The 2015 annual National Conference for Commissioning Chemotherapy Services, hosted by the NHS England Chemotherapy Clinical Reference Group (CRG), was held on 30th November 2015. The conference supported the CRGs continued aim of facilitating consistency of approach in commissioning cancer drugs and chemotherapy services. The meeting was particularly timely, providing both the presenters and the audience a first opportunity to discuss and debate the recently published Cancer Drugs Fund (CDF) consultation document.

The meeting chair, Adrian Newland (Professor of Haematology, Barts and the London NHS Trust and Clinical Member, London North East, Chemotherapy CRG), welcomed the audience to the meeting and began by discussing the context for today’s NHS. The NHS has made a number of improvements in cancer-related patient outcomes over the past decade. However, the NHS is facing a number of challenges in its drive to continue improving outcomes, including financial constraints and increasing patient numbers. These challenges can only be addressed by reducing costs and making efficiency gains.

There are a number of additional challenges for cancer services, including the introduction of cancer vanguards as part of the NHS Five Year Forward View, the spending review, the new cancer strategy, and the uncertain future of the CDF and access to increasingly expensive anticancer drugs. The CDF budget has been steadily increasing, from a budget of £200 million in 2013/2014 to £340 million from April 2015; CDF expenditure has greatly outstripped the budget, however, with projected expenditure for 2015/2016 of £410 million without further prioritisation of spending or delisting of drugs. Key questions that need to be addressed include how to balance the need to control the cancer drugs budget with the need to meet targets for improving the quality of cancer services, and how supportive care should be funded. Professor Newland concluded his opening address by noting that funding of cancer drugs comes with a considerable opportunity cost, with oncology receiving funding at the expense of a wide range of other services.
To investigate the opportunity cost of NICE-funded drugs, a threshold ICER was calculated based on expenditure across 23 Programme Budget Categories (PBCs) and health outcomes linked to ICD codes. The cost per death averted was used to estimate the cost per life year gained, which was then adjusted for quality of life and used as an estimate of cost per QALY gained. Based on these estimates, the threshold cost per QALY gained across all 23 PBCs was £12,936.1

This cost-effectiveness threshold was then used to estimate the opportunity cost of £10 million of additional NHS spending at various cost-effectiveness thresholds for a new drug. At all threshold values investigated, from £20,000 per QALY to £50,000 per QALY, funding of the new medicine was associated with a net harm to NHS patients due to the opportunity cost of providing the drug.2 This finding suggests that the cost-effectiveness thresholds used by NICE are too high, and that NICE guidance is potentially doing more harm than good. Professor Claxton then went on to examine the opportunity cost of the CDF, finding a net harm to NHS patients of approximately 14,000 to 21,000 QALYs each year (Table 1), and noting that the available data suggest that cancer patients are worth five times as much as patients with other illnesses.

Professor Claxton concluded his presentation by being the first speaker to discuss the proposed new CDF, noting that NICE will be responsible for the appraisal of new drugs, with possible assessment outcomes of a drug being recommended for use, not recommended for use, or recommended for conditional inclusion in the CDF to allow further evaluation of their benefit after 24 months. He then raised the concern that conditional approval may give drug manufacturers an incentive to seek a NICE assessment with minimal data, noting that such approaches to funding have been unsuccessful in the past. Professor Claxton’s final suggestion was that NICE implement a value-based rebate mechanism linking the NICE appraisal to the Pharmaceutical Price Regulation Scheme (PPRS) rebate. This would allow NHS England to provide prescribers with a rebate for the cost of medicines funded through baseline commissioning, with prescribers then having to use their local budget to fund drugs that are not covered by the rebate.

<table>
<thead>
<tr>
<th>Year</th>
<th>Budget</th>
<th>Health lost elsewhere (QALYs)</th>
<th>Benefits of CDF (QALYs)*</th>
<th>Net harm to NHS patients (QALYs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013/14</td>
<td>£231m</td>
<td>17,821</td>
<td>3,374</td>
<td>14,447</td>
</tr>
<tr>
<td>2014/15</td>
<td>£280m</td>
<td>21,645</td>
<td>4,098</td>
<td>17,547</td>
</tr>
<tr>
<td>2015/16</td>
<td>£340m</td>
<td>26,283</td>
<td>4,977</td>
<td>21,306</td>
</tr>
</tbody>
</table>

*19,282 patients treated in 2013/2014 and assuming a 3-month survival benefit and 0.7 quality of life. Implies £68,321 per QALY which is used to infer benefits in 2014–2016.

