Istituto di Ricerche sulla Popolazione
e le Politiche Sociali

Istituto Superiore di Sanità

SEMINARIO

L'impatto dei tumori sui sistemi sanitari: approcci ed esperienze a confronto

Aula Marconi, CNR, P.le Aldo Moro, 7 – Roma

Questione farmaci oncologici ad alto costo

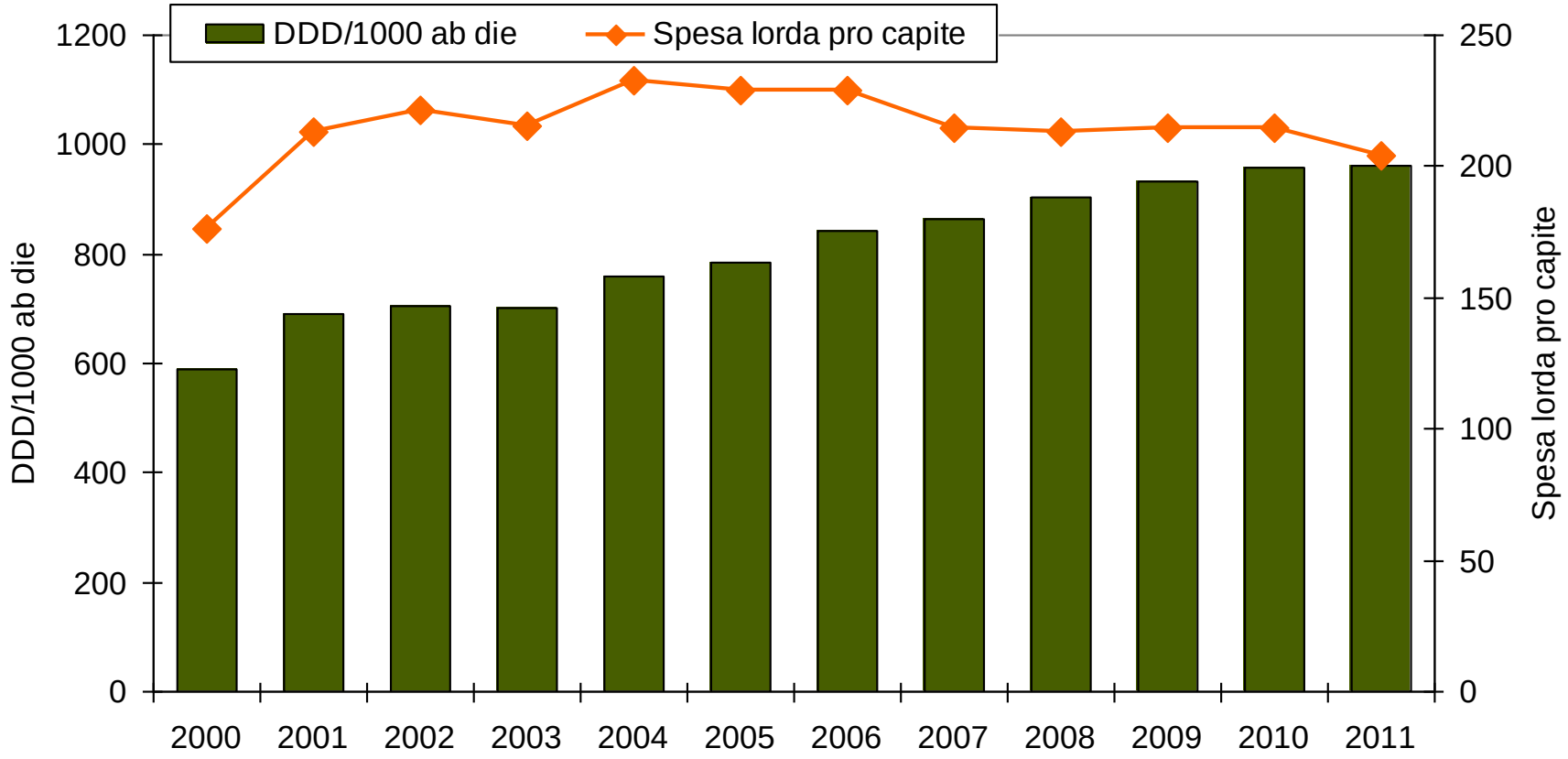
Giuseppe Traversa

Centro Nazionale di Epidemiologia, Sorveglianza e Prevenzione della Salute
Istituto Superiore di Sanità, Roma

