INNOVATIVE PAYMENT MODELS
DO CUTTING-EDGE ONE-TIME TREATMENTS NEED EQUALLY INNOVATIVE OUTCOMES OR ANNUITY BASED PAYMENT MODELS?

WORKSHOP
For distribution to ISPOR International Attendees
MAY 23, 2018

Agenda

8:30 – 8:45
CURRENT LANDSCAPE & CHALLENGES

1. Introduction
2. Current state of innovative one-time therapies in USA and the EU
3. Challenges in commercializing one-time therapies
4. Payer expectations from innovative payment models

8:45 – 8:55
INNOVATIVE PAYMENT MODELS – USA

1. Commonly proposed innovative payment models by USA payers
2. Outcome-based payment model for gene therapy
3. Annuity-based payment model

8:55 – 9:20
INNOVATIVE PAYMENT MODELS – EU

1. NICE Assessment of innovative payment models
2. Hybrid annuity payment model
3. Affordability of one-time treatments

9:20 – 9:30
STRATEGIES

1. What are the tangible steps and actions manufacturers can take to successfully commercialize innovative treatments?
2. Audience Q&A
We would like to first introduce our panellists, and welcome our guests.

MARK CHALMERS, PhD
PRINCIPAL & EU LEAD, CBPARTNERS

ISMAIL ISMAILOGLU, PhD
 SENIOR ANALYST, CBPARTNERS

OMAR ALI
VISITING LECTURER VALUE BASED PRICING & INNOVATIVE CONTRACTING, UNIVERSITY OF PORTSMOUTH

This workshop will explore the challenges in funding high-cost one-time treatments and the potential innovative payment solutions.

OBJECTIVE
Discuss pricing and reimbursement challenges posed by innovative one-time treatments and explore novel payment models and their feasibility for different global payer archetypes

GOALS
DISCUSS CURRENT LANDSCAPE & CHALLENGES
Provide an overview of the current and future landscape in innovative treatments, such as gene therapies and CAR-Ts

EVALUATE INNOVATIVE PAYMENT MODELS
Explore challenges posed by one-time treatments for payers, manufacturers and providers in USA and the EU and their expectations from novel payment models

DEVELOP STRATEGIES FOR MODEL IMPLEMENTATION
Discuss expectations from and implementation considerations for different emerging payment models from the payer, manufacturer and provider perspective
We would like to start with a few questions to understand the audience background and views on novel gene and cell therapies.

**QUESTION 1**
Do you represent the ‘manufacturer perspective’ or the ‘payer perspective’?

**QUESTION 2**
What are the biggest opportunities for gene and cell therapies (e.g., CAR-Ts)?
A. Short-term Efficacy
B. Potential for Long-term “Cure”
C. Savings to the Healthcare System
D. Other Opportunities?

**QUESTION 3**
What are the biggest challenges to the success of gene and cell therapies (e.g., CAR-Ts)?
A. Short-term Financial Impact
B. Long-term Financial Impact
C. Efficacy Concerns (short- or long-term)
D. Safety Concerns (short- or long-term)
E. Other Challenges?


Innovative gene and cell-based therapies garnered significant attention from all stakeholders with a promise to provide a “lifetime cure” for complex conditions.

**The New York Times**
Companies Rush to Develop ‘Utterly Transformative’ Gene Therapies

**BioPharma Dive**
A new wave of gene therapies ready to hit US shores

**Reuters**
Spark gene therapy improves vision, at least in short term: FDA

**P&T Community**
Yescarta Benefits 42% of Patients a Year After Infusion

Innovative gene and cell-based therapies garnered significant attention from all stakeholders with a promise to provide a “lifetime cure” for complex conditions.

Gene therapies can also provide cost-savings by “curing” chronic conditions currently treated with high-cost products, e.g., SMA, which is treated with SPINRAZA at $750,000 for the first year, …

… or hemophilia, which can cost $270 thousand - $1 million per patient per year with current treatments

Available gene and cell therapy products target small patient populations, but products for larger indications, such as hemoglobinopathies, are in the pipeline.
However, clinical and economic value driven market and pricing access challenges have emerged threatening the accessibility of gene and cell therapies.

