

Innovative Aspects of Orphan Drugs

Marc Doms (presenter)

Helena Jenzer (facilitator)


*EHP Congress on innovation
Barcelona March 2014*

Nothing to



disclose




 *Slicing your disease to orphan needs*

Orphan Drugs

FOR

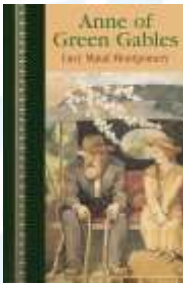
DUMMIES



A Reference for the Rest of Us!



“Medicinal products intended for the diagnosis, prevention or treatment of a life-threatening condition affecting no more than 5 in 10 000 persons in the EU”



EMA 2000

UZ
Leuven

Herengatan 49
B-3000 Leuven

www.uzleuven.be
tel. +32 (0) 30 30 33 11

UNIFORMIT HOSPITAAL LEUVEN

Chemical Classification System (WHO)

letter	code	Omschrijving hoofdgroep (eerste letter)
A	ATC code A	Spijverteringsstelsel en <u>metabolisme</u>
B	ATC code B	Bloed en bloedvormende <u>organen</u>
C	ATC code C	Cardiovasculair <u>systeem</u>
D	ATC code D	Dermatologica
G	ATC code G	Genito-urinaire <u>systeem</u> en <u>geslachtshormonen</u>
H	ATC code H	Systemische <u>hormonale preparaten</u> , met uitzondering van <u>insuline</u> en <u>geslachtshormonen</u>
J	ATC code J	Antinfectie <u>middelen</u> voor systemisch gebruik
L	ATC code L	antineoplasie en <u>immunomodulerende stoffen</u>
M	ATC code M	Spier- en skelet <u>systeem</u>
N	ATC code N	Zenuwstelsel
P	ATC code P	Antiparasitische <u>middelen</u> , insecticiden en <u>repellents</u>
Q	ATC code Q	Veterinaire <u>geneesmiddelen</u>
R	ATC code R	Ademhalings <u>systeem</u>
S	ATC code S	Sensorische <u>organen</u>
V	Varia	

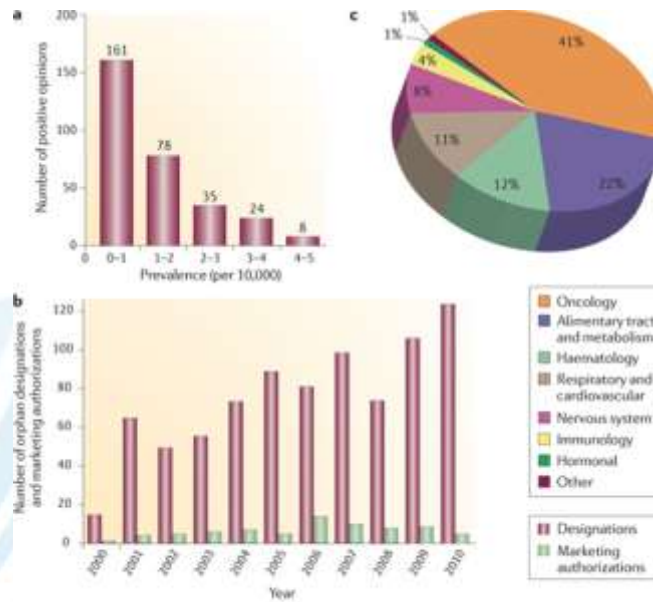




- Protocol assistance
- Market exclusivity (10 years)
- Financial incentives (fee reduction)
- Centralized EU-procedure
- National incentives (reimbursement)
- Research support
- etc...

- 73 authorised orphan drugs (1145 designated)
- 62 rare diseases
- 16 withdrawn or suspended (Afinitor, Aldurazyme, Busilvex, Fabrazyme, Glivec, Ilaris, Ixiaro, PhotoBarr, Replagal, Revolade, Somavert, Sutent, Thelin, Trisenox, Ventavis, Xyrem)

