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If so, contact Patricia McDonnell at Oncology News on T/F: +44 (0)288 289 7023, E: patricia@oncologynews.biz

European Neuro-Oncology Society Annual Conference

Date: 9-12 October 2014. Venue: Turin, Italy. Report by: Dr Helen L Fillmore, Dr Zaynah Maherally, Dr Rhiannon Lloyd, Dr John McGeehan, University of Portsmouth, UK.

The 11th Meeting of the European Association of Neuro-Oncology (EANO), 2014 was held in Turin, Italy. The meeting, which targeted neuro-oncologists, medical oncologists, neurosurgeons, neuroradiologists, neuropathologists, epidemiologists, basic and translational scientists as well as nurses, aimed to provide valuable knowledge on current studies being undertaken in areas such as cell biology and signalling, immunology and immunotherapy, in vivo and in vitro models, molecular markers and brain metastases as well as paediatrics, brain and spinal cord tumours. Special attention was also given to advances in surgery and radiotherapy. Specific sessions for neuro-oncology nurse specialists were also incorporated.

The meeting provided insightful presentations on managing the impact of brain tumour treatments on quality of life aspects. In particular, participants were brought up-to-date on the best use of new clinical studies for central nervous system tumours for improved patient outcomes and symptom management, including the latest initiatives to improve the quality of life of brain tumour patients.

The main scientific meeting was preceded by an Educational Day with parallel sessions incorporating a clinical programme on cerebral metastasis and a workshop on entitled 'Laboratory-Based Science'. These engaging sessions were supported by a comprehensive book of supporting literature for the delegates. In the Laboratory science workshop, the first of three sessions focused primarily on the collection and translation of high-quality, high-throughput, molecular data. A review on the utilisation of the very latest next generation sequencing technologies brought us usefully up-to-date in their applications expertly followed by a talk on the use of animal and 3D human in vitro models for testing new therapies. Later presentations included challenges in drug delivery across the Blood Brain Barrier (BBB) due to the complexities inherent in brain tumours and recent progress in immunotherapy. The final talks provided three perspectives on the role of cellular metabolism in neuro-oncology, focusing on the role of mitochondria and the key metabolic pathways that are intricately linked to major cancer pathways. Elegant talks covering aspects such as the 3D-protein architecture of the oxidative phosphorylation system, glutamate-glutamine cycle and hypoxia in brain tumours were given. Ongoing research in these areas could provide new targets for the development of new prognostic indicators, as well as mitochondrially-mediated chemotherapeutic approaches in the future. The concurrent nurse session addressed challenging talks highlighting quality of life of patients, privacy-solidarity conflict between doctors and patients as well as supportive and rehabilitation interventions between glioma patients and their relatives.

The main scientific meeting was built on the traditional EANO format presenting top-scoring abstracts, plenary sessions, keynote

speakers and early morning 'meet the expert' sessions. The concurrent opening sessions highlighted topics in central nervous system metastases and meningiomas, new developments in radiotherapy as well as neurotoxicity and neuroprotection. Presentation of selected oral abstracts was followed by keynote lectures then plenary sessions and evening poster viewing and networking sessions.

Two sessions for poster viewings were also allocated in the evening during the main meeting session where networking, sharing of scientific knowledge/ideas and interactive discussion regarding the so-varied yet so intense areas of research was highly valued.

On Friday afternoon, there were two plenary sessions addressing very important topics in neuro-oncology. The session on angiogenesis and issues relating to bevacizumab failure and mechanisms that brain tumours use to escape this specific treatment. In the other session, the topic was advances in brain metastasis and the first talk was given by F Winkler from Heidelberg. In his very impressive talk, he discussed dormancy, brain seeking cells, pre-existing subpopulations, brain colonisation and the perivascular niche in addition to covering specific molecules and signalling pathways involved.

In addition to several immunotherapy talks and posters, there was a plenary session on Novel avenues in immunotherapy for glioblastomas. M Gilbert from Houston gave a great talk on immunotherapy and the excitement from recent studies in melanoma patients using the immune checkpoint inhibitors, Ipilimumab and Nivolumab, to stimulate an immune response. He reviewed several immune checkpoint inhibitors being tested. He also discussed the need for immune monitoring and the absolute need to determine if there is a peripheral response. If there is not, there is probably not going to be a CNS response. There are still toxicities associated with immunotherapy and this needs to be kept in mind. He also warned of pseudo regression that can be seen in imaging following agents that target the immune system and the need for biomarkers. Lastly, Gilbert discussed other ways and potential targets to modulate the immune system. M Weller from Zurich presented work on EGFRvIII as an immunotarget in GBM and how this may be a good target that overlaps the tumour heterogeneity that we see in these tumours.

