

EC – Open Info Day

Regenerative Medicine and Advanced Therapies

ATMP Experiences from The ONE Study

Edward Geissler

Experimental Surgery

University Hospital Regensburg

University of Regensburg



Kidney Transplantation – The Problem

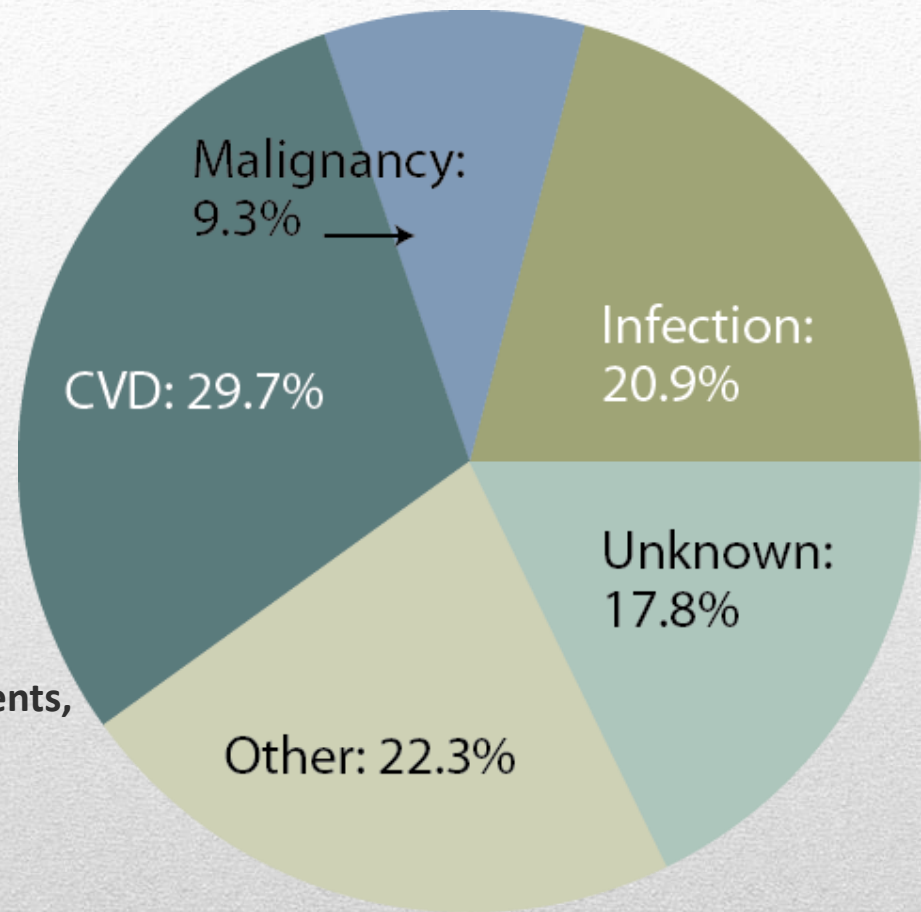


Current Graft Survival:
10 year (RTx) survival 47-61%

USRDS 2011

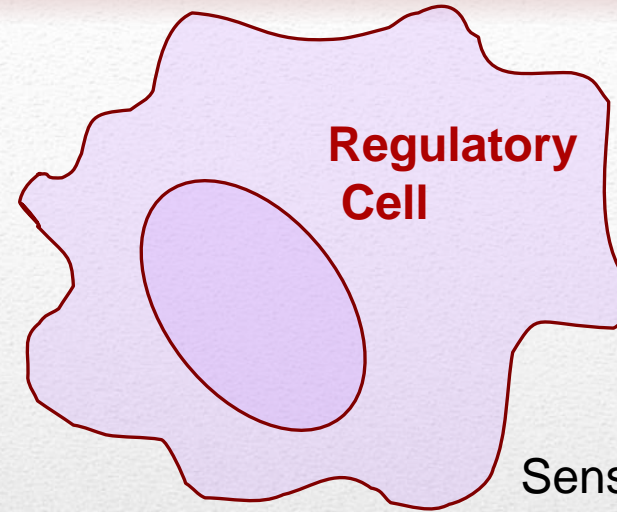
UNITED STATES RENAL DATA SYSTEM

First-time, kidney-only transplant recipients,
age 18+, 2005–2009, who died with
functioning graft.



⇒ Reduce use of pharmacological immunosuppression

Why Cell Therapy?



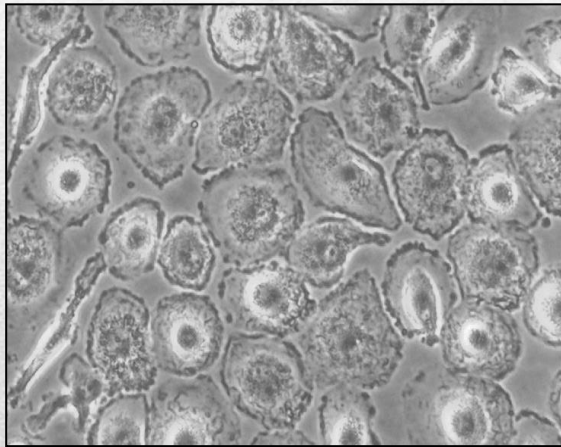
Sense signals

Integrate input

Execute complex
responses

Can turn off

Advanced-Therapy Medicinal Products (ATMPs)



