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

One Wales Medicines Assessment Group (OWMAG)

Minutes of the virtual (Teams) meeting held Monday 28 February 2022

Members in attendance:
John Watkins, Consultant in Public Health, OWMAG Chair
Andrew Champion, Assistant Director, Evidence Evaluation, IPFR representative WHSSC
Alan Clatworthy, Clinical Effectiveness and Formulary Pharmacist, IPFR representative Swansea Bay
Joe Ferris, Operations Manager, ABPI Cymru Wales
Teena Grenier, Medicines Governance Lead, IPFR representative Betsi Cadwaladr
Richard Hain, Consultant in Paediatric Palliative care, IPFR representative, Cardiff and Vale
Kathryn Howard, Head of Pharmacy, Royal Glamorgan Hospital, IPFR representative Cwm Taf Morgannwg
Malcolm Latham, Community Health Council, Lay representative
Hywel Pullen, Director of Finance, WHSSC
Berni Sewell, Senior Lecturer, Health Economist, Swansea University
Jonathan Simms, Clinical Director of Pharmacy, IPFR representative Aneurin Bevan
Michael Thomas, Consultant in Public Health, IPFR representative, Hywel Dda

AWTTC:
Karen Samuels, Head of Health Technology Appraisal
Rob Bracchi, Medical Advisor
Gail Woodland, Senior Appraisal Pharmacist
Rosie Spears, Senior Appraisal Scientist
Carolyn Hughes, Medical Writer
Rachel Jonas, Medical Writer
Laura Phillips, Admin Supervisor

Clinical experts:
Dr Wendy Ingram, Consultant Haematologist, Cardiff and Vale

List of Abbreviations:

ABPI	Association of the British Pharmaceutical Industry
AWTTC	All Wales Therapeutics & Toxicology Centre
ESR	Evidence Status Report
IPFR	Independent Patient Funding Request
NICE	National Institute for Health and Care Excellence
NMG	New Medicines Group
OWMAG	One Wales Medicines Assessment Group
WHSSC	Welsh Health Specialised Services Committee

1. Welcome and Introduction
The Chair opened the meeting and welcomed members.

2. Apologies
Ian Campbell, Hospital Consultant CAV, NMG representative
William King, Consultant in Public Health, Powys

3. Declaration of Interests/Confidentiality
The Chair reminded members that all OWMAG proceedings are confidential and should not be disclosed outside of the meeting. Members were reminded that declarations of interest and confidentiality statements are signed by each member on an annual basis. The Chair invited any declarations of interest; there were none.

4. Chair's report
The Chair noted the minutes of the last virtual face to face meeting (October 2020) and informed the group that endorsement has been received for the medicine considered at that meeting; abiraterone for prostate cancer during COVID-19, it has since superseded by NICE.

The Chair also announced that the Chief Executive Management Team has endorsed the medicines reviewed virtually in January, July, September and November 2021. They are displayed on the AWTTC website and the service has been informed.

The recommendation from today's meeting will be forwarded to the Chief Executive Management Team for their consideration on 22 March 2022.

5. Change to format of One Wales reports
Gail informed the group that the AWTTC team have revised the format of the review reports to comply with accessibility standards and to make them more streamlined. The new format will be piloted in the next two reviews and AWTTC would like feedback on the new format and welcome any comments or recommendations as to how the reports may be improved further.

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

The Chair briefly outlined the sequence of events and set the context of the meeting.

The Chair invited any declarations of interest specific to this assessment; there were none.

Gail Woodland presented the key aspects of the evidence status report.

The Chair introduced the clinical expert, Dr Wendy Ingram. The Chair described the role of the clinical expert as an invited observer of the OWMAG meeting to answer questions and input into discussions to enable members to gain a better understanding of the clinical context. The Chair highlighted that clinical experts were nominated by their specialist group or network and should not express personal opinion or promote the use of a medicine.

