by end of 2009. www.eurocadet.org For this purpose IARC collected and synthesised country-specific data on important exposures (smoking, alcohol consumption, level of physical exercise, fruit and vegetables and furthermore the level of physical exercise, where possible by SES. Relative risks were assigned based on most recent research, allowing for estimation of potential impact fraction. Furthermore trends in incidence were collected and extrapolated until 2020, so that extrapolations of these trends after this year could be affected up till 2050 by changes in exposure in the next 10–15 years. Literature overviews of effectiveness of interventions and also of barriers, e.g. legal, fiscal etc. They were explored in order to adjust to the realities in the various countries and also to identify best practices. An existing (since 20 years) computer model, PREVENT that includes latency and lag times was refined and made userfriendly, and finally introduced to epidemiologists across the EU in 5 workshops. The presentation will provide examples of prevention impact in the various countries of comparative strategies, e.g. tax increases and/or free provision of anti-smoking tools, menas to increase fruit & vegetable intake, to tackle obesity etc. Results of this project enable professionals in public health, or working in Cancer Societies to become more precise in their proposals for prevention and sketch impact of both desirable and undesirable alternatives.

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270 INVITED

Frontiers of cancer prevention research

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In this presentation, cancer prevention research will be reviewed from two perspectives; and include research that is focused on primary and secondary prevention.
Areas of primary prevention research that will be covered include successful areas (example: smoking cessation), and areas that have received massive attention but, however, with moderate success. The latter will include, among others, chemoprevention attempts (example: chemoprevention against prostate and breast cancer). The presentation will also deal with novel biomarkers (both from serum and genetic material) as predictors of different cancers. Such biomarkers (including serum proteins and genetic variants) may have the potential to be attractive targets for cancer prevention, but their test properties in relation to individual risk have been questioned, and their usefulness needs to be discussed.
The second part of the presentation will cover preventive measures of cancer deaths; mainly by early detection of cancer. This part of the presentation will mainly deal with the present status of early detection programs, such as mammography screening with the aim of preventing deaths from breast cancer, and PSA-based screening aiming to prevent prostate cancer deaths. Among several topics, the paradigm of early detection to prevent cancer deaths will be discussed.

Scientific Symposium (Wed, 23 Sep, 14:45−16:45)
Symptom management: from molecular biology to bedside including pain and cachexia

271 INVITED

Genotyping – does it matter in clinical practice for pain and cachexia?

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One of the main challenges in the clinical management of complex symptoms or syndromes such as cancer associated pain or cachexia is the early identification of specific components that are treatable. Put another way, assessment and classification of patients with such symptoms/syndromes aims to identify phenotypes that may respond optimally to available therapy. It is clear, however, that there may be genotypes that underlie such phenotypes (pharmacogenetics). Moreover, there may be genotypes that predispose patients to the symptoms/syndrome per se and which if identified might allow deployment of prophylactic therapy to specific sub-groups. The latter approach is particularly relevant to cachexia where intervention at an advanced stage of wasting may be futile and may simply increase the burden on the patient.
Cachexia is thought to arise as a result of host-tumour interaction activating the pro-inflammatory cytokine network and the neuro-endocrine stress response. Recent work has identified a single nucleotide polymorphism (SNP) in the IL 10 gene that is associated with the development of weight loss in patients with upper GI cancer. These results raise the possibility of identifying groups of patients in the pre-cachectic phase for early multimodal intervention.
With regard to differences in pain sensitivity and response to opioids, recent research has suggested that in cancer patients genetic variation in the catechol-o-methyltransferase enzyme influences the efficacy of morphine. Equally, the prevalent 118A>G polymorphism in the micro-opioid receptor has been linked with variability in the response to opioids.
Unfortunately, current data are only valid at the group level and cannot be used to predict outcome in individuals. The goal of personalised medicine for cancer pain or cachexia requires further large scale studies and more precise phenotyping to improve the quality of genotype association studies.

