QUALITY & SAFETY IN HEALTHCARE
FIRST CONGRESS
PRELIMINARY PROGRAM
THEME: STANDARDIZATION OF PRACTICES

Quality, Safety and Value of Drugs

Pierre Anhoury, MD, MPH, Clin. Oncology - Head of drug value department, Accenture

The following 7 rules describe the nature and the quality of drugs

1. The drug must be free from any acquired quality
2. The experiment must be done on a single, not a composite, condition
3. The drug must be tested on two contrary conditions
4. The potency of the drug should be equal to the strength of the disease
5. One should consider the time needed for the drug to take effect
6. The effect of the drug should be the same in all cases or, at least, in most
7. Experiments should be carried out on the human body

These were written by_____?

❑ A - HIPPOCRATE (460 BC – 370 BC)

❑ B – HUA TUO (110 – 220)

☑ C - AVICENNA (980 – 1037)

❑ D - HARVEY (1578-1657)

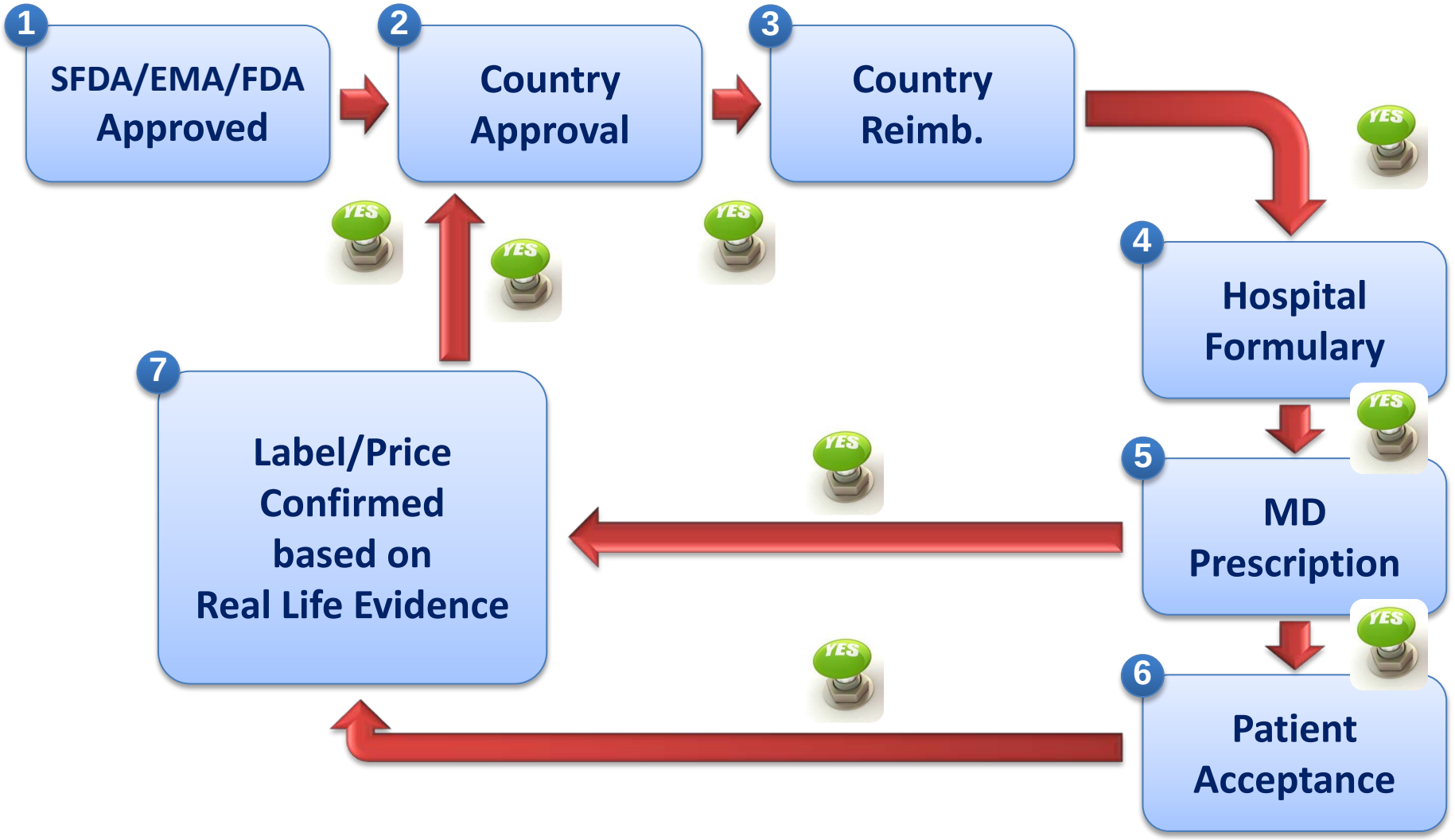
❑ E - PASTEUR (1822 – 1895)

❑ F- FRIEDRICH BAYER (1825 - 1880)

Avicenna: Canon of Medicine / Kitab El Kanoun

(980 – 1037)

7 conditions to access AND remain on the market



Sanofi Halves Price of Cancer Drug Zaltrap After Sloan-Kettering Rejection

The New York Times

By ANDREW POLLACK
Published: November 8, 2012

In an unusual move, a big drug company said on Thursday that it would effectively cut in half the price of a new cancer drug after a leading cancer center said it would not use the drug because it was too expensive.

The move — announced by Sanofi for the colon cancer drug Zaltrap — could be a sign of resistance to the unfettered increase in the prices of cancer drugs, some of which cost more than $100,000 a year and increase survival by a few months at best.

Zaltrap came to market in August at a price of about $11,000 a month. Soon after, Memorial Sloan-Kettering Cancer Center in New York decided not to use the drug, saying it was twice as expensive but no more effective than a similar medicine, Avastin from Genentech. Both drugs improved median survival by 1.4 months, doctors there said.

7 conditions to access AND remain on the market

1. SFDA/EMA/FDA Approved
2. Country Approval
3. Country Reimb.
4. Hospital Formulary
5. MD Prescription
6. Patient Acceptance
7. Label/Price Confirmed based on Real Life Evidence

Regulatory approval is simply an open door to an even riskier stage: Commercialization (Fierce Pharma, Nov 27. 2012)

Topics: Sales and Marketing

10 top drug launch disasters

Payer risk looms large as biopharma marketing snafus highlight industry's Achilles' heel

November 27, 2012

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J'aime

0

+1

Just about everyone w
experience in the drug
to the harsh realities o
10 experimental therap
an eventual regulatory
categories the succes
Research costs have

But a regulatory appro
commercialization. Ar
the rosy expectations
When payers balk or s
blockbusters wind up
transition to commercialization can end up as cautionary tales for others looking to follow the same path. Pharma, for all its deep pockets and big sales forces, often does no better. And the losers are marked down and sold off, or simply shunned by investors.

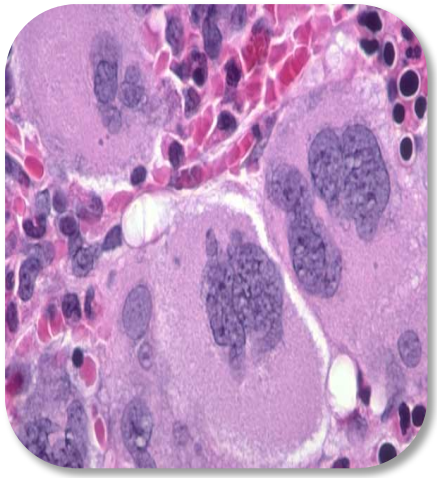
1. K-V Pharmaceuticals - Makena
2. Dendreon - Provenge
3. Sanofi - Zaltrap
4. Human Genome Sciences - Benlysta
5. Xenoport - Horizant
6. Savient - Krystexxa
7. Sanofi - Multaq
8. Somaxon - Silenor
9. AstraZeneca - Brilinta
10. Rare Disease Therapeutics - Anascorp

http://www.fiercepharma.com/special-reports/top-10-drug-launch-disasters

The Myelofibrosis business case

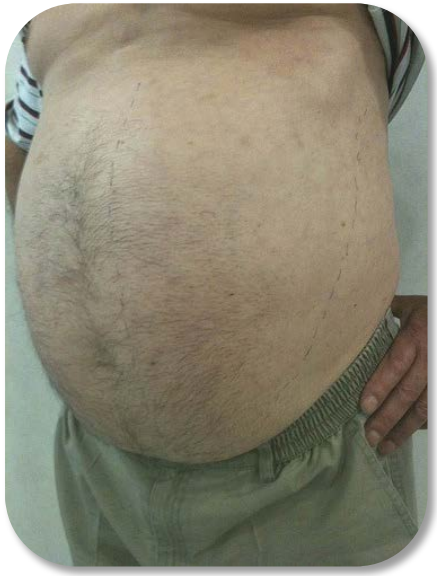
Jakafi®
ruxolitinib (tablets)
JAK targeted to make a difference

