

General introduction: challenge studies, what's in a name?

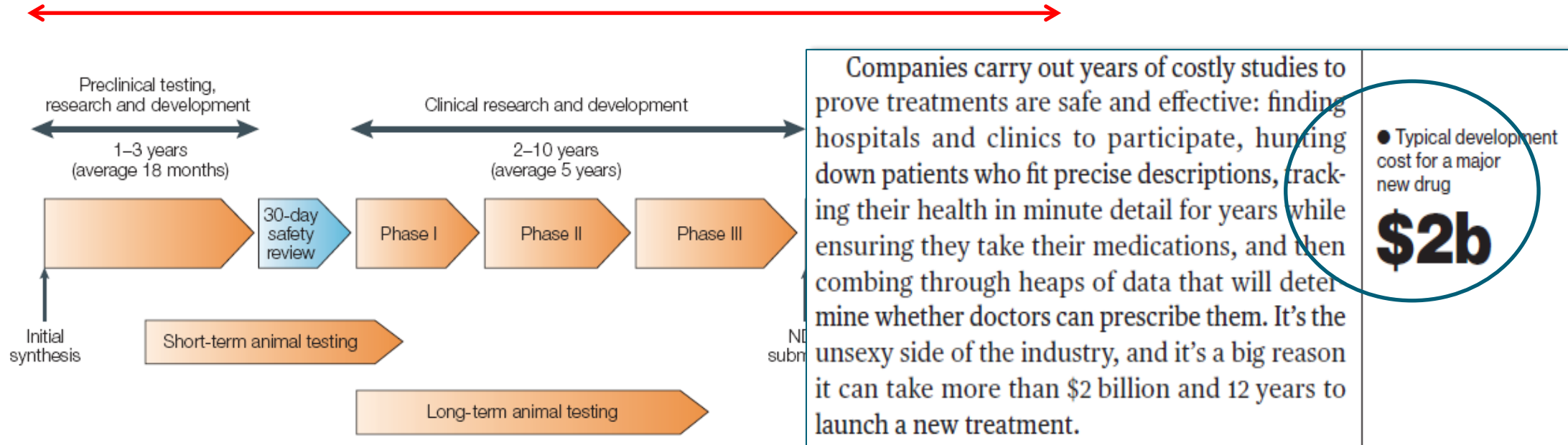
24 May 2023

Jan de Hoon, PhD, MD, MSc

University Hospitals Leuven
Campus Gasthuisberg
Leuven, Belgium

Challenge studies: what's in a name?

