from cancer therapies will be presented. The ideal criteria for reporting and grading toxicity should be objective, including biological, imaging, functional, and clinical factors. For late toxicity, the latent time to develop the toxicity should be considered. The importance of predictive and prognostic biomarkers for acute and late toxicities, mechanistic studies, and the design of clinical studies with normal tissue endpoints as a primary outcome will be discussed. A mechanism to use patient and physician reported outcomes as a follow-up tool and an indicator for intervention of treatment related toxicities will also be discussed.

Special Session (Tue, 27 Sep, 11:30−12:30)
Is the Biology of Metastatic Breast Cancer Similar to the Primary Breast Cancer?

396 INVITED

Receptors and HER2/neu Status From Primary to Metastatic Intra Patients Difference?

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A great number of studies have invariably shown discordances in hormone receptor (HR) and HER2 status between primary and metastatic breast cancer, endorsing the option to biopsy the metastatic sites to inform the choice of systemic therapy, whenever feasible. Changes in HR and HER2 status have been reported in as many as 30% of the cases, when comparing the primary tumours with either synchronous lymph node metastases or distant recurrences. The reasons for such discordances are still controversial, especially because it is exceedingly difficult to assess whether the changes actually reflect true biological mechanisms or are due to inaccurate assessment of HR and HER2 status. Indeed, the intrinsic error rate of immunohistochemical and in situ hybridisation assays used for the assessment of these markers may well be responsible for an apparent change, because any two measurements of the same variable are expected to yield discordant results unless the method is 100% accurate and perfectly reproducible. Before rendering the final diagnosis of a discordant metastasis, it may be wise to repeat the tests simultaneously on both the primary and recurrent tumour specimens, and also to use a different confirmatory test (e.g., a fluorescence in situ hybridization assay for HER2 or an mRNA based measurement for HR). Though this policy will not completely eliminate false-positive and false-negative results (because of preanalytical variables), it can reduce the technical discordance rate. Plausible biological reasons for a true change in HR or HER2 status include intratumoral heterogeneity in the expression of these markers, and the effects of the systemic interventions in clonal selection. A repeat biopsy of the metastatic site(s) may be justified when there is uncertainty about the true nature of the secondary lesion, and when the disease runs an unusual clinical course. Also, not to deny any patient the possible benefit of a targeted therapy, the repeat biopsy may be justified for patients whose primary tumour had been classified as triple negative and therefore were ineligible for any targeted treatment. A final important caveat against routine repeat measurements of receptor status on all recurrent breast cancers needs to be considered. Intratumoral heterogeneity is feature common to both the primary and the recurrent disease. Different metastatic sites in the same patient may show discordant expression of HR and HER2, so that the biopsy of a single metastasis may not be truly representative of the responsiveness of the disease to different systemic therapies. The decision to perform a repeat biopsy of the metastatic site ultimately must rely on a careful clinical judgement of the possible benefit of such intervention for the individual patients.

397 INVITED

Genomic Data on Metastatic Disease

Abstract not received

398 INVITED

Should a Biopsy Be Done in Each Patient With a Suspicion of Metastatic Relapse?

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Modern management techniques with a strong focus on adjuvant therapies have markedly reduced the risk of breast cancer recurrence. At the time of clinical or radiological suspected relapse, patients are frequently managed based on the site of relapse, the relapse-free interval, previous adjuvant therapies and the expression in the primary tumour of relevant prognostic and therapy predictive factors.

The percentage and intensity of oestrogen receptor expression together with HER2/neu status, non-amplified or amplified in the primary tumour, frequently serves the basis for management also in the metastatic disease. Previously, mostly small respective studies had revealed a lack of stability and reliable frequency both for ER and HER2/neu. Recently two prospective studies have, essentially, confirmed the presence of lack of stability for these therapy predictive markers in the comparison between the primary tumour and the corresponding relapse. In addition to this, biopsy confirmation will also discover whether the radiological lesion actually represents another primary cancer or metastatic disease from another primary tumour or even a benign lesion. The frequencies are likely to be quite/very low although for the individual patient the management may be dramatically different.
Standard radiological investigation even including CT PET scan evaluating metabolism in a tumour lesion versus the surrounding area will, of course, not be discriminative for different types of malignant lesions.
The lecture will describe an update of prospective and retrospective data on this topic and give pros and cons for biopsy verification of metastatic lesions.

Special Session (Tue, 27 Sep, 11:30−12:30)
Strategies of Prolonged Multimodality Treatment in Advanced Patients

399 INVITED

Intermittent Treatment

Abstract not received

400 INVITED

Strategies of Prolonged Multimodal Treatment on Metastatic Colorectal Carcinoma (mCRC): Maintenance Treatment With Targeted Agents

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CRC is one of the most prevalent cancers that accounts for a great number of research projects (5% of NCI budget on 2010). Common questions like the duration of treatment for metastatic patients still remains a matter of debate. Currently, this population is usually treated with chemotherapy until progression or unacceptable toxicity, in an approach that comes from the firsts studies conducted with 5-FU s/a. Nevertheless, the long-term toxicity resulting from the incorporation of new cytotoxic agents makes almost impossible to follow this strategy. Some clinical trials have been conducted to explore maintenance strategies in mCRC. Targeted agents have been incorporated in the treatment of mCRC and they have shown an improvement of efficacy with mild increase of toxicity in selected patients. The next question with these agents is whether they can contribute to improve maintenance strategies and therefore increase progression-free survival.
Anti-VEGF treatment: CONCEPT and MACRO trials suggest that maintenance treatment with Bevacizumab is feasible, but some questions regarding the correct schedules of treatment administration remain still to be answered. Currently there are 7 trials ongoing exploring different schedules with bevacizumab as part of maintenance therapy in mCRC. Mature results of CAIRO 3 and NCT 00973609 are highly awaited. For the time being, maintenance therapy with bevacizumab may be recommended as a treatment option in selected patients, although questions on cost-efficacy and patient's selection remain still unanswered. Further studies on predictive biomarkers are highly recommended.
Anti-EGFR treatment: Anti-EGFR drugs have shown s/a activity. In this field of treatment we have well-defined predictive biomarkers − KRAS mutation status − and some others that are not fully validated (like BRAF, NRAS, PIK3CA mutation status, PTEN loss, quadruple wild-type signature, and others). Nevertheless, the available studies have not explored the concept of maintenance treatment under the knowledge of predictive biomarkers, and therefore the results of COIN and NORDIC are not useful to answer this approach. Currently, there are at least 3 active clinical trials exploring combinations of chemotherapy with cetuximab or panitumumab to explore the maintenance concept. As an example, the MACRO 2 study is evaluating the feasibility and efficacy of s/a cetuximab in this setting.
Future perspectives: Further improvement in molecular biology knowledge will help to define mechanisms of primary and secondary resistance to conventional cytotoxics and targeted agents and hopefully will translate in the identification and validation of predictive biomarkers that help us to better select the treatment options in mCRC. Theoretically this approach would also help to define which patients would derive benefit from this maintenance approach and the best treatment options.