RWE generation for CAR-Ts: Payers' evolving approaches

Karen Facey k.facey@btinternet.com
Evidence Based Health Policy Consultant; FIPRA Senior HTA Advisor

Pre-Approval & **Post-Approval Challenges** in the Clinical Development & Reimbursement of CAR-T Cell Therapies
BBS – Day 2: 5 October 2023 (Virtual)

IMPACT HTA: WP10 Appraisal of Rare Disease Treatments
Workstream 4 - OBMEA
https://www.impact-hta.eu/work-package-10

European Commission (EC) funded project that completed in June 2021.
The results presented reflect the authors' views and not the views of the EC.
The EC is not liable for any use of the information communicated.

www.rwe4decisions.com

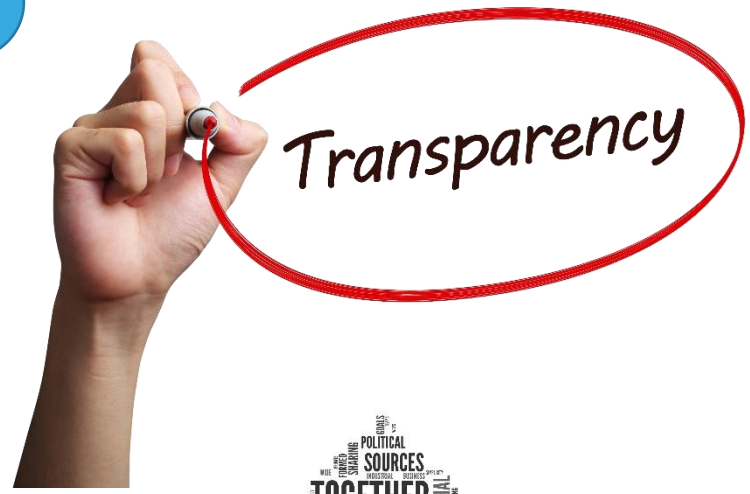
Principles

Payer-Led Multi-Stakeholder Learning Network

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

Could robust RWE fill gaps
- in clinical development, and/or
- after conditional reimbursement?

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



RWE4Decisions REAL WORLD EVIDENCE STEERING GROUP – new members

HTA bodies / Payers

Jo De Cock

Senior Adviser, **INAMI-RIZIV**

Diane Kleinermans

President of Comm. of Drug Reimbursement, **INAMI-RIZIV**

Niklas Hedberg

Chief Pharmacist, **TLV**

Piia Rannanheimo

Chief Specialist, **Fimea**

Cláudia Furtado

Head HTA, P&R Div. and Information & Strategic Planning, **INFARMED**

Laurie Lambert

Special Projects Adviser, **CADTH**

National Policy-makers

Carlos M. Saborido

Adviser, **Spanish Ministry of Health**

International Org.

Eric Sutherland

Senior Health Economist, **OECD**

Industry

EUCOPE

AstraZeneca

Boehringer Ingelheim

NOVARTIS

Pfizer

Roche

Takeda

Patient Representatives

Simone Boselli

Public Affairs Dir., **EURORDIS**

Antonella Cardone

CEO, **Cancer Patients Europe**

Chris Sotirelis

Patient Advocate for **Thalassemia**

Insurer

Hans-Georg Eichler

Consulting physician, **Austrian Social Insurance Inst.**

Clinician

Matti Aapro

Director, **Genolier Cancer Centre**

Analytics Expert

Ashley Jaksa

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

Academia

Entela Xoxi

Pharmacologist, **Uni. Cattolica Sacro Cuore**

Facilitators

FIPRA International

Karen Facey, Senior Adviser (HTA)

François Meyer, Special Adviser, HTA

Secretariat provided by FIPRA funded by EUCOPE and member companies

Registries for Evaluating Patient Outcomes: A User's Guide

Fourth Edition

AHRQ Agency for Healthcare Research and Quality

HTA Austria
Austrian Institute for Health Technology Assessment GmbH

(Good) practice organizational models using real-world evidence for public funding of high priced therapies

IQWiG

IQWiG Reports – Commission No. A19-43

Concepts for the generation of routine practice data and their analysis for the benefit assessment of drugs according to §35a Social Code Book V (SGB V)[1]

