Discussion: Interpretation of these results is difficult due to the heterogeneity of this group. Yet, despite the poor prognosis in these patients, many of whom already had multiple lines of treatment for their recurrent breast cancer, the combination of removal of macroscopic tumour, re-irradiation and hyperthermia appears to achieve a good locoregionaal control, at the cost of some severe toxicity.

387 PUBLICATION

Potential health economic benefits of adjuvant (A) trastuzumab (H) therapy of node-positive (N+) her-2+breast cancer (BC)

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Background: H, an established, effective therapy for patients (pts) with HER-2+metastatic (M) BC, has been reported to reduce the rate of relapse for pts with early stage BC (ESBC) by approximately 50% when combined with adjuvant (A) chemotherapy (CT) (NSABP and INT, HERA: ASCO 2005). There is a perception that AH might have serious negative health economic consequences. We attempted to analyse the potential cost implications of AH, in the context of current use of H in MBC (MH), and of predicted reduction in the risk of relapse.
Material and methods: We conducted a retrospective analysis of the mean per pt cost of AH and MH in St. Vincent's Hospital. All AH pts were treated on BCIRG 006, and received a mean of 27 cycles of AH over one year (12–18 weeks of weekly schedule, with three-weekly to completion of year). Based on published/presented data (BCIRG 001), we assumed a 35% risk for relapse at five years for pts with HER-2+, node+ BC receiving conventional ACT, and a 50% risk reduction (RR) for AH (ASCO 2005 data), providing an absolute benefit of 17.5%. We also costed the following drugs administered in standard A regimens: docetaxel (D-BCIRG 001), paclitaxel (P-CALGB 9344) and, filgrastim (G-CALGB 9741, dose-dense), and noted the following published absolute relapse reductions for these regimens: D-7%, P-5% and G-4%.
Results: We identified 50 and 63 pts who received AH/MH respectively. The following are the mean cost/per pt. for the listed agents in standard A regimens (Euro): AH −34 k, AD-8.8 k, AP-7.4 k, G-9.3 k. The mean cost per pt. for MH was 47 k. The following costs per relapse prevented (CRP) were calculated: AH-194 k (i.e. 3.4 m/17.5); P-(148 k); G-(231 k); D-126 k. In addition, in the absence of retreatment with MH, the incremental cost of AH for 100+ pts. is 1.8 m (100% × 34k = 3.4 M for AH, minus 35% × 47 k = 1.6 M) or 18 k/pt. Under this "no-re-treatment with MH" assumption, the cost per relapse prevented (CRP) for AH would equal 102 k.
Conclusions: 1) AH appears to be a relatively cost-efficient means of reducing relapses. 2) The optimal schedule of AH must be determined. 3) The efficacy of MH following prior AH must be determined. 4) It is possible that the impact and cost-efficiency of H will be greater in patients selected for HER-2+ by FISH.

388 PUBLICATION

Tumor characteristic and clinical outcome of elderly women with breast cancer

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Background: Breast cancer is major health problem in elderly women. Although the number of elderly patients with breast cancer is increasing, knowledge about possible differences in the biology and clinical outcomes of breast cancer according to age is limited.
Methods: Retrospectively were followed: tumor characteristic and clinical outcome of breast cancer treated women at the Surgical Clinic in Nis between 1990–1995. Patients were divided in two groups: study (⩾65 years) and control group (<65 years).
Results: The study involved 619 women (262 study group; 357 control group). The mean age was 74.3 years, study group, and 49.7 years control group. Ductal carcinoma was the most frequently observed histological type in (70.3% vs. 61.92%). The majority of our patients presented with early-stage disease (69.02% vs.60.20%). Estrogen receptor positive tumors occurred in 67.88% of elderly patients versus 28. 42% of young cases, and negative axillary lymph nodes were observed in 45.78% and 34.40% of patients in the elderly and young group, respectively. Modified radical mastectomy was the treatment of choice for both groups. There is no significant difference in disease-specific survival by age.
Conclusion: In our population the presentation, surgical treatment, and survival from breast cancer is similar in older and younger women.

