

in neurooncology (RANO) have been introduced which are based on these MR-sequences, clinical findings and the steroid medication. These criteria include newly recognized phenomena as pseudoprogression (i.e. spontaneous stabilization or regression of new contrast enhancement within 3 months after completion of radio-chemotherapy) and pseudoregression (i.e. regression of contrast enhancing tumour with concomitant progression of non-enhancing tumour on T2-w sequences). To overcome the limitation of the pathophysiologically unspecific finding on conventional MR-sequences new functional and metabolic MR-techniques have been introduced in clinical practice. This talk will briefly summarize classical MR-response criteria and will give an overview on the opportunities and current limitations of new MR-techniques.

163

INVITED

Endpoints for Phase II Trials

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Phase II trials are screening studies with a primary goal of efficiently and accurately identifying a signal of antitumour activity of promising agents that justify subsequent phase III testing. One of the major barriers in achieving this goal is the lack of good surrogates of true patient benefit, classically defined in oncology as improvement in overall survival. Overall survival can have limited utility in phase II studies because of the time required to reach this endpoint, the confounding effects of cross over or effective second line therapies.

Endpoints in phase II studies that accurately predict phase III success are needed. Historically for cytotoxic agents, tumour shrinkage and objective response rates (RR) have been used, however, novel cytostatic agents that may result in prolongation of progression free survival and overall survival with very modest RR challenge the use of objective response as an indicator of patient benefit for this class of drug. The utility of RR is further complicated in the field of neuro-oncology, where imaging changes on standard anatomic magnetic resonance imaging can be confounded by treatment. This is evident in the case of pseudoprogression (increased enhancement related to treatment effect and not tumour progression) and pseudoresponse (decreased enhancement related to reconstitution of the blood brain barrier by anti vascular endothelial growth factor receptor inhibitors and not antitumour effect).

In this presentation we will review the advantages and limitations of commonly used endpoints in efficacy evaluation of agents in phase II testing and discuss alternate endpoints. The selection of the appropriate endpoint depends on the patient population, the nature of the agent being tested and the phase II trial design. Continued research to validate alternate phase II endpoints is critical.

164

INVITED

Endpoints for Phase III Trials

M. van den Bent¹. ¹Erasmus University Medical Center, Neuro-Oncology, Rotterdam, The Netherlands

Clinical trials on novel treatments are aiming to establish the potential benefit of the new treatment. The trial must be designed to demonstrate the clinical benefit of the novel treatment, and the trial endpoints chosen should reflect that clinical benefit in a reliable way. The requirement 'reliable' implies that the endpoint can be unequivocally assessed, and can be safely assumed to reflect therapeutic efficacy of the investigational treatment. Overall Survival (OS) is generally agreed upon to reflect a clinically meaningful benefit for the patient and is easy to assess. There are however several drawbacks of this endpoint. First, cross over treatments (once the investigational compound is readily available) and effective cross in salvage treatments given at the time of progression after initial study treatment may dilute or even eradicate OS benefits. Then, OS will require a trial of longer duration and thus with higher costs. Numerous trials have used Progression Free Survival (PFS) as the primary endpoint, which endpoint is not confounded by subsequent salvage treatments. However, assessment of this endpoint is confounded by the way it is assessed and potentially by the knowledge of the given treatment. And, if the PFS endpoint is a mere radiological endpoint without clinical correlates, it becomes a pure radiological phenomenon without clinical consequences. Although it is often assumed that clinical deterioration occurs at the time of progression that deterioration has to be demonstrated in the trial to show the clinical impact of progression. Also, if an increase in PFS comes at the price of reduced quality of life because of toxicities, such increase becomes a questionable benefit. In some diseases a good correlation exists between PFS and OS, but that is not necessarily the case. Lastly, PFS depends on the ability to assess progression in a standardized fashion. In the field of neuro-oncology, pseudo-progression and pseudo-response may interfere

with the reliability of the progression assessment. Because these pseudo-phenomena are treatment related (radiotherapy, VEGF inhibitors), this implies that endpoints must also be tailored to the investigational treatment. In particular if radiological PFS endpoints are used, blinded review is required to evaluate the local diagnosis – which will not save a trial in case of systematic local biases. Clinical functioning scales are necessary to support the benefit observed in PFS or OS. Domains chosen for these co-endpoints must reflect clinically accepted areas of relevant morbidity for the disease under consideration (e.g., cognition, seizure activity). As a consequence of all this, there is no one size fits all solution for neuro-oncological phase III trials, but only tailor made solutions.

