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The American way of funding for cancer research saves lives. Where are the Europeans?

The American way to make progress against cancer is neither new nor sophisticated but is extremely successful: more money in cancer research – more lives saved. More from the American Society for Clinical Oncology 2009 meeting can be obtained free via the website by reading the daily news [1].

Cancer is a common disease. The probability that a person will be diagnosed with cancer in his or her life time is approximately one in two for men and one in three for women. No doubt, past investment in cancer research has led to significant advances in preventing, detecting and treating the disease. In the US the cancer death rate decreased by an average of 1.1% a year from 1993 to 2002 and by an average of 1.8% from 2002 to 2005. The 5-year relative survival rate for all cancers diagnosed between 1996 and 2004 was 66%, up from 50% between 1975 and 1977. After years of robust investment funding for cancer research in the US there are today more than 11 million cancer survivors in the US – up from just three million in the 1970s – and cancer death rates have dropped 18% among men and 10% among women since the early 1990s.

Robust investment in budgets of the National Institutes of Health and National Cancer Institute helps:

- **tailor treatments in elderly cancer patients** (two out of three cancer patients are older than 65 years, have decreased organ function and suffer simultaneously from significant comorbidity. Thus, it is important to **personalise standardised cancer care**) and
- **identify patients who are most likely to benefit** from particular treatments, while avoiding undesired treatment effects and costs in the others.

Many results of this public funding of cancer research are published annually at the American Society of Clinical Oncology (ASCO) meeting. Unfortunately, in most parts of Europe we do not give the same support to funding of cancer research. In comparison to the US the survival rate of cancer patients in Europe is significantly lower. We do not even know how low in some parts of Europe. This is why we should pay attention to the results presented at the ASCO meeting.

Lung cancer

Pemetrexed as maintenance therapy extends survival. A phase III study reports (663 patients) that maintenance therapy with pemetrexed (Alimta) improves survival (13.4 months versus 10.6 months) in non-squamous forms of advanced non-small cell lung cancer. Patients with the squamous subtype do not benefit. Pemetrexed is currently approved as a first-line



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treatment for advanced or metastatic non-squamous non-small cell lung cancer in combination with cisplatin and as a single agent in patients with recurrent disease (Belani et al. Abstract # CRA 8000).

Two targeted therapies are superior to one alone in maintenance therapy. A phase III trial finds that adding erlotinib (Tarceva) to bevacizumab (Avastin)-based maintenance therapy in patients with advanced or metastatic non-small cell lung cancer

delays cancer more than maintenance treatment with bevacizumab alone (Miller et al. Abstract # LBA8002).

Novel therapy that targets two receptors benefits patients with advanced lung cancer. A phase III trial (1,391 patients) demonstrates that vandetanib (Zactima), a novel drug that targets two key receptors associated with lung cancer growth, improves progression-free survival in patients with advanced non-small cell lung cancer (Herbst et al. Abstract # CRA8003).

Oestrogens and progestins linked to increased risk of death in women with lung cancer who are having menopausal hormone therapy. A secondary analysis from the Women's Health Initiative reports that use of hormone therapy with oestrogens plus progestin increases the risk of dying from non-small cell lung cancer for women with the disease (Chlebowski et al. Abstract # CRA1500).

Gastrointestinal cancers

Octreotide LAR significantly prolongs time to progression in metastatic neuroendocrine mid-gut tumours. The phase III trial (89 patients) finds that the IM injection of 30 mg octreotide (Sandostatin) every four weeks prolonged the median time to progression to 14.3 months compared to six months (placebo). The median overall survival is at present longer than 77.4 months (placebo 73.7 months).

First-ever data shows **bevacizumab as adjuvant therapy of no benefit** in UICC stage II and III colon cancer. A phase III trial (2,720 patients) finds that adding the targeted therapy bevacizumab (Avastin) to standard adjuvant FOLFOX6 chemotherapy did not improve disease-free survival for patients with locally advanced colon cancer (Wolmark et al. Abstract # LBA4).

