Governance structure CAR T community

Open call until 01.09.2019 for feedback and participation in workpackages
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Background

EBMT

- Has received in 28-02-2019 a **qualified opinion of EMA for the cellular therapy** module of the EBMT registry and a good coverage in terms of infrastructure in order to capture data from patients receiving CAR-T cell therapies
    - Is developing harmonized data sets for CAR-T cell therapy data capture with similar organizations such as CIBMTR
- Has a strong background in accreditation and quality systems for hematopoietic cell therapy delivered via **JACIE,** including specific involvement in center selection and accreditation for CAR-T cell therapy across Europe
- Connects health care professionals such as physicians, data manager, nurses and cellular therapy coordinators, apheresis staff, cellular therapy processing staff, pharmacist, as well as patient advocates
- Has an educational branch used to educate health care professionals across Europe in dealing with cellular therapies throughout the year
- Has launched a stakeholder discussion to create a core stakeholder group dealing with aspects of
    - Transparent data sharing
    - Center accreditation within the context of CAR-T cell therapies
    - Education of health care providers

National Transplantation groups which include but are not limited to GITMO (Italy), SFGM-TC (France), HOVON-SCT (The Netherlands), BSBMT (UK), DAG-KBT (Germany), GETH (Spain), and **national registries**

- Are an important bridge from the European organization EBMT to the national practice as they spread EBMT accreditation and educational activities

Clinical CAR T centers

- Are using CAR-T cell products registered by EMA
- Are testing CAR-T cell products in company sponsored clinical trials
- Are testing CAR-T cell products in investigator sponsored clinical trials
- NEEDS: education on the use of CART cells, education for achieving the qualification as CART cell centers (by companies with an approved product).

Disease oriented health care professionals organized in scientific societies which include but are not limited to EHA, ESMO, ISCT and cooperative study groups like HOVON (Netherlands), LYSARC (France), SWECARNET (Sweden) and ALL study groups (Netherlands, France), GLA (Germany), GMALL (Germany), GELTAMO (Spain), FIL (Italy) or biobanking initiatives (Cryostem, France) encompass the expertise for specific disease entities, which are suitable for CAR T therapies, which have reached market approval

- Encompass disease orientated data collections
- Perform commercial or investigator-initiated studies dealing with CAR T therapies

Pharmaceutical companies

- Provide CAR-T cell products in the context of clinical trials
- Manufacture and market CAR-T cell products approved by EMA with the obligation to capture key essential data for safety reason within the context of PASS studies as well as center accreditation

- Are capturing post marketing data contractual through the EBMT registry and/or other national registries
- Are developing products for market approval and consider the EBMT registry as a potential platform to capture post market approval data, as well as to access historical data as comparators, since many studies are non-randomized due to the nature of the drug product
- In principle the platform will be open for companies dealing with other cellular therapy products, however focus of the platform will be in the startup phase CAR-T cells

Patient advocates

- Represent patient interests for more or less specific diseases treatable with CAR-T cell therapies, either as individuals or via patient organizations. The EBMT has a Patient, Family & Donor (PFD) Committee.

HTA (health technology assessment) bodies

- Are interested in capturing follow-up data on treatment patterns in clinical practice and long term relative-effectiveness, safety and cost-effectiveness of different therapies.

Regulators (EMA & national competent authorities)

- Has the right to request and analyze data for assessing long-term safety and efficacy data for CAR-T cell therapies as outlined in the market approval statements
- Has linked the approval of CAR-T cell therapies to the qualification of personnel in centers administering CAR-T cells
- National pharmaceutical authorities
- National competent authorities for tissues and cells are responsible for cell collection as starting materials and are increasingly interested in clinical outcome as an indicator of safety and quality

Mission statement is in line with the global CAR-T cell strategy of EBMT (Figure 1).

