Access to Cancer Medicines in Australia

An Interactive Panel Discussion
Michael Powell, Gail Rowan and Dr Karim Ibrahim
Sunday 9th Nov 2014
Interactive Discussion

• We want your input, views, opinions, cases etc!
• Some slides to set the scene
• Two areas to discuss:
  • Cancer drug access – registration/reimbursement issues
  • Cancer drug shortages – “the bread and butter”
Cancer patient from Wales to move into caravan in England 50 miles from his home so he can have access to drugs on the NHS

- David Southwood, 53, is moving 50 miles in order to receive drugs
- Drug axitinib is not yet available on NHS in Wales - but is free in England
- He believes unless he moves he will die before he gets a prescription
- Now family are uprooting their lives and moving to tiny caravan in Somerset

Thirty-six wonder drugs could extend or save the lives of cancer sufferers, but our leaders just need to fund them
“Cancer Drugs Swallowing The PBS!”

• Based on Aug 2014 figures: almost 30% of total PBS/RPBS spend is oncology drugs
  • Other groups: CVS 18%, CNS 16%, GI 11%

• In 2013:
  • Total PBS/RPBS expenditure = $8.2 billion
  • Oncology expenditure = $2.1 billion: ↑ 358% since 2003
  • Non-oncology expenditure = $6.1 billion: ↑ 28% since 2003

• DOH:
  • Over last 2 years, one in four PBAC submissions were oncology drugs
  • For 2013/14: oncology spend $1.5 billion out of total $9.15 billion (i.e. 16%)

Pharma In Focus Nov 3 2014
## PBAC Agenda Nov 2014: Major Submissions

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<tr>
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<td>HER2+ metastatic breast cancer</td>
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<tr>
<td>Trastuzumab Emtansine</td>
<td>HER2+ metastatic breast cancer</td>
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<td>Trametinib</td>
<td>BRAF+ metastatic melanoma</td>
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<td>Cetuximab</td>
<td>First line treatment RAS wild type metastatic colorectal cancer</td>
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<tr>
<td>Axitinib</td>
<td>Stage IV clear cell renal cell carcinoma</td>
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<td>Ponatinib</td>
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# PBAC Agenda Nov 2014: Minor Submissions

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<td>Rituximab s/c</td>
<td>NHL</td>
</tr>
<tr>
<td>Sorafenib</td>
<td>Stage IV clear cell renal cell carcinoma after progression with first line treatment</td>
</tr>
<tr>
<td>Pomalidomide</td>
<td>Relapsed/refractory multiple myeloma after bortezomib and lenalidomide</td>
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PBAC: Types of Submissions

Key points: Types of submissions

- Submissions to list generic equivalents:
  - are usually considered only by the Pharmaceutical Evaluation Branch.

- Minor submissions to list new forms of previously listed products or changes to the conditions of use:
  - do not require an economic evaluation
  - are not evaluated by the Pharmaceutical Evaluation Section or presented to the ESC before consideration by PBAC.

- Major submissions to list new listings, including orphan medicines and significant changes to existing listings:
  - require an economic evaluation
  - are evaluated by the Pharmaceutical Evaluation Section and presented to the ESC before consideration by PBAC.

- Resubmissions:
  - are usually considered to be major submissions might be considered to be minor submissions under exceptional circumstances.
PBAC Nov 2014

- Major Submissions (New Listings/Change to Listings)
  - 29 total – 7 oncology/haem: one in four
- Minor Submissions (New Listings/Change to Listings)
  - 29 total – 4 oncology/haem
Executive Summary

The objective of the project was to conduct an international comparison of access to new oncology medicines in five countries (Australia, Canada, England, Germany and France) over a 5-year period, by examining recommendation rates and the time taken to secure access for patients.

