Personalized health care: an economic perspective

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Overview

- Background – emerging trends in cancer drugs
- The burgeoning role of health economics in drug reimbursement decisions
- Personalized medicine – a cancer case study
- Some challenges ahead – reconciling individual and population ‘paradigms’
Gene drug heralds cancer's end game

By Danny Buckland 16/09/2010

Find 'as big as penicillin'

A crucial breakthrough in the fight against cancer was unveiled yesterday.

Scientists said the "end game" was in sight after the successful trial of a wonder drug able to genetically target tumours.
Is this cancer's 'penicillin moment'? Gene targeting drug could herald 'end game' for disease

By FIONA MACRAE
Last updated at 1:40 AM on 16th September 2010

A pill that rapidly shrinks the most deadly of skin tumours has been hailed as the dawn of a new era in cancer treatment.

The finding has been likened to the discovery of penicillin.

Known as PLX4032, it is the first cancer drug to harness knowledge from the full decoding of human DNA, and has produced 'spectacular' trial results.
“Today’s remarkable medical technologies and therapies are the direct result of an innovation process that takes place not so much in quantum leaps but more in steady, iterative steps. This continually improving, evolutionary cycle is neither linear nor predictable.”

Nelson, Health Affairs 1994
Top ten drugs in BC 2007/08

<table>
<thead>
<tr>
<th>TUMOUR SITE</th>
<th>TYPE</th>
<th>DRUG</th>
<th>COST</th>
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</thead>
<tbody>
<tr>
<td>Lymphoma</td>
<td>Curative &amp; Chronic</td>
<td>Rituximab</td>
<td>$16,787,572</td>
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<tr>
<td>Breast</td>
<td>Curative &amp; Chronic</td>
<td>Trastuzumab</td>
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<tr>
<td>Prostate</td>
<td>Curative &amp; Chronic</td>
<td>LHRH</td>
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<tr>
<td>Leukemia &amp; Sarcoma</td>
<td>Curative &amp; Chronic</td>
<td>Imatinib</td>
<td>$10,991,744</td>
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<tr>
<td>Breast</td>
<td>Curative &amp; Chronic Aromitase Inhibitors</td>
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<td>$8,026,114</td>
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<td>Breast, Lung, Prostate</td>
<td>Curative &amp; Chronic</td>
<td>Docetaxel</td>
<td>$5,543,786</td>
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<tr>
<td>Colon</td>
<td>Curative &amp; Chronic</td>
<td>Oxaliplatin</td>
<td>$5,320,446</td>
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<td>Pituitary &amp; Carcinoid</td>
<td>Long-term Symptom Control</td>
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<tr>
<td>Colon</td>
<td>Chronic</td>
<td>Bevacizumab</td>
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<td>Lung, Pancreas, Ovarian &amp; Breast</td>
<td>Chronic</td>
<td>Gemcitabine</td>
<td>$2,920,565</td>
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Monthly and median costs of FDA approved cancer drugs (2007 US$)

Source: Bach, NEJM 2009
Why is economic evaluation important?

The Fourth Hurdle

Safety  Efficacy  Quality  Cost-Effectiveness

The Fourth Hurdle
Economic evaluation for reimbursement decisions

• Many jurisdictions now require economic evaluation for reimbursement decisions (primarily for drugs)
  – Accompanied by guidelines for pharmaceutical companies
  – Pricing decisions maybe linked with reimbursement decisions

• Australia: Pharmaceutical Benefits Advisory Committee (PBAC)

• England and Wales: National Institute for Health and Clinical Excellence (NICE)

• Based on ‘Acceptable’ Incremental Cost-Effectiveness Ratios (ICERs)
Economic Evaluation in Europe

Norway: Pharmacoeconomic data required for reimbursement; official guidelines in operation.

Finland: Pharmacoeconomic evidence mandatory for evaluating new therapies for reimbursement and may also be requested for existing therapies.

Sweden: Cost-effectiveness data required for reimbursement.

Denmark: Cost-effectiveness data may be requested for reimbursement decisions.

Netherlands: Pharmacoeconomic evidence explicitly required for reimbursement of new products.

Belgium: Formal requirement for economic evaluation.

France: Not a formal requirement but increasingly used in reimbursement decisions. Guidelines prepared.

Ireland: Guidelines for pharmacoeconomic studies prepared; cost-effectiveness data may be requested.


Spain: Health technology assessment at a regional level.

Portugal: Cost-effectiveness data incorporated into reimbursement decisions.

Italy: Cost-effectiveness considered in pricing and reimbursement decisions.


Greece: Guidelines for pharmacoeconomic studies prepared; cost-effectiveness data may be requested.

Source: National Centre for Pharmacoeconomics, Ireland
How big is the hurdle?

