Università degli studi di Modena e Reggio Emilia

ASSOCIAZIONE CULTURA E VITA

NUOVI ORIZZONTI DELLA BIOETICA XI

Modena, 6 Marzo 2013

LE MALATTIE RARE: UNA SFIDA ETICA

Luca Richeldi

Centro per le Malattie Rare del Polmone

Azienda Ospedaliero-Universitaria Policlinico di Modena

UNIMORE

UNIVERSITÀ DEGLI STUDI DI MODENA E REGGIO EMILIA

Cosa rara, cosa cara.

[RARO]

1. **Poco comune**

   è un caso molto raro

   è una bestia rara

2. **Poco numeroso**

   le rare persone che passavano

   c'era qualche rara nuvola

   i clienti sono diventati rari

LE MALATTIE RARE

- 1 persona su 17 sviluppa una malattia rara nel corso della propria vita.
- Il 75% delle malattie rare colpisce bambini.
- Esistono >6.000 malattie rare riconosciute.
- Complessivamente, le malattie rare *non* sono rare.

DEFINIZIONI DI MALATTIE RARE

EMEA
(European Medicines Agency)

Less than
1 in 2000
citizens

FDA
(US Food and Drug Administration)

Fewer than
200,000 people
in the U.S.
(which is less than
1 in 1500 citizens)

RARO?

In the USA 25 million patients

In the EU 30 million patients

which is 6-8%
of the EU population
(including 25 countries)

EUROPEAN RESPIRATORY *monograph*
CLINICAL HANDBOOKS FOR THE RESPIRATORY PROFESSIONAL

Interstitial Lung Diseases

Edited by R.M. du Bois and L. Richeldi

- Idiopathic interstitial pneumonias
- Extrinsic allergic alveolitis
- Sarcoidosis
- Pulmonary Langerhans' cell histiocytosis
- Lymphanioleiomyomatosis
- Puln
- Connective tissue disease-associated lung disorders
- Pulmonary vasculitis
- Occupational interstitial lung disease
- Drug-induced infiltrative lung disease
- Paediatric interstitial lung disease

≈ 30% of all lung disorders

Vol. 46, 2009

Pneumopatie Interstiziali

Secondarie a esposizione:
- Occupazionale
- Ambientale
- Farmaci

Polmoniti Interstiziali pneumonia Idiopatiche (IIP)

Malattie del connettivo:
- Sclerodermia
- Artrite reumat.
- Sjogren

Sarcoidosi

Altre:
- Vasculiti
- Istiocitosi a cellule di Langherhans
- Polmoniti eosinofile
- Neurofibromatosi
- LAM

Fibrosi pomonare idiopatica (IPF)

Polmonite Interstiziale Desquamativa (DIP)

Bronchiolite Respiratoria con malattia interstiziale (RBILD)

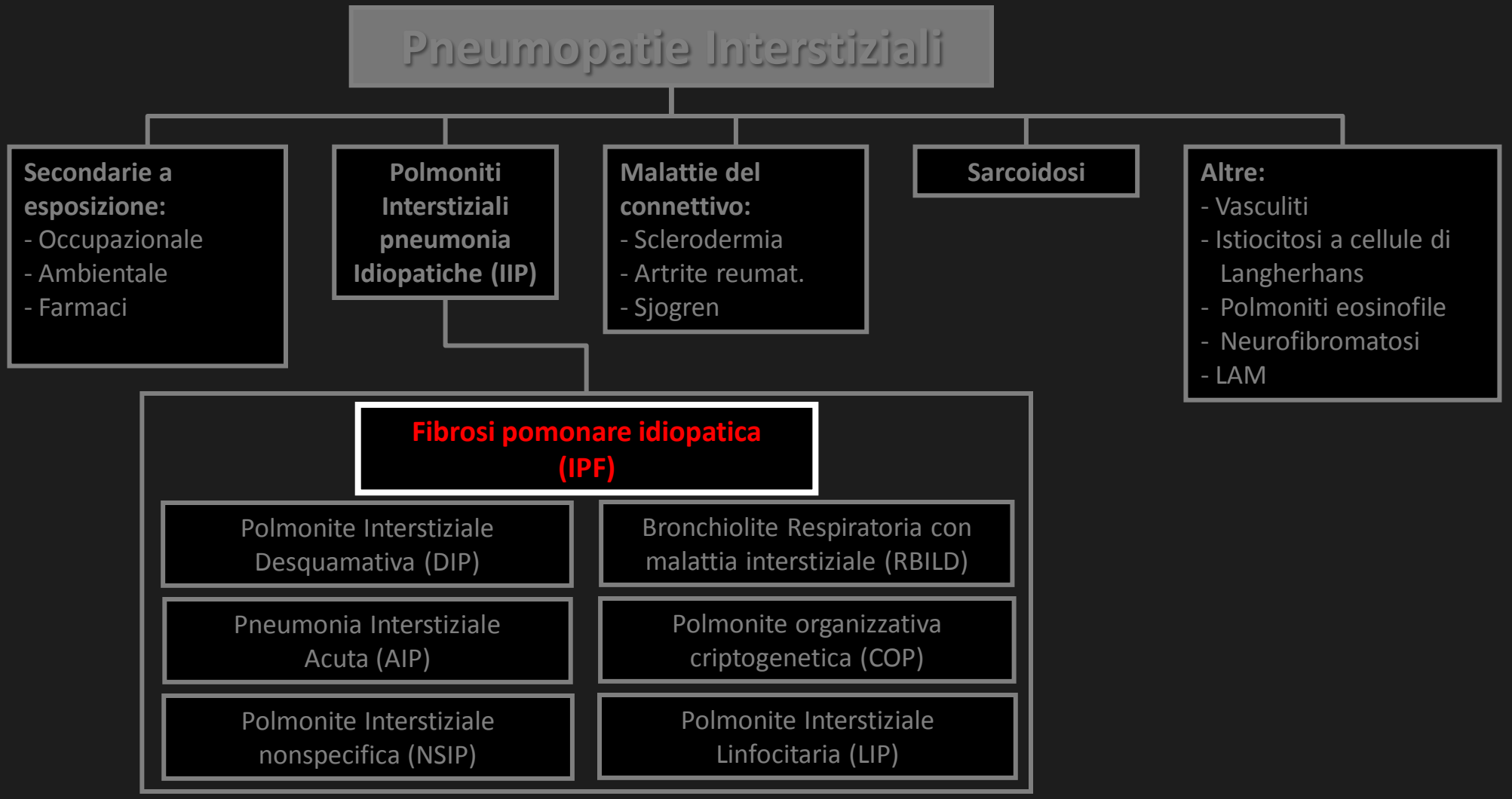
Pneumonia Interstiziale Acuta (AIP)

Polmonite organizzativa criptogenetica (COP)

Polmonite Interstiziale nonspecifica (NSIP)

Polmonite Interstiziale Linfocitaria (LIP)

ATS/ERS, 2002



ATS/ERS, 2002

Idiopathic Pulmonary Fibrosis

La più frequente e la più grave tra le IIP

≈150.000 pazienti con IPF (>50.000 morti/anno)

4,6 casi di IPF ogni 100.000 persone

Raghu G et al, *AJRCCM* 2006
Navaratnam V et al, *Thorax* 2011

CHI È “MISTER IPF”?