K Aldape gave a wonderful keynote talk on Saturday afternoon where he discussed recent work on integrating molecular genetics with histological classification of low grade gliomas and other CNS tumours for the next WHO classification. He discussed work using

unsupervised cluster of cluster analysis of molecular genetic studies and how these results relate to histology. He presented a layered model in which the molecular information is beneath the WHO grade which is based on the histology with the top layer being where the information is integrated.

On the last morning of the meeting there was an EANO-SNO session that was both enlightening and encouraging. Dr R Stupp began the session discussing lessons learned from the integrin inhibition trials (cilengitide). He discussed his views on clinical development plans. He also gave examples of how we can learn from successful failures that include successful recruitment and compliance whereas in unsuccessful failures, little information has been gleamed. Early proof of failure may also be useful in early development. The importance of statistical analysis and the greater importance on reporting the statistics were highlighted. Partnerships are key in clinical development plan and include hospitals, university scientists, commercial companies, and with expert protocol writers. The need for useful biomarkers was also mentioned. More is not necessarily better and we should consider 'moving away from yesterday'.

The second morning speaker was Dr S Chang who spoke on behalf of the Response Assessment in Neuro-oncology (RANO) group. RANO is an open working group comprised of international and multidisciplinary teams of clinicians and scientists that was formed to develop standardised methods and guidelines for assessing response to therapy in high grade gliomas. The group arose in order to gain consensus for multicentre trials and resulted in the establishment of specific criteria replacing the "Macdonald criteria". While this group have made impressive advances in specific CNS tumours, they continue to tackle all types of therapies and CNS tumours. Dr Chang brought us up to date on the groups' incredible work and advances and stressed the importance of including anyone interested in joining this group. This was an inspiring talk in that the members of this group do this on top of their 'day' job without financial compensation and that this international group works together in a joint effort to help move the treatment of brain cancer forward. This as well as the talk given by Dr Stupp was very impressive. The last scientific session was on clinical studies of malignant glioma.

A recurring theme throughout the meeting was genetic heterogeneity, with talks and posters highlighting the mitochondrial mutational landscape, different genomic subgroups within the same tumour and the nuclear genetic diversity of single cells. Understanding this heterogeneity better will be key in developing more effective treatments. The meeting was adjourned following key lecture entitled 'where is radiation oncology moving?' and announcement of the EANO Prize winners.

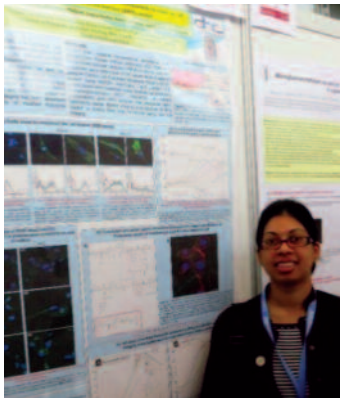
Key take home points included: Tumour heterogeneity within same tumour, advances made in immunology – therapy and basic science, advances in RANO, lessons from clinical trials and the limitations of historical controls, how much is still to be done in terms of learning about angiogenesis.

EANO Prize Winners:

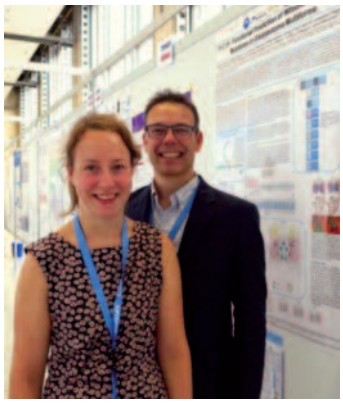
Poster Award for Basic Science: Julia Biedermann; Dresden, Germany.

Poster Award for Clinical Science: Daniel L.P. Holyoake; Cambridge, United Kingdom.

Vienna Medical Academy-Award: Simone P. Niclou; Centre de Recherche Public de la Sante, Luxembourg.



Dr Zaynah Maherally, Research Associate, Brain Tumour Research Centre, University of Portsmouth, UK.