- $100,000/QALY
- $60,000/QALY
- $50,000/QALY
## ICER thresholds in Australia

<table>
<thead>
<tr>
<th>Number</th>
<th>Incremental cost per additional life-year gained at 1998/1999 prices ($AU)</th>
<th>PBAC decision</th>
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<td>7</td>
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<td>8</td>
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<td>9</td>
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<tr>
<td>12</td>
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<tr>
<td>13</td>
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<tr>
<td>14</td>
<td>43550</td>
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<tr>
<td>15</td>
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<td>16</td>
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<td>17</td>
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<td>22</td>
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<td>23</td>
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<td>25</td>
<td>256950</td>
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</tbody>
</table>

*Source: George et al. Pharmacoeconomics 2001*
Cancer ICER thresholds in England and Wales

Figure 1: ICERs expressed as US$ (at purchasing power parity) per QALYG or LYG for condition–treatment pairs appraised by NICE

Source: Rawlings. Lancet Oncology 2007
A personalized medicine case study: Cetuximab (Erbitux) in advanced colorectal cancer (CRC)
Treatment for advanced colorectal cancer (CRC) – improves overall and progression-free survival compared to best supportive care\(^1\)

Mechanism of action - monoclonal antibody that targets epidermal growth factor receptor (EGFR), modulating tumor cell growth\(^2\)

Resistance to cetuximab is common (>50% after one treatment) - Caused by mutations in component of EGFR: *K-ras* protein, which occur in ~40% of patients\(^3\)
Cetuximab in Advanced Colorectal Cancer

Effectiveness of cetuximab (overall and progression-free survival) is significantly associated with $k$-ras mutation status ($p > 0.001$)

- Patients with wild-type $k$-ras tumors did benefit (overall survival 9.5 months)
- Patients with mutated $k$-ras tumors did not benefit (overall survival 4.8 months)$^3$

Source: Karapetis et al, NEJM, 2009
Cost-effectiveness

– Cetuximab may increase the already significant cost of managing advanced CRC, especially when provided to all patients

– Drug and administration cost of cetuximab $71,000/patient\(^4\)

– K-ras testing $450/patient\(^4\)
Cetuximab in Advanced Colorectal Cancer

Cost-effectiveness cont...

- Providing drug to all patients is not cost effective
- Incremental cost effectiveness ratio (ICER) ~$300,000 per QALY gained\(^5\)
- Targeting the therapy to patients with wild-type \(k-ras\) improves cost-effectiveness
- ICER ~$180,000/QALY\(^5\)
- Theoretical cost-savings associated with treating only wild-type \(k-ras\), $740 million (US), accounting for cost of \(k-ras\) testing
Some challenges ahead
Identifying the costs of testing strategies

- Current reimbursement systems for diagnostic tests are cost based rather than value based
- Tests for multiple markers cost thousands of dollars
- Technology is changing – cost per single-nucleotide polymorphism (SNP) analyzed is falling rapidly
- True opportunity cost is often unknown – testing may result in changes to medical utilization
- Difficult to estimate a true economic value at any given time
• Genetic tests share the same concerns about sensitivity and specificity as older diagnostics
• Patient outcomes are likely to be influenced by multiple genes, and each gene can influence multiple outcomes
• Each outcome is modified by interactions with other genes and environmental exposures – including diets, drugs and disease states
Lack of effectiveness data

- Lack of data on patient and clinician behaviour following the results of diagnostic tests, and associated patient outcomes
- Issue gets more complicated if the test indicates a patient should not get a drug
- Are there alternatives?
- If so, how does the analysis factor in the timing and sequencing of alternatives?
Lack of effectiveness data cont ...

- Inconclusive or contradictory results from small (n < 200) RCTs may be insufficient for robust estimates of effectiveness
- More decision analytic modelling required, with careful consideration of parameter and decision uncertainty
- Use of surrogate end-points, e.g. progression free survival, is likely to increase
- Cumulative synthesis of RCTs needed
• Uncertainty with the clinical value of new technologies will likely mean that the value of additional research and policy options, such as CED, should be considered.
• CED = provisional approval for coverage by payers on condition that additional data on effectiveness are collected through RCTs or patient registries.
• Registries and linkable administrative data sets will only become more important.
Some concluding thoughts
Individual vs. population ‘paradigms’

- Personalized medicine produces treatment regimens based on the molecular biology of *individuals* and their diseases
- Economic evaluation (and EBM) produces results based on responses of average patient *populations*, and considers *effectiveness* not just *efficacy*
- RCTs are limited to exceedingly homogeneous populations because of strict inclusion/exclusion criteria and tightly controlled settings
Personalized vs. stratified medicine

• Is personalized medicine more likely to lead to smaller and smaller sub-group analyses rather than ‘individualized’ care?

• Possibly, because the marginal cost of developing new drugs will outweigh the marginal benefits for pharmaceutical companies.

• RCTs and economic evaluation will not become redundant – but they will be more complex and costly.

• Linkable administrative data will be very important.
Personalized medicine promises to provide tailored therapies that take into account individual differences in risk and values.

The balance of risks and benefits for each person will differ because of preference heterogeneity.

Tailoring therapy and determining the optimal strategy will mean listening to patients’ preferences.

Economic evaluations need to model patient preferences about different treatment options.
Bevacizumab for Advanced CRC
Acknowledgements

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