HAS
HAUTE AUTORITÉ DE SANTÉ

ASSESS
HEALTH TECHNOLOGIES

METHODOLOGICAL GUIDE

Real-world studies for the assessment of medicinal products and medical devices

10 juin 2021

NICE National Institute for Health and Care Excellence

NICE real-world evidence framework

Corporate document
Published: 23 June 2022
www.nice.org.uk/corporate/ecd9

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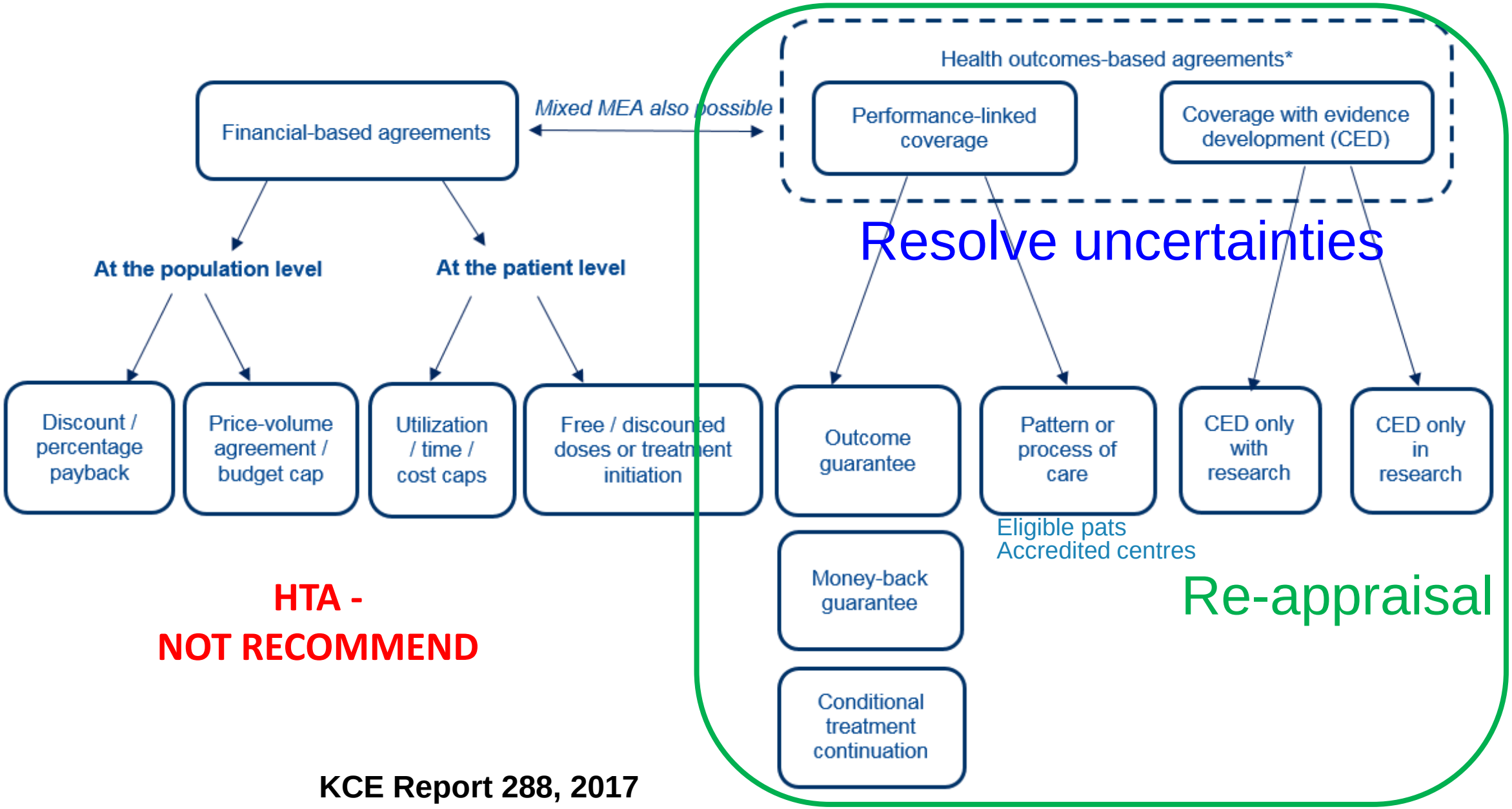
cadth Canada's Drug and Health Technology Agency

CADTH Methods and Guidelines

Guidance for Reporting Real-World Evidence

May 2023



KCE Report 288, 2017
How to improve the Belgian process for Managed Entry Agreements?

