REAL WORLD EVIDENCE

RWE4Decisions

WEBINAR

RWE over the Lifecycle of ATMPs to Meet the HTA (Regulation) Needs

10 October | 15:00 - 16:30 CEST

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HOUSEKEEPING RULES

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RWE4Decisions REAL WORLD EVIDENCE

Principles

Payer-Led Multi-Stakeholder Learning Network

Highly innovative technologies often have immature clinical evidence (and high prices)

Could robust real-world evidence (RWE) generated during the life cycle of technology development and use resolve HTA/Payer uncertainties?

Can requirements be aligned across stakeholders and health jurisdictions/payers?

… working with the RWE4Decisions multi-stakeholder community

INAMI-RIZIV

Secretariat: FIPRA

MULTI-STAKEHOLDER COMMUNITY

Clinicians/Researchers Registry-holders

Patients/Foundations

Regulators

Analytics experts/ Statisticians

Academia

Industry

HTA bodies, Payers and Health Ministries

AITHA, Austrian Social Insurance Association | INAMI-RIZIV, KCE | CADTH | Danish Medicines Council, Amgros | NICE | FIMEA | HAS | G-BA, AOK | NCPE

AIFA | ZIN | NoMA | AOMIT | INFARMED | Health Insurance Institute | Health Ministry | TLV

"Learning by Doing"

RWE4Decisions REAL WORLD EVIDENCE 2023 STEERING GROUP

HTA bodies / Payers

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AstraZeneca

Boehringer Ingelheim

NOVARTIS

Pfizer

Roche

Takeda

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Insurer

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Matti Aapro

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Analytics Expert

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Market Access Scientific Strategy Lead, **Aetion, US**

Academia

Entela Xoxi

Pharmacologist, **Uni. Cattolica Sacro Cuore**

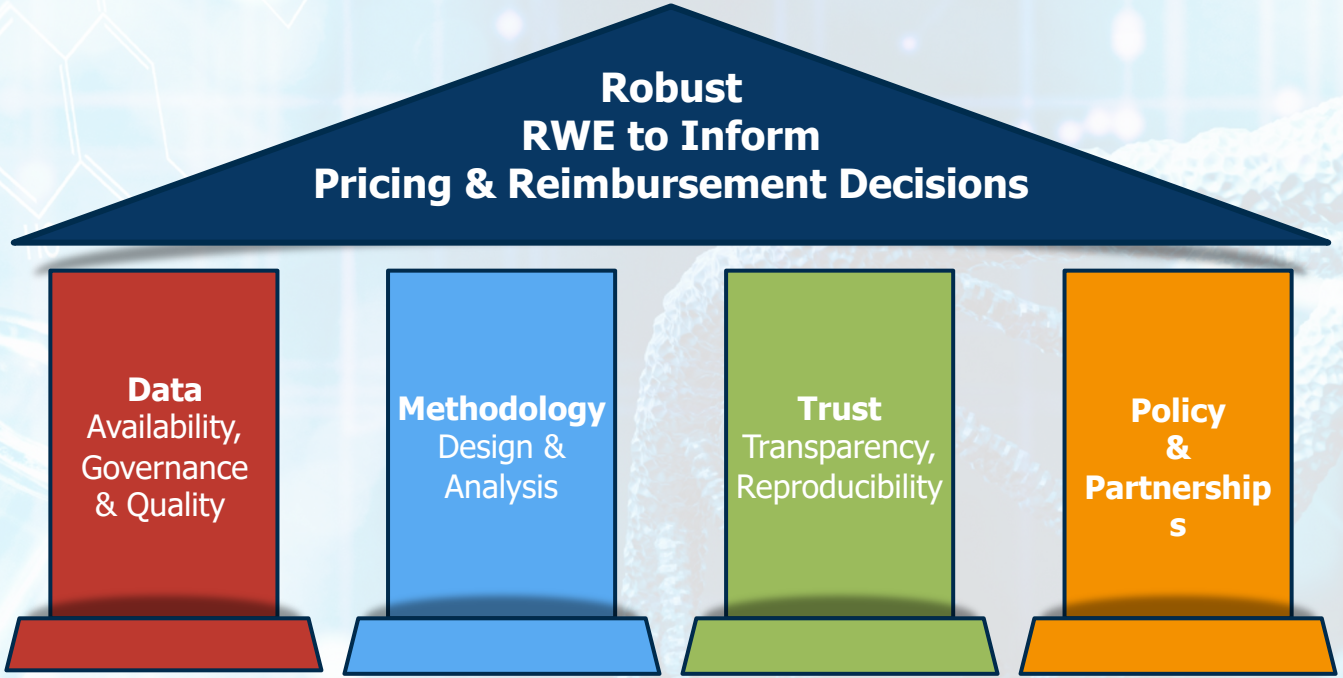
Facilitator

FIPRA Int.

