NEWSROUND

Selected press reports compiled by the ESO Cancer Media Centre

Assertive patients get better treatment

→ Journal of Clinical Oncology

Women who take greater control over choosing their breast cancer surgeon are more likely to be treated by more experienced breast surgeons and at a hospital affiliated with an accredited cancer programme, compared to women who are referred by another doctor or their health plan, according to a recent study.

A total of 1,844 women were surveyed about how their breast surgeon was selected, with choices such as 'I was referred by another doctor,' 'I chose this surgeon because of his or her reputation' or 'I wanted a surgeon who practiced near my home.'

Nearly two-thirds of the patients said they were referred to their surgeon by another doctor, with another 15% referred by their health plan. About a quarter chose their surgeon based on reputation – women with more education and higher incomes were more likely to be in this group.

The researchers found that only a third of the women were treated by a high-volume surgeon, defined as one with more than 50% of their practice devoted to breast cancer surgery. Two-thirds of the women were treated in hospitals designated as cancer centres by the National Cancer Institute or the American College of Surgeons.

Women who said they chose their own surgeon were twice as likely to see a highly experienced surgeon as were those referred by another doctor or by their health plan.

Commenting on the findings, author Steven Katz said, "Women with breast cancer should be aware that referrals from another doctor or their health plan may not connect them with the most experienced surgeons or the most comprehensive practice settings in their community. Patients might consider seeking a second opinion, especially if they are advised to undergo a particular treatment without a full discussion of the options."

■ Patterns and correlates of patient referral to surgeons for treatment of breast cancer. SJ Katz, TP Hofer, S Hawley et al. *J Clin Oncol*, 20 January 2007, 25:271–276

New tool to screen for ovarian cancer

→ Cancer

A symptom survey may provide doctors with a quick and cost-effective screening tool to detect early-stages of ovarian cancer, according to a new study. The findings reveal that early ovarian cancer may be identified by a specific set of symptoms, their frequency and duration.

Ovarian cancer is often misdiagnosed by general practitioners. There is no effective screening test to detect early-stage disease in the general population or in high-risk groups. The lack of recognised, early clinical signs and symptoms delays diagnosis until the disease is advanced. These factors combine to make ovarian cancer one of the deadliest malignancies in the world.

Recent evidence suggests that early-stage symptoms may be recognisable and could be used to develop a symptom index for early disease. Researchers led by Barbara Goff, of the University of Washington School of Medicine and the Fred Hutchinson Cancer Research Center in Seattle, compared the clinical history of women at high risk for developing ovarian cancer with that of women already diagnosed with ovarian cancer, to develop a basic symptom index.

They found "that a relatively simple evaluation of symptoms of recent onset and significant frequency" was sufficient to function as a potential screening tool. The symptom profile of 'any complaint of pelvic/abdominal pain, increased abdominal size/bloating, or difficulty eating/feeling full, that is present more than 12 days per month and for less than one year' was found to be present in 57% of cases of early disease and 80% of advanced cancers (sensitivity). Ovarian cancer was present in 90% of women over 50 years of age who identified these symptoms and in 86.7% of women under 50 years of age (specificity).

Goff plans to evaluate a simple three-question screening in a multi-year study in general clinical practice. Sherry Salway Black, from the Ovarian Cancer National Alliance in Washington, DC, explains in an accompanying editorial that, "a symptom index is only one of a number of promising research tracks the ovarian cancer advocacy community actively supports." Although years away, the development of a screening blood test would be "the real key to early detection". She continues, "Until there is a valid screening test, the symptom index could serve an important role in detecting cancers, and after a test is identified, the index could be a tool used in combination with other methods to

contribute to early detection."

In the meantime, health organisations need to continue to educate women and physicians about the symptoms of ovarian cancer. Awareness of the symptoms offers women the best hope for early detection and successful treatment of the disease.

■ Development of an ovarian cancer symptom index: possibilities for earlier detection. BA Goff, LS Mandel, CW Drescher et al. *Cancer* 15 January 2007, 109:221–227

Eating less fat may cut risk of breast cancer recurrence

→ JNCI

Women who have been treated for early-stage breast cancer may lower the chance of their cancer recurring if they reduce the amount of fat in their diet, according to a recent study.

Lead author Rowan Chlebowski, at the Los Angeles Medical Center in California, and his colleagues conducted a trial to determine whether a low-fat diet could prolong disease-free survival in women who had had early-stage breast cancer.