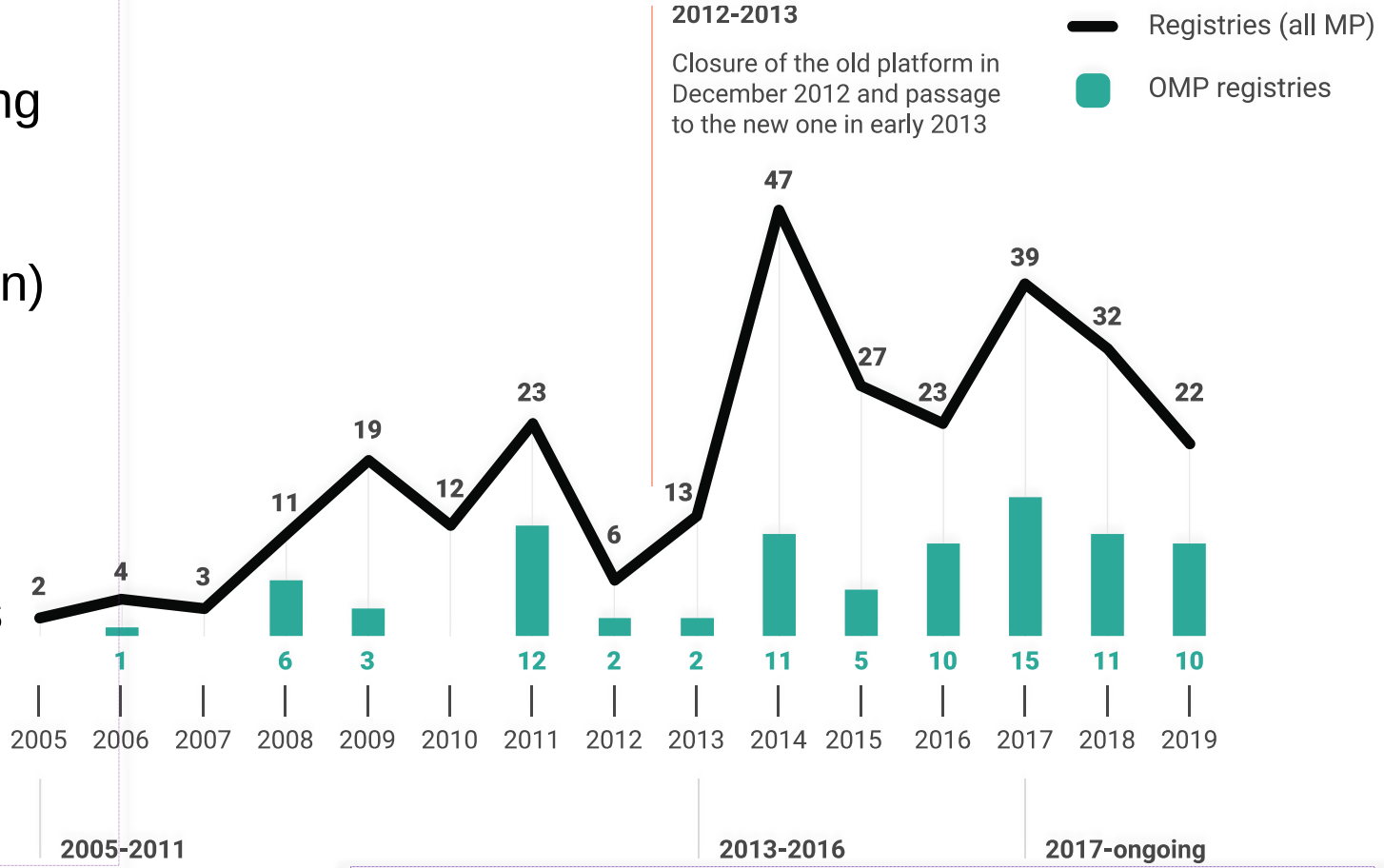
RWE4Decisions REAL WORLD EVIDENCE

AIFA (Italian Medicines Agency) Registry Platform for MEA

- National web-based registries platform co-managed by funding regions
- Prescriber must enter data to obtain access (and continuation)
- Registry funded by companies

2005-2019

- 283 indication-based registries
  - ➢ 77 have been closed
  - ➢ others are ongoing



MP, medicinal product; OMP, orphan medicinal product

XOXI E, FACEY K, CICCHETTI A. The evolution of AIFA registries to support Managed Entry Agreements for orphan medicinal products in Italy. Frontiers in Pharmacology: Drugs Outcomes Research and Policies, 2021