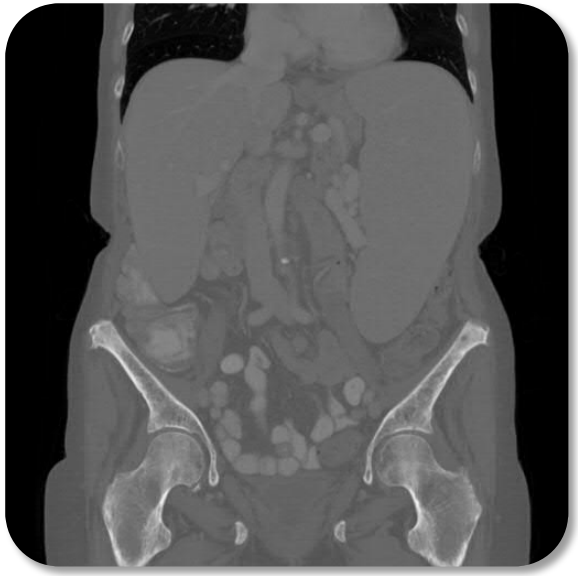
Value assessment of the new Jak2 Inhibitor

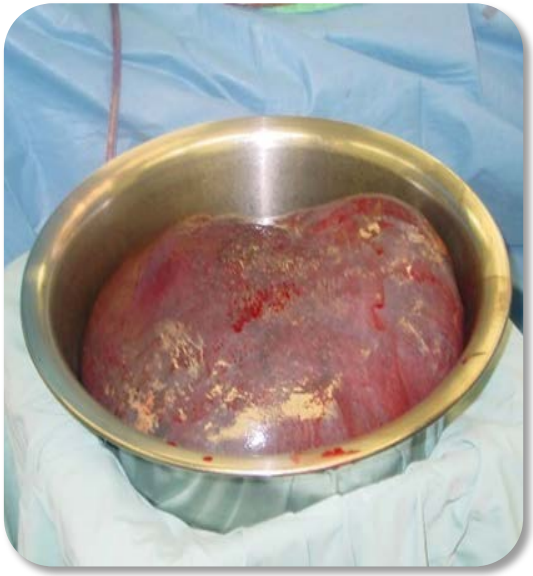


Myelofibrosis
Clinical + Biological
Abnormalities

Symptom
Fatigue
Bone pain
Fever
Pruritus
Night sweats
Symptomatic splenomegaly
Weight loss (>10%)

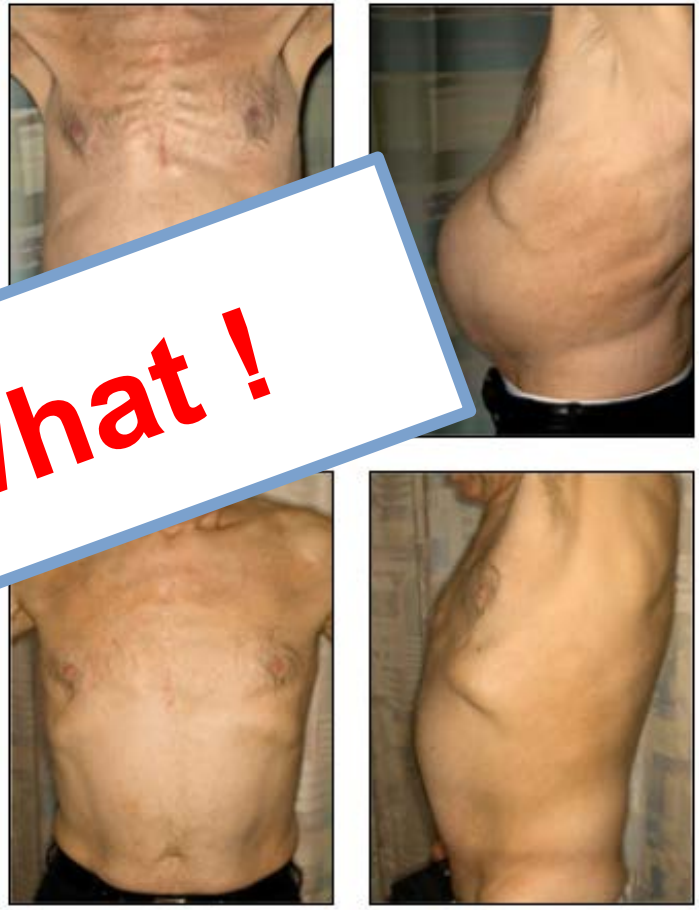






Reduction in the patient's splenomegaly

Dr. Srdan Verstovsek examines a patient whose symptoms from myelofibrosis improved during his participation in a clinical trial of a JAK2 inhibitor.



ABOVE: Photos of a patient before therapy with an experimental JAK2 inhibitor show the distended abdomen caused by the enlarged spleen, a common symptom of myelofibrosis. **BELOW:** Photos taken after 2 months of therapy with a JAK2 inhibitor show a marked reduction in the patient's splenomegaly.

FDA: So What !

Quality of life data to support and reinforce the drug's value

Contents lists available at ScienceDirect

Leukemia Research

journal homepage: www.elsevier.com/locate/leukres

The Myelofibrosis Symptom Assessment Form (MFSAF): An evidence-based brief inventory to measure quality of life and symptomatic response to treatment in myelofibrosis

Ruben A. Mesa[a,*], Susan Schwager[a], Deepti Radia[b], Andrea Cheville[c], Kebede Hussein[a], Joyce Niblack[d], Animesh D. Pardanani[a], David P. Steensma[a], Mark R. Litzow[a], Candido E. Rivera[e], John Camoriano[f], Srdan Verstovsek[g], Jeffrey Sloan[h], Claire Harrison[b], Hagop Kantarjian[g], Ayalew Tefferi[a]

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[b] *St. Thomas's, London, United Kingdom*
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[d] *CMPD Education Foundation, United States*
[e] *Mayo Clinic, Jacksonville, FL, United States*
[f] *Mayo Clinic Scottsdale, Scottsdale, AZ, United States*
[g] *M.D. Anderson Cancer Center, Houston, TX, United States*
[h] *Cancer Center Biostatistics, Mayo Clinic, Rochester, MN, United States*

Contents lists available at ScienceDirect

Leukemia Research

journal homepage: www.elsevier.com/locate/leukres

Myelofibrosis symptom assessment form 2/2

Spleenomegaly and associated mechanical symptoms

Filling up quickly when you eat (Early Satiety)	0 (Absent) 1 2 3	4 5 6 7 8 9 10 (Worst Imaginable)
	Examples: *Does not limit how much you can eat*	*Moderately limits how much you can eat* / *Severely limits how much you can eat*
Abdominal pain or discomfort	0 (Absent) 1 2 3	4 5 6 7 8 9 10 (Worst Imaginable)
	Examples: *Present but do not consider an issue*	*Definitely an issue but not requiring medications* / *Severe enough to require medications*
Inactivity	0 (Absent) 1 2 3	4 5 6 7 8 9 10 (Worst Imaginable)
	Examples: *limited only with strenuous exercise*	*Even simple walking is a difficult task* / *Mostly chair or bed ridden*
Cough	0 (Absent) 1 2 3	4 5 6 7 8 9 10 (Worst Imaginable)
	Examples: *Present but do not consider an issue*	*Definitely an issue but not requiring medications* / *Severe enough to require medications*