The Chair invited the clinical expert to give an overview of the disease and medicine being considered. The clinical expert explained that the FLT3-ITD mutated acute myeloid leukaemia (AML) is the most challenging form of AML, refractory to treatment with very few patients achieving sufficient response to chemotherapy to receive a bone marrow transplant. Monitoring for residual disease is problematic with poor sensitivity of biomarkers, currently disease status is tracked by studying the microscopic morphology of blood and bone marrow. It is therefore challenging to identify which patients are at risk of relapse, those with FLT3 mutations are at a high risk of relapse. Due to the poor sensitivity of FLT3 testing, any level of mutations measured indicates a significant risk of relapse.

The clinical expert informed the group that there is variability in post-transplant monitoring of AML patients across treatment centres in the UK. The haematology department in Cardiff and Vale University Health Board (CAVUHB) conduct intensive bone marrow and blood monitoring studying morphology and chimerism. Intensive monitoring allows intervention on relapse more quickly. The only other option available currently is donor lymphocyte infusion which is not considered very effective and carries a high risk of relapse. Although there are other medicines being explored for maintenance treatment post-transplant the expert has most experience of using sorafenib. In her experience most patients tolerate treatment well, with most requiring dose adjustments.

The Chair opened general discussion relating to the clinical effectiveness of sorafenib and questioned the possible limitations of two main studies, one being under powered and the other open label. Dr Ingram acknowledged that the majority of studies were non-randomised with historical control groups, however the European Society for Blood and Bone Marrow Transplant (EBMT) believe maintenance sorafenib should become standard of care. Midostaurin is offered to new patients with all eligible patients proceeding to transplant. The only options for maintenance treatment with an FLT3 inhibitor are through IPFR or clinical trials. There are currently clinical trials ongoing for use of two years maintenance treatment with gilteritinib, other trials are in early stages.

Members asked about the generalisability of the trial results to clinical practice, for example the age of patients. The expert explained that most patients would be eligible for transplant and from an age perspective the trials were representative of patients in practice. One member asked about patients from Wales who are treated in centres across the border in NHS England. Dr Ingram informed the group that monitoring may differ in these centres when compared to CAVUHB.

Members requested clarity as to the exact patient group under consideration. The expert clarified that sorafenib maintenance therapy would only be offered to AML patients with the FLT3-ITD mutation with treatment commencing between day 30 and 60 post-transplant. They must not have graft versus host disease and it would not be used as an alternative to transplant or as a bridge to transplant.

Members enquired as to alternative treatment options for maintenance therapy post-transplant. Dr Ingram explained that there is not as much data to support them and that they tend to be less well tolerated with higher incidences of adverse events.

The expert was asked as to the rationale for the recommended treatment duration of two years. Although the exact rationale is unclear the expert explained that the highest risk of relapse was in the first year following transplant, risk lowers in the second year and very few patients relapse after two years. In such cases an FLT3 inhibitor would be re-instated through IPFR request as this would be in a minority of cases and not considered the norm.

The Chair invited the health economist to comment on the cost-effectiveness evidence provided. The health economist highlighted the absence of any cost-effectiveness analyses. The high clinical effect and relatively low budget impact costs suggest that it could be a cost-effective option. Gail confirmed the costs that would most likely apply in NHS Wales. Members also highlighted that the medicine is off patent, the availability of generics and therefore the potential for more in the future which could drop the price further in years to come.

The Chair invited discussion on the patient and public perspective. The lay member highlighted that any medicine that extended life and improved quality of life would be appreciated by patients. Dr Ingram informed the group that the medicine not only extends life but actually offers the chance of a cure. She has received positive feedback from patients treated with sorafenib, side effects are managed to maintain quality of life during treatment with dose adjustments and treatment breaks. To date no patients treated within the centre have asked to stop treatment.

The Chair invited discussion on the wider societal and health and social care issues. No questions were raised.

The clinical expert left the meeting and members were invited to vote. The OWMAG recommendation for health board Chief Executives was agreed:

Date of advice: Monday 28 February

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.

7. AOB

The Chair opened discussion on the future format of OWMAG meeting and the possibility of moving to in-person meetings. The general consensus was to have a hybrid approach with in-person meetings occasionally and facilities for members to attend virtually.

8. Next meeting

The Chair confirmed that the next meeting will be on 28 March 2022. This is a virtual meeting to consider two reviews and voting will be by email. The Chair then thanked members for their participation and closed proceedings.