CDF, Cancer Drugs Fund; NHS, national health service; QALY, quality-adjusted life year.
Professor Peter Clark (Consultant Medical Oncologist, Clatterbridge Cancer Centre, Merseyside, Chair, Cancer Drugs Fund and Chair, NHS England Chemotherapy CRG) presented the next session, discussing the current state and future role of the CDF.

As a proportion of GDP, England has relatively low spending on healthcare compared with other countries, with a total NHS England budget of £102 billion in 2015/2016. The total spend on chemotherapy in NHS England is £1,750 million; £1,500 million of this spend is on chemotherapy drugs, £910 million of which is on patent medicines given a positive recommendation by NICE, and £415 million of which is funded by the CDF. These CDF-funded drugs represent 28% of the drug spend and 15% of chemotherapy activity. The monthly cost of individual CDF-funded drugs ranges from £1,300/month to £12,000/month.

Historically, NICE has given a positive recommendation to approximately 60% of cancer drugs; however, in recent years positive recommendations have been given to only 33% of cancer drugs, mostly due to rising costs and the increased use of assumptions in cost effectiveness models leading to greater uncertainty. As the outcome of NICE appraisals is binary, many pharmaceutical companies have introduced Patient Access Schemes (PAS) as a method of making new drugs cost effective in order to gain funding.

For those drugs which are not funded by NICE, the CDF has represented an alternative route for access to funding. However, few CDF-funded drugs have been transitioned into baseline commissioning following a NICE appraisal, leading to consistent yearly increases in the CDF budget. Furthermore, drug cost was not included as a criterion for entry into the CDF until November 2014, further adding to pressures on the CDF budget and leading to a significant overspend. There is also the view that the CDF has undermined the impact of NICE and reduced the need for NICE to assess cancer medicines in a timely manner, and growing concern that the funding of cancer drugs through the CDF allows unequal treatment of cancer compared with other diseases.

The new CDF consultation will lead to appraisal of all new drugs and indications by NICE, with technology assessment committees having three options when assessing new drugs: yes, no and a conditional yes. NICE will be required to issue final guidance within 90 days of marketing authorisation, meaning that the NICE appraisal process will have to begin much earlier. The role of the CDF will shift to an evaluation fund for drugs with uncertain cost effectiveness according to NICE criteria, providing 2 years of funding during which Pharma can collect real-world data to support reassessment and transition of drugs into baseline commissioning. The CDF budget will be capped at £340 million, and reimbursement for Pharma will be adjusted in the event of an overspend.

During the Q&A session that followed, Professor Clark remarked that one of the challenges is how the industry will collaborate with NICE to produce guidance within 90 days of marketing authorisation, noting that the current proposals carry an element of unknown financial risk for the pharmaceutical industry. However, he believes that the timescale for data collection is feasible, commenting that there are a number of discussions still to be had regarding how uncertainty around the value of drugs will be explored and resolved.
Professor Sean Duffy (National Clinical Director for Cancer) began his presentation by outlining the aims of the Independent Cancer Taskforce report, which presents a vision for improving health by targeting a number of key areas, including better prevention and earlier diagnosis of cancer, improved patient experience of treatment, and care for patients living with and beyond cancer (Figure 1). Professor Duffy continued on to discuss the improvement in cancer outcomes seen over the past 10 years, with significant improvements in survival for a wide range of cancers, and over 50% of patients now surviving for 10 years or longer. However, improvements in outcomes have been variable, with marked improvements seen in some diseases, such as breast and prostate cancer, while little progress has been made in others, particularly lung and pancreatic cancer. There is also noted to be considerable regional variations in patient outcomes across the UK.