Maschio

Età media: 65 anni

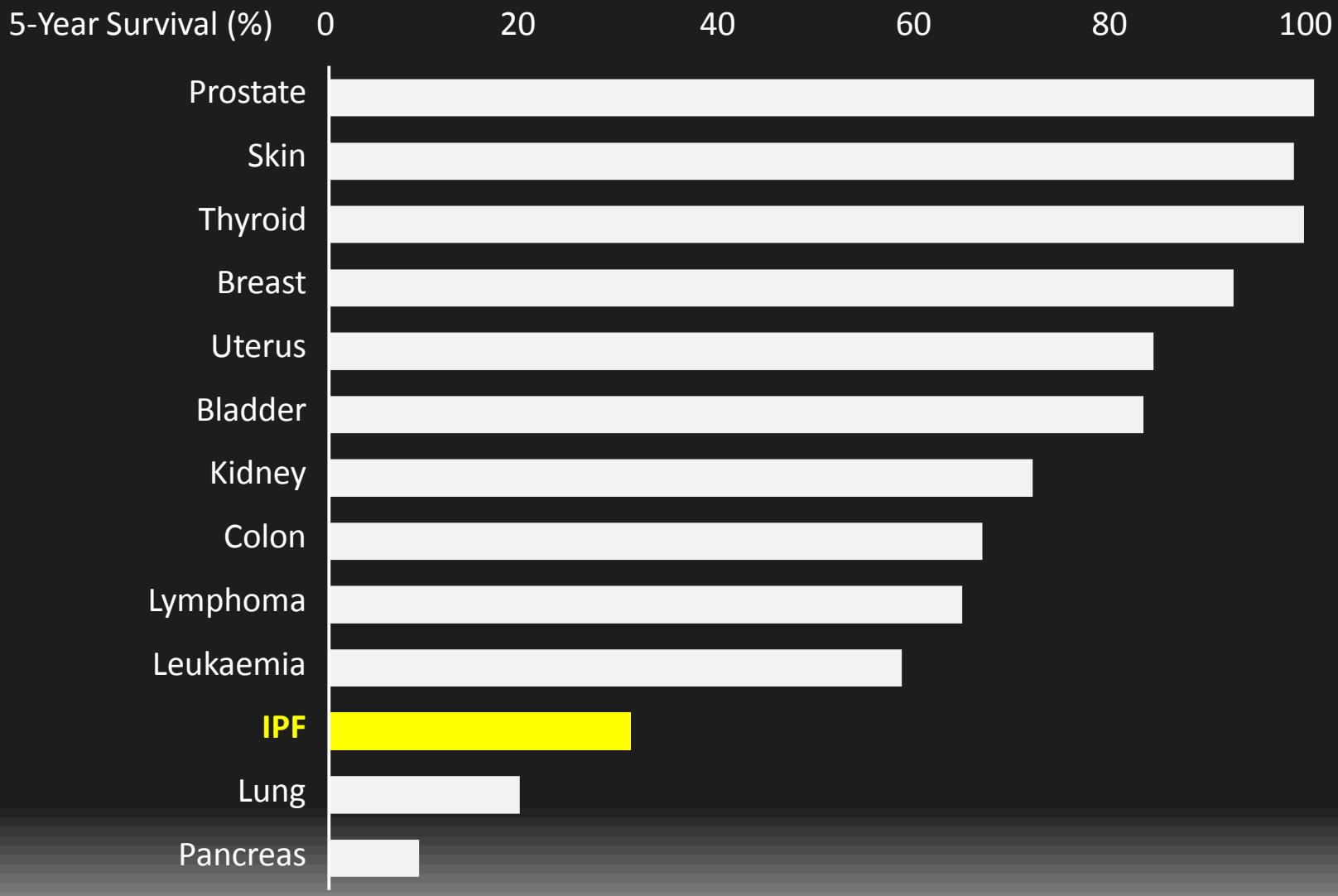
Fumatore o ex fumatore

Tosse secca

Dispnea da sforzo

Raghu G et al, *AJRCCM* 2011

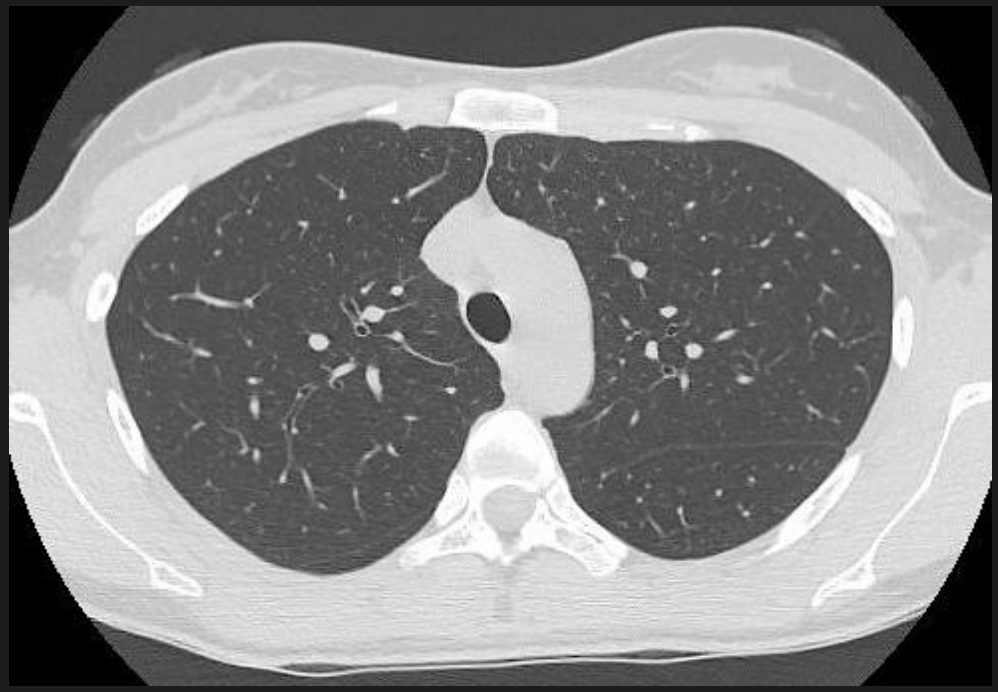
IPF: PROGNOSIS WORSE THAN MOST CANCERS



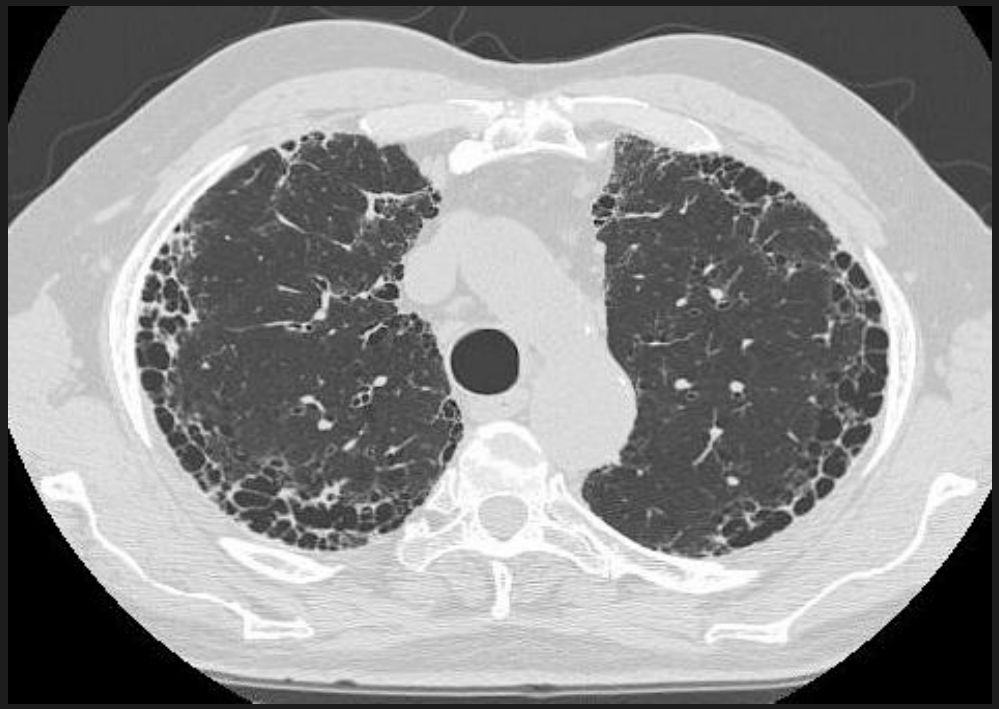
Vancheri et al, *Eur Respir J* 2010; 35: 496-504

