What Value Do We Place on a Cure?
Value Demonstration Challenges Associated with Innovator and Regenerative Therapies in the EU, North America and Asia

ISPOR European Congress, Amsterdam, Netherlands

November 2014

Several Types of Emerging Therapies Poised to “Transform” Healthcare

<table>
<thead>
<tr>
<th>Emerging technology platform/modality</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gene therapy</td>
<td>Adenosine deaminase (ADA) gene deficiency replacement (1990)</td>
</tr>
<tr>
<td>Protein/enzyme/hormone replacement (synthetic)</td>
<td>Humulin (1982)</td>
</tr>
<tr>
<td>Therapeutic antibodies (murine)</td>
<td>OKT-3, ALJ (1986)</td>
</tr>
<tr>
<td>Therapeutic antibodies (humanized)</td>
<td>Campath, Cambridge University/Miller's (2000)</td>
</tr>
<tr>
<td>Therapeutic antibodies (humanized)</td>
<td>Meditoxin, Roche (1999)</td>
</tr>
<tr>
<td>Antisense</td>
<td>Virazole, Iox (1996)</td>
</tr>
<tr>
<td>RNAI</td>
<td>No approved drug yet - several clinical trials</td>
</tr>
<tr>
<td>Therapeutic vaccines</td>
<td>Merx, Avax Technologies (2005)</td>
</tr>
<tr>
<td>Cell therapies, hematopoietic stem cells</td>
<td>First allogeneic bone marrow transplant, Sloan-Kettering, NY (1953)</td>
</tr>
<tr>
<td>Cell therapies, human embryonic stem cells</td>
<td>No approved drug yet - many clinical trials planned</td>
</tr>
<tr>
<td>Cell therapies, human adult stem cells</td>
<td>No approved drug yet - several late stage clinical studies ongoing; for example, graft versus host disease by Chris (Phosphera)</td>
</tr>
</tbody>
</table>

Source: Schmidt et al. Drug Discovery Today 2009
Growth Projections: Key Emerging Technology Categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Market 2012 ($B)</th>
<th>Market 2018 ($B)</th>
<th>CAGR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Device</td>
<td>$350</td>
<td>$440</td>
<td>4%</td>
</tr>
<tr>
<td>Cell Therapy / Regen</td>
<td>$2</td>
<td>$8</td>
<td>21%</td>
</tr>
<tr>
<td>Orphan / Rare / Specialty</td>
<td>$83</td>
<td>$120</td>
<td>7%</td>
</tr>
<tr>
<td>Immunotherapy / Vaccines</td>
<td>$64</td>
<td>$111</td>
<td>14%</td>
</tr>
<tr>
<td>Personal Med / CDx</td>
<td>$292*</td>
<td>$492*</td>
<td>11%</td>
</tr>
</tbody>
</table>

Source: Quintiles analysis of secondary sources.

What is Regenerative Medicine? (with cell therapies as a subset)

Deals with repairing or replacing tissues and organs by using advanced materials and methodologies

- **Allogeneic stem cells** – cells taken from one person and given to another person
- **Autologus stem cells** – cells taken a person and given to the same person
- **Gene therapy**
- May also involve **biocompatible matricies and/or other systems to support the cells**
- Sources of adult stem cells (multiple):
  > Bone marrow & blood
  > Skeletal muscle
  > Adipose tissue
  > Liver, brain, cord blood, placenta and umbilical cord
Many Issues Required To Understand Value Drivers for Regenerative Medicine

- Payers will look at the balance of outcomes relative to cost of entire procedure.
- How will evidence development differ from conventional therapies?
- Are available codes/tariffs sufficient for key procedure steps?
- Do we need a new code/tariff? If so, what timing and info required?
- What outcomes are important in avoiding reimbursement rejection?
- What are the key reimbursement limitations that we can expect for the therapy?
- Is payment level appropriate to support access for each step?
- What are our options for address inappropriate payment?
- How does site of care influence reimbursement potential for the therapy?
- Is special expertise required to provide the therapy?
- Are Centers of Excellence required?
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Cell Therapies & Regenerative Medicine: What is Different?