Other patient reported symptoms derived from an international patient survey

Night Sweats	0 (Absent) 1 2 3	4 5 6 7 8 9 10 (Worst Imaginable)
	Examples: *Noticeable but do not need to change garment or sheets*	*Garment change but able to sleep* / *Garment change and interferes with sleep*
Itching (pruritus)	0 (Absent) 1 2 3	4 5 6 7 8 9 10 (Worst Imaginable)
	Examples: *Present but do not consider an issue*	*Definitely an issue but not requiring medications* / *Severe enough to require medications*
Bone Pain (diffuse not joint pain or arthritis)	0 (Absent) 1 2 3	4 5 6 7 8 9 10 (Worst Imaginable)
	Examples: *Present but do not*	*Definitely* / *Severe enough to*

Itching (pruritus)

0 (Absent) 1 2 3 | 4 5 6 7 | 8 9 10 (Worst Imaginable)

Examples: *Present but do not consider an issue* / *Definitely an issue but not requiring medications* / *Severe enough to require medications*

4 changes transformed the 7 conditions to be on the market into barriers

Stakeholders & changing needs

More **challenging attitude** to concede **drug approval**

"So What" attitude

Regulators

Payers

Stronger attention to the **relationship** between **drug value** and **cost**

"Reduce Cost" trend

Focus on the **cost/benefit analysis** of the **protocols**

"Cost Effectiveness Culture"

Physician

Patients

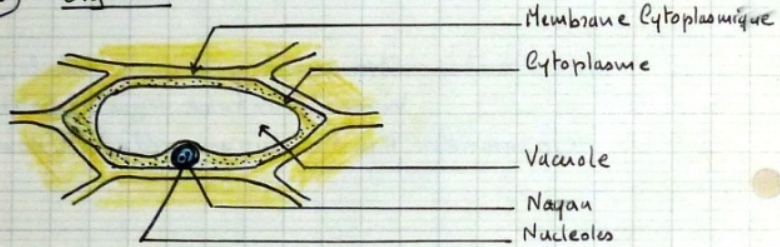
New consciousness and **influencing role** on the drug selection

"Patient Empowerment"

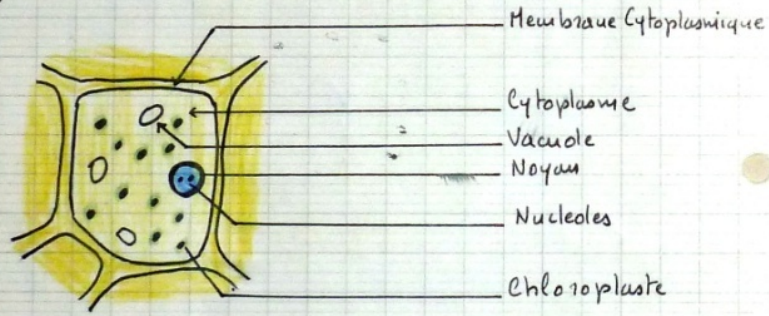
1960

Exemples de cellules :

