Are We Winning The War on Cancer?
A 40-year retrospective review of progress in the treatment of stage IV disease
Ralph W. Moss, PhD
International Clinical Hyperthermia Society
Budapest, October 2012
Launching the War…1971

- “A national crusade to be accomplished by 1976 in commemoration of the 200th anniversary of our country.”
  
A Statistical Review of Malignant Testicular Tumours Based on the Experience of the Ontario Cancer Foundation Clinics, 1938-1961

Testicular Tumors 2012

- Testicular cancer: our experience after 10 years.
- Arch Esp Urol. 2012 May;65(4):467-475

Two-thirds of the cases were detected in Stage I, and 100% of these cases showed complete remission.

Among those with higher stage tumors, two out of three patients were cured after chemotherapy. For the remaining one-third, rescue treatments managed to achieve a remission rate of 66%.
Curing Metastatic Cancers in the 1970th

- Testicular
- Hodgkin’s
- NHL
- Leukemias
- Childhood Tumors (Wilm’s, Osteogenic Sarcomas)
- Choriocarcinoma
In the last 35 years there is no one tumor type that was cured while is metastatic.
Progress in the War on Cancer?

- Reduction in cigarette smoking
- Pap test for cervical cancer
- Better molecular markers
- Secondary prevention, e.g. breast cancer
- Less disfiguring surgery
Are we winning the war?

- “Remarkable progress”
  *(Time, Nov. 8, 1982)*

- “We’ve made progress…but we still have a far way to go before we can declare victory.”

- “The challenges of defeating cancer appear ever more daunting…”
  *(Susan Gapstur, PhD and Michael Thun, MD, American Cancer Society, 2010)*
Overall trend in cancer mortality is down slightly

The joinpoint trend in US cancer mortality with associated APC(%) for cancer of all sites between 1975-2007, All Races

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<thead>
<tr>
<th>Male and Female</th>
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Stage IV colon cancer

- “Unresectable metastatic colorectal cancer is generally not curable with current technology.”
- Likelihood of benefit in a poor performance status patient is substantially diminished, and the likelihood of a serious adverse event is greatly increased.
- “It is a source of frustration and humility for investigators ... that over 50 years later [5-FU] remains at the very core of most chemotherapeutic approaches to colorectal cancer.”
Colon CA: CORRECT Trial

- Regorafenib is a new oral multi-kinase inhibitor from Bayer. CORRECT randomized trial = regorafenib + BSC vs. placebo + BSC
- Median overall survival = 6.4 mos for regorafenib and 5.0 mos for placebo
- Median progression-free survival was 1.9 mos for regorafenib vs. 1.7 mos for placebo
- Overall response rate was 1.6% for regorafenib vs. 0.4% for placebo
- Bayer is banking on drug “to be one of the future standouts in its portfolio of cancer medicines...eyeing the program to yield blockbuster returns on the company's R&D investment.” (Fiercebiotech 2012)
- Bayer expects drug will eventually top more than $1 billion in yearly revenue.

Grothey, Axel. Results of a phase III randomized, double-blind, placebo-controlled, multicenter trial (CORRECT) of regorafenib plus best supportive care (BSC) versus placebo plus BSC in patients (pts) with metastatic colorectal cancer (mCRC) who have progressed after standard therapies. J Clin Oncol 30, 2012 (suppl 4; abstr LBA385)
Top 10 Late-Stage Cancer Drugs – 2012; Fiercebiotech.com
Phase III trial-Pancreatic cancer median survival

- Gem + Tarceva = 6.37 months
- Gemzar = 5.91 months
- Moore et al

**The difference in survival = 2 weeks**
Survival in brain cancer

Glioblastoma multiforme (brain cancer)

- “In a landmark international trial, patients were randomized to radiotherapy with or without concurrent and adjuvant temozolomide. Median and 2-year survival were increased by 2.5 months and 16.1%, respectively…”

- “A randomized phase 2 trial of temozolomide versus procarbazine in 225 patients with GBM at first relapse demonstrated that treatment with temozolomide improved median progression-free survival (12.4 weeks vs. 8.3 weeks). Radiographic responses were disappointing (5.4% vs. 5.3%).

(DeVita, et al. Cancer, 9e, 2011, ch. 121)
● Comparison of trial results to EORTC "showed median survival was 15.8 months vs. 14.6 months…” Results show that only < 50% of GBM patients complete standard of care in the real-world setting and prognosis remains dismal for patients who do not receive CRT.”

Brain Tumors (GBM)

- Hyperthermia
- Alovera
- Artemisinin
- Boswellia Serata
- Bromelein
- Cat's Claw
- Chrysin
- Dichloroacetate (DCA)
- Curcumin
- D3
- D-Alpha Tocopherol Succinate
- G.L.A
- Green Tea
- ISCADOR
- IP-6
- Melatonin 20 mg
- M.S.M
- Newcastle Disease Virus
- Noscapine
- Quercetin Complex
- Resveratrol
- Ascorbic Acid
In patients with stage IV breast cancer previously treated with an anthracycline and a taxane:

- Addition of Avastin (bevacuzumab) to Xeloda (capecitabine) (Xeloda) increased response rates from 9.1 to 19.8%
- This did not result in longer progression-free survival (4.86 v 4.17 months).
- Overall survival was 15.1 with Avastin vs. 14.5 months without (non-significant difference).