Karen Facey, Senior Adviser (HTA)

Secretariat provided by FIPRA funded by EUCOPE and member companies

Four pillars to support development of robust RWE for HTA/Payer decision-making



Capkun, G et al. (2022) ***"Can we use existing guidance to support the development of robust real-world evidence for health technology assessment/payer decision-making?"*** *doi:10.1017/S0266462322000605*

AGENDA

15:05 – Keynote presentation

Ana Hidalgo-Simon, Leiden University Medical Center

15:20 – Moderated panel discussion – led by Eric Sutherland (OECD)

Alexander Natz, European Confederation of Pharmaceutical Entrepreneurs (EUCOPE)
Niklas Hedberg, Swedish Dental and Pharmaceuticals Benefits Agency (TLV)
Christoph Rupprecht, Allgemeine Ortskrankenkasse (AoK)
Simone Boselli, EURORDIS-Rare Diseases Europe

16:05 – Q&A with the audience

16:25 – Closing remarks from the panel

RWE4Decisions Webinar Series 2023

RWE over the lifecycle of ATMPs to meet the HTA(R) Needs
Tuesday, 10 October | 15.00-16.30 CET

Advanced Therapies and their challenges - why RWE is a key part of the solution

Ana Hidalgo-Simon, MD, PhD
Associate Professor Leiden University Medical Centre

Transforming lives with stem cell medicine

Leiden University Medical Center

reNEW Novo Nordisk Foundation Center for Stem Cell Medicine

Future element IV (Oocyte maturing)
www.odranoel.eu

ATMPs (Advanced Therapy Medicinal Products)

Medicines for human use that are based on genes, tissues or cells

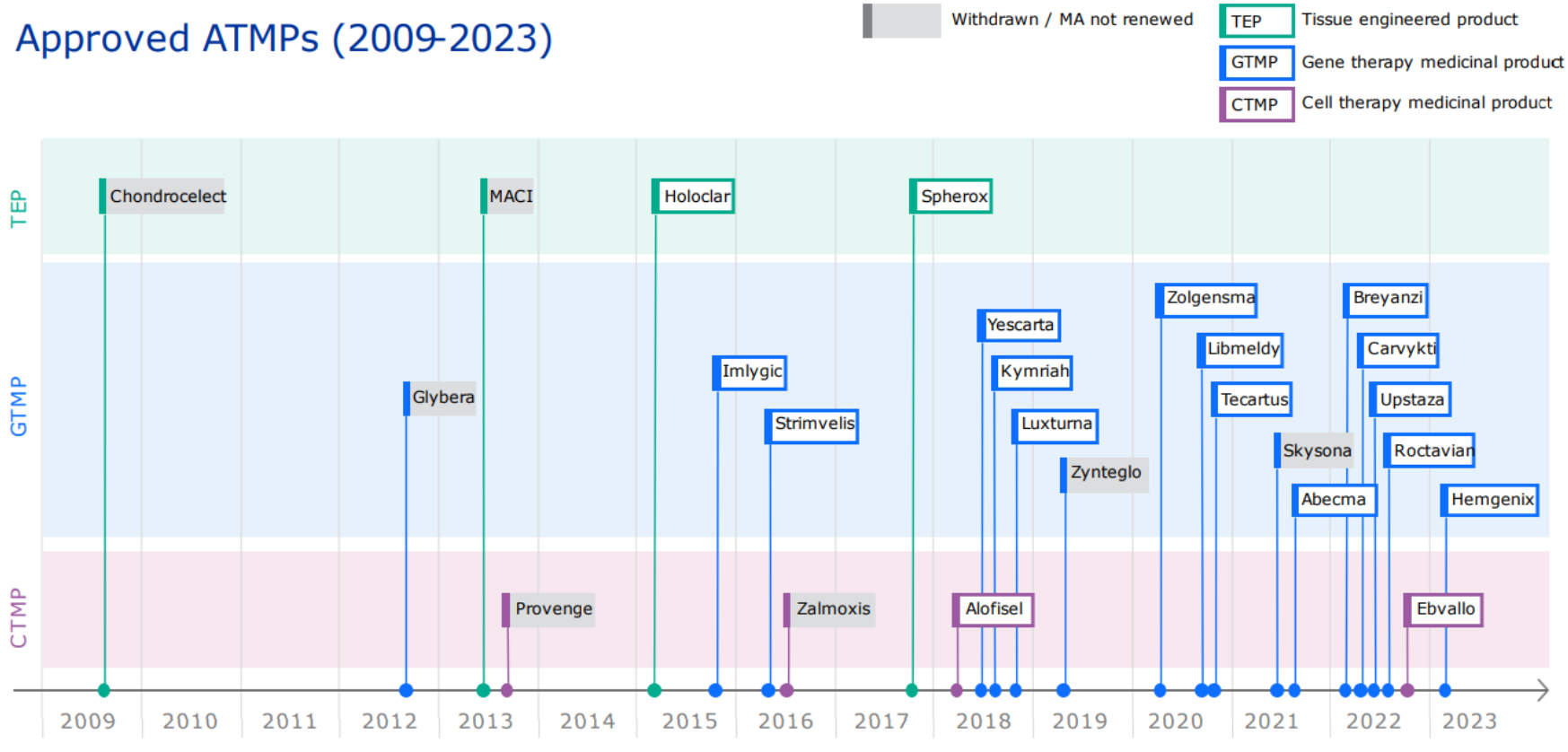
- Gene therapy medicines
- Somatic-cell therapy medicines
- Tissue-engineered medicines
- Combined ATMPs (medical devices as an integral part)