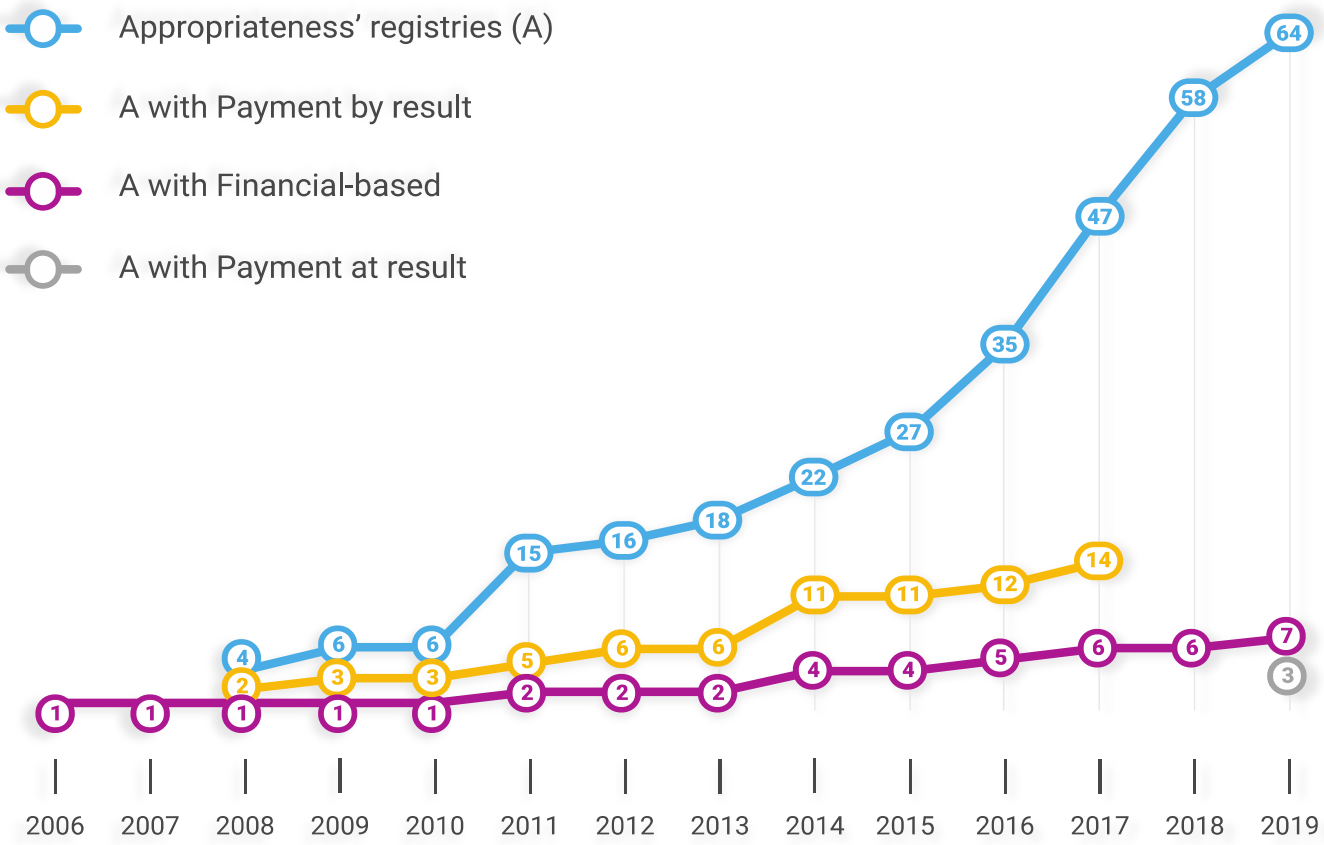
Type of Managed Entry Agreements

182 Appropriateness Only

35 + Financial-based
(cost-sharing/cost-capping

60 + Payment by result
(refund for non-responders)

3 + Payment at result
cancer cell therapies
(payment if response achieved)



XOXI E, FACEY K, CICCHETTI A. The evolution of AIFA registries to support Managed Entry Agreements for orphan medicinal products in Italy. Frontiers in Pharmacology: Drugs Outcomes Research and Policies, 2021

Australia - MSAC CED	Belgium - INAMI CED	England - Cancer Drugs Fund CED	Italy – AIFA VBA
Apr 2019 2 years	June 2019 2 (+1) years	Nov 2018/Feb 2019 4 years (ALL), 4.5 years (DLBCL)	August 2019 18 months+
Public health system data, Australian BMT registry (Pay on infusion)	Bespoke data collection by Insurers and MAH	Ongoing clinical trials NHS data (SACT) UK BMT registry	National web-based registry (Payment at Result at 0, 6, 12 months)
Acute Lymphocytic Leukaemia **Clinical/economic and financial uncertainties** Pat numbers Indications for use Non infusion PFS Durability of response Late onset AEs and use of high cost treatments – SCT, IVIG >3 years 2nd dose of any CART	ALL and Diffuse Large B-Cell Lymphoma (DLBCL) **Uncertainties: long-term safety and efficacy, added value** *Pat numbers* *Optimal population* *Non infusion* *Date of leukapheresis* *Success rate (infusion)* *PFS & OS 6, 12, 20 mos (DLBCL)* *SCT* *Medical resource use* *Tocilizumab use* *Specialist centre capacity*	ALL and DLBCL **Clinical uncertainties** ALL - Trials: OS - Registry: Stem Cell TransplantT - number, time to (if linkage possible) DLBCL - Trials: OS, PFS, IVIG use - NHS: OS, IVIG use	ALL and DLBCL **Clinical uncertainties** Diagnosis Date of Infusion (including reasons for no infusion or delay) Chemo regimen Response at follow-ups Need for other treatments Various outcomes