“\textit{We don’t know how much the company has invested} to develop the therapy and I think the first step is to be transparent \ldots Beyond considering that \textit{asking $475K} is crazy, \textit{it is essential} that \textit{MFGs specify how that price has been reached}.”
- Irene Bernal, Right to Health Foundation, Jan 09, 2017

“\textit{It is necessary to rethink}, in a global and integrated perspective, \textit{not only} the models for the financing of therapies but the health systems and the management of budgets dedicated to health spending.”
- Mario Melazzini, Director General of AIFA, Nov 30, 2017

Glybera, the first commercially available gene therapy, suffered from suboptimal efficacy and was recently pulled from the market due to lack of demand.

\textbf{ECONOMIC CHALLENGES}

\begin{itemize}
  \item Had challenges in EMA approval for LPL due to concerns about lack of benefit and small trials
  \item Despite ~1M EUR price, \textit{outcomes-based payments not possible} due to lack of a clear cut method to track the effects of the drug
  \item Used only for 1 GER patient commercially and removed from the market due to lack of demand
\end{itemize}

\textbf{FAILURE TO ENGAGE PAYERS}

\textbf{FAILURE TO PLAN FOR AN INNOVATIVE PAYMENT MODEL}

\begin{itemize}
  \item [The GER physician] had to prepare a submission as thick as ‘a thesis’ for German regulators and then personally call the CEO of DAK, one of Germany’s large sickness funds to ask [them] to pay the $1 million price tag
  \item [The GER physician] had to prepare a submission as thick as ‘a thesis’ for German regulators and then personally call the CEO of DAK, one of Germany’s large sickness funds to ask [them] to pay the $1 million price tag
\end{itemize}

\textbf{STICKER SHOCK}

\begin{itemize}
  \item “The payers said they wanted to pay up front, but that \textit{created a lot of anger in Europe}. It’s a shame. It became the one-million [Euro] therapy”
  \item “The payers said they wanted to pay up front, but that \textit{created a lot of anger in Europe}. It’s a shame. It became the one-million [Euro] therapy”
\end{itemize}

\textbf{UNIQUE GLYBERA}

€1.1M

\textbf{GENE THERAPIES}

\begin{itemize}
  \item [2012]
  \item [2018]
  \item [2019]
  \item [2020]
  \item [2021]
  \item [2022+]
\end{itemize}

\textbf{SOURCE: CBPartners secondary research}

You can access the online poll at \url{http://bit.ly/novelpayments}
Despite positive reimbursement decisions, GSK did not expect a return from Strimvelis due to small target population and recently transferred rights to Orchard.

- EMA approved for ADA-SCID, but faces challenges due to very small population (<10 patients/year) in Europe and limitation of administration to 1 center in ITA.
- AIFA payment arrangement, covering all European patients, includes staggered payments, as well as refunds if patient has to receive another therapy.
- Recently recommended by NICE based on cost-effectiveness at £100,000 threshold.

**Gene Therapies**

**GSK / ORCHARD STRIMVELIS (ADA-SCID)** £694,000

**EMA approved for ADA-SCID, but faces challenges due to very small population (<10 patients / year) in Europe and limitation of administration to 1 center in ITA.**

**AIFA payment arrangement, covering all European patients, includes staggered payments, as well as refunds if patient has to receive another therapy.**

**Recently recommended by NICE based on cost-effectiveness at £100,000 threshold.**

**Cell Therapies**

- Both YESCARTA and KYMRIAH are approved for R/R DLBCL setting (~3,500 USA patients), KYMRIAH also approved for pediatric R/R B-ALL (~600 patients).
- Despite its $373,000 price, total cost associated with YESCARTA is expected to reach ~$1M, including hospitalization and treatment of severe AEs.
- Medicare reimbursement has been delayed for both products due to uncertainty over inpatient rates.

