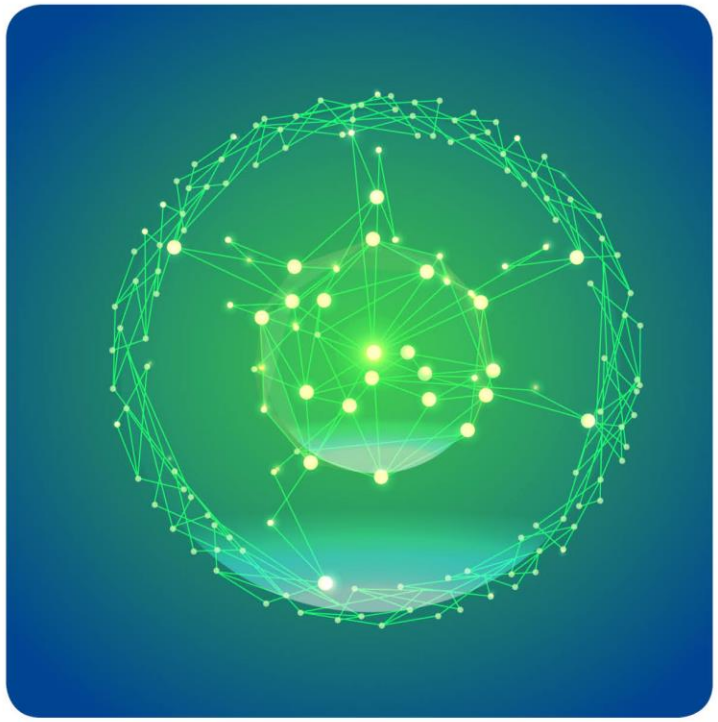


TORINO

DIPARTIMENTO DI BIOTECNOLOGIE MOLECOLARI E SCIENZE PER LA SALUTE

AULA ARISTOTELE

Via Nizza, 52

17 LUGLIO 2019

AZIENDA OSPEDALIERO - UNIVERSITARIA
Città della Salute e della Scienza di Torino

ROAD MAP CAR-T

PROSPETTIVE ATTUALI E FUTURE DELL'USO DELLE CAR-T IN ITALIA

2019 MOTORE SANITÀ
Gestire il Cambiamento

QUALI TECNOLOGIE NECESSARIE?

Dott. Silvio Falco

Direttore Generale AOU Città della Salute e della Scienza di Torino

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

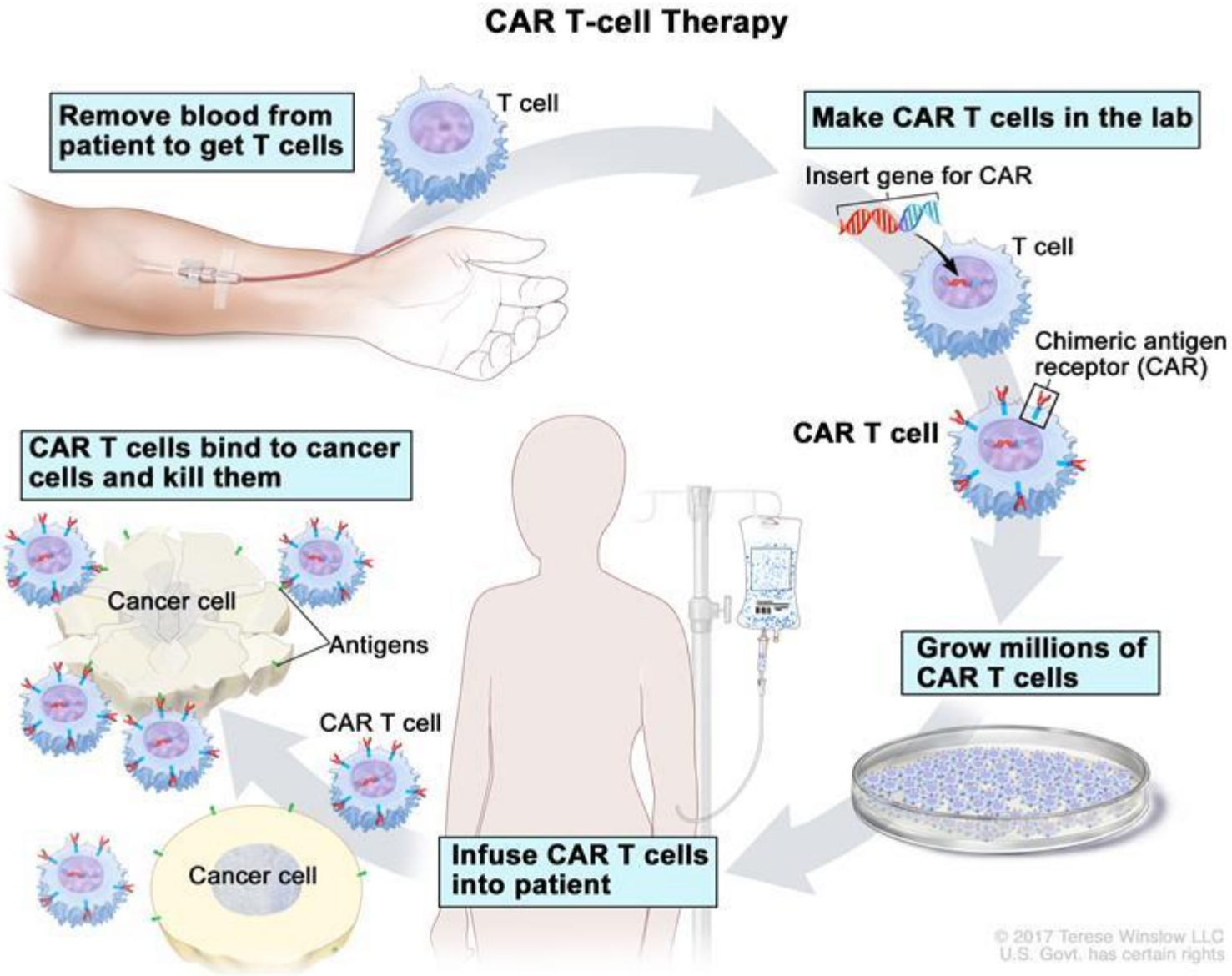
FRONTIERS IN MEDICINE

Chimeric Antigen Receptor Therapy

Carl H. June, M.D., and Michel Sadelain, M.D., Ph.D.

"Genetically engineered T cells constitute a powerful new class of therapeutic agents that offer hope for curative responses in patients with cancer. Chimeric antigen receptor (CAR) T cells were recently approved by the Food and Drug Administration (FDA) and are poised to enter the practice of medicine for the treatment of leukemia and lymphoma"

UNA PROCEDURA CLINICAMENTE COMPLESSA



UNA PROCEDURA CLINICAMENTE COMPLESSA....