I) Oignon



II) Elodée



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1970

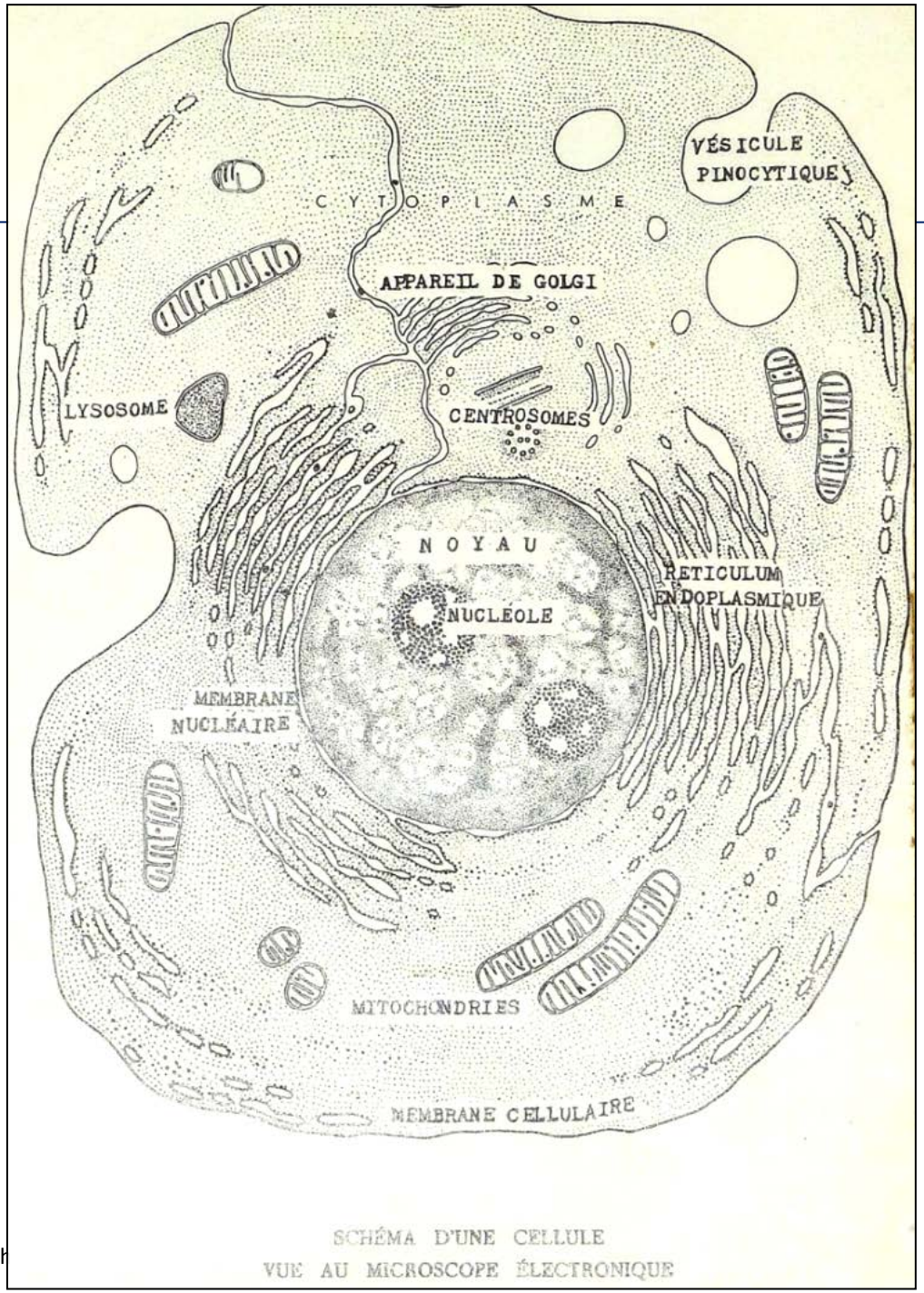
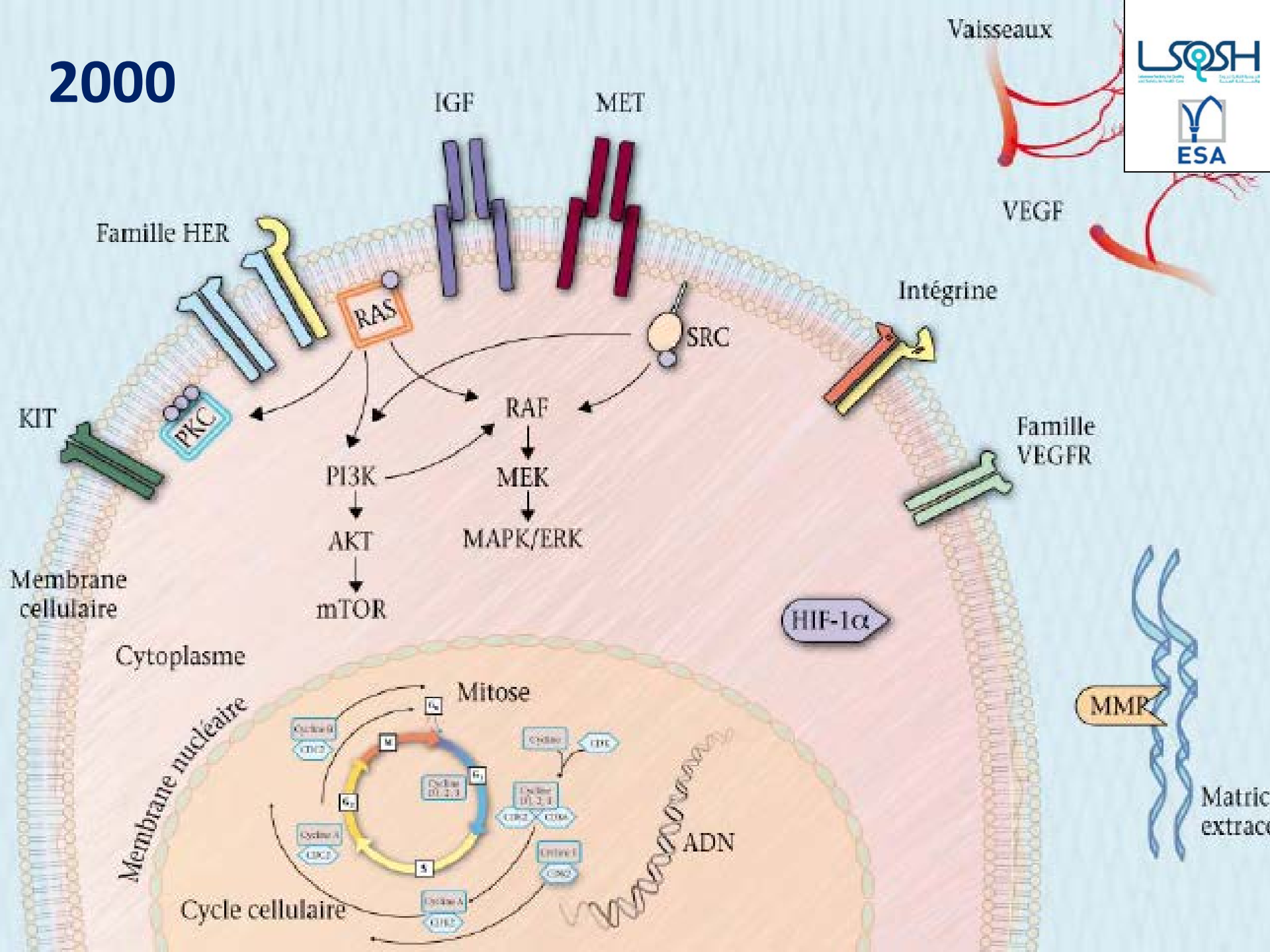
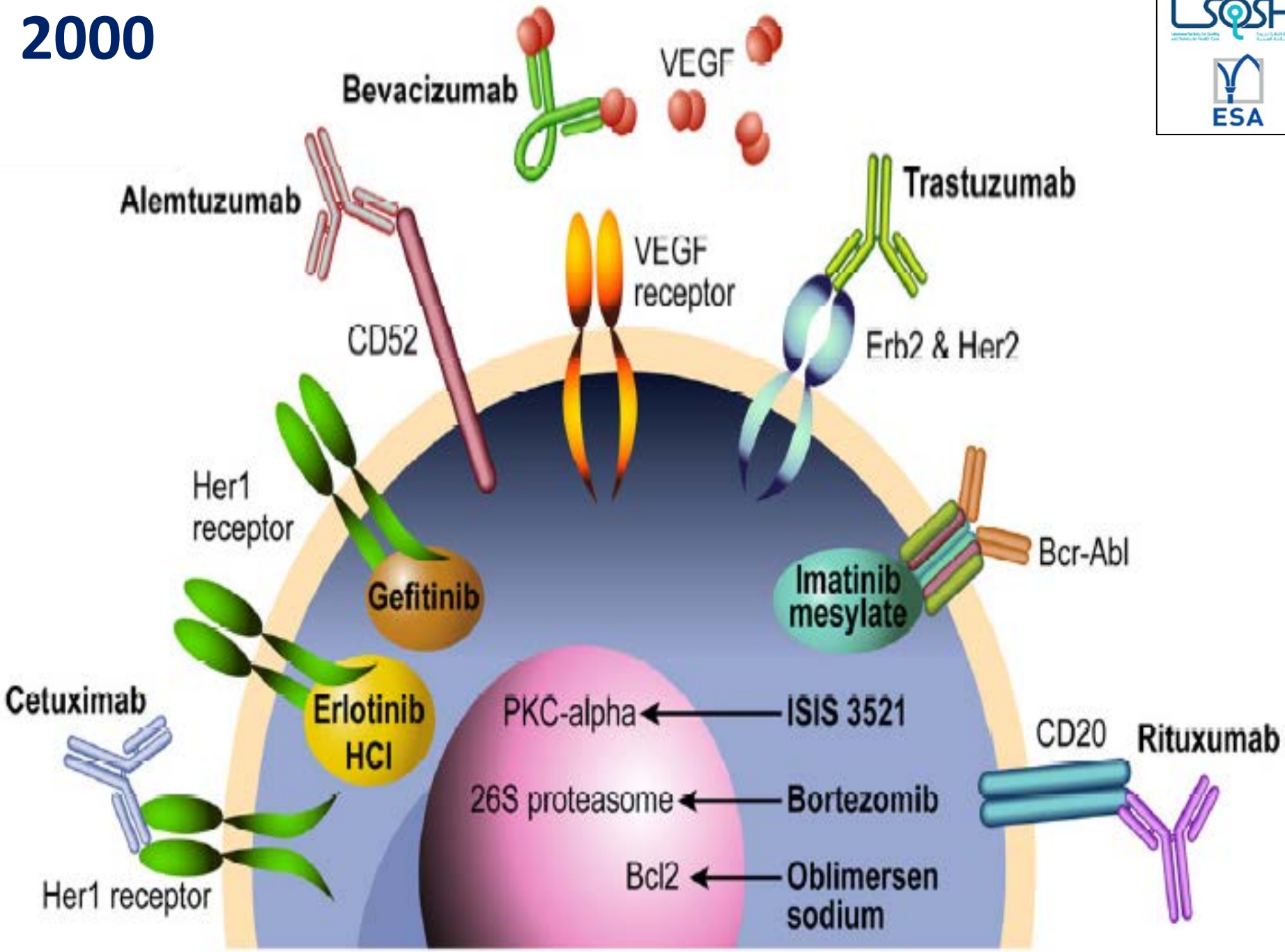


