Achieving Reimbursement for Regenerative Medicine: Building Collaboration with Payors

Richard T. Maziarz, OHSU
Robert Deans, Athersys

ISCT 2012
2010: A New Vision for Partnership

ISCT Industry Task Force
Summary of Recommendations
<table>
<thead>
<tr>
<th>CC Subcommittees</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Process and Product Development</strong></td>
<td><strong>Business Models, Reimbursement</strong></td>
</tr>
<tr>
<td>Technology</td>
<td>and COGS</td>
</tr>
<tr>
<td></td>
<td><em>To define economic aspects of manufacturing clinical cell products and tools influencing reimbursement and acceptance as standard of care</em></td>
</tr>
<tr>
<td></td>
<td><strong>Industry Education</strong></td>
</tr>
<tr>
<td></td>
<td><em>To construct educational platforms that drive commercialization objectives with external societies and industry community</em></td>
</tr>
<tr>
<td></td>
<td><strong>Clinical Development and New Product Introduction</strong></td>
</tr>
<tr>
<td></td>
<td><em>To address unmet patient needs by connecting industry, academia, and global regulatory agencies</em></td>
</tr>
</tbody>
</table>
Centralizing Perspectives

Therapeutic Area Committee

1. Open development processes and education to clinical partners and regulators

2. Scalable and economic practices sufficient to meet payer expectations and gain acceptance as SOC

Commercialization Committee

Stem Cell Committee
Reimbursement Initiative

- Structured as a subcommittee of the ISCT Commercialization Committee

- Originally targeted technology focus for COGS reduction

- Shifted when opportunity arose to co-host workshop with NMDP in September, 2011

- Gained momentum with stakeholders and is building network outside ISCT
Welcome
Richard Maziarz, MD, Co-Chair, ISCT Commercialization Committee

Opening and Introductions - Moderator
David Dilts, PhD, MBA, CMA Director of Clinical Research, Professor of Healthcare Management, Oregon Health and Science University

PART 1 – STAKEHOLDER PERSPECTIVES

Health System Overview
Michael Boo, Chief Strategy Officer, NMDP
1. General Health System Structure
2. Health Care Regulation and Reform
3. Coding Essentials

Healthcare Provider Perspective
Richard Maziarz, MD, Co-Chair ISCT Commercialization Committee, Professor of Medicine, Oregon Health and Science University
1. The nuts and bolts of healthcare delivery.
2. Provider-Payer relationships.
3. Clinical trials.
4. Implementation of newly approved therapies.

Discretionary Break

Private Payor Perspectives
Dennis Irwin, MD, National Medical Director, OptumHealth
Stephen Crawford, MD, CPHRM, FCCP, Medical Senior Director, CIGNA LifeSOURCE Transplant Network
1. Insurance Products and Payors
2. Clinical Trials
3. Coverage of New Technologies

Break

PART 2 – MODERATED DISCUSSION

Case Studies
1. Codes in Transplantation: Complexity of the Not Too Distant Future
2. Cord blood and Bone Marrow: Heterologous Use Outside Transplant
3. Adult Adherent Stem Cells: Anticipating COGS and Pricing with Approval Studies Underway

Open questions – Industry participants

PART 3 – CONSENSUS BUILDING & ACTION

- Stakeholder roles and next steps.
- Including advocacy and commercialization organizations
- ISCT and NMDP; mechanisms for influence.

Networking Lunch La Fourgasse Salon
Reimbursement Roundtable Objectives

- Educate stakeholders on the scope and complexity of the issues for regenerative medicine product and therapy reimbursement.
- Create a forum for multidisciplinary dialogue on issues and implications.
- Engage in a disciplinary approach to define a path toward adequate reimbursement for regenerative medicine product and therapy reimbursement.
Stakeholder Perspectives
The Reimbursement Environment Under Health Care Reform

Michael Boo, JD
Chief Strategy Officer
National Marrow Donor Program
Justification for Reform

What is Ailing Our Health Care System?

- Too many uninsured
  - Estimated 45.7 million
  - Nearly 16% of the US population
- We spend too much
  - More than any country; twice as much as Canada our nearest competitor ($6,697 per capita in 2005)
- We tend to reward quantity of care over quality

Hughes & Associates, Ltd.
Unsustainable Rising Costs

Projected spending on health care as a percentage of Gross Domestic Product

Percent

Source: Congressional Budget Office, 2008

Hughes & Associates, Ltd.
Overview of Affordable Healthcare Act

Major Features of Reform

<table>
<thead>
<tr>
<th>Objectives</th>
<th>Legislation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Access to affordable care</td>
<td>Expansion of coverage to 32 million uninsured; individual mandates; new insurance rules</td>
</tr>
<tr>
<td>Cost containment</td>
<td>Restructure payments to providers; fees on health industry; new taxes</td>
</tr>
<tr>
<td>Improving quality/health system performance</td>
<td>Comparative effectiveness research; bundled payments; value-based purchasing</td>
</tr>
</tbody>
</table>

Hughes & Associates, Ltd.
Clinical Trials Coverage – New Act

• **Costs** to be covered:
  - Requires health insurers to cover “routine patient costs” in clinical trials
  - Routine coverage = all items and services consistent with the coverage provided in the plan that is typically covered for a qualified individual who is not enrolled in a clinical trial
    • Hospital visits
    • Imaging or laboratory tests
    • Medications
Clinical Trials – New Act