...RICHIEDE UN SISTEMA COMPLESSO

Strutture di degenza

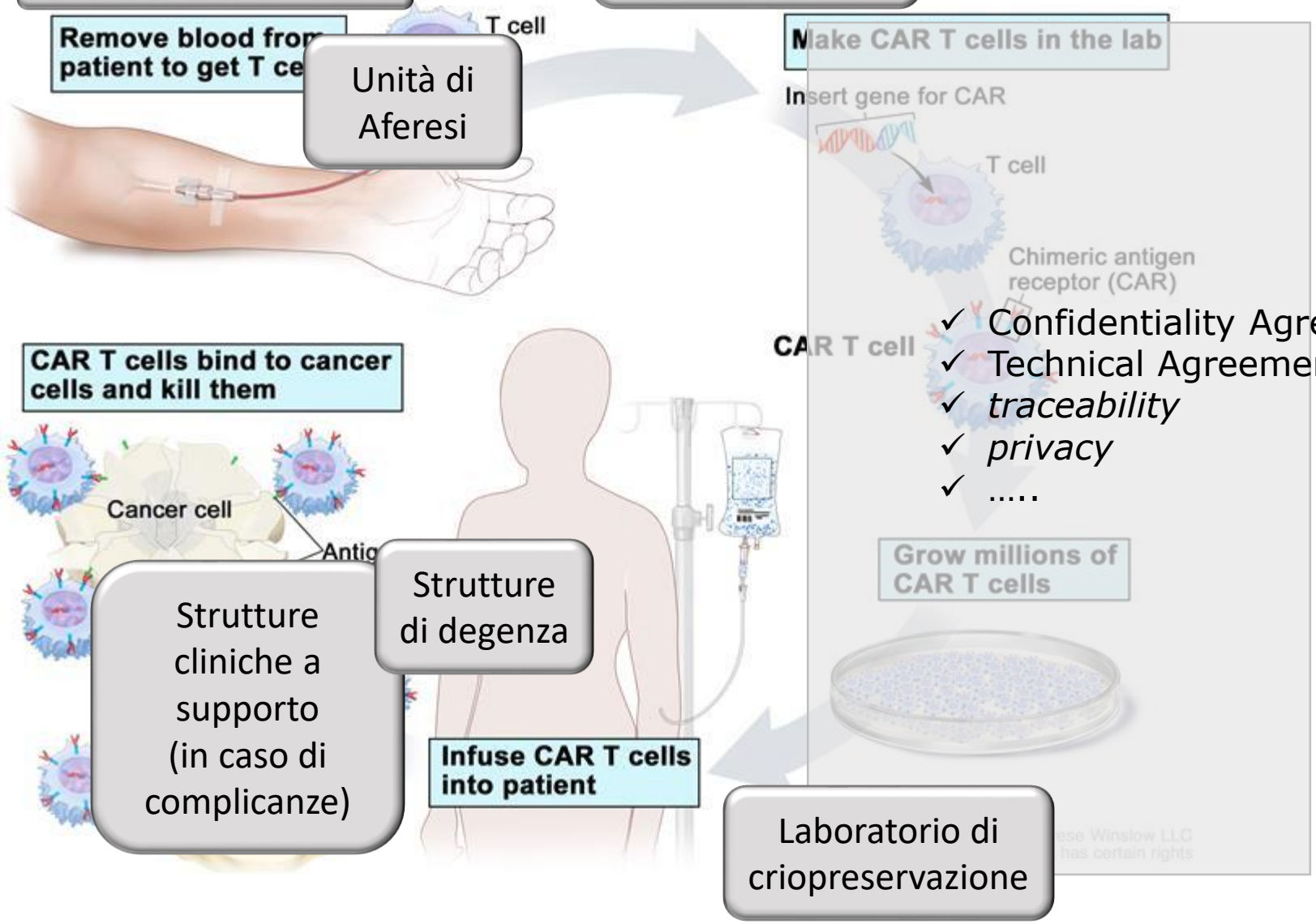
Ematologia

Onco-Ematologia Pediatrica

Trapianto Cellule

Laboratorio di criopreservazione

Unità di Aferesi



- ✓ Confidentiality Agreement
- ✓ Technical Agreement
- ✓ *traceability*
- ✓ *privacy*
- ✓ .....