Special Session (Sun, 25 Sep, 13:15–14:15) Calories and Cancer

165

INVITED

Body Mass Index and Cancer Incidence

A.G. Renehan¹. ¹University of Manchester, Department of Surgery, Manchester, United Kingdom

By 2008, we [1] and others had established that excess body mass index (BMI), as an approximation of general body adiposity and excess calorie intake, is associated with increased risk of several cancer types. These associations exist for both common (for example, colon, endometrial, post-menopausal breast, oesophageal adenocarcinoma) and less common malignancies (for example, thyroid carcinoma, non-Hodgkin lymphoma). Given the plausibility of the biological explanations, the consistency of associations, the sufficiently long latency times between BMI measurement and cancer occurrence, and the recent demonstrations of risk reversibility in morbidly obese cohorts undergoing bariatric surgery, many of these associations are probably causal. Approximately 124,000 new cancer cases may be attributable to excess BMI in Europe (2008). Since 2008, it has become clear that associations between BMI and cancer risk may be modified in the presence of other risk factors. For example, in users of hormonal replacement therapy, the associations between BMI and endometrial and post-menopausal breast cancers are attenuated. In turn, these observations point to a strong influence of oestrogen as an intermediary between obesity and cancer development in these cancer groups. Additionally, it is increasingly clear that approximations of central adiposity, for instance, waist circumference (WC), may better describe associations between adiposity and increased cancer risk, for example, in colon and rectal cancer, thus suggesting a key role for insulin resistance in these cancer types. Better understanding of these associations will facilitate refinements of approaches to prevent obesity-related cancers.

References

[1] Renehan et al. *Lancet* 2008;371(9612):569–78

166

INVITED

Starvation and Differential Stress Resistance in Cancer Treatment

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Short-term starvation (STS or fasting) provides protection to normal cells, mice, and possibly patients from a variety of chemotherapy drugs, but the possibility that it may also protect tumour cells renders its translational potential uncertain. Here we investigate the effect of fasting cycles on tumour progression independently of and in combination with toxic chemotherapy drugs, with focus on melanoma, glioma, breast cancer, and neuroblastoma *in vivo* models. We also present data on the effect of starvation on a wide variety of cancer cell lines and investigate its effect on a breast cancer cell line at the molecular level. Our studies suggest that multiple fasting cycles have the potential to protect the host against toxic chemotherapy drugs while enhancing the efficacy of the treatment.

167

INVITED

Energy Balance Including Physical Activity Influence Breast and Colon Carcinogenesis – Results From Recent Studies

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There is a growing concern among scientists and recently also oncologists around the observation that the epidemic increase in unfavorable energy balance: excess body weight and physical inactivity are associated with biological mechanisms that may favor certain types of cancer development. Determine the biological mechanisms by which these lifestyle patterns

influence colon and/or breast cancer risk and development will inform us not only about biological plausibility for the observed association, but also provide evidence for causality, and be important for practical guidelines both in prevention and importantly also for patients. Proposed biomarkers for the associations between energy imbalance and colon and breast cancer are i.e. genetic susceptibility, steroid hormones, hyperinsulinemia, insulin resistance, leptin, increased inflammation: i.e. C-reactive protein, depressed immune function, oxidative stress and DNA repair. Results from recent observational studies and cancer prevention intervention trials will be focused. Finally, some results from those few randomized controlled trials including physical activity among breast and colon cancer patients will be presented.

Special Session (Sun, 25 Sep, 13:15–14:15) Tips and Tricks to be the Best

168

INVITED

Middle Face Microvascular Reconstructions Based on Cordeiro Classification

A. Maciejewski¹, C. Szymczyk¹, M. Grajek¹, L. Krakowczyk¹, P. Jedrzejewski¹, J. Wierzon¹, R. Szumniak¹, M. Dobrut¹, R. Ulczok¹, S. Poltorak¹. ¹M. Skłodowska-Curie Memorial Institute, Department of Oncologic and Reconstructive Surgery, Gliwice, Poland

Middle face reconstructions are usually very difficult. In the reconstruction of this area we can use both artificial materials and autologous tissue, or a combination of these two. In most of the cases a free tissue transfer is used for the coverage. Each defect in this area is unique, and each must be treated individually, but thanks to Cordeiro classification we can apply a protocol of useful microvascular techniques which will provide optimal postoperative outcome in given defect's type. This presentation describes microvascular techniques in a reconstruction of middle face defects' (Type I-IV). A quality of life evaluation based on own modification of University of Washington QOL form is also described. The most important conclusion? – Proper preoperative planning and free flap(s) choice are crucial to obtain satisfactory aesthetic and functional outcome.