M reg

- Natural T regulatory cells (Tregs)
- Donor-specific Tregs
- Tr1 cells (donor-specific)
- Tolerogenic dendritic cells
- Suppressive macrophages (M regs)
- Mesenchymal Stem Cells (MSCs)

EU Thematic Priority: Health.2010.1.4-1, *Translational research on cell-based immunotherapy*

An EU funded project called - *The ONE Study*

„A Unified Approach to Evaluating Cellular Immunotherapy
in Solid Organ Transplantation“



www.onestudy.org

The ONE Study Consortium



- UCSF, San Francisco, CA, USA
- MGH, Boston, MA, USA

SAN FRANCISCO

BOSTON

- UKR, Regensburg, GER
- Charité, Berlin, GER
- Churchill Hospital, Oxford, UK
- Guy's Hospital, London, UK
- CHU, Nantes, FRA
- HSR, Milan, ITA

OXFORD

LONDON

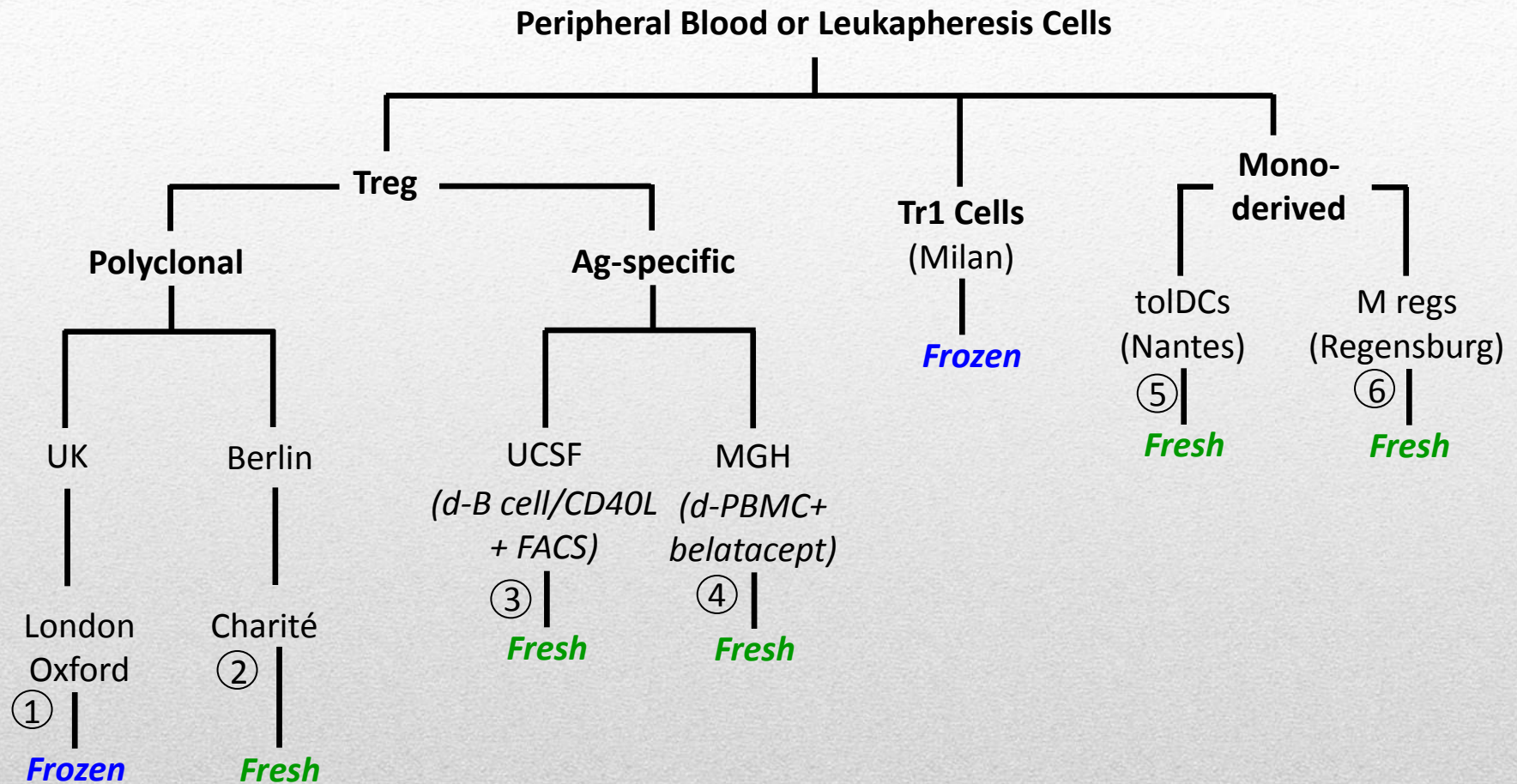
BERLIN

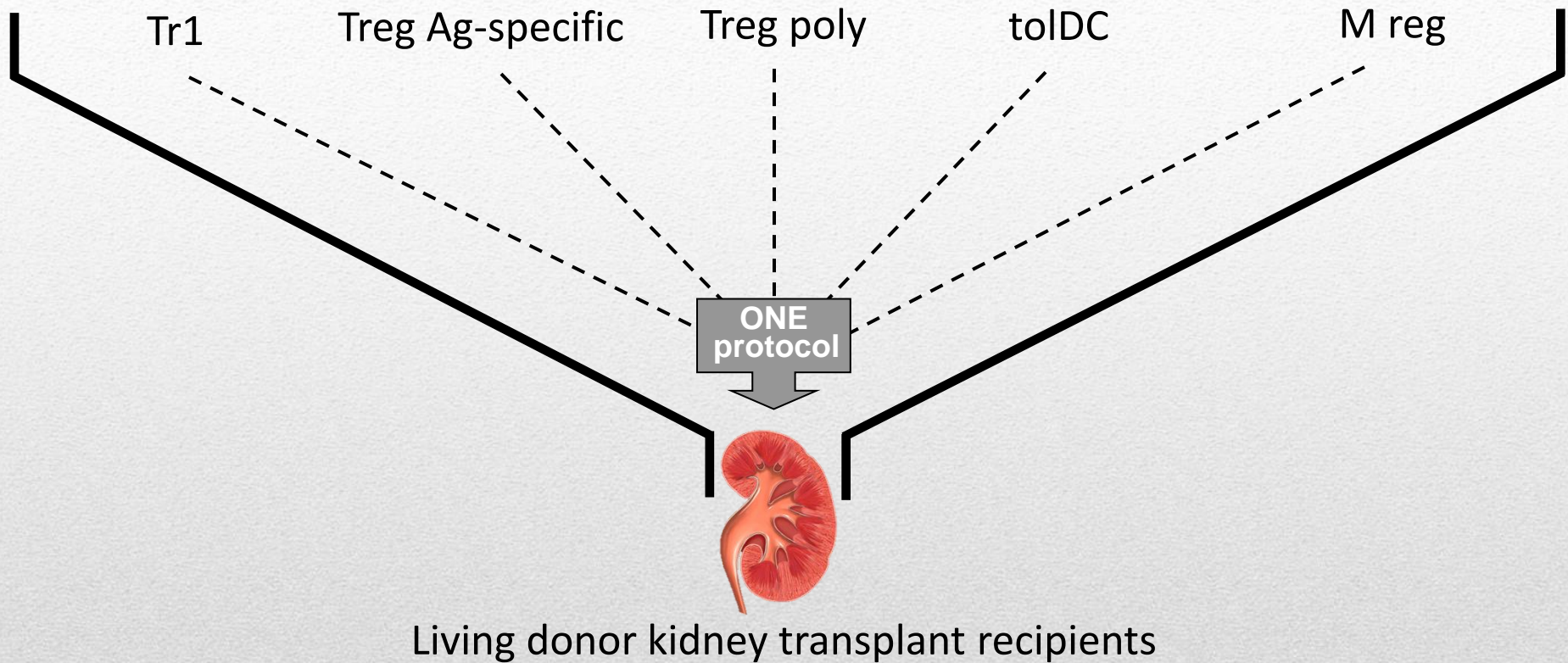
NANTES

MILAN

REGENSBURG

Miltenyi Biotec
ESI
Beckman Coulter
Köhler Eclinical GmbH



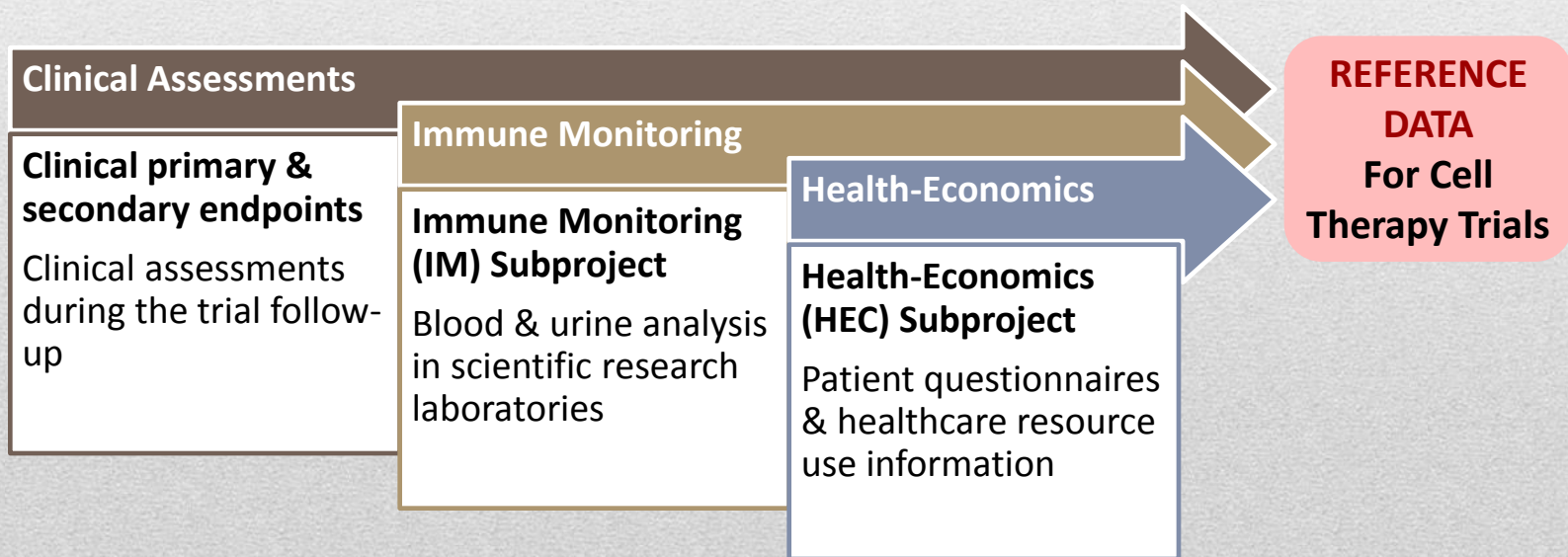


» All cells tested using the same clinical trial design/**immune monitoring program**