TC TORACE AD ALTA RISOLUZIONE (HRCT)

TC TORACE AD ALTA RISOLUZIONE (HRCT)



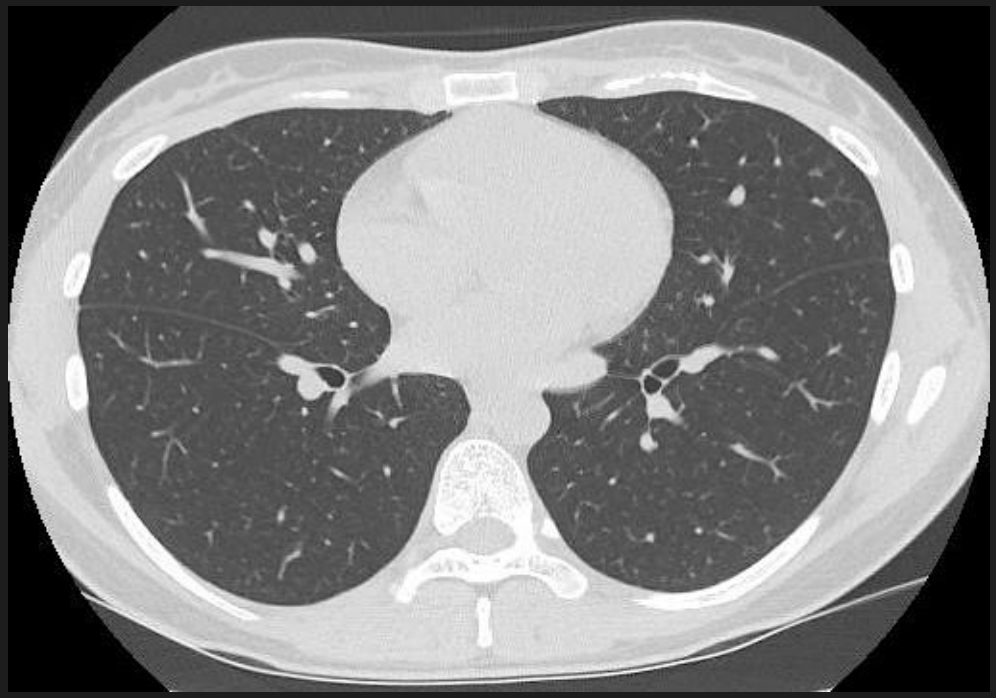
SANO



IPF

CAMPI SUPERIORI

TC TORACE AD ALTA RISOLUZIONE (HRCT)



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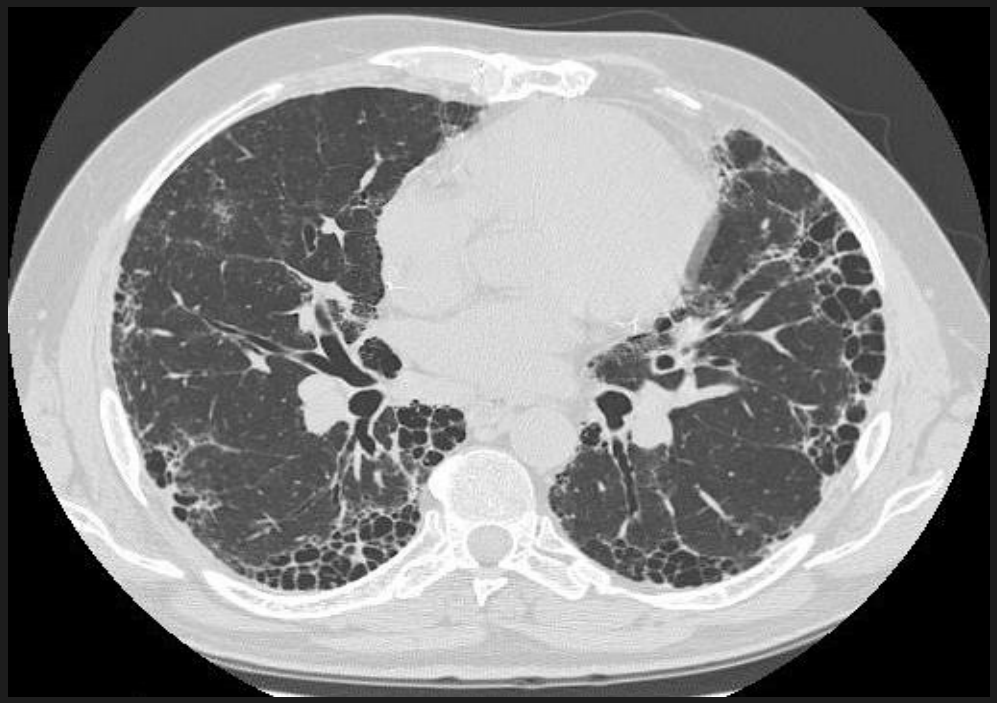
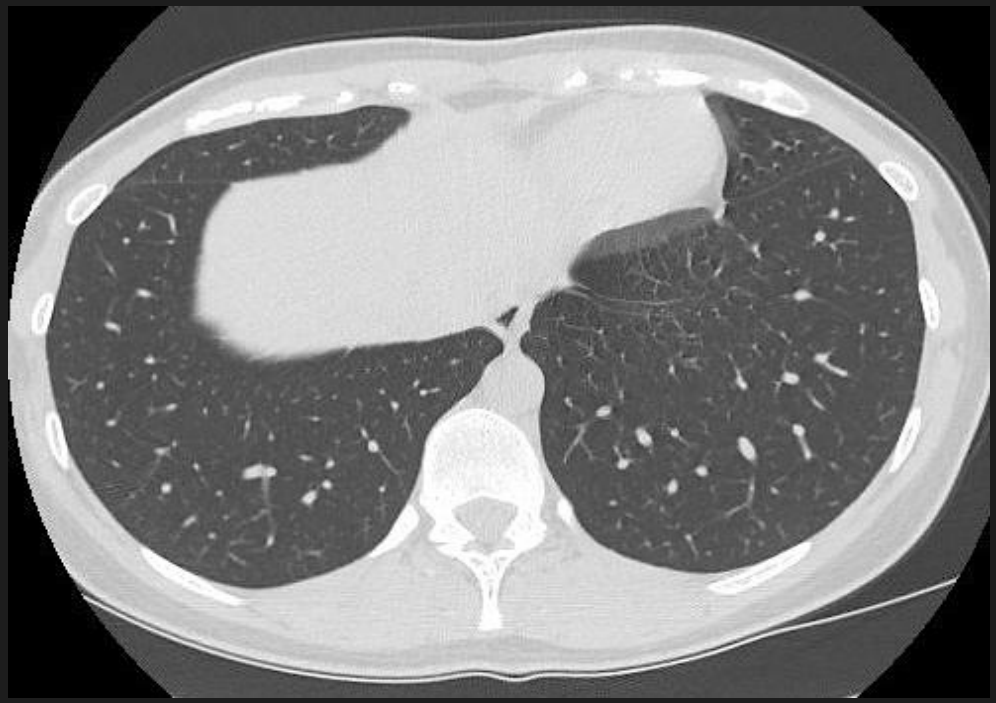


