Materials and Methods: Only a single prospective and randomized study has prospectively investigated when postoperative radiotherapy is to be integrated in relation to chemotherapy. Multiple studies have tested the effects by adding endocrine therapies to chemotherapy, and the addition of trastuzumab (T) to different chemotherapy regimens. When and how to integrate these modalities in relation to radiation will be discussed.
Results: Long term follow-up reveals increased cardiovascular toxicities by radiotherapy, although these side-effects have in the overview process been described to diminish in later studies.
The initial pooled analysis of the adjuvant US trastuzumab studies (NSABP B-31/NCCTG N9831), containing doxorubicin, cyclophosphamide (AC) and paclitaxel (P), revealed in an indirect comparison with the HERA study a "better" disease-free survival. In the US studies T was partly delivered concurrently with adjuvant P, while in the HERA study all T was given after the completion of chemotherapy and radiotherapy. The US studies, with AC, concurrent P and T, followed by radiotherapy and remaining T, revealed a likely higher risk of severe congestive heart failure (CHF) and systolic dysfunction, respectively; 0.6% in HERA compared with 2.5−3.6% CHF. Systolic dysfunction was 3.0% in the HERA study, while the concurrent strategies revealed 14−17%. In the third large US study BCIRG 006, the arm with concurrent T with docetaxel (D) and carbopaltin revealed a 0.4% risk of severe CHF, systolic dysfunction was reported in 8.6% of the patients. For the FINHER study with only nine weeks of T concurrent with D or vinorelbin at start of therapy the corresponding values were 0% and 3.5%, respectively.
Conclusion: For most patients, the likely best strategy is to deliver chemotherapy first, followed by radiotherapy and endocrine therapy. For those patients with HER2/neu positive cancers there is a potentially better effect by giving trastuzumab concurrently with taxanes, although the cardiac side-effects seem to be higher by this strategy, so the optimal strategy is so far not known.