AIM

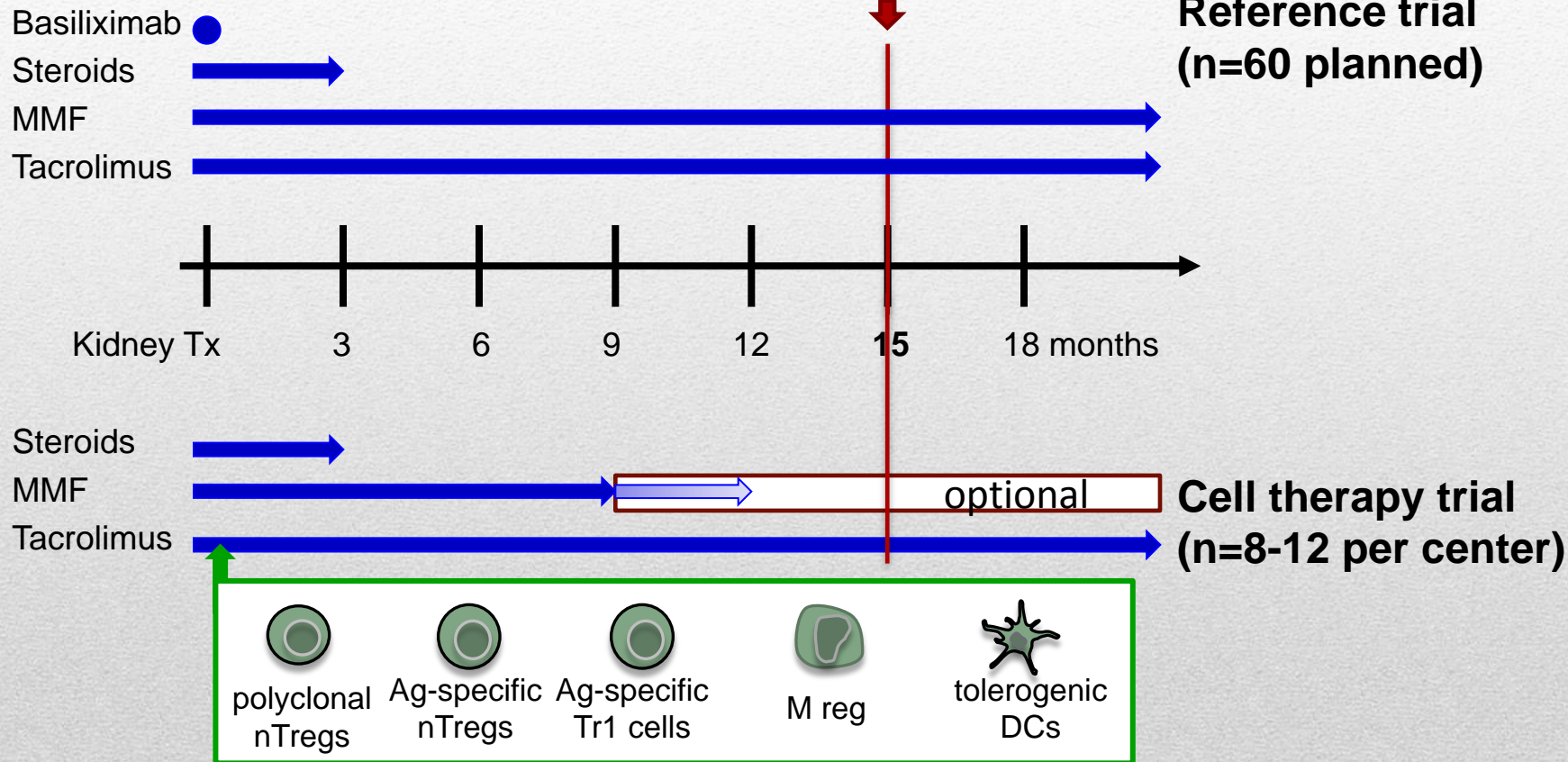
Reference Group Trial → Reference data for *The ONE Study* Cell Therapy Trials

- 60 Living-donor kidney transplant patients treated with a standard immunosuppressive regimen
- Expected acute rejection rate = approx. 10% (2.4% - 17.6%)



„Primary Endpoint“ (biopsy proven rejection)