Lung Cancer (NSCLC)

- “…patients with stage IV NSCLC typically die from their disease, with an overall median survival time of 10 to 12 months. The fraction of patients who are alive 1 year after diagnosis has increased slightly over the past decade.”
- A 2003 meta-analysis confirmed an increase in median survival of 1.5 months (from 4.5 to 6 months). As a result, the use of chemotherapy has become the standard for most patients with advanced NSCLC.

Second-line treatment with docetaxel (Taxotere) = 3.4 month median progression-free survival in wild-type NSCLC

With erlotinib (Tarceva) = 2.4 months

CR rate with docetaxel = 4.3%, PR rate = 9.6%

CR rate with Tarceva = 0%, PR rate = 2.2%

"Docetaxel is not a very good drug and erlotinib is a terrible drug.” —Steven E. Vogl, MD, (from audience)

Garrasino MC, et al. TAILOR: A phase III trial comparing erlotinib with docetaxel as the second-line treatment of NSCLC patients with wild-type (wt) EGFR. J Clin Oncol. 30, 2012 (suppl; abstr LBA7501)
How much have we spent?

- $200 billion by 2008
  (Sharon Begley, “We Fought Cancer…and Cancer Won” science editor, *Newsweek, 2008*

- Fiscal Year (FY) 2011 Budget Request: $5,264,643,000
Medical expenditure on cancer treatment $125 billion in 2010
Will rise to $158 billion p.a. by 2020
Could reach as high as $207 billion p.a.

(JNCI, Jan. 12, 2011)
Cancer is Big Business

- Cancer is “one of the most important growth segments among the pharmaceutical markets…”

- At $47.7 billion per year for drugs alone, “cancer is one of the largest, fastest growing markets in the pharmaceutical industry.”

Per person cost of drugs

- Avastin (bevacuzumab) for colon, etc. = $88,000 per person
- Provenge for prostate cancer: $31,000 per injection = $93,000 per person
- Yervoy (ipilimumab) for melanoma = $30,000 per infusion = $120,000 for four months
- Herceptin + Perjeta = $187,000 p.p. (18 mos.)
- Meanwhile, many inexpensive drugs are in short supply.

The Treadmill Effect

- **Study 1**
  - Arm A Median Survival = 8 months
  - Arm B Median Survival = 10 Months
  - \( B > A \)

- **Study 2**
  - Arm B median Survival = 8 months
  - Arm C Median Survival = 10 months
  - \( C > B \)
  - C is more expensive than B
A multi-centre randomized, open-label phase II trial of continuous erlotinib plus gemcitabine or gemcitabine as first-line therapy in ECOG PS2 patients with advanced non-small cell lung

- Australia
- Oncology Reports, March 2012
- Gemzar +/- Erlotinib

**Median Survival**
- Gemzar alone = 21 weeks
- Gemzar + Erlotinib = 26 weeks
Comparison of radiotherapy alone and radiotherapy with chemotherapy using adriamycin and 5-fluorouracil in bronchogenic carcinoma

- From Newport Chest Clinic, Newport, and Velindre Hospital, Cardiff
- Thorax, 1981, 36, 190-193
- Eighty-two patients with histologically confirmed lung cancer were randomly allocated to receive either radiotherapy alone or the same dose of radiotherapy followed by four cycles of adriamycin and 5-fluorouracil.
Stable disease

● Only 5-8 years ago when we claimed that hyperthermia can arrest the growth of cancer cells and patients live longer with the cancer (=stable disease) we were considered “Charlatans” and “illusioning” patients.

● Now-days, ”stable disease” became the backbone of all the new drugs and therapeutics
SLOPS

Years
Months
Weeks
Days
Promise of CAM

- Complementary and alternative medicine (CAM) is a great repository of new concepts and treatments.
- Results with integrative oncology (IO) are better than with conventional oncology.
- E.g., 38 months vs. 20 months overall survival in stage IV BC
- “There currently is no drug that has demonstrated the potential to double the life expectancy of metastatic breast cancer patients, as evidenced in these findings.”

LOOKING AT CANCER FROM THREE DIFFERENT ANGLES

Dr. JOSEPH BRENNER

- Medical Oncologist
- Expert in Integrative cancer therapies
- Cancer victim

Dr. BRENNER with Prof. DI-BELLA
Conclusions

- “War on cancer” has been expensive and disappointing
- Progress, when measured by improvement of survival in stage IV disease) has been minimal
- Needs of Big Pharma basically drive major developments in oncology
- Cancer remains Big Business
- Fundamentally new strategies are necessary to bring about major changes
Let’s revitalize the War on Cancer by focusing on CAM treatments

“Now is the time to commit ourselves to waging a war against cancer as aggressive as the war cancer wages against us.”

—President Barack Obama, quoted in People, June 3, 2009
Contact info

- Ralph W. Moss, PhD
  Cancer Communications, Inc.
  PO Box 1076
  Lemont, PA 16851
  814-238-3367
  www.cancerdecisions.com

- Editor, ADVANCES in Cancer Treatment
  (monthly online newsletter)
- “War on Cancer” columnist, Townsend Letter
‘Cherry picking’ patients in trials

- Inclusion & exclusion criteria lead to ‘cherry picking’ patients in clinical trials.
- Exaggerated claims of benefit in general population
- Trial patients are younger, healthier, more likely to be married and better educated.
- Thus, survival after chemo in stage IV colon CA is **30% shorter** in elderly Medicare patients than in clinical trial participants.


WHEN CANCER CURE FOUND