Zorginstituut Nederland

CAR-T RWD DLBCL
A case study on the use of Real World Data

L. Timmers, PharmD, PhD

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CAR-T: Challenges to HTA

- Phase I/II data in combination with claims of curation.

1. Short-term evidence is not (usually) enough to substantiate the claim
2. Data on hard end-points is (usually) not (yet) available
3. A go/no-go decision has to be made
4. Current (cost-)effectiveness methodology and policy frameworks do not facilitate better decision making

Assessment and appraisal of CAR-T Therapies in the Netherlands

Acute lymphatic leukemia (ALL) (till 25 jaar)

- Kymriah®
- 10 patients/year
- Budget impact: €2,1 million
- Pharmacotherapeutic evaluation
- No CE evaluation

Diffuse large cell B-cel lymphoma (DLBCL)

- Kymriah® & Yescarta®
- 90-135 patients/year
- Budget impact: €32-48 million
- Pharmacotherapeutic evaluation
- CE evaluation

Assessment and appraisal of CAR-T Therapies

Acute lymphatic leukemia (ALL) (till 25 jaar)
Kymriah®

ZIN advice

- Therapeutic added value
- No pharmaco economic evaluation
- Out of Dutch ‘lock procedure’ without price negotiation

Assessment and appraisal of CAR-T Therapies

Diffuse large cell B-cel lymphoma (DLBCL)

ZIN advice Yescarta®

- Therapeutic added value
- ICER €46.048/Qaly – €600.262/Qaly (!) -> long term efficacy?
- Only after price negotiation available

ZIN advice Kymriah®

- Therapeutic 'less value'
- Due to insufficient scientific foundation.
- uncertainty because of low quality of evidence
- Not available in the Netherlands

Questions left

Dilemma is making an accurate assessment of the long-term value

- How will the treatment be used in clinical practice?
- What is the rol of time from extraction to infusion in practice?
- What will the (cost-)effectiveness be in clinical practice?
- Can pay-for-performance schemes based on RWE be used?

- -> iterative process

Real World Evidence

RWE studies aim to improve health care decision making

RWE can inform the application of evidence from RCTs to health care decision making and provide insights beyond those addressed by RCTs.

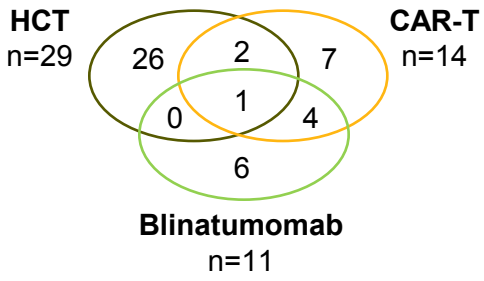
Joint ISPOR/ISPE taskforce RWE

CAR-T products have been approved by FDA 2 years earlier

- Give insight in use in clinical practice
- Follow-up on clinical effectiveness and cost-effectiveness
- Re-evaluate products' performance in real-life

CAR-T Real World Data Project 1

Demonstrate how to use RWD to make an accurate assessment of the long-term value and impact of CAR-T for ALL



Study partners:

VANDERBILT UNIVERSITY

Nashville Biosciences

VitalTransformation
The impact of health technology made simple

Results and discussion from project 1

- “CAR T is not curative”
- CAR-T is seen as a bridging therapy to HCT
- Patients with longest RFS got combination therapy (e.g. CAR T + Allo-BMT)
- Budget impact of combination therapies (e.g. CAR T + Allo-BMT)
- Comparison of USA and Europe (the Netherlands).
- Hospital exemption products?

CAR-T Real World Data DLBCL (Project 2)

Second project on CAR-T:

- DLBCL indication
- Including data from Europe: EBMT
- Multi-stakeholder involvement (incl. CBG-MEB/EMA)
- Feasability study
- Iterative, RWD-based assessment

Research questions (1)

1- What are the current clinical treatment pathways for DLBCL treatments, in the USA and in Europe?

2- How are licensed CAR-T therapies (Kymriah® and Yescarta®) being developed and used in clinical practice for the treatment of DLBCL?

3- How are unlicensed CAR-T therapies (hospital exempted; HE) being manufactured and used in clinical practice for the treatment of DLBCL?

4- What is the effectiveness and cost-effectiveness of licensed CAR-T therapies and how does this compare to HE for patients with similar characteristics?

Research questions (2)

5- What is the total time required from T-cell extraction to (re-)infusion in clinical practice for licensed CAR-T therapies when compared to HE for DLBCL?

6- What are the similarities and differences in DLBCL treatment pathways and (relative) effectiveness and cost-effectiveness of licensed CAR-T therapies between the USA and Europe?

Scientific Advisory Board

Vanderbilt University Medical Centre (VUMC)
The Amsterdam Medical Centre (AMC)
The University Medical Centre Utrecht (UMCU)
The (Dutch) Medicines Evaluation Board (CBG-MEB)
The European Medicines Agency (EMA)
The Medicine Evaluation Committee (MEDEV)
The Norwegian Medicines Agency (NoMA)
The Institute for Quality and Efficiency in Health Care (IQWiG)
The Dental and Pharmaceutical Benefits Agency (TLV)
The European Network for HTA work package 5b (EUnetHTA WP5b)

Time Schedule

- April to July 2019: Public tendering procedure
- Mid-July 2019: start of project/ kick-off meeting
- Mid-December 2019: discussing preliminary findings
- February 2020: Final report
- ..: Impact on decision making (?)

Thank your for your attention

ltimmers@zinl.nl
+31 6 12038017