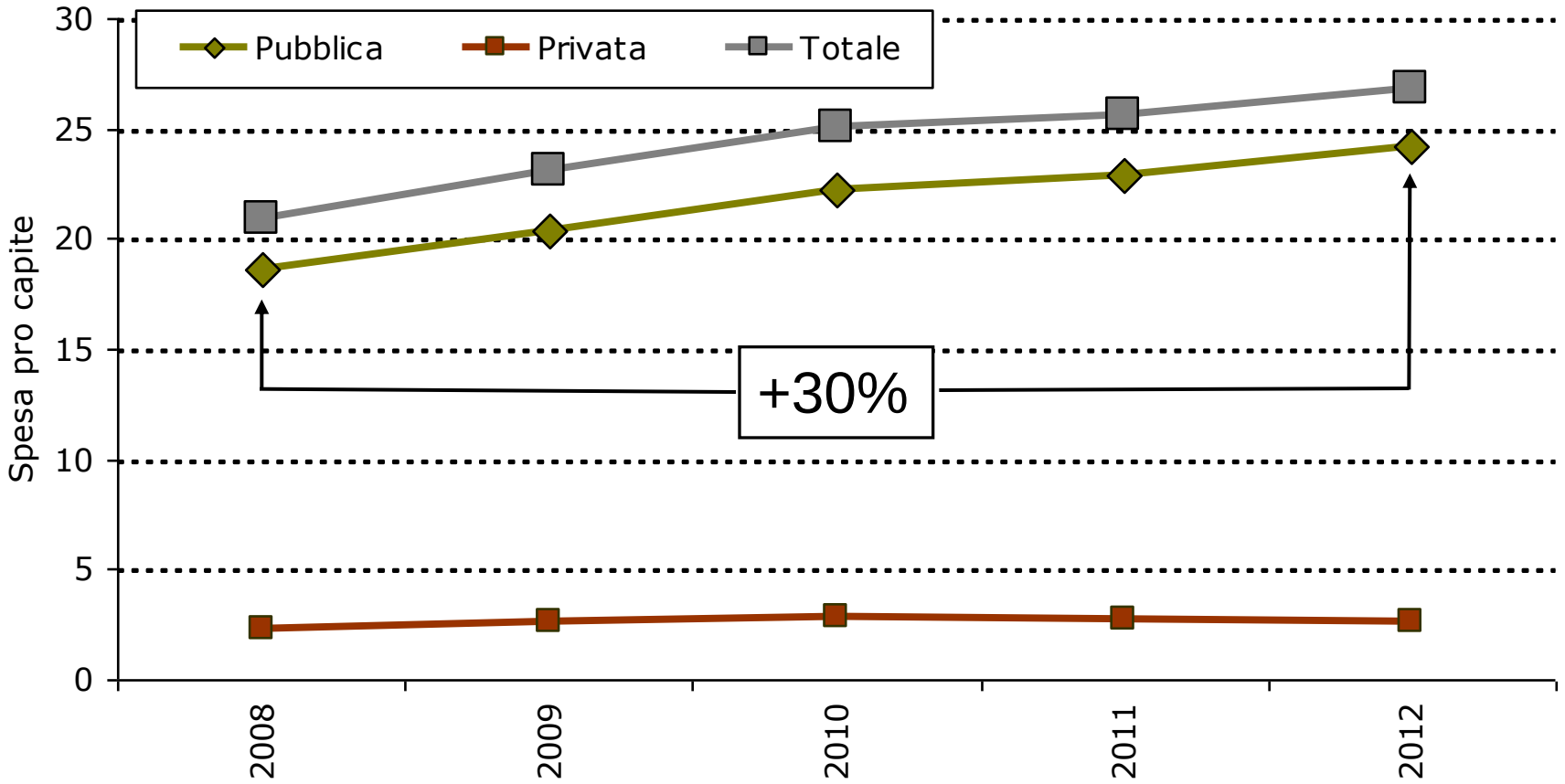
Gli argomenti

- Inquadramento sulla spesa farmaceutica
- Perché aumenta la spesa dei farmaci oncologici
- Le strategie per il controllo della spesa in Italia
- I possibili scenari
- Conclusioni

