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

One Wales Medicines Assessment Group (OWMAG)

Minutes of the hybrid meeting held Monday 19 June 2023

Members in attendance:
John Watkins, Consultant in Public Health, OWMAG Chair
Andrew Champion, Assistant Director, Evidence Evaluation, representative WHSSC, Deputy OWMAG Chair
Joe Ferris, Operations Manager, ABPI Cymru Wales
Malcolm Latham, Community Health Council, Lay representative
Shaun Harris, Health Economist, Swansea University
Alan Clatworthy, Clinical Effectiveness and Formulary Pharmacist, representative Swansea Bay
Jonathan Simms, Clinical Director of Pharmacy, representative Aneurin Bevan
Kathryn Howard, Head of Pharmacy, Royal Glamorgan Hospital, representative Cwm Taf Morgannwg
Teena Grenier, Medicines Governance Lead, representative Betsi Cadwaladr
Michael Thomas, Consultant in Public Health, representative Hywel Dda
Timothy Banner, Clinical Director Pharmacy and Medicines Management, representative Cardiff and Vale
William King, Consultant in Public Health, representative Powys
Bethan Tranter, Chief Pharmacist, representative AWPAG/Velindre

AWTTC:
Rachel Jonas, Medical Writer
Laura Phillips, Admin Supervisor
Rosie Spears, Senior Appraisal Scientist
Gail Woodland, Senior Appraisal Pharmacist

Clinical expert:
Craig Barrington, Consultant in Oncology, Swansea Bay UHB

Observer:
Will Hardy, Health Economist, Bangor University

List of Abbreviations:

ABPI	Association of the British Pharmaceutical Industry
AWTTC	All Wales Therapeutics and Toxicology Centre
ESR	Evidence Status Report
IPFR	Individual 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

Hywel Pullen, Assistant Director of Finance, Cardiff and Vale, representative Finance Directors
Ian Campbell, Hospital Consultant CAV, representative NMG
Richard Hain, Consultant in Paediatric Palliative care, representative Cardiff and Vale

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. Ratification

The chair informed the group that since the last meeting we have received ratification from Welsh Government of the assessment considered at the March meeting; rituximab for the treatment of myasthenia gravis in adults.

5. Assessment

Dostarlimab (Jemperli®) for locally advanced treatment-naïve stage II/III deficient mismatch repair (dMMR) / high microsatellite instability (MSI-H) rectal cancer

The Chair welcomed clinical expert, Dr Craig Barrington, Consultant in Oncology, Swansea Bay UHB. 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 provided an overview of the order of considerations for the meeting.

Rosie Spears presented an overview of the key aspects of the dostarlimab evidence status report (ESR).

The Chair invited the clinical expert, Dr Barrington, to give an overview of the disease and experience of using dostarlimab as a first line treatment. The clinical expert explained that patients are wanting to avoid stomas and organ preservation for rectal cancer is not a new entity, with international recommendations published in 2019. There has been good success seen with total neoadjuvant therapy (TNT) in current practice. Dostarlimab would be potentially providing a new addition to patient

treatment options. The extent of surgery was explained to members – highlighting the potential for total pelvic exenteration, with life changing implications.

It was confirmed the patient numbers quoted in the ESR are realistic to clinical practice, future predictions are more difficult as there are more DMMR or MSI-H colorectal cancers in general, with a variety of reasons why clinicians think that's the case. Cancers in the rectum are typically associated with Lynch syndrome and those with MSI-H typically do not respond to chemotherapy and have a poor prognosis, but respond even better than the sporadic MSI-H population to immunotherapy. There are also the current changes in bowel cancer screening, it is anticipated that by 2025, all members of the population of the age of 50 will be sent for screening. So, it is likely more cancers will be detected even earlier and raise the patient numbers, especially as there are more MSI-H tumours being detected. The median age of 50 is thought to be in line with clinical experience and the increased quality of life impact associated with patients in a younger age, such as living longer with a stoma.