Overall the project found that while recommendation rates in Australia were broadly comparable with those in other countries, on average it took more time to achieve access.
Specifically, the project found that:

- Australia’s recommendation rate for new and subsequent listings was comparable with Canada, with around 25% of new cancer medicines failing to secure reimbursement in these jurisdictions.
- Australia’s recommendation rate for new and subsequent listings appears to be lower than the corresponding rates in France and Germany.
- Australia’s recommendation rate was greater than that for England, but the creation of the Cancer Drugs Fund has led to a recent major improvement in access.
- The mean time from registration to listing in Australia was longer than in most other countries for both new and subsequent listings.
- Access to new medicines for certain cancers such as colorectal cancer, non-small-cell lung cancer and breast cancer seems to be poorer in Australia.
The project also noted that:

- Price reductions were invariably required to obtain a recommendation or listing in Australia, Canada and England
- Risk share arrangements are often associated with listings
- The average number of submissions required to attain a positive PBAC recommendation ranged from 2.3 to 2.5 respectively for new and subsequent listings
## International Comparisons for New Listings

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Dr Klein: Ipilimumab

- TGA approved since July 2011 as monotherapy for patients with advanced/metastatic melanoma who have failed or are intolerant to prior therapy
- PBS reimbursed since August 2013 (reinduction permitted)
- PBS does not allow Ipilimumab treatment prior to BRAF inhibitor treatment in patients with BRAF mutated melanoma
TGA Process

Pre-submission: -3 mths
Submission: 0 mths
Delegate’s Recommendation: -6 weeks
ACPM: 7 mths
TGA approval: 8 mths

PBAC Process

Submission: -17 weeks
March
July
November
PBAC: March
July
November
PBS Listing: Minimum of +5 mths
Added complexities.....targeted therapies

• Co-dependent submission process required:
  • Targeted therapies with a targeted biomarker
  • E.g. BRAF inhibitors
  • Combined MSAC/PBAC submission for BRAF diagnostic testing/BRAF inhibitor for listing on MBS (BRAF testing) and PBS (BRAF inhibitor)
    • MSAC = Medical Services Advisory Committee
    • MBS = Medical Benefits Scheme
On 1 April 2013, NHS England took on responsibility for the operational management of the Cancer Drugs Fund (CDF).

The CDF provides an additional £200m each year to enable patients to access drugs that are not routinely funded by the NHS. It was established in 2010 and will run until the end of March 2016.

There is now a single, national list of drugs and indications that the CDF will routinely fund and standard operating procedures for administration of the fund.

The list of drugs and indications has been compiled by NHS England Clinical Reference Group (CRG) for Chemotherapy working with the local clinician leads who oversaw the administration of the ten regional CDFs.
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<td>3. 2nd or subsequent line treatment post 1st line combination chemotherapy</td>
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Case Study: A Political Football

• BS, 18yo female
• Diagnosed with Atypical Haemolytic Uraemic Syndrome) at 7 months old
  • aHUS = chronic, uncontrolled complement activation causing formation and accumulation of microthrombus in blood vessels throughout body (thrombotic microangiopathy)
  • Affects 60-70 people in Australia
• Went into remission
• Recurrence in 2013
Case Study: A Political Football

• Supportive treatment includes plasma exchange, dialysis and transplantation
• Eculizumab (Soliris)
  • TGA approved 2012
  • Not currently PBS subsidised for aHUS
  • On LSDP for treatment of paroxysmal nocturnal haemoglobinuria (PNH)
• Mum very active in media, involving local/federal MPs
• Self funded for 5 treatments – out of money
• After much wrangling, hospital MAC agreed to fund with regular efficacy reviews every 6 weeks
• Entry onto access program agreed with Alexion from end of Oct
Case Study: A Political Football

• PBAC recommended the PBS listing of Soliris for the treatment of aHUS under a Managed Entry Scheme.
  • “The PBAC considered that the medicine could be cost-effective if the sponsor rebated part or all of the price of the drug depending on how well the patient responds to treatment.”
  • “This means that all eligible patients could be treated with PBS-subsidised Soliris but the price paid by the Government should vary depending on the magnitude of the benefit gained by individual patients.”
  • “Scaled rebates would be applied for those patients who do not achieve complete remission at 6 months.”

