therefore the need to develop a critical thinking to assess their merit. The reasoning involved in this process is, from the statistical point of view, very similar to the steps one takes when designing and conducting a clinical trial to its end.
Whether you write or read a scientific paper, start by identifying the objectives, then read the methods and the results, and then make your own judgment about their value before reading/writing the discussion and conclusion. Make this with a fresh mind, free of prior beliefs and with logic and objectivity!
Be mindful that bias may be introduced at every step of a clinical experiment:
– By construction (if e.g. endpoints or follow-up assessments systematically favor one group, or by selection of a suboptimal comparator)
– In the conduct (selection bias, selective reporting of events, operational bias − this one comes when intermediate results are divulged that influence the further conduct of the experiment)
– In the data analysis (sub-grouping, data dredging, hindsight bias − a natural human tendency to try to confirm prior beliefs, disconfirmation bias − the opposite tendency to scrutinize more the results that go against prior beliefs)
– In the presentation of the results (when more focus is given to the significant findings, even if they are secondary/exploratory; when effect estimates are not reported thus clincal significance cannot be assessed)
– In the interpretation of the results (a tendency to confirm prior beliefs and to see causality)
– In the publication of the results (publication bias: a tendency to make more publicity for positive results than for negative results).

Modern clinical trials are becoming increasingly complex due to the increasing economical pressure and to the growing scientific knowledge. Trials that use adaptive designs, surrogate endpoints or sophisticated pharmaco-genomic classifications are at particularly high risk of bias. In reading articles, be mindful that intermediate endpoints may not always be surrogates for long term clinical benefit; that adaptive designs carry the risk of operational bias or require appropriate safeguards and that the risk of false positive findings must be controlled by appropriate measures whenever analyses in subgroups or interim analyses are conducted.
Find current reporting guidelines on www.equator-network.org

359 INVITED

How to Get Good Evidence Based Information

Abstract not received

Tuesday 27 September 2011

Scientific Symposium (Tue, 27 Sep, 09:00−11:00) Relieving Symptoms of Hormonal Therapies in Patients With Breast Cancer

360 INVITED

Endocrine Symptom Assessment in Women With Breast Cancer

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Background: Toxicity and tolerability profiles of endocrine treatments in breast cancer trials are usually derived from physician-recorded adverse events. However, there is some evidence that these proxy rating do not adequately reflect endocrine symptom burden experienced by women with breast cancer.
Objective and Methods: The objective is to give an overview of measures used to assess self-reported symptoms related to endocrine therapy in women with breast cancer, to summarise major findings of clinical trials including self-reports of endocrine symptoms and their impact on quality of life (QoL), and to discuss implications for clinical practice.
Results: Several valid tools are available to assess self-reported endocrine symptoms in breast cancer clinical trials. These tools encompass subscales of commonly used cancer-specific QoL measures (e.g. Functional Assessment of Cancer Therapy − Endocrine Subscale; FACT-ES) or checklists specific to endocrine or menopausal symptoms (e.g. Breast Cancer Prevention Trial (BCPT) Symptom Checklist). In contrast, the Checklist for Patients on Endocrine Therapy (C-PET) was developed for the individual assessment of patients' experience with endocrine treatment at clinical visits in order to facilitate communication between the patient and the treatment team. Prevalence rates for most endocrine symptoms are higher when self-reported compared to physician ratings published in pivotal clinical trials. Studies that assessed subjective endocrine symptoms focused on treatment comparisons rather than on the associations between endocrine symptoms and QoL measures. Regarding the impact of endocrine treatment on QoL, findings are not consistent.
Conclusion: The use of endocrine agents, particularly aromatase inhibitors like anastrozole, letrozole and exemestane will extend in earlier stages of disease and for longer periods of time. It's therefore important to collect data on patients' self-reported symptom burden from clinical trials. This information is relevant to inform women about the potential physical sequelae of different endocrine agents, to interpret the association between symptoms and QoL, and to symptom management.

361 INVITED

Evidence-based Management of Symptoms Related to Endocrine Treatment

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Endocrine treatment will be a major part of breast cancer therapy for postmenopausal women with hormone-sensitive early breast cancer for years to come, the safety and long-term tolerability of the treatment are therefore important considerations. Like all adjuvant therapies, endocrine treatment has symptoms and side effects associated with their use, many of which resemble symptoms common to menopause. There is a great need to support patients to tolerate and effectively manage and/or prevent these symptoms. Educating patients about anticipated symptoms and side effects may help them understand, accept, and cope with treatment long-term. This presentation reviews symptoms and side effects associated with different adjuvant endocrine treatments and highlight some strategies to manage them effectively. It also highlights the importance of patient education regarding endocrine therapy and involvement in treatment decisions, which may lead to better long-term adherence and ultimately to better outcomes.

