The problem of support to patients at every stage of their illness and their professional and social reinsertion is also an issue of great social importance. Access to insurance policies, loans and insurance has, until recently, not been facilitated in France.
There is much to do in terms of medical education: France suffers from a tremendous lack of oncologists and cancer specialists with expertise in cancer care. In terms of research, the 1,000 cancer research units and 4,000 cancer researchers are a symptom of insufficient coordination and lack of coherent funding. In fact, compared to the USA, the French cancer research budget amounts to 3 US$ per capita compared to 14 US$ for the USA. There is also a lack of genomic and post-genomic platforms, of tumour collections and insufficient translational research. With 260 new trials per year and 1,750 ongoing trials, France also lacks independent funding in clinical research as well as public health and social sciences research.
In this rather mixed context, cancer was qualified as “one of the greatest challenges of our century” by President Jacques Chirac, a proposition conveyed during the World Summit against Cancer in 2000 by the signature of the Charter of Paris under the motto “Cancer will not be defeated in one day, but one day, it will be defeated!” The Charter of Paris reflected the first global call to action against cancer and recognized it as an international priority in all its aspects: prevention, therapy, psychology, sociology, economics and spirituality.
As a result of this awareness and in order to implement the seventy measures of the National Cancer Plan launched in 2002, the French National Cancer Institute (INCa) was founded in May 2005. With an overall budget of €1.5 billion, an increase from the €175 million in 2002, the Cancer Plan aims to create a critical mass of cancer research in France, pooling the expertise and resources necessary to increase European and international visibility and to facilitate strategic funding. As well as coordinating cancer research and stimulating clinical research, the INCa plays a major role in global patient care and aims to mobilize all those involved in the fight against cancer in France through strategic actions covering prevention, screening, treatment, patient support, training and education.
One of its major actions concerns breast cancer: decreasing cancer mortality for this pathology is directed through organized screening and public information. In this spirit the Institute initiated a large campaign in 2004 to stimulate women to participate in organized breast cancer screening across France. This campaign aimed to control both the quality of the mammography and radiologists’ skills through double reading of mammograms and guiding patients for optimal care. The number of women who took part in this screening increased from 33% to 41%.
An effort has been made to increase access to medical imaging with, for example, an increase in the number of PET scans from 8 to 72. Moreover, more than 15,000 tests of genetic screening for susceptibility to cancer have been performed in France. Two types of criteria are now taken into account in the treatment of patients: quantitative, with a sufficient level of activity to ensure the quantity of surgical acts in all cancer centres, and qualitative through a multidisciplinary, personalized approach, at all stages, including diagnosis, underpinned by an effective continuing medical education system.
The INCa is also working to improve access to the most innovative drugs (for example, with Herceptin for HER2 positive breast cancer) and to set best practice guidelines. All cobalts will be replaced by new generation accelerators. In clinical research, the Institute has set a target of one in ten new cancer patients being offered inclusion in recognized clinical trial protocols. To achieve this goal, clinical research groups are being created specific to each type of tumour and regional data centres will ensure rigorous and coherent methodology in clinical trials and the coordination of data collection.
The Cancer Plan has provided the means to federate cancer research in France through the creation of seven regional research hubs, known as ‘cancéropôles’, bringing together private and public sector partners in basic, translational and clinical research. The INCa plays a key role in coordinating these cancéropôles, fostering synergies within and between them.
Funding (50 M€) is channeled through both open and targeted calls for proposals uniting 3 or 5 teams on 3 year projects benefiting from international evaluation. The Institute is also developing disease-specific national networks of excellence (the PNES). The first two, launched in late 2005, target lung and kidney cancers.
Since “cancer knows no borders”, international fellowships and joint research projects have been set up by the Institute. Moreover, the European Alliance against Cancer, in which the INCa plays a key role, aims to be active on the European scene, through its work on a virtual tumour bank and a proteomic biomarkers discovery programme.
Over the coming years, the INCa will carry forward the spirit of the Cancer Plan to ensure that every cancer patient in France has equal access to quality care, support and innovation in the framework of a coordinated care pathway, adapted both to the characteristics of their cancer and to their own personal history.