273 INVITED

Cancer pain treatment. New approaches based upon the WHO pain ladder

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World Health Organization guidelines have provided an important template for cancer pain management. The majority of poorly-controlled cancer pain on a world-wide basis could be improved by following these guidelines. However, individual management often needs a refinement to optimize analgesia and minimize side-effects. In addition, difficult to control pain such as movement-related pains, spontaneous pain at rest and other types of neuropathic pain, can provide a challenge. Imrpoved pain assessment is key. We are developing an improved understanding of both key clinical questions in the oncology setting and also more objective clinical findings using techniques such as quantitive sensory testing. Optimum use of morphine and alternative opioids remains crucial. The recent availability of fast-acting fentanyl preparations will clearly be of use for some types of breakthrough pain. The newer antidepressants, such as duloxetine, provide the opportunity of both using a drug which can be easily titrated to both an antidepressant dose and an effective neuropathic pain dose with a much improved side-effect profile over the older antidepressants. Understanding the role of topical analgesia, eg lidocaine, capsaicin, is of increasing importance as we learn to combine skilfully systemic and topical preparations acting on different receptor profiles. Assessment and management of interventional analgesia (including domicillary), is an important area. Appropriate use of implantable intrathecal pumps can improve both pain and quality of life substantially. A greater understanding of the peripheral and central mechanisms of pain and integration with other factors has been central to the expansion of the analgesic armamentarium. The mechanisms and management of cancer treatment-related pain has attracted more attention as patients live longer and the treatment armamentarium expands further.
The expanded WHO analgesic ladder and its many applications will be discussed in relation to both cancer and cancer-treatment related pain.

274 INVITED

Treatment of cachexia-a preventive or symptomatic approach?

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Cancer cachexia is a very frequent and burdensome complication of advanced cancer, characterized by increased nutritional intake and appetite, an altered metabolism causing a catabolic drive, associated with neuroendocrine alterations. It is a continuum reaching from pre-cachexia to the full anorexia/cachexia syndrome to late irreversible cachexia. In pre-cachexia typical characteristics are present, but weight loss is not obvious. While in the full syndrome weight loss is >5% in 6 months and <2% in 2 months. Treatment of cachexia encompasses pharmacological, nutritional, behavioral and educational interventions. The therapeutic targets are increase of nutritional intake by cognitive control of eating, improvement of dietary habits, oral supplements or enteral or parenteral nutrition, reversal of the catabolism by antiinflammatory agents and/or effective antineoplastic interventions and they include also improvement of muscle function by physical activity training and development of drugs to reverse muscle proteolysis and increase protein synthesis. As a wealth of data documenting that inflammatory weight loss and/or loss of appetite is associated with decreased response to anti-cancer treatment, increase of toxicity and finally survival.
There is good evidence (grad A) that nutritional continuous counseling, including but not limited to supplements increases survival and treatment tolerability in curative rectum and head and neck cancer situations, also

there is good evidence that in low catabolic situations nutrition can be of beneficial effect.
In advanced cancer patients, early nutrition counseling stabilizing weight before there is a involuntary weight loss can be effective in early phases of cachexia, therefore a preventive approach or an early treatment before severe symptoms approach, seems justified.
However clinical trials for pre-cachexia management are required. Patients who have beginning loss of appetite, early satiety, increasing physical function and beginning weight loss should therefore early receive multi model interventions. For patients having physical fatigue and decreased physical function as main symptomatic concern, its important to estimate the likelihood that the tumor situation the cachexia can be controlled to achieved a stabilization of muscle mass or even increase in muscle function and overall physical function.
For that a staging of cachexia syndrome is necessary including nutritional intake and appetite, early satiety, catabolic drive with inflammation, tumor situation and muscle mass (important in patient where obese or with fluid retention). The alleviation of anorexia alone by appetite stimulant seems justified in rare cases, but appetite stimulation without improving muscle mass and physical function is unlikely to improve quality of life. Likewise short term corticosteroids might be justified for 1 or 2 weeks, however a long term treatment is clearly contraindicated because it worsened cachexia syndrome.
Conclusion: Both preventive treatment of cachexia is justified, namely applied as early interventions of pre-cachexia. In addition advanced cancer patients symptomatic approach is important, especially if the tumor situation and the catabolic drive can be controlled and improved. The symptomatic treatment including education and behavior interventions to relieve cachexia related suffering is an effective palliative cancer care intervention. Further research is needed to develop further multi-model approaches.