• PBS from 1 Dec 2014?
Access to Cancer Medicines in Australia

Karim Ibrahim
Senior HEM/BMT Pharmacist
St Vincent’s Hospital, Sydney
Case Study

• Mr. PM a 56 year old male

• Diagnosed with Hodgkin’s Lymphoma 2001-received ABVD-complete remission

• Relapsed in 2002, further chemotherapy escalated BEACOPP then autologous BMT in 2003

• Relapsed then allogeneic BMT from an unrelated donor in 2004, then relapses in 2007, 2009 and 2010 treated with radiotherapy and DLI, then radiotherapy and vinorelbine and gemcitabine chemotherapy.

• Failed bendamstine chemotherapy in 2013 and then responded to 3 doses of Brentuximab in 2013. Patient does not want any more transplants.
Case study

• Patient has unfortunately relapsed again with bulky abdominal and lung disease. He wants further treatment!

• Team would like to use another 3-6 further doses of Brentuximab

• Dose of brentuximab is 1.8mg/kg every 3 weeks. Mr PM's weight is around 95-100kg, which means he will need 4 vials per dose. Each dose will cost $21,200.

• 3 doses will cost $63,600. 6 doses will cost $127,200

• Drug is not currently subsidised under PBS. Patient is working full-time but can not afford to pay.

• Request to drug committee ? approve

• BTW. Patient is a staff member!!!!
Issues on access to cancer medicines in Australia

• Timeframe to gain PBS listing can be lengthy

• Coverage of indications and reimbursement restrictions

• Barriers arising from state/federal arrangements

• Public hospital formularies

• Private health insurance

• Value of cancer medicines $$$$

• Discussions about when to stop vs. continue treatment
The Bread and Butter

What happens when the basics run out?
The Small Fry Problems...

• Out of stocks

• The global / Australian market

• The PBS...
Out of stocks

• What do we do when things are out of stock?

• How long do we spend sorting out and discussing these issues...

• Cyclophosphamide oral tablets...
• Liposomal doxorubicin...
The Local Market

- Local supply can be determined by international decisions
- 2012 – Mitomycin C withdrawn from Australian market

- COSA and CPG influential in ensuring supply continued
- Impact on anal cancer
- Impact on bladder cancer

- Agreement to continue supply
The Local Market

- Etoposide Phosphate
- 2013 – notice to consider withdrawal from Australian market due to equivalence pricing on PBS
- Letter composed outlining potential impact on cancer services – not drug acquisition costs
- Letter of support for PBAC
- Focus on 4 areas
  - Compounding time
  - Stability
  - Administration time
  - Reaction risk and treatment costs
- Single institution 3 month period 330 doses
  - Etoposide PO4 – 15 min infusion = 82.5 hours
  - Etoposide base – 30-60 min infusion = 330 hours
Bladder

