Special Session (Mon, 26 Sep, 13:15−14:15)
Health Status in Screening in Elderly Patients − Is This the Way Forward?

311 INVITED

Geriatric Evaluation is the Principle Way of Assessing the Elderly Patients

Abstract not received

312 INVITED

The Use of Screening Tools in Geriatric Oncology

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Older patients represent the majority of cancer patients, and therefore a substantial proportion of patients in any oncology practice. Geriatric oncology research has demonstrated that these patients have a significant amount of geriatric problems, and that these problems impact the patient's prognosis and management independently from classic oncologic predictors.
However, the multidisciplinary assessment offered in specialized geriatric oncology programs is beyond what many oncology practices can do. A solution that has emerged is a two step approach: First, use a short screening tool on every patient. Then refer the patients screening positive for multidisciplinary work-up in parallel with their oncology work-up and reach an integrated treatment plan. In this presentation, we will discuss the short screening instruments that have been tested in cancer patients, their sensitivity and specificity for geriatric problems, and their practical integration into the patients' management. Notably discussed will be: the abbreviated CGA, the G8, the Gronigen Frailty Index, the Senior Adult Oncology Program 2 (SAOP2) questionnaire, the Triage Risk Screening Tool, and the Vulnerable Elders Survey 13 (VES13) questionnaire. Sensitivity is a key issue for screening tools and a high sensitivity is an important requirement for these tests. Some of these instruments meet it better than others: ranges in studies go from 65% to 100%. Such sensitivity usually comes at the cost of specificity and therefore it is important that the patients be further worked up to distinguish true from false positives and the impact of the true positive findings on the treatment plan.

Scientific Symposium (Mon, 26 Sep, 14:45−16:45)
Breast Conservation in Young Women With Early Breast Cancer

313 INVITED

The Role of Radiotherapy in Reducing Local Relapse Risk in Young Women

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Data from the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) clearly demonstrate the significant reduction in risk of local failure from radiotherapy following breast conserving surgery in the treatment of early stage disease. An approximate 70% reduction in the risk of local recurrence with radiotherapy was observed across multiple trials following treatment to the conserved breast compared to lumpectomy alone. Age was shown to impact risk of failure; however only limited information is available specifically on outcome of BCT in young women (defined as under 40 years of age) as analyses thus far from the EBCTCG present outcomes collectively in women <50 years of age compared to women 50−59, 60−69, $\geqslant$70 years. These results demonstrate a similar proportional reduction in local recurrence with radiotherapy irrespective of age, with a much greater absolute benefit in women under 50 years compared women 50 years and older. These results underscore the importance of radiotherapy in younger women but also highlight the underlying increased baseline risk of recurrence associated with younger age.
Review of the literature suggests the presence of biologically more aggressive disease in young women that impacts both local and systemic failure irrespective of local treatment. Diagnostic and treatment-related factors have thus been shown to result in significant improvements in outcome following BCT particularly in young women. Improvements in imaging can help to better select young women who are acceptable candidates for BCT. Surgical margins are now carefully assessed to negative margins can be achieved. Use of a boost dose of radiotherapy to the tumour bed has been shown to significantly reduce the rate of in-breast tumour recurrence. Indications for systemic therapy have expanded to include most patients with invasive disease and some with DCIS. And choice of systemic therapy is being increasingly individualized based upon tumour characteristics including histologic sub-type and receptor expression. Thus, agents such as trastuzumab are being increasingly used with further reduction in local recurrence. And finally, the interplay between local and systemic control suggests gene profiling for systemic risk may help predict those patients at increased risk for local failure. Preliminary results are promising; prospective validation is forthcoming.

314 INVITED

What Are the Sources of Local Relapse?

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Breast-conserving therapy is the preferred treatment for patients with early-stage breast cancer. It offers equal local control and overall survival and superior psychosocial outcomes compared with modified radical mastectomy. However, an ipsilateral breast cancer recurrence can be traumatizing and can lead to death. There are three possible explanations for ipsilateral breast cancers: 1) a regrowth of clonogenic cells that were not removed by surgery or killed by radiotherapy that can be referred to as true recurrences, 2) a new primary tumour that arises from the remaining breast tissue and 3) a radiation-induced new primary breast cancer. Several definitions have been used to distinguish true recurrences from new primary tumours. Initially, these distinctions were based on spatial and temporal characteristics of the ipsilateral breast cancer (i.e., the farther from and the later after the initial primary tumour, the more likely it is to be a new primary tumour) and on shared common histopathologic criteria (e.g., type, grade, and hormone receptor status). In the quest for additional ways to distinguish new primary breast tumours from true breast cancer recurrences, biologic studies of clonal relationships between the new and original tumour have also been performed. These studies have relied on ploidy, loss of heterozygosity, p53 analysis, or X chromosome inactivation or have been based on DNA copy number alterations (CNAs). New gene-expression data also support the possibility to diagnose radiation-induced breast cancers. We will discuss the potential implications of better defining the pathogenic nature of ipsilateral breast cancers, both clinical − in terms of prognosis and treatment − and scientific.