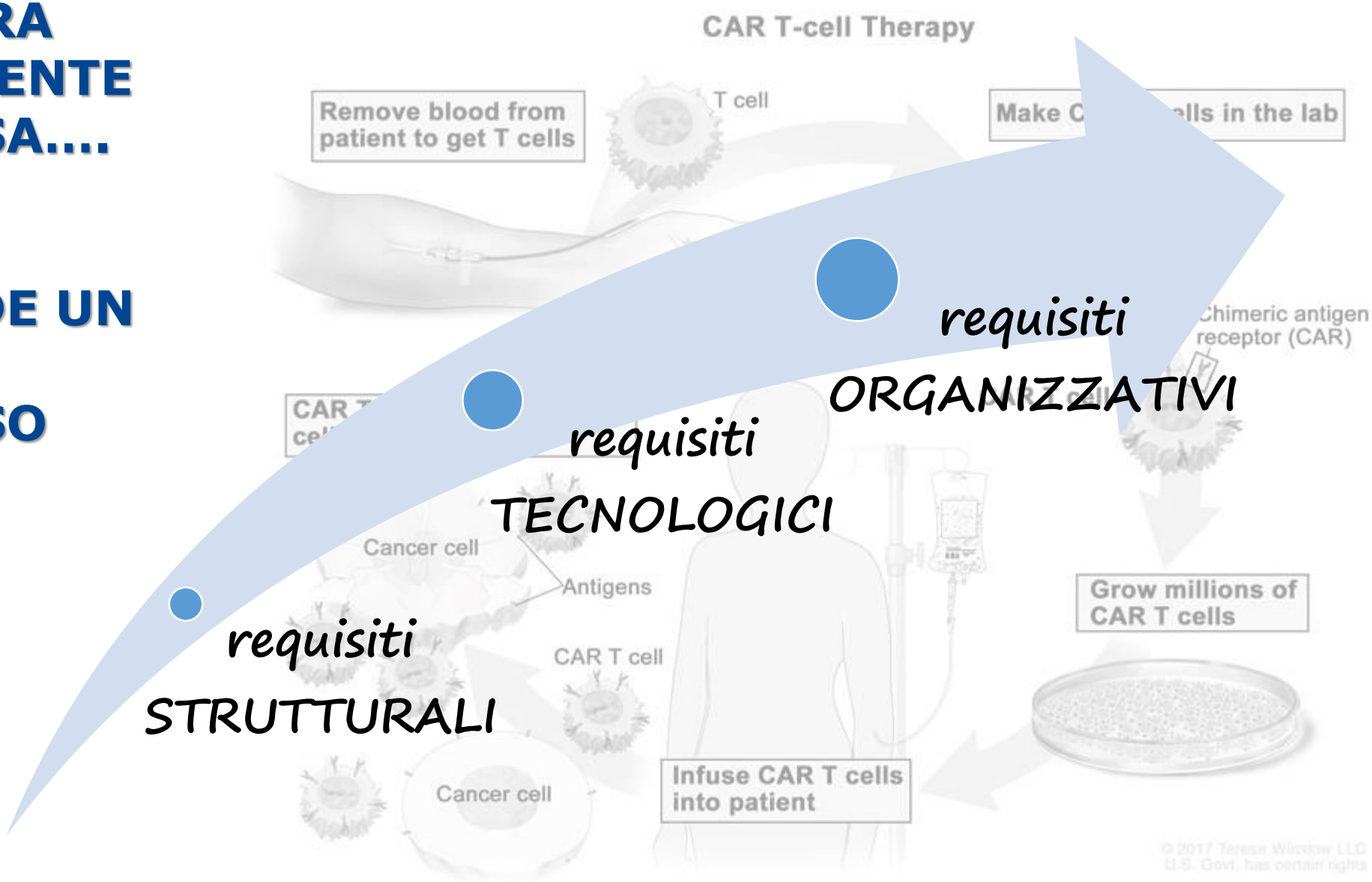
Strutture di degenza

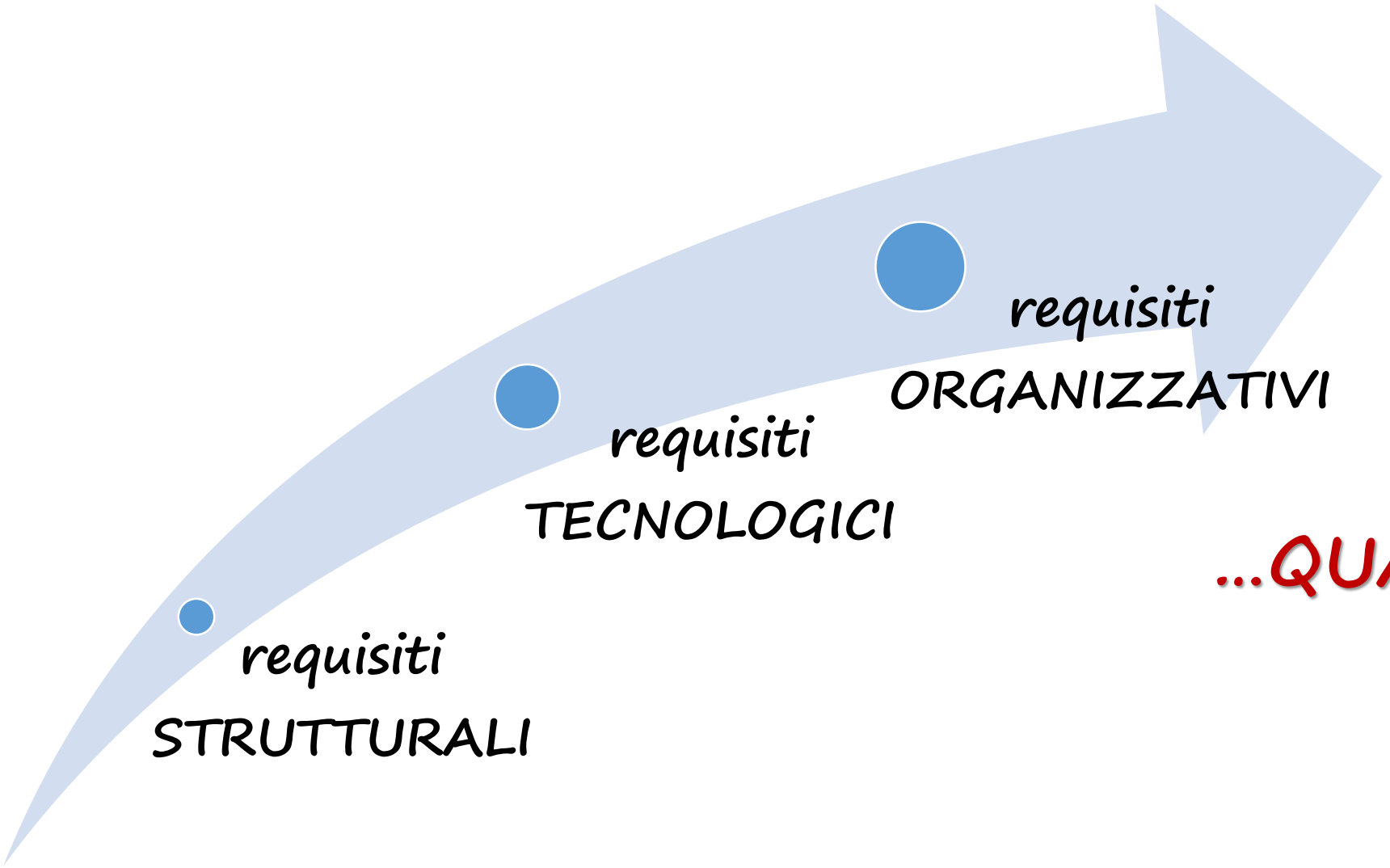
Strutture cliniche a supporto (in caso di complicanze)