SCHÉMA D'UNE CELLULE
VUE AU MICROSCOPE ÉLECTRONIQUE

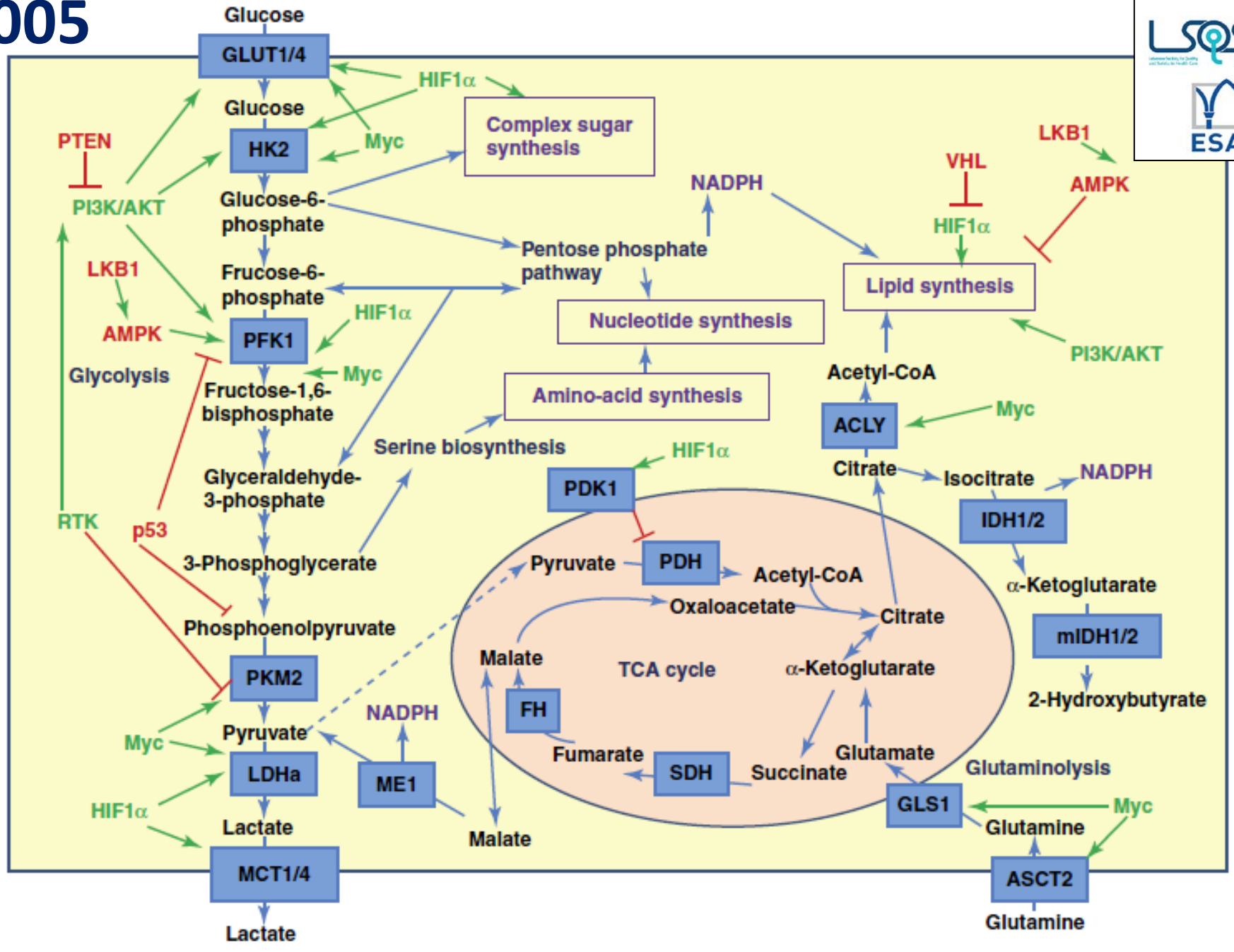
2000


Vaisseaux
IGF
MET
VEGF
Famille HER
RAS
SRC
Intégrine
KIT
PKC
RAF
PI3K
MEK
AKT
MAPK/ERK
Famille VEGFR
Membrane cellulaire
mTOR
HIF-1α
Cytoplasme
Mitose
MMP
Membrane nucléaire
ADN
Cycle cellulaire

2000

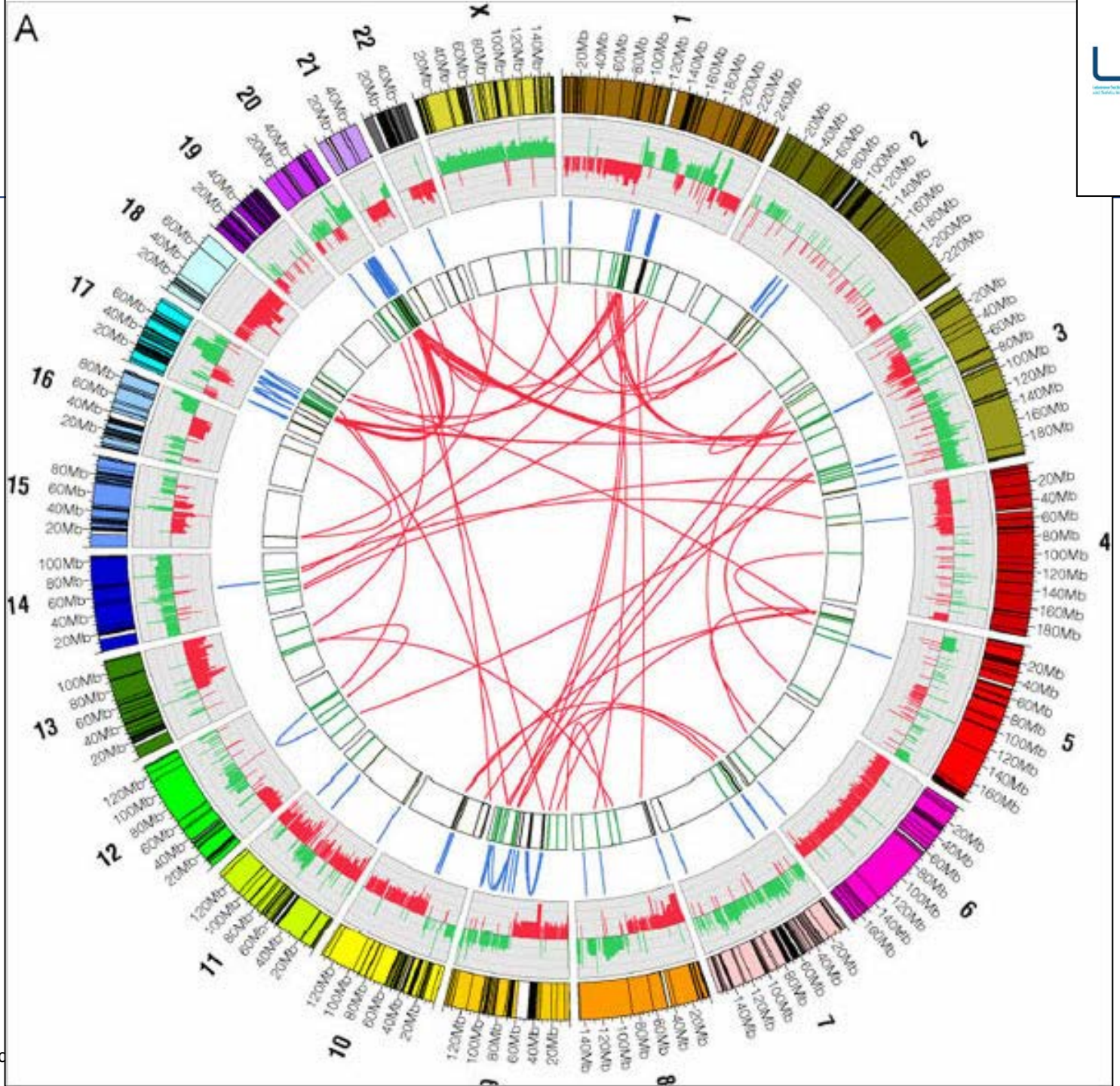

Bevacizumab
VEGF
Alemtuzumab
Trastuzumab
VEGF receptor
CD52
Erb2 & Her2
Her1 receptor
Gefitinib
Imatinib mesylate
Bcr-Abl
Cetuximab
Erlotinib HCl
PKC-alpha
ISIS 3521
CD20
Rituxumab
26S proteasome
Bortezomib
Bcl2
Oblimersen sodium
Her1 receptor

2005



Drug Discovery Today

2011



The new complexity is offering hospitals a new role in drug value assessment

- Molecular biology is the main R&D driver in an unbelievably complex environment with many uncertainties regarding the real clinical outcomes and long-term human impact