Between February 1994 and January 2001 nearly 2,500 women who had been treated for early-stage breast cancer were enrolled in the trial. Forty percent of the women were randomly assigned to a dietary intervention group and 60% made up the control group. Data were collected until 31 October 2003, a median follow-up of 60 months.

The goal of the women in the intervention arm was to reduce their dietary fat to just 15% of their total calorie intake. They attended counselling sessions twice a week for eight weeks and kept records of their daily fat intake. Dieticians contacted or met with the women every three months and the women could attend optional monthly dietary group sessions. The control group met with a dietician when they started the trial and were contacted by dieticians every three months.

At the beginning of the study, both groups consumed 56–57 g fat per day. After one year, the women on the diet consumed an average of 33 g per day, while the control group consumed 51 g per day). The two groups' body weight was similar at the beginning of the trial. Five years later, the women on the diet weighed an average of six pounds less than the women in the control group.

Women in the dietary intervention group had a 24% lower risk of relapse than those in the control group. Nearly 10% of women on the diet had some form of recurrence compared to 12% of the women in the control group. The researchers concluded that a lifestyle intervention designed to reduce dietary fat intake may improve relapse-free survival of breast cancer patients receiving conventional cancer management.

■ Dietary fat reduction and breast cancer outcome: interim efficacy results from the Women's Intervention Nutrition Study. RT Chlebowski, GL Blackburn, CA Thomson et al. *JNCI* 20 December 2006, 98:1767–76

Trastuzumab improves early survival in HER2+ breast cancer

→ The Lancet

Treatment of women with HER2-positive breast cancer with trastuzumab (Herceptin) for one year following standard chemotherapy can improve survival according to the two-year follow-up data of the HERA (Herceptin Adjuvant) study, which was published recently in the *Lancet*.

A total of 1,703 women were randomised to receive treatment with trastuzumab for one year after surgery and chemotherapy, and 1,698 women were assigned to the control group (observation only). After two years of follow-up it was found that more deaths occurred in the observation group than in the group of women treated with trastuzumab (90 versus 59), which corresponds to an absolute survival benefit of 2.7% (92.4% vs 89.7%) after three years.

Of the 172 women who stopped trastuzumab early, only 115 (6.8%) stopped because of safety issues. There were no cardiac deaths in the trastuzumab group; however, severe and symptomatic congestive heart failure occurred in more women on trastuzumab than in the observation group. Seventy-two women (4.2%) discontinued trastuzumab because of heart problems.

According to the paper's main author Ian Smith, from the Royal Marsden Hospital in London, "The survival benefit that has emerged over such a short period emphasises the potential of this approach and underlines the importance of developing further specific targeted therapies in breast and other cancers."

■ Two-year follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer: a randomised controlled trial. I Smith, M Procter, RD Gelber et al. *Lancet* 6 January 2007, 369:29–36

Gemcitabine can delay pancreatic cancer recurrence

→ JAMA

A recent study has shown that adjuvant use of gemcitabine can significantly delay the recurrence of pancreatic cancer following surgery. Helmut Oettle, from the Charite School of Medicine, Berlin, Germany, and colleagues, conducted an open-label, randomised, controlled trial that compared the use of gemcitabine with observation in 368 patients who had undergone complete surgical resection for their pancreatic cancer (R0 or R1) and received no prior chemotherapy or radiotherapy. Patients in the gemcitabine arm received, on average, six cycles of treatment.

More than 80% of the patients had gross complete resection of their pancreatic cancer. With a median follow-up of 4.5 years, cancer had recurred in 74.3% of patients in the gem-

citabine group and 92% of patients in the control group. The median disease-free survival was 13.4 months and 6.9 months in the control group. Grade 3 or 4 toxicities rarely occurred and there was no difference in quality of life between the two groups.

Subgroup analyses showed that the effect of gemcitabine on disease-free survival was significant in patients who had had a gross complete surgical resection. However, there was no difference in overall survival between the gemcitabine group (median, 22.1 months) and the control group (median, 20.2 months).

The authors concluded that adjuvant gemcitabine offers a good, and currently perhaps the best, chance for delaying the development of recurrent disease in patients who have undergone certain types of surgical resection for pancreatic cancer.