315 INVITED

What Are the Effects of Systemic Therapy in Reducing Local Relapse Risk?

S. Aebi[1]. [1]*Luzerner Kantonsspital, Medical Oncology, Lucerne, Switzerland*

Systemic therapies (adjuvant endocrine treatments, chemotherapies, and adjuvant trastuzumab) reduce the risk of recurrence and death from breast cancer. Locoregional relapses indicate a high risk of distant metastatic disease. The likelihood of a local recurrence is determined by biological properties of the cancer as well as the extent of surgery and the use of radiation therapy. The metaanalyses of the EBCCTG reveal that polychemotherapy (cyclophosphamide, methotrexate, and fluorouracil (CMF)-based and anthracycline-based) reduce the relative risk of locoregional recurrence by more than 60 percent; similarly, tamoxifen diminishes the same risk by about 50 percent. More recent developments of adjuvant drug therapy yield similar results: Aromatase inhibitors reduce the risk of local recurrences by at least an additional 30 percent as compared to tamoxifen monotherapy. Certain but not all trials investigating taxane-based chemotherapies report superior protection from locoregional recurrences as compared to non-taxane-containing chemotherapies. Trastuzumab reduces the risk of locoregional recurrence in patients with HER2 amplified/overexpressing breast cancer.
The effect of systemic therapies on the risk of locoregional recurrence will be reviewed. Preliminary conclusions suggest that more efficient therapies which are associated with a lower risk of recurrence will also protect from locoregional relapse.

316 INVITED

Breast Conservation in Young Women With Early Breast Cancer

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In the last ten years a number of revolutions have occurred in our understanding of the biology of breast carcinoma and have deeply influenced our approaches to the disease in terms of prevention, detection and treatment.

1. The genetic studies have identified subgroups at high risk of developing the disease creating the premises for programs of targeted chemoprevention.
2. Endocrine modulators and other active principles like retinoids have shown to be effective in reducing breast cancer incidence in specific subgroups of patients.
3. New developments in imaging procedures have made possible the detection of very early carcinomas greatly increasing the curability rates.
4. The analysis of the genetic profile of the cancer cells will be fundamental for prognostic evaluation and to assess the likelihood of response to medical treatments.
5. More and more non palpable tumours will be identified and destructed. Radio guided techniques to remove those occult lesions are now available.
6. Mastectomy is abandoned in favor of breast conservative treatments.
7. Thank to the Sentinel Node Biopsy procedure, the dissection of regional lymph nodes will be limited to patients with positive nodes.
8. Radiotherapy fields are being progressively reduced and partial breast irradiation is becoming a realistic perspective for the future.
9. Systemic treatments will be decided mainly according to the prediction of response to specific endocrine or chemical drugs.
10. New types of drugs built to meet specific biomolecular targets, expressed by mutated genes, are appearing as a result of the postgenomic research.
11. The cancer “stem cells” concept will open new roads in treatment.
12. TNM classification is being deeply modified.

All these new facts are at the root of dramatic changes in paradigms for prevention, detection and treatment of breast cancer. The main shift refers to the progressive awareness of the importance of quality of life, which is changing the traditional approach based on the “maximum tolerated treatment” to the “minimum effective treatment”. This new trend has led to limited surgery (instead of mutilating operations), more targeted radiotherapy (instead of large field involving the regional nodes), less aggressive chemotherapy (instead of the high dose approach). This new trend will motivate more women to participate in early detection programmes, which in turn will lead to the reduction of mortality rates.

Scientific Symposium (Mon, 26 Sep, 14:45−16:45) **Contributors to Better Survival in Colorectal Cancer**

317 INVITED

The Contribution of Evidence Based Guidelines and Compliance to Colon Cancer Cancer Survival

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Evidence based guidelines have played an ever increasing role in the practice of medicine over the last thirty years. National guidance for the management of colorectal cancer (either comprehensive guidance for all aspects of the condition from diagnosis to terminal care, or specific to a particular problem such as liver limited metastatic disease) has existed in many countries for the last fifteen or so years. But has the provision of such guidance led to any improvement in outcomes?