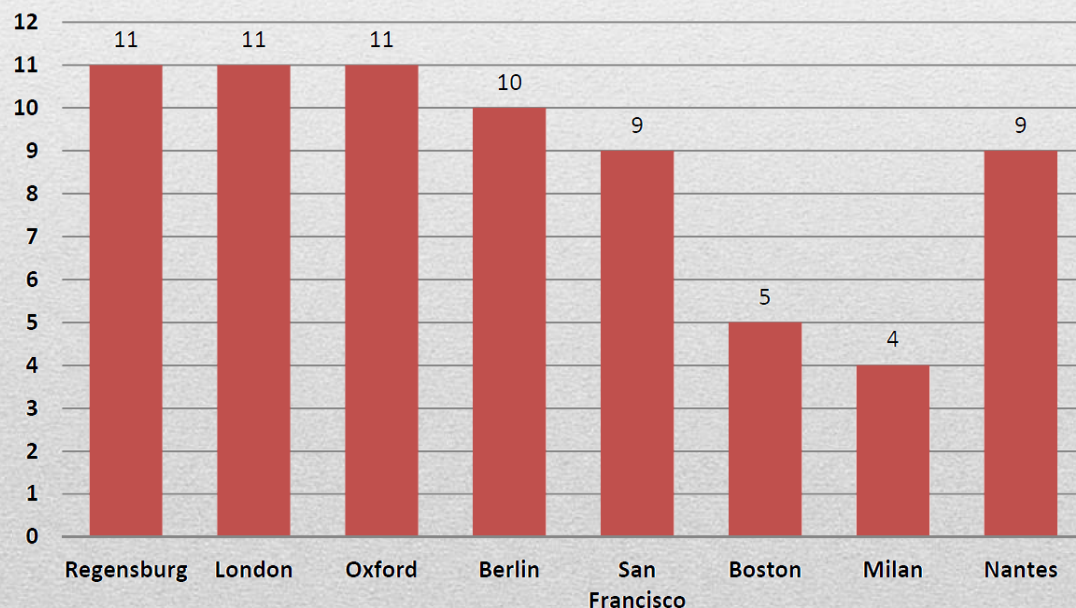
Observation Period



Reference Group Trial Update

- ▶ enrollment of 70 patients complete; all patients in for >12 months
- ▶ Immune monitoring program operational at all sites
- ▶ number of informative patients = 61 (planned 60)

ONErGt11: Number of Patients Enrolled



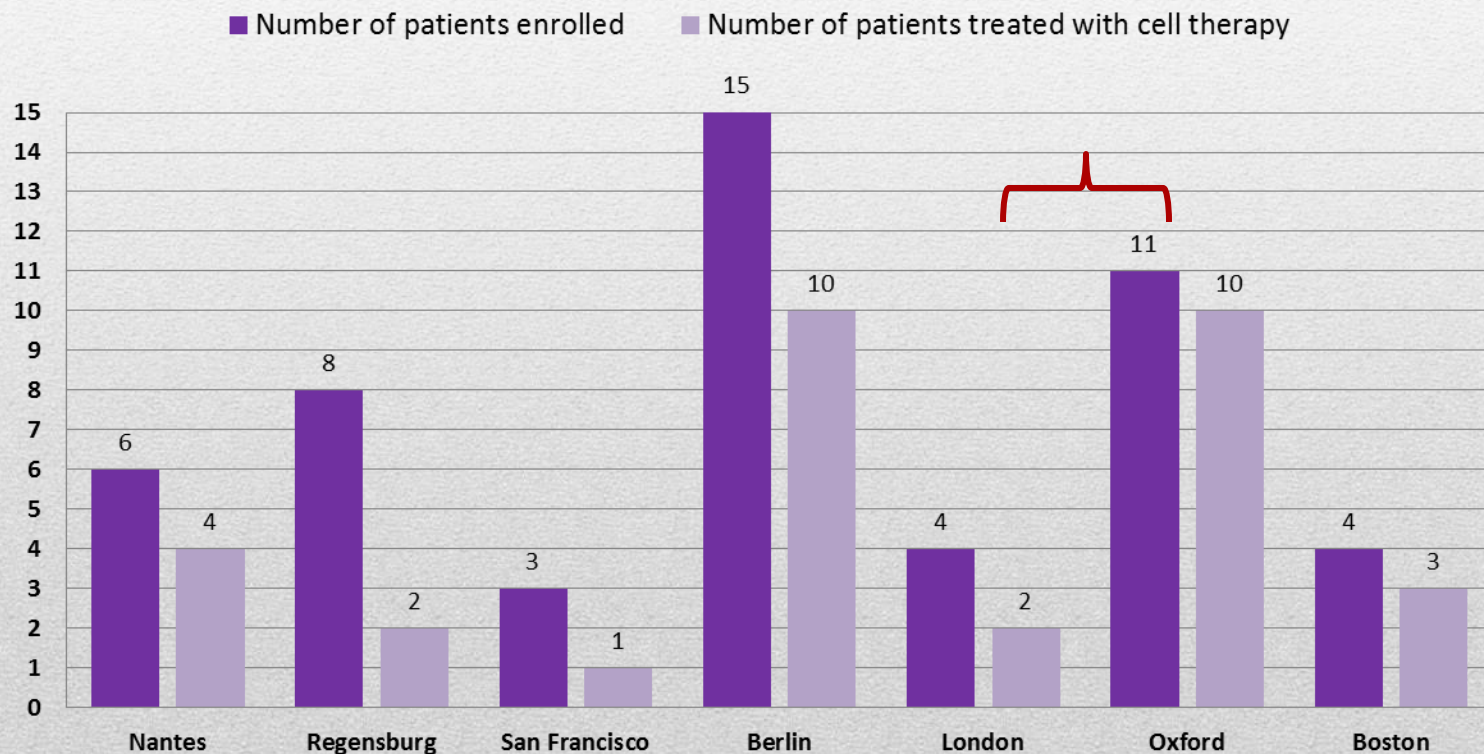
Primary endpoint (BPAR):