- **Creating transparent data access and an improved data collection** for data captured through the EBMT registry for CAR-T cell therapies in line with the mandatory “must have” data sets defined by EMA and study protocols for different stakeholders such as EMA, companies, HTA bodies cooperative groups, and biobanks. Additional aims are:
    - Linking the EBMT registry to other registry data efforts (HARMONY) or biobanking efforts such as envisioned by CRYOSTEM
    - Developing a patient orientated report for CAR-T cell therapies together with patient advocates
- Developing a **qualification / accreditation process** which covers immune effector cells (IECs) but independent from a defined product, through the identification of commonalities / redundancies across the different processes
- Developing an **educational program** for physicians, data managers, apheresis nurses, cell therapy technologists, pharmacists, and nurses dealing with CAR-T cells either the supply chain or the patient care, but independent from a defined product
- Scouting the development of new **European policies and legislation**. Commenting ongoing European policy and legislation initiatives from the perspective of different stakeholders.

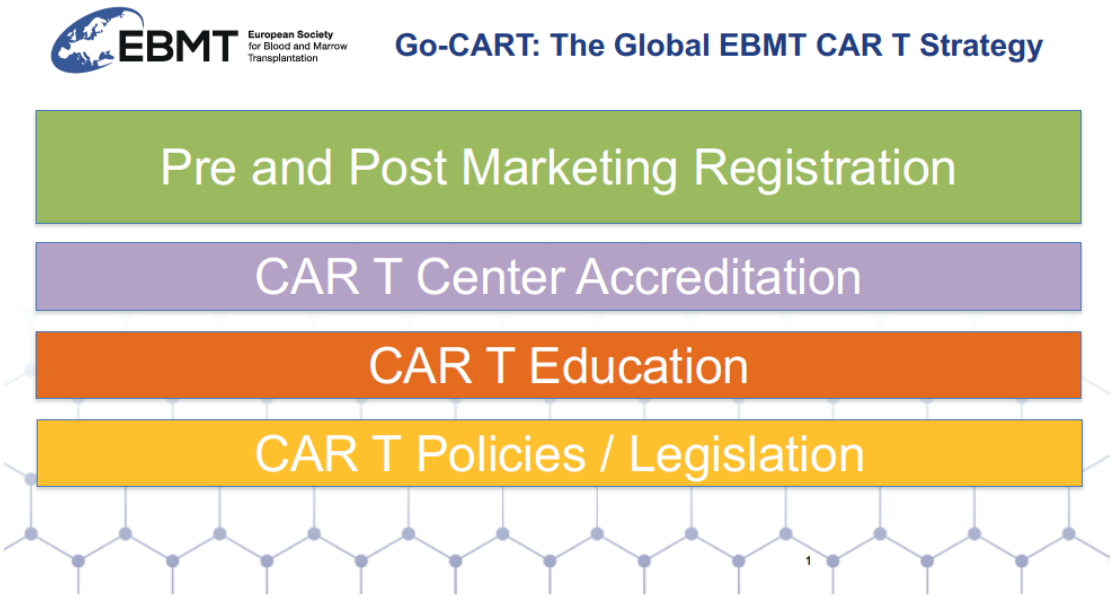

Figure 1. Global EBMT CAR T Strategy

Process and contact points with different stakeholders to create a governance structure (Figure 2).

- **Pharmaceutical stakeholders:** pharmaceutical stakeholders have been identified during the EMA CAR T registry workshop as well as during different annual meetings in 2018 (EBMT, ASH, EHA) and contractual interactions have been initiated
- **HTA stakeholders** have been identified during the qualified opinion process of EBMT with EMA and EUnetHTA has been identified next to Dutch, German, French and British, and Spanish HTA bodies as key players. A first focused stakeholder meeting was performed in April 2019 in Leiden.
- **Medical stakeholders:** During different meetings at the 1st CAR T cell meeting in Paris in 2019, the 45th annual meeting of EBMT in 2019 medical stakeholders have been approached and identified for further discussion. Follow up meetings are planned during the EHA meeting in 2019.
- **Patient representative:** EBMT launched an international patient representative group in 2018 and the chair of the group has been representing the interests of the group during different meetings at EBMT.