Drs Rhiannon Lloyd, Research Fellow, Brain Tumour Research Centre (left) and John McGeehan, Reader in Structural Biology (right), Institute of Biomedical and Biomolecular Science, University of Portsmouth, UK.

Dr Helen L. Fillmore Principal Research Fellow, Brain Tumour Research Centre, University of Portsmouth.

A newcomer's view by Dr John McGeehan

"I was privileged to be asked to speak at EANO 2014 as part of the Educational Day Workshop, although the thought of presenting structural biology to a room full of senior neuro-oncologists was rather daunting at first. I was pleasantly surprised that our work combining mitochondrial genetic studies on GBM with my own speciality, protein X-ray crystallography, provided a platform for hugely productive discussions throughout the course of the meeting. Engagement with neurosurgeons and clinicians really opened my eyes to the huge challenges in this field and I gained a deeper understanding of the complexities of these diseases. I became convinced that the bringing together of multiple diverse techniques is really a powerful way forward. I am pleased to report that as a result of open discussions over coffee, and in some cases over fine Italian wine, our group left the meeting with a succession of new contacts and several exciting collaborative opportunities. I would like to thank the organisers for providing such a conducive atmosphere and the delegates for their enthusiasm and friendliness."

European Society of Medical Oncology

Date: 26-30 September 2014; Madrid, Spain. Report by: Janet Fricker, Medical Journalist.

ESMO reports practice changing studies in melanoma

Notable melanoma research presented at ESMO included studies demonstrating that inhibiting two pathways was better than one, the first ever phase 3 trial of a PD1 inhibitor, and abstracts exploring two different approaches in cutaneous melanoma for inducing local and systemic immune responses.

Commenting on the phase 3 COMBI-v and CoBRIM studies Reinhard Dummer, ESMO faculty coordinator for melanoma, said, "While monotherapy with a BRAF inhibitor is currently considered as a standard of care for patients with BRAF-mutated advanced melanoma, the data from these two trials provide convincing evidence that combination therapy with either dabrafenib and trametinib or vemurafenib and cobimetinib will be the standard systemic therapy for this patient population." The rationale for combination therapy is that tumours develop resistance to BRAF inhibitors via the MAPK pathway which can be blocked by a MEK inhibitor.

In the CoBRIM study, presented by Grant McArthur from the Peter MacCallum Cancer Centre, Melbourne, 495 patients were randomized 1:1 to vemurafenib plus the MEK inhibitor cobimetinib (n=254) or vemurafenib alone (n=239). Results show patients in the combination arm achieved a median progression free survival of 9.9 months compared to 6.2 months with monotherapy (HR=0.51, 95% CI, 0.39 to 0.68 P<.0001). The frequency of complete and partial responses was 68% for the combination arm versus 45 % for vemurafenib (P<0.0001), and the interim overall survival analysis showed a 35% reduction in risk of death favouring combination treatment (HR=.65; P<.05). Notably, combination therapy reduced cutaneous squamous cell carcinoma from 11% to 3%, and of keratoacanthoma from 8% to 1%.

In the COMBI-v trial, presented by Caroline Robert from the Institut Gustave-Roussy, Paris, 704 patients with advanced BRAF-positive melanoma were randomized to the BRAF inhibitor dabrafenib plus the MEK inhibitor trametinib (n=352) or vemurafenib monotherapy (n=352). In the interim analysis, which became the primary analysis when the trial was stopped for efficacy, median overall survival was 17.2 months with vemurafenib alone and had not been reached for combination treatment (HR 0.69, 95% CI 0.53-0.89 p=.005). The median progression free survival was 11.4 months for the combination therapy versus 7.3 months for monotherapy (HR 0.56, 95% CI 0.46-0.69, P<0.001). Cutaneous malignancies occurred in 1% of patients taking combination treatment arm versus 18% on monotherapy.

In advanced melanoma patients who have limited options after progressing on approved agents ipilimumab and BRAF inhibitors, nivolumab produced 'impressive' durations of response. Nivolumab is a PD-1 immune checkpoint inhibitor that works by preventing the programmed cell death ligand from binding to its receptor, thereby stimulating the immune system.

In the phase 3 open-label trial ,405 patients with advanced melanoma who progressed on or after anti-CTLA-4 therapy and a BRAF inhibitor (for BRAF V600 mutation positive disease) were randomized 2:1 to receive nivolumab (n=268) or investigators' choice chemotherapy (ICC), either dacarbazine or carboplatin plus paclitaxel.