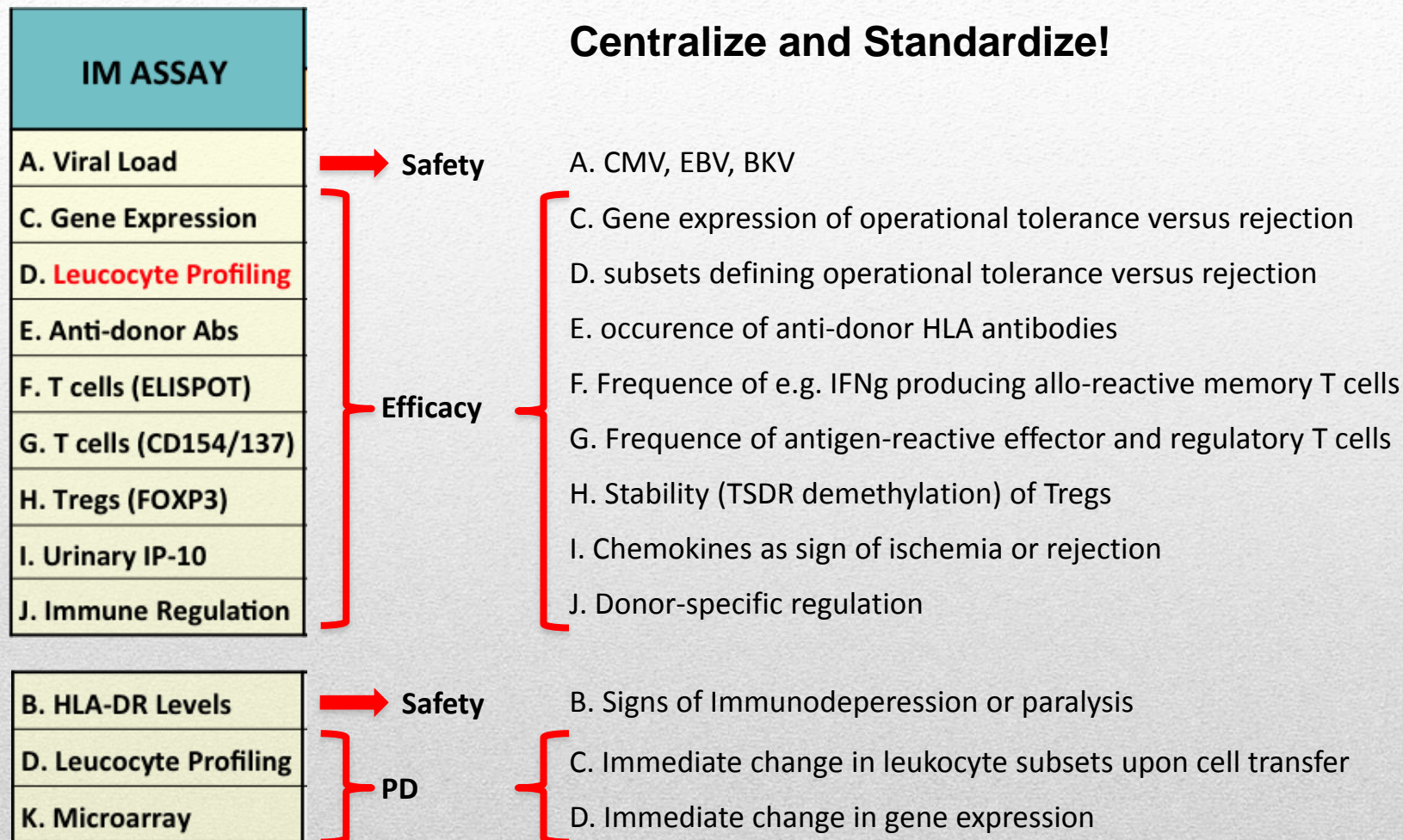
» 9 patients with BPAR (14.8%)

Patient Recruitment & Treatment Status:

51 patients enrolled

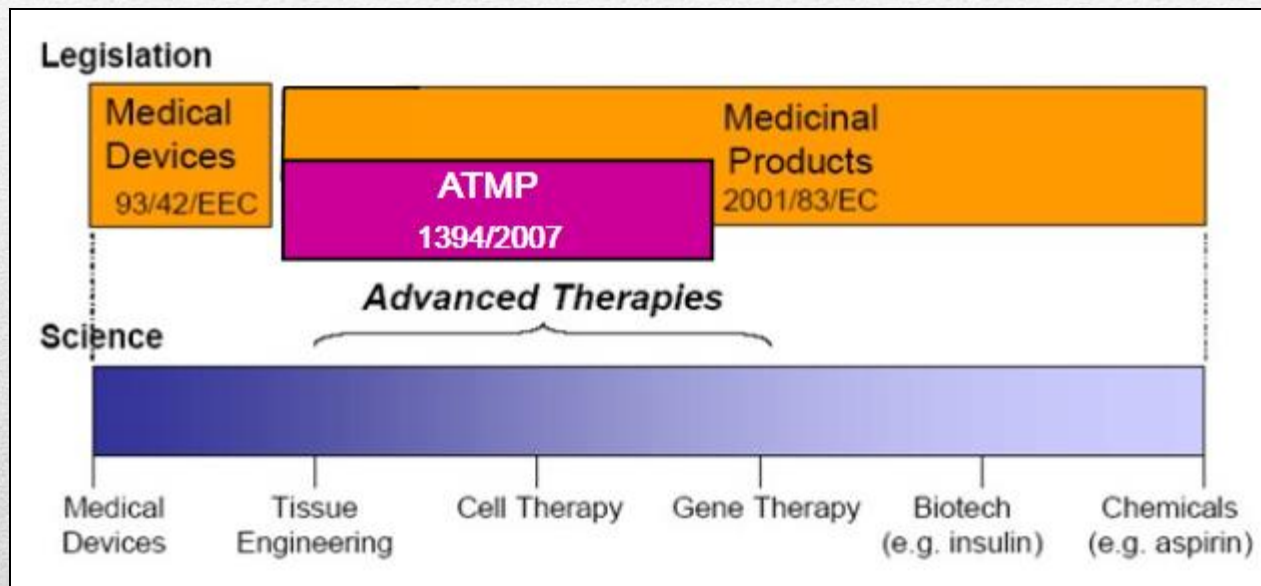
32 patients treated (confirmed)