- **Costs not covered:**
  - “The investigational treatment, device, or service itself,”
  - Often covered by trial sponsor or NCI
  - “Items and services that are provided solely to satisfy data collection and analysis needs and that are not used in the direct clinical management of the patient”
  - “A service that is clearly inconsistent with widely accepted and established standards of care for a particular diagnosis”
Clinical Trials – New Act

- **Trials covered:**
  - Phase I-IV clinical trial that is conducted in relation to the prevention, detection, or treatment of cancer or other life-threatening disease or condition that is
    - Federally funded, or
    - Conducted under an investigational new drug application (IND) reviewed by the FDA, or
    - Drug trials that are exempt from having an IND under 21 CFR 312.2(b)(1)
Clinical Trials – New Act

• Applies to:
  – Any group health plan or insurance issuer
  – Federal Employee Health Benefit Plan
• Minimum standards for states; does not pre-empt more generous state law requirements
• CMS clinical trials rules remain for Medicare:
  – Broader definition of what can be investigated
  – Narrower: may not cover Phase I and II trials
Conclusions

- Positives for transplantation
  - More patients will have insured access
  - Mechanisms to look at cost of transplant more globally
  - Comparative effectiveness research will encourage data driven coverage decisions
  - Clinical trial coverage should improve
Conclusions

• Concerns for transplantation
  – Does not change current reimbursement issues
    • Search and procurement coverage
    • Indications coverage
  – Still face limited economic resources for Medicaid
  – High cost service in a shared risk environment
Medicare Coverage and Reimbursement
Medicare Coverage – Professional Services and Products and Supplies

• Health Care Common Procedure Coding System (HCPCS)
    • identify medical services and procedures furnished by physicians and other health care professionals
  – Level II - primarily to identify products, supplies, and services

• Differing reimbursement pathways for in-patient vs out-patient treatment
The CPT Process

Proposal submitted to AMA

AMA staff determines it is a new issue or new information received on previous item

Request referred to CPT Advisory Committee

Change recommended or no agreement reached

CPT Editorial Panel resolves request

AMA Staff determines request is not a new issue

No new code needed

Add new code or revise existing

Request further info

Reject an item
Issues

• New technologies
  – Replace or enhance existing service
  – Perform different function
  – Treat new diseases

• Reimbursement considerations
  – Impact on Medicare eligible population
  – Bundled services
  – Comprehensive Cancer Center Network
Maturing Industry Perspectives on Reimbursement

Robert Deans, PhD
Chair ISCT Commercialization Committee
Executive Vice President of Regenerative Medicine,
Athersys, Inc.
Demographics Impacting Healthcare Costs

The largest “at-risk” population will continue to substantially increase in the coming decades.

Estimated Population Change by Age Group 2010-2030

By 2030, the number of people in the U.S. age 65 or older will increase by ~80%

Source: www.census.gov

Courtesy of Gil van Bokkelen
62% of Healthcare Costs Treat Chronic Conditions

Costs for assisted living and nursing home care of a single Parkinson's patient can cost as much as $100,000 per year.

---

Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion

Drug therapy for Parkinson's disease costs more than $6 billion a year. Costs such as rehabilitation and home care can run as high as $150,000 per patient, per year.

---

Mayo Clinic, College of Medicine. “Parkinson’s Disease Information”

Courtesy of Gil van Bokkelen
Candid Concerns

- We simply can’t afford to pay for the promises we have made to ourselves

- If nothing changes, we simply won’t have the infrastructure or resources to provide adequate care for many people

- *Ceteris paribus*...limited resources and excess need inevitably leads to healthcare rationing
Capital and Technology Trends in Cell Therapy
Cell Therapy Development Models and Trends

- HSC Transplant
- Engineered T Cells
- Heterologous HSC
- Engineered Tissue
- Mesenchymal SC
- Personalized Medicine
- Universal Donor Product
- Biologics/Drug Paradigm
- ES, iPS Technology
- Tissue Regeneration
- Approval for Cartilage, Skin Products
- Autologous and Allogeneic
- Transplant Product Paradigm
- Patient Designated
# Cell Therapy Development Timelines

Current technologies build on 50 years of research

<table>
<thead>
<tr>
<th>1960s</th>
<th>1970s</th>
<th>1980s</th>
<th>1990s</th>
<th>2000s</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1993 – ViaCell Begins Banking Cord Blood</td>
<td>Late 1990’s – Multiple FDA Approvals</td>
<td>Dermagraft - FDA Approval 2001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1986 – First Mouse Cloned</td>
<td>Carticel (1997)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1998 – Human ESCs isolated</td>
<td></td>
<td>2005 Use of unrelated cord blood in BMT</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1998 – Human ESCs isolated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2007 – iPSCs from Humans</td>
</tr>
</tbody>
</table>

- 1968 – ALL patient irradiated, infused with identical twin BMT
- 1990 – Geron Founded
- 1997 – Dolly the Sheep cloned
- 1998 – Human ESCs isolated
- 2001 – RhBMP-7 Approved
- 2005 Use of unrelated cord blood in BMT
- 2007 – iPSCs from Humans
Regenerative Medicine Investment Cycles

RM Market: On 2nd Half of the Gartner Curve

Visibility
- 1998 Human ESCs first derived
- 1997 Dolly the sheep
- 1997 First FDA approved cell therapy (Carticel)
- 1999 TE bladders in clinic
- 1999 First FDA approved TE product (Apligraf)
- 2000 Time Magazine: TE No. 1 job

