Special Session (Tue, 22 Sep, 13:30–14:30)
The management of GIST tumours

123 INVITED

Surgery perspective

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Surgery is the standard treatment for primary, resectable gastrointestinal stromal tumor (GIST). However, surgical resection often is not curative, particularly in cases of large GIST. By 5 years after complete removal of their tumor, half of patients so treated have relapsed. The efficacy of imatinib in the treatment of advanced GIST has aroused interest in the therapeutic potential of multimodality approaches to management that combine surgery with systemic therapy. The approval of imatinib as an adjuvant after GIST resection larger than 3 cm in the US and in patients with significant risk of recurrence in Europe makes it necessary to carefully evaluate the following aspects: 1. The data to be derived from intraaoperative findings as tumor rupture or the necessity of performing a multivisceral resection pose the patient at considerable risk for recurrence. 2. Neoadjuvant treatment of locally advanced GIST has been proven to be well tolerable effective in the RTOG-132 study. The german so-called Apollon trial proved that organ-preserving surgery with very low postoperative morbidity is a major outcome effect of pretreatment and improves patient's QOL 3. In patients with primary GIST who are at high risk for postoperative relapse the Z9001 randomized phase 3 trial comparing imatinib and placebo given for 1 year after primary R0 resection showed significantly shorter time to relapse, but details of tumor pathology and mutation data need to influence the decision whom to treat. 4. The more recent data-driven classification by Miettinen and Lasota is going to replace the Consensus (2002) system and clearly depicts groups of patients with real high risk of recurrence and those in whom – irrespective of tumor size – no adjuvant therapy is indicated. A third group with thorough counseling of the patient can also be defined. 5. Long-term results of surgery in patients with response to imatinib show encouraging results and guide the way towards a phase III study with surgical resection of responsive, residual tumor as the interventional arm versus imatinib alone.

124 INVITED

Gastro-intestinal stromal tumors (GIST): the model for solid tumors treated with tyrosine kinase inhibitors

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Gastro-intestinal stromal tumors (GIST) are rare tumors from the digestive tract. Despite their rarity, they are of great importance for oncology by being one of the first tumor entities for which a cancer-cell specific therapy became available. Through advances in molecular biology, it was revealed that GIST is driven by mutations in the *c-KIT* and/or *Platelet-derived growth factor receptor A (PDGFRA)* gene yielding receptors that are constitutively activated. Imatinib is a tyrosine kinase inhibitor (TKI) targeting these receptors and its advent has dramatically improved the outcome of advanced GIST patients. Meanwhile other TKIs exhibiting anti-tumor activity against GIST have been identified. Despite the recent introduction of these compounds for GIST patients, major improvements have already been accomplished concerning insight into the mechanism of action, resistance, and patient management issues. In particular insight into resistance has improved. It appears that there are two types of resistance; primary and secondary resistance, the first referring to mechanisms already present before treatment initiation and the latter acquired during therapy. In both primary and secondary resistance, differences in pharmacokinetics between individuals were recently identified to be involved. However, the most important cause underlying primary resistance is the mutational status of *c-KIT* or *PDGFRA*. This mutational status is of clinical relevance given differences in sensitivity to imatinib between the products from these diverse mutations. As a consequence, the initial dose of imatinib is tailored according to the underlying *c-KIT* mutation. Mutations in *c-KIT* and *PDGFRA* are also the main culprit for secondary resistance. Although several of these novel mutated products can be inhibited by other TKIs, progressive GIST almost always harbors numerous variant mutations differing in sensitivity to TKIs. As a result, it is unlikely that all these different products can be inhibited by a single TKI, while combinations of TKIs are hardly tolerable due to toxicity. Consequently, novel ways to treat GIST progressing under TKIs are needed. All together, lessons learned from GIST are widely applicable to other tumor entities rendering GIST the paradigm of solid tumors treated with TKI. This presentation addresses GIST, in particular its treatment, mechanisms accounting for resistance, and potential future perspectives.

Special Session (Tue, 22 Sep, 13:30–14:30)
Palliative cancer care

125 INVITED

Optimal approaches to persistent and chronic pain: new perspectives on an old problem

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Pain is among the most common and distressing symptoms encountered by patients with advanced cancer. The relief of pain is one of the most important clinical tasks of palliative care. The challenge of this task is to achieve effective relief with minimal side effects and to deliver this service to all patients in need of these interventions. Identification of barriers to implementation of effective strategies, determination of strategies to overcome these obstructions, and the monitoring of outcomes for purposes of quality improvement are important aspects.
Although many factors are contributing to the problem of unrelieved pain, patients reluctance to report pain, misconceptions about tolerance, addiction, physical dependency, concerns about side-effects of pain medication, and concerns about the use of pain medication around the clock prevent patients from reporting pain and taking adequate pain medication are important barriers inhibiting adequate management of pain. As the number of cancer patients is growing, there is an urgent need to develop a home monitoring system that makes data immediately available for review by a multidisciplinary pain or palliative team. Systematic approaches to pain management, by means of "disease management" hold the promise of realizing more of the potential benefit of self-monitoring pain, patient adherence to medication (compliance) pain education and instruction by means of teleguidance, improved self-management, and awareness of clinical alerts.

126 INVITED

Advanced disease: managing the complex journey of cancer recurrence towards end-of-life care

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Although the interface between cancer care and palliative care remains evident, the recent revision of the 1990 WHO definition of palliative care to an approach to care beyond malignant disease (WHO 2002) has led to criticism that palliative care is now less clear in its goals and objectives. Similarly, the development of supportive oncology and the interpretation of the use of *palliative* chemotherapy and radiotherapy for symptom management also creates anomalies for patients and families. It is suggested that the term palliative care does not give clear signals to the patient and family about the transition and future consequences of advanced disease (Illhardt 2000).
In this presentation, the impact of this shft will be reflected in relation to the patient and family experience of transition to palliative care services and how a professional re-interpretation of language can confuse and misinform patients about the reality of thier future. The findings of a study into the the transition experiences of patients with advanced cancer will be used as a template to debate the impact of cancer recurrence and the facing of end-of-life on patients and families. A multidisciplinary "total pain" approach will be advocated in order to enable a positive experience of living well until death to occur. Finally, the psychological impact of understanding the finite life wil be addressed and how cancer care practitioners can shape their practice to support patient's at life's end.

Special Session (Tue, 22 Sep, 13:30–14:30)
Synthetic lethality as a novel strategy of cancer therapy

127 INVITED

Hitting cancer where it hurts most: the RNAi strategy to discover synthetic lethal interactions in cancer

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The search for novel therapeutic agents in cancer relies on the identification and validation of new molecular targets. Ideally, inhibition of such targets would have detrimental effects in tumor cells where normal cells would not be affected. Tumor cells have acquired multiple mutations associated with different properties of malignant transformation. However, gain of these