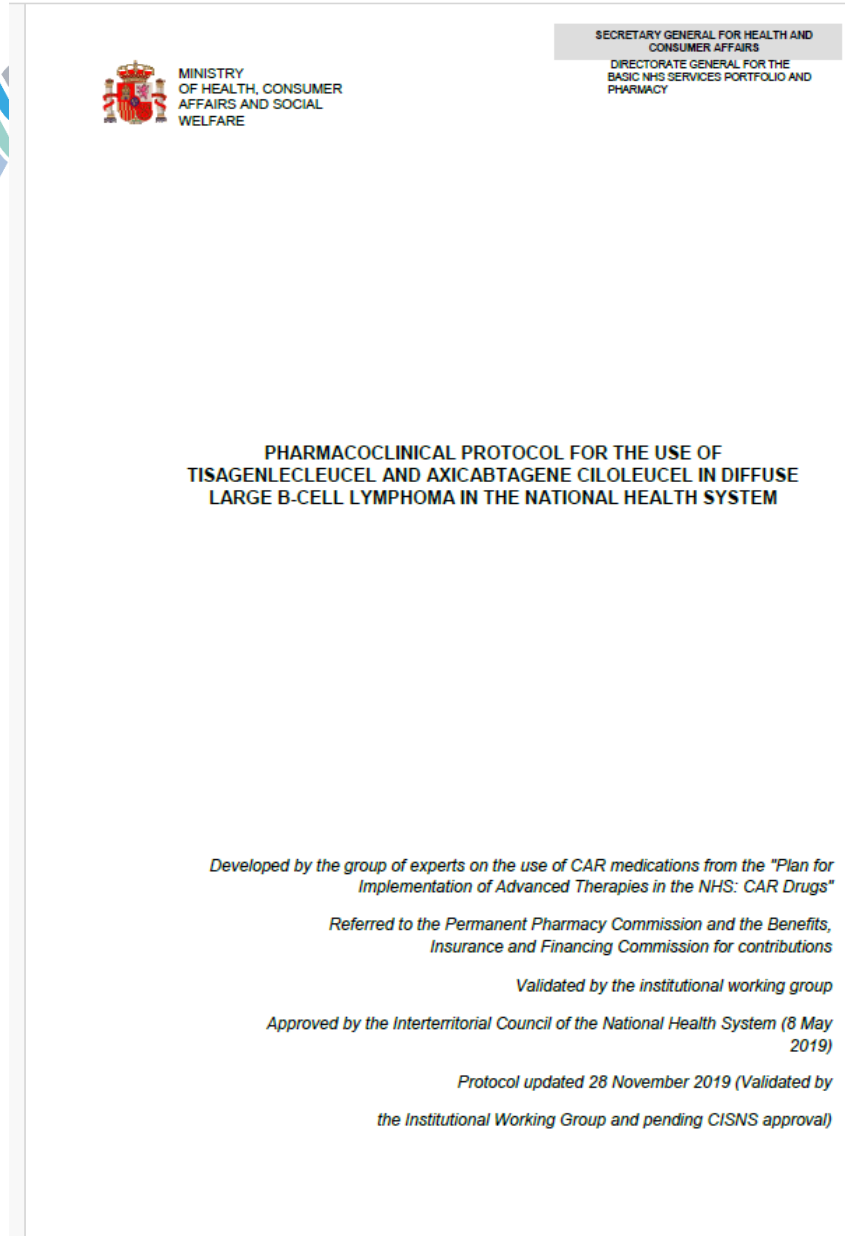
Valtermed protocols and reports

https://www.sanidad.gob.es/en/profesionales/farmacia/valtermed/home.htm

GOBIERNO DE ESPAÑA MINISTERIO DE SANIDAD

› Protocolos Farmacoclínicos:

- Tisagenlecleucel en leucemia linfoblástica aguda de células B **Escuchar** (versión en inglés **Escuchar**)
- Tisagenlecleucel y axicabtagén ciloleucel en linfoma B difuso de células grandes **Escuchar** (versión en inglés **Escuchar**)
- Inotuzumab ozogamicina en leucemia linfoblástica aguda **Escuchar** (versión en inglés **Escuchar**)
- Darvadstrocel en fístulas perianales complejas en enfermedad de Crohn **Escuchar** (versión en inglés **Escuchar**)
- Lumacaftor/ivacaftor y tezacaftor/ivacaftor en el tratamiento de la fibrosis quística **Escuchar** (versión en inglés **Escuchar**)
- Dupilumab en el tratamiento de la dermatitis atópica grave en pacientes adultos **Escuchar** (versión en inglés Will open in a new window to the page docs/20200131_Protocolo_dupilumab_dermatitis_atopica__grave_adultos.pdf
- Remdesivir en el tratamiento de la enfermedad por COVID-19 **Escuchar** (versión en inglés **Escuchar**)
- Burosumab en el tratamiento del raquitismo hipofosfatémico ligado al cromosoma X **Escuchar** (versión en inglés **Escuchar**)
- Voretigén neparvovec en el tratamiento de la distrofia retiniana asociada a la mutación *RPE65* bialélica **Escuchar** (versión en inglés **Escuchar**)



