

## CDDF 8th Alpine Conference

**Date:** 2-4 March 2015. **Venue:** Innsbruck, Austria.

Greater interaction is needed between the European Medicines Agency (EMA) and different health technology assessors across Europe for effective delivery of approved drugs, was the recurring message from speakers at the 8th ALPINE Cancer Drug Development Forum (CDDF) meeting, held in Innsbruck, in March, 2015.

"The Alpine meeting provides a unique forum for stakeholders including regulators, academia, industry and patient groups to come together and hear presentations on a wide range of drug development topics," said Professor Heinz Zwierzina, one of the conference chairs from Innsbruck Medical University, Austria. "Discussions and delegate feedback allows us to identify key topics to be addressed in future CDDF workshop meetings."

The prospect for a centralised, EU-wide Health Technology Assessment (HTA) process Bruno Flamion, a past chair of the Committee for Reimbursement of Medicines in Belgium, told delegates, is now 'on the table'. Such developments, he explained, have been made 'workable' by directive 2011/24/EU from the European Parliament and Council on application of patient rights in cross border healthcare.

"The idea of HTA is to provide policy makers with accessible, usable evidence based information," said Flamion, from the University of Namur, Belgium. However, the reality is that with 28 European member states each conducting separate HTA pricing/ reimbursement assessments the system has become fragmented. Differences include France considering the value of new therapies in the context of drug budgets; the UK considering value in terms of health care budgets; and Sweden considering value in terms of wider societal budgets. "In future we may see patient participation increase harmonisation of HTA evaluation. They want access to products based on efficacy and safety and have a right to ask for this," said Flamion.

Stiina Aarum, from the European Medicines Agency (EMA), highlighted the need for developers to interact with regulators and HTAs in parallel. Currently regulators and HTAs, she said, often answer different questions and have different evidence requirements. Such variance in standards can result in divergent appraisals of risk benefit versus cost effectiveness. "There's a need for stakeholders to come together early to devise optimised development plans discussing issues such as trial populations, comparators, and endpoints," said Aarum.

The EMA, she said, has completed 34 parallel procedures with HTA bodies from England, Italy, Germany, Sweden, France, Netherlands, Spain and Belgium for a broad range of indications including lung, breast and pancreatic cancers and melanoma. This year, said Aarum, around 23 parallel scientific advice



Stiina Aarum



Tatiana Prowell

procedures are ongoing.

The adoption of break through therapy designations, Francesco De Lorenzo, President of the European Cancer Patient Coalition (ECPC) told delegates, does not solve the problem of patient access to innovative drugs. "The safest, most effective drug that arrives too late is of no benefit for patients," said De Lorenzo, a colorectal cancer survivor, medical doctor, and former Italian minister of health. Inequalities in cancer care, he said, are a reality for Europe. Average cancer expenditure per citizen varies from 182 in Germany, to 16 in Bulgaria. One possible solution, he suggested, would be for cost-effectiveness to be evaluated as part of the market authorization process. Patients are ready to accept the risk of adaptive licensing/ break through designations, he said, but require good information. "We need shorter simpler consent forms of two to three pages rather than the current 20 plus pages. Governments have to invest more in education and advice," said De Lorenzo.

The FDA wants to proactively engage sponsors to discuss trial designs to improve consistency of Patient Reported Outcome (PRO) data, said Tatiana Prowell, the FDA Breast Cancer Scientific Lead. To this end, the FDA has recently appointed PRO leads for each of its three divisions in the Office of Hematology & Oncology Products.

The 2012 FDA Safety and Innovations Act, Prowell explained, created a mandate to include patient perspectives in drug development. "PRO data can support accelerated or regular approval, but should be held to the same high standards as other endpoints," said Prowell.

Patient-reported symptoms, studies have shown, demonstrate better correlations with disease status than clinician-reported symptoms but issues remain around PRO reproducibility. "Most importantly, can you detect responses to the intervention that represent clinically meaningful changes for patients?"

The demonstration of spleen size reduction in myelofibrosis patients treated with ruxolitinib offers a good example of a successful PRO programme that achieved accelerated approval in a trial involving just 300 patients. Here sponsors engaged early with FDA advisors to discuss trial endpoints resulting in the development of a simple PRO tool including six symptoms of direct relevance to patients. "While it took time for the companies to meet with FDA and develop the PRO tool, the process resulted in a better development and registration strategy," said Prowell, adding that the FDA is in the process of building a PRO research agenda.