# Treatment affordability and strategies for expanding access

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# The Price Tag on Progress — Chemotherapy for Colorectal Cancer

Deborah Schrag, M.D., M.P.H.

N ENGL J MED 351;4 WWW.NEJM.ORG JULY 22, 2004

**Table.** Estimated Drug Costs for Eight Weeks of Treatment for Metastatic Colorectal Cancer.

| Regimen | Drugs and Schedule of Administration | Drug Costs* |
|---|---|---|
| | | $ |
| **Regimens containing fluorouracil** | | |
| Mayo Clinic | Monthly bolus of fluorouracil plus leucovorin | 63 |
| Roswell Park | Weekly bolus of fluorouracil plus leucovorin | 304 |
| LV5FU2 | Biweekly fluorouracil plus leucovorin in a 48-hr infusion | 263 |
| **Regimens containing irinotecan or oxaliplatin** | | |
| Irinotecan alone | Weekly bolus | 9,497 |
| IFL | Weekly bolus of fluorouracil plus irinotecan | 9,539 |
| FOLFIRI | LV5FU2 with biweekly irinotecan | 9,381 |
| FOLFOX | LV5FU2 with biweekly oxaliplatin | 11,889 |
| **Regimens containing bevacizumab or cetuximab** | | |
| FOLFIRI with bevacizumab | FOLFIRI with fortnightly bevacizumab | 21,399 |
| FOLFOX with bevacizumab | FOLFOX with biweekly bevacizumab | 21,033 |
| Irinotecan with cetuximab | Weekly irinotecan plus cetuximab | 30,790 |
| FOLFIRI with cetuximab | FOLFIRI and weekly cetuximab | 30,675 |

**The near doubling of median survival has been accompanied by a 340-fold increase in drug costs**

Effect x 2 =

Cost x 340

# How is cost-effectiveness measured?

## Cost per Life Year gained:

If new treatment B costs $50,000/yr & standard treatment A costs $1,000/yr

& in an RCT patients live a median 6 months longer with B

**Then added cost per Life-Year gained is $98,000**

## What cost per LY gained is cost-effective?

- In Chicago, Paris or Montreal, publicly-funded health-care systems can generally afford up to $60,000, but not more than $100,000 per LY gained
- In Cairo, Calcutta or Lagos health-care systems can afford much less

# Some estimates of cost per Life Year gained

Statins for prevention of CAD in moderate-high risk patients: $10,000

Adjuvant CMF: $500-1,000

Adjuvant FEC-D: $30,000

Adjuvant trastuzumab (> 10 studies): Range is ~ $15-45,000

**Adjuvant trastuzumab is cost-effective in wealthy countries**

# Small gains at high price



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# When Are "Positive" Clinical Trials in Oncology Truly Positive?