169

INVITED

Tips and Tricks How to be the Best – Clinical Oncologist

S. Sleijfer¹. ¹Erasmus University Medical Center, Department of Medical Oncology, Rotterdam, The Netherlands

There are several aspects in Medical Oncology in which physicians can be successful: patient care, teaching, and research. With respect to research, several parameters can be used to measure someone's success such as number of publications, impact factor of journals in which manuscripts are published, number of citations, oral presentations, grants awarded, appointments and several others.

As holds true for every aspect of life, success in research is a combination of own capacities and opportunities from which several can be influenced, but others not. Furthermore, opportunities to become successful in research will differ per country, institute and department.

In this presentation, a personal view on how to be successful in cancer research as a clinical oncologist will be given.

170

INVITED

Radiation Oncologist

D. Zips¹. ¹TU Dresden, Radiation Oncology UK Carl Gustav Carus, Dresden, Germany

To successfully perform clinical work, research and teaching is often a challenging task. Working as a clinician scientist and university lecturer I will report my experiences and techniques to cope with this challenge. A personal view on for example how to combine experimental research with clinical duties, the impact of mentors and the use of having a fellowship abroad will be discussed.

Special Session (Sun, 25 Sep, 13:15–14:15) The European Network for Cancer Research in Children and Adolescents (ENCCA) FP7 Project

171

INVITED

The European Network for Cancer Research in Children and Adolescents(ENCCA) FP7 Project

R. Ladenstein¹, G. Vassal², K. Pritchard-Jones³, M. Schrappe⁴.

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ENCCA is a 'Network of Excellence', funded by the European Union's FP7 Programme under the health topic 'Structuring clinical research in paediatric and adolescent oncology in Europe'. The ENCCA consortium is composed of 33 partners from across Europe, including research institutes and organisations recognised as being at the forefront of excellence in paediatric oncology.

The objective is to reduce knowledge fragmentation and enhance their communication, collaboration and management in an effort to advance clinical research in Europe. ENCCA will restructure knowledge-sharing through the integration of the whole chain of stakeholders from the European paediatric oncology community bringing together their expertise and viewpoints to ensure that ENCCA is all-encompassing but remaining patient-centred. Ultimately ENCCA aims to create a sustainable 'European Virtual Institute' to serve as future platform for clinical and translational research in childhood and adolescent cancers in Europe.

The ENCCA consortium is dedicated to

1. Promoting innovative methodologies and designs for clinical trials
2. Harmonising therapeutic strategies by enabling better access to innovative therapies, knowledge and technology in the field of paediatric tumour biology
3. Improving substantially the quality of life of children and adolescents with cancer with a particular emphasis on long term treatments side effects
4. Proposing common ethical definitions, monitor ethical issues present in the implementation of the European clinical research agenda
5. Providing a comprehensive education and training programme, enhancing research mobility, sustainable clinical trial design, training coordination and information to benefit patients' families.

To achieve the ultimate goal of becoming the 'stepping stone' towards an interactive and sustainable European Institute, the ENCCA network will deliver over the next 4 years 18 work packages with a total of 80 milestones and 82 deliverables, streamlined through 3 main channels of activities embracing all tumours groups: Integrated Activities, Joint Research Activities and Spread of Excellence.

The ENCCA consortium envisions a dynamic and open network that can benefit the entire paediatric oncology community in Europe to overcome also current major hurdles like difficulties to run investigator driven clinical trials within the 2004 clinical trial directive and the extremely poor access to new drugs despite the 2007 Paediatric Medicine Regulation.

172

INVITED

'Spread of Excellence' (Dissemination) Activities of the European Network of Excellence for Cancer Research in Children and Adolescents (ENCCA)

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Good communication, sharing of knowledge and international coordination of research into paediatric cancer underpins continued advances in this field which are sorely needed. Cancer in children remains a significant public health issue as some 15,000 new cases are diagnosed every year in Europe. Although 80% of cases are cured by multidisciplinary treatments, still 3,000 cases will not survive. The ENCCA network aims to improve the current situation by reducing as far as possible the existing hurdles and pitfalls in paediatric oncology. ENCCA's ultimate goal is to build a sustainable virtual European institute to serve cancer research in children and adolescents for the next decades, including coordinating training opportunities for clinical and non-clinical researchers to significantly improve cure rates and quality of cure for patients.

The 'Spread of Excellence' work packages include disseminating the work of ENCCA to patients, parents, academic researchers and industry to improve partnerships and knowledge of opportunities for participation in clinical trials, research training and collaboration. A specific work