Symposium (Thu, 27 Sep, 09:00−11:00)
Quality improvement strategies in cancer

192 INVITED

A mixed Dutch approach in the European perspective

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Being examples of performance The Netherlands did well in European comparisons of participation in EORTC studies of cancer treatment, of the presence of effective mass screening programmes (for cervical and breast cancer) and active participation in studies of screening for lung and prostate cancer; generally, it exhibited reasonably good results within the Eurocare studies, covering the diagnostic periods 1978−85, 1985−89, 1990−94 and 1995–2002, respectively with increasing populations covered, as well as in various high resolution care pattern studies of breast, colorectal, testis and prostate cancer. Although, and a bit later than desired, a huge government stimulated investment effort in radiotherapy equipment and manpower took place since 2001, there was great anxiety on the needed capacity and efficiency of the health sector, partly evoked by 'silent' demographic changes and permanent uncertainties on income of and power over doctors, who also became scarce due to inadequate deliberate ministerial policies to keep the number of medical students low since the mid 1980s; but they were doubling again since 2000 and training opportunities have enlarged in the meantime.
Since 2000 there have been several, seemingly uncoordinated but necessarily related, initiatives to come to a national cancer plan. On the one hand several explorative reports on the future of cancer prevention and cancer care have been published under the auspices of the Dutch Cancer Society, the major player in the domain of cancer research by fund raising and patient education: 3 reports on prevention (summarizing the evidence) by prudent exposure to UV (2002), diet (2004), physical exercise (2005), a report on colorectal cancer screening preaching diversity (2004), a report on the bright future of imaging (2005), a report on molecular diagnostics (2007) and biobanking, a report on waiting times (2006); they were also supported by an extensive report on trends in prevalence (incidence and survival) during the period 1990–2015 (2004). This latter report still provokes discussion on how to adress the rising demand for care (the number of cancer patients alive rising from about 500,000 in 2005 to 800,000 in 2015), especially in the domain of breast and colorectal cancer, skin cancer and related to older patients, for whom special care programs are needed that also adress co-morbidity, especially for the rapidly rising numbers of patients with cancer and diabetes. The aim of all these scenario-type of reports have been to stimulate the various players to take their responsabilities in terms of training, regionalization (here supported by the 9 Comprehensive Care Centres – CCC's – responsible for the promotion of quality of care at regional level), delegation of tasks to nurse-practioners and in fact promoting early diagnosis and also reluctance with cancer screening with its modest benefits and large resource & care implications.
Simultaneousy, In the period 2003−06 a major political change gave the health insurance companies responsability for buying health services, also competing on price and quality (as always difficult to measure etc), for which the Ministry of Health and new independent supervising bodies are trying to create optimal conditions, e.g. by promoting incentives for such competition, efficiency, patient safety ans also the introduction of electronic patient records. But also efforts to heva new (expensive) cancer drugs sooner available. Although aimed at greater efficiency, more restricting rules and controls are also resulting and care providers like GP's suffer. The results are mixed for the various specialists whose numbers are increasing rapidly.
A substantial, rather heavy, effort to write a national plan was also undertaken by the major players (the Dutch Cancer Society, the 'united' CCC's, Insurance companies, cancer patient societies and the Ministry of Health). A large report arrived in 2004, but was not received with much enthousiasm, because it lacked a perspective (except for wider application of psychosocial care) especially with respect to research and development and in fact there had been little professional involvement. Recently, some efforts take place in reviving, but in fact many professionals are making hteir own plans in accordance with the new regime of governance by insurance companies.
The importance of professional involvement can be underscored by many examples, the best (in my opinion) being the impressive improvements in rectal surgery and preoperative irradiation which have taken place in the last 15−20 years; they are currently followed in the domain of colon cancer management and many other initiatives at regionalization of surgical oncological care.
Conclusion: through a diversity of professional initiatives cancer care is definitely improving in the Netherlands. The best policy is to support this.

193 INVITED

The UK programme

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Abstract not received.

194 INVITED

The French approach – The French Cancer Plan and its instrument the French National Cancer Institute (INCa): A centre of hope in the fight against cancer

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Fighting cancer in the world, and particularly in France, means more than just taking up a public health challenge. Among the 10 million new cases and 6 million deaths worldwide in 2000, France accounted for 280,000 new cases and 150,000 deaths. By 2020, it could kill 10 million people worldwide every year.
Beyond the disease strictly speaking, cancer leads to a number of social inequalities, ranging from exclusion and discrimination to psychological problems. With the ultimate goal of cure, science plays a key role in the fight against cancer, basing its research both on simple mechanistic paradigms of cancer and more complex process-based ones. Considering the huge increase in medical needs – as regards the epidemiology and chronicity – and the cost and complexity of the new treatments, the next step consists in transferring relevant information and updated knowledge from the laboratory to the bedside (through translational research and valorisation), thus adhering to the objective of putting patients at the heart of cancer care – both in access and quality.
The landscape for cancer in France reflects the challenges of the disease. Although the country has the best survival rate after cancer in Europe, the number of cases doubled between 1980 and 2000. In addition, a lack of public health policy is evident in a country where there is the highest premature mortality in men. The principle of universal and unlimited access to care in France results in 3 million mammograms, 1.5 million colonoscopies and 6 million Pap tests administered every year, undermined by a lack of organization and cost-efficiency.
The French healthcare landscape shows geographical discrepancies as well as a lack of equipment and of respect to patients, despite a high level of access to modern medicine. In 2002, France had 10.3 scanners per million inhabitants, 3.8 MRIs and 0.2 PET scans with waiting times of 41 days for a scanner and 39 days for an MRI. There is also an increase in the demand for health services with, for example, a 12% per year increased demand for chemotherapy. French cancer patients have insufficient access to non-medical care (including rehabilitation and counselling) and ambulatory care (despite a significant progress made in the palliative care and pain management areas.)

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

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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

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Abstract not received.

197 INVITED

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

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