Laboratorio di criopreservazione

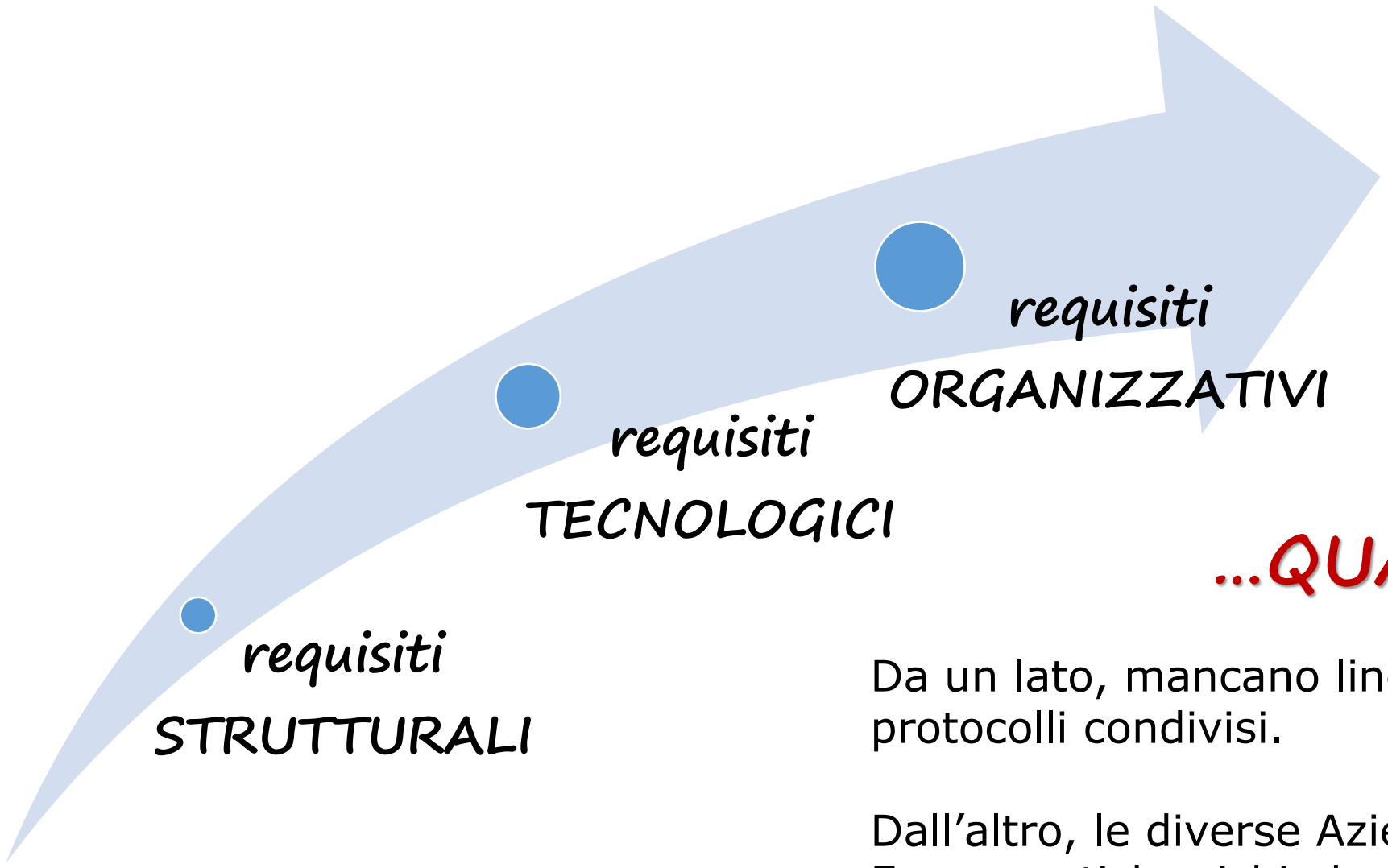
UNA PROCEDURA CLINICAMENTE COMPLESSA....

...RICHIEDE UN SISTEMA COMPLESSO




requisiti
STRUTTURALI
requisiti
TECNOLOGICI
requisiti
ORGANIZZATIVI

...QUALI?



...QUALI?

Da un lato, mancano linee guida e protocolli condivisi.

Dall'altro, le diverse Aziende Farmaceutiche richiedono requisiti ed apparecchiature eterogenee.

Il prodotto esce
dall'Ospedale congelato
e ritorna congelato

Apparecchio di aferesi
in uso presso l'AOU

Il prodotto esce
dall'Ospedale non congelato
e ritorna non congelato

Apparecchio di aferesi
della Ditta

Il prodotto esce
dall'Ospedale non congelato
e ritorna congelato

Apparecchio di aferesi
in uso presso l'AOU

Contenitore criogenico per conservazione del materiale cellulare in azoto liquido, con sistemi di monitoraggio della temperatura ed allarme remoto (con conseguenti necessità organizzative)

Etichettatrici

Sacche di raccolta e over-pouches (sacche di sicurezza)

Tracciabilità del percorso (integrazione con i sistemi informativi Aziendali, sia sanitari che amministrativi)

ETEROGENEITÀ delle TECNOLOGIE RICHIESTE

Ad oggi, le diverse Ditte Farmaceutiche hanno richieste eterogenee in termini di organizzazione, apparecchiature, requisiti ….

necessario ottimizzare risposte Aziendali il più possibile 'trasversali', anche in funzione di eventuali ulteriori richieste future.

importanti problematiche nella formazione del personale coinvolto, e nel mantenimento delle competenze !

ETEROGENEITÀ degli SCENARI GIURIDICO-AMMINISTRATIVI

Ad oggi, le diverse Ditte Farmaceutiche hanno percorsi eterogenei di registrazione e approvazione del farmaco, con proposte eterogenee alle Aziende Sanitarie

NOVARTIS

PEDIATRICO: Sperimentazione Clinica
ADULTO: commercializzazione ?

Celgene

Sperimentazione Clinica

Kite
A GILEAD Company

GILEAD

Uso compassionevole ?

- **Percorsi amministrativi eterogenei**

- **Rischio di un ruolo 'passivo' dell'AOU nell'accettare quanto proposto dalla Ditta Farmaceutica, non sempre privo di criticità (es. esclusione dell'uso compassionevole dalla polizza assicurativa Aziendale)**

MULTIDISCIPLINARIETÀ DEL PERCORSO DI CURA

Il percorso del paziente coinvolge diverse Strutture, non solo cliniche.

Necessità di forte integrazione tra le differenti realtà coinvolte…

…a chi il ruolo di coordinamento, pianificazione e monitoraggio ?

CRITICITA' ORGANIZZATIVE

1. **le CAR-T sono terapia genica con microorganismi geneticamente modificati (MOGM)!**

   NECESSARIA LA NOTIFICA DI IMPIANTO E DI IMPIEGO
   (NB il vettore lentivirale NON è replicazione competente, e NON sono necessarie precauzioni particolari per lo smaltimento dei rifiuti clinici contaminati)

2. **le CAR-T escono dall'Ospedale come cellule, e vi rientrano come farmaco !**

   autorizzazione al non-transito da parte della Farmacia Ospedaliera

PROBLEMI APERTI

1. STIMA DEL FABBISOGNO

«quanti e quali pazienti?»

Quali Centri clinici, e come?
È sufficiente il modello hub&spoke?
Quale programmazione Regionale?

Siamo in grado di prevedere la mobilità inter-regionale, anche alla luce degli imminenti obblighi di trasparenza sui trials clinici previsti dal D.Lgs. N.52/2019 ?

PROBLEMI APERTI

2. IDENTIFICAZIONE DEI REQUISITI PER I CENTRI CLINICI

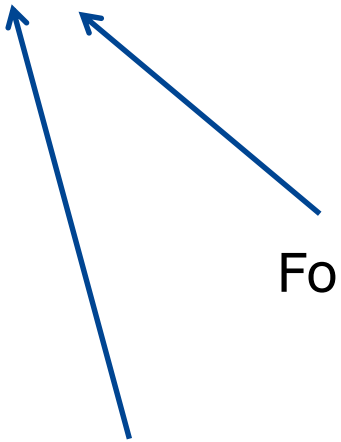
«quali strutture, e quali tecnologie?»
«quali processi di accreditamento e certificazione?»