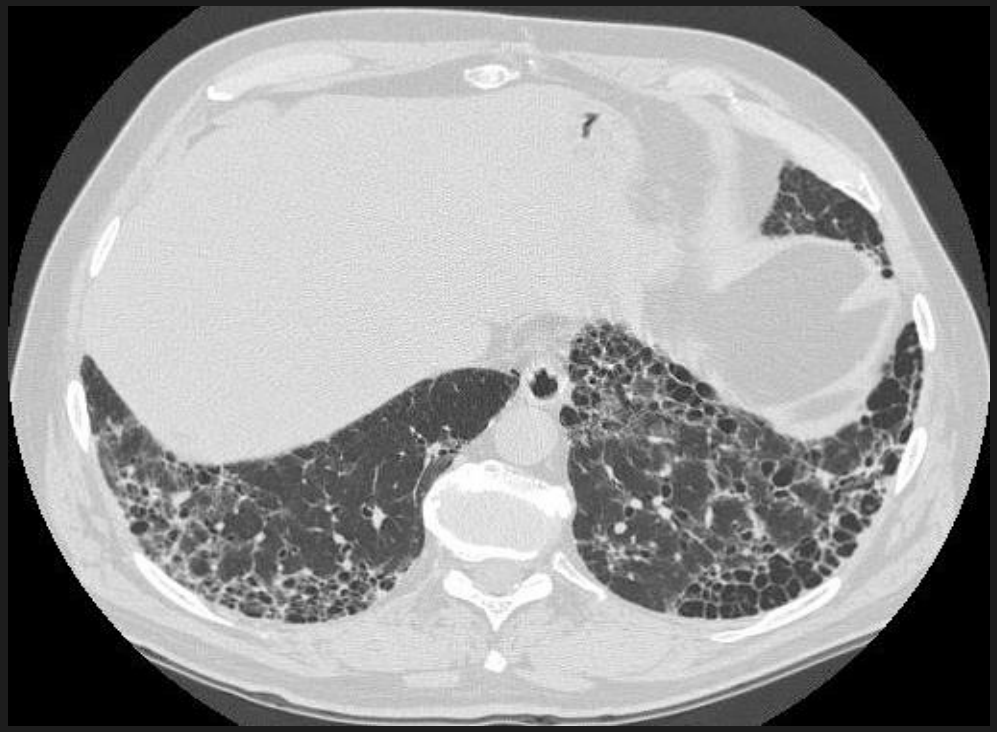
IPF

CAMPI MEDI

TC TORACE AD ALTA RISOLUZIONE (HRCT)



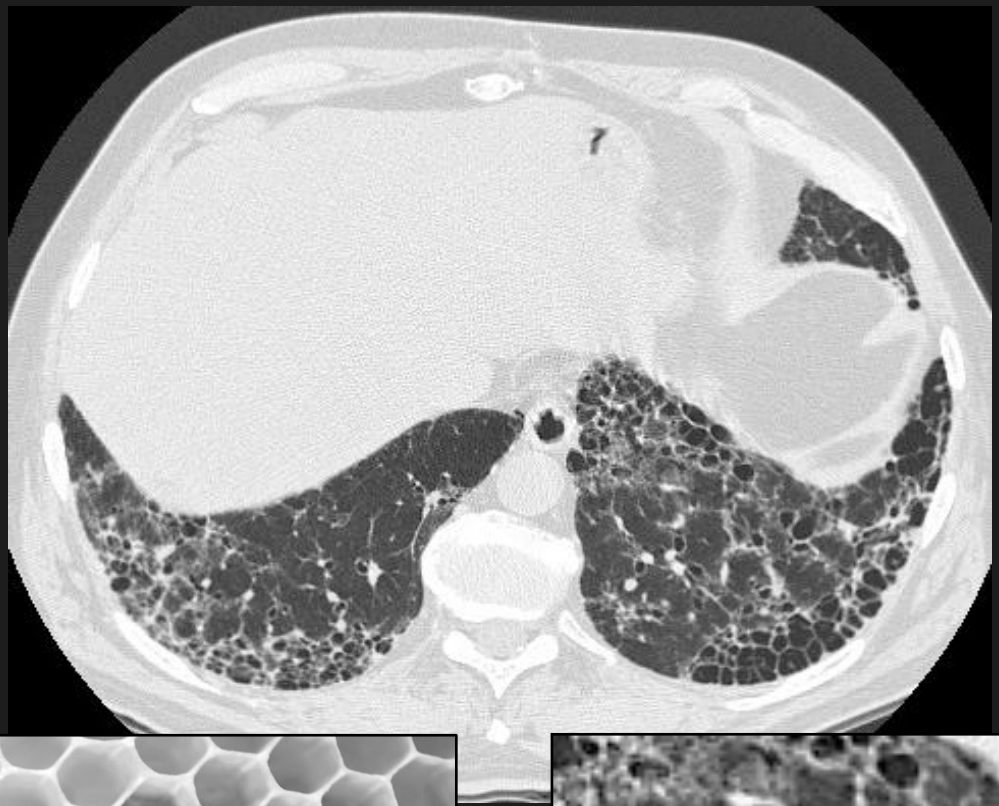
SANO

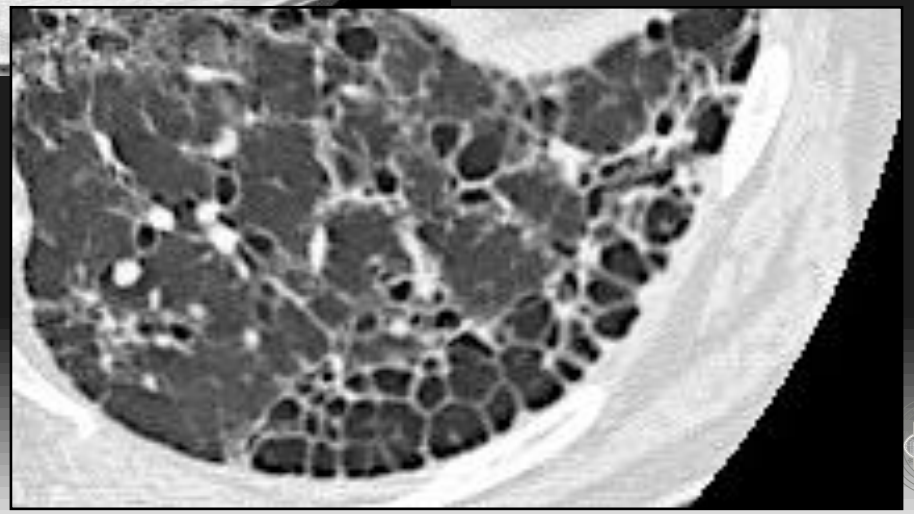


IPF

CAMPI INFERIORI

“POLMONE AD ALVEARE”





COME RICONOSCERE Mr. IPF?