**Car-Ts offer great promise for late stage cancer patients, but utilization has been limited due to hurdles in reimbursement.**

- Both YESCARTA and KYMRIAH are approved for R/R DLBCL setting (~3,500 USA patients), KYMRIAH also approved for pediatric R/R B-ALL (~600 patients).
- Despite its $373,000 price, total cost associated with YESCARTA is expected to reach ~$1M, including hospitalization and treatment of severe AEs.
- Medicare reimbursement has been delayed for both products due to uncertainty over inpatient rates.
One-time funding of innovative treatments pose diverse clinical and economic challenges for manufacturers and payers.

<table>
<thead>
<tr>
<th>STAKEHOLDERS</th>
<th>CLINICAL CHALLENGES</th>
<th>ECONOMIC CHALLENGES</th>
<th>STAKEHOLDERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>MFG</td>
<td>HARD TO ASSESS AND COMMUNICATE BENEFIT</td>
<td>PSYCHOLOGICAL STICKER SHOCK</td>
<td>MFG</td>
</tr>
<tr>
<td>PAY</td>
<td>UNCERTAINTY OF LONG-TERM CLINICAL BENEFIT</td>
<td>REALIZE LIFETIME REVENUE AT ADMINISTRATION</td>
<td>PAY</td>
</tr>
<tr>
<td>MFG</td>
<td>UNCERTAINTY OF LONG-TERM SAFETY</td>
<td>AFFORDABILITY &amp; HIGH UPFRONT COSTS</td>
<td>PAY</td>
</tr>
<tr>
<td>MFG</td>
<td>COMPLEX ADMINISTRATION AND FOLLOW-UP</td>
<td>COLLECTIVE BUDGET IMPACT (NEW PATIENTS, NEW PRODUCTS &amp; NEW INDICATIONS)</td>
<td>PAY</td>
</tr>
</tbody>
</table>

SOURCE: CBPartners secondary research and experience

There are different needs and expectations of MFGs and payers / providers when it comes to innovative payment models.

<table>
<thead>
<tr>
<th>STAKEHOLDER NEEDS / EXPECTATIONS FROM INNOVATIVE PAYMENT AGREEMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>FINANCIAL PREDICTABILITY &amp; STABILITY</td>
</tr>
<tr>
<td>TAILORED CONTRACTS</td>
</tr>
<tr>
<td>PUBLIC PERCEPTION</td>
</tr>
<tr>
<td>REFUNDS, IF FAILURE</td>
</tr>
<tr>
<td>MINIMIZE ADMINISTRATIVE BURDEN</td>
</tr>
<tr>
<td>MINIMIZE FINANCIAL UNCERTAINTY</td>
</tr>
<tr>
<td>EXTRACT INCOME FOR VALUE PROVIDED</td>
</tr>
<tr>
<td>TIMELY AND BROAD ACCESS</td>
</tr>
<tr>
<td>PUBLIC PERCEPTION</td>
</tr>
<tr>
<td>EVIDENCE DEVELOPMENT</td>
</tr>
</tbody>
</table>

Payer challenges caused by one-time therapies are generally aligned between USA and the EU, but manifestations diverge due to differences between healthcare systems.

A clear understanding of payer and provider expectations is a must for successful development of innovative payment models.

SOURCE: CBPartners secondary research and experience
Innovative payment models have been proposed in USA and EU, but payer interest has remained low due to implementation challenges and failure to meet needs.

