that is easy to understand and permanently available. It is evident that this information is evidence based if possible, usually conventional wisdom and always conscious based searching for optimal medical treatment. Europa Uomo expects and does receive this information, yearly updated, from our scientific committee.
Next to this highway of high quality information we see patient-centered care as our domain where we welcome professional help but want to be involved from the start on any project or progress in patient care be it psychological, social, financial or involving quality of life and/or health economics.
Entering the labyrinth of medical care requires consistent quality aid and specific objective guidance to follow a care path in our social health care system. We claim patient rights but also patient obligations.
The choice of your treating specialist or rather the treating multiprofessional team is a first step to a better outcome of treatment.
The net results of the many uncertainties in the dialogue to a shared decision on primary treatment are stress and anxiety leading to fatigue and psychiatric treatment. Determining the individual disease treatment and the outcomes that matter to each patient are essential to reach the expected health related quality of life (HRQoL). Next to cure or control of the cancer patients worry most of the side-effects of treatment and the impact on their lifestyle as well as on the lifestyle of their partner. We hope to see the publication of outcomes of all procedures and treatments in an updated database which is easier to understand then sophisticated statistics, p-values and confidence intervals.

245 INVITED

The Concept of Prostate Cancer Units

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Background: In prostate cancer (PC) multiple treatment/observational options are available. Multidisciplinary (MD), multiprofessional management facilitates high-quality medical procedures, collaboration among dedicated specialists, preventing and managing physical and emotional disease- or treatment-induced complications.
Materials: Following the experience with breast cancer, in 2010 the European School of Oncology promoted the identification of general recommendations as well as mandatory requirements for the set up of PCU in a discussion paper. A PCU should be referred $\geqslant$100 newly diagnosed PC cases each year. Therapeutic/observational protocols should be carried out under the direction of PCU. Data should be recorded and available for audit once a year. A PCU should have a core team trained in PC who dedicates an agreed time to PCU and attends MD meetings (MDM): PCU Clinical Director, $\geqslant$1 uro-pathologists, $\geqslant$2 urologists, $\geqslant$2 radiation oncologists, $\geqslant$1 medical oncologists, 1 nurse specialist in PC, $\geqslant$1 data managers, 1 professional responsible for the compilation of patient data. The PCU should have access to associated services and non-core personnel: $\geqslant$1 radiologists, $\geqslant$1 medical physicists, $\geqslant$2 radiation therapy technologists, $\geqslant$1 physiotherapists, $\geqslant$1 palliative care specialists, 1 clinical psychologist, 1 sexologist/andrologist, 1 geriatrician, $\geqslant$1 clinical trial coordinators, patient advocates.
One urologist, one radiation oncologists and one medical oncologist (if possible and whenever indicated, a psychologist) should participate synchronously or in rapid succession in a weekly MD clinic. Advanced, recurrent or metastatic PC patients (pts) should be offered clinic every 2 weeks. Follow up should be supervised by PCU core members. All options should be offered and the pt's right to information and self-determination ensured.
In weekly MDM min 90% PC cases should be discussed and decisions documented in charts.
PCU should possess or have access to all the technological equipment for imaging, radiotherapy, pathology.
Conclusions: The set up of PCU requires to reorganize services, workflow and attitudes but it should have a favorable economic impact and avoid multiple consultations and inappropriate treatments. PCU certification should be considered the necessary step forward to ensure optimal treatment and care. The aim of this symposium is to start discussing about the set up of PCU in Europe.

References

Valdagni et al *Eur J Cancer* 47, 2011
Gomella et al *JOP* 6, 2010
Bellardita et al *JOP* 7, 2011

Monday 26 September 2011

Scientific Symposium (Mon, 26 Sep, 09:00−11:00) How to Understand and to Reverse Drug Resistance in Metastatic Breast Cancer

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Functional Genomic Approaches to the Dissection of Cancer Drug Resistance Mechanisms

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Drug resistance contributes to early treatment failure and deteriorating quality of life for patients with cancer. Deriving gene expression based predictors of drug sensitivity from microarray data is an associative learning process that is inherently vulnerable to the over-fitting of data. Such statistical considerations may require new approaches to the discovery of predictive biomarkers of drug response. Functional genomics screening approaches using RNA interference technologies have begun to dissect drug sensitivity pathways, revealing molecular mechanisms that may influence response to endocrine, cytotoxic and targeted therapeutic approaches in the clinical setting. Results from such functional genomics-driven biomarker discovery strategies and potential caveats in the search for novel predictive biomarkers will be discussed.

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PARP Inhibitors Sensitivity and Resistance

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Inherited mutations in either the *BRCA1* or *BRCA2* genes provide an increased risk for breast cancer. Cancers defective in either of the *BRCA* genes also have a defect in homologous recombination (HR), which will increase the genetic instability in the cancers and drive disease progression. Previously, we and others identified that *BRCA* mutated tumours are highly sensitive to inhibitors of the DNA repair enzyme Poly(ADP-ribose) polymerase (PARP). Interestingly, PARP inhibitors are only toxic in the *BRCA* mutated cells and hence there is a synthetic lethal relation between PARP and BRCA. The underlying mechanism for the PARP-BRCA synthetic lethality was initially attributed to accumulation of DNA strand breaks after PARP inhibition that required BRCA-mediated HR for repair. Here, I will provide evidence that this simple explanation is incomplete and that other complex underlying mechanism are also relevant. Importantly, some *BRCA* mutated cancers fail to respond to PARP inhibitors in clinical trials and many responding *BRCA* cancers eventually develop resistance to PARP inhibitors. Here, different mechanisms for PARP inhibitor resistance are discussed. Furthermore, novel strategies to overcome PARP inhibitor resistance are presented.

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How to Reverse the Resistance to Trastuzumab

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Several preclinical studies have suggested that activation of mTOR pathway, through PTEN loss and PIK3CA mutations, could mediate resistance to trastuzumab. Based on this background, a clinical research program has been launched to adress the hypothesis that mTOR inhibitors could reverse resistance to trastuzumab.
Phase I trials have allowed detecting first signals for efficacy and finding the doses for further studies. In the phase I trials combining paclitaxel, trastuzumab and everolimus (mTORC1 inhibitor), 44% of the patients have presented an objective response. This phase I study proposed a 10 mg daily schedule for further development. In the phase I trial combining vinorelbine, trastuzumab and everolimus, the response rate was 19% and the 5 mg daily dosage for everolimus was selected for further studies. Two phase II trials have been done, that confirmed that mTOR inhibitors reverse resistance to trastuzumab. In the phase II trial developed by MD Anderson, patients were selected to present a resistance to trastuzumab, and were treated with trastuzumab and mTOR inhibitors, without any cytotoxic agents. In this study, the response rate was 13%. Based on the results of these phase I/II trials, two randomized trials have been started. In addition to clinical development, several teams are developing biomarker programs in order to better identify which patients should be proposed a mTOR inhibitor.