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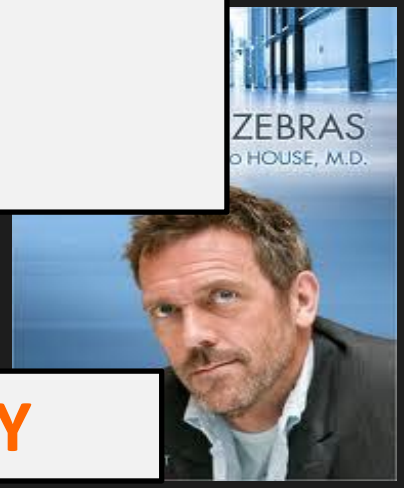
"If you h
think horses, not zebr

- **Low numbers**
- **Complex management**
- **Generally poor prognosis**
- **Lack of specific formation**



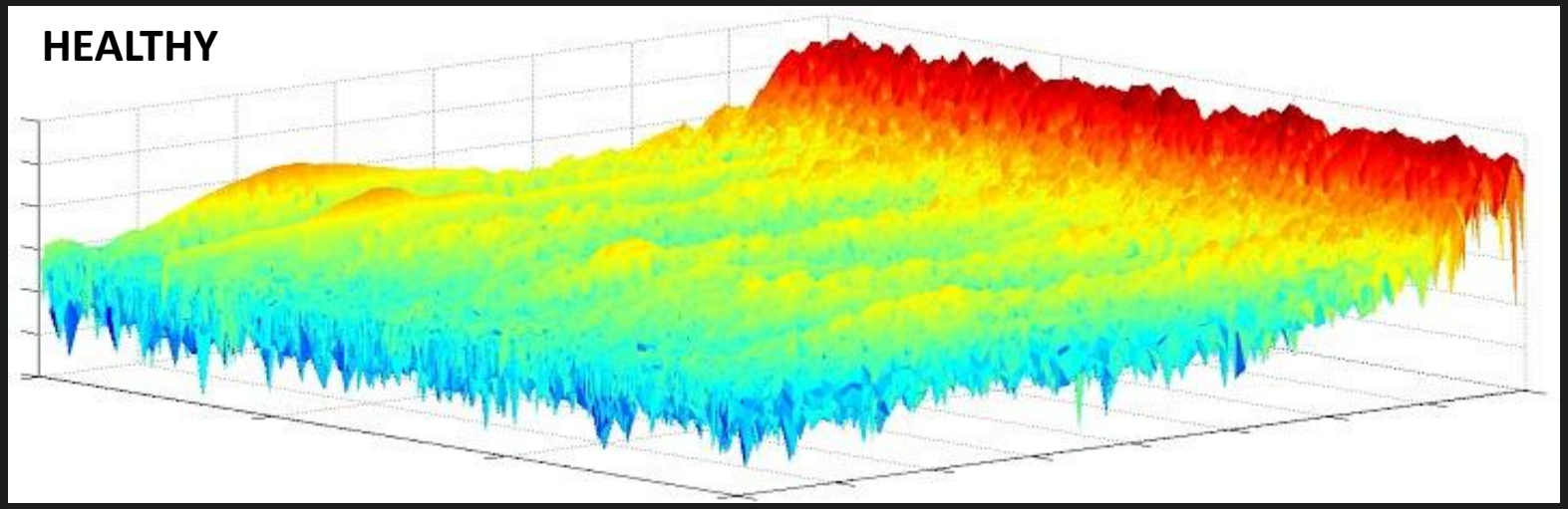
DIAGNOSTIC DELAY

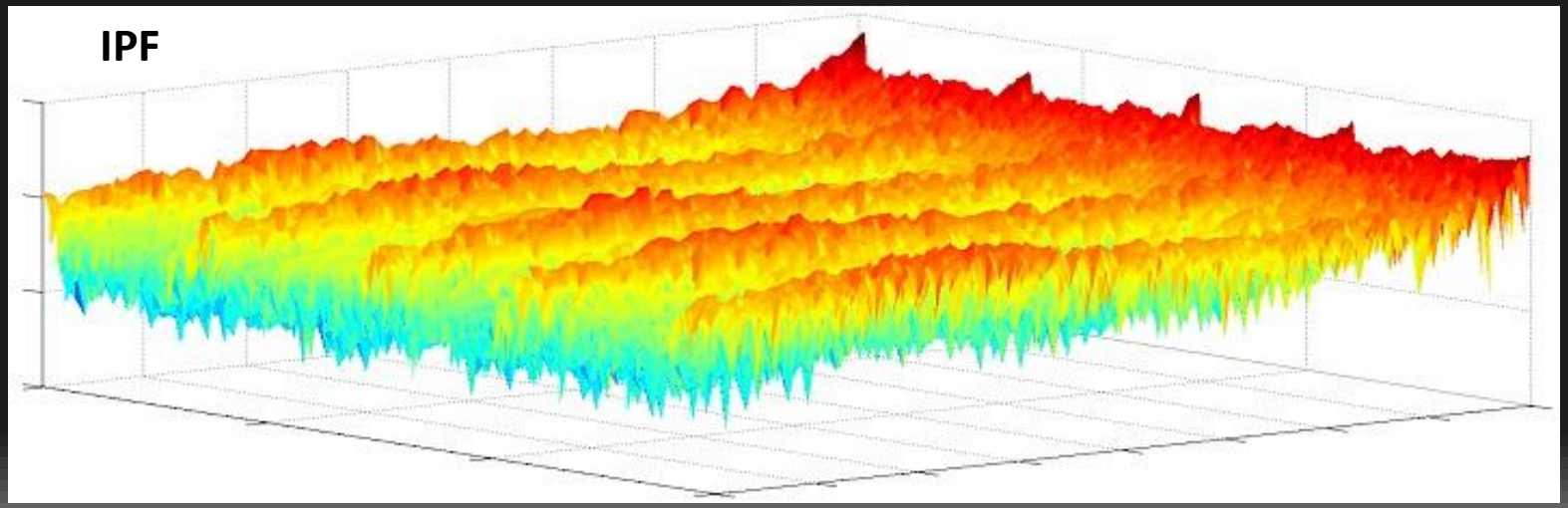
Increase in costs

Reduction of potential beneficial effects of early interventions

Ruolo dei suoni polmonari?

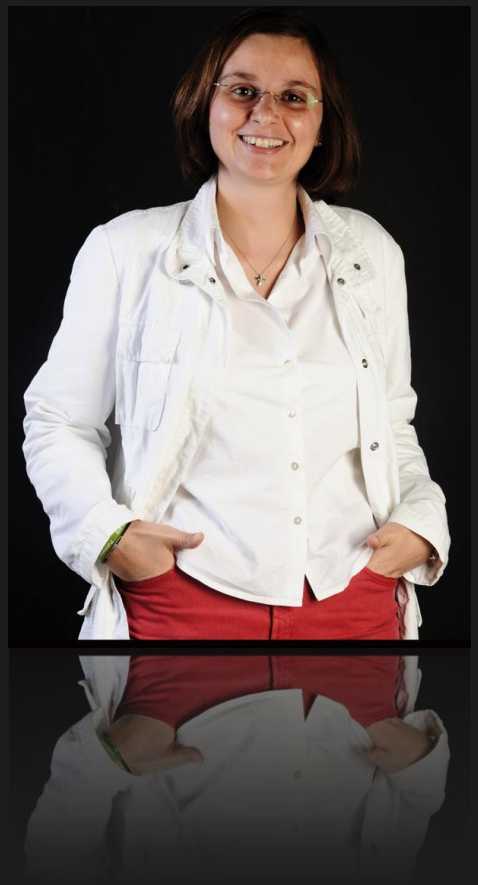
3M™ Littmann® 3200


HEALTHY


IPF

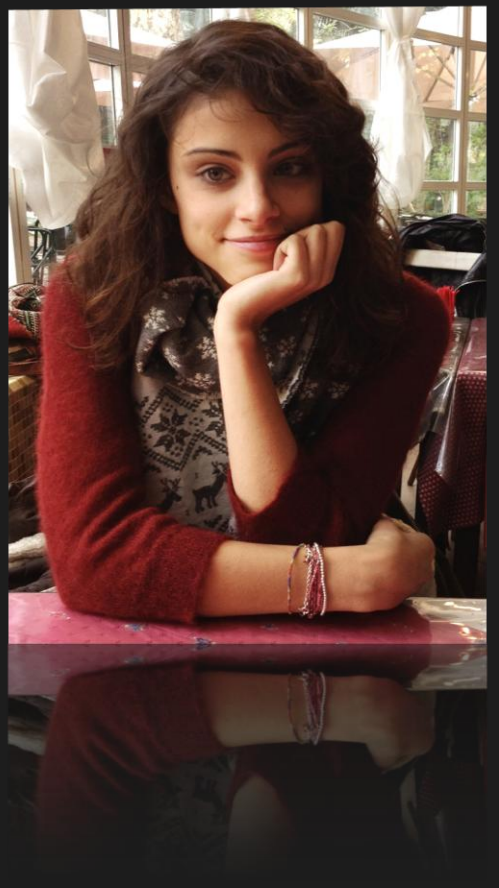
G. Della Casa

S. Cerri



G. Sgalla

M. Ori



Con il contributo di:

InterMune®
Leader in IPF

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Si può anche trovare una donna che non ha avuto esperienze amorose, ma è raro tuttavia trovarne una che ne ha avuta solo una.