La prescrizione farmaceutica territoriale in Italia: DDD e spesa lorda dal 2000 al 2011



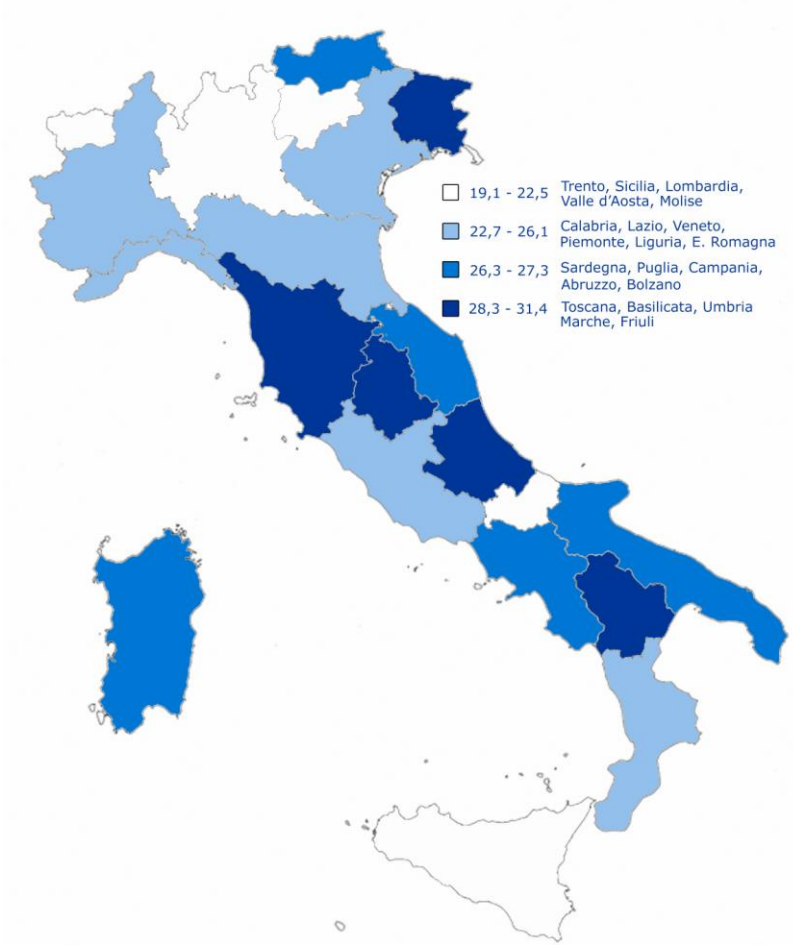
Andamento della spesa pro capite per farmaci oncologici (ATC: L01), (2008-2012)



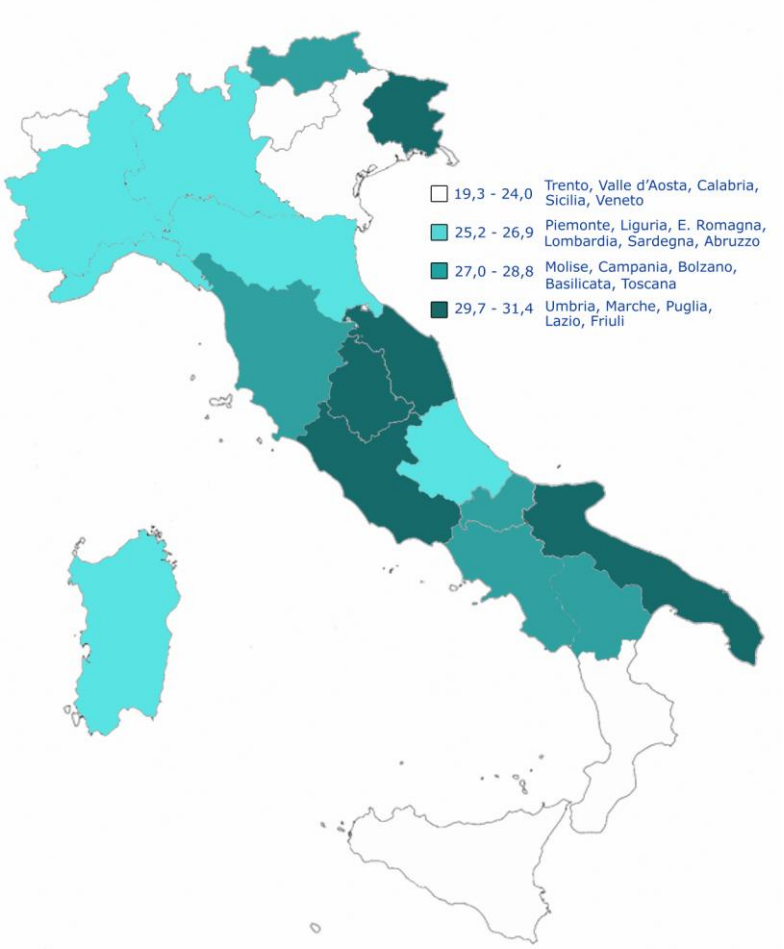
Fonte: Tracciabilità del farmaco - Ministero della salute