È (e sarà) sufficiente l'accreditamento JACIE
(Joint Accreditation Committee of ISCT and EBMT) ?

PROBLEMI APERTI

3. LA QUALITÀ DELLE CURE E LA SICUREZZA DEI PAZIENTI

«quali Linee Guida?»
«quali percorsi formativi?»



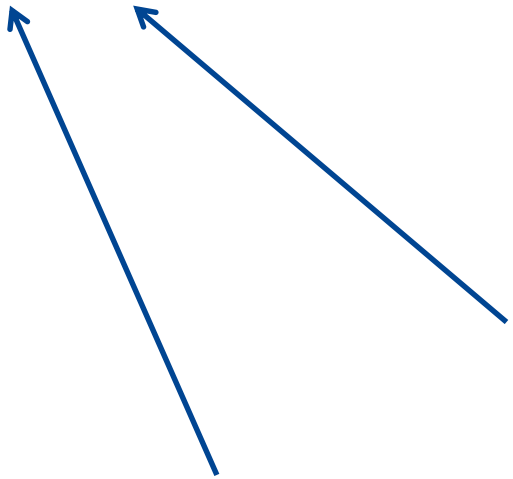
Forte necessità di Linee Guida e protocolli condivisi

E’ possibile immaginare dei ‘car-T team’ multidisciplinari dedicati ?

PROBLEMI APERTI

4. LA SOSTENIBILITÀ

«chi paga, e cosa?»



Quali profili di rimborsabilità?

Quale ruolo per le
Ditte Farmaceutiche?

To date, most centres have limited experience and there has, as yet, been no guidance as to the optimal models of care for CAR T cell recipients, either in the short or long term. However, current FACT- JACIE standards now cover immune effector cells (IECs), with a view to providing quality standards for the facilities, infrastructure and training and to ensure competency across clinical, pharmacy and scientific staff in the administration of CAR T cells and the management of complications. In addition, centres require adequate data managementinfrastructure to meet the regulatory requirement for mandatory reporting of follow-up for 15 years.

Follow-up

G Model
RETRAM 3229 No. of Pages 10

ARTICLE IN PRESS

Current Research in Translational Medicine xxx (2019) xxx–xxx

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www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en

Original article

An international survey on the management of patients receiving CAR T-cell therapy for haematological malignancies on behalf of the Chronic Malignancies Working Party of EBMT

P.J. Hayden[a,*], T. Sirait[b], L. Koster[b], J.A. Snowden[c], I. Yakoub-Agha[d]

[a] Dept. of Haematology, Trinity College Dublin, St. James's Hospital, Dublin 8, Ireland
[b] EBMT Data Office, 2300 Leiden, the Netherlands
[c] Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK
[d] CHU de Lille, IJRIC, INSERM U995, Université de Lille, 59000, Lille, France

Table 2
Cities and countries.

Country	City	N (%)	N (Country)
USA	Seattle	3 (7)	16
	Tampa	3 (7)	
	Portland	2 (5)	
	Chicago	1 (2)	
	Jacksonville	1 (2)	
	Not disclosed	1 (2)	
	Nashville	1 (2)	
	New York	1 (2)	
	Philadelphia	1 (2)	
	Rochester	1 (2)	
	Saint Louis	1 (2)	
France	Paris	3 (7)	6
	Lille	2 (5)	
	Lyon	1 (2)	
Spain	Madrid	2 (5)	5
	Badalona	1 (2)	
	Barcelona	1 (2)	
	Salamanca	1 (2)	
Germany	Cologne	1 (2)	3
	Hamburg	1 (2)	
	Würzburg	1 (2)	
UK	Bristol	1 (2)	3
	London	1 (2)	
	Manchester	1 (2)	
Saudi Arabia	Riyadh	2 (5)	2
Italy	Milano	1 (2)	2
	Rome	1 (2)	
Netherlands	Amsterdam	1 (2)	2
	Utrecht	1 (2)	
China	Hangzou	1 (2)	1
Israel	Tel Hashomer	1 (2)	1
Total			**41 (100)**

There is no common model of care for the long-term follow-up (LTFU) of recipients of these new therapeutic agents at this early stage. Although the issue of relapse is of prime importance in the

Table 10
Follow-up from discharge to Day+100.

Follow-up from hospital discharge to day +100		N (%)
How frequently should the patient attend ambulatory clinics (in patients without an overt complication and not including hospitalization for transfusion)?		
During the first month following discharge	Total answers	33 (80)
	1 time / week	8 (24)
	2 times / week	**14 (43)**
	3 times / week	11 (33)
	1 time / month	0 (0)
	Don't know	0 (0)
During the second month following discharge	Total answers	33 (80)
	1 time / week	**13 (39)**
	2 times / week	3 (9)
	1 time / 2 weeks	**13 (39)**
	1 time / month	4 (12)
	Don't know	0 (0)
During the third month following discharge	Total answers	33 (80)
	1 time / week	7 (21)
	2 times / week	0 (0)
	1 time / 2 weeks	12 (36)
	1 time / month	**13 (39)**
	Don't know	1 (3)

JACIE (or FACT) accreditation provides the broader quality management system required to support LTFU of patients receiving CAR T therapy. Although the standards pertaining to immune effector cell therapies (i.e. section B7.11 of the 7th edition, https://www.ebmt.org/jacie-accreditation) are most directly relevant to the early aspects of CAR T-cell administration, the more general integration of CAR T administration into the broader quality management systems required for accreditation will necessitate document-controlled policies, procedures and service level agreements (SLAs) including MDTs for LTFU. Incorporation of transitional and shared care arrangements should provide an effective means of delivering quality assured LTFU in this complex patient group alongside mandatory data reporting.

Although being cell-based therapeutics, CAR-T cells qualify in European member states as ‘‘gene therapy medicinal products’’, a subcategory of Advanced Therapy Medicinal Products or ATMPs, as defined in European regulation EC 2007/1394. They qualify as ATMPs since the collected cells are engineered and thus subject to substantial manipulations. They are gene therapy medicinal products since the product of the expression of the recombinant DNA sequence is responsible for therapeutic effects. Being genetically engineered, CAR-T Cells further qualify as ‘‘geneticallymodified organisms’’ (GMO)

Manufacturing of hematopoietic cellular therapies and in particular of autologous CAR-T cells also borrows to medical practices that have been in use for decades in the field of hematopoietic cell transplantation [15]. In particular, cell procurement is similarly regulated by the content of directives 2004/ 23/EC, 2006/17/CE and 2006/86/CE, and relies on apheresis techniques. Although pharmaceutical companies may consider operating their own apheresis facilities in the future, they have so far subcontracted with hospital-based or blood bank based collection facilities. This creates a peculiar situation in which a hospital or a blood bank acts as the provider of the starting material or raw material necessary to initiate the manufacturing process, and thus must comply with its client requirements, including requests for periodic auditing as well as proofs of evidence for training, retraining, habilitation of involved personnel and proper maintenance and use of infrastructures and equipment.