362 INVITED

Identification and Management of Treatment-Related Symptoms for Breast Cancer Patients Receiving Adjuvant Endocrine Therapy

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Data from several multi-national clinical trials have demonstrated that adjuvant endocrine treatment significantly reduces the risk of recurrence and death in women with ER+ breast cancer. It is however difficult to determine which patients actually need treatment: many with early stage disease will be cured of their cancer by adequate surgical and radiation therapy. Consequently some women may receive adjuvant hormone therapy for 5−10 years and experience considerable iatrogenic harms without deriving any discernable benefit. Some of the rarer harms e.g. thromboembolic events and endometrial cancer maybe life-threatening. More commonly experienced harms that are quality of life threatening include: vaso-motor complaints, loss of libido, vaginal dryness and arthralgias. If these are left untreated they can compromise adherence to therapy. We need to minimise the impact of these troublesome side-effects by careful monitoring and prompt implementation of ameliorative interventions. Some of the methods for managing symptoms are reviewed and areas that demand more research to demonstrate efficacy will be outlined.

363 INVITED

Non-compliance in the Adjutant Endocrine Treatment of Women With Breast Cancer

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Enhanced therapeutics and treatment options have improved outcomes of patients with endocrine responsive early breast cancer. Contribution from both physicians and patients is necessary to translate this progress for the overall population into benefit for the individual patient. To ensure the latter one, potential and actual adverse events and respective management options as well as the importance of compliance need to be addressed and discussed openly with empathy and self confidence before and during the course of therapy.
Oral therapies are used increasingly in the treatment of all cancers, especially breast cancer accommodating most women's preferences for tablet therapies. For that reason, patient compliance with recommended treatment is crucial to successful outcomes. However, a 2003 study among 2,378 women with early stage breast cancer revealed that overall adherence to tamoxifen decreased to 50% by the fourth year of therapy. These results were confirmed by more recent studies for patients prescribed tamoxifen or anastrozole. Reasons for non-adherence

are diverse and may include side effects, duration of treatment, poor patient education about the benefit of treatment, and forgetting to take drugs. Communicating possible side effects that affect quality of life and offering respective management options will help patients being prepared for these events and curb the influence on daily life. In the context of adjuvant endocrine therapy menopausal symptoms and arthralgia/myalgia may be more relevant to the patient's perception of tolerability than the effect on bone mineral density. Proactive communication can credibly inform that these events have also been reported by a large number of patients in the placebo arm of a clinical trial (MA.17 n = 5170, hot flashes: 54% vs.58% placebo vs. AI, arthralgia: 21% vs. 25%, and although this does not change the symptoms it illustrates that non-adherence with therapy is not an effective strategy either.
Conclusions: Although accommodating patients' preferences, oral therapies are associated with a disturbingly high rate of non-adherence. With the increasing number of oral treatment options and the increasing duration of therapy adherence is vital to effective therapy. Hereby it is essential to communicate how adjuvant therapy works, the impact of non-adherence on the risk of recurrence, and of course the potential side effects of therapy together with management options minimizing the impact on daily life.

Scientific Symposium (Tue, 27 Sep, 09:00−11:00)
Partial Breast Irradiation

364 INVITED

Clinical Radiobiology of Partial Breast Irradiation

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During the last decades, the conceptual approach to breast cancer treatment has shifted from radical mastectomy to local treatment that preserves the breast and axillary lymph nodes along with adjuvant systemic therapy. Breast-conserving surgery followed by postoperative whole breast external beam radiotherapy is now the standard of care for suitable patients with early breast cancer. External beam radiotherapy is a safe and effective treatment; the risk of side-effect is low. However, despite its many positive benefits, radiation therapy is also associated with some disadvantages, the foremost of which is perhaps the fact that it is a relatively complex and expensive treatment. Although many studies have failed to identify a subgroup of patients in whom radiotherapy can be completely avoided, whether irradiation of the whole breast is necessary in all or a subgroup of patients remains unclear. An important rationale for considering less than whole-breast treatment concerns the patterns of breast tumour recurrence in patients treated with breast conservation without adjuvant radiation therapy. Data from clinical trials suggest that of the 30% of patients who experience breast tumour recurrence when radiation therapy is not delivered, the vast majority (approximately 80%) will have the recurrence develop at the site of the original disease. In addition, the absolute percentage of recurrences that develop in a location far away from the tumour bed ist low, ranging from 3% to 5%. From these data, many researchers have hypothesized that treatment directed solely to the site of the primary tumour may be adequate. Therefore, partial breast irradiation (PBI) utilizing irradiation of the tumour bed with an associated margin in early breast cancer patients is being investigated. A number of methods of PBI exist: 1) External-beam radiotherapy (EBRT) 2) Intraoperative radiotherapy (IORT) 3) Brachytherapy. Irrespective of modality, the majority of treatments are prescribed using hypofractionated accelerated courses, which are termed accelerated partial breast irradiation (APBI). Determining the dose used and the expected toxicity for each modality requires knowledge of the radiobiologic concepts of both the tumour and the technique used. Understanding the radiobiological principles behind the different APBI techniques enables a more informed prediction of disease control and toxicity and enables quantitative comparisons between techniques and regimens. Patients vary in their response to a specific course of radiation. In the future, translational research may give us the ability to identify genotypic and phenotypic factors, which may enable us to predict which APBI technique may prove more suitable for an indivual patient.

