NRAS oncogenes. Many other molecular abnormalities have been reported in other genes such as PI3K, PTEN, AKT1, MDM2, APC, HER2, KDR, MET, CTNNB1, ATM, BRAF, AKT1 and more recently ALK as well as FGFR1. Of note FGFR1 amplification has been reported in up to 20% of squamous cell carcinoma and 5% of adenocarcinomas.
Beyond the now classical oncogene-drivers represented by EGFR mutation and ALK translocation, many other molecular abnormalities could be used for selection of specific therapies such as amplification of HER2 and FGFR1; or activating mutations of HER2, HER3, HER4, FGFR2, KDR. . . Nevertheless the correlations between the presence of such abnormalities and clinical response are still not firmly documented, although some interesting case reports have been reported. The table below provides a summary of specific alterations, their frequencies and their potential corresponding molecular targeted interventions. DNA repair markers are also potential predictors of standard anti-cancer therapies (ERCC1, MSH2, BRCA1, PARP).

Scientific Symposium (Sun, 25 Sep, 14:45−16:45) **Improved Pain Control Through a Collaborative Approach Between Oncology, Pain and Palliative Care Specialists**

189 INVITED

How to Improve Cancer Pain Control Through European Guidelines for Opioid Treatment and Cancer Pain Diagnosis

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The principle for optimal cancer pain control with primary focus on the use of opioids was published as a second edition by WHO in 1996. The analgesic ladder concept, in which the choice of analgesics is determined by the severity of the pain, is the central idea behind the opioid guidelines. Despite the global impact of the WHO guidelines, 50% of cancer patients with pain are not adequately treated. Barriers to optimal pain control may be linked to 1) insufficient knowledge about the pathophysiology of cancer pain, 2) inferior assessment and classification of cancer pain, 3) sub-optimal treatment, and 4) inadequate implementation of evidence-based knowledge into clinical practice. An updated version of the European Association for Palliative Care (EAPC) guidelines were published in 2001. The guidelines have been criticized for the non-systematic approach in the development, and incomplete review of available literature. Therefore a rigorous evidence-based methodology and a wide international development process was initiated, and in 2011 the Evidence-based Guidelines for the use of Opioid Analgesics in the Treatment of Cancer Pain: the 2011 EAPC Recommendations are emerging. The present version of the EAPC guidelines contain substantial novelties, also in content. One relevant change regards the content of recommendation 2, which modifies the original role of oral morphine as a first step-three opioid. This recommendation values the available evidence from studies with other opioids (hydromorphine and oxycodone), but also acknowledges the lack of evidence supporting the description of first choice for any of these drugs.

190 INVITED

Chemotherapy Including Modern Targeted Therapies to Prevent and to Treat Cancer Pain

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Despite decades of research the evidence that palliative chemotherapy prevents or relives cancer pain is very limited. Although it is widely held that tumour shrinkage is generally associated with relief of pain there is a profound paucity of data concerning the analgesic benefits of cytotoxic chemotherapy and biological therapies. Direct evidence of analgesic benefit is restricted to a very small number of trials mainly in pancreatic cancer and prostate cancer. Bone modifying agents such as bishosphonates and denusumab have, overall, shown only limited analgesic effects and there major benefits have been related to the prevention of painful bone related events. This presentation will review existing data and propose that pain related data be collected in amore systematic manner in clinical trials, particularly among patents with advanced cancers.

191 INVITED

What is the Place for an Effect of Surgery to Prevent And/or to Treat Cancer Pain

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The paradox when considering surgery to prevent/treat cancer pain is of course that surgery itself causes pain. Post-operative pain usually subsides within 1−2 weeks but sometimes can be longlasting which has been emphasized in a review by Perkins and Kehlet. They concluded that long lasting post-operative pain has an incidence of up to 50% or more in studies of breast surgery, thoracotomy, and amputations.
Besides pain, surgery is inevitably connected with other types of morbidity and even mortality. This makes the decision when to make use of surgery indeed challenging. A conscious calculation of pros and cons has to conclude that the advantages dominate. If the realistic goal of care is cure, radical surgery is the main option in many cancer diseases. The meticulous use of skin incisions and tissue friendly dissection techniques that minimizes the risk of nerve injuries are known to decrease the frequency of post-operative neuropathic pain.
In a palliative context performance status, length of survival, chance of effect, risk of complications, time to recovery, and patient's acceptance of the proposed surgical intervention are factors to be included in the decision making process. When estimated survival prognosis is less than a couple of months large surgery is, in principle, contraindicated. Minimal invasive techniques may still be justifiable if the non-surgical treatment alternatives have failed or are likely to have little or no effect.
Stabilizing orthopedic surgery for painful skeletal metastases, stenting, by-passing or venting procedures for mechanical obstructions of bowel, bile or urinary tracts, limb amputation in selected cases of sarcoma or melanoma, neuroablative or neurostimulatory procedures, implantation of neuropharmacologic delivery systems are examples of surgical procedures that can increase pain relief. Meticulous patient selection and timing is of outmost importance to succeed.

192 INVITED

What is the Place and Effect of Radiotherapy and What is the Optimal Schedule for Cancer Pain

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The place for radiotherapy in cancer pain, is any situation where pain can be related to a mass effect or infiltration of a local tumour. The mechanism of pain may be complex and radiotherapy may affect not only the tumour bulk itself, causing extensive cell death but also the release of nociceptive cytokines and nerve conduction. It is therefore active both in visceral, musculoskeletal and neuropathic pain.
Pain relief after radiotherapy is generally good with both high response rates and durable response seen. As an example, metastatic bone pain will respond in 70 to 80% of patients with a durable response for many months often spanning the remaining life expectancy of the patient. Similar response is seen with bone related neuropathic pain, pain from non small cell lung cancer (NSCLC) and from progressive liver metastases.
The optimal schedule for cancer pain in the palliative setting is the lowest amount of radiotherapy which is compatible with effuicacy. As a basic principle if this can be achieved with a single dose of radiation this will be the optimal schedule.
There is good level 1 evidence to support this policy in metastatic bone pain, neuropathic pain, and NSCLC. Short fractionated schedules delivering 5 to 10 treatments may be preferred in some settings, for example in brain metastases, where there may be impending spinal canal compression or pathological fracture from painful bone metastases and in NSCLC patients who have good performance status and limited metastatic disease.
In summary, radiotherapy is the most effective treatment for cancer pain in many settings where the mechanism of pain is due to direct tumour growth with 70% or so of patients having durable response from low dose treatment often requiring a single exposure of radiation.

193 INVITED

A Future Research Agenda to Improve Pain Control Through Collaborative Efforts

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Many of the cancer patients suffer from pain during their illness. Mostly the analgesia follows the WHO ladder approach. For severe pain we use