Francois de la Rochefoucauld

Regulatory Information

Legislation

- Federal Food, Drug, and Cosmetic Act (FD&C Act)
- Significant Amendments to the FD&C Act
- Orphan Drug Act

Resources for You

- Developing Products for Rare Diseases & Conditions
- 21 CFR Part 316/ Proposed amendment to 1992 Orphan Regulations

Orphan Drug Act

Orphan Drug Act – Excerpts
(Public Law 97-414, as amended)

CONGRESSIONAL FINDINGS FOR THE ORPHAN DRUG ACT
The Congress finds that—

(1) there are many diseases and conditions, such as Huntington's disease, myoclonus, ALS (Lou Gehrig's disease), Tourette syndrome, and muscular dystrophy which affect such small numbers of individuals residing in the United States that the diseases and conditions are considered rare in the United States;
(2) adequate drugs for many of such diseases and conditions have not been developed;
(3) drugs for these diseases and conditions are commonly referred to as "orphan drugs";
(4) because so few individuals are affected by any one rare disease or condition, a pharmaceutical company which develops an orphan drug may reasonably expect the drug to generate relatively small sales in comparison to the cost of developing the drug and consequently to incur a financial loss;
(5) there is reason to believe that some promising orphan drugs will not be developed unless changes are made in the applicable Federal laws to reduce the costs of developing such drugs and to provide financial incentives to develop such drugs; and
(6) it is in the public interest to provide such changes and incentives for the development of orphan drugs.


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Languages EN | FR | DE | ES | IT | PT | RU
About Orphan Drugs
"Orphan drugs" are medicinal products intended for diagnosis, prevention or treatment of life-threatening or debilitating rare diseases. They are "orphans" because the pharmaceutical industry has little interest under normal market conditions in developing and marketing drugs intended for only a small number of patients suffering from very rare conditions.
What is an orphan drug?
"Orphan drugs" are medicinal products intended for diagnosis, prevention or treatment of life-threatening or very serious diseases or disorders that are rare.
Promoting orphan drug development
The growing number of rare diseases awaiting treatment are an important public health issue. Often the scarcity of incentives for drug manufacturers and the lack of...
Orphan drug designation
The first step in the development of any orphan drug is to obtain designation as an Orphan Medicinal Product.
What are you looking for:
eNews
Find out the latest news from the rare disease community!
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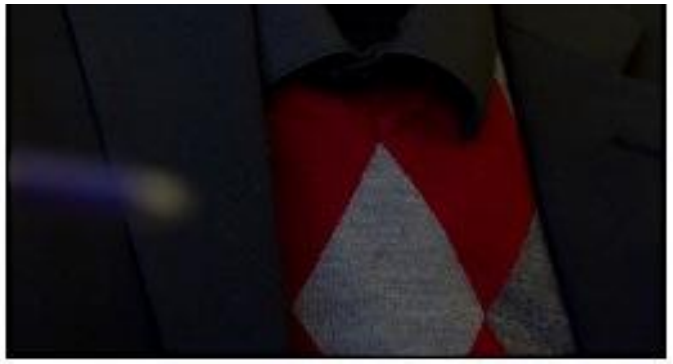
The New York Times BUSINESS DAY THURSDAY, JANUARY 31, 2013

Making 'Every Patient Counts' a Business Imperative

BY KATIE THOMAS
JANUARY 31, 2013

Customers are few for an orphan drug, but so are competitors.

tended its relationship with Mr. Jablonski, helping to finance his nonprofit, the Short Bowel Syndrome Foundation, and flying company leaders to visit him in Lincoln. On Jan. 15, he met with the chief executive and strategized with marketing employees about how to promote Gattex to his social network of 1,000 patients and caregivers.



Human medicines
- European public assessment reports
- Patient safety
- Pending EC decisions
- Withdrawn applications
- Paediatrics
- Rare disease designations
- Medicines under evaluation
- Medicines for use outside the EU
- Veterinary medicines
- Herbal medicines for human use

Home ▸ Find medicine ▸ Human medicines ▸ European public assessment reports

Esbriet

pirfenidone

Email Print Help Share

About | Authorisation details | Product information | Assessment history

Next tab »

This is a summary of the European public assessment report (EPAR) for Esbriet. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Esbriet.

Expand all items in this list

- **What is Esbriet?**
- **What is Esbriet used for?**
- **How is Esbriet used?**
- **How does Esbriet work?**
- **How has Esbriet been studied?**
- **What benefit has Esbriet shown during the studies?**
- **What is the risk associated with Esbriet?**
- **Why has Esbriet been approved?**
- **What measures are being taken to ensure the safe use of Esbriet?**
- **Other information about Esbriet**

Name	Language	First published	Last updated
Esbriet : EPAR - Summary for the public	EN = English GO	11/03/2011	18/01/2012

AUTHORISED
This medicine is approved for use in the European Union

Esbriet RSS feed

Related information

Esbriet: Orphan designation

The NEW ENGLAND JOURNAL of MEDICINE

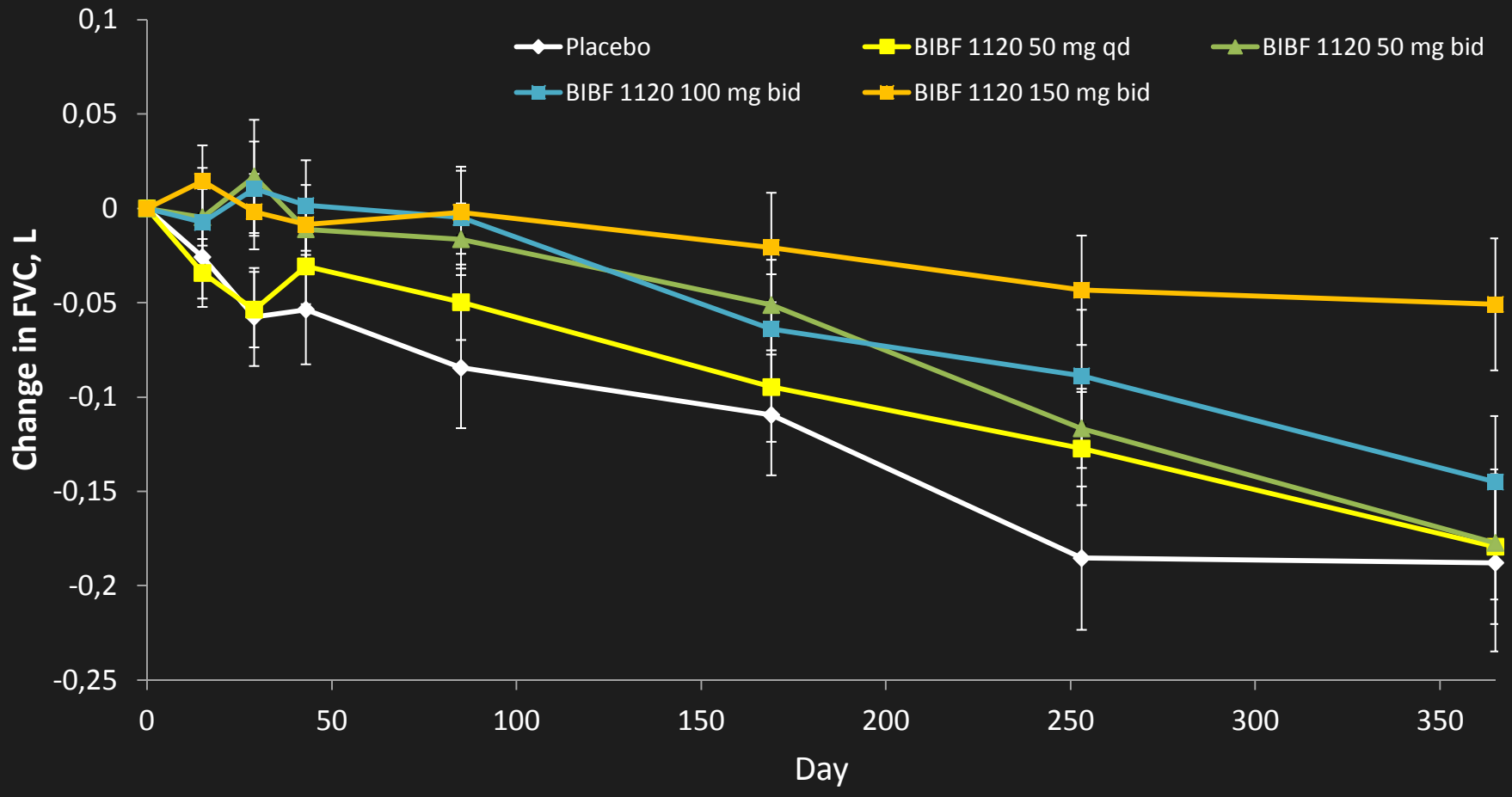
ESTABLISHED IN 1812 SEPTEMBER 22, 2011 VOL. 365 NO. 12