MINISTRY
OF HEALTH, CONSUMER
AFFAIRS AND SOCIAL
WELFARE

SECRETARY GENERAL FOR HEALTH AND CONSUMER AFFAIRS
DIRECTORATE GENERAL FOR THE BASIC NHS SERVICES PORTFOLIO AND PHARMACY

PHARMACOCLINICAL PROTOCOL FOR THE USE OF TISAGENLECLEUCEL AND AXICABTAGENE CILOLEUCEL IN DIFFUSE LARGE B-CELL LYMPHOMA IN THE NATIONAL HEALTH SYSTEM

Developed by the group of experts on the use of CAR medications from the "Plan for Implementation of Advanced Therapies in the NHS: CAR Drugs"

Referred to the Permanent Pharmacy Commission and the Benefits, Insurance and Financing Commission for contributions

Validated by the institutional working group

Approved by the Interterritorial Council of the National Health System (8 May 2019)

Protocol updated 28 November 2019 (Validated by

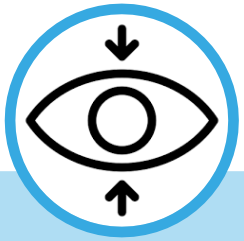
the Institutional Working Group and pending CISNS approval)

- Lots of inclusion and exclusion criteria
- 3 pages of pre-treatment preparation
- Baseline: Demographics, Disease characteristics including detailed evaluation of relapse/refractory/unresponsive, Clinical data
- Leukapheresis/CAR-T production: 8 variables
- Treatment administration: 5 variables
- Monitoring
- Response

DESCAR-T, NATIONAL REGISTRY FOR PATIENTS WITH HEMATOLOGICAL MALIGNANCIES, ELIGIBLE FOR CAR T-CELL THERAPY

The DESCAR-T study is a national registry to follow-up patients who have been treated with CAR T-cells. The collected data will allow to better understand the short- and long-term efficacy and safety profile of these new therapies in real-life setting.

2021 Coverage with Evidence Development (CED) OBMEA Fictitious case study multidisciplinary workshops



Objectives

- Review recent experiences of use of OBMEA for CED aimed to resolve HTA/Payer decision-relevant uncertainties for later re-appraisal
  - GetReal
  - EUnetHTA PLEG
  - IMPACT HTA WP10
- Agree a RWE evidence generation framework for CED of 2 fictitious cases

Scope of June webinars

Case 1: therapy given to children on an ongoing basis at point of diagnosis of a rare neuromuscular disease

Case 2: a one-off cell therapy given to adults in a late-stage cancer

Multi-stakeholder discussions

Agreement on Uncertainties

- ? Data sources for CED
- ? Pros and cons of different data sources
- ? Challenges in accessing data
- ? Good practices
- ? How to develop data collection protocol
- ? Alignment of data collection requirements

Outputs

RWE4Decisions recommended actions for stakeholders to support payer/HTA decisions about highly innovative technologies

RWE4Decisions REAL WORLD EVIDENCE

INAMI

RWE4Decisions REAL WORLD EVIDENCE

RWE4Decisions Case Studies Workshops – June 2021

Generating Real-World Evidence in Outcomes-Based Managed Entry Agreements: Two Fictitious Case Studies

Report of Proceedings

Executive Summary

Coverage with Evidence Development (CED) is a form of Outcomes-Based Managed Entry Agreements (OBMEA) that can enable patient access to promising treatments whilst collecting additional data to enable re-appraisal. CED in clinical practice is complex and the ability of such schemes to deliver sufficient data to influence pricing and reimbursement renegotiations or alteration of treatment use is often questioned. However, with the increasing number of highly innovative treatments coming to market with limited clinical data, and advancements in digital health, there is renewed interest in use of CED. Alongside this, there is recognition that CED should only be instigated when "decision relevant" uncertainties can be resolved by data collection within a timeframe that will inform re-appraisal. Furthermore, they should be the "exception and not the norm".

With this context, RWE4Decisions held trans-national multi-stakeholder workshops to discuss CED plans for two fictitious highly innovative treatments for rare disorders. The nature of the fictitious treatments was contrasting as one treatment was life-long and the other once-in-a-lifetime. Each rare disease had no existing disease modifying treatments, and the new treatments had a high price and major uncertainties in the evidence base available to HTA/Payers.

