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SCIENCE MEDICINES HEALTH

Regulatory Perspective on Post-licensing Evidence Generation (PLEG)

Qualification of EBMT registry for post-licencing evidence generation for CAR-T cells authorised for haematological malignancies

Presented by Spiros Vamvakas on 18 June 2019

Overview

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- **Role of PLEG for regulators, guidance**
- **Examples PLEGs in Scientific Advice, Marketing Authorisation**
- **Tools for cooperation**
- **Way forward**

PLEG: what and why

To address remaining uncertainties that we cannot answer in pivotal data at Licensing and for strengthened life cycle approach

- **PLEG scope of data / studies**
  - both randomised and non- randomised studies
  - Data from trials, and data from clinical practice (RWD)

  High quality timely data and methods: control of chance, bias and confounding

Existing Regulatory guidance on PLEG

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Scientific guidance on Post-Authorisation Efficacy Studies PAES

- Categories of uncertainties
- Distinguish data source (primary/secondary) from study design (RCT & NonRCT)
- e.g. Registries can allow variety of observational study design options
- Data quality crucial. Measures include common terminologies, quality control and standards, Limitations acknowledged

Other guidance; PASS, pregnancy, advanced therapies

Regulatory experience-scientific advice (SA) on PLEG

- Advice on PLEG can take place pre or post MAA for safety or efficacy issues
  - ➢ Neurological condition - registries Post licensing- long term control for outcomes; Pre MAA
  - ➢ Rare condition, imposed registry for Post Authorisation Safety Study (PASS) - Post MAA discussion – HTA observers
  - ➢ Pre-licensing discussion gene therapy for rare cancer, thalasaemia: long-term safety and efficacy

Toolbox for cooperation in PLEG

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Opportunities for **parallel consultations** involving other stakeholders in planning Post Launch Evidence Generation:

- Parallel consultation – product specific
- (Parallel) qualification advice / opinion– not product specific
- Public workshops

Qualification of EBMT registry

European Society for Blood & Marrow Transplantation (EBMT) registry qualification for post-licensing evidence generation for CAR-T cell products authorised for haematological malignancies

- *CHMP, CAT and PRAC involvement*
- *Participation of patient representatives and HCPs*
- *Procedure observed by EUnetHTA as part of EMA/ HTA alignment*

CAR-T cells workshop organised by EMA (9 February 2018)

To agree on recommendations on core data elements to be collected, patient consent, governance, quality assurance and registry interoperability.

✓ Openness from all stakeholders in maximising output of resources

Report published on 22 May 2018

Qualification of EBMT registry

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EBMT interactions with EMA

2015 – First contacts with EMA under Patient Registry Initiative

2016 – Invited to participate in EMA CAR-T and Registry events

Oct 2017 – Formally requested qualification opinion from the CHMP

Feb 2018 – Face-to-face discussion meeting with SAWP & CAR-T cells workshop

Data that regulators & developers want

Data that registries can pragmatically collect

Jun 2018 – Start of public consultation of draft qualification opinion

Feb 2019 – Final qualification opinion published

Qualification of EBMT registry

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Qualification opinion included:

- **Context of use**

Study aims

The current status of the cell therapy module of EBMT registry may allow its **use as a data source for regulatory purposes** in the context of the following studies **concerning CAR-T cell therapies authorised for haematological malignancies**:

- ✓ **Drug utilisation studies**
- ✓ **Drug efficacy / effectiveness studies**
- ✓ **Drug safety evaluation**

Qualification of EBMT registry

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Individual study considerations

- Individual studies should be conducted under a **study protocol**.
- **Early tripartite interaction** with EBMT, regulators and Applicants is encouraged.
- **Source data verification and periodic auditing** should be conducted using a risk-based approach. As a general rule, data source verification for a minimum of 10% of registered patients in individual study centres would be required.
- Procedures to **assure sequential inclusion of all patients treated**, to **identify and collect missing data** as well as to **minimize patient lost to follow up** should be detailed.
- **Modifications to the current cell therapy module** may be implemented **for additional data collection**, e.g. to address a particular research question.

Qualification of EBMT registry

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Expected impact of qualification opinion

- **Revisions of EBMT registry** to better address the needs of stakeholders in post-licensing evidence generation for CAR-T cell products.
- **Harmonization and agreement on standardisation of data elements/fields** in all centres and between EBMT and other registries.
- **Collaboration** with other registries, regulatory authorities and stakeholders in order **to facilitate the development of a policy on sharing aggregate, pseudo-anonymised, and individual patient data** and establish a process for requesting and obtaining data.
- **Collection of Quality of Life data** is encouraged.

Thank you for your attention

Further information

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