195 INVITED

Prospective clinical trials on quality improvement

C.J.H. van de Velde. *Leiden University Medical Centre, Department of Surgery, Leiden, The Netherlands*

As a result of the Eurocare study it is evident that major oncological outcome differences per country are observed. Worldwide there are major initiatives in order to improve the quality by quality measurements and outcome based restructurization of care. A very important component is the surgical performance which is more complicated to control than radiation-oncology and medical oncology. In several studies a large variability between surgical outcome of individual surgeons and institutions is observed requiring quality assurance to achieve a treatment result that meets a certain standard.
Several prospective randomized clinical trials were conducted in which surgical quality control was implemented also with the use of extensive standardization of pathology examination of the operative specimen. These studies in GI cancer led to vast improvements in terms of local control as well as overall survival.
A study on gastric cancer was performed studying the effects of limited lymph node dissection and extended lymph node dissection. Every surgical procedure was supervised and the performance reported back to the individual surgeons. Although morbidity was higher in the D2 resection arm, present updated results at 14 years indicate a survival benefit overall for D2 dissection in terms of local control and survival. Newer developments are selection of patients on the basis of prognostic and predictive markers as well as co morbidity. This leads to further improvements in locoregional control in the treatment of gastric cancer. The dispute that still exists between the Eastern and Western approach of gastric cancer will through this structure be solved, although in low incidence countries this type of surgery should be concentrated in high volume hospitals and preferably patients and doctors should participate in prospective auditing programs.
Another example is rectal cancer where the major problem in the past was local recurrence rates varying between 15 and 30%. In a study with video instruction, supervision as well as standardization of pathology, local recurrence rates were reduced by half and survival improved by 10%. Standardized preoperative short-term radiation therapy improved local control further, although not for patients with a positive circumferential resection margin. In those countries were training programs and auditing has been performed disease-free and overall survival after rectal cancer treatment have improved dramatically. Further improvements can be made by proper selection by well trained teams preoperatively to the different multimodality treatments that eventually will tailor the treatments to the individual patient. These developments have changed the pattern of recurrence of rectal cancer patients with major impact on local recurrence to now focus to systemic treatment. Updates, analyses of the Dutch TME as well as of five major European rectal studies will be presented. In both high as well as low volume cancer treatments pre- ad postoperative multidisciplinary team conferences are mandatory, but also outcome monitoring should be part of the local as well as national structures. Patients that participate in prospective clinical trials preferably also with translational research questions will help further improve not only the standards of care but also enable refinements of treatment to the individual patient. Scientific societies in Europe should further strive to accomplish and facilitate the auditing program to further improve outcome.

Symposium (Thu, 27 Sep, 09:00−11:00)
Impact of gene expression profiling on the treatment of patients with leukaemia and lymphoma

196 INVITED

Diffuse large B-cell lymphoma

B. Coiffier. *France*

Abstract not received.

197 INVITED

Hodgkin lymphoma: Impact of molecular techniques for better diagnosis and treatment

V. Diehl. *Klinik I für Innere Medizin der Universität, German Hodgkin Study Group, Köln, Germany*

For more than 160 years Hodgkin Lymphoma (HL) was thought to be an inflammatory or infectious disease. Only recently we were able to

culture the pathognomonic Hodgkin- Reed- Sternberg cells in vitro and characterize by molecular techniques, using the micro dissection technique, the nature and origin of these cells as monoclonal germinal- center- derived pre-apoptotic B-lymphocytes that are protected from apoptotic cell kill by numerous mechanisms including mediators and cells of the innate immune system.
Gene expression profiling data have shown that HL cells have a unique signature of specific genes that differ considerably from other B-cell Non Hodgkin Lymphomas and make this lymphoma entity an unique target for new avenues of molecular approaches, using small molecules and antibodies directed against specific transcription factors leading to aberrant cell proliferation, inhibition of apoptotic cell death or constitutive expression of tumor molecules that are absent in the normal cellular counterparts.
There is however no Imatinib for HL and also there is not yet "Philadelphia chromosome" found in HL which drives the malignant process and offers the deadly target for imatinib! There, also, no antibody that acts like Rituximab in NHLs for this HL entity, so doctors depend still mainly on the old chemo- and/or radio- therapies, however, with a very high success rate of curing more than 85−90% of patients with HL in all stages of the disease.

198 INVITED

Acute lymphoblastic leukaemia

D.F. Hoelzer. *Germany*

Abstract not received.