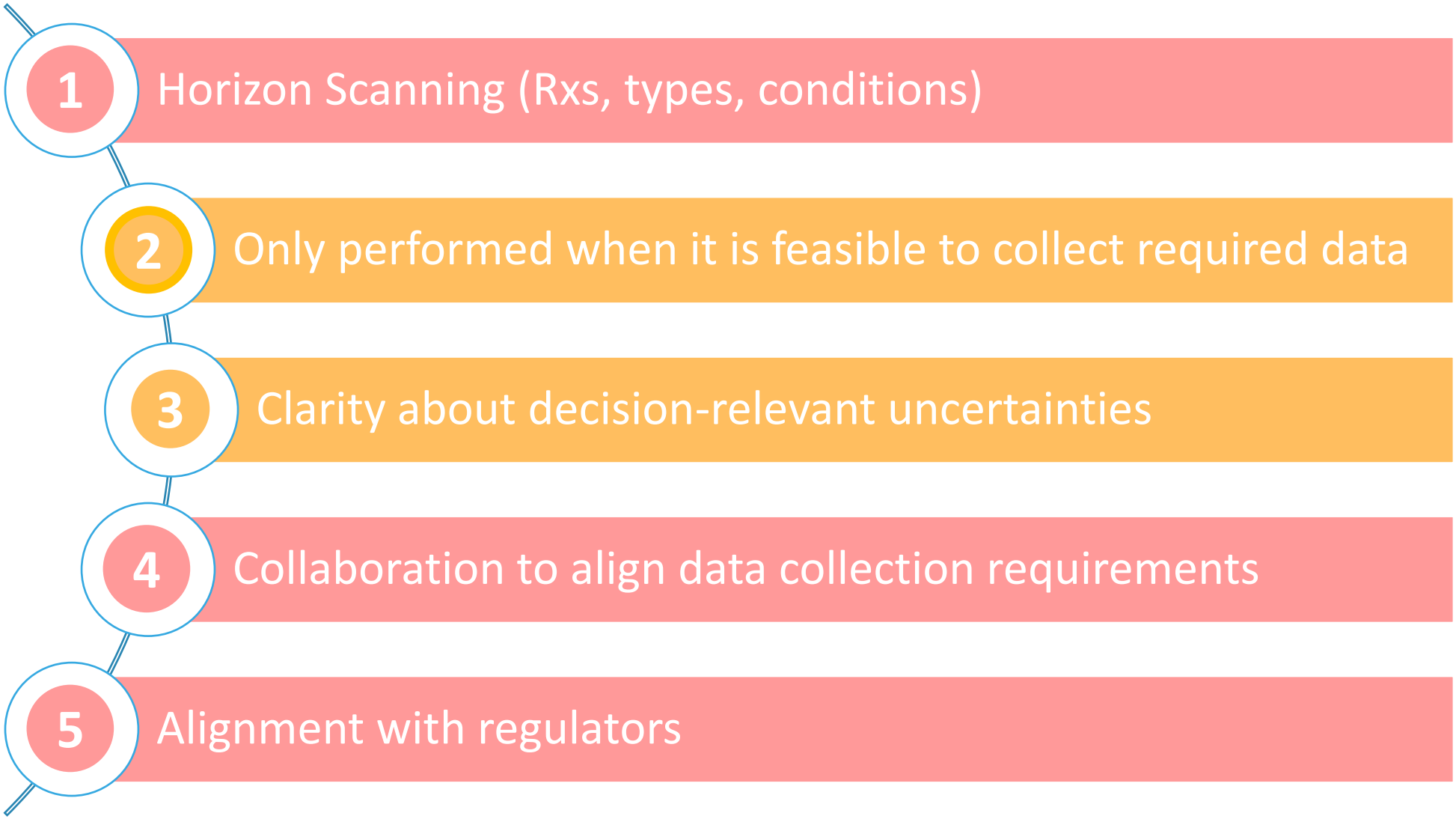
Pros and cons of real-world data sources that might resolve the decision-relevant uncertainties were considered. Challenges in accessing the data arising due to the rarity of the condition, alignment of post marketing data collection requirements, publication of detailed data collection plans and data governance of data provided by highly specialised centres were discussed. Potential actions that could be taken by individual stakeholders or collaborative initiatives were agreed.