<table>
<thead>
<tr>
<th>Issue</th>
<th>Cell Therapies &amp; Regenerative Medicines</th>
<th>Conventional Biologics</th>
<th>Implications</th>
</tr>
</thead>
</table>
| Well understood & accepted by payers and physicians | Not well, at present perceived as truly novel | Yes | • Payers and physicians may place higher scrutiny on value demonstration  
• Commercialization may involve additional educational efforts and/or complexities |
| Involves multiple procedural steps that may be separately reimbursable (including in cell extraction, purification and processing, and administration that may include imaging) | Often | Rarely | • More like reimbursement for a device/procedure  
• Failure to achieve reimbursement of any component part may jeopardize reimbursement of the entire procedure  
• HTA will focus on the cost-effectiveness of the entire procedure |
| HTA will focus on the cost-effectiveness of the entire procedure | Yes | Not often applicable | • Requires HEOR data collection regarding the entire procedure |

Faulkner E (chair and presenter), Brot K, Spinner D, Payne K. How will innovator technologies fare in an increasingly restrictive global reimbursement environment?: lessons from comparison of cell and gene therapies to conventional biopharmaceuticals. International Society for Pharmacoeconomics and Outcomes Research, 14th Annual European Congress, Madrid, Spain, November 2011.
Cell Therapies & Regenerative Medicine: What is Different?

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<tr>
<th>Issue</th>
<th>Cell Therapies &amp; Regenerative Medicines</th>
<th>Conventional Biologics</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>May involve multiple billing codes / tariffs and/or payment centers</td>
<td>Yes</td>
<td>No</td>
<td>• Lack of appropriate codes/tariffs or payment may limit or preclude access and uptake</td>
</tr>
<tr>
<td>for reimbursement of the full procedure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>May involve requirements for longer-term data collection to</td>
<td>Yes</td>
<td>Sometimes</td>
<td>• This is a top HTA criticism of most cell therapies in global markets to date</td>
</tr>
<tr>
<td>demonstrate value (including post-market follow-up data)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strong potential to be more costly than standard of care (SOC)</td>
<td>Often</td>
<td>Sometimes</td>
<td>• Higher cost means that therapies must demonstrate significant outcome</td>
</tr>
<tr>
<td>alternatives</td>
<td></td>
<td></td>
<td>improvements vs. SOC comparators</td>
</tr>
<tr>
<td>May enable a disease cure or prolonged therapeutic effect</td>
<td>Yes</td>
<td>Rarely</td>
<td>• Can alter the balance of benefit-cost tradeoffs in value assessment</td>
</tr>
</tbody>
</table>

Faulkner E (chair and presenter), Bröt K, Spinner D, Payne K. How will innovator technologies fare in an increasingly restrictive global reimbursement environment?: lessons from comparison of cell and gene therapies to conventional biopharmaceuticals. International Society for Pharmacoeconomics and Outcomes Research, 14th Annual European Congress, Madrid, Spain, November 2011.

How Does the Global Regenerative Medicine & Cell Therapy Market Look?

• Larger than you might think…

• Cell Therapy Group reports ~250 companies (globally) with >300 products in development in 2008*

<table>
<thead>
<tr>
<th>Phase</th>
<th>Today</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I</td>
<td>89</td>
</tr>
<tr>
<td>Phase II</td>
<td>77</td>
</tr>
<tr>
<td>Phase III</td>
<td>32</td>
</tr>
<tr>
<td>Commercial</td>
<td>68</td>
</tr>
</tbody>
</table>

• Alliance for Regenerative Medicine Reports around 700 products in preclinical & clinical development in 2014

• Some therapies may be “home brew” in-hospital products and not commercial therapies

• Market entry by big pharma has just started (Pfizer, Roche, J&J, Novartis)