Overall across the breadth of medicine, the evidence suggests that the introduction of guidance does lead to improvement in outcome in over ninety per cent of cases [1]. However, the methodology and degree of rigor applied to the methodology in the creation and introduction of such guidelines is very variable, and there are many models of methodology with which guidelines can be constructed. Furthermore the size of outcome improvement following the introduction of guidelines varies widely.

Another problem in measuring the impact of the implementation of guidelines in oncology is the coincidence of the guideline publication with a simultaneous major breakthrough in disease detection or therapy. Furthermore, implementation and audit of outcomes of guideline recommendations may vary considerably at the local level.

The presentation will review the impact of a number of major national guidelines for the management of colon cancer from the author’s perspective as Chair the National Institute of Clinical Excellence’s colorectal cancer guideline development group.

References

[1] Grimshaw JA and Russell IT. Lancet 1993; 342: 1317−22

318 INVITED

Better Survival due to Improved Staging in Colon Cancer. the Sentinel Node Reappraised

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Background: The value of the sentinel lymph node (SLN) procedure in colon cancer patients remains a matter of great debate. The objective of this systematic review is to summarize the potential advantages of SLN procedure in colon cancer patients particularly focussing on the identification rate and sensitivity of the SLN procedure as well as on upstaging and on the possible impact on outcome.

Methods: A systematic review of the literature was performed since the first use of the SLN procedure in colon cancer patient in 1997 up to now. This review therefore represents a synthesis of the most relevant data regarding SLN procedure in colon cancer patients including data from our Swiss multicenter study.

Results: There are only a few prospective, multicenter studies − including one randomized controlled trial − in the literature. In the hand of experienced surgical oncologists, the SLN identification rate is close to 100% and the sensitivity around 85%. However, these rates are lower early in the learning curve. There is no universally accepted standardization of the SLN procedure (e.g., in vivo vs. ex vivo tracer injection; type of tracer used, amount of tracer injected, defined learning curve for the procedure). Due to in-depth analysis of the SLN (ultrastaging), small nodal tumour infiltrates are found in a relevant proportion of patients initially classified as node negative; upstaging rates around 15% are published in the literature.

Conclusions: The SLN procedure for colon cancer has good identification and accuracy rates, which further improve with increasing experience. Patients remaining node negative after ultrastaging of the SLN represent a subgroup of colon cancer patients with excellent prognosis. Most importantly, the SLN procedure results in an upstaging of 15% of node negative patients. The potential advantage of performing the SLN procedure appears to be particularly important in these patients as they may benefit from adjuvant therapy, which consequently may result in better disease-free and overall survival.

In the future, it is crucial to further explore different strategies to improve either lymph node staging (e.g. by One-Step Nucleic Acid Amplification [OSNA] of lymph nodes) or the SLN procedure in colon cancer patients (e.g. by using an intraoperative near-infrared fluorescence imaging system [FLARE]).

319 INVITED

Neoadjuvant Treatment in Colon Cancer

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With the advent of more active combination chemotherapy (CT) than just single agent FU, resections of unresectable liver metastases (mets) have been reported. Since then disease downstaging has become a relevant endpoint of “conversion therapy”. “Neoadjuvant CT” of resectable mets was also investigated, within the frame of a “perioperative strategy”. In addition to unresectable and resectable mets, “potentially resectable” mets are usually considered a third category, although CT used in this setting should be regarded as conversion therapy. Conversion therapy is most challenging, since it is directed against macroscopic mets with the aim of shrinking them or altering their structure, whereas perioperative therapy is directed against micrometastases. A recent systematic review of 23 neoadjuvant CT trials on resectable colorectal liver mets reported a median RR of 64%, with R0 resection rate of 93%, and median DFS of 21 months. In the only phase III study available, these figures dropped to 43%, 87% and 19 months, respectively. These studies do not allow a conclusion on the optimal neoadjuvant CT for resectable mets, because the phase III investigated FOLFOX CT vs surgery alone, and the other studies are single arm phase II. In nonresectable mets the Tournigand study provide a randomized comparison between FOLFOX and FOLFIRI reporting a higher RR for FOLFOX with corresponding liver mets R0 resection rate of 22% compared to 9% with FOLFIRI. This conversion rate of FOLFOX was confirmed (33% on 43 patients) in a phase II study. In a randomized phase III trial, Falcone et al. demonstrated an increased RR (66% vs 41%) and R0 resection rate (36% vs 12% in patients with liver only mets) for the triplet regimen FOLFOXIRI compared with FOLFIRI. Further increased RR is reported with the addition of monoclonal antibodies to standard CT. At least 4 studies showed consistent improvements in RR (ranging from 59% to 79%) with addition of Cetuximab to CT. In the phase III CRYSTAL trial the rate of R0 liver resection increased from 1.5% with CT only to