Professor Duffy noted that patient outcomes in England could be improved by targeting a number of key areas. Examples included improvements in diagnostic services and addressing socioeconomic inequality in early diagnosis of cancer, which has been demonstrated to improve patient outcomes; another example noted by Professor Duffy was the need to address inequality, with a high incidence of some cancers linked with preventable causes associated with socioeconomic deprivation. As improving patient experience and long-term outcomes are a key aim of the strategy, their improvement should be prioritised equally with clinical outcomes in clinical practice and in trials. Finally, every patient should have access to a recovery package when they have completed their treatment.

In order to modernise cancer services, acute workforce deficits need to be fixed and a strategic review of future workforce requirements needs to be undertaken. Centralisation of services will help to maximise efficiency and improve patient outcomes. Key steps to support commissioning include the creation of new Cancer Alliances, which will be committed to improving patient outcomes, and the creation of cancer dashboards, which will show all of the data needed to manage services.

The earliest priorities of the taskforce are to introduce a 4-week wait standard from the time of GP referral to diagnosis. Piloting of new methods of commissioning services is also underway, with NHS England having already implemented a number of vanguard sites. Professor Duffy then concluded by stating that the taskforce has set ambitions, and is now reaching out to those involved in patient care to help deliver them.
Developments in Acute Oncology

Dr Ernie Marshall (Consultant Oncologist, Clatterbridge Cancer Centre) presented the next segment of the meeting, discussing developments in acute oncology services (AOS). Dr Marshall began by commenting that there has been considerable enthusiasm towards acute oncology, and that it has captured the imagination of a number of disciplines. This has led to a number of innovations and widespread uptake of AOS, with acute oncology teams now well established across the country using a range of different service models. At the present time, there are a total of 221 whole time equivalent acute oncology nurses, representing 7% of all nursing staff, and 13% of all oncologists have an acute oncology role.

The 2015 AOS survey showed that acute oncology teams have reduced hospital admissions, although this reduction appears to have plateaued, with most patients admitted due to advanced disease. The introduction of acute oncology teams has also reduced the average patient length of stay by approximately 3 days and improved patients’ experience of care. Staffing remains a key issue in the service, with about half of the respondents agreeing there was insufficient resource. Specialist nurses play a key role in the service, not only in delivering treatment, but in providing leadership.

In light of these observations, a draft AOS specification was published in June 2015, with Dr Marshall commenting that the service specification needs to be translated into a framework for good clinical practice. Some of the current recommendations include the implementation of multidisciplinary teams (MDTs), emphasis of the importance of avoiding unnecessary admissions, alignment of the AOS with acute care and the forging of links between the AOS and primary care. It is also important that the AOS provides comprehensive 7-day services, and works with local commissioning and network performance monitoring.

To improve the service and patient outcomes, the AOS working group has identified four key areas to focus on: metrics; education and training; primary care; and IT innovation. A national minimum dataset is needed to provide metrics with which to drive improvement, and should be aligned with NHS Quality Surveillance Team quality indicators. Finally, as AOS sits across multiple organisations, it is essential that the service has network functionality in order to effectively deliver treatment; to achieve these goals, the service is collaborating with Macmillan and is working to engage key stakeholders. These goals were also discussed at the service’s first annual AOS conference in 2015, and the service is looking to launch an acute oncology website too in the near future.

During the following Q&A session, Dr Marshall commented that it is important for acute oncology teams to engage with primary care and educate the public to increase awareness of the support available to patients and physicians.
Dr Andrew Wardley (Consultant, The Christie Hospital, Manchester) talked about end-of-life care, beginning by stating that a way needs to be found to merge cancer care and end-of-life care, as this would help to both improve patient outcomes and reduce emergency admissions. A number of changes have been made to the provision of end-of-life care at The Christie Hospital. These include:

- Better identification of patients with progressive disease
- Introduction of MDT meetings
- Holistic needs assessment of patients
- A change of terminology from end-of-life care to supportive care
- Earlier involvement of the supportive care team when appropriate

Importantly, the new service has strong links to the community, which greatly assists in providing holistic care for patients. The service works across the whole breast disease group, helping nurses and clinicians identify, treat and support patients with advanced disease. The service also ensures that all patients with advancing disease undergo a holistic needs assessment. In addition to these changes, Macmillan is funding a Breast Palliative Care project, with the aim of increasing communication with community teams and increasing advanced care planning discussions. The aim of the project is to integrate supportive care in the whole group and support the transition of patients from chemotherapy to supportive care or early phase clinical trials.