Alberto Ocana, Ian F. Tannock

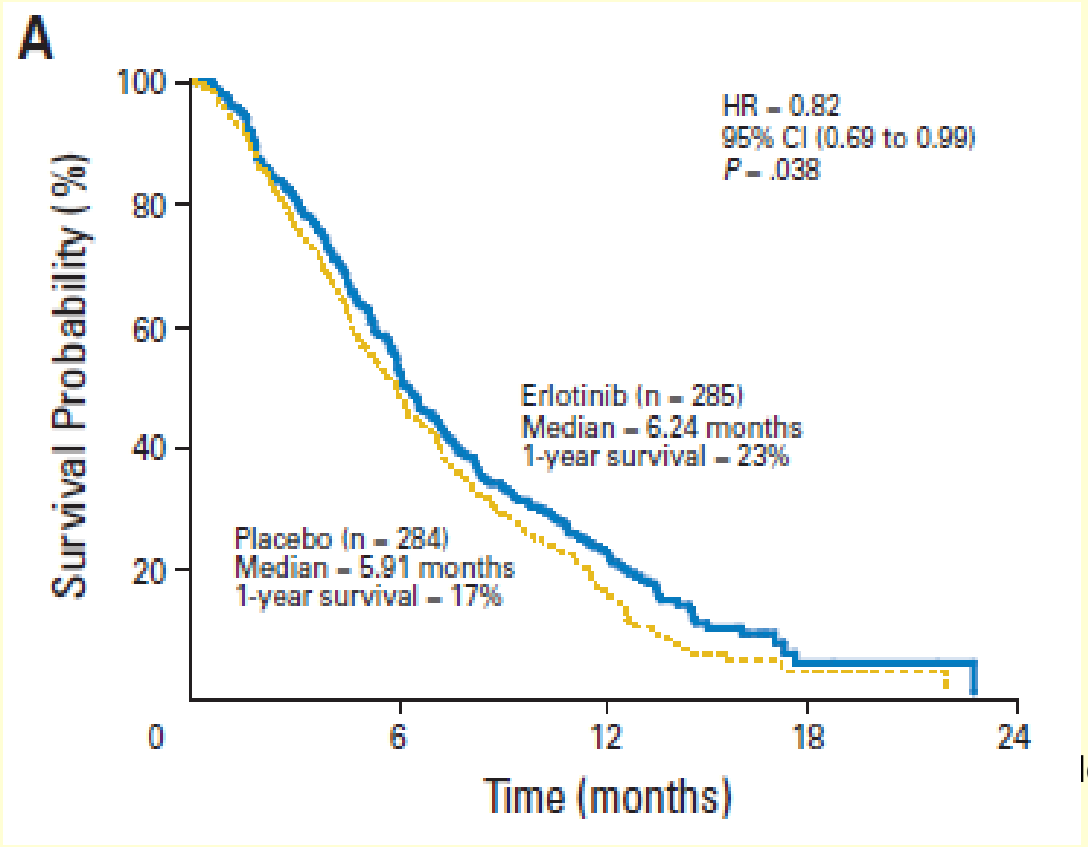
J Natl Cancer Inst 2010;103:1–5

- Trials are designed to demonstrate or rule out a difference (δ) in outcome between their arms that should be clinically important
- However several trials have reported a smaller difference, but because the trial was very large this was statistically significant
- FDA and EMA have approved drugs based on any significant difference in overall survival
- This encourages ever larger trials to demonstrate clinically meaningless but statistically significant differences
- This is a waste of scarce resources and should stop

# Erlotinib Plus Gemcitabine Compared With Gemcitabine Alone in Patients With Advanced Pancreatic Cancer: A Phase III Trial of the National Cancer Institute of Canada Clinical Trials Group

J Clin Oncol 25:1960-1966. © 2007

*Malcolm J. Moore, David Goldstein, John Hamm, Arie Figer, Joel R. Hecht, Steven Gallinger, Heather J. Au, Pawel Murawa, David Walde, Robert A. Wolff, Daniel Campos, Robert Lim, Keyue Ding, Gary Clark, Theodora Voskoglou-Nomikos, Mieke Ptasynski, and Wendy Parulekar*




**Despite this trivial difference, the p-value was <0.05, and …**

**....Gemcitabine + Erlotinib was approved by the FDA for treatment of pancreatic cancer**

lontreal

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# The obscene cost of new drugs

## Does it relate to their effectiveness?

# Oncogenic Targets, Magnitude of Benefit, and Market Pricing of Antineoplastic Drugs

J Clin Oncol 29. © 2011

*Eitan Amir, Bostjan Seruga, Joaquin Martinez-Lopez, Ryan Kwong, Atanasio Pandiella, Ian F. Tannock, and Alberto Ocaña*

**Three groups of agents FDA approved since 2000:**

- **(A) Targeted agents where the target population is selected by a biomarker**
- **(B) Less specific biological targeted agents**
- **(C) Chemotherapeutic agents**

| Group | No of drugs/ trials | HR for OS | HR for PFS | Median monthly cost (in USA) |
|---|---|---|---|---|
| A | 6/7 | 0.69 (0.59-0.81) | 0.42 (0.36-0.49) | $5,375 |
| B | 7/14 | 0.78 (0.74-0.83) | 0.57 (0.51-0.64) | $5,644 |
| C | 8/12 | 0.84 (0.79-0.90) | 0.75 (0.66-0.85) | $6,584 |
| P-value | | 0.003 | <0.0001 | NS |

