EASD 2010: Innovations and challenges facing the diabetes care IVD industry

The concept of an "artificial pancreas" – technology that can monitor a diabetic patient's levels of blood sugar and insulin and deliver the hormone precisely as it is needed – is a longed-for development in the treatment of diabetes. The dream is finally becoming a reality, according to data presented at last year's EASD conference. Michaela Miller and Joshua Guthermann of Boston Biomedical Consultants attended the meeting

Accuracy of monitoring and patient enablement were among the key focal points of the in vitro diagnostic product demonstrations and topical discussions at the most recent meeting of the European Association for the Study of Diabetes (EASD). The annual conference, held in Stockholm, Sweden from 20-24 September, is the single largest pan-European exhibition specifically dedicated to diabetes and attracted over 17,300 delegates and nearly 100 industry exhibitors from across the globe. Despite slowed market growth, heightened regulatory scrutiny, and increased pressure on margins, the number of competitors in the diabetes monitoring space continues to increase as evidenced by the sheer number of smaller device exhibitors at the show. With growing pressure on governments to reduce diabetes related healthcare expenditures, cutbacks (implicit or otherwise) in test strip reimbursement for non-insulin-dependent type II diabetes mellitus patients have been implemented across Europe.

BGM technology

Innovation in blood glucose monitoring (BGM) technology displayed at the EASD meeting was focused on improved accuracy, ease of use, and enabling patient action. Technical improvements ranged from the ability to selectively mark BGM test results, to the integration of lancing technology, and connectivity to smartphones. With strong influences from the consumer electronics industry on product design, display technology, user interfaces, device connectivity, and data management have become growing research and development focal points.

Sanofi-Aventis made a splash at the EASD with its iBGStar BGM module, which connects to the Apple iPhone and iPad. The conference marked the company's

© Informa UK Ltd 2011

official unveiling of its new comprehensive approach to providing diabetes patient care. Facing key patent expirations including that covering insulin analogue blockbuster Lantus, Sanofi-Aventis announced its intention to diversify through the launch of BGM systems, and potentially other devices including insulin infusion pumps. At the conference, Sanofi-Aventis revealed its first two BGM meters, stemming from an alliance with Salem, New Hampshire-based AgaMatrix. The company's future offerings will be based on a four-pronged portfolio consisting of diagnostics, delivery devices, therapeutic products, and services. The BGStar and iBGStar are slated for commercialisation in 2011, starting in Europe, most likely France, where Sanofi-Aventis has the strongest brand equity. Both products are based on patented Dynamic Electrochemistry technology currently sold under the WaveSense brand by AgaMatrix and various distributors. The pending introduction of the iBGStar will also mark Apple's first official entry into the medical device space.

Roche promoted its advances in the development of BGM and insulin delivery technology as well as data management systems. The company most recently introduced the first "continuous strip"-based BGM system (Accu-Chek Mobile), which was one of Roche's centrepieces at the EASD. Messaging highlighted the product's ease of use, lack of strip handling, simplified patient training, as well as related reduction in patient errors and improved patient compliance. Roche also promoted the Accu-Chek Combo, one of the only handheld insulin infusion pump controllers available in Europe.

Roche stressed the importance and value of data management tools and published additional study data highlighting the economic and clinical benefits of structured BGM. Roche has increased its communication on the topic in response to the ongoing debate about the value of at-home BGM for non-insulin-dependent diabetes patients.

LifeScan, the BGM business of Johnson & Johnson, displayed its existing portfolio and emphasised the accuracy of its OneTouch Ultra technology. The company drew attention to the dangers associated with using GDH-PQQ enzyme chemistries (which the OneTouch Ultra does not utilise) given the potential for maltose interference. In 2009, the FDA informed manufacturers that it would not approve BGM products based on the GDH-PQQ enzyme and advised healthcare institutions against their use. Select European authorities, including France, have also insisted on shifting from the GDH-PQQ enzyme.

