Method and Purpose: A census of the specialist nursing workforce from England, Wales, and Northern Ireland was conducted in November 2008 in an attempt to establish baseline data.
Results: Census response rates ranged from 66% to 100% across the three countries. There were inconsistent numbers of nurse specialists compared to published cancer incidence figures. It did not appear that workforce intelligence had driven staff recruitment. There was also a marked variation in the the number of specialist titles used (England recorded 17 different titles).
Conclusions: The large number of specialist titles could undermine the consistent development of specialist nursing practice; it may be useful to standardise titles. England and Northern Ireland have already used this data to commission additional specialist posts. This census has been an extremely powerful management tool and the information gathered has been used in education, policy development, and workforce design. Other European countries may benefit from conducting their own census activity.

Scientific Symposium (Wed, 23 Sep, 09:00−11:00)
Current avenues in clinical trials for melanoma treatment

203 INVITED

Melanoma vaccines – quo vadis?

G. Parmiani[1]. [1]*San Raffaele Hospital, Unit of Immuno-Biotherapy of Melanoma and solid Tumors, Milan, Italy*

Background: Metastatic melanoma is a disease for which no effective therapy is available with the possible exception of IFN-α in stage III patients. The immunotherapy approach to such a tumor was started on more convincing scientific basis 15 years ago thanks to the molecular characterization of melanoma antigens (Ags) recognized by T cells (e.g. MAGE, Melan-A/MART1, etc.). In fact, no therapeutic activity was previously obtained after immunotherapy with anti-melanoma and anti-idiotypes antibodies or with vaccine based on autologous/allogeneic melanoma cells.
Results: Approximately 10 years of clinical studies of immunotherapy, while generating important immuno-biological information on the patient immune functions and a remarkable frequency of anti-vaccine immune responses in patients treated with the self (differentiation or cancer/testis) Ags, failed to induce a significant clinical outcome both as tumor response and survival. However, the new generation of immunotherapy studies of the last 3−5 years based on the wealth of new information obtained both in the laboratory and in the clinic and by the application of the genome and post-genome analysis, has provided a more detailed picture of the relationship between tumor and host (including the role of tumor microenvironment). These data have suggested how to obtain not only an increased frequency and strength of the immune response to the different vaccination approaches but how to improve the clinical outcome.
Emerging principles for a successful vaccination of metastatic melanoma include, a) vaccination with multiple Ags (particularly under the form of peptides, perhaps long peptides) to avoid tumor escape caused by immune selection, including Ags belonging to different subgroups (e.g. differentiation, cancer/testis, universal, mutated) and recognized both by CD8 and CD4 T cells; b) new TLR-binding immune adjuvants; c) combination with immunomodulating antibodies (e.g. anti-CTLA4) or cytokines (IFN-α, IL-2, IL-12); d) administration of reagents that can counteract the immunosuppressive environment (anti-Treg, anti-TGFβ antibodies, etc.).
Recent studies also show a relevant increase of clinical response in metastatic melanoma patients receiving adoptive immunotherapy with Ag-specific T cells after immune depletion including pharmacological treatment and total body irradiation. Finally, a clinical phase III study of peptide-based immunotherapy combined with IL-2 has been presented at ASCO 2009 that showed significant increase of frequency of tumor regression in patients receiving such a biological combination therapy compared to patients arm given IL-2 only.
Conclusion: Therefore, though we are still waiting for a large, perspective, phase III study that may unequivocally document the clinical success of vaccination strategy in metastatic melanoma, the future remains promising for this area of investigation even taking into account the recent results of clinical studies of vaccination in other dreadful tumors like non-small cell lung cancer and prostate cancer.

204 INVITED

Angiogenesis in melanoma

P. Lorigan[1]. [1]*The Christie NHS Foundation Trust, Medical Oncology, Manchester, United Kingdom*

Angiogenesis is essential if metastatic melanoma is to grow beyond a size of 2−3 mm^3. This 'angiogenic shift' occurs when melanoma cells start to produce several growth factors, including vascular endothelium growth factor (VEGF). The process of angiogenesis depends on an interaction between tumour cells, stromal cells, endothelial cells and bone marrow-derived cells. The vascular endothelial growth factor family of growth factors, their receptors, and a number of cofactors, are key components of angiogenesis. There is evidence for expression of angiogenic factors being both prognostic and predictive. However, not all melanomas express VEGF and other angiogenic factors are also important. Considerable evidence has emerged for the central role of bone marrow-derived endothelial and myeloid cells in tumour related angiogenesis. Tumor-associated macrophages (TAM) are major infiltrates of human solid malignancies and release a number of potent proangiogenic factors. Dendritic cells produce a wide range of angiogenic and angiostatic factors, and are inhibited by VEGF.
A number of drugs have been developed to specifically target the components of these pathways. How these drugs result in inhibition of angiogenesis is unclear, but effects are likely to include inhibition of new growth, induction of endothelial cells apoptosis, and effects on vascular including vascular constriction and vascular normalisation, and effects on cell-cell and cell-matrix interactions. Early phase studies with bevacizumab, afibercept and axitinib have shown evidence of activity, though the addition of sorafenib to carboplatin and paclitaxel chemotherapy in both the first and second line metastitic settings showed no impact on survival. This is at odds with the outcome seen for this regimen in lung cancer, and other combinations in breast and colerectal cancer. Since angiogenesis is critical for invasion and metastasis, adjuvant therapy is an important area to explore. The AVAST-M study is a large randomised study comparing bevacizumab with routine follow-up in patients with resected high risk stage II and stage III disease. Targeting angiogenesis has been successful in a number of common cancers. Whether this will also be the case for melanoma remains to be seen.

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Molecular imaging of cancer

206 INVITED

Reporter gene imaging in cancer: from mouse to man

R. Blasberg[1]. [1]*Memorial Sloan Kettering Cancer Center, NeuroOncology Laboratory, New York, USA*

Molecular-genetic imaging in living organisms has experienced exceptional growth over the past 10 years, and can be defined as "the macroscopic visualization of cellular processes in space and time at the molecular level of function". It has its roots in molecular and cell biology as well as in imaging technology, chemistry and radiochemistry. Three imaging strategies: based on "direct" and "indirect" assessments of molecular-genetic processes, as well as "bio-marker" or "surrogate" imaging have been combined with three imaging technologies: radionuclide-, magnetic resonance- and optical-based imaging systems.
The "direct" imaging motif builds on established relationships between chemistry/radiochemistry and imaging. Bioconjugate chemistry linking specific binding motifs and bioactive molecules to paramagnetic particles for MR imaging or to radionuclides for PET and gamma camera imaging. This interactive relationship has existed for many years and continues to expand through the development of new relationships and focused interactions between molecular/cellular biologists, chemists, radiochemists, imagers and clinicians. The next generation of direct molecular imaging probes will come from better interactions between pharmaceutical companies, academia and hospitals. Such interactions are now being pursued with the objective to develop and evaluate new compounds for imaging; compounds that target specific molecules (e.g., DNA, mRNA, proteins) or activated enzyme systems in specific signal transduction pathways. However, a constraint limiting direct imaging strategies is the necessity to develop a specific probe for each molecular target, and then to validate the sensitivity, specificity and safety of each probe for specific applications prior to their introduction into the clinic.
Biomarker or surrogate imaging that reflects endogenous molecular/genetic processes is particularly attractive for expansion and translation into clinical studies in the near-term. This is because existing radiopharmaceuticals and imaging paradigms may be useful for monitoring down-stream changes