Peak of Inflated Expectations
- 2001 Ortec FDA approved
- 2001 Dermagraft FDA approved
- 2001 Bush "partial ban" on hESCs

Trough of Disillusionment
- 2002 ISSCR Founded

Slope of Enlightenment
- 2005 CIRM Founded

Plateau of Productivity
- 2007 iPS Technology Developed
- 2007 Apligraf - 200,000 Patients Treated
- 2006 Carticel - 10,000 Patients Treated
- 2009 Pfizer & Athersys: $111M Deal
- 2009 Obama Ends Ban on hESCs
- 2008 Genzyme-Osiris $1.25B Deal
- 2007 Shire Acquires ABH: $750M
- 2010 Cephalon & Mesoblast $2B Deal
- 2010 Dendreon's Provenge Approved

Technology Trigger
- 1980 Early TE research (MIT)
- 1986 ATS and Organogenesis founded
- 1988 SyStemix founded
- 1992 Geron founded

Stage of Development
- 2002 ATS + Organogenesis file Chapter 11

CONFIDENTIAL 4

COURTESY OF GREG BONFIGLIO
State of the Market

RM Market is Maturing: Key Metrics

Rapidly Expanding Market:
- $1.6B in 2010
- $20.0B in 2025
- CAGR of 18.34%

Dramatic Revenue Growth
- $130M in 2001
- $1.6B+ in 2010

Worldwide funding for research increasing
- $2.5B Now
- $14B in 10 Years

Clinical Programs
- Over 3600 Clinical Trials
- Over 400 ex-Oncology

Commercial Products
- 400 on Market ( Mostly Skin, Tools Media, & Devices);
  - 900+ in Development
- 44 Cell Therapies on Market
  - $1B Revenues
  - 400 in Development
  - 28 in PIII/Pivotal Trials

1.2M+ Patients Treated with RM Products.
  - 320K+ Cell Therapy Patients

RM Companies
- 700+ Co’s involved in RM
- 50+ Public Co’s;
  - $8-$10B Total Market Cap
- 250+ Private Co’s

COURTESY OF GREG BONFIGLIO – PROTEUS VENTURES
Adherent Stem Cell Technology

Shifting the paradigm for treatment from transplant to biologics
Over 5400 patients have now received adherent stem cell (MSC) treatment, in over 100 trials in over 14 indications.

Global regulatory approaches towards adherent stem cell therapy have common elements:
- Qualified ex vivo expansion process using flasks, cell factories
- Lot release requirements well defined
  - Identity, viability, potency, cytogenetics, sterility
- Acute and long term safety evaluation expected
  - Infusional toxicity and immune sensitization
  - Ectopic tissue and tumorigenicity

Ankrum, J 2010 Trends Mol Med
Geographic Distribution of Reported Clinical Studies – Adherent Stem Cells

Ankrum, J 2010
Cumulative Dose per Patient – Selected Clinical Studies
Wide Range for Treatment COGS: Reimbursable?

**Strategy:**
- Test multi-dose treatment approaches, at highest safe doses
- Power POM study to show efficacy

**$1,500 - $72,000**
**$15/million cells**

**$10 million COGS for 200 patient trial**

* Assumes 100 kg patient
What Hurdles Does Industry Face?

- Establishing reimbursement principles around therapeutic value and healthcare cost economics
- Financial
  - Defining pharmacoeconomic benefit...communicating a compelling value proposition
  - Establishing product reimbursement history in this space
- Clinical Validation
  - Addressing investor uncertainty (access to capital & potential for liquidity events)
- Physician Acceptance
  - Clear illustration of how the product can achieve a better clinical outcome...and ideally, a much more cost effective outcome
  - Ease of use
  - “No hassle” reimbursement (and do clinicians get to charge for a procedure?)
- Patient Acceptance
Now, a ground floor view: the individual perspective
TAKE COVER!!
THE DEATH PANELS
IS COMING!!
Who are the “Death Panels?”

- Payers??
- Big Business??
- Health Care Administrations??
- Physicians??
Healthcare Provider view:
The nuts and bolts of healthcare delivery

*HSCT as case study for regenerative medicine*

Richard T. Maziarz, MD
Co-Chair ISCT Commercialization Committee
Professor of Medicine, OHSU
Provider Principles

- Primary goal is the direct delivery of care to patients
- The patient is the center of our attention.
- Ability to deliver care is subject to multiple factors.
National Marrow Donor Program

- Facilitate transplants worldwide (more than 50,000 since 1987)
- Support patients and physicians
- Advance transplant research
- Operate the Be The Match Registry®