# Are targeted agents cost-effective?

Ocana A, Seruga B, Amir E, Kwong R,Tannock IF

- We identified 25 new drugs approved by FDA for 17 malignant diseases in 2000-2010, and estimated the cost per life-year gained
- For only 37% of new agents was the cost per life-year gained less than $100,000
- The cost of new targeted agents needs to be reduced by a median 78% to render them cost effective, even for Western countries
- We suggest that registration of new anticancer drugs require value-based pricing that renders them cost-effective



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# "Rationing" of health-care

- Most European countries (and Canada) believe that all of their citizens have a right to expect a certain level of health care
- They use a form of cost-effectiveness in planning distribution of resources to hospitals, health professionals, diagnostic procedures etc.
- This leads to some restriction in access to drugs, based on demonstrated cost-effectiveness
- "Rationing of health-care" is essential to ensure fair distribution of limited resources – no matter how wealthy the country

# Market forces largely control the cost of drugs

- Pricing is based on maximizing profit
- The decision to assign a high price for a limited market versus a lower price to allow broader access is not based on maximizing clinical benefit
  - quite contrary to the philosophy behind funding of public health services

It is the major cause of limited availability of off-patent drugs such as methotrexate and doxorubicin

# Teaching old drugs to do new tricks

**The profit motive for drug development makes it very difficult to evaluate new roles for old drugs**

# Question: Why was premetrexed ($$$) evaluated in a large RCT for mesothelioma?

Answer: Because responses were seen with methotrexate (e.g. 37% CR+PR among 63 patients in a Norwegian trial: Solheim et al. Br J Cancer 1992;65:956-60)

Is methotrexate as effective as premetrexed?

We will never know, because there is no incentive to do large trials with cheap (older drugs)

# Effectiveness or Cost-effectiveness as the preferred criterion for approving new drugs?



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# Arguments for approving drugs based only on effectiveness include:

1. The profit motive is a powerful incentive for investment in development of new therapies
2. Patients, physicians, insurance companies, public health providers, and countries can make their own judgments about benefit relative to cost
3. Cost is not stable and an expensive drug today will become more affordable
4. Drug pricing is driven by the US and attempts to control pricing might lead to non-availability of a drug in a particular country or region.



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# Argument for approving drugs based only on cost-effectiveness include:

1. Limited health care resources are distributed more equitably
2. New therapies which lead to small improvements in clinical outcome will be cheaper than those that cause dramatic improvements.

# If FDA and EMA changed policy to require cost-effectiveness for drug approval……

…with the caveat that it would have to allow companies to recover the real costs of research:

1. Pricing of drugs would be related to drug effectiveness
2. It would stimulate more equitable distribution of drugs that is based on effectiveness rather than price.

# And in routine oncologic practice…

- Oncologists are encouraged constantly (and subtly) by Pharma reps to prescribe more expensive drugs
- Oncologists should be aware of the relative costs of drugs and where there are equal options, select the cheaper
- "Educational" events sponsored by a single company are aimed at marketing, not education
- There is no free lunch!

# Some statistics from a colleague, Dr Zeba Aziz (Lahore, Pakistan)

- Health insurance covers only 5% of the population
- Trastuzumab is given to 5-7% of Her2+ women. We try to give 9 weeks as in the FinHer study. We participate in trials (ALTTO) so eligible women can get trastuzumab or lapatinib or both
- Aromatase inhibitors and taxanes are not used routinely

"It seems when I go to Western meetings we are living in a different world and when we are back we practice entirely in a different scenario"

# A wild idea ….

If our mission is to maximize therapeutic benefit for all patients with cancer

One strategy is to lobby EMA/FDA such that the approval process for new therapies in wealthy countries…

is linked to an agreement by companies to provide such therapies to patients in countries that cannot afford them

# If you are buying a....

Ford

## You shouldn't have to pay for a...

Ferrari