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

Interim Pathways Commissioning Group (IPCG)

Minutes of the meeting held Friday, 27th May 2016 in the Academic Centre, University Hospital Llandough, Cardiff CF64 2XX

Members in attendance:
Sharon Hopkins, Director of Public Health, IPCG Chair
Fiona Woods, Director, WMIC, IPFR C&V
Brian Hawkins, Chief Pharmacist, IPFR CT
Jonathan Simms, Clinical Director of Pharmacy, IPFR AB
Alan Clatworthy, Clinical Effectiveness & Formulary Pharmacist, IPFR ABMU
Stuart Bourne, Deputy Director Public Health, IPFR Powys
William Oliver, Assistant Director of Therapies & Health Science, IPFR HD
Fraser Campbell, Assistant Medical Director, IPFR BCU
Stuart Davies Finance Director, WHSSC
Rick Greville, ABPI Cymru Wales, Industry Representative
Geoff Greaves, Lay representative
Debra Fitzsimmons, Health Economist, WHESS
Sue Jeffs, Consultant Anaesthetist, AWPAG representative
Jason Lester, Consultant Oncologist, Deputy Clinical Director, VCC representative
Marysia Hamilton-Kirkwood, Assistant Medical Director, Public Health, AB

AWTTC:
Phil Routledge, Clinical Director, AWTTC
Karen Samuels, Head of Patient Access, AWTTC
Gail Woodland, Senior Appraisal Pharmacist, AWTTC
Rosie Spears, Senior Appraisal Scientist AWTTC

Observers:
Ann-Marie Matthews, IPFR Manager/Lead for Value-based Healthcare, AB;
Anthony Williams, Senior Appraisal Pharmacist, Team Manager, AWTTC;
Jessica Davis, Medical Writer, AWTTC;
Ruth Lang, Head of Liaison and Administration, AWTTC.

List of Abbreviations:

AB	Aneurin Bevan
ABPI	Association of the British Pharmaceutical Industry
ADT	Androgen deprivation therapy
ASAR	AWMSG Secretariat Assessment Report
AWPAG	All Wales Prescribing Advisory Group
AWTTC	All Wales Therapeutics & Toxicology Centre
BCU	Betsi Cadwaladr University
CT	Cwm Taf
C&V	Cardiff and Vale
ESR	Evidence Status Report
GCSF	Granulocyte colony stimulating factor
HB	Health Boards
HD	Hywel Dda

ICER	Incremental cost-effectiveness ratio
IPCG	Interim Pathways Commissioning Group
NMG	New Medicines Group
NICE	National Institute for Health and Care Excellence
OS	Overall survival
P	Powys
RCC	Renal cell carcinoma
SMC	Scottish Medicines Consortium
VCC	Velindre Cancer Centre
WHSSC	Welsh Health Specialised Services Committee

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

2. Apologies
Ian Campbell, NMG Clinical Representative
James Coulson, Clinical Pharmacologist
Teena Grenier, Medicines Governance Lead, BCU.

3. Declaration of Interests / Confidentiality
The Chair reminded members that all IPCG proceedings are confidential and should not be disclosed outside of the meeting. Members were asked to ensure they had signed and returned the confidentiality statements to AWTTC. The Chair invited any declarations of interest – there were none.

4. Assessment 1
Axitinib (Inlyta®▼) for the treatment of advanced renal cell carcinoma (RCC) after failure of prior treatment with pazopanib.

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 forthcoming.

The AWTTC lead highlighted the key aspects of the evidence status report.

The Chair introduced the clinical experts, Dr Jake Tanguay, Consultant at VCC and Prof. John Wagstaff, Honorary Consultant, ABMU. The Chair described the role of the clinical experts as invited observers of the IPCG meeting to answer questions and input into discussions to enable members to gain a better clinical 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 stated that the clinical experts would declare any personal or non-specific interests and will leave the meeting prior to the vote.

The Chair opened general discussion in relation to clinical effectiveness. Clinical experts started by highlighting evidence of two clinical trials one of which demonstrated preference by patients for pazopanib over sunitinib (70% versus around 20% [PISCES]) and another which demonstrated no difference in efficacy between the two medicines (COMPARZ). The experts expressed that in practice the

preference would be for pazopanib for first line treatment of RCC however the marketing authorisation for axitinib currently precludes its use as a second line treatment after pazopanib. If axitinib is not supported for use post pazopanib then sunitinib would have to be used in first line treatment which is less favourable for patients in terms of quality of life (QoL) and adverse effects. The efficacy of axitinib was briefly discussed with the clinical expert informing the group that median survival of patients was improved with treatment with axitinib. Quality of life with axitinib was discussed; clinical experts stated that the evidence for improved QoL for pazopanib over sunitinib in the PISCES study essentially covered relevant QoL issues. Members asked the clinicians if there were any adverse effects of concern for axitinib, clinical experts described the medicine as well tolerated.