Farmaci oncologici (ATC L01), distribuzione in quartili della spesa pro capite pubblica e totale (anno 2012)

Pubblica



Totale



Fonte: Tracciabilità del farmaco - Ministero della salute

Perché aumenta la spesa dei farmaci oncologici

- L'aumento dei farmaci efficaci
- L'aumento delle terapie combinate
- L'aumento dei prezzi dei singoli farmaci
  - Relazione fra prezzi e valore aggiunto
- **...**

blood

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The price of drugs for chronic myeloid leukemia (CML) is a reflection of the unsustainable prices of cancer drugs: from the perspective of a large group of CML experts

Experts in Chronic Myeloid Leukemia

As a group of more than 100 experts in chronic myeloid leukemia (CML), we draw attention to the high prices of cancer drugs, with the particular focus on the prices of approved tyrosine kinase inhibitors for the treatment of

editorial addresses the multi
involved in cancer drug pricin
impact on individual patients
care policies, and argues for t

Through positive collaborations with Pharma, experts in chronic myelogenous leukemia (CML) have been fortunate to have 3 drugs approved by the US Food and Drug Administration (FDA) in 2012 for the treatment of CML: bosutinib, ponatinib, and omacetaxine. This is in addition to 3 others approved in the last decade: imatinib, dasatinib, and nilotinib. The 3 new drugs, however, have been priced at astronomical levels: ponatinib at $138 000 per year, omacetaxine at $28 000 for induction and $14 000 per maintenance course, and bosutinib at ~$118 000 per year.[1]

Should NICE's threshold range for cost per QALY be raised?

NICE has recently raised the threshold for end of life drugs. **Adrian Towse** argues it should consider doing the same for other treatments, but **James Raftery** believes that the threshold is already too high

BMJ | 31 JANUARY 2009 | VOLUME 338

Le strategie per il controllo della spesa in Italia

- I registri
- Il rimborso condizionato
  - payment by result e risk sharing
- I tetti di spesa
- La ricerca indipendente

Verificare l'appropriatezza d'uso

Agenzia Italiana del Farmaco

AIFA

Unità Registri del protocollo dei farmaci

Scheda di monitoraggio Zytiga® (abiraterone acetato)

E	Campo obbligatorio ai fini dell'eleggibilità
O	Campo obbligatorio

Legenda:

RP	**R**egistrazione **P**aziente
E_DC	**E**leggibilità e **D**ati **C**linici
RF	**R**ichiesta **F**armaco
DF	**D**ispensazione **F**armaco
RV	**RiV**alutazione
FT	**F**ine **T**rattamento

Classe di rimborsabilità H

Scenari per garantire l'assistenza e contenere la spesa

- Uso appropriato
  - Innanzitutto registri, linee guida e audit
- Diffusione di generici e biosimilari
- Prezzi e rilevanza clinica
  - La domanda di fondo: cosa aggiunge il nuovo farmaco rispetto alle alternative terapeutiche esistenti?
- Produzione di nuove evidenze
  - Domande prive di interesse commerciale

Quando una differenza è sufficientemente rilevante?

