(AEs). The most common grade 3 to 4 AEs were neutropenia (11.3%), febrile neutropenia (6.3%), anemia (2.8%), fatigue (2%), neutropenic sepsis (1.8%), vomiting (1.3%), and diarrhea (1%). Eight (2%) treatment-related deaths were reported.

The investigators concluded that CUP/EAP provides additional safety data for CbzP in a routine clinical practice patient population with heavily pretreated mCRPC. Treatment was tolerable, with a predictable and manageable toxicity profile consistent with data reported for TROPIC and product labeling.

Affordability of Cancer Care: A Global Perspective

Increasing Cancer Burden and Globalization

The incidence of cancer is expected to rise substantially by 2030, because of the increasing world population, aging, and the introduction of cancer risk factors from developed countries to risks that already exist in low- and medium-resource countries. An expected 1% per annum increase in cancer incidence will result in approximately 26 million new cases in 2030, with most of the increased in developing countries [Thun MJ et al. *Carcinogeneis* 2010]. Patients in low-resource countries typically present with advanced cancer. Obstacles to prevention, early detection, and therapy include scarce human resources, financial barriers, lack of radiotherapy facilities, limited access to anti-cancer drugs and palliative care, and insufficient coordinated action.

According to Peter Boyle, PhD, DSc, International Prevention Research Institute, Lyon, France, the current model is broken. An international policy based on collaboration is needed, with a global consortium that involves governmental and nongovernmental organizations, the pharmaceutical industry, and other partners.

Successful models for tackling this critical problem include: the Academic Model Providing Access to Healthcare, which aims to deliver essential primary care services, control HIV, and mitigate the social and economic consequences of HIV/AIDS; the School of Nursing and Midwifery, University of Dundee, Scotland, UK, which provides distance health education in low- and middle-income countries; Hospice Africa Uganda, which provides palliative care and education in palliative care; and the Susan G. Komen Global Alliance in low-income countries.

Cost and Effectiveness of New Cancer Treatments

Ian Tannock, MD, PhD, University of Toronto, Toronto, Ontario, Canada, discussed the high cost of cancer treatments relative to their effectiveness. Many new drugs provide small gains at a high price.

Dr. Tannock and colleagues found that only 37% of 25 new targeted agents approved by the US Food and Drug Administration (FDA) cost <$100,000/life-year gained. The cost of new targeted agents needs to be reduced by a median 78% to be cost-effective, even in Western countries. The investigators recommended that registration of new anticancer drugs should require value-based pricing that renders them cost-effective. In addition, healthcare rationing is essential to ensure fair distribution of limited resources, regardless of a country's wealth.

Drug pricing is based more on maximizing profits than clinical benefit and is the major cause of the limited availability of off-patent drugs, such as methotrexate and doxorubicin. The profit motive for drug development makes it difficult to evaluate new roles for old drugs, which is important in developing countries. Drug pricing is based on effectiveness measures in clinical trials and is driven by the United States. Drug approvals based on cost-effectiveness would lead to more equitable distribution. Oncologists should be aware of the relative costs of drugs and choose cheaper alternatives when options are equal.

A strategy to maximize therapeutic benefits for all patients is to lobby the European Medicines Agency and the FDA to link approvals for new therapies in wealthy countries to agreements by drug manufacturers to provide the therapies at a much lower price to countries that cannot afford them.

Barriers and Challenges to Cancer Research

Access to cancer drugs and new diagnostic procedures is critical to cancer control around the globe. Studies show that patients enrolled in clinical trials have improved care and outcomes. Participation in clinical research enables quick and smooth introduction of new, effective treatments in standard practice. According to Tanja Cufer, MD, PhD, University Clinic Golnik, Ljubljana, Slovenia, only about 3% of cancer patients worldwide are participating in clinical trials.

Last year, the ASCO International Affairs Committee conducted a web-based survey of 300 oncologists from 24 countries on challenges to clinical cancer research. Eighty oncologists responded, 41 from high income countries (HIC) and 39 from low- and middle-income countries (LMIC; Table 1). Most respondents had participated in up to 10 trials in the previous 5 years. A significantly higher percentage of oncologists from HIC versus LMIC participated in >10 clinical trials during this time. More respondents from LMIC reported it took >120 days from regulatory initiation to enrollment of the first patient.