The Chair invited general discussion of any cost effectiveness issues. It was highlighted that there are no cost effectiveness calculations for the use of axtinib in this indication. The Chair invited discussion of any budget impact issues. Members were informed of the availability of a confidential Patient Access Scheme which offered a price reduction for axitinib. Licensed alternatives to axitinib were discussed, and it was noted that although everolimus is licensed for this indication it is not recommended by NICE. The statement from NICE supporting the use of axitinib post pazopanib was re-iterated. Clarification was requested on the number of cycles used to calculate the budget impact; 5 cycles was the median number of cycles used in clinical trials and in the budget impact.

The Chair invited members to discuss the patient/public perspective. The clinical expert informed members that some HBs have already agreed the provision of axitinib post pazopanib and he highlighted potential inequity of access across Wales.

The Chair invited members to discuss wider societal issues. It was highlighted by a member that axitinib is available post pazopanib for treatment of RCC in England through NHS commissioning.

The Chair thanked the clinical experts and asked them to leave the meeting.

Proceedings were concluded by the Chair and members asked to vote.

IPCG recommendation for Health Boards Chief Executives:

Axitinib (Inlyta®▼) for the treatment of adult patients with advanced renal cell carcinoma (RCC) after failure of prior treatment with pazopanib.
Axitinib (Inlyta®▼) can be made available within NHS Wales to treat adult patients with advanced renal cell carcinoma (RCC) after failure of prior treatment with pazopanib.

5. Assessment 2
Docetaxel (Taxotere®) in combination with androgen deprivation therapy for the treatment of hormone naive metastatic prostate cancer

The Chair invited any declarations of interest, there were none forthcoming.

The AWTTC lead highlighted the key aspects of the evidence status report.

The Chair introduced the clinical experts, Dr Jake Tanguay, Consultant at VCC and Prof. John Wagstaff, Honorary Consultant, ABMU. The Chair described the role of the clinical experts as invited observers of the IPCG meeting to answer questions and input into discussions to enable members to gain a better clinical 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 stated that the clinical experts would declare and personal or non-specific interests and will leave the meeting prior to the vote.

The Chair opened general discussion in relation to clinical effectiveness. Prof Wagstaff informed members that he was a co-author on the pivotal STAMPEDE clinical trial and that the improvement in median survival for patients given docetaxel with ADT is large compared to those given ADT alone. The fall-off rate for treatment with docetaxel was discussed. Clinical experts confirmed that with 74% of patients receiving the full treatment this fall-off rate would be expected with this kind of treatment. Fall-off is mainly due to tolerance issues, in particular the development of neutropenia. It was highlighted that there was a higher response rate in patients who received all 6 cycles of treatment. Clarification around the benefit in patients with metastatic cancer compared to those with non-metastatic was requested; clinical experts explained that in the trial to date the cohort of non-metastatic cancer patients was underpowered and data is immature at present to evaluate efficacy in this patient group. Members asked about the likelihood of patients receiving two courses of treatment with docetaxel with a second course after the development of castration-resistant prostate cancer. It was noted that in the two published trials approximately 28% and 13.6% received a second course of treatment on development of castration resistance. Clinical experts highlighted that NICE had published a recommendation for use of cabazitaxel post docetaxel although in practice it is more likely that a second dose of docetaxel would be offered. Members questioned the GETUG-AF15 study where no overall survival (OS) benefit was demonstrated for docetaxel in this group. Clinical experts explained that the study was under powered and that the hazard ratio was of the same magnitude of that in studies which demonstrated OS benefit. A network meta-analysis which included this trial data showed significant OS benefit. Members asked if there is a licensed alternative for use in this indication, clinical experts responded that there is not. Clinical experts clarified the patient group who would be eligible for this treatment as those with high risk metastatic prostate cancer who are fit enough to receive treatment. They also highlighted another groups of patients who may be considered - patients with high risk locally advanced prostate cancer. The Chair stated that as this is outside the indication under discussion it would not be discussed further within the meeting.

The Chair invited discussion on cost effectiveness and budget impact issues. Members were made aware of Velindre and South West Wales Cancer Care costings for implementation of this medicine. Gail Woodland highlighted that the budget impact estimate in the ESR was significantly higher as it did not take into account local negotiated agreements. Members asked if there was any sensitivity analysis particularly around toxicity. Debra Fitzsimmons stressed that the cost effectiveness calculations are not robust due to paucity of good QoL data and that all caveats highlighted in the ESR should be noted. Treatment of patients with granulocyte colony stimulating factor (GCSF) was discussed; clinical experts were of the opinion that in practice clinicians were more likely to dose reduce on development of neutropenia and upfront prophylactic GCSF would not be considered standard practice. Gail Woodland clarified that GCSF was not included in the ESR budget impact. Members noted that in practice docetaxel acquisition costs would be less. It was noted that if the costs submitted by VCC and SWW were taken into account then the total budget impact would be approximately one third of the price stated in the ESR. Members were informed that contract prices were normally re-negotiated on an annual basis and that list prices are fixed.