NMDP Transplants by Cell Source

<table>
<thead>
<tr>
<th>Year</th>
<th>Bone Marrow</th>
<th>Peripheral Blood Stem Cells</th>
<th>Cord Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>'68</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'69</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'70</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'71</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'72</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'73</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'74</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'75</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'76</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'77</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'78</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'79</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'80</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'81</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'82</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'83</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'84</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'85</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'86</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'87</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'88</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'89</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'90</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'91</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'92</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'93</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'94</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'95</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'96</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'97</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'98</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'99</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'00</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'01</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'02</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'03</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'04</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'05</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'06</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'07</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'08</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'09</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'10</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>'11</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Source: National Marrow Donor Program FY 2011
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone marrow transplant</td>
<td>$1,282,645,000</td>
<td>15,100</td>
<td>84.9%</td>
<td>51.3%</td>
<td></td>
</tr>
<tr>
<td>Open prostatectomy</td>
<td>$1,032,016,000</td>
<td>88,500</td>
<td>68.6%</td>
<td>40.8%</td>
<td></td>
</tr>
<tr>
<td>Aortic resection; replacement or anastomosis</td>
<td>$1,872,908,000</td>
<td>61,600</td>
<td>38.5%</td>
<td>31.9%</td>
<td></td>
</tr>
<tr>
<td>Cancer chemotherapy</td>
<td>$2,616,504,000</td>
<td>187,400</td>
<td>33.2%</td>
<td>14.2%</td>
<td></td>
</tr>
<tr>
<td>Spinal fusion</td>
<td>$8,863,922,000</td>
<td>350,700</td>
<td>29.5%</td>
<td>15.6%</td>
<td></td>
</tr>
<tr>
<td>Lobectomy or pneumonectomy</td>
<td>$1,757,748,000</td>
<td>81,400</td>
<td>29.2%</td>
<td>24.9%</td>
<td></td>
</tr>
<tr>
<td>Incision and drainage, skin and subcutaneous tissue</td>
<td>$1,108,187,000</td>
<td>158,600</td>
<td>28.6%</td>
<td>31.5%</td>
<td></td>
</tr>
<tr>
<td>Arthroplasty knee</td>
<td>$9,217,740,000</td>
<td>605,200</td>
<td>27.5%</td>
<td>25.7%</td>
<td></td>
</tr>
<tr>
<td>Nephrotoomy and nephrostomy</td>
<td>$682,609,000</td>
<td>38,600</td>
<td>25.3%</td>
<td>11.7%</td>
<td></td>
</tr>
<tr>
<td>Mastectomy</td>
<td>$660,173,000</td>
<td>70,100</td>
<td>23.8%</td>
<td>3.6%</td>
<td></td>
</tr>
<tr>
<td><strong>Total for top 10 procedures</strong></td>
<td><strong>$29,094,452,000</strong></td>
<td><strong>1,657,100</strong></td>
<td><strong>32.3%</strong></td>
<td><strong>22.2%</strong></td>
<td></td>
</tr>
</tbody>
</table>

*2004 costs were adjusted to 2007 dollars using the overall Consumer Price Index.
2005-11: 108% increase in billed charges (allo)*

- 7,300 total transplants

2009 – BMT has highest percentage growth in costs of any hospital procedure (AHRQ HCUP)

2011: Estimated 20,000 Transplants per year in U.S.

~$10 Billion spent on HCT/BMT

*Data courtesy of Milliman Cost of Transplant Report, 2005, 2011
Shift in Payor Mix:
High-Margin Contracts to Govt. Payors

2007 Payors

2012 Payors

- Medicaid
- Medicare
- Comm HP
- Self
Defining the Need—2015???

- By applying the optimal transplant rate to the U.S. population, the need for allogeneic (related and unrelated) transplant is 18,000 per year.
  - Related – 5,500 per year
    - 30% of patients have a related/sibling match
  - Unrelated – 12,500 per year

- NMDP Facilitated Unrelated Transplants:
  - 2011 = ~5,000 per year
    - Double from just a few years earlier
  - 2005 = ~2,500 per year
Lessons from the Field: Understanding the Rules of the Game

1. The Provider as Gate Keeper - follow the numbers

   » e.g.: NMDP 1 yr risk adjusted survival ~ 62% for all patients

   » e.g.: Allogeneic transplant for advanced heme malignancy (not in CR; beyond CR2)- 40% 100 day mortality

   » Institutional contracting for Center of Excellence status
     • Expectations for 100 day survival 60-80% sib; 60-70% unrelated and 55-65% at one year (summary of 5 payers)

   » Stem Cell Transplantation Outcomes Database (SCTOD)
     • “Transparency” of outcomes for public consumption; risk adjustment still under development

   » Pay for Performance/ Accountable Care Organizations as a future
Accountable Care Organizations

• Provider led organization with emphasis on primary care
  – Collectively accountable for quality and total per capita costs for a set patient population
• Payments linked to quality improvements that reduce overall costs
  – Risk sharing arrangements will vary
• Reliable and sophisticated performance improvement to demonstrate savings are achieved through realized improvements in care
Lessons from the Field: Understanding the Rules of the Game

2. Regulatory
   » Foundation for Accreditation of Cell Therapy (FACT)
   » FDA
   » Institutional QA
     • CMS Value Based Purchasing (VBP)
     • Hospital Consumer Assessment of Healthcare Providers & Systems (Patient experience data)
     • Falls, BSI, readmission rates
Amount of Money at Risk

Payment Implementation

- 2013 → 1% of payment
- 2014 → 1.25%
- 2015 → 1.5%
- 2016 → 1.75%
- 2017 → 2%

- Percent of earn back is based on a point system and a straight exchange function:
  - 50 VBP points = 50% of reimbursement earned back
  - 75 VBP points = 75% of reimbursement earned back
How VBP score calculated