Early provision of supportive care carries a number of benefits for patients, including improved quality of life, a reduced need for aggressive interventions and improved survival. This has led to a cultural change in the palliative care team, who have refocused their activity on delivering enhanced supportive care with the aim of avoiding unnecessary hospitalisation. As a result, the team has noted an improvement in patients’ prognosis and understanding of where they are in the disease process.

Dr Wardley concluded by touching on the next steps for the service, which include identifying community-based sites that are more appropriate for patients to receive long-term supportive care than admission to a tertiary centre, and investigating options for developing community outreach, such as setting up a mobile chemotherapy unit.
Dr James Larkin (Consultant Medical Oncologist, The Royal Marsden Hospital) discussed the development of new treatments for melanoma, a therapy area in which he specialises. Historically, there have been few effective medical therapies available for the treatment of metastatic melanoma, with treatment options consisting of cytotoxic chemotherapy and cytokines. Due to the lack of effective therapies, overall survival (OS) in this patient group has been poor.

The treatment of melanoma has advanced considerably in recent years, with the introduction of targeted therapies and checkpoint inhibitors over the last 4 years. Targeted therapy with the BRAF inhibitors vemurafenib and dabrafenib has revolutionised the treatment of melanoma, with both drugs demonstrating significant improvements in progression-free survival (PFS) compared with existing therapies.\textsuperscript{3,4} Subsequently, the combination of dabrafenib and the MEK inhibitor trametinib demonstrated a significant improvement in PFS compared with vemurafenib alone (Table 2).\textsuperscript{5–7} Dr Larkin then touched on efforts to identify an effective therapy for the 2% of melanoma patients with KIT-mutant disease, with initial trials indicating that treatment with therapies targeted at KIT show some promise in this patient group.\textsuperscript{8–10} Development of therapies for this rare subgroup of melanoma patients presents a number of challenges, from difficulty evaluating drug sensitivity to the difficulties of disseminating data in a timely manner. Dr Larkin then concluded his discussion of targeted therapies by noting that all tumours eventually develop resistance to treatment.

The presentation then switched to the checkpoint inhibitors, a group of drugs which are designed to take the brakes off the immune system. A 5-year OS analysis of ipilimumab demonstrated a plateau at the end of the survival curve (Figure 2), suggesting a long-lasting benefit of treatment with this drug class in some patients.\textsuperscript{11} This has been further investigated in the CheckMate 067 trial, which is investigating the combination of ipilimumab and nivolumab, with the combination showing a significant improvement in PFS compared with either therapy alone.\textsuperscript{12} Although the combination regimen is associated with a higher side effect burden than monotherapy with either drug, it is also associated with rapid and durable responses in patients who discontinue treatment due to toxicity.

### Table 2. Progression-free survival in patients with metastatic melanoma treated with BRAF and MEK inhibitor combinations

<table>
<thead>
<tr>
<th>Trial</th>
<th>Median progression-free survival</th>
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<tbody>
<tr>
<td>Dabrafenib + trametinib vs vemurafenib\textsuperscript{5}</td>
<td>11.4 vs 7.3 months&lt;br&gt;Hazard ratio (HR) 0.56, p&lt;0.001</td>
</tr>
<tr>
<td>Dabrafenib + trametinib vs dabrafenib\textsuperscript{6}</td>
<td>9.3 vs 8.8 months&lt;br&gt;Hazard ratio (HR) 0.75, p=0.03</td>
</tr>
<tr>
<td>Vemurafenib + cobimetinib vs vemurafenib\textsuperscript{7}</td>
<td>9.9 vs 6.2 months&lt;br&gt;Hazard ratio (HR) 0.51, p&lt;0.0001</td>
</tr>
</tbody>
</table>
As there is no accepted standard of care for metastatic melanoma, there are considerable information needs with regards to selecting patients who will benefit from treatment with targeted therapies and immunotherapies. These should include the route of administration and tolerability of a treatment, disease characteristics and the patient’s preference. Dr Larkin also noted that the checkpoint inhibitor pembrolizumab is an expensive drug, and as yet long-term survival data are unavailable, making assessment of the drugs benefit difficult. Nonetheless, these drugs are now being investigated in combination with other therapies to see if further survival gains can be made.
Commissioning Chemotherapy Services 2015
Report from a National Chemotherapy Clinical Reference Group Conference