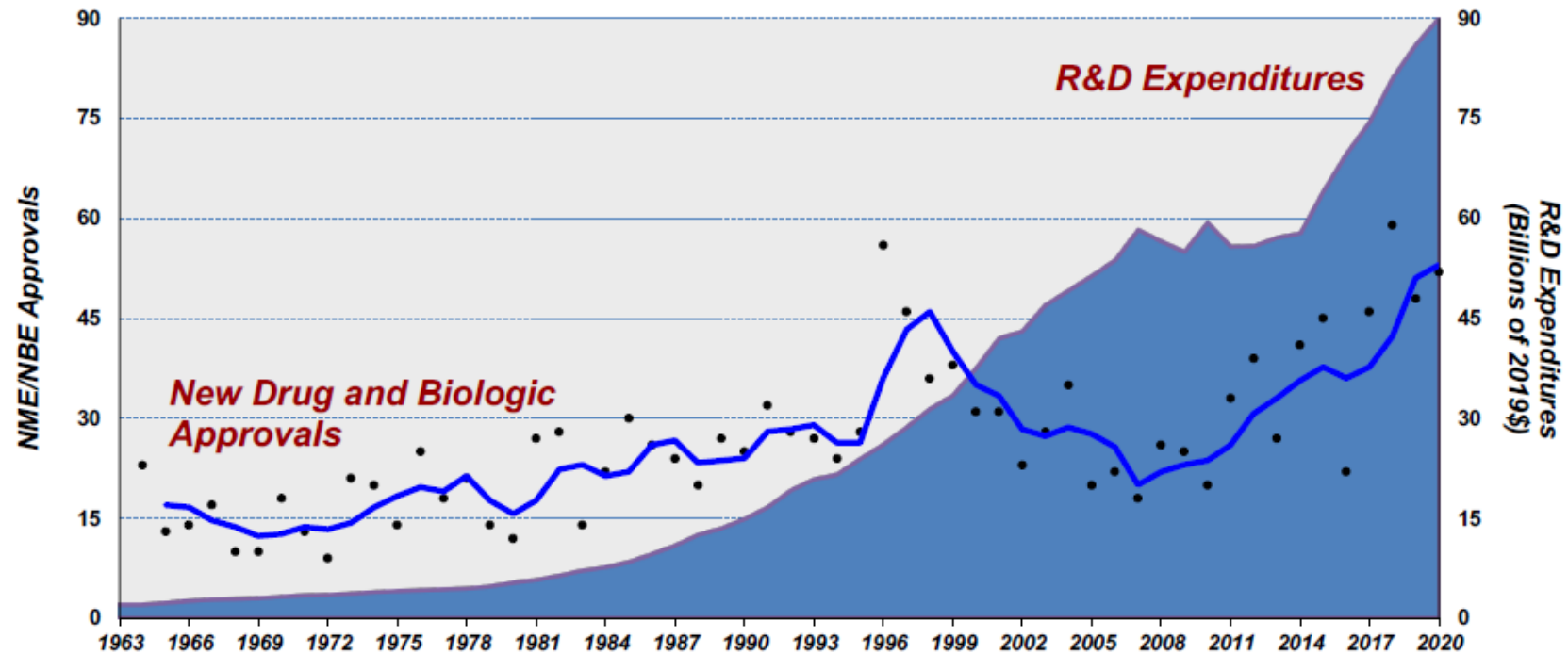
The background



Challenge studies: what's in a name?

The background

New Drug and Biologic Approvals Are Not Keeping Pace with Rising R&D Costs



* Trend line is 3-year moving average; R&D expenditure adjusted for inflation (2020 estimate)

Source: Tufts CSDD, 2021; R&D expenditures from PhRMA Industry Profile 2019

Challenge studies: what's in a name?

The background

FDA approves Lundbeck's Vyepti, the first CGRP inhibitor for migraine delivered IV
With little difference in efficacy or price, the CGRP competition will boil down to delivery, frequency and access