Overall VBP Score

- HCAHPS
- Clinical

International Society for Cellular Therapy
ISCT
<table>
<thead>
<tr>
<th>AMI</th>
<th>Threshold</th>
<th>Benchmark</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMI-7a Fibrinolytic therapy received within 30 minutes of hospital arrival</td>
<td>65.48%</td>
<td>91.91%</td>
</tr>
<tr>
<td>AMI-8a Primary PCI received within 90 minutes of hospital arrival</td>
<td>91.86%</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Heart Failure</th>
<th>Threshold</th>
<th>Benchmark</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF-1 Discharge instructions address all required elements</td>
<td>90.77%</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pneumonia</th>
<th>Threshold</th>
<th>Benchmark</th>
</tr>
</thead>
<tbody>
<tr>
<td>PN-3b Blood culture performed before first antibiotic received in hospital</td>
<td>96.43%</td>
<td>100%</td>
</tr>
<tr>
<td>PN-6 Appropriate antibiotic selection</td>
<td>92.77%</td>
<td>99.58%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Surgical Care Improvement</th>
<th>Threshold</th>
<th>Benchmark</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCIP-Inf-1 Prophylactic antibiotic received within 1 hour prior to surgical incision</td>
<td>97.35%</td>
<td>99.98%</td>
</tr>
<tr>
<td>SCIP-Inf-2 Prophylactic antibiotic selection for surgical patients</td>
<td>97.66%</td>
<td>100%</td>
</tr>
<tr>
<td>SCIP-Inf-3 Prophylactic antibiotics discontinued within 24 hours after surgery end time</td>
<td>95.07%</td>
<td>99.68%</td>
</tr>
<tr>
<td>SCIP-Inf-4 Cardiac Surgery patients with controlled 6AM postoperative serum glucose</td>
<td>94.28%</td>
<td>99.63%</td>
</tr>
<tr>
<td>SCIP-Card-2 Surgery patients on a beta blocker prior to arrival that received a beta blocker during the perioperative period</td>
<td>95.00%</td>
<td>100%</td>
</tr>
<tr>
<td>SCIP-VTE-1 Surgery patients with recommended VTE prophylaxis ordered</td>
<td>93.07%</td>
<td>99.85%</td>
</tr>
<tr>
<td>SCIP-VTE-2 Surgery patients who received appropriate VTE prophylaxis within 24 hours prior to surgery to 24 hours after surgery</td>
<td>93.99%</td>
<td>100%</td>
</tr>
</tbody>
</table>
## 8 HCAHPS Measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>Rating Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Communication with Nurses</td>
<td>Never, Sometimes, Usually, Always</td>
</tr>
<tr>
<td>Communication with Doctors</td>
<td></td>
</tr>
<tr>
<td>Responsiveness of Hospital Staff</td>
<td></td>
</tr>
<tr>
<td>Pain Management</td>
<td></td>
</tr>
<tr>
<td>Communication about Medicines</td>
<td></td>
</tr>
<tr>
<td>Hospital Cleanliness and Quietness</td>
<td></td>
</tr>
<tr>
<td>Discharge Information</td>
<td>No, Yes</td>
</tr>
<tr>
<td>Overall Rating of Care</td>
<td>0 - 10</td>
</tr>
</tbody>
</table>
Value Based Purchasing — *Future Measures*

<table>
<thead>
<tr>
<th>Mortality</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality 30-AMI</td>
<td>Acute Myocardial Infarction (AMI) 30-day mortality rate</td>
</tr>
<tr>
<td>Mortality 30-HF</td>
<td>Heart Failure (HF) 30-day mortality rate</td>
</tr>
<tr>
<td>Mortality 30-PN</td>
<td>Pneumonia (PN) 30-day mortality rate</td>
</tr>
</tbody>
</table>

**Hospital Acquired Conditions**

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foreign Object Retained After Surgery</td>
</tr>
<tr>
<td>Air Embolism</td>
</tr>
<tr>
<td>Blood Incompatibility</td>
</tr>
<tr>
<td>Pressure Ulcer Stages III &amp; IV</td>
</tr>
<tr>
<td>Falls and Trauma: (includes Fracture, Dislocation, Intracranial Injury, Crushing Injury, Burn, Electric Shock)</td>
</tr>
<tr>
<td>Vascular Catheter-Associated Infections</td>
</tr>
<tr>
<td>Catheter-Associated Urinary Tract Infection (UTI)</td>
</tr>
<tr>
<td>Manifestations of Poor Glycemic Control</td>
</tr>
</tbody>
</table>

**AHRQ Patient Safety Indicators (PSIs), Inpatient Quality Indicators (IQIs) and Composite Measures**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSI 06</td>
<td>Iatrogenic pneumothorax, adult</td>
</tr>
<tr>
<td>PSI 11</td>
<td>Post Operative Respiratory Failure</td>
</tr>
<tr>
<td>PSI 12</td>
<td>Post Operative PE or DVT</td>
</tr>
<tr>
<td>PSI 14</td>
<td>Post Operative wound delhiscence</td>
</tr>
<tr>
<td>PSI 15</td>
<td>Accidental puncture or laceration</td>
</tr>
<tr>
<td>IQI 11</td>
<td>Abdominal aortic aneurysm (AAA) repair mortality rate (with or without volume)</td>
</tr>
<tr>
<td>IQI 19</td>
<td>Hip fracture mortality rate</td>
</tr>
<tr>
<td></td>
<td>Complication/patient safety for selected indicators (composite)</td>
</tr>
<tr>
<td></td>
<td>Mortality for selected medical conditions (composite)</td>
</tr>
</tbody>
</table>
Lessons from the Field: Understanding the Rules of the Game

3. Coding - adventures and misadventures
   - Compliance
   - Reimbursement
   - Risk assessment
   - Severity of illness index

United Healthsystems Consortium (UHC)
   - Outcome measures: what is the proper metric??
     - “Death in hospital during transplant stay”
   - Transparency
Lessons from the Field:
Understanding the Rules of the Game

4. Reimbursement: Medicare
   • Pricing: will the DRG payment cover the cost?
   • Timing of benefit delivery
   • Coverage: No preauthorization; review and coverage decision is post procedure

**COVERED - Allogeneic**
Leukemia or Leukemia in remission; Aplastic anemia
Severe combined immunodeficiency disease (SCID)

**NON-COVERED**
Multiple Myeloma

**Coverage with Evidence Development (CED)**
Myelodysplasia

**NOTE:**
All other indications for stem cell transplantation remain at local contractor discretion. Many institutions will not allow procedures for undetermined diagnoses, given risk of nonreimbursement.