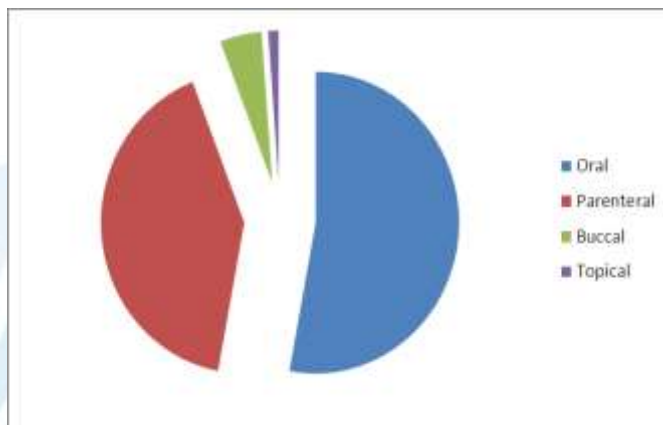


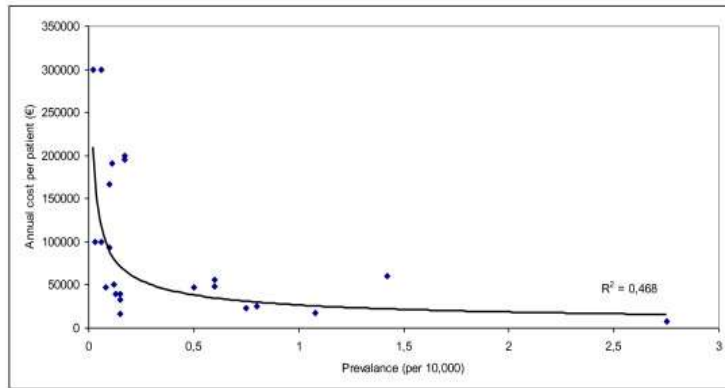


Nature Reviews | Drug Discovery



Route of administration



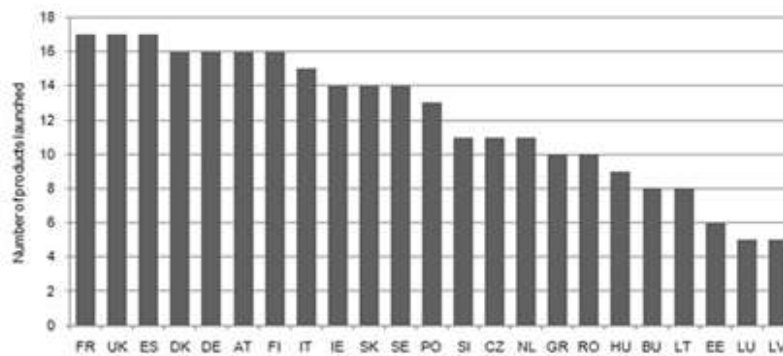


Bron : prof. dr. Steven Simoens - Onderzoekscentrum voor Farmaceutische Zorg en Farmaco-economie

UZ Leuven | Herestraat 49 | 3000 Leuven | www.uzleuven.be | tel. +32 (0) 30 30 30 11 | SANPHORIT HOSPITAAL LEUVEN

Reimbursement in Europe

Total number of orphan drugs launched in 2001-2009 per country



Prevention

NO orphan autorisation

- Folic acid 0,4 mg / 4 mg



Orphan Autorisation

- Japanese encephalitis vacc



Proteïnekinase inhibitors



NO orphan drug autorisation

- Caprelsa (vandetanib)
- Inlyta (axitinib)
- Iressa (gefitinib)
- Tarceva (erlotinib)
- Tyverb (lapatinib)
- Votrient (pazopanib)
- Xalkori (crizotinib)
- Zelboraf (vemurafenib)

Orphan drug autorisation

- Glivec (imatinib)
- Nexavar (sorafinib)
- Sprycel (dasatinib)
- Tassigna (nilotinib)
- Sutent (sunitinib)

NO Orphan drug autorisation

- Iressa (gefitinib)
- Sutent (sunitinib)



Orphan drug autorisation

- Caprelsa (vandetanib)
- Glivec (imatinib)
- Inlyta (axitinib)
- Nexavar (sorafinib)
- Sprycel (dasatinib)
- Tarceva (erlotinib)
- Tassigna (nilotinib)
- Tyverb (lapatinib)
- Votrient (pazopanib)
- Xalkori (crizotinib)
- Zelboraf (vemurafenib)



Oliver Twist, Roman Polanski, Charles Dickens.

M. Dooms



Zinc acetate





Trully Innovative

Life-threatening
condition

&

Unmet Medical Need



**“On fera sécher au
soleil le sang
tiré d’un jeune
homme sain ...”**

Lemery, Pharmacopée
Universelle. 1647



Advanced Therapy Medicinal Products



77 DESIGNATIONS AND 1 AUTHORISATION

- **ATMP**

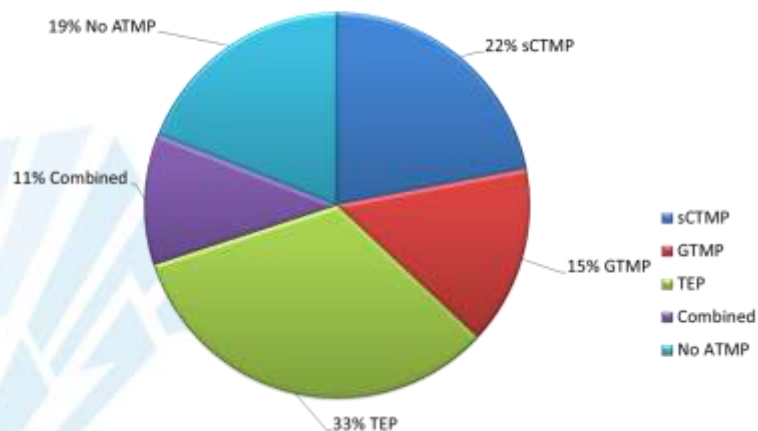
- products in gen therapy (GTMP)
- products in somatic cell therapy (sCTMP)
- products in tissue engineering (TEP)
- combined products (Combined)
- 'Manipulated': minimum 1 of the 2 criteria