199 INVITED

Acute myeloid leukaemia

A. Burnett, K.I. Mills. *Cardiff University, Department of Haematology, Cardiff, United Kingdom*

Acute myeloid leukaemia is a heterogeneous disease with respect to morphology immunophenotype, cytogenetic abnormalities and mutations that occur. Some of these features have prognostic implications and are increasingly being used to make treatment choices. The balance of these features changes with age. Older patients tend to be characterised by a preponderance of adverse features whereas the opposite is true in younger patients. Biologically it is thought that most cases originate in a cell which is equivalent to the normal haemopoietic pluripotent stem cell, which however may have phenotypic characteristics by which it can be identified.
Gene expression analysis has a number of potential uses in this disease, and a number of questions arise. First, is the signature of the cell population thought to represent the leukaemic stem cell different from the blast cell population which form the bulk of the tumour? Relatively few studies have been done to address this issue but these provide reasonable confidence to suggest that the CD34 positive population is representative of the blast population. Morphological and immunophenotypic criteria have been established in order to diagnose AML. In addition non-random chromosome changes occur in the majority of cases. Careful correlative studies have clearly demonstrated that unsupervised analysis, using robust microarray platforms, such as the Affymetrix Oligonucleotide arrays, can identify the morphologically, immunophenotypically and cytogenetically defined categories with a high (>99%) degree of accuracy. Cytogenetics subclassification is now well established to be predictive of response to all forms of treatment. Expression signature can identify the major prognostic subgroups and in some cases individual karyotype. It can be seen from a diagnostic point of view that all the major information can be provided by DNA microarray technology. This may even be a more qualitatively robust and even cost effective approach. Most of these studies have been conducted as a collaborative approach within the European LeukemiaNET (ELN Work package 13, chaired by T Haferlach). In an international project – the MILE study – microarray characterisation of >2500 cases of all leukaemia subtypes have been completed within 17 defined subgroups. Signatures have been identified which are now being prospectively validated with a view to developing a leukaemia diagnostic chip.
One of the subjective areas of morphology is the distinction of cases that are high risk Myelodysplasia from those that are AML, recognising that the former can often progresses into the latter. Recent evidence suggests that microarray can throw light on this issue and identify patients with an increased risk of transformation.
The concept exists that microarray definition could not only identify existing disease categories, but also define new ones. Further prognostic information is now emerging from the recognition of various mutations within or across the cytogenetic categories. Although it is harder to identify gene expression signatures for these mutations across the leukaemia sub-groups, they can be identified within specific and relevant categories. However, there is much optimism, as yet unfulfilled, that more accurate prognostic information could be provided either to indicate likely disease response to treatment, or indeed prediction of toxicity, with the hope that sensitivity to individual agents can also be identified. This challenge required the characterisation of large numbers of patient's samples – preferably in setting of a standardised approach to treatment. This combined with other molecular approaches of identifying disrupted pathways hold out some hope for future new drug development.

Special session (Thu, 27 Sep, 11:15−12:15)
Impact of HPV vaccination in oncology in Europe

200 INVITED

What is known about HPV natural history? Current trends and variation in incidence, mortality and relation to screening programmes in Europe

X. Bosch. *Spain*

Abstract not received.

201 INVITED

Types of HPV vaccination in the pipeline and dreamed/proven efficacy and effectiveness at short/long term

C.J.L.M. Meijer. *The Netherlands*

Abstract not received.

202 INVITED

Scenarios for application of human papillomavirus vaccination

S. Franceschi. *International Agency for Research on Cancer, Infections and Cancer Epidemiology Group, Lyon, France*

Background: A dozen high-risk types of human papillomavirus (HPV) are recognised to be the necessary, though not sufficient, cause of almost all cervical cancer cases worldwide (approximately 500,000 new diagnoses and 240,000 deaths per year).
Materials, methods and results: HPV 16 and 18 infections alone account for over 70% of invasive cervical cancer (Smith et al., Int J Cancer, 2007), and a fraction of ano-genital cancer and oral cancers. Thus HPV is considered responsible for nearly 5% of cancer in women in developed countries, and this proportion triples when we consider developing countries. The prevalence of HPV in cancer-free women varies substantially from one population to another (2−30% in women 15−64 years of age, Franceschi et al., Int J Cancer, 2006), but it is the most common sexually transmitted infection in most areas of the world.
Although both prophylactic and therapeutic vaccines against HPV are under evaluation, major breakthroughs in the last years have been reported only with respect to prophylactic vaccines. These vaccines have been shown to be safe and highly efficacious in preventing persistent HPV infection (Harper et al., Lancet, 2006), and cervical intraepithelial neoplasia 2 and 3 (Garland et al., N Engl J Med, 2007; FUTURE II Study Group, N Engl J Med, 2007). The main differences between the two products are the HPV types included (i.e., quadrivalent, HPV 6/11/16/18, versus bivalent, HPV 16/18), and the adjuvant used (aluminium or a new ASO4 adjuvant). Some cross protection from the bivalent vaccine has been reported against the relatively common HPV types 31 and 45 (Harper et al., Lancet, 2006). Studies of HPV vaccines have never been done in Africa, and Asia has been only minimally involved. Furthermore, information on duration of protection is limited to 3-to-5 years, and so is the long-term effect in women who have been infected by vaccine types but spontaneously cleared the infection.
Conclusions: Full benefits from HPV vaccines will only be possible, however, if mass immunisation campaigns for girls not yet exposed to HPV can be implemented, notably in developing countries, but, at present, the main obstacle is the high cost. Long-term monitoring of HPV vaccination and cervical screening is essential for finding the most effective strategies for cervical cancer control.