Example: OHSU pt with 2° MDS with MM history just denied payment; appeal process unclear
Lessons from the Field: Understanding the Rules of the Game

5. Reimbursement: Medicaid
   • Variability is vast across states
     – Oregon examples
       • Eligibility of reimbursement determined by pairing of diagnosis with effective treatment
       • 5 year survival mandate
       • One transplant in your lifetime
       • Evidence based (Health Resource Commission advisory to Health Services)
       • Reduced intensity allogeneic tx- excluded until this past year, due to absence of randomized trials and long term outcome data
Lessons from the Field: Understanding the Rules of the Game

6. Reimbursement: Private Payers
   • Procedure caps
   • Lifetime caps
   • Preexisting condition clauses
   • Preauthorization procedures
   • Clinical trials
Lessons from the Field: Understanding the Rules of the Game

7. Reimbursement: uninsured individuals

- Access to care variable across states
- Very little transplant activity in the US in this circumstance
- Institutional support - Office of Financial and Medicaid Specialists for defining assistance programs - often based on # individuals in family and % income above or below poverty line. *Transplant-related services are not a part of the services that are discountable.*
- CAWEM coverage for illegal aliens - allows emergency coverage; OHSU excludes HCST, as defined by institution as elective procedure - not “essential benefit”
Lessons from the Field:
Understanding the Rules of the Game

8. Reimbursement: Clinical Trials
   • Many states with legislation for mandated coverage of clinical trials
   • Participation in trials can be allowed, selectively allowed (no phase I or II), or not permitted
   • Close scrutiny to separate trial specific vs SOC costs
   • Indemnity issues
Lessons from the Field: Understanding the Rules of the Game

9. Evidence based medicine-
   • “FDA approval is not evidence.”- Helfand, 2011
   • GRADE (Grading of Recommendations Assessment, Development, and Evaluation) Working group
   • Evidence-based Practice Center (EPC)- supported by AHRQ → multiple evidence reports and Comparative Effectiveness Reviews (CERs)
   • “Evaluation of consistency, ideally requires an evidence-base with independent replication of findings; therefore, EPCs cannot properly evaluate consistency in an evidence-base with the single study. EPC’s cannot be certain that a single trial, no matter how large or well-designed, presents the definitive picture to any particular clinical benefit or harm for a given treatment. Thus, it is recommended that EPC’s judge single study evidence bases as “consistency unknown (single study)”, which would generally decrease the strength of evidence grade. Owens et al, Methods Guide for Comparative Effectiveness Reviews, 2009.
Comparative Effectiveness Research (CER)

- ARRA allocates $1.1 billion in 2009/2010 for CER
  - creates Federal Coordinating Council
  - Calls on the IOM to establish research priorities

- Previously estimated $627M/year on CER and $155M on CEA
- No past experience with CER (priority setting or conduct of research)
- AHRQ Effective Health Care Program (EHCP) had $30M in funding in 2008
  - Conducts CER on relevant topics including cardiovascular disease; diabetes; mental health; bone and joint conditions; cancer; and obesity
Summary: Informational Needs

- Should we pay for this service? = Coverage
- Did we pay for the correct service correctly? = Payment
- Was the service we paid for performed optimally? = Quality
- Do patients and providers have sufficient information to make choices? = Transparency
Managed Care Benefit Management
Rules of the Games: the Payer Community

Dennis Irwin, MD
September 14, 2011
Benefit determination: Who is covered

Eligibility
- A patient must be primary with this plan
- Medicare: primary payer | secondary payer
- Medicaid: primary payer | secondary payer

Three important dates:
The patient must be a member of the plan on all three dates before you will get a coverage determination and/or payment:

1. Date first eligible
2. Date of request
3. Date of service

Is Medicare the primary payer?
- If Medicare is primary, Medicare coverage rules apply
  – See National Coverage Determination (NCD) and Local Coverage Determination (LCD), if any
  – Commercial plans will refer you to your Medicare Fiscal Intermediary for coverage determinations
- If Medicare is secondary, commercial plan rules apply

Is Medicaid the primary payer?
Benefit determination: Plan design

Benefits and exclusions

• Inclusions (those services that are covered)
• Exclusions (those services that are specifically not covered)
• There may or may not be contingency clauses for life threatening conditions
• Many plans have Designated Networks for BMT and other low-frequency, high-cost services

Covered Health Service

Those health services, including services, supplies, or pharmaceutical products, which we determine to be all of the following:

• Medically necessary
• Described as a Covered Health Service in this Certificate under Section 1: Covered Health Services and in the Schedule of Benefits
• Not otherwise excluded in this Certificate under Section 2: Exclusions and Limitations

Exclusion

Experimental or Investigational and Unproven Services and all services related to Experimental or Investigational and Unproven Services are excluded.