1- "Substantial manipulation" :

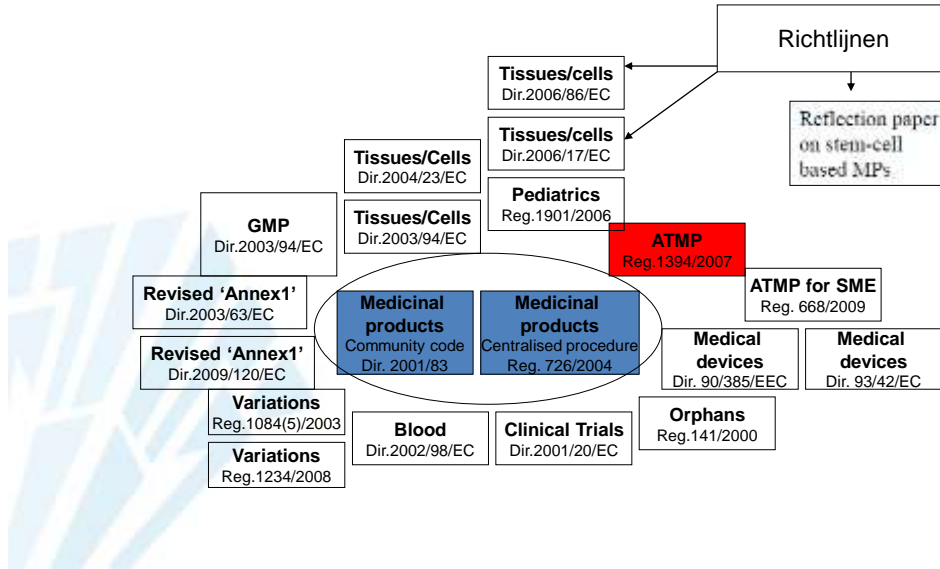
- a) NOT: cut, centrifuge, sterilise, freeze,... (Annex I)
- b) BUT: cell expansion, ex vivo cell activation or – differentiation, ...

2- Not the same essential function in receiver and donor.

23



European Legislation



Hospital exemption in Europe

LIDSTAAT	NATIONALE AUTORITEIT	RICHT-SNOER	BIET-ROUWREMATIG	IMPORT/EXPORT	GMP	GP	TOEGEREKTE ATMPs (5,7)
UK	MHRA	Ja + Specials (8)	Aparte richtsnoer (8)	Nee (5) Wettelijke zielehuizen binnen de UK. WDL (6)	Ja (8) (8) (11)	Nee (5)	Tegenstrijdige bronnen: 1 of 0?
Ierland	IMB	Ja	f	f	Ja (8)	f	0
Frankrijk	ANSM	Nee	f	Nee (5)	Ja (5)	verantwoordelijke persoon gespecteerd (9)	0
Duitsland	PEI	Ja	Specificatie in de AMG (sectie 4b §2) (12)	Nee (11) Ongespecificeerde instelling voor gezondheidszorg (bv. artsengastijk) in TFG (sectie 14, sub-sectie 2) (11)	f	Specifieke voorwaarde in AMG (sectie 15, sub-sectie 3a) MAAR ook zo voor hospital exemption? (10)	0
Oostenrijk	BASGIAGES	Nee	f	f	f	f	0
Nederland	IGZ	Ja	Opgenomen in richtsnoer van ME (12)	Nee (12)	Ja (12)	Ja (12,13)	3 (13)