Results showed the objective response rate was 32% for nivolumab compared with 11% for chemotherapy, and the median duration of response was 3.6 months in the chemotherapy arm and had not been reached in the nivolumab arm. Treatment with the PD1 inhibitor was associated with a lower frequency of adverse events compared to ICC, with discontinuation due to drug side effects occurring in 2.2% of nivolumab patients versus 8% of chemotherapy patients.

"The impressive data on duration of response suggest there will be significant prolongation of progression-free and overall survival when the analysis of those data is mature," said presenter Jeffrey Weber, from the Moffitt Cancer Center, Tampa, Florida.

The poster session 'Melanoma and other skin tumours' on Sunday featured T-VEC oncolytic viral immunotherapy and PV-10, two intralesional therapies for cutaneous melanoma where injections are leading to tumour regression not only in the injected lesions, but also in 'bystander' lesions suggesting the strategy is augmenting immune response. Both agents are believed to have local ablative effects that stimulate the immune system. Talimogene laherparepvec (T-VEC) is a herpes simplex virus type 1-derived investigational oncolytic immunotherapy; while PV-10 is a 10% solution of the dye Rose Bengal.

An extension study of the phase 3 OPTiM study showed patients can benefit from longer durations of T-VEC treatment (abstract 1102P). At ASCO 2014 the investigators had reported that the median overall survival was 23.3 months in the T-VEC arm versus 18.9 months in the granulocyte macrophage colony-stimulating factor (GM-CSF) arm (HR 0.79, P=0.051). The extension study was made available to patients who did not have clinically relevant progressive disease or had a complete response and then developed a new lesion within 12 months from the end of last treatment. Altogether 31patients were enrolled into the extension trial, including three from the GM-CSF arm and 28 from the T-VEC arm who continued on randomized treatment for up to 12 months.

Results showed that best overall responses improved in seven patients in the T-VEC arm, with five patients who had a partial response in the main trial achieving complete responses and two patients who had stable disease in the main trial achieving complete responses. "We were able to show that in some patients whose disease had returned we could get them back into remission by re challenging them with the agent," said investigator Kevin Harrington, from Institute of Cancer Research, London.

The latest analysis from a phase 2 study evaluating intralesional injection of PV-10 in 80 patients with stage IIIB-IV melanoma, showed progression free survival relates to the number of lesions injected (abstract 1120P). The 28 patients who had all their lesions injected had a progression free survival of 9.8 months compared to seven patients with a median of five untreated lesions who had a progression free survival of six months.

"The progression free survival of 9.8 months compares favourably with historical progression free survivals of less than 2.5 months for DTIC/TMZ, "said first author Sanjiv Agarwala, from St. Luke's Hospital and Health Network, Bethlehem, Pennsylvania. Such data he added, suggests PV-10 will deliver significant progression free survival effects in the phase 3 study, due to start Q4 2014. "The abstract also shows us that we're likely to get the highest responses when all lesions are injected," added Agarwala.

9th International Conference of Anticancer Research

Date: 6-10 October 2014. Venue: Sithonia, Greece. Report by: Rebecca Mather, Kathleen Keatley and Samah Jassam - PhD students at the University of Portsmouth Brain Tumour Research Centre.

Focus on Brain Tumours

The scientific program of the 9th International Conference of Anticancer Research was comprised of six parallel sessions covering research into varying types of cancer, cancer treatment, diagnosis and novel therapies. It featured three dedicated brain tumour sessions, as well as separate talks and posters investigating glioma.

The first brain tumour session focused on the heterogeneity of glioma, its microenvironment and therapeutic resistance. Professor G. Pilkington opened this session with an overview of the brain tumour microenvironment, before Professor R Bjerkvig discussed anti-vascular therapy, describing the effects of bevacizumab on the infiltrative growth of glioblastoma multiforme (GBM) cells xenografted into nude rats. In a talk focused on the perivascular glioma niche, Dr. H. Fillmore described therapeutic resistance with a focus on MMPs and their roles in glioma invasion. Professor C Herold-Mende then presented her group's studies into the role of the immunological microenvironment on GBM survival. Her talk recognised and identified a number of immunological adaptations within the GBM tumour microenvironment, which correlated with patient outcome. Dr H Motaln from The National Institute of Biology, Slovenia discussed the role of mesenchymal stem cells (MSCs) in the GBM microenvironment utilising co-cultures to investigate the interaction between MSCs and GBM cells.

