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117 INVITED

Treatment options for glioblastoma failing standard first-line treatment

W. Wick. *University of Heidelberg, Neurooncology, Heidelberg, Germany*

Primary treatment with radiotherapy and concomitant and adjuvant temozolomide has resulted in a progression-free survival (PFS) of 7.2 months in the experimental arms of EORTC 26981/NCIC CE3 newly diagnosed glioblastoma. Salvage therapies in this study added another 7.4 months. This observation highlights the importance of second-line treatment to improve overall survival and illustrate that current treatment concepts can be improved. Interestingly, patients who were stable for a longer time after primary temozolomide treatment may have another prolonged stabilization on second-line TMZ therapy. Moreover, evidence from one-armed trials suggests that TMZ at dose-dense regimens may be more efficacious than conventional dosing schedules. At recurrence, a reoperation should generally be considered. Further a second radiotherapy, in circumscribed tumors or out-of-field recurrences or at a longer interval from primary treatment (>12 months) should be evaluated. Chemotherapy has a defined role at recurrence. In addition to the intensified temozolomide protocols that might be effective not only after completion of standard treatment but also in pateinst that progress under standard temozolomide nitrosourea-containing protocols should be considered. Interstitial treatment with BCNU (Gliadel) exhibited only marginal efficacy in a randomized study and is therefore not considered outside clinical studies. Outside clinical studies the combination of imatinib-mesylate (Gleevec) and hydroxyurea is used. Results of the direct comparison to hydroxyurea alone are expected. The randomized immunotoxine studies have been negative (IL-13/Precise) or prematurely terminated (Transmid). The same applies for a randomized trial comparing the antiangiogenic compound Enzastaurin and CCNU. Generally, prospective studies analyzing the inhibition of migration, invasion and angiogenesis are lacking. Therefore, substances such as Enzastaurin, Cilengitide and Avastin should be analyzed within clinical studies. The latter has exerted interest because of an unusual high response rate of 61% in a unicenter study in combination with irinotecan. An EORTC study comparing CCNU and CCNU plus Avastin is currently under preparation. There are no new results on somatic gene therapy from randomized studies. Novel approaches include pathway inhibitors tackling the EGF receptor signalling (nimotuzumab), PI3-Kinase or mTOR (Temsirolimus).

Award lecture (Tue, 25 Sep, 17:00−17:45)
FECS Clinical Research Award Lecture

118 FECS Award

The pivotal role of the surgical oncologist in the improvement of cancer outcome

C. van de Velde. *Leiden University Medical Centre, Afdeling Chirurgie, Leiden, The Netherlands*

Translational cancer research holds the promise to realize a paradigm shift in medical technology and its therapeutic applications and effects. Biomarkers can lead to better stratification of the patient and the tumor with respect to e.g. metastatic behaviour leading to personalized treatments: the extent of surgical resection and the use of additional treatments. These approaches will lead to more effective treatments and therefore more cures of our future patients. Surgeons play an important role in tumor/serum banking to make this translation possible. The multidisciplinary approach mandates the Commitment, Competence and Continuity of the surgical oncologist but unlike the other team members the amount of skills can make a major difference for the individual patient. Recent developments in Quality Assurance both in clinical trials as well of by auditing processes have made improvements that have a greater impact on survival than that of any of the adjuvant therapies currently under study. Several examples in gastric, colorectal and breast cancer will be given showing the immediate advantage for the patient being part of such a programme. Quality improvement not only translates into better loco-regional control but also in close cooperation with the diagnostic modalities (radiology/pathology) improves organ preservation and quality of life. Further and direct measurable improvements can be made by (inter)national outcome-based quality improvements: one of the coordinating tasks of the European Society of Surgical Oncology. Improvements should be made in analyses identifying best practices and broad implementation of these. Technological innovations are rapidly integrated leading to a continuous adaptation of these. Our future surgical oncologists will be leaders in multidisciplinary care and certainly not any more the ones who will treat first but have a duty in quality control and assurance.

Wednesday, 26 September 2007

Special session (Wed, 26 Sep, 09:00−11:00)
The European Association for Cancer Research (EACR)

119 EACR award

DNA replication repair: molecular insights towards new approaches to targeted anti-cancer therapy

T. Helleday. *University of Oxford, Radiation oncology and biologyPRI Churchill Hospital Headington, Oxford, United Kingdom*

Background: Recent studies suggest the existence of tumorigenesis barriers that slow or inhibit the progression of preneoplastic lesions to neoplasia. It will be presented in this seminar how oncogenes are responsible for induction of the DNA damage checkpoint pathway leading to apoptosis, cell cycle arrest as well as oncogene-induced senescence.
Results: We show that overexpression of the oncogene cyclin E is associated with signs of DNA replication stress, such as reduced replication elongation and prematurely terminated DNA replication forks that are associated with DNA double strand breaks (DSBs). The replication lesions caused by oncogenes are tumour specific and indicate that an increase in DNA damage is associated with tumour development. Oncogene-induced DNA replication lesions are also similar to those produced during radiation- or chemotherapy to kill tumour cells. A new concept for cancer therapy is to amplify endogenous DNA single-strand breaks, to specifically kill tumour cells. This can be achieved following inhibition of Poly(ADP-ribose) polymerase (PARP). Here, we provide an example how endogenous tumour lesions may be amplified to kill tumour cells; this idea has been put into practice for cells that are mutated in the breast cancer susceptibility genes BRCA1 or BRCA2, encoding proteins involved in homologous recombination repair. Heterozygous carriers of a mutation in one of these have a considerably increased risk of breast or ovarian cancers that arise from cells that have lost the wild type copy. The loss of homologous recombination accelerates genetic instability, which likely drives the cancer development. We show that homologous recombination defective cell lines are sensitive to a PARP inhibitor, in particular those homozygous for the BRCA2 mutation. These cells were 100–1000 fold more sensitive to PARP inhibitors than the heterozygote or the wild-type cell lines and regression of tumours derived from BRCA2 mutated cells was observed.
Conclusions: The use of an inhibitor of a DNA repair enzyme alone, to enhance oncogene-induced DNA lesions to selectively kill a tumour represents a new concept in cancer treatment. In this lecture, novel anti cancer treatments using the same concept will also be presented.

120 INVITED

Should the coordination of the European cancer research and care be built on national programmes?

C. Lombardo. *Belgium*

Abstract not received.

121 INVITED

Network analysis of cellular signalling

F.M. White[1], P. Huang[1], W.K. Cavenee[2], F.B. Furnari[2]. *[1]MIT, Biological Engineering, Cambridge, USA; [2]Ludwig Institute for Cancer Research UCSD, Medicine and Cancer Center, La Jolla, USA*

Background: EGFRvIII is a truncated mutant of the epidermal growth factor receptor (EGFR) which is implicated in the progression of glioblastoma multiforme. While much work has been done to elucidate the pathways initiated by EGFRvIII, the global map of its signaling network