Lack of funding was the most important obstacle and patient accrual the least important for academia-driven clinical trials

in HIC and LMIC. The second most important obstacle in HIC was lack of time or competing priorities and in LMIC, it was regulatory issues.

Table 1. Major Obstacles to Cancer Research.

	Average Rank	HIC (n=41)	LMIC (n=39)
Competent authorities procedures	4.25	4.61	3.87*
Ethics committee procedures	4.55	4.80	4.28*
Insurance/indemnification coverage	4.55	4.54	4.56
Lack of patients/patient accrual	5.43**	5.27**	5.59**
Lack of funding	3.16***	3.15***	3.18***
Lack of research materials (eg, drugs)	4.49	4.49	4.49
Lack of trained personnel	5.00	4.90	5.10
Lack of time or competing priorities	4.58	4.24	4.92

*marks change in obstacle distribution when stratified by country income; ** patients versus rest (except personnel) significant; ***fuding versus significant.

Future Global Cancer Research

According to Richard L. Schilsky, MD, University of Chicago, Chicago, Illinois, USA, cancer is a systems issue that encompasses biological, healthcare delivery, clinical trial information, and patient support systems. Researchers are recognizing that every tumor has a unique profile, with multiple molecular subtypes within each histologic type. A schema of personalized medicine developed by MacConnaill and Garraway [*J Clin Oncol* 2010] based on DNA profiling and targeted therapies is being challenged by emerging data on intra-patient tumor heterogeneity [Gerlinger M et al. *N Engl J Med* 2012] and evolution of histologies and genotypes.

The vision of personalized care faces many challenges, including the need for molecular pathway analysis, validated biomarker assays, an information infrastructure able to support decision-making and patient monitoring, multiple effective therapies, and increasing regulatory complexity. The success rate of bringing drugs to market is 5% to 8%, resulting in great inefficiencies and costs.

To address these challenges, new learning structures are needed, including global research consortia, community-based networks, and learning healthcare systems. There is a need to move toward trials that have the greatest potential to provide benefits for patients, with selection of participants based on molecular characteristics. Pragmatic clinical trials in community clinical practice are also important. Patient-centered, rapid-learning cancer care systems, such as ASCO Cancer-LINQ, that incorporate data collection and comparative effectiveness research with implementation, assessment, and refinement of new evidence are needed.

Targeted Therapy Issues in the Age of Personalized Medicine

Biomarkers and Oncology Drug Development

Elizabeth Mansfield, PhD, US Food and Drug Administration (FDA), Silver Spring, Maryland, USA, discussed the use of biomarkers and biomarker tests for prediction, prognosis, and patient selection in targeted drug development trials. Once identified a test must be developed that measures the biomarker in a useful way. Some biomarkers are both prognostic and predictive, but trials must be designed to demonstrate the marker's value for one or the other. Selective biomarkers are neither prognostic nor predictive but are used to select a treatment population.

In 2011, the FDA published the Companion Diagnostic Draft Guidance, announcing that if a companion diagnostic test is necessary to find a drug to be safe and effective, the FDA must approve at least one instance of that test. Table 1 shows examples of pairs of diagnostic tests and biomarkers. Test selection and development must take into consideration appropriate measurement characteristics, be analytically validated, be uniformly used in registration trials, and be available for approval together with the drug.

Table 1. Types of Companion Diagnostic Tests.

Use	Type
Identify patients likely to respond or not respond to a partiuclar therapeutic product	**Predictive**
Identify subgroups of the larger population with poor prognosis who are likely to benefit from a particular therapeutic product	**Prognostic**
Identify patients likely to be at increased/decreased risk for serious adverse reactions from a particular therapeutic product	**Safety**
Monitor response to treatment for the purpose of adjusting treatment (schedule, dose, etc) to achieve improved safety or efficacy	**Monitoring**
Individualize the dose of particular therapeutic product	**Dosing**
Use as integral part of therapeutic clinical trials conducted to support market approval of a therapeutic product	**Selection**

Preselection is difficult, because all or most included patients are marker-positive and different tests with different performances are likely to have been used. External or non-Clinical Trial Assay tests may bias an enrolled population. In addition, no negative markers are available to validate the test or drug performance.

To gain approval, patients with acceptable benefit-to-risk profiles should be selected and any serious safety