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JOURNAL OF CLINICAL ONCOLOGY

COMMENTS AND CONTROVERSIES

Incremental Advance or Seismic Shift? The Need to Raise the Bar of Efficacy for Drug Approval

Alberto Sobrero, *Ospedale San Martino, Genova, Italy*
Paolo Bruzzi, *Istituto Nazionale per la Ricerca sul Cancro, Genova, Italy*

15 farmaci per tumori solidi registrati

- Guadagno mediano di sopravvivenza: 2 mesi

Incremental Advance or Seismic Shift? The Need to Raise the Bar of Efficacy for Drug Approval *(Sobrero & Bruzzi, JCO 2009)*

Premessa

- Differenze statisticamente significative ma non sempre clinicamente rilevanti
- Molti farmaci approvati in base a miglioramenti di indicatori surrogati
- Costi rilevanti anche a fronte di benefici non chiari

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JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

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

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

From the Divisions of Medical Oncology, Hematology, and Surgical Oncology, Princess Margaret Hospital, Toronto; National Cancer Institute of Canada Clinical Trials Group, Kingston; Algoma District Cancer Program, Sault Ste Marie, Ontario; Cross Cancer Institute, Edmonton, Alberta, Canada; the Australasian Gastrointestinal Tumor Group, Sydney, Australia; Norton Healthcare Pavilion, Louisville, KY; UCLA Medical Center, Los Angeles, CA; M. D. Anderson Cancer Centre, Houston, TX; OSI Pharmaceuticals, Boulder, CO; Sourasky Medical Centre, Tel Aviv, Israel; Great Poland Centre for Oncology, Poznan, Poland; Confidence Medical Centre, San Isidro, Argentina; and the National University Hospital, Singapore, Singapore.

Submitted June 26, 2006; accepted November 8, 2006; published online ahead of print at www.jco.org on April 23, 2007.

Supported in part by OSI Pharmaceuticals, Melville, NY.

Presented in part at the American Society of Clinical Oncology Gastrointestinal Symposium, Hollywood, FL, January 27-29 2005; and the 41st Annual Meeting of the American Society of Clinical Oncology, Orlando, FL,

ABSTRACT

Purpose

Patients with advanced pancreatic cancer have a poor prognosis and there have been no improvements in survival since the introduction of gemcitabine in 1996. Pancreatic tumors often overexpress human epidermal growth factor receptor type 1 (HER1/EGFR) and this is associated with a worse prognosis. We studied the effects of adding the HER1/EGFR-targeted agent erlotinib to gemcitabine in patients with unresectable, locally advanced, or metastatic pancreatic cancer.

Patients and Methods

Patients were randomly assigned 1:1 to receive standard gemcitabine plus erlotinib (100 or 150 mg/d orally) or gemcitabine plus placebo in a double-blind, international phase III trial. The primary end point was overall survival.

Results

A total of 569 patients were randomly assigned. Overall survival based on an intent-to-treat analysis was significantly prolonged on the erlotinib/gemcitabine arm with a hazard ratio (HR) of 0.82 (95% CI, 0.69 to 0.99; $P = .038$, adjusted for stratification factors; median 6.24 months *v* 5.91 months). One-year survival was also greater with erlotinib plus gemcitabine (23% *v* 17%; $P = .023$). Progression-free survival was significantly longer with erlotinib plus gemcitabine with an estimated HR of 0.77 (95% CI, 0.64 to 0.92; $P = .004$). Objective response rates were not significantly different between the arms, although more patients on erlotinib had disease stabilization. There was a higher incidence of some adverse events with erlotinib plus gemcitabine, but most were grade 1 or 2.

Conclusion

To our knowledge, this randomized phase III trial is the first to demonstrate statistically significantly improved survival in advanced pancreatic cancer by adding any agent to gemcitabine. The recommended dose of erlotinib with gemcitabine for this indication is 100 mg/d.

Incremental Advance or Seismic Shift? The Need to Raise the Bar of Efficacy for Drug Approval *(Sobrero & Bruzzi, JCO 2009)*

Premessa

- Differenze statisticamente significative ma non sempre clinicamente rilevanti
- Molti farmaci approvati in base a miglioramenti di indicatori surrogati
- Costi rilevanti anche a fronte di benefici non chiari

Proposta alternativa

- Alzare l'asticella

Incremental Advance or Seismic Shift? The Need to Raise the Bar of Efficacy for Drug Approval *(Sobrero & Bruzzi, JCO 2009)*

