.

About neoadjuvant vismodegib

Vismodegib is an oral tablet which blocks one of the key cell signalling pathways that causes BCCs to grow and become locally advanced. This signalling pathway is called the Hedgehog (Hh) signalling pathway. Vismodegib is proposed as a neoadjuvant for the treatment of locally advanced BCC for lesions likely to result in functional sequelae or significant aesthetic sequelae, for a defined period of up to 10 months, prior to treatment with curative surgery and/or curative radiotherapy. The aim of the treatment is to downstage locally advanced BCC in order to de-escalate the extent of curative treatment required.

Vismodegib is licensed for use in adult patients with symptomatic metastatic BCC and locally advanced BCC inappropriate for surgery or radiotherapy. The neoadjuvant use of vismodegib as outlined in this policy is off-label.

NICE Technology Appraisal (TA) TA489 covers the use of vismodegib for the treatment of BCC in adults. NICE TA489 recommended that vismodegib not be made available for its licensed indications. This was due to uncertainty in the evidence and lack of cost-effectiveness. The population covered in this NHS England clinical commissioning policy policy differs from the population covered by NICE TA489. NICE TA489 covers the licensed use of vismodegib for adult patients with symptomatic metastatic BCC or locally advanced BCC that is inappropriate for surgery or radiotherapy. The neoadjuvant use of vismodegib for locally advanced BCC in this policy is off-label, and therefore is outside of the scope of NICE TA489. In addition, patients included in this policy must be suitable, or potentially suitable, for curative treatment at baseline and will receive neoadjuvant for a maximum duration of 10 months only.

Epidemiology and needs assessment

The incidence of BCC varies across the UK. The highest incidence of BCC rates was observed in Southwest England at 362 per 100,000 of the population per year (Venables et al. 2019). BCC is less prevalent in non-Caucasian racial ethnic groups, but when they occur they tend to be diagnosed at a later stage. The median age of diagnosis for BCC is 71 years (Venables et al. 2019).

It is estimated that only 0.8% of BCCs become locally advanced (Goldenberg et al. 2016). In England this translates to around 530 individuals with locally advanced BCC. The population eligible for neoadjuvant treatment (treatment administered prior to curative treatment) with vismodegib in this policy is patients who are suitable or potentially suitable for curative treatment at baseline (curative surgery and/or curative radiotherapy) and who have lesions likely to result in functional sequelae or significant aesthetic sequelae. Clinical consensus estimates that there are likely to be approximately 120 patients per year who would be eligible for neoadjuvant treatment with vismodegib.

Locally advanced BCC is rarely the primary cause of mortality in the population of interest. The intent of treatment with neoadjuvant vismodegib is to reduce morbidity.

Implementation

Inclusion criteria

Adult patients (aged 18 years and above) should be considered for neoadjuvant treatment with vismodegib if they meet **ALL** of the following criteria:

- A confirmed histopathological diagnosis of locally advanced, non-metastatic basal cell carcinoma

  AND

- Have an Eastern Cooperative Oncology Group (ECOG) performance status of ≤2 at baseline

  AND

- Have been determined by an appropriate MDT[1] to have a lesion likely to result in functional sequelae or significant aesthetic sequelae[2] and to be suitable or potentially suitable for curative treatment at baseline.

All patients considered potentially suitable for treatment with neoadjuvant vismodegib by an appropriate local MDT, in line with the eligibility criteria, will be referred to the Specialist Skin Cancer MDT (SSMDT) for a final decision regarding treatment. Indications constituting functional sequelae or significant aesthetic sequalae and which would indicate eligibility for treatment with neoadjuvant vismodegib are as below:

  - Total or partial removal or alteration of an organ[3] that will result in a functional impairment
  - Total or partial loss or alteration of a limb that will result in functional impairment
  - Large radiotherapy field size likely to result in significant complications including, but not limited to chronic radiation damage, radiation-related skin toxicity, potential changes to underlying structures and/or detrimental impact on surgical wound healing
  - Where curative treatment will result in severe disfigurement (significant aesthetic sequelae) that is likely to cause significant psychological distress

Exclusion criteria

Patients are excluded if they meet **ANY** of the following criteria:

- Patients covered by NICE TA489 for adult patients with symptomatic metastatic BCC or locally advanced BCC that is inappropriate for surgery or radiotherapy
- Patients under the age of 18 years
- Patients who are pregnant or breastfeeding
- Patients of childbearing potential who do not comply with the Erivedge Pregnancy Prevention Programme
- Patients who are determined to be unsuitable for curative treatment at baseline
- Patients who have previously received neoadjuvant treatment with vismodegib, or any other Hedgehog pathway inhibitor, for the treatment of the same lesion(s)

Stopping criteria

Treatment will be stopped in patients who meet **ANY** of the following criteria:

- An optimal response has been reached to facilitate curative treatment as determined by treating clinician(s)

[1]An appropriate MDT should, as a minimum, have representation from the following specialties: a consultant clinical oncologist, a consultant dermatologist and a consultant surgeon with expertise appropriate to the disease-specific area.
[2]There is no formally agreed, standardised criteria for determining whether a patient may be suitable or potentially suitable for curative treatment. It is suggested that the categorizations used by Bertrand et al. 2021 would provide a suitable framework to aid an MDT it its decision-making process. The Bertrand et al. 2021 table is located in Annex A.
[3] This includes sensory organ(s)

- A maximum treatment duration of 10 months is reached
- Disease progression whilst on treatment
- Unacceptable toxicity
- Patient decision to stop treatment

Dosing

The neoadjuvant use of vismodegib to treat locally advanced BCC prior to curative treatment for lesions likely to result in functional sequelae or significant aesthetic sequelae is off-label and Trust policy regarding off-label use of medicines should apply.

The recommended dose for the neoadjuvant treatment of locally advanced BCC is 150mg taken once daily. Dose adjustments are not permitted. Treatment break(s) are permitted to allow toxicity to improve. Where a treatment break of more than 6 weeks beyond the expected 4-week cycle length is needed, completion of a treatment break approval form to restart treatment is required.