365 INVITED

Partial Breast Irradiation With External Beam Radiotherapy

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Over the past ten years a increasing number of papers have been published detailing various approaches of Partial Breast Irradiation (PBI), utilizing accelerated fractionated external beam radiation therapy or single dose intraoperative (IORT) or brachytherapy techniques. Very recently both the American and European Societies of Radiotherapy (ASTRO & ESTRO) have developed, independently, some recommendations providing a clinical guidance for the use of PBI outside the context of a clinical trial. With some minor differences, ASTRO and ESTRO guidelines proposed the selection criteria to define a low-risk group of patients, suitable to be treated. Main characteristics are age over 50 years for ESTRO (60 years for ASTRO), unifocal small ductal carcinoma (up to 3 cm and up to 2 cm, respectively) and negative axilla, wide free margins, no additional pathological risk factors such as EIC, LVI, BRCA mutation, and others. Among the different techniques used to perform PBI, external beam radiotherapy has increased rapidly in popularity. 3D-CRT and IMRT can be used safely to partially irradiate the breast. The high conformality of these techniques allows a precise targeting of the lumpectomy cavity and tumour index quadrant, with good dose homogeneity within the target volume. PBI can also be realized using external electron beam in intraoperative setting. IORT allows to realize a high radiation dose to the index quadrant, eliminating the treatment to the tissue remote from the tumour bed, and using only one single session. The comparison between the current standard for early stage breast cancer with early data coming from PBI techniques poses a dilemma as to when preliminary results are sufficiently mature to be allow practitioners and patients to consider a new treatment approach as safe. Since up to now there were few study identifying groups of patients that would benefit from this new approach, the general recommendation is not to consider this technique as the therapeutic standard for all, but to limit the use to proper selected patients. For this reason, further mature data coming from the multi- or unicenter large phase III ongoing trials in US and Europe comparing standard irradiation with the different PBI/IORT schedules and techniques will hopefully support the movement into routine clinical practice (GEC-ESTRO, NSABP B39/RTOG 0413, ELIOT, TargIT, and others). Upadted results of these will be reported and discussed, both with emerging issues of PBI, including new imaging modalities to define the target, biological profiles for selection of cases, and progress in technologies.

366 INVITED

Brachytherapy Options for Partial Breast Irradiation

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Recent years, Accelerated Partial Breast Irradiation (APBI) has been under investigation as a treatment technique to deliver radiation after breast conserving surgery to a smaller breast volume in a short treatment time. in a subset of carefully selected patients with a small risk for having tumour cells left at a distance from the primary tumour site APBI can be considered as an alternative to whole breast irradiation and boost.
Multicatheter brachytherapy is the oldest technique that has been tested as modality for APBI in a large number of phase II trials with up to 12 year follow and a phase III trial. It has demonstrated an annual local recurrence rate of 0.6% similar to whole breast irradiation but with a better cosmetic outcome. Based on this success other techniques have been developed such as single catheter balloon HDR brachytherapy ,3D conformal external beam radiotherapy or intraoperative irradiation with electron beams (ELIOT) and kilovoltage photon beam (TARGIT). From the early experience these new developments seem to be challenging, but short term follow-up data should be looked at with caution.
The Multicatheter technique with a stepping source afterloader allowing for dwell time optimization is able to deliver a very conformal treatment, limiting the treated volume strictly to the target and allowing for maximal skin sparing. The technique requires skilled and experienced radiation oncologists, with attention for details and precision.
To decrease the existing barrier against the widespread use of multi-catheter BT, the MammoSite™ device, has been promoted as technically less demanding and has become increasingly popular in the US but has been commented more critically by the European experiences. The main problems are the conformance of the balloon to the cavity and to the asymmetrical target as well as the difficulty to avoid skin toxicity when the balloon surface is at less than 15 mm beneath the skin, leading to a high rate of balloon explantation.
Therefor several new BT devices have been developed to combine the advantages of multi-catheter and MammoSite® balloon BT, blending the versatility and flexibility of interstitial BT for dose shaping with the simplicity and convenience of a single-entry device These SAVI® (Strut-Adjusted Volume Implant), the SenoRx Contura®, and the ClearPath® applicators are a marriage of the two techniques and use multiple struts, which can be differentially loaded aiming to maximize tumour bed dose and minimize normal tissue dose According to the limited experience with these hybrid breast BT applicators, skin dose can be reduced significantly without comprising PTV coverage Obviously, these applicators offer an alternative method of APBI for a selected group of patients but their short and long term efficacy has still to be proven.