The Chair invited discussion on patient and societal issues. Clinical experts stressed the significance of this treatment and confirmed that patients living in England access the medicine via NHS England commissioning. The Chair invited discussion on any wider issues not covered previously. Members asked if the target patient group could be narrowed down; however, clinical experts stated that this would not be possible as response is uniform across the patient group. Clinical experts highlighted a significant increase in workload for cancer centres as patients are currently treated in urology departments and oncology departments would be required to take over the treatment of patients. It was noted that starting and stopping criteria for the treatment are presented in the NHS England commissioning document.

The Chair thanked the clinical experts and asked them to leave the meeting.

Proceedings were concluded by the Chair and members asked to vote.

IPCG recommendation for Health Boards Chief Executives

Docetaxel in combination with androgen deprivation therapy
for the treatment of hormone-naive metastatic prostate cancer
Using the agreed starting and stopping criteria, docetaxel, in combination with androgen deprivation therapy, can be made available for the treatment of men with hormone-naive metastatic prostate cancer

6. Assessment 3
Bevacizumab (Avastin®) at a dose of 7.5 mg/kg in combination with carboplatin and paclitaxel for the front-line treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer

The Chair invited any declarations of interest, there were none forthcoming.

The AWTTC lead highlighted the key aspects of the evidence status report.

The Chair introduced the clinical expert, Dr Louise Hanna, Consultant Clinical Oncologist, VCC. The Chair described the role of the clinical experts as invited observers of the IPCG meeting to answer questions and input into discussions to enable members to gain a better clinical 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 stated that the clinical experts would declare any personal or non-specific interests and would leave the meeting prior to the vote.

The Chair opened general discussion in relation to clinical effectiveness. The clinical expert clarified that she was expressing the collective opinion of health professionals treating gynaecological malignancies across Wales. The main evidence is from the ICON7 clinical trial; patients with stage III, debulked with > 1 cm residual tumour and stage IV cancer patients were considered to be the most likely group to derive benefit from this treatment and this high risk sub-group was a planned sub-group. She also highlighted an audit of real life data from the South West Wales cancer centre which mirrors the results found in the ICON7 study. The clinical expert confirmed that the number of patients estimated in the ESR was reasonable and that the average number of cycles is approximately 10. Members were informed that currently this patient group has poor clinical outcomes and there are no new treatments forthcoming. The findings of the ICON7 study were questioned by the panel who highlighted that patients were not blinded and the subgroup analysis was not robust. Clarification was sought in relation to the availability of an alternative licensed treatment for this indication; the clinical expert informed the group that there was no alternative available and standard treatment in the UK is based on the ICON7 study. The clinical expert noted that access to clinical trials can depend on availability of bevacizumab.

The Chair invited discussion around issues of cost effectiveness. It was noted that the cost-effectiveness calculations were based on those submitted to the SMC. The health economist, Debra Fitzsimmons described the calculations as well described and likely to be robust.

The Chair invited discussion on the budget impact. Members discussed the number of patients likely to be treated. Based on local intelligence, the number of eligible patients would exceed that estimated in the ESR. However the clinical expert noted that the number of patients eligible according to the indication under consideration was different and the numbers quoted in the ESR were reasonable.

The Chair invited discussion on patient and public issues. Clarification of the effects of treatment on QoL was sought. The clinical expert explained that whilst on treatment, overall patients experienced a decrease in QoL but they do remain active whilst on treatment. In clinical practice, patients with high risk disease tended to tolerate the treatment better. It was noted that in ICON7 there were no significant differences in QoL scores in those patients with high risk disease compared to the control group. Members acknowledged the availability of the treatment in Scotland and in England.

The Chair thanked the clinical experts and asked them to leave the meeting.

Proceedings were concluded by the Chair and members asked to vote.

IPCG recommendation for Health Boards Chief Executives

Bevacizumab (Avastin®) 7.5 mg/kg dose in combination with carboplatin and paclitaxel for the front-line treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer

It is the view of the Interim Pathways Commissioning Group (IPCG) that bevacizumab (Avastin®) 7.5 mg/kg dose in combination with carboplatin and paclitaxel should not be supported within NHS Wales for the front-line treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer.

In making this recommendation IPCG considered all levels of risk for this population.

7. Date of next meeting

The Chair confirmed the date of the next meeting on Monday 27th June 2016 in Cardiff and closed proceedings. *(Post meeting note: June meeting subsequently cancelled).*