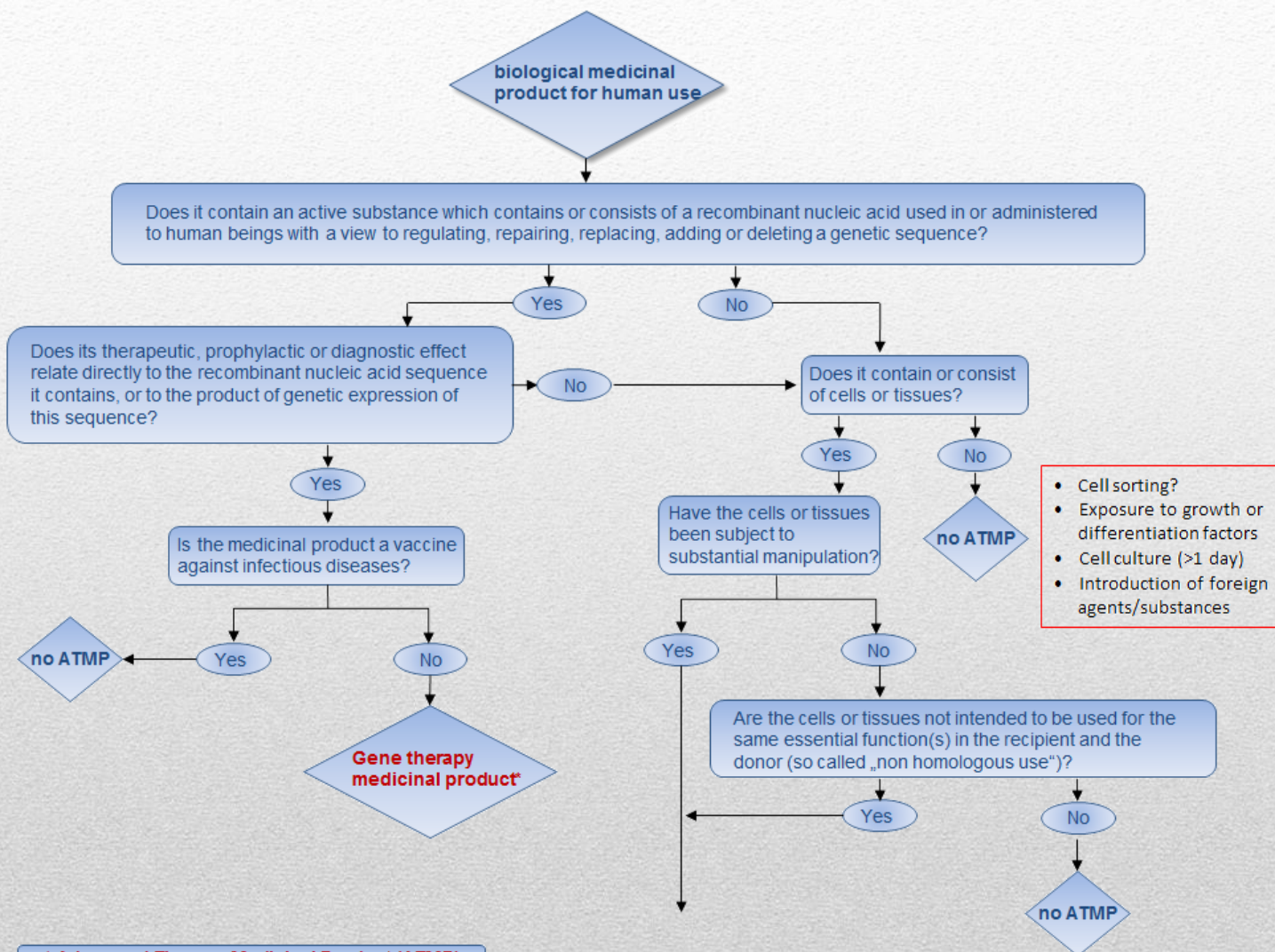




Do you have an ATMP?