Scientific Symposium (Wed, 23 Sep, 14:45−16:45)
Special therapies for special sarcoma subtypes

275 INVITED

Taxanes in angiosarcomas

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Rationale: Angiosarcomas of soft tissue represent a heterogenous group of rare sarcomas with specific clinical behaviour and risk factors. Paclitaxel has been suggested to induce tumor control in a higher proportion of patients with angiosarcoma, as compared to other sarcomas. The objective of this retrospective study was to assess the antitumor activity of this compound in a multicenter setting.
Method: Clinical cases of angiosarcomas of soft tissue treated with single agent paclitaxel were collected from centers of the Soft tissue and Bone sarcoma Group of EORTC, using a standardized data collection form. Paclitaxel could be given every three weeks, or weekly. Statistical analysis was performed using SASS software.
Results: Data from 32 patients were collected from 10 centers. There were 17 males, 15 females, with a median age of 60.4 years (range 25−91). Primary angiosarcomas were located in scalp and face in 8 patients (25%) and at other primary sites in 24 patients (75%) All patients had intermediate (n = 13) or high grade (n = 19) primary tumors. 13 (40%) patients had been pretreated with doxorubicin based first-line-chemotherapy and three of them (9%) also with 2nd-line chemotherapy with ifosfamide. 11 (34%) patients had been irradiated before as treatment for angiosarcoma. In 8 (25%) patients the angiosarcoma occurred at sites of prior radiation therapy for other malignancies. The response rate was 62% (21/32) in the whole series, 75% (6/8) in scalp angios, and 58% (14/24) in tumors from other primary sites. The median time to progression was 7.6 months (1−42) for the whole group. For the face/scalp group it was 9.5 months, and for patients with angiosarcomas at other sides 7.0 months respectively.
Conclusion: Paclitaxel was found to be an active agent in angiosarcoma of soft tissue in this retrospective study. These results need to be confirmed in a prospective randomized phase II study.

276 INVITED

Aromatase-inhibitors in gynaecological sarcomas

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Introduction: Endometrial sarcomas are uncommon malignancies, comprising less than 1% of all gynecological cancers and around 5% of uterine cancers.
Stage is the most significant predictor of outcome: survival is 60−70% after surgery when the tumor is confined to the uterus, being pelvis, upper abdomen and lungs major sites of failure.
Histological classification of endometrial sarcomas includes two categories: pure sarcomas (leiomiosarcomas, mullerian and endometrial stromal sarcomas) and mixed sarcomas (carcinosarcomas and adenosarcomas). Recurrence rates are higher for mixed (63%) than for pure (44%) endometrial sarcomas.
Precise role of adjuvant treatment remains unclear being median survival with advanced or recurrent disease less than one year. The role of radiation therapy is controversial without prospective randomized trials and prognostic imbalances between irradiated and non irradiated patients in most retrospective series.
Systemic treatment: According to phase II trials efficacy of chemotherapy in uterine sarcomas is moderate with response rate of 25% for doxorubicin (leiomiosarcomas) and less than 20% for cisplatin or paclitaxel (carcinosarcomas).
Endometrial stromal sarcoma (ESS) constitutes about 0.2% of all genital tract malignancies. ESS usually expresses steroidal receptors and is regarded to be hormones-sensitive. Most women with ESS undergo bilateral salpingo-oophorectomy as part of its primary treatment but estrogen can also be produced by extra-ovarian via. This extra-ovarian production of estrogen depends on conversion of circulating androgens to estrogens via the aromatase enzyme pathway. The efficacy of aromatase-inhibitors is probably due to the reduction of estrogen levels by inhibiting estrogen synthesis not only in peripheral sites but also in the tumor cells themselves.
Due to the rarity of this tumor type only some cases series and no prospective studies are published, with multiple case reports of efficacy of aromatase inhibition, specially in low-grade ESS.
Conclusion: Aromatase-inhibitors are active in the treatment of some gynecological sarcomas, specially low-grade ESS. Despite of the rarity of these tumor types, rare tumours study groups such us Rare Tumors Working Group within Gynecological Cancer Intergroup (GCIG) should make an effort to prospectively define the utility of these treatments.

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