389 PUBLICATION

Suggestions for follow-up (FU) strategies according to the risk of recurrence in patients with T1N0M0 breast cancer (BC): a single-institution experience

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Background: The risk of recurrence for early stage (T1N0M0) BC after multimodal therapies is not well defined and the FU strategies are still controversial.
Materials and methods: We retrospectively evaluated 214 T1N0M0 BC patients (pts) diagnosed at Istituto Clinico Humanitas/Cliniche Gavazzeni during April 1999-June 2003. Fifty-eight pts(27%) had T1a-b and 156 pts(73%) T1c BC. Pts characteristics(T1a-b/T1c, respectively): premenopausal 26/36%; invasive ductal 71/79%, invasive lobular 4/11%, other histology 25/10%; G1–2 90/80%, G3 10/12%; ER+ 93/88%, PgR+ 86/82%. Most pts were treated with conservative surgery(91/90%) followed by radiotherapy. In T1a-b group 4 pts(7%) received adjuvant chemotherapy vs 63 pts(40%) in T1c. Pts with ER+ and/or PgR+ received adjuvant tamoxifen(TAM) ± LHRH-analogues according to menopausal status; 8(14%) T1a-b and 43(26%) T1c pts received or switched to aromatase inhibitors due to contraindications or intolerance to TAM.
Results: At a median FU time of 34.7 mos (range 8.6–64.6) we observed 3 recurrences(5%) in T1a-b group:2 relapses in homolateral breast and 1 in chest wall with lung metastasis. In T1c group there were 7 recurrences(4%): 2 local relapses(1%) and 5 (3%) metastatic diffusions in bone (2pts), liver (1pt), supraclavicular lymphnodes (1pt) or other site (1pt). Second tumours in controlateral breast were observed in 1 (2%) T1a-b pt and 6 (4%) T1c pts. All the bone recurrences were diagnosed after bone scan for pain; lymphnode recurrence by ultrasonography(US) and fine needle agobiopsy(FNA) after clinical evidence of lymphoadenopathy; liver recurrence by routine US and confimed by FNA; lung recurrence by routine chest X-ray. All the homolateral relapse and controlateral BC were detected by routine mammography(Mx).
Conclusions: Our data show that T1N0M0 BC has a very low risk of early recurrence after multimodal therapies. At a median FU time of about 3 yrs, no differences in the recurrence rate were found between T1a-b and T1c BC, with a trend (not statistically significant) for higher incidence of distant metastases in T1c group. These observations suggest that in this group of pts early FU strategies should be targeted to detect local relapses more than distant metastases. Medical interview, physical examination, Mx and breast US are strongly recommended but there is not enough evidence to support the routine use of other diagnostic exams without specific clinical indications.

390 PUBLICATION

The implications of delaying the start of aromatase inhibitor (AI) therapy

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Background: The introduction of AIs has transformed adjuvant hormonal therapy for postmenopausal women with early breast cancer (EBC). However, debate continues as to the optimal AI administration strategy.
Methods: Initial adjuvant trials randomise patients (pts) about to begin adjuvant therapy to tamoxifen (T) or an AI for 5 years. Switching trials randomise pts partway through a 5-year course of adjuvant therapy and compare the relative efficacy of continuing with T or switching to an AI. Extended adjuvant trials enrol pts after completion of 5 years' T and evaluate the efficacy of additional therapy with an AI versus placebo or no treatment. Switching and extended adjuvant trials select pts who have already responded to 2–3 years' or 5 years' T, therefore, pts with an early recurrence will be excluded from such trials. Results from trials using an AI initially versus sequencing will not be available for several years
Results: Modelling indicates that the risk of recurrence and especially the years of life lost to recurrence are always lower over the first 10 years of follow-up when an AI is initiated first. Switching to an AI will reduce the risk of recurrence, compared with continuing on T, but even after 10 years recurrences are more likely than in those who received an AI from the outset. This is particularly apparent in the progesterone receptor (PgR)-negative subgroup, but the results are model dependent for the PgR-positive subgroup. The ATAC trial, a double-blind randomised trial, compared anastrozole with T as initial adjuvant therapy in 6241 postmenopausal women with EBC. Risk: benefit data from ATAC (68 months' median follow-up) show that, compared with T, anastrozole