## Evidentiary Criticisms in HTA
### Differences Among Markets

### Evidence Consideration

<table>
<thead>
<tr>
<th>Evidence Consideration</th>
<th>AU</th>
<th>CA</th>
<th>FR</th>
<th>DE</th>
<th>IT</th>
<th>ES</th>
<th>SE</th>
<th>UK</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insufficient evidence of value</td>
<td>S</td>
<td>S</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>S</td>
<td>Y</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Insufficient number/quality of studies</td>
<td>S</td>
<td>S</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Y</td>
<td>Y</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Lack of comparative data</td>
<td>S</td>
<td>S</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Y</td>
<td>Y</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Lack of long term data (&gt;1 year)</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>NA</td>
<td>NA</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>S</td>
</tr>
<tr>
<td>Inconclusive or inconsistent outcomes</td>
<td>S</td>
<td>N</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>N</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Focus on surrogate outcomes</td>
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<td>S</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>S</td>
<td>Y</td>
<td>N</td>
<td>S</td>
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<tr>
<td>Inappropriate endpoints</td>
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<td>NA</td>
<td>Y</td>
<td>Y</td>
<td>S</td>
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<tr>
<td>Concerns regarding safety</td>
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<td>N</td>
<td>Y</td>
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<td>NA</td>
<td>N</td>
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<td>NA</td>
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<td>Y</td>
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<td>S</td>
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<tr>
<td>Insufficient cost-effectiveness</td>
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*Y = yes, in all assessments (yellow); S = some (green); N = no (red); NA = not available. Abbreviations: AU = Australia, CA = Canada, FR = France, DE = Germany, IT = Italy, ES = Spain, SE = Sweden, UK = United Kingdom, and US = United States. *Note: due to the limited number of assessments in some markets and variability of information reported in HTAs and reimbursement policies, results should be interpreted with caution. N = 48 HTAs and reimbursement policies from Australia, Canada, France, Spain, Sweden, the UK and US.

Aside from the US, Australia had the most HTAs (n=15). Many were horizon scanning reports and virtually all rejected the technology based on level of evidence/maturity and some due to insufficient marginal improvement to address unmet need.

Spain and Sweden had few HTA reviews on regenerative medicine and premature to draw conclusions on payer position + perspectives.
Evidentiary Criticisms in HTA
Differences Among Markets

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<td>Insufficient efficacy</td>
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Many US HTAs were noncoverage policies for technologies not yet on the market. Main reason is likely to prevent broader hospital use through existing reimbursement mechanisms for “unproven technologies”

Percentage of HTAs that Noted Key Evidentiary Criticisms

Study design quality is key. Device-like studies = high rejection potential

N = 48 HTAs and reimbursement policies from Australia, Canada, France, Spain, Sweden, the UK and US
Empire Strikes AHEAD: US Payer Preemptive Noncoverage Policies for Regen. Therapies

Sample target indications currently *not covered* by leading US payers:

- Myocardial infarction
- Congestive heart failure
- Multiple sclerosis
- Systemic lupus erythematosus
- Systemic sclerosis
- Rheumatoid arthritis
- Juvenile rheumatoid arthritis
- Idiopathic thrombocytopenic purpura
- Dermatomyositis
- Polymyositis
- Autoimmune cytopenia
- Diabetes mellitus (type I)
- Systemic vasculitis
- Celiac disease
- Crohn's disease
- Oncology (select indications/applications)

**Implications for Regenerative Medicine:**

- Payers are concerned about unproven, hospital-based cell therapies
- Policies will change as evidence for tested products matures in the marketplace

Source: Indications identified through evaluation of multiple US MCO coverage policies.
Focus on Outcomes that Matter for Regenerative Med

Level of importance regarding assessment of regenerative medicines for reimbursement: 1 = lowest and 10 = highest

- Effectiveness – based on hard endpoints (i.e., mortality, morbidity)
- Durability of treatment effect
- Evidence of safety (including treatment related adverse events)
- Comparative effectiveness vs. SOC alternatives
- Established scientific rationale for clinical response
- Cost of the cell/gene therapy component
- Overall procedure costs
- Quality of life impacts
- Availability of long-term data
- Effectiveness – based on surrogate outcomes
- Physician/medical society support

Based on a US 2013 survey of the National Association of Managed Care Physicians, including 60% payer and 40% provider respondents. N = 20

US Perspective on Paying for Regenerative Medicine Value

What degree of increase in payment could regenerative medicines potentially capture under the following circumstances?

