ISPOR 19th Annual European Congress Vienna 2016
Congress Report
November 2016
Costello Medical Consulting recently attended the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 19th Annual European Congress in Vienna, Austria, with over 4,700 other delegates from 29th October to 2nd November 2016. This year’s congress was entitled “Managing Access to Medical Innovation: Strengthening the Methodology-Policy Nexus”.

There were over 120 events to attend, including three plenary sessions and over 2,000 poster presentations. Figure 1 below presents a word cloud of the most commonly cited words across all of the session abstracts at the congress.

Figure 1. ISPOR Vienna 2016 Word Cloud Describing the Key Topics Covered at the Congress

Key Themes of the Congress

This report focuses on eight key themes that were widely discussed at this year’s congress:

- Impact of Pricing on Access and Innovation
- Collaboration Between Health Technology Assessment (HTA) Bodies and the European Medicines Agency (EMA)
- Value Assessment and Reimbursement of Medical Devices
- Value Assessment and Pricing of Biosimilars
- Novel Uses of Real-World Evidence (RWE) and Appropriateness for HTA
- Patient Engagement in HTA Processes
- Pricing, Reimbursement and Patient Engagement in Rare Diseases
- Advances in Health Economic Modelling
Impact of Pricing on Access and Innovation

Several sessions discussed the pricing of medicines and the impact of price on access and innovation. The second plenary session explored the use of differential pricing in Europe, given the differences in ability to pay and willingness to pay. Differential pricing was deemed to be a policy that could improve access, but barriers exist in Europe such as international reference pricing, parallel trade, and the difficulty of political feasibility.

As well as differential pricing across countries, one presentation explored how prices of orphan drugs in oncology varied depending on patient population sizes, and found no clear association, highlighting the multi-faceted nature of drug pricing.

Several key challenges were identified when pricing medicines, such as limited evidence, the speed of HTA being a limiting factor, and balancing the value of a product with the recuperation of the investment costs. Reference pricing, negotiations, and risk sharing were noted as options to tackle these problems.

One presentation explored a flexible pricing model, which used real time outcomes-based pricing, which could reflect value, be market-based, incorporate RWE, and potentially lead to earlier access to medicines and better value.

Collaboration Between HTA Bodies and the EMA

The first plenary session of the congress discussed the synergies that could be created between the EMA and national HTA bodies. The benefits of such a collaboration were presented by Guido Rasi from the EMA and included the possibility for faster patient access, resource savings for regulators/HTA bodies and the mitigation of reputational and political risk for regulators/HTA bodies across Europe. Wim Goettsch from the European Union Network for HTA (EUnetHTA) also discussed the huge progress in interaction between the EMA and HTA bodies and that a new workplan between the EMA and EUnetHTA is being developed in the coming months.

Finally, a European Commission initiative on strengthening European Union (EU) cooperation on HTA is also underway, and the inception impact assessment was published in September 2016 with five possible future policy options for this collaboration (Figure 2).

![Figure 2. Future Options for HTA and EMA Collaboration](image)

<table>
<thead>
<tr>
<th>Option 1</th>
<th>Option 2</th>
<th>Option 3</th>
<th>Option 4</th>
<th>Option 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Status quo – voluntary cooperation</td>
<td>Long-term voluntary cooperation (beyond 2020)</td>
<td>Cooperation through the collection, sharing and use of common tools and data</td>
<td>Cooperation on production of joint REA (relative effectiveness assessments) reports</td>
<td>Cooperation on production of joint Full HTA reports (REA + economic)</td>
</tr>
<tr>
<td>Non-legislative / voluntary</td>
<td>Legislative / voluntary + mandatory</td>
<td></td>
<td></td>
<td></td>
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</tbody>
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+ Issues to be addressed
- Scope
- Funding mechanism
- Coordination/secretariat

Value Assessment and Reimbursement of Medical Devices

The challenges associated with the value assessment and reimbursement of medical devices were a key theme at this year’s congress. Health care systems typically spend twice as much on pharmaceuticals than devices yet there are almost 300 times more medical devices on the market and their commercial lifecycle is typically only 2–3 years (Figure 3). An issue panel highlighted how ‘fast-followers’ can often claim ‘substantial equivalence’ of a medical device, which avoids the need for costly clinical studies but further discourages novel research.