Efficacy of a Tyrosine Kinase Inhibitor in Idiopathic Pulmonary Fibrosis

Luca Richeldi, M.D., Ph.D., Ulrich Costabel, M.D., Moises Selman, M.D., Dong Soon Kim, M.D., David M. Hansell, M.D., Andrew G. Nicholson, D.M., Kevin K. Brown, M.D., Kevin R. Flaherty, M.D., Paul W. Noble, M.D., Ganesh Raghu, M.D., Michèle Brun, M.Sc., Abhya Gupta, M.D., Nolwenn Juhel, M.Sc., Matthias Klüglich, M.D., and Roland M. du Bois, M.D.

NEJM 2011; 365: 1079-87

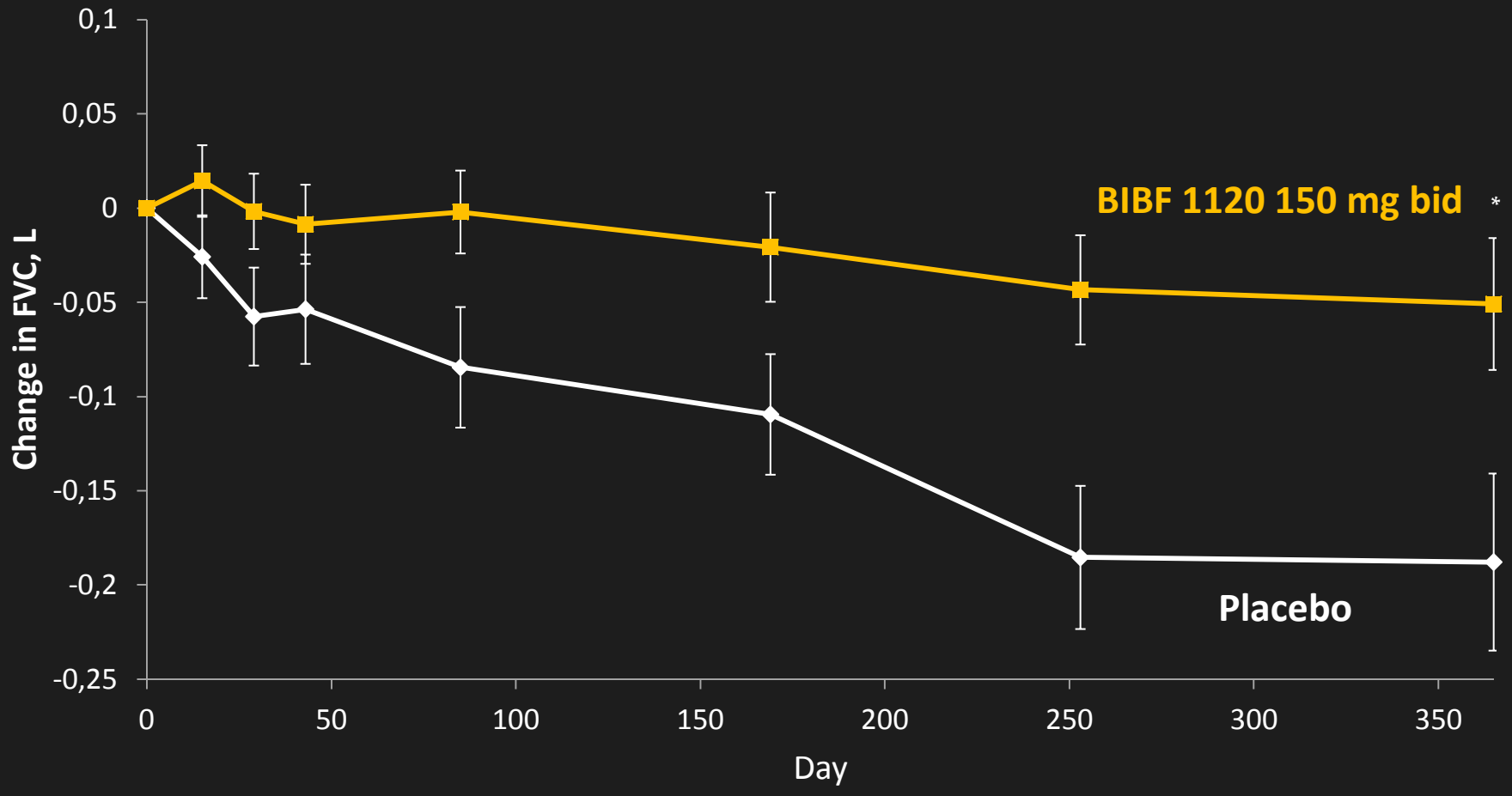
CHANGE IN FVC FROM BASELINE OVER TIME



Day	0	15	29	43	85	169	253	365
N	428	419	416	415	398	385	372	317

Mean (SE)