- Disease is cured [permanently]
- Prolonged duration of therapeutic effect 2-3 years longer than any established alternative
- Prolonged duration of therapeutic effect 6-12 months longer than any established alternative

- 60% said >51%
- 45% said >26%
- 20% said 51%

Based on a US 2013 survey of the National Association of Managed Care Physicians, including 60% payer and 40% provider respondents. N = 20
Call to Action: NICE to Reconsider HTA of “a Cure”

- House of Lords Science and Technology committee to review policy on HTA of potentially curative therapies
- Recognizing >34 cell & gene therapies in pipeline in UK
- Current HTA models do not take into account:
  - High start up manufacturing costs for cell therapies
  - Wider economic & social benefits of a cure
  - Integration of cures into value-based pricing schemes
- Some initial technologies may be allowed higher pricing and then NHS will demand economies of scale for later entrants

Will a Single Payment for a Cure Fit into Reimbursement Processes?

The special case of gene therapy pricing

- Approval of [regenerative] products will be based on data from trials captured over a period of time shorter than the expected duration of the therapy. Payers may be reluctant to structure a one-time payment over a ‘projected’ duration of efficacy.
- Criticisms may emerge, despite the fact that effective [regenerative] therapy may reduce the overall financial burden to the healthcare system
- Example: Lost in the discussion was the fact that Sovaldi ($84K per year) was not priced higher than less effective alternatives it represented a cure of a prevalent infectious disease
- Pay for Performance Solution - annuity system that is a true risk sharing arrangement where continued reimbursement is dependent on measurement of clinical efficacy

Measure Twice and Cut Once for Regenerative Medicine Value Prep

- Regenerative medicine value demonstration requires evaluation of multiple “layers”…just like Precision Medicine…there are more layers to this onion than conventional therapies


Paying for a Cure: Key Considerations for Discussion Today

- We aren’t generally used to paying upfront for a cure…requires us to rethink system & incentive issues
- What models could we consider?
  - Pay for Performance
  - Amortization
  - Novel financing schemes
  - Other???
- Where will the funding come from?
- What is likely to actually be accepted and by whom?
- How will we handle scenarios where multiple cures are found if regenerative therapies achieve their promise?
- What about broader vs. orphan indications?

Image source: www.bing.com
What value do we place on cure?

Value demonstration challenges associated with innovator and regenerative therapies in the EU, North America and Asia

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(2) Adjunct Professor, Department of Epidemiology and Community Medicine, University of Ottawa
(3) Senior Scientist, Institute for Public Health, Medical Decision Making and Health Technology Assessment

UMIT - Private Universität für Gesundheitswissenschaften, Medizinische Informatik und Technik GmbH
Literacy: What is a cure?

• Cure or temporary health state?
  – A1C/FPG (diabetes), HCV SR (chronic hepatitis C infection), >5 yr PFS (various cancers)

• No chance of re-entering suboptimal health state from same disease
  – Gene therapy
  – Autologous transplant

Numeracy: What are the numbers?

• What am I willing to give up?

• Is it ~ cost of production in a competitive market, “i.e., what must be given up to produce the commodity.”

• “... there is no competitive or any other production of lives, independent of the people concerned. My life is unique, no other lives compensate me for the loss of it.”

“Evans, Strained Mercy
The Economics of Canadian Health Care, 2007
Numeracy: What are the numbers?