Vantaggi

- Stimolo all'innovazione
- Immissione in commercio solo di farmaci più rilevanti
- I costi dei nuovi farmaci diventano più «ragionevoli»
- Necessari meno pazienti nelle sperimentazioni cliniche

Svantaggi

- Rischio di non riconoscere piccoli incrementi che sommati ne danno uno grande

La ricerca indipendente

Erlotinib versus docetaxel as second-line treatment of patients with advanced non-small-cell lung cancer and wild-type *EGFR* tumours (TAILOR): a randomised controlled trial

Marina Chiara Garassino, Olga Martelli, Massimo Broggini, Gabriella Farina, Silvio Veronese, Eliana Rulli, Filippo Bianchi, Anna Bettini, Flavia Longo, Luca Moscetti, Maurizio Tomirotti, Mirko Marabese, Monica Ganzinelli, Calogero Lauricella, Roberto Labianca, Irene Floriani, Giuseppe Giaccone, Valter Torri, Alberto Scanni, Silvia Marsoni, on behalf of the TAILOR trialists

Summary

Background Erlotinib is registered for treatment of all patients with advanced non-small-cell lung cancer (NSCLC). However, its efficacy for treatment of patients whose tumours are *EGFR* wild-type—which includes most patients—is still contentious. We assessed the efficacy of erlotinib compared with a standard second-line chemotherapy in such patients.

Methods We did this randomised controlled trial in 52 Italian hospitals. We enrolled patients who had metastatic NSCLC, had had platinum-based chemotherapy, and had wild-type *EGFR* as assessed by direct sequencing. Patients were randomly assigned centrally (1:1) to receive either erlotinib orally 150 mg/day or docetaxel intravenously 75 mg/m² every 21 days or 35 mg/m² on days 1, 8, and 15, every 28 days. Randomisation was stratified by centre, stage, type of first-line chemotherapy, and performance status. Patients and investigators who gave treatments or assessed outcomes were not masked to treatment allocation, investigators who analysed results were. The primary endpoint was overall survival in the intention-to-treat population. The study is registered at ClinicalTrials.gov, number NCT00637910.

Findings We screened 702 patients, of whom we genotyped 540. 222 patients were enrolled (110 assigned to docetaxel *vs* 112 assigned to erlotinib). Median overall survival was 8·2 months (95% CI 5·8–10·9) with docetaxel versus 5·4 months (4·5–6·8) with erlotinib (adjusted hazard ratio [HR] 0·73, 95% CI 0·53–1·00; p=0·05). Progression-free survival was significantly better with docetaxel than with erlotinib: median progression-free survival was 2·9 months (95% CI 2·4–3·8) with docetaxel versus 2·4 months (2·1–2·6) with erlotinib (adjusted HR 0·71, 95% CI 0·53–0·95; p=0·02). The most common grade 3–4 toxic effects were: low absolute neutrophil count (21 [20%] of 104 in the docetaxel group *vs* none of 107 in the erlotinib group), skin toxic effects (none *vs* 15 [14%]), and asthenia (ten [10%] *vs* six [6%]).

Interpretation Our results show that chemotherapy is more effective than erlotinib for second-line treatment for previously treated patients with NSCLC who have wild-type *EGFR* tumours.

Funding Agenzia Italiana del Farmaco.