By Hongjiang Li, Staff Writer | Feb 22, 2020 2:38 AM CET

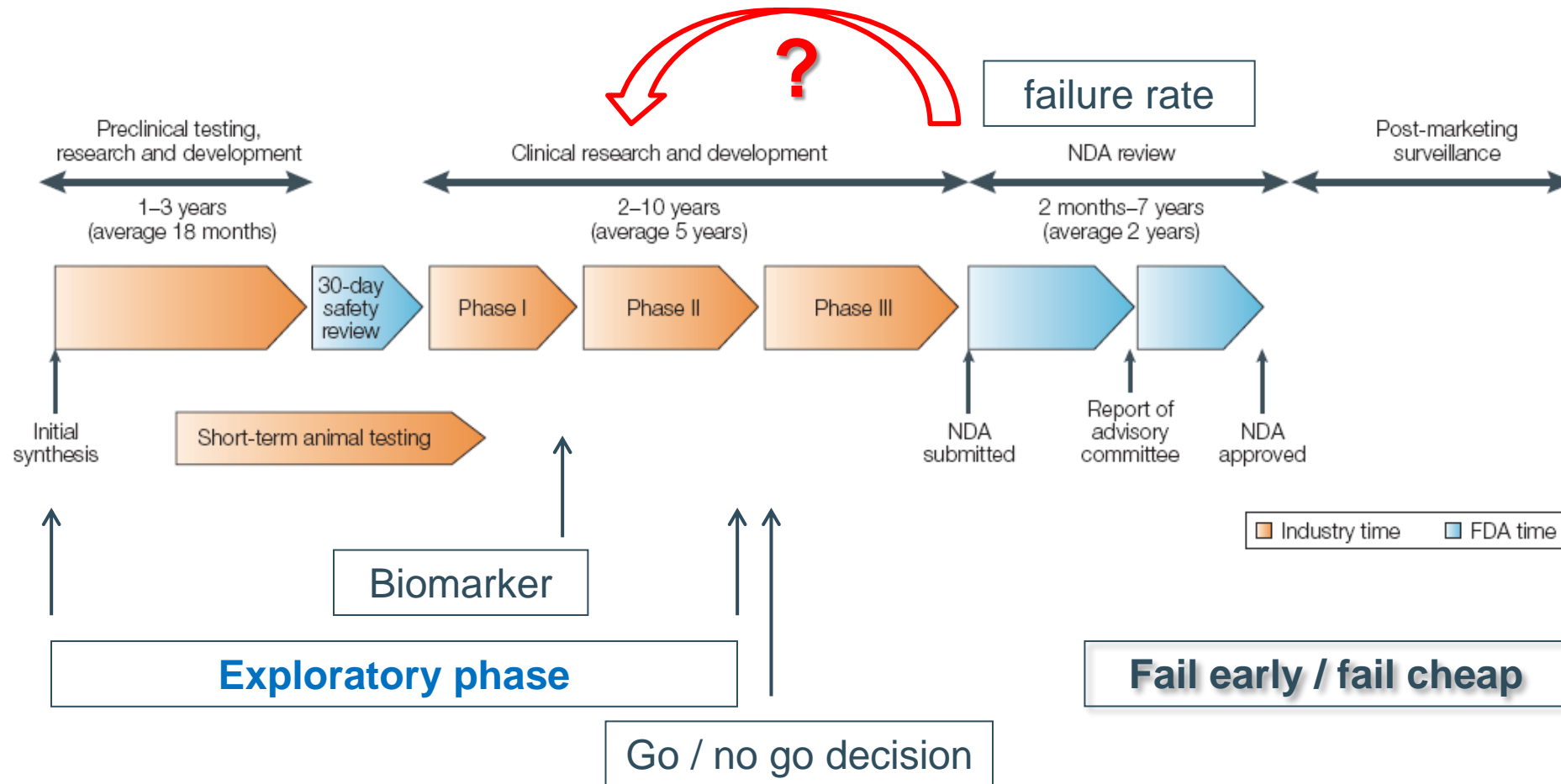
FDA's approval of Vyepti eptinezumab from Lundbeck is the first for an IV-delivered CGRP inhibitor for migraine prevention, but the therapy will face competition from established subcutaneous drugs in its class.

The company gained Vyepti in October through its \$1.95 billion takeout of migraine company Alder BioPharmaceuticals Inc., now known as Lundbeck Seattle BioPharmaceuticals Inc. (see "[Lundbeck Enters Migraine Race](#)").



Challenge studies: what's in a name?

The background



Challenge studies: what's in a name?

What is a challenge?

Cambridge dictionary:

1. ... a call to someone to participate in a competitive situation or fight to decide who is superior in terms of ability or strength.
2. ... a call to prove or justify something.
3. (Medicine) the administration of an immunogenic or infectious agent to an animal or person, in order to study the resulting immune response or measure the efficacy of a vaccine.



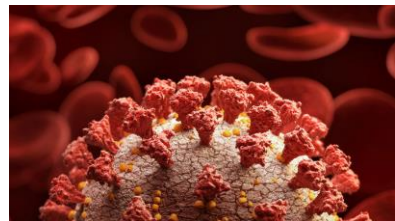
Challenge studies: what's in a name?

What is a challenge study?

A **human challenge study**, also called a challenge trial or controlled human infection model (**CHIM**), is a type of clinical trial involving the intentional exposure of the trial participant to the condition tested...

Boosted by the **SARS-CoV-2 pandemic** in order to test:

- pathophysiology of the infection
- vaccines
- monoclonal antibodies
- antiviral treatments
- ...



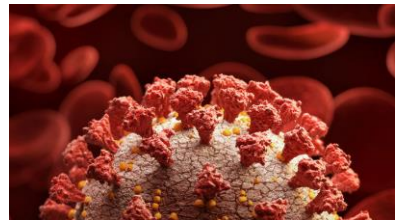
Challenge studies: what's in a name?