Dr Barrington explained his current clinical experience using dostarlimab in three patients. In the Cercek study, it was queried what the anticipated outcome would have been for patients not receiving dostarlimab and the credibility of results from a trial with no control arm. It was reiterated this population have a poor prognosis, with about 4% of all metastatic colorectal cancer patients being MSI-H. The keynote, 177 trial 70% are alive at three years with monotherapy so this treatment can potentially revolutionise the outlook for this cohort. The results from NICHE-2 trial also report 67% pathological complete response and 95% major pathological response after two cycles of treatment, however these results are yet to be peer reviewed.

The potential positioning of new treatments such as contact radiotherapy in the pathway was queried, Dr Barrington explained the differences between long course chemoradiotherapy, external beam treatment is offered in the three centres in Wales routinely. Contact radiotherapy delivers a high dose of radiotherapy direct to the tumour and it's usually used for early stage to stage two with better organ preservation seen in trials. Contact radiotherapy response is not demonstrating the 100% complete response that is being reported with dostarlimab. It is about opening treatment options to this patient group. The effects of radiotherapy were also highlighted, such as effect on fertility.

The dosing of nine cycles was discussed and Dr Barrington confirmed the intended treatment in trials was dostarlimab then long course chemoradiotherapy with a TNT approach, this stepwise approach has not been used due to the complete clinical response seen with dostarlimab. The dose regimen in the trial is likely sufficient treatment due to the results currently being reported. Members queried the potential availability for licensed treatments for this indication in the near future. Dr Barrington highlighted ongoing studies of immunotherapies for all dMMR/MSI-H tumours. Rosie Spears informed the group that the AZUR-1 study is being conducted by the marketing authorisation holder for dostarlimab with primary completion in 2025 and full completion in 2029 so licencing is a few years away. NICE are currently

assessing use of pembrolizumab for previously treated dMMR/ MSI-H solid tumours with publication expected in September 2023, however this is at a different place in the treatment pathway. Access to dostarlimab may affect future treatment choices as the benefits of immunotherapy (PDL-1 inhibitors) is likely to be a class effect.

Shaun Harris presented an overview of the key aspects of the dostarlimab health economics.

There was a discussion around the quality of life data and the possible reasons there are for not seeing higher results with the organ preservation approach. The increased surveillance implications with a watch and wait approach was discussed. The impact of immunotherapy toxicity was discussed and Dr Barrington highlighted there is a risk with any treatments and in clinical experience, most immunotherapy toxicities can be very easily managed as an outpatient and don't require inpatient admission. Differences in US costs and treatment pathways compared to the UK NHS perspective were highlighted as a limitation of the Cui study.

The Chair opened discussion on the patient and public perspective. The lay representative, Malcolm Latham, emphasised the current clinical effectiveness results reported and the benefits of organ preservation on patient's quantity of life. He discussed the potential value of having this accessible to patients as a routine option.

Potential benefits on service impact by reducing the need for surgery and radiotherapy (and the associated resource used with these interventions) was raised.

It was confirmed patients in Wales are currently accessing dostarlimab via IPFR. There will be some clinical trial centres in England, with competitive enrolment. Place of treatment for those patients living on the border will need to be confirmed to ensure there is access to treatment. If there is a positive recommendation, then start stop criteria and patient reported outcome measures will be put in place. There is ongoing work in Wales looking at organ preservation monitoring strategies.

The clinical expert was thanked and left the meeting. The Chair summarised the mornings' discussions and asked the group if there were any other points to raise.

The Chair closed discussion and invited members to vote:

Date of advice: Monday 19 June 2023

Using the agreed starting and stopping criteria, dostarlimab can be made available within NHS Wales for the treatment of locally advanced treatment-naïve stage II/III deficient mismatch repair (dMMR) / high microsatellite instability (MSI-H) rectal cancer. Dostarlimab should be prescribed on the basis of lowest acquisition cost.

6. Review

Mepolizumab (Nucala®) for the treatment of chronic eosinophilic pneumonia

Rosie Spears presented an overview of the key aspects of the mepolizumab review.

It was highlighted that mepolizumab is the only non-recommendation currently active for One Wales which has been in place since 2019 and been reviewed annually. There followed a discussion around clinician engagement and current patient access.

Members were invited to vote on the mepolizumab review. The OWMAG recommendation was to continue to not recommend this treatment in Wales for chronic eosinophilic pneumonia. The next review by OWMAG will be in three years or earlier if new evidence becomes available.