Bayer highlighted its newest diabetes care products at the EASD meeting, including the CONTOUR USB BGM meter, which was initially commercialised in late 2009. Since the launch, Bayer has promoted its value as turning "knowledge into insight". The meter stands out due to its colour screen, built-in USB port, rechargeable battery, and onboard data management software. Of secondary emphasis was the DIDGET, the first high-profile BGM product to work with a Nintendo DS game console. Distribution of the DIDGET has been limited to few international markets.

Abbott utilised the EASD as a venue to promote its improved FreeStyle test strip. Much emphasis was placed on the introduction of the new test strip in Europe and its ZipWik tabs technology. The alteration of the test strip is aimed at improving the blood application process, minimising waste, and shortening the testing process. The test strip has been reconfigured to FAD-GDH chemistry and features no coding. The changes were promoted as improvements to the accuracy of the technology as well as ease of use. Abbott CE marked the device in October 2009, and the new test strip was available in 15 European markets by mid-2010.

Sanofi-Aventis was not the only new company to announce its intention to enter the BGM market. Newcomer Mendor introduced the Discreet BGM system, which has an integrated lancing device and 25-test strip cartridge. The design of the device resembles that of a mobile phone. The start-up company is run by a young management and engineering team who formerly worked for Nokia, and who are using social networking and web-based marketing tools such as Twitter and Facebook to promote its products and disseminate company news. The product was first commercialised in Finland in late 2010 with a broader global release underway.

Other secondary competitors in the BGM space also introduced new products at the conference. These included ARKRAY, Menarini, ForaCare, Nova Biomedical, Terumo, and many smaller international players. Several pursue positioning based on price, which adds to the pressure on margins and reinforces the importance of low manufacturing costs. While historically, innovation and quality of smaller vendor systems have fallen below industry standards established by the "Top Four" competitors, these gaps are disappearing; product differentiation has been easier to copy and first-to-market advantages yield shorter-term benefits.

CGM & advances with the artificial pancreas

Advances made with continuous glucose monitoring (CGM) technology were discussed at the meeting, as was progression in the development of an automated artificial pancreas. Multiple presentations were given, serving as a forum for discussions and debate. CGM reimbursement across Europe has been established at a slow pace, perhaps owing to the publication of data questioning its value in improving glycaemic control and minimising adverse events.

However, positive clinical data published by the Junior Diabetes Research Foundation in 2009 and Medtronic in 2010, indicating that the use of CGM was both a safe and effective means for improving or maintaining HbA1c control in T1DM patients, has led to notable forward momentum in CGM reimbursement in the US. Consistent release of information proving clinical and economic value of CGM will be necessary to drive similar movement across Europe.

In the absence of established reimbursement for CGM sensors and systems, product adoption across Europe has been slow. Prices range from €30 to nearly €90 per sensor depending on the country. To date, the Europe CGM market is primarily driven by healthcare provider purchases for temporary patient use and treatment assessment rather than for patient home use. Nonetheless, industry continues to pursue market development and all of the commercial CGM products were showcased at the EASD, including the DexCom SEVEN Plus, which was introduced in Europe in early 2010 through various distributors. The product has been available in the US since March 2009 and the company currently holds an estimated 24% market share in the US. DexCom also promoted the first-generation GlucoClear hospital CGM, an in vivo sensor developed in collaboration with Edwards LifeSciences. The system is currently in pilot studies in eight different countries. A second-generation hospital CGM device aimed at wider commercialisation is in development.

Medtronic, the market leader in the area of CGM, officially introduced the iPro2 professional CGM device in Europe. Promoted as "Put it on and go", the iPro2 requires minimal patient training and can

© Informa UK Ltd 2011

be worn for up to six days, after which the data is analysed by the physician. In addition to the iPro2, Medtronic promoted CGM integration in its insulin infusion pumps, including the MiniMed Paradigm Veo, which is positioned as a first step toward an artificial pancreas. The Paradigm Veo was first introduced in Europe in 2009.