What is a challenge study?

17 February 2021: The U.K. approved the world's first COVID-19 human challenge trial...

It will deliberately infect people to find out how much coronavirus it takes to sicken someone

- Researchers call on healthy young people to volunteer for the study, which will play a key role in developing effective Covid-19 vaccines and treatments.
- Up to 90 volunteers aged 18 - 30 years will be exposed to Covid-19 in a safe and controlled environment to increase understanding of how the virus affects people.



Challenge studies: what's in a name?

Controlled Human Infection Model Studies: CHIM studies

Controlled Human Infection Model Studies

Summary of a workshop held on 6
February 2018



Executive summary

Controlled Human Infection Model (CHIM) studies, trials that purposely infect human volunteers with infectious agents (known as challenge agents), are an essential component of pathology, immunology and vaccines research. There are unique ethical, safety and scientific challenges associated with CHIM studies that mean that robust governance and appropriate regulation is essential to their effective use and continued growth.

There continues to be significant investment in CHIM studies as part of a wider goal of tackling endemic, pandemic and emergent infectious diseases. Such funding, driven by Wellcome, the Medical Research Council, the Bill & Melinda Gates Foundation and Horizon 2020, among others is targeted towards areas of ongoing unmet need, such as malaria and leishmaniasis, as well as pandemic outbreaks.

Challenge studies: what's in a name?

Controlled Human Infection Model Studies: CHIM studies

Controlled Human Infection Model Studies

Summary of a workshop held on 6
February 2018



Human challenge trial workshop: Focus on quality requirements for challenge agents, Langen, Germany, October 22, 2019

Isabelle Bekeredjian-Ding^{a,b}, Wim Van Molle^c, Marc Baay^d, Pieter Neels^{e,*}, on behalf PEI speakers and session chairs (Nele Berthels^f, Christoph Conrad^g, Angela van Diepen^h, Sarah Fortuneⁱ, Karen Goetz^j, Andrew Gorringer^k, Daniel Hoft^l, Robert A. Johnson^m, Peter Kremsnerⁿ, Oleg Krut^o, Yves Levy^p, Wolfram Metzger^q, Volker Oeppling^r, Scott Stibitz^s, Kawsar R. Talaat^t, Stephen Thomas^u, Adrian Wildfire^v, Beno Nyam Yakubu^w)

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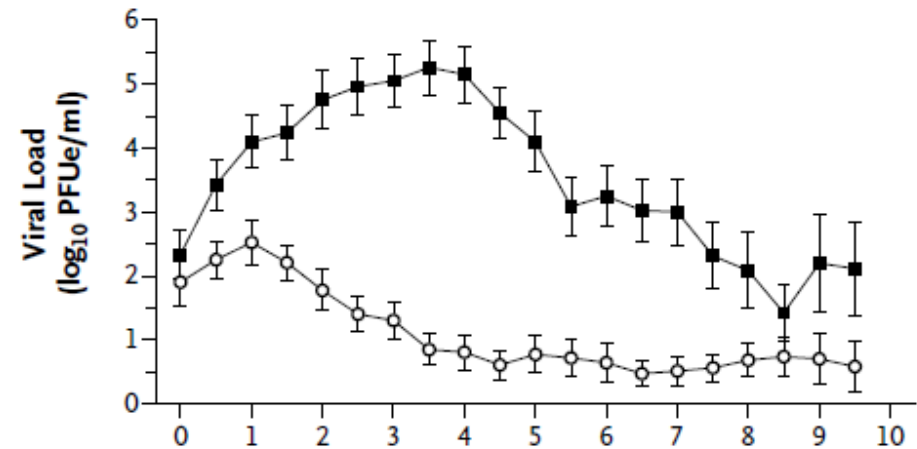
Controlled Human Infection Model Studies: CHIM studies

Infectious agents

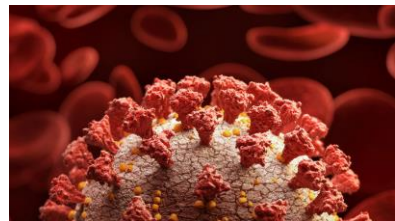
- ✓ Virusses:
 - ✓ Influenza
 - ✓ Rhinovirus
 - ✓ RSV
 - ✓ SARS-CoV-2

ORIGINAL ARTICLE

Oral GS-5806 Activity in a Respiratory Syncytial Virus Challenge Study



N Engl J Med 2014; 371: 711-722



Challenge studies: what's in a name?