Definition of Experimental and Investigational

Medical, surgical, diagnostic, psychiatric, substance abuse or other health care services, technologies, supplies, treatments, procedures, drug therapies, medications or devices that, at the time we make a determination regarding coverage in a particular case, are determined to be any of the following:

• Not approved by the U.S. Food and Drug Administration (FDA) to be lawfully marketed for the proposed use and not identified in the American Hospital Formulary Service or the United States Pharmacopoeia Dispensing Information as appropriate for the proposed use
• Subject to review and approval by any institutional review board for the proposed use. (Devices which are FDA approved under the Humanitarian Use Device exemption are not considered to be Experimental or Investigational)
• The subject of an ongoing clinical trial that meets the definition of a Phase 1, 2 or 3 clinical trial set forth in the FDA regulations, regardless of whether the trial is actually subject to FDA oversight

Based on standard UnitedHealthcare plan language. Other insurers and self-funded payers may have different language.
## Benefit determination: Plan design

### Benefits and exclusions

<table>
<thead>
<tr>
<th>Inclusions (those services that are covered)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exclusions (those services that are specifically not covered)</td>
</tr>
<tr>
<td>There may or may not be contingency clauses for life threatening conditions</td>
</tr>
<tr>
<td>Many plans have Designated Networks for BMT and other low-frequency, high-cost services</td>
</tr>
</tbody>
</table>

### Life-threatening sickness or condition

"If you have a life-threatening Sickness or condition (one that is likely to cause death within two years of the request for treatment) we may, in our discretion, consider an otherwise Experimental or Investigational Service to be a Covered Health Service for that Sickness or condition. Prior to such a consideration, we must first establish that there is sufficient evidence to conclude that, albeit unproven, the service has significant potential as an effective treatment for that Sickness or condition, and that the service would be provided under standards equivalent to those defined by the National Institutes of Health."

### Medicare Advantage

Medicare Advantage plans will have their own coverage rules. For example, United Healthcare Medicare and Retirement plans (formerly Ovations) generally do not cover clinical trials

### Note

Self-funded employers can and do create benefits and exclusions not supported by available science. Their plan document is the governing benefit plan

---

Based on standard UnitedHealthcare plan language. Other insurers and self-funded payers may have different language.
Benefit determination: Medically necessary

Medical Policy

- Evidence based
- Not based solely on expert opinion
- Final step, not the first step, in the benefit determination process

Medical Policy developmental hierarchy in descending order of importance:

- Centers for Medicare and Medicaid Services (CMS) National Coverage Decisions (NCDs) — *This is the highest level for Medicare beneficiaries*
- Statistically robust, well-designed randomized controlled trials
- Statistically robust, well-designed cohort studies
- Large, multi-site observational studies
- Single-site observational studies

Based on UnitedHealthcare Medical Policy development policies and procedures. Other insurers and self-funded payers may have different Medical Policy development schemes.
Benefit determination: Medically necessary

**Medical Policy**

- Evidence based
- Not based solely on expert opinion
- Final step, not the first step, in the benefit determination process

**Medical Policy developmental hierarchy in descending order of importance:**

- In the absence of incontrovertible scientific evidence, medical policies may be based upon national consensus statements by recognized authorities. The following stratification describes the hierarchy of use of medical policies and clinical guidelines within UnitedHealthcare:
  - National guidelines and consensus statements, e.g., United States Preventive Services Task Force (USPSTF), National Institutes of Health (NIH) clinical statements, Agency for Health Care Research and Quality (AHRQ) clinical statements
    - NCCN guidelines are given regard re: cancer therapies
  - Evidence-based nationally recognized clinical guidelines
  - Centers for Medicare and Medicaid Services (CMS) National Coverage Decisions (NCDs)
  - Clinical position papers of professional specialty societies, e.g. American College of Physicians (ACP), American College of Cardiology (ACC), American College of Chest Physicians (ACCP), when their statements are based upon referenced clinical evidence
- Expert opinion using Cochrane grading

Based on UnitedHealthcare Medical Policy development policies and procedures. Other insurers and self-funded payers may have different Medical Policy development schemes.
Hierarchy of coverage determination

Eligibility → Mandates and Medicare → Benefits and exclusions → Medical Policy
Reinsurance: The elephant in the center of the room

This is a fact of life for the self-funded employer: it is the relationship with their reinsurance carrier that determines many payer decisions

• Self-funded employers will typically reinsure unless they are so large they can underwrite their entire risk
• Typical stop-loss thresholds (specific deductible) are $50–$500,000 averaging depending on the size of the employer
• Reinsurance carriers may exclude experimental and investigational treatment even if it is a benefit of the plan
• Reinsurance carriers will interpret the employer’s benefit plan and their reinsurance contract with the employer strictly, i.e., absolutely no room for interpretation even if the decision makes little clinical or economic sense from your perspective
  – Not surprising since the stop-loss carrier is bearing the brunt of the risk for the very high-dollar claims. Any claim avoided remains the responsibility of the primary payer.

This explains the inflexibility of many self-funded payers
Procedures For Handling Requests for Coverage of Stem Cell “boost”, “re-infusion”, “support” or “rescue”.

Stephen Crawford, MD
Medical Senior Director, CIGNA Life SOURCE Transplant Network
Case Study 1

Codes in Transplantation: Complexity of the not too distant future
Case Study 1:

54-year-old male patient with AML; inter. Risk cytogenetics, in CR2. Female sibling donor, G5P4M1, PBSC only.