Mike Drummond (Centre for Health Economics, University of York) discussed how a post-market research collaboration scheme could be a possible solution, to enable RWE to be gathered as quickly as possible without the burden of research costs lying with the first-to-market manufacturer.

In addition, medical device reimbursement typically occurs at a local hospital-level through the Diagnosis Related Group (DRG) system, which can lead to the under-reimbursement of high-cost innovations to cheaper existing DRGs. A presentation evaluating national HTA body assessment of devices in England and France concluded that although the involvement of national HTA bodies could speed-up the adoption of novel devices and provide uniform availability, their current role and scope across Europe varies substantially.

The new EU Medical Device Regulations (to be published at the end of 2016 with rules applying in 3 years) were also discussed in which high-risk devices will be subject to additional assessments and there will be stronger pre-market scrutiny and post-marketing surveillance.

Value Assessment and Pricing of Biosimilars

As more biosimilars are developed and enter the market with the promise of cost savings for healthcare systems, increased choice for prescribers and broader access for patients, questions of how they should be valued, considered by HTA bodies, and their position alongside originator biologics were of particular interest at this year’s congress.

During an issue panel on whether biosimilars should undergo HTA, it was proposed that while arguably any potential for greater cost-effectiveness with biosimilars should be reviewed, HTA is a lengthy and expensive process.

Figure 3. The Medical Devices Sector in Context

<table>
<thead>
<tr>
<th>Healthcare System Expenditure</th>
<th>Number of Approved Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical devices</td>
<td>&gt;500,000 approved medical devices</td>
</tr>
<tr>
<td>Pharmaceuticals</td>
<td>1,453 approved pharmaceuticals</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nature and Number of Companies</th>
<th>Commercial Lifecycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;25,000, mostly SMEs</td>
<td>2 to 3 years</td>
</tr>
<tr>
<td>~90, mostly MLEs</td>
<td>8 to 12 years</td>
</tr>
</tbody>
</table>

The decision to conduct HTA should be considered in terms of its ability to maximise access to the drug for the patients most likely to benefit. If HTA is carried out, it should be of a suitable length and depth, with an appropriate comparator, depending on the local approval status of the originator biologic and whether the biosimilar is being directed towards the same indication(s) or new ones.

It was also highlighted that governments are struggling to decide on pricing policies for biosimilars, and information on the cost of switching patients to biosimilars from originator biologics is scarce in Europe, with respect to modelling their budget impact. The future of biosimilars as a genuine alternative is likely to depend on positive attitudes of payers and the general public, appropriate pricing, and their ability not just to replace originator biologics, but to be used for treatment innovation in their own right.

**Novel Uses of RWE and Appropriateness for HTA**

The integration of RWE with randomised controlled trial (RCT) evidence was a running theme throughout the congress. Novel techniques presented included estimating drug efficacy by integrating RCT data on that treatment with RWE from a similar treatment that is already on the market. Additionally, methods that would allow the integration of RWE data to improve survival curve estimates from short-term RCT data were also explored.

Propensity score matching is a frequently used method of synthesising treatment effects on an individual patient level, when no control is available. This technique was used to inform several poster and podium presentations on a range of topics, from the financial burden of obstructive sleep apnoea in the elderly to the perception of marijuana use in the USA. The matching-adjusted indirect comparison method, which weights individual patient data from one trial so that the overall baseline characteristics are similar to that of another trial, was also explored as a potential way of incorporating single-arm or disconnected evidence into a network meta-analysis.