  - Different jurisdictions
  - New legislation
  - If needed: EMA classification service @ https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/advanced-therapies/advanced-therapy-classification

Novel and very different therapies

	Traditional therapies	Advanced therapies
Size and complexity	Low	High – very difficult to copy
Treatment administration	Regular, frequent	One or two administrations
Duration of effect	Reversible, wash off	Permanent (e.g. gene editing)
Treatment location	Home, ambulatory, pharmacy	Specialized centers only
Costs	Low	Very high
Access to patients	Easy and generally fast	Delayed, limited
HTA	Review and decision paths exists	Complex and limited acceptance
Sustainability of the health system	Under control	Not clear

Approved ATMPs (2009-2023)



CAT quarterly report, July 23, accessed Oct 2023

Leiden University Medical Center

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Narrow evidence base

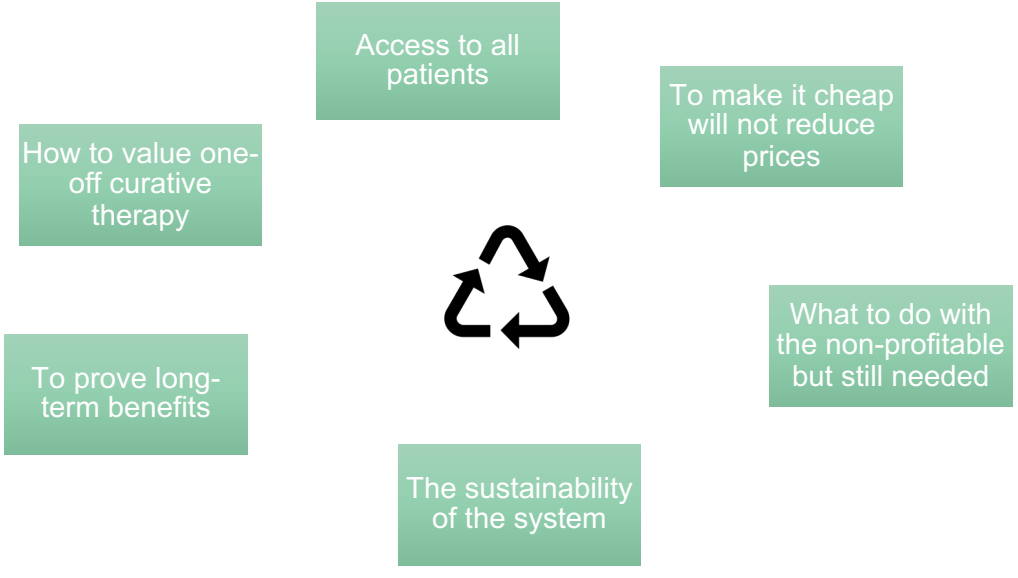
	Average no in CT pre-MA	Product	Short indication	Orphan	Marketing authorisation	Date of approval
Somatic cell + tissue engineered	**In the low 100s**	Zalmoxis	Hematopoietic Stem Cell Transplantation Graft vs Host Disease	Yes	Conditional	23/08/2016
		Alofisel	Rectal Fistula	Yes	Full	23/03/2018
		Holoclar	Stem Cell Transplantation Corneal Diseases	Yes	Conditional	19/02/2015