In this session post-graduate students were given the opportunity to present. Carmen Rapp from the University of Heidelberg presented her studies into the T-cell target repertoire in primary and recurrent glioblastoma, while Steffen Dettling discussed the impact of the microenvironment on T-cells infiltration in low-grade glioma. From the University of Portsmouth, Samah Jassam hypothesised the role of CD15 and E-selectin in metastasis. Kathleen Keatley then presented her work using three-dimensional structural analysis to predict the role of mitochondrial DNA mutations in GBM and Rebecca Mather introduced the deacetylation of GD3A as a potential therapeutic strategy for paediatric medulloblastoma.

The second session entitled Brain Cancer Treatment: Epigenetic Networks, was a special symposium which covered a broad range of topics including epigenetic regulation, DNA damage and repair, tumour microenvironment and the use of nanoparticles in the treatment of glioma. This session featured a presentation by Professor D Schiffer on the histopathology of the perivascular and perinecrotic niches in glioblastoma. In this talk he described the theories of palisade formation in the perinecrotic niches.

The final brain tumour session discussed new insights into brain tumours. This included talks from both clinicians and scientists and highlighted differences between tumour and stem cell populations. Highlights from this session include Dr N Goffart's talk on GBM stem cell invasion via the CXCL12/CXCR4 axis in the adult mouse sub-ventricular zone. In this study GBM cell lines were xenografted into the mice, which were then treated with a CXCR4 antagonist, which significantly reduced invasion to the sub-ventricular zone.

As well as the three specific brain tumour sessions, many other talks featured brain tumour research. Dr A Dovas of Columbia University Medical Centre presented recently published data on cell type-specific gene expression at the infiltrative margins of glioma, highlighting the intratumoural heterogeneity. Professor RM Snapka, whose group primarily look at the mechanism of anticancer agents, presented inhibition of glioblastoma cell growth using thymoquinone.

The conference also provided useful insight into topics such as metastasis, apoptosis and metabolism; which raised potential questions that could be applied to brain tumour research in the future. Talks of particular interest included a presentation on the establishment of 3D in vitro tumour stroma model by Professor MM. Mueller and an investigation into signalling cascades, invasion and metastasis in breast cancer by Dr G Giamas.

The British Skull Base Society Annual Conference

Date: 29-30 January, 2015. Venue: Dublin, Ireland.

Preview

The British Skull Base Society is the not-for-profit, multidisciplinary and multi-professional body that represents the major United Kingdom and Irish centres involved in the care of patients with problems around the base of the skull. Its members are made up of clinical specialists responsible for the treatment of patients with skull base tumours and other disorders of the skull base, and come from a number of disciplines including otolaryngology, neurosurgery and oncology.

The society aims to raise the standards of clinical care in the field of skull base medicine through support of multidisciplinary practice and collaborative research and the provision of a forum for the dissemination of knowledge. The BSBS also acts as a professional advisory body to other groups including government agencies.

This year's British Skull Base Society annual conference organised by Aesculap Academia, will be held in the prestigious Royal College of Surgeons in Ireland. The organising committee from the Beaumont Hospital, which consist of Mr Rory McConn Walsh, Mr Daniel Rawluk and Mr Mohsen Javadpour look forward to welcoming delegates to Dublin.

Beaumont Hospital is a large academic teaching hospital 5km north of Dublin city centre. The hospital plays a leading role in the transformation process in the Irish health services, including the establishment of a number of clinical directorates and the development of formal academic and service development links with sister hospitals as part of an academic and regional network.

There will be an opportunity to present research either orally or in the open poster sessions – a great opportunity for researchers and clinical specialists to present to their colleagues and peers. If you wish to submit an abstract please download a submission form from the Aesculap Academia website and send this to academia.bbmuk@bbraun.com by Wednesday 31st December 2014.

Aesculap Academia – the organisers of The British Skull Base Society Annual Conference, are the educational arm of B Braun Medical Ltd, providing continued education for healthcare professionals including surgeons, physicians, nurses and anaesthetists. To reserve your place for next year's BSBS Annual Conference at the Royal College of Surgeons in Ireland please contact Mrs Aynsley Pix, Event Manager +44 (0) 114 225 9034.

Please visit www.aesculap-academia.co.uk