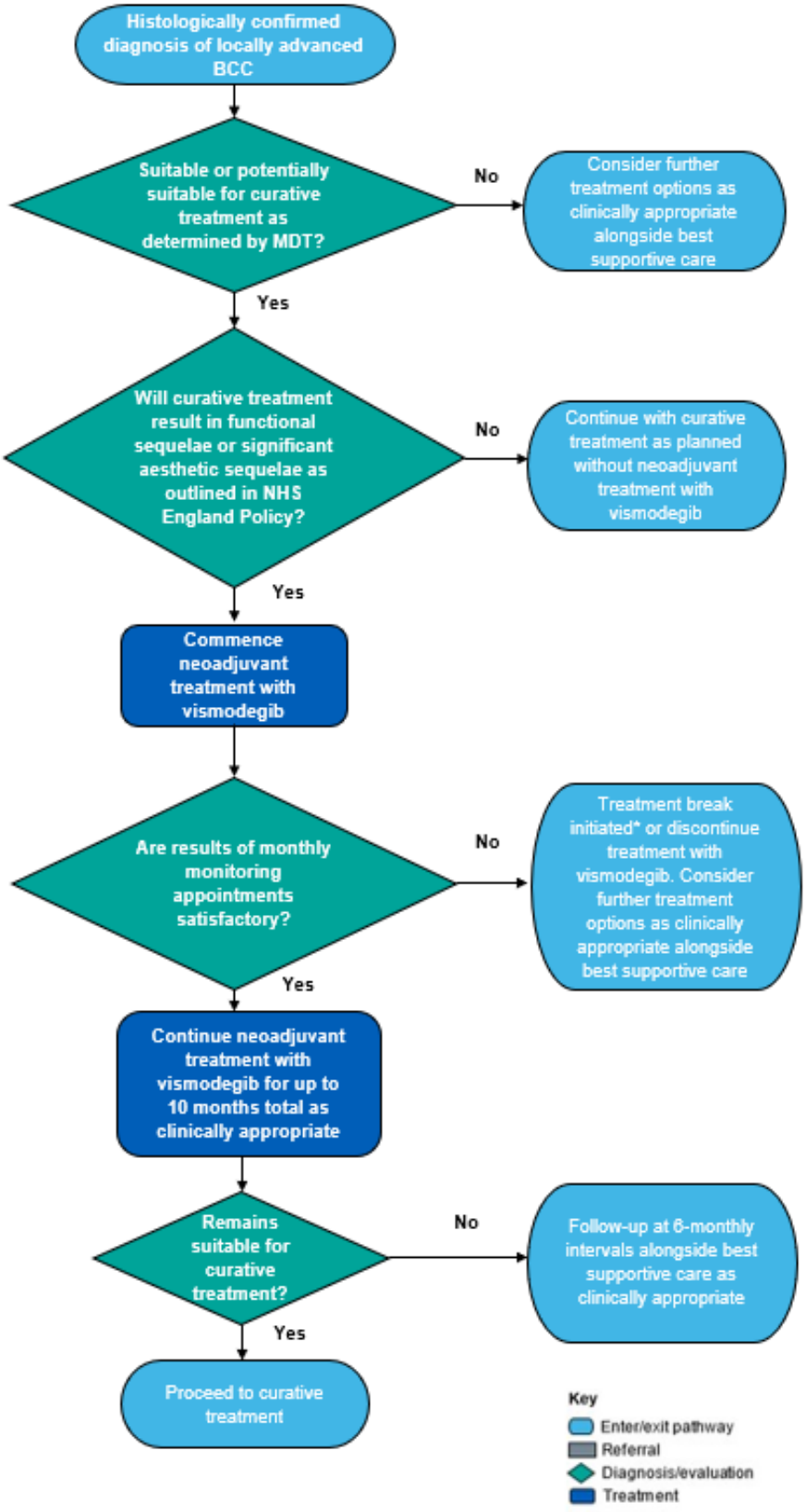
Monitoring

A formal medical review should take place prior to initiation of treatment with neoadjuvant vismodegib with appropriate baseline investigations including imaging if required. Further medical reviews to assess the tolerability of treatment, and to determine whether or not the treatment should continue to be carried out, should take place monthly from the date of treatment initiation.

Patients who receive treatment with neoadjuvant vismodegib for a maximum duration of 10 months and who subsequently elect not to undergo curative treatment, or for whom curative treatment is no longer indicated (e.g., due to histological remission), should be offered lifelong follow up by a suitable clinician at 6-monthly intervals[4] with appropriate monitoring investigations including imaging if required. If tumour recurrence occurs during this follow-up period, curative treatment can be initiated before the recurrent lesion spreads to become locally advanced. Patients who have previously undergone neoadjuvant treatment with vismodegib for a locally advanced BCC would not be eligible for a further round of neoadjuvant treatment for the same lesion(s) in the event of a recurrence.

[4] Follow-up appointments at shorter intervals would only be required if the patient noticed a sooner recurrence.

Patient pathway



* Where a treatment break of more than 6 weeks beyond the expected 4-week cycle length is needed, completion of a treatment break approval form to restart treatment is required.

Governance arrangements

Service Specification: Cancer: Chemotherapy (Adult) B15/S/a

Provider organisations must register all patients using prior approval software and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined. Any provider organisation treating patients with this intervention will be required to assure itself that the internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the Trust's Drugs and Therapeutics committee (or similar) and NHS England may ask for assurance of this process.

Please note that the neoadjuvant use of vismodegib is off-label, therefore Trust policy regarding unlicensed medicines should apply.

Mechanism for funding

Vismodegib is categorised as a high-cost drug to be reimbursed under the cost and volume process.

Audit requirements

All systemic anti-cancer treatments (SACT) must be recorded via the SACT portal as required within the NHS standard contract. There are no specific audit requirements, however data collection using case report forms (CRF) to facilitate a multicentre service evaluation is strongly encouraged.

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

Cryotherapy	The use of extreme cold to freeze and remove abnormal tissue.
Curative	Treatment given with the aim of achieving complete remission (cure) and preventing recurrence.
Neoadjuvant	Treatment administered before the main treatment (e.g., radiotherapy or surgery), to reduce the size of a tumour or to help prevent a disease coming back
Radiotherapy	The use of high energy rays (radiation) to treat cancer.
Sequelae	The aftereffect(s) of a disease or condition.

References

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