*Sally Greenbrook (Policy Manager, Breast Cancer Now)* presented a project investigating health technology assessments (HTA) commissioned by Breast Cancer Now in collaboration with Prostate Cancer UK. The project was undertaken by independent health economists, and compared UK HTA systems with those of Sweden, France, Germany, Australia and Canada, with the aims of determining what these countries did differently from the UK when assessing drugs and identifying lessons that could be learned for the UK. The project was undertaken after the last six breast cancer drugs and five of the last six prostate cancer drugs assessed by NICE were given a negative opinion, while many of these drugs are routinely funded in other parts of Europe.

In the UK, HTAs are the deciding factor in whether a product will be made available on the NHS; a negative decision means that a drug will not be routinely funded, with the exception of drugs funded by the CDF. Patients play a central role in drug assessment, although this does not always translate into patients gaining access to a drug. Drug price is also an important factor, with manufacturers offering discounts to the NHS through the use of PASs.

HTAs in other countries make use of a variety of pricing methods when assessing drugs, with some countries making drugs with limited clinical value available at a reduced price. France, for example, adjusts the price of a drug across its licensed indications depending on a rating of its clinical value in each indication. Such pricing methods allow the needs of industry to be balanced against the budget restrictions of healthcare payers.

Overall, the comparison of UK HTA systems with those in other countries highlights that there is general agreement that patients should be involved in the assessment process, but there is no agreement as to how the patient view should be taken into account. Other countries also demonstrate that flexible pricing can work, and that value-based assessments are beneficial in assessing cancer therapies. Faster assessment of new drugs is likely to mean less uncertainty for patients and faster access to new treatments.

Ms Greenbrook concluded by noting that there is no easy answer for how new cancer treatments can be made available to patients at prices that are both affordable to the NHS and acceptable to the pharmaceutical industry, although the situation could be helped by offering more flexible pricing and reimbursement arrangements. There is also the question of how NICE will resource the accelerated appraisals outlined in the CDF consultation, with the time taken for drug assessments being reduced from the current timescale of up to 2 years to a maximum of 90 days under the revised guidance. However, it is clear that the issue of access to cancer treatments is not going away.
Dr David Dodwell (Chief Knowledge Officer, National Cancer Intelligence Network) was the final presenter of the meeting, providing an update on the SACT dataset. Dr Dodwell began by commenting that commissioning was not the main reason for the development of SACT when it was first proposed; however, because of the introduction of high-cost drugs, the use of SACT data in the commissioning process has come to the fore in recent discussions. This is particularly important, as there is likely to be a shift from conducting large randomised trials to collection of real-world data.

Future commissioning models are expected to include a component of real-world data collection, which will feed back into the commissioning process. At the present time, a lot of the SACT data that have been collected are good and very complete; however, outcome-related data remain incomplete and are sometimes of poor quality. Challenges that need to be addressed to ensure more complete and higher quality data collection include boosting the uptake of e-prescribing.

Dr Dodwell then touched on some of the data analyses that are underway, noting that there was a good match between SACT and chemotherapy waiting time data, then moving on to present an overview of an analysis of 30-day post-chemotherapy mortality in breast and lung cancer patients. Although the data presented were preliminary, they show that real-world mortality is approximately three times higher in patients with lung cancer than in clinical trials, a result which was not apparent for breast cancer. A finding such as this is of particular importance to commissioners, as this difference in mortality negates much of the benefit of treatment. The challenges of collecting SACT data for CDF drugs was then briefly discussed, with few outcome data for CDF drugs available at the present time.

Dr Dodwell concluded by stating that proper resourcing and careful use of SACT data appears to be the way forward. Referring to the CDF consultation document, he commented that it is not yet clear what data are to be collected, how they will be collected, and who will collect them. However, the SACT dataset would be well placed to evaluate the value of cancer drugs, and would be a better solution to this problem than developing a new method of data collection solely for drugs with interim funding.
Meeting close

Professor Newland brought the meeting to a close, thanking the presenters and audience members for their participation in the conference, saying that he looked forward to the next meeting in 2016.

References