• Already mitomycin C problems
• Now BCG – OncoTICE – out of stock
• Alternative BCG products – difficult to source, short supply
• Alternative installation agents available – are they as good????
• Are they funded????
<table>
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<th>Dose</th>
<th>Protocol</th>
<th>Response rates</th>
<th>Toxicity</th>
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| BCG       | 2-8 x 10^8 CFU (contents of one vial) | Induction: weekly x 6 weeks then maintenance: monthly for 12 months | 2003 meta-analysis 700 patients with CIS  
  - CR: 68% BCG versus 51% chemotherapy. 3.6-year follow-up:  
    - durability of response: 47% BCG 26% mitomycin  
  Systematic Review 585 pt Ta or T1 disease  
  - Recurrence: TURBT plus BCG significantly fewer recurrences at 12 months compared with TURBT alone (odds ratio [OR] 0.30, 95% CI 0.21-0.43) |  
  - frequency (71%), cystitis (67%), fever (23%), haematuria (23%)  
  - No reported BCG-associated deaths  
  - Localised and systemic infectious complications can occur. Do not administer with traumatic catheterization, active cystitis, or persistent gross haematuria following TURBT | The 70 to 86% percent survival rate at 4-5 years with BCG is similar to immediate cystectomy  
  References:  
  Mungan Br J Urol 1998; 82:213  
  Sylvester J Urol 2005; 174:86  
  Bohle Urology 2004; 63:682 |
| Mitomycin-C | 20mg to 40mg daily or 40mg standard | Induction: weekly x 6 weeks then maintenance: monthly for 12-24 months |  
  493 pts assigned BCG (wkly x 6), mitomycin (20 mg wkly x6), or mitomycin (20 mg wkly x6, then monthly for three years)  
  - three-year recurrence-free rates with six-week courses of either BCG or mitomycin were inferior to that achieved with maintenance mitomycin (66 and 69 percent versus 86 percent).  
  - Minimally absorbed into the systemic circulation  
  - Myelosuppression is uncommon  
  - Chemical cystitis (self-limiting) reported in approx. 40% rarely progresses to bladder contraction  
  - hypersensitivity reaction (rash)  
  - Incomplete bladder wound healing post mitomycin |  
  - Most commonly used chemotherapy agent  
  - Not PBS funded | References:  
  Friedrich Eur Urol 2007; 52:1123  
| Gemcitabine | 1500mg to 2000mg | Induction: weekly x 6 weeks then maintenance: monthly for 12 months | 2012 systematic review gemcitabine versus placebo or another agent:  
  Compared with mitomycin C gemcitabine resulted in:  
  - lower rate of recurrence (26% v 39%)  
  - lower rate of progression (11% v 18%) NS  
  - significantly lower incidence of adverse events (39% v 72%)  
  Compared to BCG:  
  Different outcomes depending on the patient population;  
  - untreated Ta-T1 without CIS, equivalent to BCG for recurrence rates (25% v 30%) and risk of progression.  
  - high risk patients, significantly higher recurrence rate (53% v 28%) and significantly shorter time to recurrence (26 v 30 months).  
  - recurrence after BCG (compared to continued BCG), significantly fewer |  
  - compared with intravesical BCG, gemcitabine associated with significantly less dysuria (13% v 45%) and frequency (10% v 45%)  
  - Alternative to BCG or for patients who have progressed on BCG  
  - Unrestricted PBS listing | References:  
  Serrretta Urology 2005; 65:65  
<table>
<thead>
<tr>
<th>Agent</th>
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| Epirubicin | 50 mg | Induction: weekly x 6 weeks Possible maintenance: three times weekly doses every three months for 36 months | more active than either placebo or Interferon (IFN) alpha Trial of 957 patients with intermediate- and high-risk Ta and T1 papillary bladder cancer shown to be less active than BCG Compared to BCG:  
• BCG showed longer time to first recurrence and a higher three-year recurrence-free survival (65% vs 49%)  
• median follow-up 9.2 years, risks of first recurrence and distant metastases significantly lower with BCG (38% vs 53% & 5% vs 8.6%)  
• Death from all causes and death from bladder cancer significantly reduced with BCG (31% vs 38% & 3.4% vs 6.8%) | Limited systemic absorption following intravesical instillation. |
| Interferon   |      |          |                                                  |                                                                          | • Studies have demonstrated activity for this and other anthracyclines, but role remains limited  
• PBS subsidised                                                                 |
| Thiotepa  | 30mg or 60mg | Randomized trial by National Bladder Cancer Collaborative Group showed that intravesical thiotepa (30 or 60 mg) was associated with a significant reduction in recurrence rate | Irritative voiding symptoms in up to 69 percent of patients Because of its relatively small molecular weight (186 daltons), thiotepa is absorbed systematically, and the incidence of myelosuppression may be as high as 54 percent [109, 134]. Furthermore, thiotepa is a potent carcinogen and has been linked to the development of secondary leukemia in patients treated for non-muscle invasive bladder cancer | • Approved for use in the United States for Intravesical administration by the FDA  
• Not PBS subsidised                                                                 |

References: 
Van der Meijden J Urol 2001; 166:476 
Sylvester Eur Urol 2010; 57:766 
Jimenez-Cruz Urology 1997; 50:529 
Prout J Urol 1983; 130:677