**PAYMENT DETAILS**

1. **ANNUITIZED PAYMENTS**
   - Payments spread over years to overcome affordability issues and soften “sticker shock”. Regardless of performance

2. **PAY-FOR-PERFORMANCE**
   - Payment only initiated if predetermined goals are met or rebate issued if goals are missed

3. **ANNUITIZED PAYMENTS + PAY-FOR-PERFORMANCE**
   - Similar to annuitized payments, but payment only sent if treatment goals are met

4. **DISCOUNT BASED ON % PAID UP-FRONT**
   - Payment is spread over time, but payer receives a discount based on initial payment percentage

**CHALLENGES**

1. One-time hit avoided, but long-term budget impact remains unchanged
   - Patient might leave plan

2. Need to define and track outcomes long-term
   - Need to define and track outcomes long-term
   - Patient might leave plan

3. Does not protect from risk of treatment failure

**SOURCE:** CBPartners experience

Despite launching at a high list price, LUXTURNA has obtained broad coverage from commercial plans due to small patient population with high unmet need.

**SPARK - LUXTURNA**

| FDA Approval | 2017 |
| Condition | Biallelic RPE65 mutation associated retinal dystrophy |
| Incidence | ~0.3 – 0.6:100,000 |
| MoA | Viral vector carrying RPE65 gene |
| Treatment Alternatives | N/A |
| Outcomes | Median change in MLMT* score from the baseline to year one: 2 |
| Price | $850,000 |

**Payer Response**
- Proposal for annuitized payment model with deeper rebates
- Coverage with pay-for-performance agreements

"VN's price exceeds usual thresholds for cost effectiveness, but it is the first treatment available for this serious, ultra-rare disorder."
- ICER Assessment Report, Feb. 2018

**SOURCE:** Nature Biotechnology; US Food and Drug Administration; “MLMT: Multi-Luminance Mobility Testing

Spark Therapeutics offers a performance-based agreement to insurers to make LUXTURNA’s almost $1M price more palatable.

**ADMINISTRATION**
- Payment to Spark directly from Insurer, eliminating buy-and-bill cost

**SHORT-TERM FOLLOW-UP**
- Rebate, if performance criteria not met

**LONG-TERM FOLLOW-UP**
- Rebate, if performance criteria not met

**POSITIVES AND NEGATIVES FROM THE STAKEHOLDER PERSPECTIVE**
- Timely access
- Revenue
- Positive public perception (stand behind product)
- Need to track outcomes
- Long-term financial uncertainty
- Avoid paying for non-responders
- Alleviates long-term risk
- Does not soften “sticker shock”
- Need to track outcomes
- Uncertainty if patients change plans
- Timely access
- Avoid large outlay for procurement
- No “buy-and-bill” gain for administration
- Does not soften “sticker shock”
- Increased administrative burden

**SOURCE:** CBPartners secondary research

An annuity payment model can allow tying payments to outcomes, but parameters including payment duration, size and outcome goals must be carefully defined.

POSITIVES AND NEGATIVES FROM THE STAKEHOLDER PERSPECTIVE

- Timely access
- Positive public perception (stand behind product)
- Revenue spread over a long timeframe
- Need to track outcomes
- Long-term financial uncertainty

- Avoid paying for non-responders
- Alleviates long-term risk
- Softens “sticker shock” in short-term
- Need to track outcomes
- Uncertainty if patients change plans

- Timely access
- Avoid large outlay for procurement
- Softens “sticker shock” in short-term
- No “buy-and-bill” profit
- Increased administrative burden

SOURCE: Hypothetical model based on CBPartners experience

You can access the online poll at http://bit.ly/novelpayments

Agenda

8:30 – 8:45
CURRENT LANDSCAPE & CHALLENGES

1. Introduction
2. Current state of innovative one-time therapies in USA and the EU
3. Challenges in commercializing one-time therapies
4. Payer expectations from innovative payment models

8:45 – 8:55
INNOVATIVE PAYMENT MODELS – USA

1. Commonly proposed innovative payment models by USA payers
2. Outcome-based payment model for gene therapy
3. Annuity-based payment model

8:55 – 9:20
INNOVATIVE PAYMENT MODELS – EU

1. NICE Assessment of innovative payment models
2. Hybrid annuity payment model
3. Affordability of one-time treatments

9:20 – 9:30
STRATEGIES

1. What are the tangible steps and actions manufacturers can take to successfully commercialize innovative treatments?
2. Audience Q&A

You can access the online poll at http://bit.ly/novelpayments
NICE - Exploring the assessment and appraisal of regenerative medicines and cell therapy products – What is the price of a Cure?