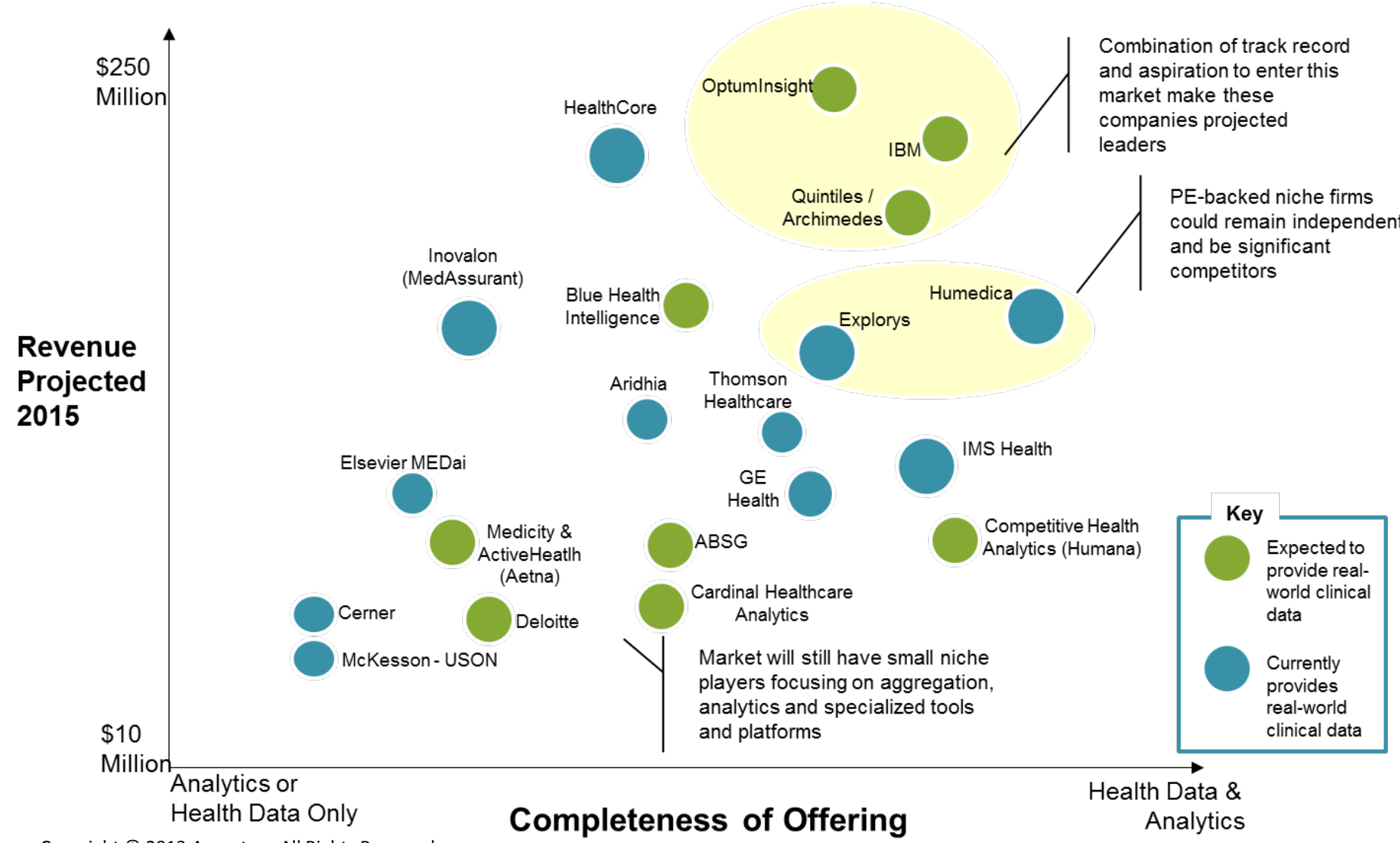
- New drugs are targeting smaller populations and are more expensive

- New drugs are approved for several indications, targeting the same mechanism of action in different diseases (inflammatory diseases, neurology, oncology,…)

- Randomized Clinical Trials are not sufficient to document the full value of a drug. Value dossier are strongly challenged by regulators, HTA agencies and payers

Real life evidence is becoming more systematic for the evaluation of the drug in the real world. Hospitals are the first contributors to data collection from patient records

Health data and analytics competitive environment



Drug value is also an issue in the generic business

Médicaments : les nouveaux faussaires

Par *Pierre Demoux* | 06/11 | 18:06

La contrefaçon de médicaments est devenue une activité très rentable pour des trafiquants qui profitent des possibilités d'Internet et des failles dans les systèmes de santé. Pays pauvres comme pays riches sont touchés, avec des risques sanitaires graves.

Les Echos
LE QUOTIDIEN DE L'ÉCONOMIE

7 novembre 2013

The growth of biosimilars will encourage HTA agencies to require more real life evidence

Classic molecule, chemical synthesis

Complex molecule, biological synthesis

Princep drug

Traditional generic

Biosimilar

Due to the **high complexity of biologicals and their production**, biosimilars **cannot guarantee** the exact structure and conformation **similarities** with the princep drugs

Due to these differences, **real life evidence** generation will become key in **demonstrating the real effects of biosimilars** and will be expected from payers and regulatory authorities

Only a fraction of generics actually are efficient, making the need for control very important

Empty pill boxes

Original drugs

Counterfeit drugs

Substandard drugs

"Perfect" generic

Counterfeit and Substandard

- Counterfeit:
  - Missing key ingredients
  - Too strong or too weak
  - With the wrong active ingredients
  - With dangerous contaminants
  - In unsanitary or unsterile conditions
  - Using unsafe methods
  - With improper labels

SAFEMEDICINES.org

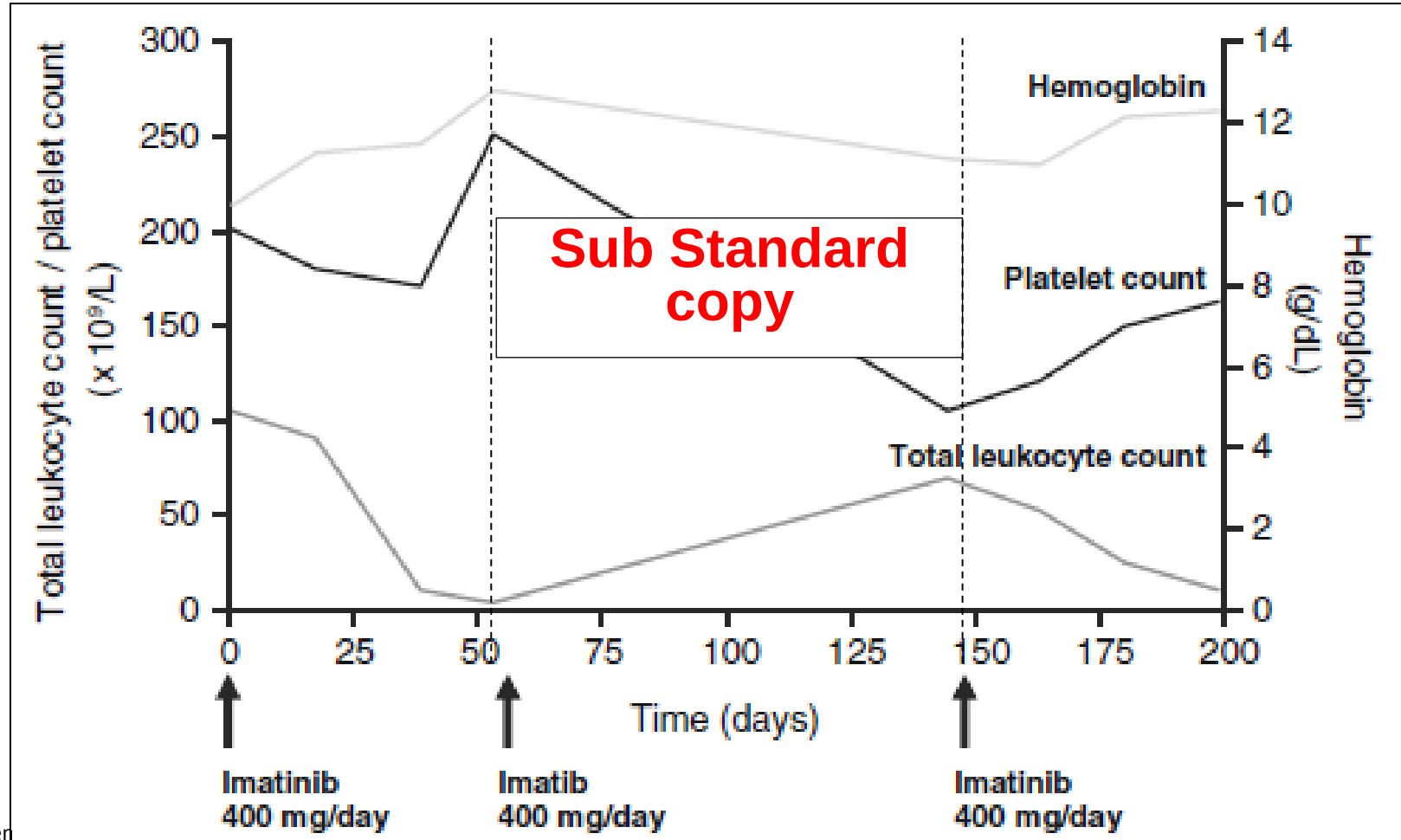
- Substandard:
  - Result of manufacturer that do not follow approved “Good Manufacturing Practice” regulated by the FDA or EMA
  - No intent to fool or defraud the consumer
  - Drugs fall below the established standard

Int J Hematol
DOI 10.1007/s12185-009-0431-1

CASE REPORT

Failure of copy Imatib (CIPLA, India) to maintain hematologic and cytogenetic responses in chronic myeloid leukemia in chronic phase