Adjuvant treatments for pancreatic cancer compared. A phase III study comparing the adjuvant treatments most commonly used for pancreatic cancer in Europe and the US (gemcitabine and 5FU/Folinic acid, respectively) found that there is no difference in survival between the two regimens, though gemcitabine was associated with fewer side effects (Neoptolemos et al. Abstract # LBA4505).

The current standard is supported for anal cancer. The largest study to date confirms continuous radiation combined with 5FU and mitomycin-C chemotherapy. A phase III trial (940 patients) finds that this current standard treatment for anal cancer should not be changed and that maintenance therapy (cisplatin and 5FU) after initial treatment is not effective (James et al. Abstract # LBA4009).

Local tumour control is not improved by adding oxaliplatin (Eloxatin) to preoperative chemoradiotherapy for locally advanced rectal cancer. A preliminary analysis suggests the treatment may reduce distant metastases, however. In this phase III trial, 747 patients with locally advanced rectal cancer were randomised to receive standard preoperative chemoradiotherapy (50.4 Gy in 28 daily fractions and 5FU 225 mg/m²/day) or the standard plus oxaliplatin (+ weekly 60 mg/m² x 6 (Aschele et al. Abstract # CRA4008).

Trastuzumab improves survival for patients with HER2-positive locally advanced, recurrent, or metastatic gastric cancer. Among patients with gastric cancer tumours that express high levels of the HER2 protein, those who received trastuzumab (Herceptin) plus chemotherapy (5FU or capecitabine and cisplatin) lived significantly longer than patients who received standard chemotherapy alone, with a 26% reduction in the risk of death. In this large phase III trial (3,807 patients) median overall survival was 13.8 months in the trastuzumab group versus 11.1 months in the chemotherapy only group (Van Cutsem et al. Abstract # LBA4509).

Breast and gynaecological cancers

New class of targeted therapy: PARP inhibitors. Two new studies reported results on the effect of so-called PARP (Poly (ADP-Ribose) Polymerase) inhibitors on traditionally difficult-to-treat breast cancer, what is known as ‘triple negative’ (ER, PR, HER2 negative) breast cancer.

Cancer cells use the PARP enzyme to repair DNA damage, including the damage inflicted by chemotherapy drugs. The first study, a randomised phase II study (86 patients) shows that women with metastatic triple-negative breast cancer who received the investigational PARP inhibitor BSI-201 in combination with conventional chemotherapy (gemcitabine plus carboplatin) lived significantly longer and experienced significantly better progression-free survival than women who received standard chemotherapy alone. Approximately 62% of patients receiving BSI-201 showed clinical benefit compared with 21% in the chemotherapy-only group. The overall

response rate to treatment with the drug combination containing BSI-201 was significantly greater (48%) than in the group receiving only chemotherapy (16%). Women who received BSI-201 had a median survival of 9.2 months compared with 5.7 months in women who received chemotherapy alone (O’Shaughnessy et al. Abstract # P3).

The other study, a small phase II trial on 54 patients with BRCA-deficient breast cancer, showed that PARP inhibitor olaparib induces tumour response as single agent. Tumours that arise in patients with BRCA mutations have a defect in their ability to repair DNA. By adding olaparib, the tumour cells are deprived of another DNA repair mechanism. It is thought that this added inhibition of DNA repair with olaparib then leads to cancer cell death. In this study, 40% of the patients responded to olaparib. Olaparib was well tolerated, with the common side effects being mild fatigue, nausea and vomiting (Tutt et al. Abstract # CRA501).

Adding gemcitabine to chemoradiation improves survival in women with locally advanced cervical cancer.

A phase III multicentre study (259 patients) showed that adding gemcitabine (125 mg/m² weekly x 6 doses with concurrent radiation and then two adjuvant 21-day cycles at day 1 and 8 at a dose of 1,000 mg/m²) to a regimen that includes cisplatin (50 mg/m² on day 1), radiation (50.4 Gy in 28 fractions) and brachytherapy (30–35 Gy) extends overall survival among women with locally advanced cervical cancer. Brachytherapy is radiation treatment given by placing radioactive material directly in or near the target, which is often a tumour.

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