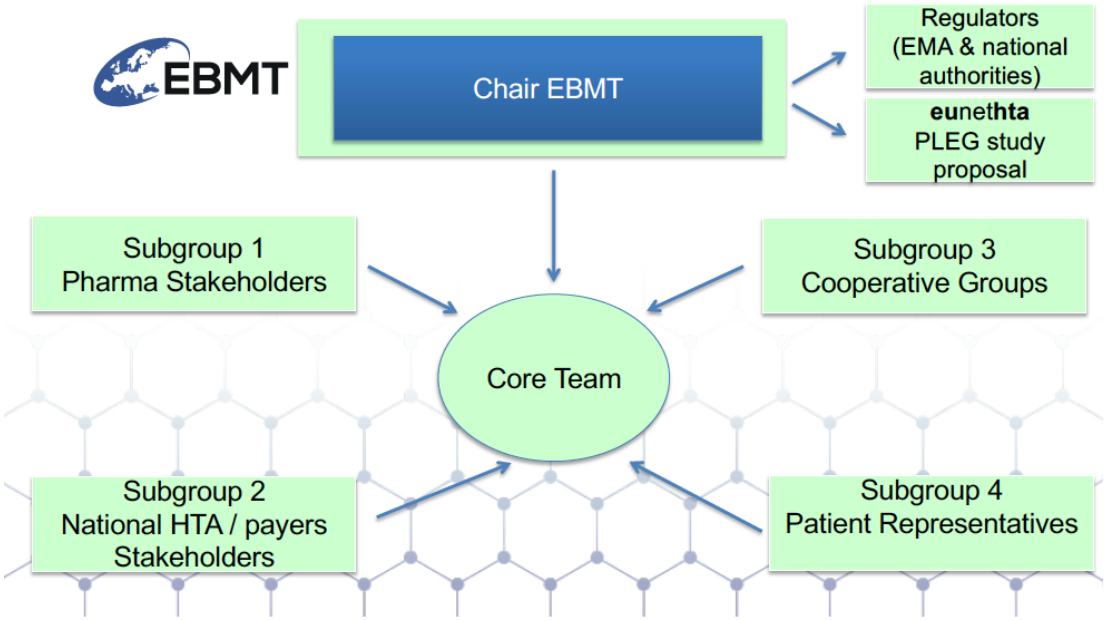

Figure 2: Different interaction during 2018 and 2019 to connect different stakeholders

Governance structure

Executive committee

The steering committee will be coordinated by an **executive committee** with maximum of 4 representatives representing medical societies (EBMT and EHA) supported by the program manager. It will be explored to expand later the executive committee towards two members representing ESMO. The executive committee oversees overall activities and will further work on details of the governance structure in order to clarify e.g. approval processes for defined work packages. The executive committee will also oversee participants of the stakeholder meeting and is working in an "inclusion model" while also considering operational aspects in terms of group sizes for defined work packages.

Steering committee

A steering committee will oversee different operational activities. The steering committee will define work packages, distribute different stakeholders to defined work packages, and appoint work package leaders. The steering committee will discuss final deliverables of different work packages and is working in a consensus model.

The precise number of the steering committee members will be developed during the process until Q3/2019 and depend on operational aspects and interest of different groups.

Different members will represent different stakeholders. Members of the steering committee are:

1.) EBMT (5 representatives and providing the chair) will, as registry holder and representative of core CAR-T cell activities, chair the steering committee, guide the discussion, coordinate the agenda, invite steering committee members, appoint candidates, and implement working groups. The chairperson will rotate between the 5 key units:

- EXCOM representative

- EMA/EU contact: LRAC
- Center Qualification / Accreditation (JACIE representative)
- Science: CTIWP (focus scientific activities)
- Education: Educational representative

2.) Pharma (representatives)

- Companies with contractual CAR-T cell data delivery to EBMT
- Companies with planned activities

3.) HTA Bodies

- Positioning of EUnetHTA will be defined during the ongoing interaction with EUnetHTA
- National HTA representative if requested

4.) Payers

- National payers representative if requested

5.) Medical professional organizations

- EHA
- ESMO
- cooperative study groups

6.) Patient advocates

7.) Regulators

The following themes will be overseen by the steering committee.