Abbott promoted the FreeStyle Navigator CGM following a temporary distribution disruption earlier in the year; new transmitters and receivers remain unavailable in the US. Since its European launch at the end of 2007, Abbott invested in differentiating the CGM based on its built-in FreeStyle BGM, five-day sensor life, and minute-by-minute results and trending.

The only other CGM device that is currently commercially available is the GlucoDay S by Menarini. Unlike other electrochemical systems, the GlucoDay S is a micro-dialysis based device and largely used for clinical research.

Stand-alone CGM technology continues to be pursued for commercial purposes, but is frequently thought of as one component of a larger ambition, the development of a closed-loop system or artificial pancreas. At the EASD, results and evidence were presented from current studies evaluating different artificial pancreas algorithms. Findings revealed that basal control was easily obtained through current algorithms.

The development of an artificial pancreas that can also adequately adjust for bolus insulin injections still appears to be an engineering challenge. In a November 2010 interview, FDA representatives indicated that available CGM systems were solely approved to track and trend glycaemia – a long step from utilising the data to automatically drive insulin dosing, a requirement for an artificial pancreas. The agency believes that it may be five years from realistically evaluating its first automated artificial pancreas product submission.

Disease diagnosis via HbA1c testing

One topic of interest at the EASD 2010 conference was the use of HbA1c testing for the diagnosis of diabetes. Until recently, the standard for diagnosis consisted of a fasting plasma glucose (FPG) or an oral glucose tolerance test (OGTT), both of which suffer from multiple potential pre-analytical and analytical errors. Many healthcare professionals use handheld consumer glucose meters, which are inherently less accurate than laboratory methods.

In 2009, an International Expert Committee representing the EASD, the American Diabetes Association and the International Diabetes Foundation released new guidelines for diabetes diagnosis including the use of a laboratory HbA1c test with a cut-off point of ≥6.5% or ≥47mmol/mol. The committee cited a number of benefits of the HbA1c test including assay traceability and standardisation and no requirement for patient fasting. It is a time averaged assay, and correlation between HbA1c and specific diabetes associated complications exists.

Based on these benefits, at the EASD 2010, the World Health Organization (WHO) announced new provisional guidelines for diabetes diagnosis including the HbA1c assay with a cut-off point of ≥6.5% or ≥47mmol/mol in addition to the established FPG or OGTT diagnostic criteria. The recommendations specify that an HbA1c test is appropriate for diagnosis only if "stringent quality assurance tests are in place and assays are standardised to criteria aligned with international reference values, and that there are no conditions present which preclude its accurate measurement." The WHO previously considered HbA1c as a diagnostic test in 1999 and 2006, but rejected it on both occasions due to concerns surrounding assay traceability and standardisation.

Amidst the announcement of the WHO provisional guidelines, a number of papers were published at the EASD meeting indicating that the FGP, OGTT, and HbA1c diagnostic criteria do not correlate, leading to the potential for variations in diagnosis based on testing protocols. With these concerns in mind, diabetes specialists and general practitioners are now trying to understand what tests and cut-offs should be used to diagnose diabetes in future.

** Boston Biomedical Consultants is based in Waltham, Massachusetts. To contact Michaela Miller or Joshua Guntherman, email info@bostonbiomed.com*

Ask the Analyst

Phil Greenfield Christopher Bowe Ian Schofield Ashley Yeo Dr Peter Charlish

OUR EXPERTS ARE NOW *YOUR* EXPERTS Free to subscribers

Ask the Analyst gives you direct access to our expert analyst team. Simply ask your research questions and our analysts will do the research and get back to you personally with the information you need.

Our experts can you help by:

- Producing regulatory and legal guidance tailored to your needs
- Advising you on how to navigate through diverse international regulatory & legal requirements
- Enhancing your Strategic Planning

Regulatory Affairs Medtech

For more information or to submit your question, please visit: **www.regulatoryaffairsmedtech.com/asktheanalyst**

 © Informa UK Ltd 2011