		Spherox	Cartilage Diseases	No	Full	10/07/2017
Gene therapy	**In the low 400s**	Imlygic	Melanoma	No	Full	18/12/2015
		Strimvelis	Severe Combined Immunodeficiency	Yes	Full	30/05/2016
		Yescarta	Lymphoma, Follicular Lymphoma, Large B-Cell, Diffuse	Yes	Full	27/08/2018
		Kymriah	Precursor B-Cell Lymphoblastic Leukemia-Lymphoma Lymphoma, Large B-Cell, Diffuse	Yes	Full	27/08/2018
		Luxturna	Leber Congenital Amaurosis Retinitis Pigmentosa	Yes	Full	22/11/2018
		Zynteglo	beta-Thalassemia	Yes	Conditional & accelerated	29/05/2019

Design features of pivotal clinical trials for the approved advanced therapy medicinal products in the EU

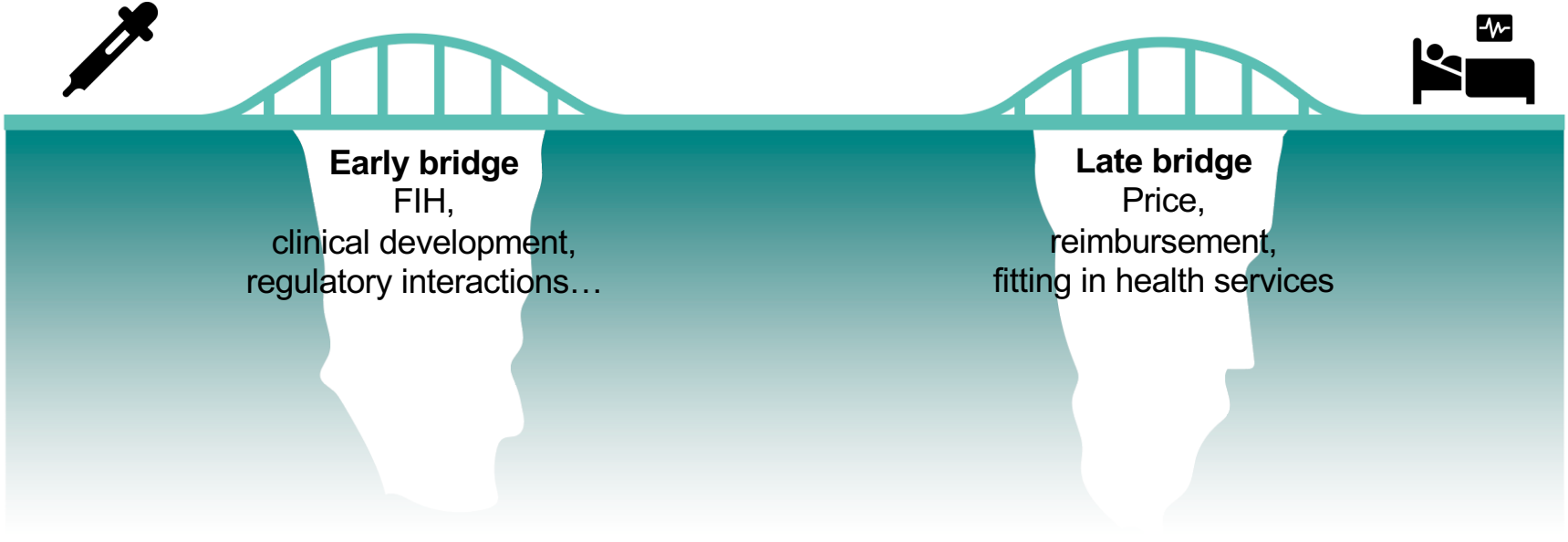
Trade name	Pivotal study	Non-randomized	Non-controlled	Historical control	Intermediate endpoints	Population/no. of patients (enrolled)
Gene therapy medicinal products						
Kymriah (ALL)	Phase II	✓	✓	✓	✓	Children/92
Kymriah (DLBCL)	Phase II	✓	✓	✓	✓	Adults/147
Yescarta	Phase I/II	✓	✓	✓	✓	Adults/111
Tecartus	Phase II	✓	✓			Adults/105
Imlygic	Phase III				✓	Adults/437
Glybera	3 Phase II/III	✓	✓		✓	Adults/45
Strimvelis	Phase I/II	✓	✓	✓		Children/12
Luxturna	Phase III				✓	Children and adults/31
Zynteglo	Phase I/II and Phase III	✓	✓		✓	Children and adults/41
Zolgensma	Phase III	✓	✓	✓		Children/22
Libmeldy	Phase I/II	✓	✓		✓	Children/22
Skysona	Phase II/III	✓		✓		Children/32[a]
Abecma	Phase II	✓	✓	✓	✓	Adults/140