An accompanying editorial pointed out that "It is unlikely that these small steps alone will provide the necessary enhancements of benefit beyond the improvements in surgery to profoundly alter the course of this most challenging of cancers."

■ Adjuvant chemotherapy with gemcitabine vs observation in patients undergoing curative-intent resection of pancreatic cancer: a randomized controlled trial. H Oettle, S Post, P Neuhaus. *JAMA* 17 January 2007, 297:311–313

IARC issues warning on rising cancer burden

→ IARC

The latest figures released by the International Agency for Research on Cancer (IARC), and published online in the Annals of Oncology, reveal that 3.2 million new cases of cancer were diagnosed in Europe in 2006. The equivalent figure for 2004 was 2.9 million, indicating a rise of 300,000 new cases over the two-year period.

IARC director Peter Boyle, who prepared the report with colleagues, warned that despite better prevention and treatments, Europe faces a major increase in the cancer burden because of the ageing population. He said urgent action is needed now to tackle cancer, particularly in Central and Eastern Europe.

Breast cancer incidence has increased by 16% since 2004. It has now overtaken lung cancer as the most common cancer diagnosis, with 429,900 new cases reported in 2006 (13.5% of all cancer cases). Though much of this increase is due to better early detection, death rates continue to rise.

The number of new cases of colorectal cancer rose to 412,900 (12.9% of all cancer cases), making this the second most common cancer in Europe. Colorectal cancer remains the second biggest killer, with mortality rates increasing by 1.8% since 2004.

Lung cancer is now the third most common cancer diagnosis, with 386,300 new cases reported in 2006 (12.1% of all cancer cases); however, it remains the biggest killer.

Commenting on the report, Boyle said, "urgent action is particularly vital now to take preventive action against cancer, especially in Central and Eastern Europe, with strong and effective measures to curb the tobacco epidemic and more widespread screening programs for breast, cervix and colorectal cancers."

■ IARC press release no 174, www.iarc.fe, and Estimates of the cancer incidence and mortality in Europe in 2006. J Ferlay, P Autier, M Boniol et al. Ann Oncol published online 7 February 2007, doi:10.1093/annonc/mdl498

Zoledronic acid can protect against bone loss from hormone treatment

→ Journal of Clinical Oncology

Two recently published studies suggest that zoledronic acid can prevent loss of bone mineral density (BMD) in both pre- and post-menopausal women. BMD loss is a side-effect of aromatase inhibitors, which are used to treat early hormone-receptor-positive breast cancer in post-menopausal women, leaving them more susceptible to bone fractures. The results could therefore be important to this group of patients.

In one of these studies, known as Z-FAST, scientists looked at the effect of adding zoledronic acid to adjuvant endocrine therapy with the aromatase inhibitor letrozole, to see whether this protected against loss of BMD.

A total of 602 post-menopausal patients receiving treatment with letrozole were randomly divided into two groups. The first group was given zoledronic acid from the beginning of their letrozole treatment. The second group was given a delayed dose of zoledronic acid after their BMD had reduced (when lumbar spine or total hip T score decreased to less than –2.0 or when a non-traumatic fracture occurred). The researchers measured the BMD in the lumbar spine and hip to compare the results.

The study found that after 12 months the lumbar spine BMD was 4.4% higher in the group that received zoledronic acid straight away compared to the delayed group, and total hip BMD was 3.3% higher. The upfront group also had less enzymes, which show up active bone disease, whereas concentrations of these enzymes increased significantly in the delayed group. The authors concluded that within one year of follow-up, results indicate that upfront zoledronic acid therapy prevents BMD loss in the lumbar spine in post-menopausal women receiving adjuvant letrozole for early-stage breast cancer.

The other study looked at using zoledronic acid to prevent bone loss associated with adjuvant hormone therapy in pre-menopausal women – a group of patients in whom use of aromatase inhibitors is still under evaluation. This randomised phase III trial compared tamoxifen plus goserelin with or without zoledronic acid against anastrozole plus goserelin with or without zoledronic acid for three years in pre-menopausal women with hormone-responsive breast cancer.

A total of 401 patients underwent BMD

measurements at intervals throughout the three-year period. The results showed that hormone treatment without zoledronic acid led to significant overall BMD loss after three years of treatment. The loss was significantly greater in patients receiving anastrozole/goserelin compared with patients receiving tamoxifen/goserelin.