One issue panel focused on the value of RWE, exploring how this type of data could be integrated into the HTA process. It was argued that observational data is generally of a lower quality than RCT data, and may therefore increase the risk of an incorrect decision. However, the overall opinion was that RWE data, combined with RCT data, can be a helpful and a relatively cost-effective tool for determining drug efficacy and safety if appropriate methods are used.

**Patient Engagement in HTA Processes**

There was a strong emphasis on patient engagement in HTA processes at this year’s conference. Sheela Upadhyaya (Highly Specialised Technologies [HST] Programme, National Institute for Health and Care Excellence [NICE]) provided a helpful overview of where patient input is most valued for their appraisal programme – notably in providing clarification around patient numbers and key aspects of disease burden, as well as insight into likely uptake of new therapies and subsequent adherence.

Poor penetration of the patient voice into HTA where it is not supported by quantitative evidence was openly acknowledged at one issue panel, though speakers also argued for the need to demonstrate the qualitative value of collected outcomes to patients. Samantha Parker from Lysogene provided an interesting summary case study, describing her concerted efforts to not only collect sleep pattern data but to then conduct rigorous, semi-structured interviews to qualitatively demonstrate the value of these altered sleep patterns to patients.

Ultimately, payer and patient value frameworks do overlap. As patient engagement in HTA expands, increasing patient involvement in evidence generation for these joint areas of interest will help manufacturers to develop cases for access that resonate with both the payer and the patient.

**Pricing, Reimbursement and Patient Engagement in Rare Diseases**

Consistent with the increasing industry and public interest in orphan and ultra-orphan indications, this year’s conference featured a number of presentations focused on the importance of pricing, reimbursement and patient engagement in rare diseases.

The HST programme at NICE was discussed in detail. During an issue panel focused on off-label treatments in rare diseases, Pilar Pinilla-Dominguez (Technical Adviser, NICE Scientific Advice) discussed how the broader criteria that are considered in HST decision-making are better able to capture the value of orphan drugs, which frequently lack high quality evidence.
During the same issue panel, Jack Scannell (Co-head European Pharmaceuticals, UBS Investment Bank) presented the case for off-label use as a source of under-appreciated innovation, while we heard from Oliver Timmis (CEO, AKU Society) about the problems faced by patients that have been prescribed off-label medications, including inequality in access, lack of informed consent and lack of clinical follow-up (Figure 4).<sup>20</sup>

During another issue panel, the question of whether “rarity” is sufficient to justify treating orphan or ultra-orphan conditions differently to more common conditions in HTA was raised by Ron Akehurst (Strategic Director, BresMed Health Solutions).<sup>21</sup> He noted that characteristics commonly seen amongst rare diseases, such as disproportionately affecting the young and the large QALY gains, are not unique to rare diseases; therefore, perhaps these characteristics should be given appropriate weighting regardless of the size of the affected population. Furthermore, he highlighted the uncertainty in terms of appropriate research and development investment and pricing in the rare disease area – a topic that was touched upon in the follow-up discussion, which challenged high prices proposed by industry for orphan medications. To conclude this panel, Alastair Kent (Director, Genetic Alliance UK) brought home the importance to society of therapies that address the unmet needs of the rare disease patient population, and the difficulty in accurately measuring this value.<sup>21</sup>

**Advances in Health Economic Modelling**

Several presentations focussed on ongoing advances in health economic modelling. Oncology was a key theme, with sessions covering novel approaches to long-term survival analysis through incorporation of real-world data and dynamic extrapolation modelling.<sup>21</sup> A new working group set up to improve input sourcing when modelling advanced cancers, particularly related to costs and utility values, also reported their findings to date.<sup>22</sup>

Improved approaches to modelling methodology were also addressed in several sessions. These included a new short course on the recently developed Discretely Integrated Condition Event (DICE) simulation,<sup>23</sup> a workshop introducing a platform in development for carrying out rapid Value of Information analysis,<sup>24</sup> and a second workshop introducing new global technical verification checklist to complement the existing structural checklists and improve quality control of economic models.<sup>25</sup>