CAR-T cell therapy for relapsed/refractory B-cell Lymphoma

<table>
<thead>
<tr>
<th>Assumed Individual patient level incremental QALY gain</th>
<th>Bridge to HSCT TPP</th>
<th>Curative Intent TPP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assumed Price (acquisition cost of the therapy)</td>
<td>£356,100</td>
<td>£528,600</td>
</tr>
</tbody>
</table>


NICE - Exploring the assessment and appraisal of regenerative medicines and cell therapy products – Curative intent scenario

NICE - Exploring the assessment and appraisal of regenerative medicines and cell therapy products – Curative intent scenario

Table 3: Outcomes from Curative Intent Target Product Profile (minimum evidence set)

<table>
<thead>
<tr>
<th>Scenario</th>
<th>ICER NICE QALY (£)</th>
<th>Incremental NHE QALY (£)</th>
<th>Probability of Cost Effectiveness</th>
<th>Consequences of Decision Uncertainty</th>
<th>Expert Panel &quot;Decision&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discount of 10% on base case price with lifetime leasing (£2,985 per month)</td>
<td>£45,592</td>
<td>27.2 (£1,350,584)</td>
<td>97.2%</td>
<td>Yes</td>
<td>Assumed Yes</td>
</tr>
<tr>
<td>Same pricing as lodging to NICE TPP (£30,110 per patient)</td>
<td>£34,337</td>
<td>27.2 (£1,350,584)</td>
<td>97.2%</td>
<td>Yes</td>
<td>Assumed Yes</td>
</tr>
<tr>
<td>Same total cost as lodging TPP with lifetime leasing (£7,333 per month)</td>
<td>£33,277</td>
<td>27.2 (£1,350,584)</td>
<td>97.2%</td>
<td>Yes</td>
<td>Assumed Yes</td>
</tr>
<tr>
<td>Same total cost as lodging TPP with lifetime leasing and 10% discount (£1,660 per month)</td>
<td>£29,713</td>
<td>27.2 (£1,350,584)</td>
<td>97.2%</td>
<td>Yes</td>
<td>Assumed Yes</td>
</tr>
</tbody>
</table>

You can access the online poll at http://bit.ly/novelpayments

Upcoming publication!

Establishing the Cost of Implementing a Value-Based, Managed Entry Agreement for a Hypothetical CAR T-cell Therapy

Panos Kefalas¹, Omar Ali⁵, Jesper Jorgensen⁶, Nick Mevius⁷, Tim Richardson⁸, Adam Meads⁹, Laura Munro⁴, Matthew Duddy⁵

¹ Catapult Cell and Gene Therapy, Guy’s Hospital, London UK, ² Verona, BasCity, Nottingham UK
³ CONTACT Panos Kefalas, Panos.Kefalas@catapult.org.uk Catapult Cell and Gene Therapy, Guy’s Hospital, London UK

You can access the online poll at http://bit.ly/novelpayments
Under an innovative payment model, continued effectivity of treatment will need to be monitored on a regular basis.


Under an innovative payment model, continued effectivity of treatment will need to be monitored on a regular basis.

