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

Sorafenib for maintenance treatment following allogeneic haematopoietic cell transplantation for acute myeloid leukaemia associated with a FLT3-ITD mutation (OW18)

Feburary 2022 OWMAG

ONE WALES INTERIM DECISION

Sorafenib for maintenance treatment following allogeneic haematopoietic cell transplantation for acute myeloid leukaemia associated with a FLT3-ITD mutation

Date of advice: February 2022

The following One Wales Medicines Assessment Group (OWMAG) recommendation has been endorsed by health board Chief Executives.

Using the agreed starting and stopping criteria, sorafenib can be made available within NHS Wales for maintenance treatment following allogeneic stem cell transplantation for acute myeloid leukaemia associated with a FLT3 ITD mutation.

The risks and benefits of the off-label use of sorafenib 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 Group 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 promotes consistency of access across NHS Wales.

Starting and stopping criteria for sorafenib for the maintenance treatment following allogeneic haematopoietic cell transplantation for acute myeloid leukaemia associated with a FLT3-ITD mutation

Developed in collaboration with the haematological cancer services, Cardiff and Vale University Health Board.

This treatment is not to be used as a bridge to transplant or as an alternative option to haematopoietic cell transplantation.

Starting criteria:
Patients who have received an allogenic haematopoietic cell transplantation for acute myeloid leukaemia and where:

- There was presence of the FMS-like tyrosine kinase-3 internal tandem duplication (FLT3-ITD) mutation at the time of diagnosis or AML relapse.
- There is no evidence of graft versus host disease (GvHD)
- There are no contraindications to the use of sorafenib
- The patient is not eligible for entry into a clinical trial

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

The recommended dose is 800 mg/day in two divided doses to be adapted according to tolerance. Treatment should start 30-60 days post-transplant and may continue up to a maximum of two years.

Monitoring:

- Full blood count
- Urea and electrolytes
- Liver function tests
- Phosphate and calcium
- Blood glucose

The above tests should be done weekly for month 1 then monthly for 2 months, extended to every two months if the patient is well.

- Blood pressure every 1-2 months
- Thyroid function test (if clinical signs of hypo/hyperthyroidism)
- Electrocardiogram every 1-2 months
- Bone marrow monitoring (morphology, MRD, chimerism) at month 1, 2, 3, 6, 12,18 and 24 post-transplant, but monitoring can be increased as required.
- Clinical symptoms of GvHD
- Clinical evaluation of side effects, refer to Summary of Product Characteristics.

Any other monitoring should be in accordance with the Summary of Product Characteristics for sorafenib. Sorafenib should be transiently discontinued in the case of

GvHD requiring systemic treatment with corticosteroids, but may be cautiously resumed once remission of GvHD is documented.

Stopping criteria:

- evidence of morphological relapse on bone marrow examination
- toxicity; a dose reduction may be considered, follow the guidance in the Summary of Product Characteristics.
- patient request
- after two years of sorafenib.

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

One Wales Medicine Assessment Group summary of decision rationale

Medicine: **sorafenib**
Indication: **for maintenance treatment following allogeneic haematopoietic cell transplantation for acute myeloid leukaemia associated with a FLT3-ITD mutation**
Meeting date: **28th February 2022**

Criteria	OWMAG opinion
Clinical effectiveness	OWMAG notes that the main clinical effectiveness evidence is from two clinical trials. All studies identified concluded that sorafenib maintenance therapy reduces the risk of relapse. There is no official published treatment protocol for maintenance sorafenib to treat AML associated with a FLT3-ITD mutation. Maintenance therapy duration is not firmly established, but SORMAIN was based on 24 months of maintenance therapy, depending on tolerance. OWMAG considers that the evidence provided demonstrated clinical effectiveness.
Cost-effectiveness	OWMAG notes that no cost effectiveness studies have been undertaken. There is insufficient information available to provide cost effectiveness analyses.
Budget impact	OWMAG considers that the clinical estimate of patient numbers reported is reasonably accurate. OWMAG acknowledges that budget impact estimates are subject to uncertainty but that overall the budget impact is relatively small. There is particular uncertainty around maintenance therapy duration, a two-year projection was used in line with recommendation by the European Society for Blood and Marrow Transplantation (EBMT).
Other factors	OWMAG considers that entry into a clinical trial would be the preferred option for eligible patients within this cohort. This will be incorporated in to the start/stop criteria.
Final recommendation	OWMAG recommends that sorafenib is made available for maintenance treatment following allogeneic haematopoietic cell transplantation for acute myeloid leukaemia associated with a FLT3-ITD mutation. This recommendation is subject to the development of appropriate start/stop criteria.
Summary of rationale	There is some evidence to suggest that sorafenib is clinically effective for the treatment of acute myeloid leukaemia associated with a FLT3-ITD mutation treatment following allogeneic haematopoietic cell transplantation and may be associated with greater tolerability in a predefined cohort of patients. It would appear to offer reasonable value for money with a relatively low budget impact.