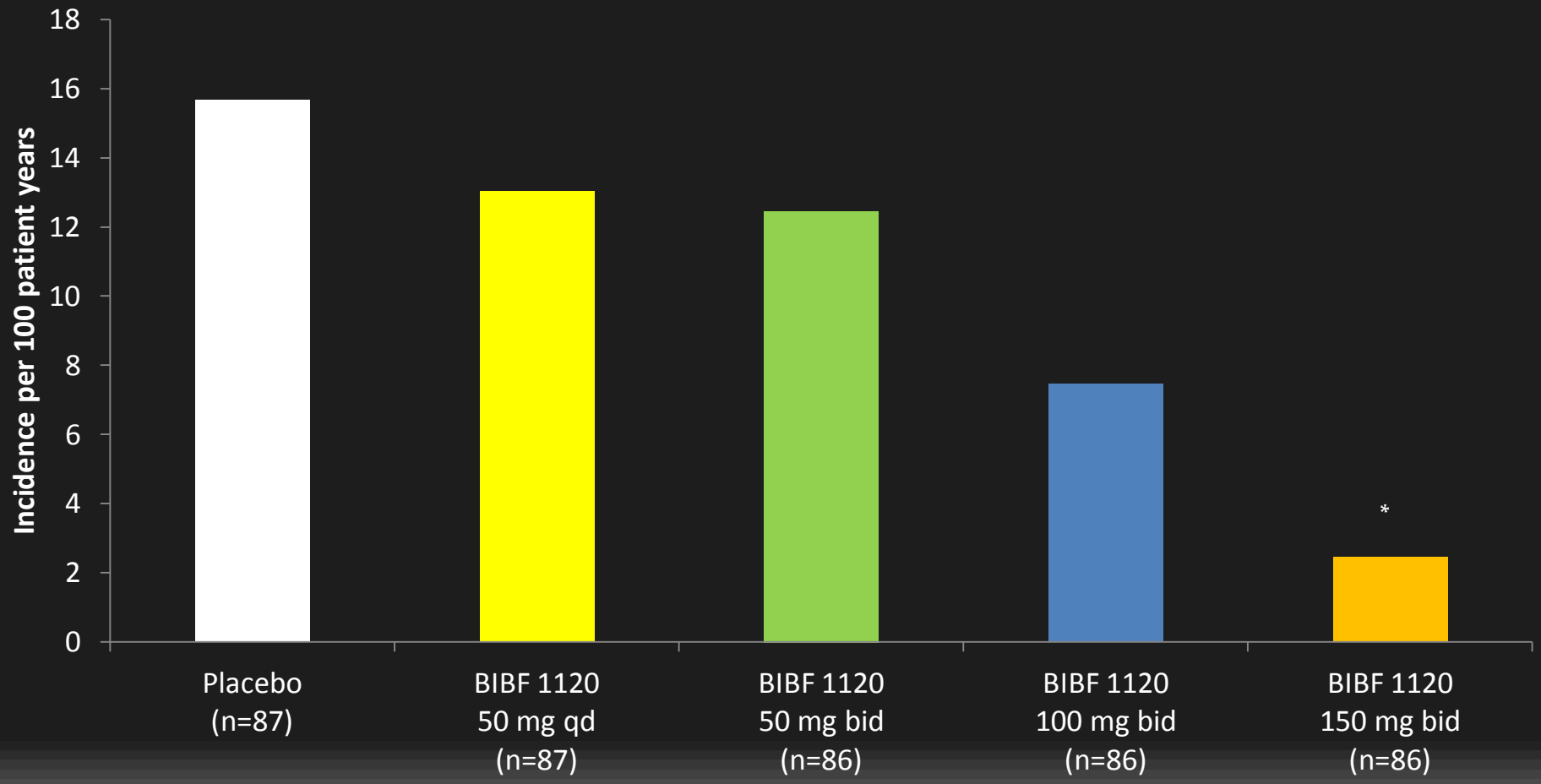
CHANGE IN FVC FROM BASELINE OVER TIME



*p=0.014 (nominal value vs. placebo); p=0.064 (closed testing procedure for multiplicity)

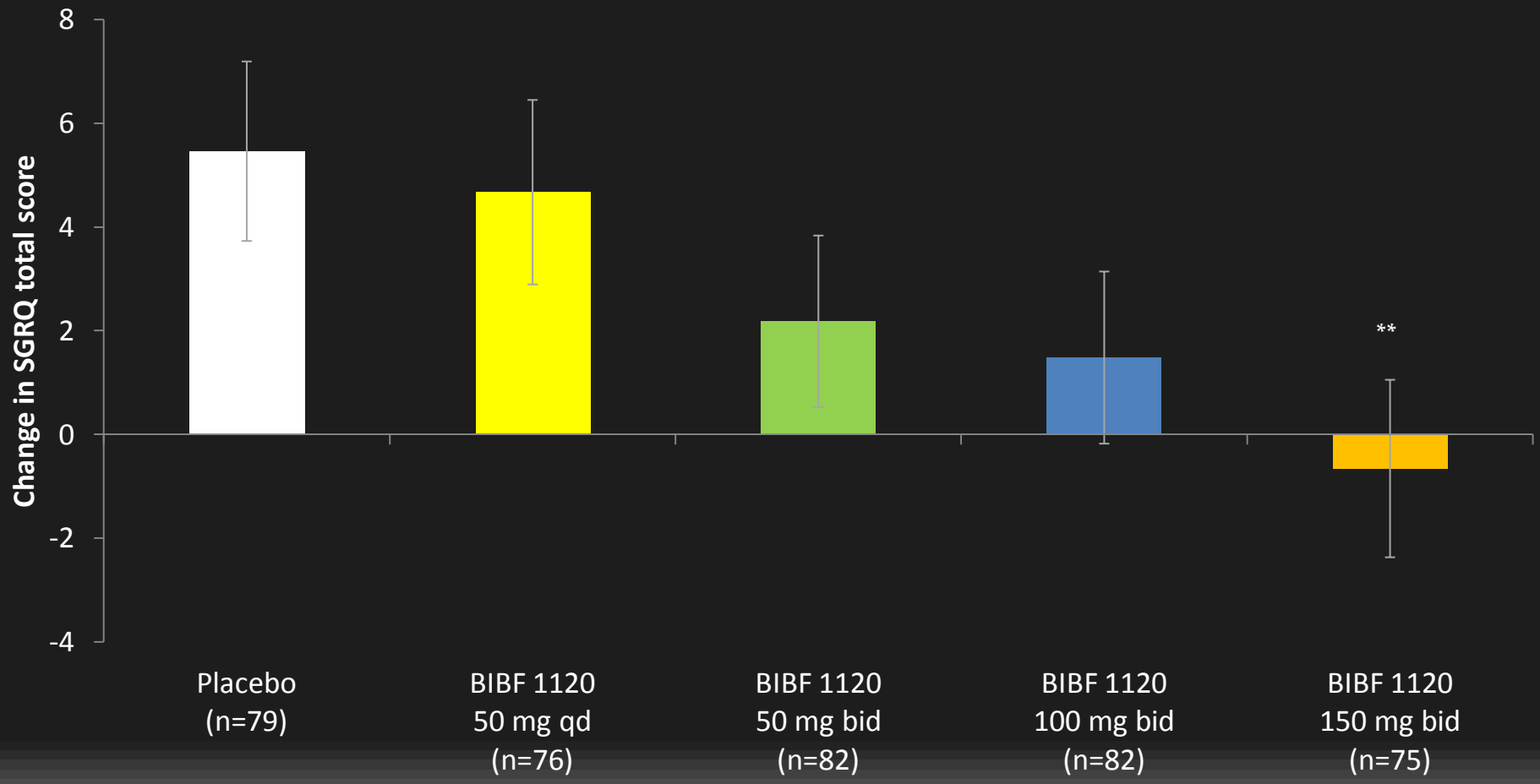
Mean (SE)

INCIDENCE OF ACUTE EXACERBATIONS



*p=0.02 vs placebo

CHANGE IN SGRQ TOTAL SCORE



LOCF. Mean (SE). **p<0.01 vs placebo
Adjusted based on an ANCOVA with terms for treatment

PHASE III TRIALS WITH NINTEDANIB
INPULSIS 1 AND INPULSIS 2

- Two identical 52-week Phase III placebo-controlled trials to evaluate the efficacy and safety of nintedanib 150 mg bid in 1,066 IPF patients completed enrolment on 17 September 2012 (trials NCT01335464 and NCT01335477).
- Primary endpoint: change in FVC at week 52.

www.clinicaltrials.gov

I veri amici sono rari, perché la domanda è minima.

Marie von Ebner-Eschenbach

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The 17th International Colloquium on Lung & Airway Fibrosis

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Organized by the Center for Rare Lung Diseases,
University of Modena & Reggio Emilia


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PARMAREGGIO
TERRAQUILIA


LASA METALLI
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There is no disease so rare that it does not deserve attention

Orphanet

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Modena, 6 Marzo 2013

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Azienda Ospedaliero-Universitaria Policlinico di Modena

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