

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

Overview



- 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



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

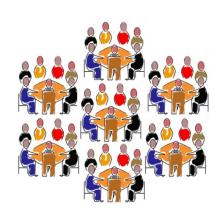
- Advice on PLEG can take place pre or post MAA for safety or efficacy issues
 - ➤ Neurological condition registries Post licensing- long term control for outcomes; Pre MAA
 - ➤ Rare condition, imposed registry for Post Authorisation Safety Study (PASS) Post MAA discussion HTA observers
 - ➤ Pre-licensing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

Toolbox for cooperation in PLEG



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





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



Support #

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 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



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.



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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