• "When given a choice between preventive and curative interventions, more subjects preferred the preventive intervention (37% vs 21%, p=0.002)."


Numeracy: What are the numbers?

<table>
<thead>
<tr>
<th>Table 6: Marginal effects for population average models</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Predictor</td>
<td>δ Uₜ - Uₜ*</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Lives saved</td>
<td></td>
</tr>
<tr>
<td>Cure(B - A)⁻¹</td>
<td>-0.2118</td>
</tr>
<tr>
<td>AgeGrp1(B - A)⁻¹</td>
<td>0.3222</td>
</tr>
<tr>
<td>AgeGrp2(B - A)⁻¹</td>
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<tr>
<td>AgeGrp3(B - A)⁻¹</td>
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</tr>
<tr>
<td>Evidence(B - A)⁻¹</td>
<td>0.1714</td>
</tr>
<tr>
<td>Fault(B - A)⁻¹</td>
<td>-0.1455</td>
</tr>
</tbody>
</table>

Numeracy: What are the numbers?

- So age, available treatments, “type” of patient, level of income may be a factors in valuing a cure¹

- Of course we may also want to consider
  - Amount of potential life lost
  - State of health at cure


*Ensure that the value of what is gained from an activity outweighs the value of what is sacrificed*” (Williams)
Numeracy: What are the numbers?

Model description and Symbols:
- **Boxes**: Decision-making bodies.
- **Circles**: Data requirements, tools, etc. which impact process.
- **Broken Arrows**: May or may not impact decision.
Ecolacy: And then what?

• Global budget envelope provided to hospital based on demographics and service levels
• Budget impact first and then (possibly) HTA - Rarely, hospital HTA although opportunity cost stems from hospital budget constraint.
• Only one cell therapy (Prochymal) licensed so far

Ecolacy: And then what?

• Physicians likely to use existing physician fee schedule codes to cover new procedures (not always)
• New code development largely out of control of new entrants – feasibility of implementation also an issue (who is responsible?).
Summary

• “Value” in Canada (or elsewhere) has little to do with whether intervention is a “cure” or not
• High upfront costs are a significant barrier to adoption due to finance structures.
  – Small budgets and no real potential for innovative financing
  – Much uncertainty re: feasibility of implementation
  – Even an economically attractive price may not be enough to ensure uptake
Background

- Recent innovations have brought the concept of a “cure” into increased prominence for the public, payers, and governments.

- Potential for a substantial number of new products to enter the medical marketplace with the ability to “cure” diseases.

- Few currently in the marketplace
Regenerative Medicine and Advanced Therapy Overview

- **247** Total Therapeutic COMPANIES
- **466** Total Unique Therapeutic PRODUCTS
- **699** Total Preclinical & Clinical Stage TRIALS

Marketed products in the U.S.

- Dermagraft
- Osteocel
- PureGen
- BioDfactor
- BioDfence
- IaViv
- Provenge
- Carticel
- Epicel

- Nucel
- Apligraf
- GINTUIT
- Trinity Evolution
- Grafix
- DeNovoET
- Prokera
- AmnioGraft

Alliance for Regenerative Medicine Annual Report, 2014
Potential Value of a cure for Duchenne muscular dystrophy

Challenges: Data needs

- Long-term data
  - Mortality
  - Quality of life
  - Post market follow-up
    - Registries
    - Coverage with evidence development

- Subgroups
  - Multiple comorbidities
  - Disease stage
  - New starts vs. Prevalent cases
Value and Timing

- Timing of intervention in patient’s life/disease cycle is key
- Sovaldi in incarcerated populations
  - Treating all patients with Hep C
    - ~30,000/QALY
    - $48 billion dollars
  - Treating only patients with advanced fibrosis
    - ~14,000/QALY
    - $3.8 billion

Affordability/Financing

- The total cost of curative treatments for common diseases may be prohibitive even if they demonstrate good value.
  - Disease areas for many new product targets are common.
    - 3.2 million hepatitis C patients in U.S.: ~$200 billion
- Challenge of a large upfront cost
  - “Think about AIDS treatment as paying a mortgage. Sovaldi is like buying a house with cash.” – NY Times
U.S. Challenges

Multi Payer system:
- Limited time to capture the downstream cost savings

20% continued with the same insurance plan at 3 years

Additional Challenges: U.S.

