AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

One Wales Medicines Assessment Group Recommendation:
Dabrafenib (Taflinar®) and trametinib (Mekinist®) for the treatment of inoperable BRAF V600E variant anaplastic thyroid cancer (OW27)

April 2024

ONE WALES MEDICINES ASSESSMENT GROUP (OWMAG)

Dabrafenib (Taflinar®) and trametinib (Mekinist®) for the treatment of inoperable BRAF V600E variant anaplastic thyroid cancer

Date of advice: April 2024

The following One Wales Medicines Assessment Group (OWMAG) recommendation has been endorsed by the All Wales Medicines Strategy Group (AWMSG) and ratified by Welsh Government.

Using the agreed starting and stopping criteria dabrafenib (Taflinar®) and trametinib (Mekinist®) in combination can be made available within NHS Wales for the treatment of inoperable anaplastic thyroid cancer with the BRAF V600E variant.

The risks and benefits of the off-label use of dabrafenib (Taflinar®) and trametinib (Mekinist®) for this indication should be clearly stated and discussed with the patient to allow informed consent.

Providers should consult the relevant guidelines on prescribing unlicensed medicines before any off-label medicines are prescribed.

This advice will be reviewed after 12 months or earlier if new evidence becomes available.

Clinician responsibility
Clinicians will be obliged to collect and monitor patient outcomes. Evidence of clinical outcomes will be taken into consideration when reviewing the One Wales Medicines Assessment decision.

Health board responsibility
Health boards will take responsibility for implementing One Wales Medicines Assessment Group decisions and ensuring that a process is in place for monitoring clinical outcomes.

One Wales advice assists consistency of access across NHS Wales.

Starting and stopping criteria for the treatment of inoperable BRAF V600E variant anaplastic thyroid cancer

Developed in collaboration with oncologists in Wales.

Starting criteria:
Patients must satisfy all of the following criteria. Treatment may be considered in patients who:

- have BRAF V600E mutation-positive anaplastic thyroid cancer confirmed by a validated test through the All Wales Medical Genomics Service (AWMGS)
- have cancer that is deemed to be not operable at the time treatment is commenced with dabrafenib and trametinib*
- an Eastern Cooperative Oncology Group (ECOG) performance status of between 0 and 2.
- are not pregnant. Patients of childbearing potential must be willing to use an adequate method of contraception.

*patients who are down-staged following initial treatment with dabrafenib and trametinib and undergo surgical resection with curative intent will continue to be eligible for treatment.

A full list of precautions is included in the Summary of Product Characteristics (SmPC)[1,2].

Dabrafenib and trametinib should always be initiated by an experienced oncologist following a multidisciplinary team (MDT) discussion.

Patients who satisfy the eligibility criteria will be prescribed dabrafenib and trametinib following consultation with the patient and/or carer after consideration of potential adverse effects, cautions, contraindications and an explanation of alternative treatment options. This consultation should be recorded in the patient's notes.

The recommended total daily dose of dabrafenib is 300 mg (two 75 mg capsules twice a day), and the recommended dose of trametinib is 2 mg once daily[1,2]. Treatment is continued until disease progression or unacceptable toxicity occurs. Dosing delay or discontinuation may be required based on individual safety and tolerability. Recommended modifications to manage adverse reactions are provided in the SmPC[1,2].

Monitoring:

- Full blood count
- Urea and electrolytes
- Liver function tests
- Thyroid function test
- Blood pressure
- ECG (+/- echocardiogram and MUGA scan as appropriate)
- Clinical evaluation of side effects, refer to SmPC

The above tests should be done at baseline. Repeat blood tests, blood pressure and ECG repeated every four weeks in clinic. Refer also to local protocols on scheduling tests.

Whilst on treatment a computed tomography (CT) will be performed every 3 months, according to response to treatment.

Skin examination should be performed prior to initiation of therapy with dabrafenib and trametinib and monthly throughout treatment and for up to six months following discontinuation of dabrafenib or until initiation of another anti-neoplastic therapy. If patients report new visual disturbances, such as diminished central vision, blurred vision or loss of vision at any time while on dabrafenib and trametinib, a prompt ophthalmological assessment is recommended[1,2].

This list is not exhaustive. Any other monitoring should be in accordance with the SmPC for dabrafenib and trametinib[1,2].

Stopping criteria:

- evidence of clinically significant disease progression or symptomatic deterioration as agreed in the MDT
- toxicity; dosing delay may be considered, follow the guidance in the SmPC.
- patient request

Patients who have received treatment with dabrafenib and trametinib who subsequently undergo surgical intervention to improve local control are likely to need to continue treatment post-surgical resection, unless MDT discussion deems that the adequacy of resection was such that adjuvant treatment with dabrafenib and trametinib is no longer indicated.

Only one course of treatment may be issued in accordance with this advice. Requests for repeat courses should be explored through funding mechanisms such as the individual patient funding request process.

Other considerations:

- It is important that outcomes are collected for this patient cohort and the outcomes will be reviewed by the One Wales Medicines Assessment Group after 12 months.
- Clinicians may wish to use one of the Cancer Research UK consent forms for SACT (Systemic Anti-Cancer Therapy) to help ensure your patient is fully informed when consenting to SACT.

References

1. Novartis Pharmaceuticals UK Ltd. Taflinar®. 75 mg hard capsules. Summary of Product Characteristics. Jul 2023. Available at: https://www.medicines.org.uk/emc/product/7837/smpc. Accessed Mar 2024.
2. Novartis Pharmaceuticals UK Ltd. Mekinist®. 2 mg film-coated tablets. Summary of Product Characteristics. Jul 2023. Available at: https://www.medicines.org.uk/emc/product/5072/smpc. Accessed Mar 2024.