Transplant center: ex vivo T cell depletion to decrease GVHD risk, following CTN 0303 protocol (Devine et al, BBMT 2011)

Post transplant: Donor-derived mature DC generated in vitro from CD14(+) monocytes, loaded with HLA Ag-restricted peptides derived from PR1 and WT1 for repetitive stimulation donor CD8(+) T cells in the presence of IL-2 and IL-7. Stimulated donor T cells were infused 28, 56, and 112 days after transplantation (Bornhauser, Blood, 2011)
## CMS Reimbursement: Current HSCT Procedures-Outpatient

<table>
<thead>
<tr>
<th>CPT/HCPCS</th>
<th>Description</th>
<th>2011 Payment Rate</th>
<th>%Change since 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>36511</td>
<td>Apheresis wbc</td>
<td>$853.18</td>
<td>5.99%</td>
</tr>
<tr>
<td>36515</td>
<td>Apheresis, adsorp/reinfuse</td>
<td>$2,166.33</td>
<td>-3.55%</td>
</tr>
<tr>
<td>36516</td>
<td>Apheresis, selective</td>
<td>$2,166.33</td>
<td>-3.55%</td>
</tr>
<tr>
<td>36522</td>
<td>Photopheresis</td>
<td>$2,166.33</td>
<td>-3.55%</td>
</tr>
<tr>
<td>38206</td>
<td>Harvest auto stem cells</td>
<td>$853.18</td>
<td>5.99%</td>
</tr>
<tr>
<td>38207</td>
<td>Cryopreserve stem cells</td>
<td>$233.61</td>
<td>2.51%</td>
</tr>
<tr>
<td>38208</td>
<td>Thaw preserved stem cells</td>
<td>$233.61</td>
<td>2.51%</td>
</tr>
<tr>
<td>38209</td>
<td>Wash harvest stem cells</td>
<td>$233.61</td>
<td>2.51%</td>
</tr>
<tr>
<td>38210</td>
<td>T-cell depletion of harvest</td>
<td>$418.39</td>
<td>7.25%</td>
</tr>
<tr>
<td>38211</td>
<td>Tumor cell deplete of harvest</td>
<td>$418.39</td>
<td>7.25%</td>
</tr>
<tr>
<td>38212</td>
<td>Rbc depletion of harvest</td>
<td>$418.39</td>
<td>7.25%</td>
</tr>
<tr>
<td>38213</td>
<td>Platelet deplete of harvest</td>
<td>$418.39</td>
<td>7.25%</td>
</tr>
<tr>
<td>38214</td>
<td>Volume deplete of harvest</td>
<td>$418.39</td>
<td>7.25%</td>
</tr>
<tr>
<td>38215</td>
<td>Harvest stem cell concentrate</td>
<td>$418.39</td>
<td>7.25%</td>
</tr>
<tr>
<td>38220</td>
<td>Bone marrow aspiration</td>
<td>$257.53</td>
<td>23.25%</td>
</tr>
<tr>
<td>38221</td>
<td>Bone marrow biopsy</td>
<td>$257.53</td>
<td>23.25%</td>
</tr>
<tr>
<td>38230</td>
<td>Bone marrow collection</td>
<td>$2,166.33</td>
<td>-3.55%</td>
</tr>
<tr>
<td>38240</td>
<td>Bone marrow/stem transplant (allogeneic)</td>
<td>$2,166.33</td>
<td>-3.55%</td>
</tr>
<tr>
<td>38241</td>
<td>Bone marrow/stem transplant (autologous)</td>
<td>$2,166.33</td>
<td>-3.55%</td>
</tr>
<tr>
<td>38242</td>
<td>Lymphocyte infuse transplant</td>
<td>$853.18</td>
<td>5.99%</td>
</tr>
</tbody>
</table>

**Notes:**
- RTM: see my addition
- Two codes for the same procedure / rate?
Questions - Current Transplant Codes

- How can new treatments and manipulations be accommodated within the system?
  - What is the cost of T cell depletion?
  - If the decision to TCD is to decrease long term costs, how do we achieve reimbursement within time determined case rates?

- How do we recapture the cost of goods & manufacturing of the infusion of the donor derived, HLA-restricted, peptide-specific, T cell lines?

- Do these infusions fall within the framework of existing procedure codes?

- Is there a need for new CPT codes for cellular therapies? How soon can they be developed?
  - The only new procedural codes currently in existence are for unilateral application of autologous bone marrow derived mononuclear cells for critical limb ischemia- “T” codes (no value yet assigned)

- How do we achieve these goals?
How Do We Create Our Future?

- Educate and better understand our relationships in healthcare management
- Develop principles which foster economic success for stakeholders
- Keep patient care as the primary driver for therapy advancement
The problem:
Consensus Building & Action

- Stakeholder Roles & Next steps
  - Advocacy
  - Coding

- Mechanisms for Influence:
  - ISCT
  - NMDP
  - ARM
  - Other
Networking and Influence

- Reimbursement panel participation at Stem Cells on the Mesa, 12/2011
  - Affiliation with ARM/ CIRM

- Participation at Avalere sponsored workshop on Diabetes Wound Healing Reimbursement
  - Affiliation with ARM

- ISCT Workshop 6/12
- Healthcare Financial Management Association 6/12
- IBC Cell Therapy Clinical Development, 9/12

- Engaged by National Managed Care Providers (NMCP) for crossover workshop
  - Leadership role on newly formed Regenerative Medicine subcommittee

- Drafted position paper from NMDP workshop

- Re-focus ISCT Reimbursement Committee—advocacy and education

Volunteers?