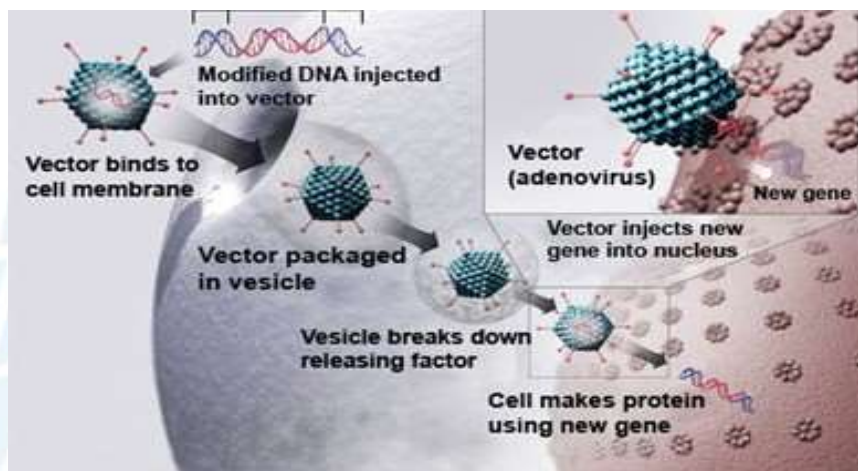
Kalydeco (ivacaftor)



- Subpopulation CF (genetic mutation G551D)
- Personalized medicine: treats genetic defect
- PPP: contributions of the CF community & research funded by NIH et al
- Clinical trials in CF patients



Glybera (Alipogene Tiparvovec)



Brentuximab Vedotin Mechanism of Action

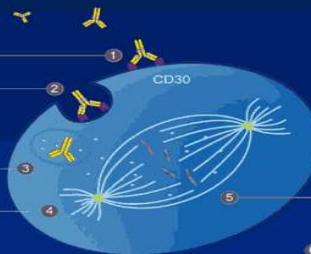


Brentuximab vedotin (SGN-35) ADC
monomethyl auristatin E (MMAE), potent antitubulin agent
protease-cleavable linker
anti-CD30 monoclonal antibody

ADC binds to CD30
ADC-CD30 complex
traffics to lysosome

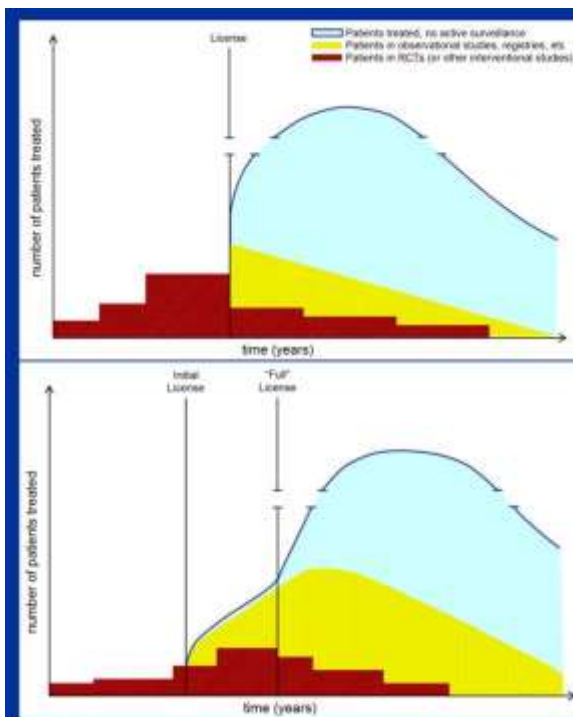
MMAE is released

MMAE disrupts
microtubule network



G2/M cell
cycle arrest

Apoptosis



Current scenario:

Post-licensing, treatment population grows rapidly
treatment experience does not contribute to evidence generation

Adaptive Licensing:

after initial license, number of treated patients grows more slowly, due to restrictions; patient experience is captured and contributes to real-world information



First-Aid-Kit



Home treatment



3D Printing in Medicine





- Performance based agreement
- Early treatment access
- Conditional reimbursement
- Multi-criteria decision analysis



Multi-criteria decision analysis

- A set of methods and approaches to aid decision making, where decisions are based on more than one criterion, which make explicit the impact on the decision of all the criteria applied and the relative importance attached to them.





Integrated Delivery Systems



TheKingsFund >

Ideas that change
health care

Canterbury
District Health Board
To Four Heales & Stables

Approach to coordinated care

Maccabi has a comprehensive, fully integrated health information and communication system with a comprehensive database that includes more than 18 years of data on almost 2 million members. Maccabi functions on the basis of a decentralized organizational approach.

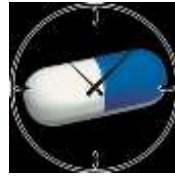


Figure 1: Maccabi coordinated care. Networking and Decision Support Systems are at the heart of delivering coordinated care to Maccabi members.

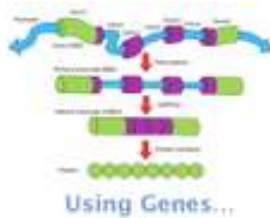
Maccabi, 2011 - <http://www.intel.co.uk/content/dam/www/public/us/en/documents/white-papers/coordinated-health-care-from-maccabi-an-intel-paper.pdf>

CONTRA-INDICATION





Synthetic Biology



to Program Cells to
Become
Cellular Factories ...



to Make
High Value Products