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See **Comment** page 916

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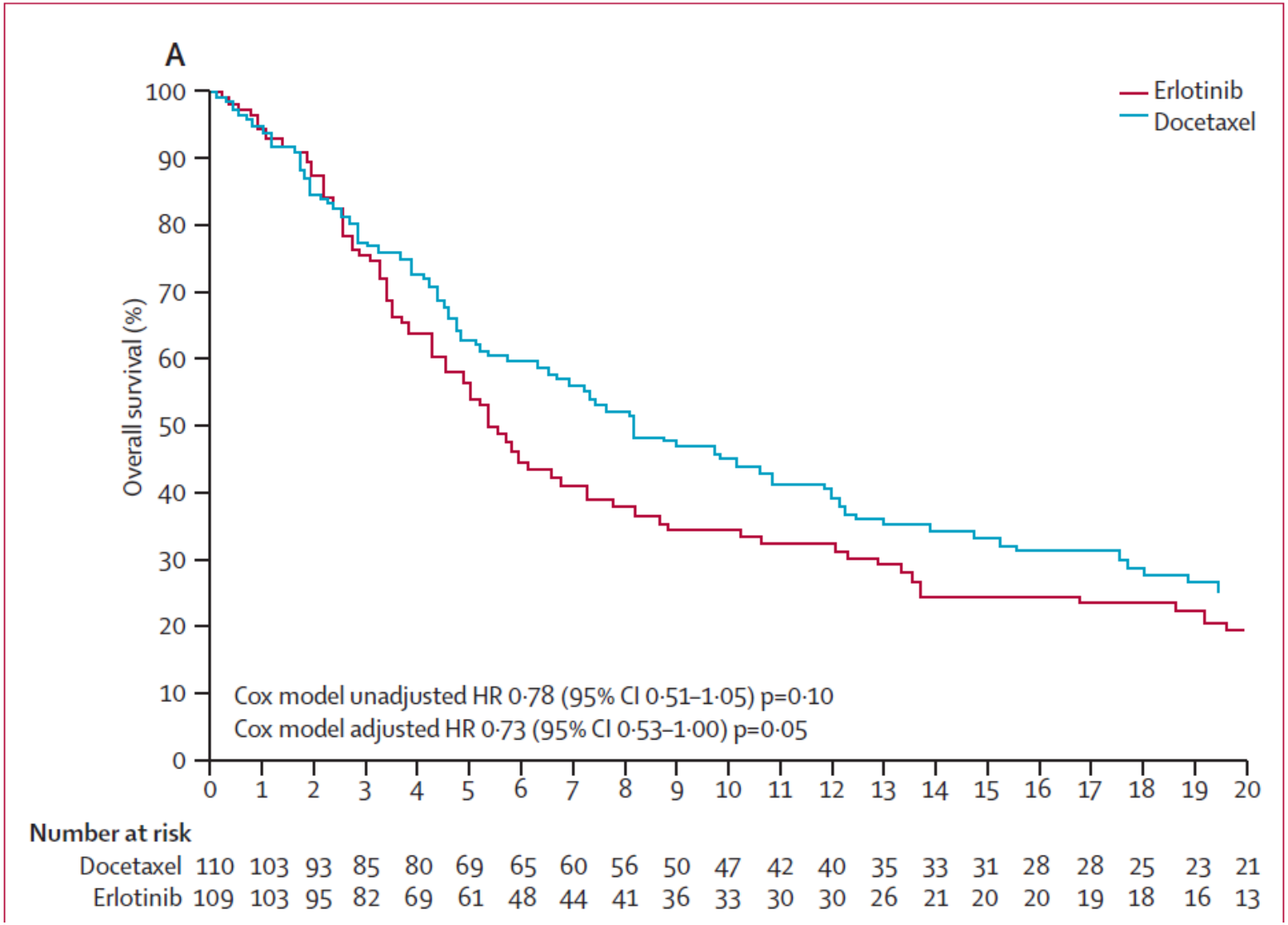
Erlotinib versus docetaxel as second-line treatment of patients with advanced non-small-cell lung cancer and wild-type EGFR *(Garassino et al., Lancet oncol 2013)*



Erlotinib versus docetaxel as second-line treatment of patients with advanced non-small-cell lung cancer and wild-type EGFR *(Garassino et al., Lancet oncol 2013)*

- Risultati dell'uso dell'erlotinib
  - peggioramento in termini di tempo alla progressione della malattia e di sopravvivenza complessiva
  - costo aggiuntivo di circa 2.000 euro per paziente

- Implicazioni dello studio
  - salute: l'erlotinib sarebbe potuto diventare il farmaco di riferimento per questi pazienti (il 90% circa dei pazienti con questo tumore)
  - riduzione spesa SSN: in 2-3 anni, più del finanziamento Aifa per tutti i progetti del 2007 (circa 13 milioni di euro)

In conclusione

- La spesa per i farmaci oncologici aumenta in assoluto e come peso relativo
- Chiarire quali miglioramenti terapeutici sono di interesse e devono essere garantiti dal SSN
  - Condivisione con i cittadini
  - Comprensibilità per le aziende farmaceutiche
- Prezzi maggiori per farmaci con profilo B/R superiore, ma simili per B/R simile
- Interventi per favorire l'uso appropriato
- Migliorare le evidenze disponibili
  - Necessità di studi post autorizzativi profit e non-profit