Chemotherapy Protocol

BASAL CELL CARCINOMA (BCC)

VISMODEGIB

Regimen

- BCC - Vismodegib

Indication

- The patient either has;

    a. Gorlin Syndrome with non-locally advanced, non-metastatic basal cell carcinomas (BCC) (greater than or equal to 6) clinically evident at the point of decision to treat BCCs of which 3 are at least 5mm OR
    b. Non-locally advanced, non-metastatic multiple BCC (greater than or equal to 6) clinically evident at the point of decision to treat BCCs of which 3 are at least 5mm AND are appropriate for surgery i.e., surgically appropriate eligible tumours.

- The patient has at least 6 operable clinically evident non-locally advanced, non-metastatic BCC with surgically eligible tumours of 3 lesions of at least 5mm diameter, of which 1 is histopathologically confirmed.

- The patient is suitable for surgical intervention, but surgical intervention alone has the potential for substantial disfigurement.

- Vismodegib will be prescribed at a dose of 150mg daily OR an intermittent schedule, until disease progression or adverse effects which necessitate stopping

- The patient is aged 18 years and above.

- Vismodegib must not be used during pregnancy and female and male patients will be counselled as describe below.

    - Counselling for female patients:
    The patient must be counselled about the adverse use of vismodegib in pregnancy AND, if a woman of child-bearing potential, has been advised that she should use two forms of contraception (including one highly effective method and one barrier) during vismodegib therapy and for 24 months after the final dose, AND has had a negative medically supervised pregnancy test within the past seven days.

    - Counselling for male patients:
    The patient has been counselled about the adverse use of vismodegib in relation to pregnancy and has been advised that he should always use a condom (with spermicide if available), during vismodegib therapy and for 2 months after the final dose.

- ECOG performance status of 0, 1 or 2

Adverse Effects

Drug	Common Side Effects
Vismodegib	Decreased appetite, dysgeusia, ageusia, nausea, diarrhoea, constipation, vomiting, dyspepsia, alopecia, pruritus, rash, muscle spasms, arthralgia, pain in extremities, amenorrhoea, weight loss, fatigue, pain

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

- FBC prior to each cycle.
- U&Es and LFTs prior to each cycle.
- For all women of childbearing potential, a negative pregnancy test conducted by a healthcare provider must be obtained within 7 days of treatment initiation and then every 4 weeks whilst on treatment.

Dose Modifications and Discontinuation

Haematological

Haematological toxicity is uncommon. Consider blood transfusion or the use of erythropoietin according to NICE TA323 if patient symptomatic of anaemia or where the haemoglobin is less than 8g/dL (80g/L).

Criteria	Eligible level
Neutrophil	$1x10^9$/L or greater
Platelets	$100x10^9$/L or greater

If below the eligible level discuss with consultant before continuing treatment.

Hepatic Impairment

No dose adjustment is required in patients with mild, moderate, or severe hepatic impairment (as defined by National Cancer Institute Organ Dysfunction Working group criteria for hepatic impairment).

Renal Impairment

Mild and moderate renal impairment is not expected to impact the elimination of vismodegib, and no dose adjustment is needed. Very limited data is available in patients with severe renal impairment. Patients with severe renal impairment should be carefully monitored for adverse reactions.

Pregnancy

Vismodegib is contraindicated in women of childbearing potential who do not comply with the pregnancy prevention programme. A medically supervised pregnancy test,

conducted by a health care provider, should be performed within 7 days prior to initiating treatment and monthly during treatment. Pregnancy tests should have a minimum sensitivity of 25 mIU/mL as per local availability. Only 28 days of treatment can be supplied at one time to women of childbearing potential. Persistent lack of menses during treatment with vismodegib should be assumed to indicate pregnancy until medical evaluation and confirmation. In case of pregnancy in a woman treated with vismodegib treatment must be stopped immediately.

Counselling points for women of childbearing potential

- Vismodegib exposes a teratogenic risk to the unborn child
- She must not take Vismodegib if she is pregnant or plans to become pregnant.
- She must have a negative pregnancy test, conducted by a healthcare provider within 7 days before starting vismodegib treatment.
- She must have a negative pregnancy test monthly during treatment, even if she has become amenorrhoeic.
- She must not become pregnant whilst taking vismodegib and for 24 months after her final dose.
- She must use two methods of recommended contraception including one highly effective method and a barrier method during vismodegib therapy and for 24 months after the final dose.
- She must use 2 methods of recommended contraception while she is taking vismodegib unless she commits to not having sexual intercourse.
- She must tell her healthcare provider if any of the following occur during treatment and for 24 months after her final dose:
    - If she becomes pregnant or think for any reason that she may be pregnant.
    - If she misses her expected menstrual period.
    - If she stops using contraception unless she commits to not having sexual intercourse.
    - If she needs to change contraception during treatment.
- She must not breast-feed while taking vismodegib for 24 months after the final dose.