- High(est) costs
  - Sovaldi costs in U.S.: $1,000 per pill
  - Sovaldi costs in Egypt: $1,000 per patient
- Many payers can’t say no
- Drugs vs. Procedures
- Bundled payments
- Accountable Care Organizations
National Association of Medicaid Directors (NAMD)

• “Policymakers have failed to address the cost and reimbursement issues associated with faster or increased pathways for the development of high-cost therapies and treatments.”

• “While the immediate focus and challenges present with hepatitis C treatments, we know this is a harbinger of the promises and challenges that will emerge in the years ahead.”

• “The challenge...is the intersection of a high-cost therapy and a potentially large population eligible for the therapy.”

• “It is not practical to expect Medicaid programs to finance the significant upfront costs of Sovaldi...on the promise of seeing savings 10, 20, or 30 years later.”

NAMD policy suggestions

• Direct price controls for public payers
• Federal purchasing (negotiated discount) and distribution to public programs (e.g. vaccines)
• Mandated rebates for high volumes (i.e. Price volume)
• Modify “best price” to include selling price in other countries (reference pricing)
• Allow Medicaid programs to utilize cost-effectiveness research to identify whether or not a particular drug will be included in the program’s formulary by granting Medicaid the flexibility to exclude products that are found to not be cost-effective
• Allow innovative payment arrangements. For example, allow states to enter into outcomes-based contracts with manufacturers, where payment is made per successful course of treatment rather than per pill.
Performance-based Risk-Sharing Arrangements

- Outcomes guarantee
- Annuity: Payer pays per year if patient remains “cured”
  - Max payment
  - Difficult in U.S. context → member turn-over

*All Headaches instantly Cured or Money Refunded.*

*Dr. Emerson’s Bromo-Seltzer, the most successful American Remedy, is an effervescent Powder, taken in water. If these dose do not cure any Headache, no matter how caused, send the bottle to us and you will at once refund the price. Very useful in colds, coughs, toothache, etc.*
Regenerative Medicine: A European HTA perspective

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Agenda

• Regenerative medicine: definition and value
• Regenerative medicine in Europe
  • Treatments with EMA authorisation
  • Their reimbursement status in Europe
• Other regenerative treatments
• HTA and Budget Challenges
• Ways forward
Regenerative Medicine: Definition

- "Regenerative medicine replaces or regenerates human cells, tissue or organs, to restore or establish normal function."\(^1\) Includes different types of therapies. For instance\(^2\):
  - Stem cell therapy
  - Cellular therapy
  - Tissue engineering
  - Gene therapy (sits between stem cell and cellular therapy)

- Regenerative medicine has the potential to "deliver new, innovative therapies, or even cures, where conventional approaches do not provide adequate solutions.\(^3\)


Treatments with EMA authorisation

- **Glybera (2012):** Gene therapy to treat lipoprotein lipase deficiency.
- **Chondrocelect (2009) and MACI (2013):** Tissue-engineered products to treat cartilage defects in knees.
- **Provenge (2013):** Cell therapy to treat prostate cancer.
Reimbursement status in Europe

- Glybera: launch delayed to add data (expected in the fourth quarter of 2014/first quarter of 2015).
- Chondrocelect and MACI: in scoping stage in NICE. Additionally, Chondrocelect is currently available for patients and reimbursed in Belgium, the Netherlands and Spain. HAS, in France, has published a negative opinion of Chondrocelect due to paucity of clinical evidence.
- Provenge: company plans to make it available in Europe (announced in March 2014), starting with UK and Germany. NICE and IQWiG have not yet expressed an opinion on this product.