Financial compensations for performing aphereses and providing the starting material remain to be defined, whether limited to already existing payment by private or public insurances for these services, or paid for by the manufacturer of the medicinal product.

When the medicinal product is shipped back from the manufacturing site to the clinical site as a cryopreserved cell suspension, French regulations rule that the hospital pharmacy (dispensary, ‘‘Pharmacie a` Usage Inte´ rieur’’, PUI) is responsible for proper receiving, temporary storage and distribution. However, very few hospital pharmacies operate a cryobiology infrastructure, and expertise in handling and thawing of cell-based therapeutic products is essentially present in tissue establishments (TE) or cell processing facilities that support cell and tissue transplant activities at academic facilities.

A pressing issue will be to decide on a national organization providing equitable access to all patients affiliated with the global and public health coverage (‘‘Assurance maladie’’). Identification and designation of ‘‘expert centres’’ or ‘‘centres of excellence’’ – similarly to what is currently required by the Food and Drug Administration, FDA in the USA – should result of an open and transparent process involving pharmaceutical companies that develop CAR-T Cells and sponsor clinical trials as well as French competent authorities and healthcare payers with a view to promote fair access and financial control; such decisions should be supported by adaptive definitions or guidelines included in European or EU member state regulations, including periodic reviews as clinical trials expand, and CAR-T Cells reach the market.

The administration of CAR T-cells requires a highly coordinated interaction of multiple specialists belonging to different infra-structures within health establishments in order to ensure the safety of the patients

Current Research in Translational Medicine 66 (2018) 57–58

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www.em-consulte.com

Brief communication

Clinical units to (CAR T-cells): B Society of Bone (SFGM-TC)

Ibrahim Yakoub-Agl

[a] Maladies du sang, unité d'allogre
[b] IURIC, INSERM U995, Université d

4. Recommendations

The administration of CAR T-cells requires a highly coordinated interaction of multiple specialists belonging to different infrastructures within health establishments in order to ensure the safety of the patients. For patient management, the SFGM-TC recommends minimum prerequisites likely to be completed by the specific requirements for each protocol and each type of CAR T-cells:

- A JACIE accreditation. Indeed, the JACIE committee is working on the implementation of the next edition of the FACT-JACIE standards, of a section that will be specifically dedicated to the therapeutic management of immunotherapies.
- A clinical unit with an optimal nurse/patient ratio to insure a continuous monitoring of patients at risk of developing acute immune complications (ideally 1 nurse/4 patients) [5,2].
- Medical and paramedical staff with documented experience:
  - in the administration of combinations of cytotoxic and immunosuppressive drugs
  - in the administration of previously cryopreserved cellular therapy products (Standard B3.7, B3.7.3.3, 3.7.4.3 of the FACT-JACIE International Standards for Hematopoietic Cellular Therapy v6.
  - in the man complicatio time
- A physician sp duty 24/7.
- Availability of tocilizumab (or another drug likely to attenuate the side effects according to the requirements of the sponsor and specificity of the CAR T-cell products) at the pharmacy of the establishment with a supply in the care unit that is available immediately.

Taking into account the time to occurrence of cytokine release syndrome reported in the literature, the SFGM-TC recommends that the minimum initial hospitalization duration should be of 14 days after the administration of the CAR T-cells. For patients developing profound neutropenia, the hospitalization in a protected room is recommended. It is also recommended that the CU organizes systematic evaluation of patients by an ICU specialist at regular-basis in order to undergo pre-emptive interventions whenever necessary. The ICU specialist should be familiar with the specific CAR T-cell complications.

Staff members have to be informed on the nature and risks/absence of risks for the environment/the operators associated with the administration of CAR T-cells that are GMO (refer to manual of confined use of GMOs in the setting) [6].

5. Conclusion

To our knowledge, the SFGM-TC recommendations are the first to set up a framework that take into account primarily the safety of patients undergoing CAR T-cell therapy. These recommendations will evolve as our experience progresses.

The Francophone Society of Bone Marrow Transplantation and Cellular Therapy (SFGM-TC) hold its eighth practice harmonization workshops on September 2017. In a workshop dedicated to chimeric antigen receptor T-cell therapy (CAR T-cells), the society issued recommendations regarding the prerequisite for hematopoietic cellular therapy programs to set up CAR T-cell therapy. In this article we focused on the prerequisite needed, in France, for a hematopoietic transplantation unit to start a CAR T-cell program with industrial manufactured cells within investigational products or after market access authorization.

[12,13]. Moreover, there is a need for the mandatory reporting of data to the EBMT Registry, an EMA requirement that will reside with the administering centre for 15 years.

Novartis – sperimentazione pediatrico, adulto fermi – parte congelato torna congelato
Celgene – sperimentazione – parte e torna fresco (NO criopreservazione)
Gilead-Kite – uso compassionevole? – parte fresco torna congelato

Controllo e allarme temperatura sui tank

Punti critici: LG, protocolli condivisi ???
Formazione
Rimborsabilità
Assicurazione?

PROGRAMMA GESTIONE CARTS MDACC: CARTOX COMMITTEE

Drs. Ethan Dmitrovsky, George Wilding, Aman Buzdar

Co-Chairs – EJ Shpall, MD and Patrick Hwu, MD

Principal Investigators

Leukemia
- William Wierda
- Nitin Jain

Lymphoma and Myeloma
- Sattva Neelapu
- Jason Westin
- Michael Wang

Stem Cell Transplantation and Cellular Therapy
- Elizabeth Shpall
- Partow Kebriaei

Gynecologic Oncology
- Amir Jazaeri

Investigational Cancer Therapeutics
- David Hong

Pediatrics
- Michael Rytting

Sarcoma Medical Oncology
- Dejka Araujo

Thoracic / Head and Neck Medical Oncology
- John Heymach
- George Blumenschein
- Vincent Lam