Iglesias-Lopez C, Agustí A, Vallano A, Obach M. Current landscape of clinical development and approval of advanced therapies. Mol Ther Methods Clin Dev. **2021** Nov 11;23:606-618. doi: 10.1016/j.omtm.2021.11.003. PMID: 34901306; PMCID: PMC8626628.

The access problem – most ATMPs originate from research in academic (non-profit) institutions



Evidence from academic research **for translation** needs to be solid and serve several masters



The two masters

Regulators

Benefit risk is positive in at least a subset of the population

Role is to balance the size of clinical benefits of medicines against their harmful effects, considering the uncertainties in both measures

HTAs/payers

How much better is this treatment to what is already available, taking the price into consideration

Role is to evaluate drug effects compared with available alternatives

What would help:

- Increased coordination between regulators and HTA bodies
- Reduced the level of uncertainty by more/better data/knowledge → RWE

Production of evidence

Regulatory and HTA/payers decision-making grade evidence

- Platforms
- Streamlined production
- More AI/Automatization
- Involvement of patients and end-users
- Alternative pathways
- Better use of RWE/RWD

Uncertainty and decision making I

Regulators:

High promise and high expectations vs limited data and high risks

Clear wiliness by regulators to consider RWE in their decisions

Growing demands from third-party payers, & HTAs for RWE evidence

Traditional clinical trials generally do not work for ATMPs

RWD is already part of the decision-making process:

To monitor and evaluate the post-MA safety of approved drugs

To support effectiveness

To compensate and fill the gaps (e.g. orphan single-arm trials with external control arms)

Uncertainty and decision making II

When is that RWE start to be produced?	What RWE to produce:	Where are RWE data holders:

• Need early engagement and early data collection
• RWE used:
  • At MA: Natural history…
  • Post-MA: pharmacovigilance, renewal…
  • For HTAs: reimbursement
	• What to collect
	• Compatibility of sources, methods, quality of data…
	• Sharing issues
	• Evidence needs to serve several decision makers
		• Many on academic hands
		• Burden of data collection (i.e. on doctors and HCPs)
		• Academic publications and data protection

From “post-MA too high” as the way to monitor, confirm, improve and guide developmental strategy

For discussion

To a high-level approximation:

- Uncertainty at marketing approval is inevitable – should be minimized as much as possible
- Uncertainty for HTAs/reimbursement/payers – is currently too high needs to be addressed
- Uncertainty post-MA – is part of the approval, can be minimized (good plans, early action…)
- Uncertainly long-term – can be managed in all aspects (safety, efficacy, price, value to society…)

RWE has a role in all the above, and in many instances may be the best approach

Thank you!

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https://renew.science/

Leiden University Medical Center

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Novo Nordisk Foundation Center for Stem Cell Medicine

MODERATED PANEL DISCUSSION

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QUESTIONS?

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