Other regenerative treatments

Not EMA regulated, treated as surgical interventions

- Bone marrow transplantation: often used to treat conditions which damage bone marrow, such as leukaemia, so that it is no longer able to produce normal blood cells.
- Replacement skin cells, grown by a process called tissue culture, can be used to help burn wounds heal.
- Pancreatic islet transplantation: islet cells make and release insulin. After this procedure diabetic patients can become insulin-independent.
  - NICE has issued an interventional procedures guidance [IPG274] about autologous pancreatic islet cell transplantation for improved glycaemic control after pancreatectomy.

These are typically reviewed at a provider level with some payer input.

HTA and Budget Challenges

• "Cures" are, in effect, disease modifying therapies for chronic diseases with all of the associated problems
  • Short term trials using surrogate markers may not produce relevant clinical outcomes
  • Outcomes may not be sustained over time
  • Safety problems may emerge
• Value of information approach can help choices between (i) adopt, (ii) delay and trial, (iii) adopt and trial (CED). Risk sharing can enhance value of (iii).
• Real challenge is not HTA but budget impact
  • Can we tackle high upfront costs of a cure that was cost-effective using the appropriate cost-effectiveness threshold?
  • Three possible routes?

Ways forward (1): “Pay for performance”

• Eliminate any perverse incentive to prioritise investment in repeatedly administered therapies over one-time treatments.
• Pay for performance with periodic payment as long as gene therapy "works".
• At its simplest (i) annual health check (still cured?) (ii) runs for several years / lifetime
• But many issues in structuring a PBRSA
  • Transaction costs
  • Patient “churn” – does money follow the patient?
  • May not be a simple "works" yes/no? measurement / threshold issues
  • Dying of something else...

Ways forward (2): “Amortisation”

• Payment models that spread the potentially high upfront costs over the time during which benefits are realized, which would allow the cost of treatment to be amortised over many years.

• This is how capital equipment is treated. But:
  • Still pay upfront for uncertain benefit
  • It meets accruals principle but does it meet the prudence principle?

• They make the point that a third party could get involved. This is equivalent to leasing e.g. when we buy a car. But with a car we get a warranty and we know the residual value over time.

• A medical equipment alternative is that the innovator retains ownership of the “asset” and contracts to provide a flow of services - P4P!


Ways forward (3): Innovative financing mechanisms

• In global health there are examples. Notably, the International Finance Facility for Immunisation, (IFFIm) which raised US$bn1.

• Donors pledge up front and payback over time. Upfront money is spent by LICs on vaccines – equivalent to a “cure”

• But inserting a third party between manufacturers and payers / insurers to make upfront payments is problematic:
  • It is efficient for innovators to bear some if not all of the performance risk
  • Insurers are already pooling patient population risks

Source: 1 Larry Elliot (2006).
Summary points

• Regenerative medicine shows potential
  • Might even provide cures in some cases.

• Only four treatments have had regulatory approval in Europe so far.
  • Only one of them is reimbursed centrally, in four European countries. Turned down by HAS.

• In HTA terms, “cures” are, in effect, disease modifying therapies for chronic diseases with the associated problems

• High upfront costs might pose a barrier to adoption.
  • PBRSAs / MEAs offer a way forwards
  • Accounting changes “amortisation” and “innovative financing mechanisms” may (?) offer a way forward

References

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Key Questions: Putting it All Together

- How are regenerative therapies potentially different in terms of value characterization?
  - Clinical trial & economic expectation
  - “Fit” into reimbursement systems/health systems

- What key opportunities and barriers to you see to addressing and paying for curative therapies?
  - Scenarios with low cost alternative or crowded indications

- What methodological changes are key to addressing curative therapies or therapies with prolonged duration of therapeutic effect?

- Which reimbursement approaches are likely to be successful here?
  - Risk sharing models (e.g., annuity models/pay for performance)
  - Novel coding & payment schemes

- Where should we go from here?