Why do commercial airlines ‘lease’ jet engines rather than ‘buy’ them?

the engine is the most complex and expensive part of the airplane
the engines are monitored & maintained by Rolls Royce

“we are not in the business of selling engines, but more so in the business of selling thrust“
Role of OBIC levers in bridging CSI for Pharma & Payers

1. Homogenize areas of common agreement
2. Bridge major CSI differences
3. Provide platform to negotiate the ‘quarrel house’

You can access the online poll at http://bit.ly/novelpayments

IOBC Architecture

You can access the online poll at http://bit.ly/novelpayments
IOBC Architecture

ACHIEVE OBIC BENEFITS FOR BOTH PARTIES

Pharma

- Commercial list price ~$1,000,000
- Minimal discount
- Access to patients (direct purchase)
- Mindful of pipeline gene therapies

Payer

- Household quarrels (negotiables)
- No Response
- No Payment
- Maximal discount

Risk taken on both sides: Simple contract, low admin costs & auditability; Patient adherence improved; Minimize off-label, off-pathway & non-traced costs; Long-term (CEO) OK; Pre-OBIC offers not required; Not to undermine patient visits; Reduce duration to & frequency of relapse/recurrence/rescue treatments; Doesn’t drain payer funds at EOL


Are we agreed on innovation?

How ugly is my child?

You can access the online poll at http://bit.ly/novelpayments

Agenda

8:30 – 8:45  
CURRENT LANDSCAPE & CHALLENGES

1. Introduction
2. Current state of innovative one-time therapies in USA and the EU
3. Challenges in commercializing one-time therapies
4. Payer expectations from innovative payment models

8:45 – 8:55  
INNOVATIVE PAYMENT MODELS – USA

1. Commonly proposed innovative payment models by USA payers
2. Outcome-based payment model for gene therapy
3. Annuity-based payment model

8:55 – 9:20  
INNOVATIVE PAYMENT MODELS – EU

1. NICE Assessment of innovative payment models
2. Hybrid annuity payment model
3. Affordability of one-time treatments

9:20 – 9:30  
STRATEGIES

1. What are the tangible steps and actions manufacturers can take to successfully commercialize innovative treatments?
2. Audience Q&A

You can access the online poll at http://bit.ly/novelpayments
Early engagement with payers, consideration for payment models in development and communication are key recommendations for manufacturers of novel therapies.

FOR DISCUSSION

ENGAGE PAYERS EARLY ON TO UNDERSTAND EXPECTATIONS

PLAN FOR INNOVATIVE PAYMENT MODELS EARLY IN DEVELOPMENT

COMMUNICATE OPENNESS TO INNOVATIVE CONTRACTING

ESTABLISH SYSTEMS TO TRACK OUTCOMES WITH MINIMAL BURDEN

DETAIL
• Understanding payer and provider decision-makers and influencers, as well as their motivations, is critical to designing mutually-beneficial and net value-add payment models
• Available evidence will inform the structure of innovative payment models and clinical and non-clinical evidence generation activities should be planned with this consideration
• Realizing the value perception benefits of innovative contracting requires a communication strategy to accompany payer and provider stakeholder engagement
• Added burden of outcome tracking is a strong detractor for payers and providers, which can be a roadblock for innovative payment models

TANGIBLE ACTIONS
• Discuss payment models and reimbursement strategy
• Tailor payment models to individual payer needs
• Consider implications for outcome-based agreements in trial design
• Plan evidence generation activities that can support novel payment models
• Include innovative contracting plans as part of the overall value proposition
• Engage providers to understand how outcome tracking can be supported
• Collaborate with patient communities and registries

SOURCE: CBPartners experience; manufacturer and payer perspective

You can access the online poll at http://bit.ly/novelpayments

Q&A / Conclusion

The panelists will now field any additional questions from the audience.

Visit us at cbpartners.com for a summary of today’s discussion and our other thought leadership posts!

You can still access our online poll at http://bit.ly/novelpayments

Thank you for your participation!
If you are not using the online poll, please use the colored cards that were distributed earlier.

You can access the online poll at http://bit.ly/novelpayments

**QUESTION 4**

In your opinion, what is the likelihood of success for each of the mentioned payment models in the USA?

A. Annuitized Payments
B. Pay-for-Performance
C. Annuitized Payments + Pay-for-Performance
D. Discount Based on % Paid Up-front
E. Leasing Model

**QUESTION 5**

...In Europe?