Consultants

Critical Care
- Cristina Gutierrez
- Joseph Nates

Emergency Medicine
- Patricia Brock
- Terry Rice

Neuro-Oncology
- Sudhakar Tummala
- Monica Loghin
- John de Groot

Nursing
- Patty Johnston
- Joaquin Buitrago
- Venice McDougle

Pharmacy
- Alison Gulbis
- Sandra Horowitz

EHR / Information Services
- Andrew Lee
- Cary Goodman

Division of Cancer Medicine
- Suzanne Davis

PROGRAMMA GESTIONE CARTS MDACC: CARTOX COMMITTEE

1) Incontri settimanali di discussione pazienti in terapia con CARTs
2) Gruppo multidisciplinare di gestione CARTs
3) Creazione di protocolli di gestione pazienti in terapia
4) Adeguata formazione del personale che utilizzerà CART (medici, infermieri, farmacisti)
5) Discussione dei trial in corso e dei risultati pubblicati

LA SOMMINISTRAZIONE DI CARTs AVVIENE SOLO IN AMBIENTI SPECIFICI DELL'OSPEDALE

PROGRAMMA GESTIONE CARTS MDACC: CARTOX COMMITTEE

- Team NEUROLOGI: valutazione status neurologico del paziente giornaliera
- Team INTENSIVISTI: valutazione condizioni cliniche giornaliera, se peggioramento rapido assiste il trasferimento del paziente in ICU
- Team FARMACISTI: si assicurano della disponibilità di farmaci salvavita per gestione CRS (tocilizumab, almeno 2 dosi per paziente secondo FDA)
- Supporto ELETTRONICO: strumenti informatici che facilitano la raccolta omogenea dei dati circa la valutazione delle tossicità delle CARTs (CRS, CRES)

PROGRAMMA GESTIONE CARTS MSKCC

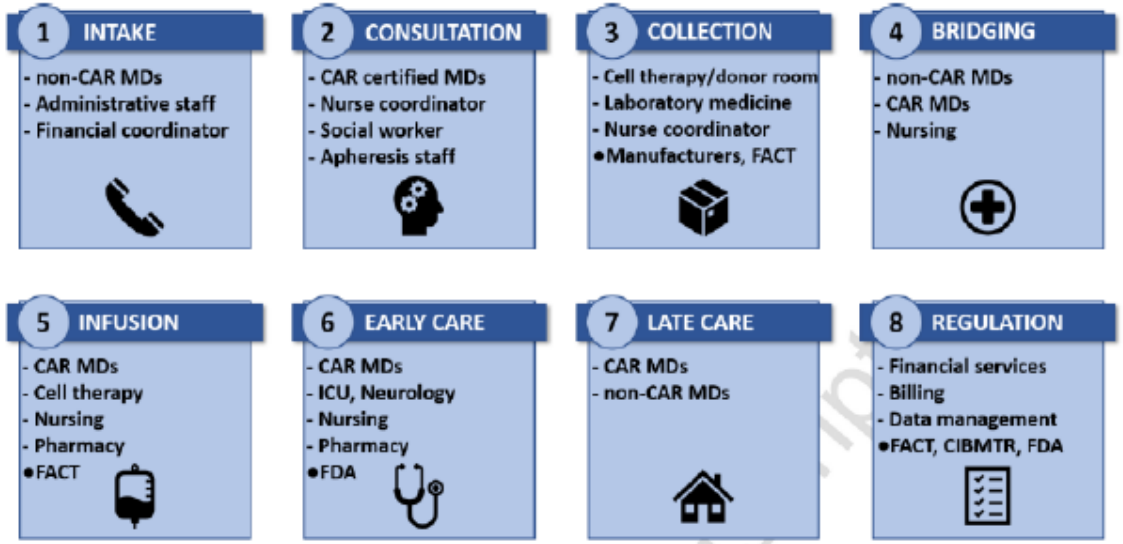

Figure 2: The eight essential steps required to establish a CAR T cell program and the personnel required to implement them. Key regulatory agencies involved in each step are denoted by a bullet.

Giralt SA, BBMT 2018

RACCOMANDAZIONI EUROPEE SU GESTIONE CARTS

Table 4

Recommended Site Capabilities and Education for Tisagenlecleucel Therapy Implementation

Site Capabilities	Education
FACT- or JACIE-accredited, transplant-capable treatment center	Medical/treatment center staff
Management of bridging chemotherapy administration and AEs	CAR-T cell therapy technology
Management of lymphodepleting chemotherapy administration and AEs	Product handling procedures for collection (leukapheresis), cryopreservation, storage, transport, receipt of finished product, thawing, and infusion
Communication with manufacturing team and courier services; adjustment of chemotherapy schedule as needed	Monitoring and management of AEs (recognizing CRS symptoms, admitting severe cases to ICU, prescribing anti-IL-6 therapy (tocilizumab) and appropriate supportive ca
Establishment of "chain of custody" or "chain of identity" process to track product for each patient[54]	
Biosafety officer	Non-medical staff education[49]
	Couriers: temperature and timing requirements for product storage and transport
	Social workers: transportation and lodging needs as dictated by treatment schedule; insurance reimbursement and other support as needed
	Patient and families: recognition and reporting of CAR-T cell therapy AEs (including CRS, neurological toxicities, and fever)

AE = adverse event, CAR-T = chimeric antigen receptor T cell, CRS = cytokine release syndrome, FACT = the Foundation for the Accreditation of Cellular Therapy, ICU = intensive care unit, IL-6 = interleuki
JACIE = Joint Accreditation Committee—International Society for Cellular Therapy (ISCT) and European Society for Blood and Marrow Transplantation (EBMT).

Buechner J, Hemasphere

OGNI PAESE HA UN ENTE REGOLATORIO DI RIFERIMENTO PER LE TERAPIE CELLULARI

Table 3

Useful Government and Society Websites

Government/Society	Website
EMA	http://www.ema.europa.eu/ema/
EMA: Advanced Therapy Medicinal Products	http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000294.jsp
EMA: Genetically Modified Organisms (Directive 2001/18/EC)	http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1407852294664&uri=CELEX:32001L0018
EMA: List of National Competent Authorities in the European Economic Area	http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/general/general_content_000155.jsp&mid=WC0b01ac0580036d63
Foundation for the Accreditation of Cellular Therapy	http://www.factwebsite.org/
Joint Accreditation Committee—International Society for Cellular Therapy (ISCT) and European Society for Blood and Marrow Transplantation (EBMT)	http://www.jacie.org/
Austrian Network for Gene Therapy	http://angt.austrianova.com/angt/
British Society of Gene Therapy	https://www.bsgct.org/
European Society of Gene and Cell Therapy	https://www.esgct.eu//Home.aspx
Finnish Gene Therapy Society	http://fsgt.fi/
French Society of Cellular and Gene Therapy	https://www.sfcg.fr/
German Gene Therapy Society	http://www.dg-gt.de/
Netherlands Society of Gene and Cell Therapy	http://www.nvgct.nl/
Spanish Society of Gene and Cell Therapy	https://www.setgyc.es/
Swedish Society for Gene and Cell Therapy	http://www.ssgct.org/

EMA = European Medicines Agency, ICH = International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use.