prevented an excess of 40 recurrences, 17 distant recurrences and 14 deaths following recurrence during the first 2.5 years. At 5 years, these figures increased to 82, 44 and 28, respectively. In addition, anastrozole has a generally more beneficial adverse-event profile compared with T, with fewer gynaecological, ischaemic cerebrovascular and venous thromboembolic adverse events.
Conclusions: Therefore, initiating T with the intention of changing to an AI after 2 to 3 years (switching) or after 5 years (extended adjuvant) would lose these early benefits of anastrozole over T. Based on current data, offering anastrozole at the earliest opportunity appears to be the best strategy.

391 PUBLICATION

Extended role of radioguided occult lesion localization in early stage breast cancer

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Objective: Presentation of our experience in radioguided occult lesion localization (ROLL) and sentinel node biopsy with axillary dissection in early stage breast cancer.
Methods: Retrospective analysis of clinical, surgical, pathological and oncological data on patients with non-palpable breast lesions treated in Clinical Hospital Split, Croatia, within two years time period. We injected 5–10 MBq of ^{99m}Tc-labeled colloidal particles of human albumin peritumorally in 102 consecutive patients enrolled in study. The sentinel lymph node in each case was visualized by lymphoscintigraphy. During the surgery, occult breast lesion was localized using ROLL technique and the sentinel lymph node was identified and removed by monitoring the acustic signal from a hand-held gamma ray-detecting probe. Complete axillary dissection was carried out only in 56 (55%) patients with confirmed pathologic positive sentinel lymph node for micrometastasis.
Results: In all the patients non-palpable breast lesion was detected by ROLL. The sentinel lymph node biopsy was identified in 96 (95%) patients. In 56 patients complete axillary dissection was carried out due to positive sentinel node biopsy. There were 5 (5%) false-positive findings. Complication rate in all patients were extremely low (0.5%). All the patients received surgical and adjuvant therapy according to stage, menopausal and receptor status.
Conclusions: ROLL followed by sentinel lymph node biopsy using a gamma ray-detecting intraoperative probe allows detecting of occult breast lesions, one step staging of the axilla with high accuracy in patients with primary early stage breast cancer. Axillary dissection may be avoided in patients with negative sentinel node biopsy for micrometastesis. The potential benefits are several: reduced morbidity, definitive surgical treatment performed in a single procedure, improved staging and more rational and selective use of systemic therapy.

392 PUBLICATION

3-year survival of the patients with stage II breast cancer, received an adjuvant hormone therapy with Toremifene (primary results)

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Background: Long term research of Oxford Group (EBCTCG) has demonstrated that used an adjuvant hormone therapy with Tamoxifene at the patients with operable breast cancer reduced the incidences of relapses and mortality. According the data of some various trials, use of second generation antiestrogen Toremifene in the adjuvant hormone therapy allows improving results of the treatment of the treatment compared to Tamoxifene. Concerning this, the aim of our clinical research was comparative study of efficiency of an adjuvant hormone therapy with Toremifene and Tamoxifene at the patients with stage II breast cancer.
Materials and methods: 181 receptor status not considered patients with stage II breast cancer were involved in this clinical trial. Patients were divided on 3 groups. 61 patients (group I) were treated with Tamoxifene at a dose of 60 mg once daily. Adjuvant hormone therapy with Tamoxifene at a dose of 20 mg once daily was administrated in 63 patients and 57 did not receive hormone therapy. To the patients with normal ovarian function were used castrations by radiotherapy or chemical castration. Patients were treated with adjuvant hormone therapy during all term of observation after radical surgical treatment and adjuvant chemotherapy. All patients were under control no less than 3 year. Efficiency of the treatment determined with following criteria: side effects and 3-year survival without recurrence.
Results: In the first group 3-year survival was 93.4%, in the second group 82.5%, in the third group 63.2%. Study of side effects of adjuvant hormone therapy with Toremifene has demonstrated more safe toxic profile compared to Tamoxifene.
Conclusions: The result of this study had indicated higher efficiency and safe toxic profile of adjuvant hormone therapy with Toremifene compared to Tamoxifene. On the base of this data we can recommend Toremifene in adjuvant hormone therapy for the treatment patients with stage II breast cancer.