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**Figure 4. Is Off-Label Drug Use Enhancing or Limiting Access for Patients with Rare Diseases?**

**A) The Pros and Cons of Off-Label Drug Use**

- Provides patient access to drugs that wouldn’t otherwise be available
- Field based discovery as a source of under-appreciated innovation
- Able to address substantial unmet need
- Greater acceptance of real-world data
- Development of mechanisms for recording and systematically reviewing off-label use
- Official recommendation and funding for follow-up studies
- Planning and early engagement

**B) What Can, or Should, be Done to Improve this Issue?**

**Improve Methodologies**

- Formal recognition of off-label use
- Incentivise user-led innovation
- Maximise use of existing programmes (eg. HST, NICE evidence summaries)
- Stricter requirements governing information given by doctors when prescribing off-label
- Development of reimbursement rules for off-label prescriptions

**Improve Data Collection and Synthesis**

- Greater acceptance of real-world data
- Development of mechanisms for recording and systematically reviewing off-label use
- Official recommendation and funding for follow-up studies
- Planning and early engagement

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Adapted from Issue Panel IP21: Is Off-Label Drug Use Enhancing or Limiting Access for Patients with Rare Diseases? ISPOR 19th Annual European Congress, Vienna, 2016. For further details of this issue panel, please contact Annabel Griffiths (annabel.griffiths@costellomedical.com).
Spotlight: Value Frameworks in the US

Rising drug costs, increasing patient financial burden, and a greater need for value in the healthcare system have led to the development of several third party value frameworks in the US and an overview of these frameworks was provided in an educational symposium at the congress. The frameworks discussed included the American Society of Clinical Oncology (ASCO) Value Framework, the Memorial Sloan Kettering Cancer Center (MSKCC) DrugAbacus, the National Comprehensive Cancer Network (NCCN) Value Framework, and the Institute for Clinical and Economic Review (ICER) Value Framework.

Many of these frameworks focus on oncology and report on the value of interventions to the health care system, and in some instances show what the intervention should be worth. Several challenges for these frameworks were raised, most notably data gaps, a lack of awareness from payers, and criticisms of the methodologies used. It was agreed that it would be important to include the appropriate metrics, for the assessments to be conducted by a neutral party, and for there to be a rigorous methodology behind any frameworks used.

Based on lessons from the usage of value frameworks in Europe, it was suggested that the frameworks used would need to fit the underlying value position on equity, efficiency, and personal responsibility, in addition to the institutional context within which it is used. It was also suggested that any framework would require periodic review, as well as feedback from stakeholders and the general public.

The ISPOR 22nd Annual International Meeting will be held in Boston, US, from May 20th–24th 2017.

Costello Medical Consulting

Costello Medical provides scientific support to the healthcare industry in the analysis, interpretation and communication of clinical and health economic data. Due to growing demand across an increasing range of service offerings and geographies, Costello Medical has grown organically since foundation in 2008 to a team of over 90 based in Cambridge and Singapore.

Alongside our widening technical and creative capabilities, we remain committed to our core values of high quality scientific work coupled with exceptional customer service at competitive and transparent prices. Our talented team has experience with a variety of leading pharmaceutical companies and a track record of success in a broad range of disease areas. For more information on our services in HTA and Health Economics, Evidence Development, Market Access, Medical Affairs, Publications, Medical Devices, Visual Communication, Public Sector work or charitable pro bono projects please visit our website at www.costellomedical.com.

Further Assistance

If you would like any further information on the themes or research presented above, please do not hesitate to contact Jeanette Kusel at: jeanette.kusel@costellomedical.com. Many of the presentations from the congress can be found at http://www.ispor.org/Event/ReleasedPresentations/2016Vienna.
## References