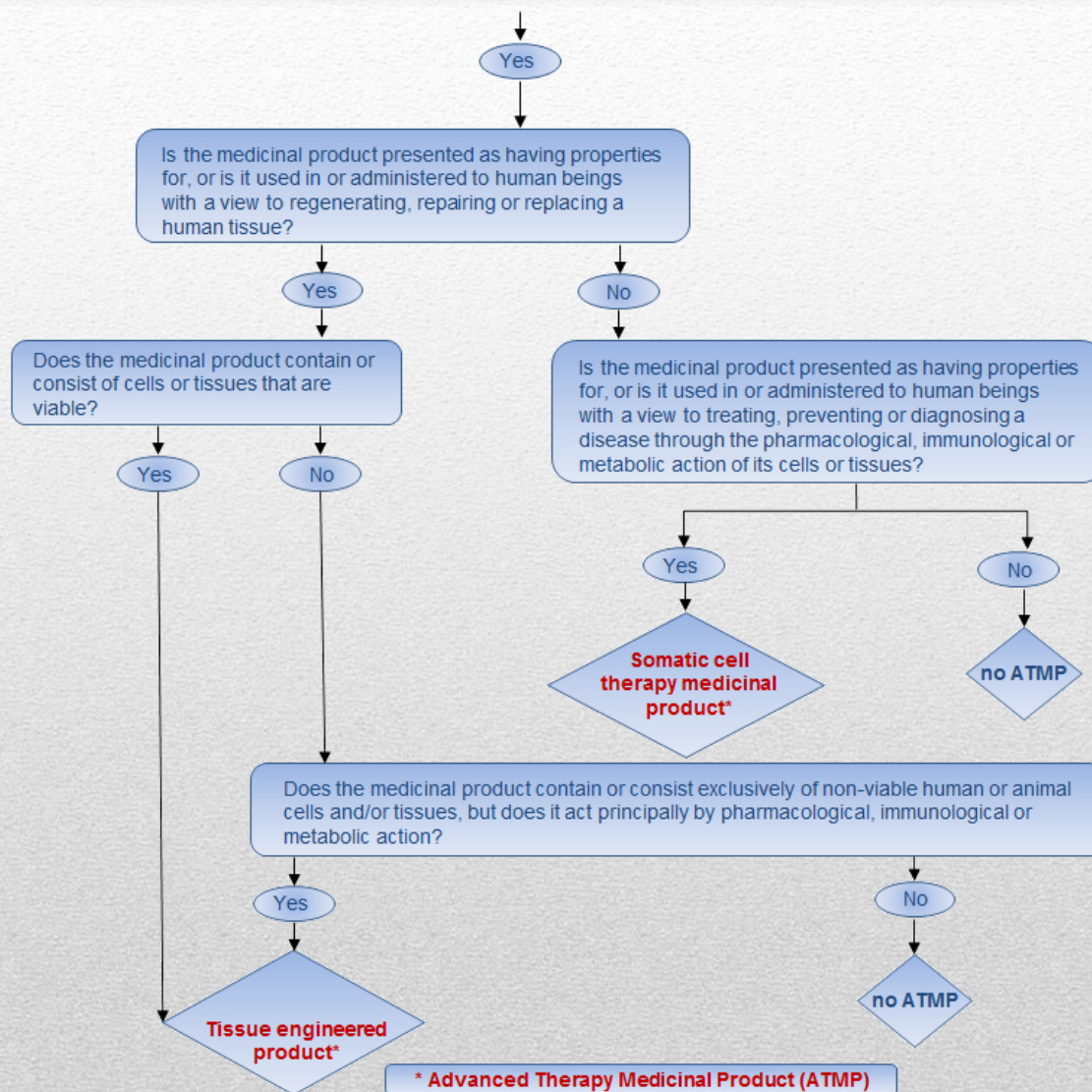


ONE Study Lessons – Do you have an ATMP?



- Cell sorting?
- Exposure to growth or differentiation factors
- Cell culture (>1 day)
- Introduction of foreign agents/substances

ONE Study Lessons – Do you have an ATMP?



Getting ATMP approvals by your Regulatory Authority:

- ⇒ Get good advice from experts – choose wisely
- ⇒ Bring strong arguments for your choices on manufacturing and protocol design
- ⇒ Go to the authorities early, but not too early for advice
- ⇒ Don't re-invent the wheel; share methods within your consortium
- ⇒ Share IMPDs/INDs amongst your consortium
- ⇒ Have one person lead the regulatory effort!!!
- ⇒ Remember that regulations are different between countries



Manufacturing considerations:

- ⇒ Find a GMP facility with a vested interest
- ⇒ Keep the manufacturing procedure as simple as possible
- ⇒ Set simple and limited product release criteria
- ⇒ ATMP stability is a critical issue
- ⇒ Eliminate serum use if possible
- ⇒ Keep clinical trial protocol flexible regarding ATMP delivery timing

Patient recruitment considerations:

- ⇒ Develop a brochure for patients
- ⇒ Minimize exclusion criteria
- ⇒ Only partner with a motivated, responsible, clinician
- ⇒ If possible, use more than one recruitment site
- ⇒ Go step-wise; use a multi-step or dose-escalation design

Other General Advice:

- ⇒ Pick your partners wisely; pick the best and keep them connected
- ⇒ Be creative in your trial design
- ⇒ Do a control group!!!
- ⇒ Do things right; don't skip steps in ATMP development!!!
- ⇒ Think ahead towards commercialization (avoid ***Valley of Death***)
- ⇒ Set serious milestones to make a „friendly“ competition
- ⇒ AND most of all.....

There are no shortcuts to any place worth going.....
Beverly Sills

*Success is the ability to go from one failure to
another without loss of enthusiasm.....*

Winston Churchill

The ONE Study Group