Action	Lead Stakeholder
1. To enable rapid implementation of an Outcomes-Based Managed Entry Agreements (OBMEA) using Coverage with Evidence Development (CED), the potential need for post reimbursement data collection should be discussed in advance. **National or collaborative horizon scanning processes should identify products that might require OBMEA and undertake iterative dialogues (scientific consultations) with the sponsor company, regulators, clinical experts and patient groups to discuss potential data sources (e.g., disease registries, health system data, patient reported outcomes, regulatory studies).** This should include initiation of governance processes to access data. This could be undertaken for a particular disease, or type of therapy, as well as individual treatments.	Horizon scanning collaboratives

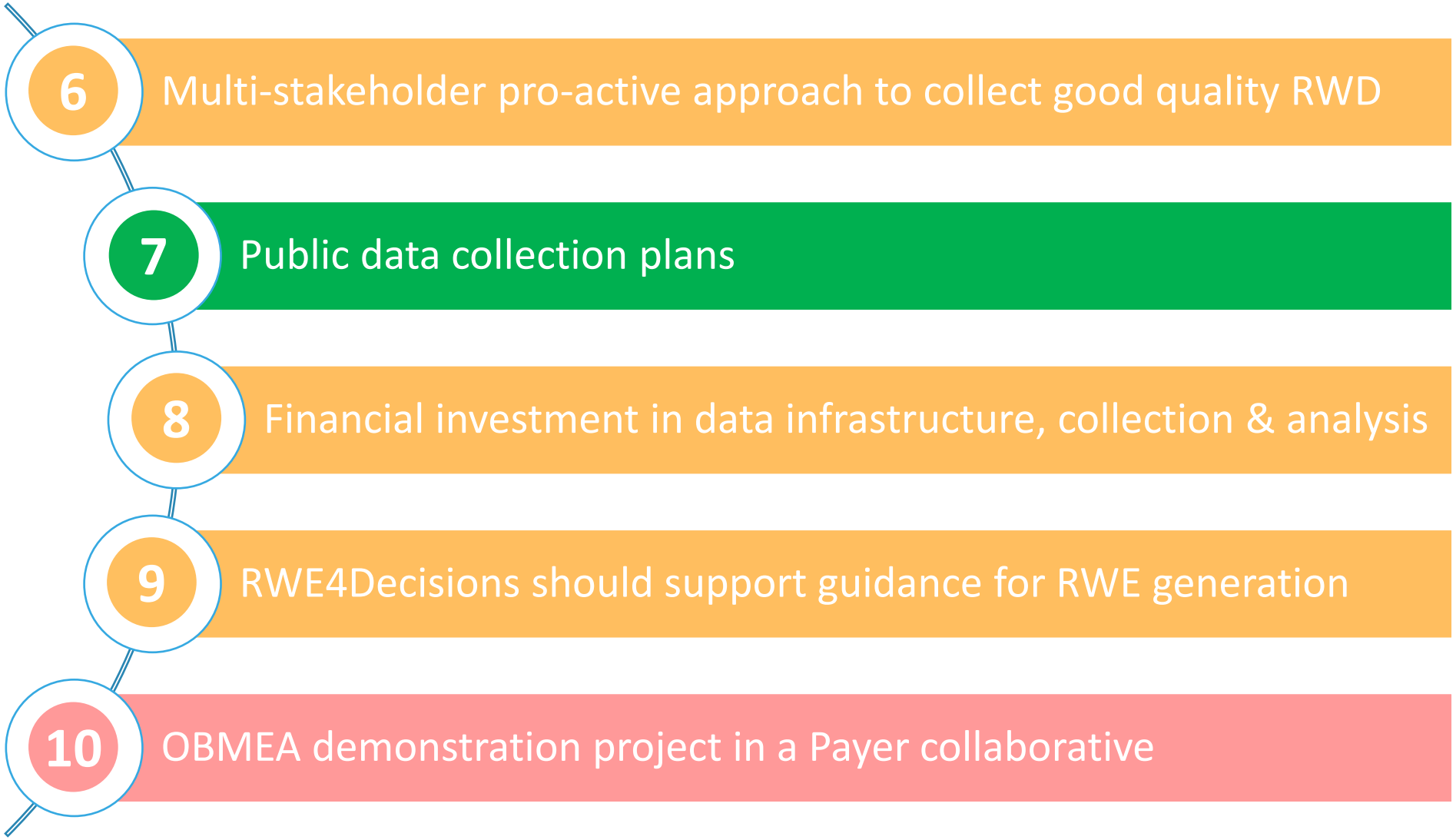
Status of Actions – September 2023?

R, Y, G

Getting better RWE from Coverage with Evidence Development (CED) Agreements that seeks to resolve uncertainties for Payer renegotiations



Getting better RWE from CED Agreements



ISPOR Transparency Initiative

Post Launch Evidence Generation

- Planning: England now require proposals for OBMEA in submission (including detail of data sources)
- Commitment: Netherlands Formal OBMEA – Letter of Concordance among stakeholders with ministerial sign-off
- Monitoring of sites and overall study to improve data quality – alliances with registries (national ala DESCAR-T? or via EBMT?).
- Analysis for re-appraisal and treatment optimization from VBA and CED

Life cycle of RWE generation