Counselling for male patients

- Vismodegib is contained in semen. To avoid potential foetal exposure during pregnancy, a male patient must understand that:

    1. Vismodegib exposes a teratogenic risk to the unborn child if he engages in unprotected sexual activity with a pregnant woman.

    2. He must always use a condom (with spermicide, if available), even after a vasectomy, when having sex with a female partner while taking vismodegib and for 2 months after the final dose.

3. He will tell his healthcare provider if his female partner becomes pregnant while he is taking vismodegib or during the 2 months after his final dose.

4. He should not donate his semen while taking vismodegib and for 2 months after the final dose.

Prescribing and dispensing restrictions

The vismodegib pregnancy prevention programme (PPP) pharmacist dispensing checklist should be completed prior to all supplies.

Blood donation

Patients should not donate blood while taking vismodegib and for 24 months after the final dose.

Regimen

28 day cycle continued for as long as the patient is deriving benefit from therapy without unacceptable toxicity (12 cycles will be set in Aria)

Drug	Dose	Days	Administration
Vismodegib	150mg once daily*	1-28	Oral

*Continuous daily administration or an intermittent unlicensed schedule may be used:

a) vismodegib 12 weeks; off treatment 8 weeks; vismodegib 12 weeks; off treatment 8 weeks; vismodegib 12 weeks; off treatment 8 weeks; vismodegib 12 weeks OR

b) vismodegib 24 weeks; off treatment 8 weeks; vismodegib 8 weeks; off treatment 8 weeks; vismodegib 8 weeks; off treatment 8 weeks; vismodegib 8 weeks.

The licensed continuous dose will be set in ARIA.

Dose information

- Vismodegib is available as 150mg capsules.

Additional therapy

The following two agents will be included in the ARIA regimen on cycle one only. Thereafter they can be added from the supportive treatment tab if required.

- Domperidone 10mg three times a day when required, orally
- Oral loperamide 4mg after the first loose stool and then 2mg every two hours up to a maximum of 16mg a day.

Administration Information

- Vismodegib capsules must be swallowed whole with water, with or without food. The capsules must not be opened.

- If a dose of Vismodegib is missed, patients should be instructed not to take the missed dose but to resume with the next scheduled dose.

Additional information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to Vismodegib.

References

1. Dreno, B., Kunstfeld, R., Hauschild, A. et al. Two intermittent vismodegib dosing regimens in patients with multiple basal-cell carcinomas (MIKIE): a randomised regimen-controlled, double-blind, phase 2 trial. Lancet Oncology (2017); 18:404-12.
2. Roche (2021). Erivedge 150mg hard capsules summary of product characteristics. Available from https://www.medicines.org.uk/emc. Accessed 27/06/2022.

REGIMEN SUMMARY

Vismodegib

Cycle One – Day One

1. Warning – Pregnancy Prevention Programme
   Vismodegib is associated with a pregnancy prevention programme. Please ensure this is completed for all patients.

2. Vismodegib 150mg once a day continuous oral
   Administration Instructions
   Oral SACT
   Pregnancy Prevention Programme
   Swallow this medicine whole. Do not chew or crush.

3. Domperidone 10mg three times a day when required.
   Administration Instructions
   Please supply 30 tablets or nearest whole pack equivalent

4. Loperamide 2mg when required.
   Administration instructions
   Take 4mg after the first loose stool and 2mg after each loose stool or every two hours thereafter.
   Maximum 16mg in a 24-hour period. Please supply 28 capsules or nearest whole pack equivalent.

Cycle Two – Day One Onwards

5. Warning – Pregnancy Prevention Programme
   Vismodegib is associated with a pregnancy prevention programme. Please ensure this is completed for all patients.

6. Vismodegib 150mg once a day continuous oral
   Administration Instructions
   Oral SACT
   Pregnancy Prevention Programme
   Swallow this medicine whole. Do not chew or crush.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	July 2022	N/A	Alexandra Pritchard Pharmacist	D C Liberscoli Consultant Clinical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Trust

Whilst every effort is made to ensure the accuracy of the information given in this protocol it cannot be guaranteed that the protocol is fully up to date. Because of the dynamic nature of cancer treatment, decisions on SACT must be based on the independent judgement of the clinician with reference to changing information on the medicine (e.g., available literature and SmPC) and evolving medical practices.