Mervat Mattar



There is a real risk to have sub-standard copies

Hematologic Relapse after 2 Years on a Non-Authorized Copy Version of Imatinib in a Patient with Chronic Myeloid Leukemia in Chronic Phase: A Case Report

Zoubir Chouffai

Clinique Belvedere, Casablanca, Morocco

Failure of a non-authorized copy product to maintain response achieved with imatinib in a patient with chronic phase chronic myeloid leukemia: a case report

Hadi Alphonse Goubran

Address: Professor of Medicine and Clinical Haematology, Faculty of Medicine, Cairo University, 73, Maadi, 1431, Cairo, Egypt

The Docetaxel example

ORIGINAL ARTICLE

Pharmaceutical quality of docetaxel generics versus originator drug product: a comparative analysis

Jérôme Vial, Mélanie Cohen, Patrick Sassiat and Didier Thiébaut

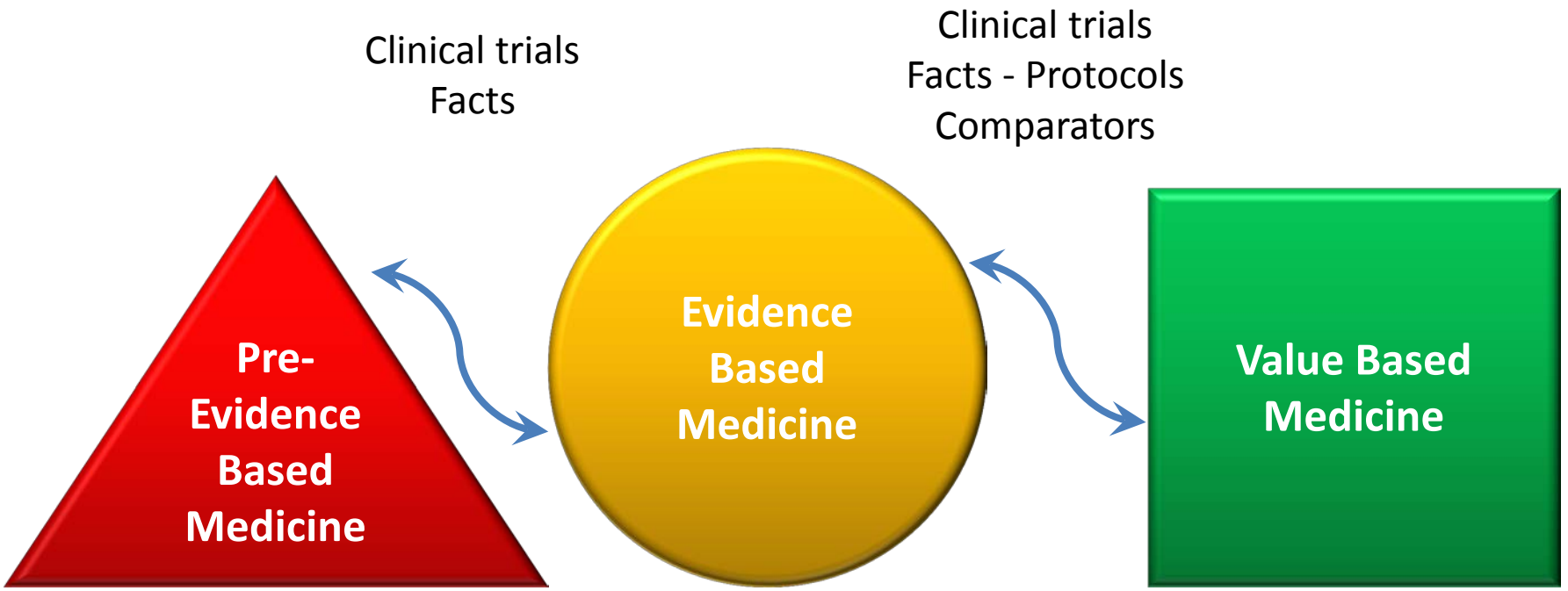
Laboratoire Environnement et Chimie Analytique, Paris, France

Address for correspondence: Jérôme Vial, Labora
ESPCI – CNRS UMR 7121, 10 rue Vauquelin, 75
Fax: +33 1 40 79 47 76; jerome.vial@espci.fr

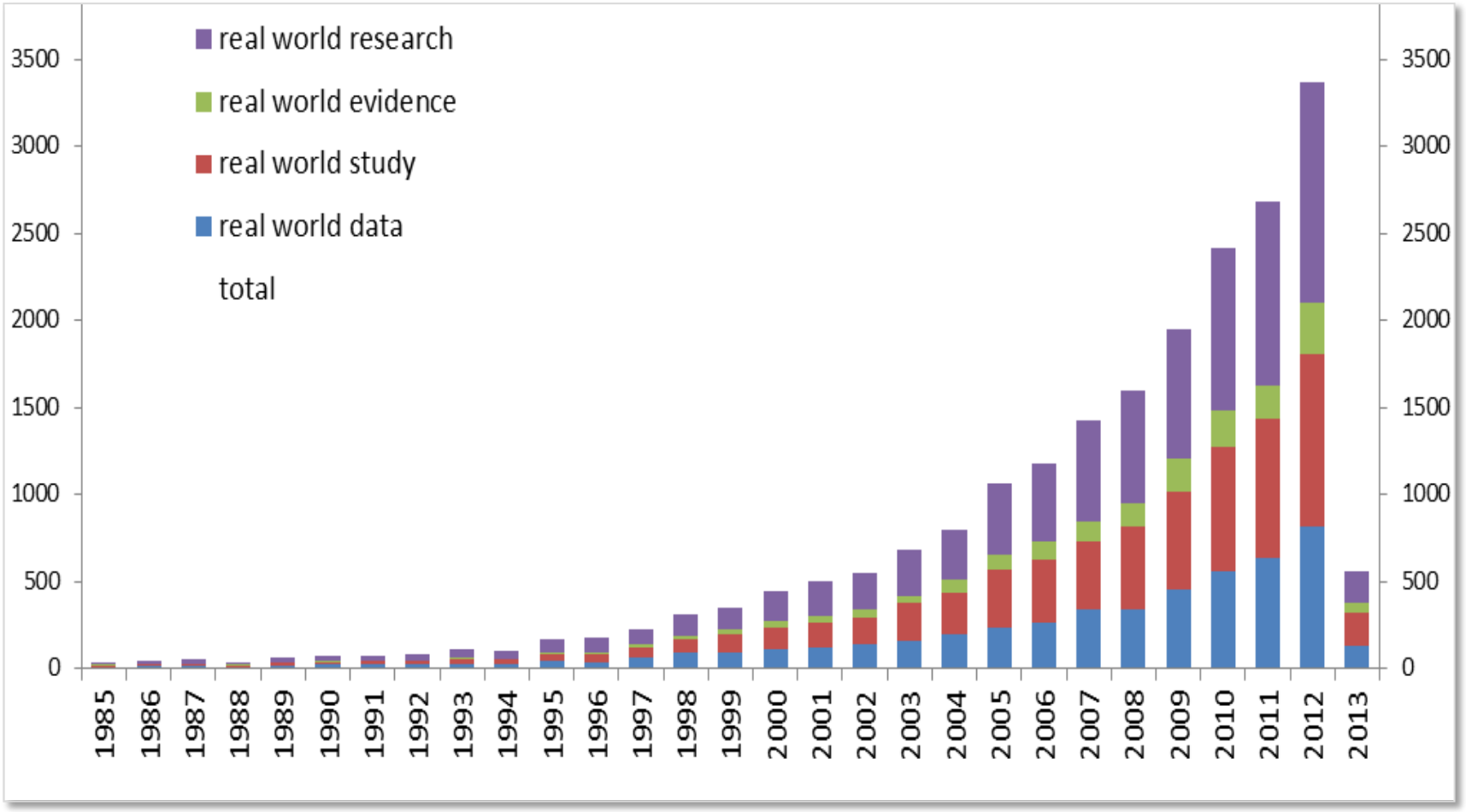
Key words: Desirability analysis – Docetaxel – C
graphy – Taxotere

Conclusions: This study demonstrated that from an analytical point of view, 90% of the generic docetaxel formulations evaluated contained insufficient active drug, high levels of impurities or both. This has the potential to affect both efficacy and safety of the drug.