However, BMD remained stable in both groups of patients treated with 4 mg zoledronic acid every 6 months. No interactions with age or other risk factors were noted. The authors conclude that patients undergoing hormone therapy should have regular BMD measurements, and zoledronic treatment should be considered for patients experiencing bone loss.

■ Zoledronic acid inhibits adjuvant letrozole-induced bone loss in postmenopausal women with early breast cancer. A Brufsky, WG Harker, JT Beck et al. *J Clin Oncol* published online 11 December 2006, doi: 10.1200/ JCO.2005.05.3744 Zoledronic acid effectively prevents cancer treatment-induced bone loss in premenopausal women receiving adjuvant endocrine therapy for hormone-responsive breast cancer: a report from the Austrian Breast and Colorectal Cancer Study Group. MFX Gnant, B Mlineritsch, G Luschin-Ebengreuth. *J Clin Oncol* published online 11 December 2006, doi: 10.1200/JCO.2005.02.7102

ICMJE trial registration standards starting to pay off

➜ New England Journal of Medicine

Eight percent of the 2,983 clinical trials sponsored by pharmaceutical companies in 2006 and entered into the ClinicalTrials.gov website did not include information on the outcomes being measured, compared with 26% of 5,355 trials registered prior to 2006, according to an editorial published recently in the *New England Journal of Medicine*. In 2006, none of the filings omitted the name of the drug being tested, compared with a small number that excluded drug names from the registry before 2006.

The editorial, written by *NEJM* Editor in Chief Jeffrey Drazen and Deborah Zarin of the National Library of Medicine, praised the increase in quality of registration but called for researchers to avoid registration duplication. Evidence of such duplication came to light after an article about the treatment of renal cancer with sunitinib was considered for publication by the *NEJM*.

The journal's staff routinely check the quality of registrations in ClinicalTrial.gov to see whether they meet the standards set by the International Committee of Medical Journal Editors (ICMJE). The registration for the sunitinib study did not meet these standards because information filed by the study's sponsor Pfizer was missing from the outcome-measured field.

However, further investigation revealed that one of the co-authors had also registered the trial through one of the cancer centres. This second registration did meet the ICMJE standards.

The editorial sent a message to investigators: "Before you enrol a patient in a study, be sure that there is a full and appropriate registration of the trial in a public database approved by the ICMJE (www.icmje.org). It could salvage a study report that otherwise would not be published."

■ Salvation by registration. JM Drazen, DA Zarin. *New Engl J Med* 11 January 2007, 3562 184–185

Radiotherapy cuts risk of recurrence after breast-conserving surgery

➜ Cancer

Radiotherapy after breast-conserving surgery for breast cancer reduces recurrence and prevents development of additional breast tumours in older women with early-stage breast cancer, according to a new study. The findings also suggest that women benefit from the recommended five years of tamoxifen treatment for hormone responsive tumours.

Women over 65 are at highest risk for breast cancer and make up half of those diagnosed. However, they are less likely than younger women to receive standard therapy, particularly radiotherapy after breast-conserving surgery. Making treatment recommendations for older patients is complicated because of the under-representation of older women in clinical trials and prognostic studies.

A total of 1,837 women over 65 years of age who were operated for early-stage breast cancer were followed for 10 years to examine the impact of choice of treatment on the occurrence of recurrent and additional breast tumours.

The researchers found that, regardless of age or comorbidities, women who underwent breast-conserving surgery but no radiotherapy were more likely to have recurrence of disease or develop additional breast tumours compared to women who received breast-conserving surgery and radiation or mastectomy alone. The risk was highest for local and regional recurrence. These results held, regardless of whether the women were treated with tamoxifen, suggesting that adjuvant radiation treatment was highly effective.

The researchers also found that women who received less than one year of tamoxifen were more likely to have disease recurrence or develop additional breast tumours compared to women who completed the recommended five-year course.

Based on these study findings, the authors recommend that mastectomy or breast conserving surgery with radiation therapy, along with adequate duration of adjuvant hormonal therapy for hormone-responsive tumours, be considered standard therapy in women of all ages and comorbidities, excepting those with very limited life expectancies.

■ Recurrences and second primary breast cancers in older women with initial early-stage disease. AM Geiger, SS Thwin, TL Lash et al. *Cancer* published online 22 January 2007, doi: 10.1002/cncr.22472