Buechner J, Hemasphere 2018

LA SITUAZIONE REGOLATORIA EUROPEA

REQUISITI EUROPEI

1)CARTS comprese nella categoria "Advanced Therapy Medicinal Products" (Regulation EC n°1394/2007 e direttiva 2001/18/EC)

2)CARTS considerate come OGM pertanto vanno seguite norme di protezione ambientale e del personale specifiche (Direttiva 2001/18/EC e Decisione della Commissione 2002/623/EC)

Buechner J, Hemasphere 2018

LA SITUAZIONE REGOLATORIA EUROPEA

REQUISITI NAZIONALI SPECIFICI

Country/site-specific requirements
- Manufacturing authorization according to good manufacturing practice standards (Commission Directive 2003/94/EC)
- Clinical trial authorization (Directive 2001/20/EC; to be replaced in 2019 by Clinical Trials Regulation EU No 536/2014)
- Ethics and biosafety committee approvals
- "Chain of identity" requirements
- Unique rules for product storage
- Importation and customs requirements

Buechner J, Hemasphere 2018

RIMBORSI FDA

1. KYMRIAH, Novartis (pediatric ALL) → 475.000 USD
2. YESCARTA, Gilead (adult NHL) → 373.000 USD

Nel prezzo non è compresa la spesa per gestire ricovero e possibili complicanze del paziente. In tale caso possibili anche spese aggiuntive comprese tra 100.000 USD e 300.000 USD.

(Rimborsabilità trapianto allogenico cellule staminali pari a 80.000-100.000 euro + spese aggiuntive per complicanze)

www.medscape.com accessed 08/03/2018

PROPOSTE

1. Implementazione standard di qualità per terapie cellulari (e identificazione centri di riferimento):
   - regolare EFFICIENTEMENTE la gestione dei trial (creazione di rete interospedaliera di riferimento)
   - maneggiare IN SICUREZZA le CARTS (creazione di standard di qualità terapie cellulari, vedi FACT-IEC)
   - amministrare il prodotto IN SICUREZZA (personale formato e creazione di rete intraospedaliera)
2. Creazione di un registro nazionale/europeo per raccolta dati su terapia cellulari (vedi esempio CIBMTR ed EBMT)

Ministero della Salute

DIREZIONE GENERALE DELLA PROGRAMMAZIONE SANITARIA

PROPOSTA DI DELIBERAZIONE CIPE PER IL RIPARTO DELLE RISORSE STANZIATE DALL'ART. 1 COMMA 555, DELLA LEGGE 30 DICEMBRE 2018, N. 145, E DELLE RISORSE RESIDUE DI CUI ALL'ART. 2 COMMA 69, DELLA LEGGE 23 DICEMBRE 2009, N. 191 PER LA PROSECUZIONE DEL PROGRAMMA STRAORDINARIO DI INVESTIMENTI IN SANITÀ ART. 20 DELLA LEGGE 11 MARZO 1988, N. 67, E SUCCESSIVE MODIFICAZIONI.
RICHIESTA ACQUISIZIONE INTESA DELLA CONFERENZA PERMANENTE PER I RAPPORTI TRA LO STATO, LE REGIONI E LE PROVINCE AUTONOME DI TRENTO E BOLZANO

Tabella 1

PROPOSTA DELIBERAZIONE CIPE
PROGRAMMA INVESTIMENTI ART. 20 LEGGE 67/1988

RIPARTO RISORSE LEGGE N. 145 DEL 30 DICEMBRE 2018
E RISORSE RESIDUE LEGGE N. 191 DEL 23 DICEMBRE 2009

Regioni	Quota d'accesso del FSN 2018 al netto delle P.A Trento e Bolzano	Importo
Piemonte	7,53%	301.337.883,29
Valle D'Aosta	0,21%	8.592.551,11
Lombardia	16,82%	672.620.506,12
P.A. Bolzano*	0,00%	-
P.A. Trento*	0,00%	-
Veneto	8,25%	330.156.845,63
F. Venezia Giulia**	2,10%	83.973.045,98
Liguria	2,75%	110.097.081,15
E. Romagna	7,56%	302.427.964,22
Toscana	6,42%	256.783.807,67
Umbria	1,52%	60.912.866,50
Marche	2,62%	104.901.558,52
Lazio	9,84%	393.504.872,64
Abruzzo	2,24%	89.553.634,33
Molise	0,53%	21.141.681,58
Campania	9,47%	378.951.360,64
Puglia	6,76%	270.259.132,05
Basilicata	0,96%	38.366.547,61
Calabria	3,26%	130.455.585,90
Sicilia	8,36%	334.231.428,94
Sardegna	2,79%	111.731.646,15
TOTALE	**100,00%**	**4.000.000.000,00**
TOTALE QUOTA RISERVATA, DA RIPARTIRE CON SUCCESSIVI PROVVEDIMENTI, PER: - Realizzazione n. 6 Centri di eccellenza per sviluppare una rete nazionale in grado di effettuare attività di ricerca, produzione e trattamento del paziente affetto da patologie tumorali eleggibili alla terapia genica CAR T- Cell - € 60.000.000,00; - Riserva per interventi urgenti - € 635.000.000,00. ***		**695.000.000,00**
TOTALE GENERALE		**4.695.000.000,00**

* le risorse non vengono ripartite in applicazione delle disposizioni di cui all'articolo 2, comma 109, della legge 23 dicembre 2009, n. 191

** L'importo comprende 80 milioni di euro oggetto di accordo fra il Governo e la Regione sottoscritto a febbraio 2019

*** Importo comprensivo dell'autorizzazione di spesa di 82,164 mln di euro prevista dal decreto-legge recante misure emergenziali per il Servizio sanitario della Regione Calabria

Il Parlamento ha già stanziato 5 milioni di euro per il 2019 per un progetto di ricerca relativo alle Car-T, e altri 5 milioni sono stati stanziati per la medesima finalità dalla legge 17 dicembre 2018, n. 136.
La Camera dei Deputati, con l'Ordine del giorno del 30 dicembre scorso, ha delineato il complessivo percorso attuativo, impegnando il Governo ad assumere una serie di iniziative. Lo stesso ordine del giorno indicava come componenti del gruppo per la definizione del progetto di fattibilità rappresentanti dell'Ospedale S. Gerardo-Fondazione Tettamanti di Monza, della società Molmed e dell'Istituto di Biostrutture e Bioimmagini del CNR di Napoli, nonché gli IRCCS della Rete oncologica ed anche l'Ospedale pediatrico bambino Gesù di Roma e l'Ospedale San Raffaele di Milano.