Evidence based medicine is not enough:
Value Based Medicine is the driver



Real Life Evidence Publications



Documenting the value of the drug is a continuous process

Value Dossier

Phase I | Phase II | Phase III | Launch | Phase IV

Phase I | Phase II | Phase III | Launch | Phase IV

Continuous value documentation

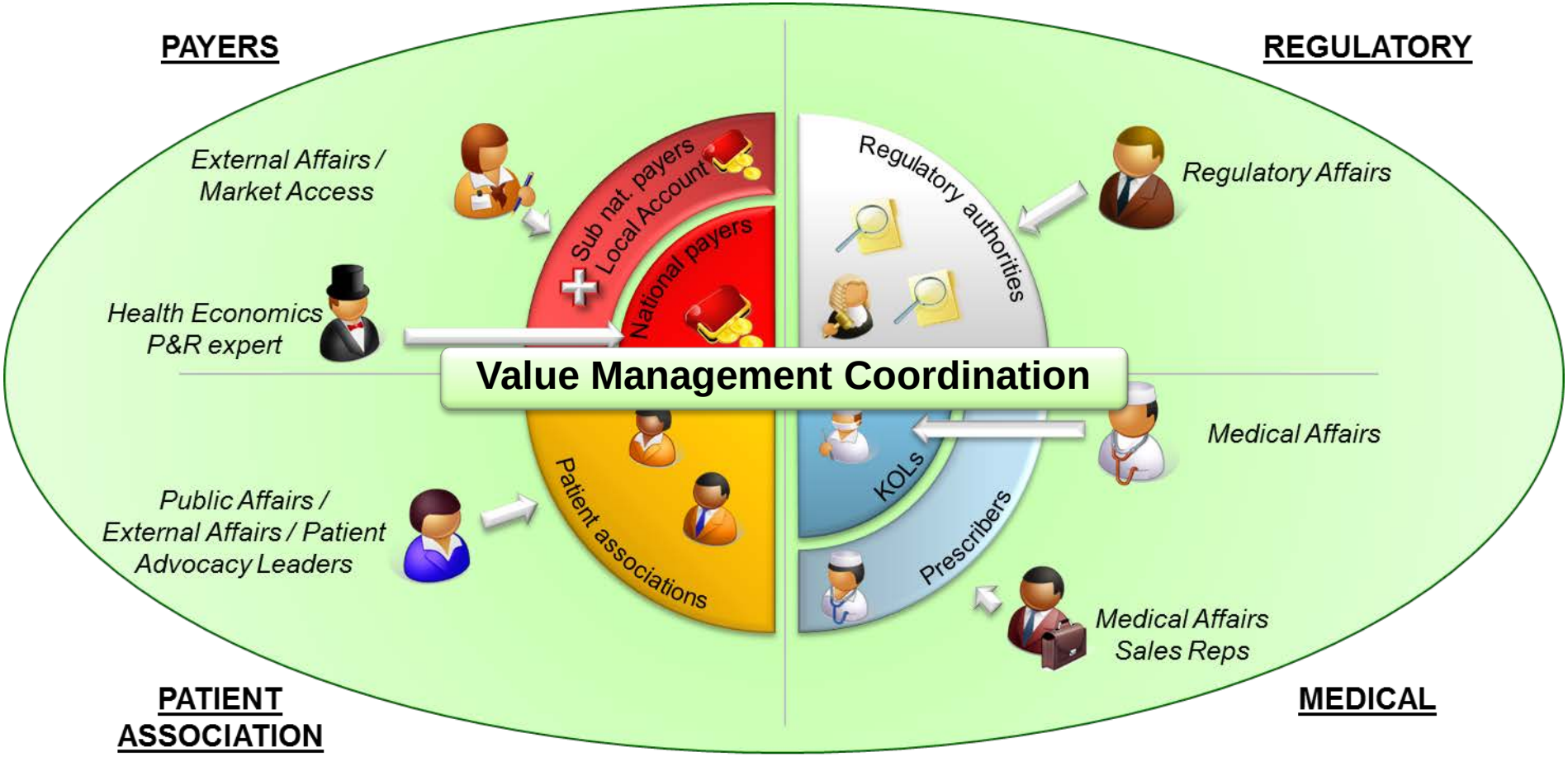
With Real World Data becoming mandatory, it's time to switch from Pharmacovigilance to Valuevigilance

Pharmacovigilance

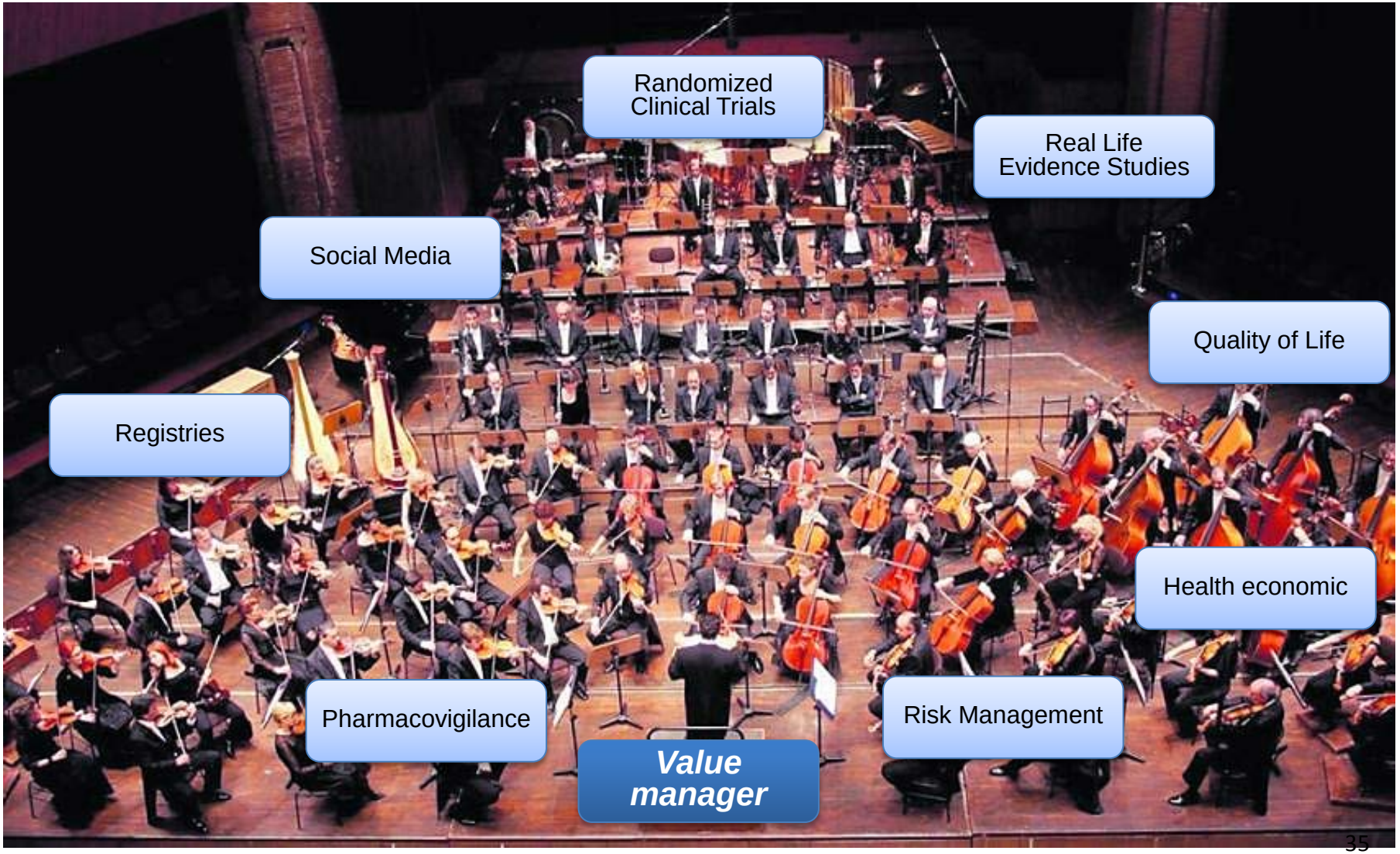
Value Vigilance

- Pharmacovigilance
- Benefits
- Quality of Life
- Economic Impact

Value management is a cross functional exercise…



…and probably an art



Thank You !

pierre.anhoury@accenture.com