Controlled Human Infection Model Studies: CHIM studies

Infectious agents

- ✓ Viruses:
 - ✓ Influenza
 - ✓ Rhinovirus
 - ✓ RSV
 - ✓ SARS-CoV-2

- ✓ Bacteria:
 - ✓ Shigella species
 - ✓ Clostridium difficile
 - ✓ TBC



Challenge studies: what's in a name?

Controlled Human Infection Model Studies: CHIM studies

Infectious agents

- ✓ Viruses:
 - ✓ Influenza
 - ✓ Rhinovirus
 - ✓ RSV
 - ✓ SARS-CoV-2

- ✓ Bacteria:
 - ✓ Shigella species
 - ✓ Clostridium difficile
 - ✓ TBC

- ✓ Parasites:
 - ✓ Malaria (Plasmodium falciparum)
 - ✓ Hookworm (Necator americanus)



Challenge studies: what's in a name?

Controlled Human Infection Model Studies: CHIM studies

Ethical concerns

Risks related to

- ✓ the “IMP” being tested
- ✓ the infectious agent involved

Considered acceptable

- ✓ scientifically sound and well designed
- ✓ ethically valid, well-informed consent
- ✓ voluntarily and free participation
- ✓ rigorously conducted under well-controlled circumstances (GLP)



Guidance document WHO May 2020: criteria for conducting challenge trials.

Challenge studies: what's in a name?

Challenge studies beyond infectious agents

Biomarker:

An objectively measured characteristic as an indicator of: normal process, a pathological process, a pharmacological response to a (therapeutic) intervention or ... *a physiological response to a (non-therapeutic) intervention.*

Challenge agent:

Substance inducing a (patho)physiological response to assess the pharmacological action of an IMP.

Challenge studies: what's in a name?

Challenge studies beyond infectious agents

Challenge agent	Activity	Route of administration
allergens	allergic reaction	skin prick / inhalation
acetylcholine	M-receptor agonist	inhalation / IA
histamine	H1- H2 agonist	skin prick / IA
isoprenaline	β -receptor agonist	IV
substance P	NK-receptor agonist	skin prick / IV / IA
serotonin	5-HT agonist	
P450 probes	CYP450 ph	

(Based on ABPI Guideline for phase 1 clinical trials)

Novel antibody cocktail targeting Bet v 1 rapidly and sustainably treats birch allergy symptoms in a phase 1 study Check for updates

Philippe Gevaert, MD, PhD,^{a,*} Jarno De Craemer, MD,^{a,*} Natalie De Ruyck, MS,^a Sylvie Rottey, MD, PhD,^b Jan de Hoon, MD, PhD,^c Peter W. Hellings, MD,^{a,d,e} Bram Volckaert, MD,^f Kristof Lesneuck, MS,^f Jamie M. Orengo, PhD,^g Amanda Atanasio, MS,^g Mohamed A. Kamal, PhD,^g Hisham Abdallah, PhD,^g Vishal Kamat, PhD,^g Robert Dingman, PhD,^g Michelle DeVeaux, PhD,^g Divya Ramesh, PhD,^g Lorah Perlee, PhD,^g Claire Q. Wang, PhD,^g David M. Weinreich, MD,^g Gary Herman, MD,^g George D. Yancopoulos, MD, PhD,^g and Meagan P. O'Brien, MD^g Ghent, Leuven, and Antwerp, Belgium; Amsterdam, The Netherlands; and Tarrytown, NY

Challenge studies

**Use a non-IMP
to show the IMP
hits the target**

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