Theme 1.1) Transparent Data definition, capture, and access <u>from PASS studies (commercial administration and data collection)</u>

- Data are owned by the patient
- All centers have at any time free access to data coming from their center.
- EBMT is, as registry holder, the data controller of the sum of all introduced data.
- Leading in data access and distribution to the sum of all data is the legal obligation through EMA and accompanying contracts with individual pharmaceutical companies within the context of the requirements for post marketing authorization and delivery of data to authorities
- All stakeholders can propose additional scientific projects that will be discussed within the stakeholder group.
- The stakeholder group will prioritize projects within a scientific committee representing EBMT, EHA, ESMO as well as cooperative group representatives and patient advocates
- The role of data controller and data processor will be defined for each project and contracts with different parties used to define the project as well as data handling in line with GDPR. Publication guidelines – including authorship - will be developed. This activity will be performed in close collaboration with the data safety officer of EBMT as well as the scientific council of EBMT

Additional aspects

- Technical connections between different data bases will be explored for technical and financial feasibility

Theme 1.2) Transparent data definition, capture, and access from <u>clinical trials and hospital exemption programs</u>

- Data are owned by the patient
- All centers have at any time free access to data coming from their center.

- EBMT and CAR T centers can limit data access of others during clinical trial or defined hospital exemption programs
- EBMT is as registry holder data controller
- All stakeholders can propose additional scientific projects which will be discussed within the stakeholder group. Whenever feasible, the steering committee will favor collaborations and connections, leading to the constitution of consortia able to candidate for various funding including EU Funding.
- The stakeholder group will prioritize projects within a scientific committee representing EBMT, EHA, as well as ESMO representatives and patient advocates
- The role of data controller and data processor will be defined for each project and contracts with different parties used to define the project as well as data handling in line with GDPR. This activity will be performed in close collaboration with the data safety officer of EBMT as well as the scientific council of EBMT

Theme 2) Center accreditation process

- JACIE is continually appraising the development of CAR-T cells and other immune effector cells (IECs) and their impact on clinical, aphersesis and processing laboratory practice across the landscape of hematopoietic cell therapy.
- Further development of quality standards for CAR-T cells and IEC will therefore be continually integrated within the JACIE organizational structure and operations, with the JACIE committee overseeing the inspection and accreditation process across centers.
- Demands for various approaches are being actively scoped, ranging from the current 'Integrated', where accreditation for IECs is an integral part of hematopoietic cell transplant (HCT) practice, to a parallel system for IEC in a neutral language, similar to FACT Common Standards, which could either be adopted or developed de novo by JACIE according to demand.
- Business planning will be a central consideration in the sustainable delivery of any accreditation process, whether it be 'integrated' within or delivered alongside current JACIE operations.

Theme 3) Educational Events for centers dealing with CAR T Therapies

- The Scientific Council (SC) and the Representative for Education of the SC and the CTIWP of EBMT will develop an education program.
- The educational planning will therefore fall within the educational structure of EBMT.
- Education activities will be also discussed and partially aligned with EHA which is representing the different disease groups as well as ESMO if solid tumors are involved as indications

Theme 4) European policies and legislation

- Policy focusing groups of different stakeholders will be invited to generate an agenda of topics that need to be commented during European legislation

Based on the discussion with different stakeholders in 04/2019 the following work packages with the defined teams will be prioritized for 2019-2020

Process
At the first stage the call is open to all stakeholders to indicate in which work package and topic they want to participate. Participation needs to be linked to a stakeholder and name/ email address of a defined person.

At a second stage different work package participants will revisit and fine tune defined tasks for further clarification. Then time lines will be defined as well as an overall work package leader chosen in a consensus model. This process will provide to the different group maximal flexibility to adopt the project in line with the needs perceived by all experts.

The chosen work package leader will report to the project manager on progress and deliverables and report to the executive and steering committee.

WP1) Harmonization of core data sets, data protection, and exploration of future data sets

Team composition:
- EBMT
- EHA
- Interested stakeholders

WP2) Center accreditation standards

Team composition:
- JACIE Committee (EBMT, ISCT)
- Pharmaceutical companies with approved CAR-T cell medicinal products or CAR-T cells close to being placed on the market
- Patient advocate representative
- MO = EBMT Medical Officer

WP3) Center educational standards

Team composition:
- Educational units EBMT and EHA
- Pharmaceutical companies with approved CAR-T cells medicinal products or CAR-T cells close to being placed on the market
- Patient advocate representative

WP4) The registry from an HTA perspective

Team composition
- EUnetHTA
- EBMT

WP5) Scientific excellence

Team composition:
- EBMT
- EHA
- Cooperative groups
- Scientific branch of companies

WP6) Moving European policies and legislation forward

The project will be developed in close collaboration with regulators