393 PUBLICATION

Toremifen in treatment of precancerous breast diseases

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Background: One of the probable mechanisms in the development of dishormonal hyperplasia and breast cancer is hyperestrogenemia on a basis of insufficiency in progesterone. We represent the treatment's results of 46 patients with diffused forms of hyperplasia by a new anti-estrogen drug Toremifen.
Material and methods: The age of women was 39–52 years, i.e. premenopausal period. The evidence of hormonal status has shown an authentic increase of estradiol in the lutheal phase, reduced contents of progesterone, and moderate hyperprolactinemia. The dose of Toremifen was 30 mg once a day, during 1 month.
Results: Clinical improvement was found in 35 patients (76.1%), in 9 patients the use of this drug was stopped, due to menstrual disorders, 2 patients had intermenstrual bleeding. A softening, reduction of intensity and decrease of pain in the breast was marked. Hormonal status has shown authentic decrease in estradiol, increase in progesterone in the second phase of the menstrual cycle, however compensational increase of prolactin was noted. In 2 patients with tendention to located forms of hyperplasia, a decrease of focal condensation to complete disappearance was marked in 4 cases. In ultrasonic examination of the breast we have noted a reduction in the density of fibrotic component, reduction in diameter of small cystical formations. The clinical effect of one month's treatment with Fareston lasts 3 to 4 months.
Conclusions: We would like to emphasize that the high efficacy and good tolerance of Toremifen make it possible to administer such drug in the combined treatment of mastopathy in women with survived menstrual-ovarian function.

394 PUBLICATION

Efficiency of Toremifen in the treatment of diffuse mastopathy

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Background: Diffuse mastopathy is the most common disease of breast of women. By the data of various authors the frequency of mastopathy occurs at the reproductive females is 24–40%. The rate of annual morbidity increase is 8–10%. The pathogenetical treatment of diffuse mastopathy is therapy with hormonal drugs. The aim of the research was comparative study of efficiency of Toremifen in the complex therapy of patients with diffuse mastopathy.
Materials and methods: 254 patients with diffuse mastopathy were involved in this trial. Patients were divided on 2 groups. Patients of first group (n = 136) were treated with Toremifen at a dose of 20 mg once from 5th to 25th day of regular menstrual cycle or daily with impaired menstrual function and in menopause. The patients of second group (n = 118) were treated by phytotherapy. Duration of treatment in both group patients was 6 months. Efficiency of the treatment was determined with following criteria: dynamics of pain syndrome and changes of mammagraphic density of breast.
Results: In the group of patients treated with Toremifen 122 (89.7%) patients had complete response, which was defined as the disappearance of any pain, 14 (10.3%) had reduction of pain. In the group of patients treated by phytotherapy, results were following: 22 (18.7%) patients had complete response, which was defined as the disappearance of any pain, 64 (54.2%) had reduction of pain, 32 (27.1%) had no response. The dynamics of changes of mammagraphic density in breast was following: in the first group 92 (67.6%) patients had the normal mammography, 29 (21.3%) patients had reduction of indurations, 15 (11.1%) patients had no changes in mammography. The results of second group patients were following: 11 (9.3%), 25 (21.2%) and 82 (69.5%) patients respectively.
Conclusions: The results of our study had demonstrated high efficiency of Toremifen compared to phytotherapy in the treatment of diffuse mastopathy.