

The parallel journeys from Academia to Company and from ITF to Scientific Advice

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EUROPEAN MEDICINES AGENCY
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Conflict of interest and support

- This lecture presents IP owned by Med. Univ. Gdańsk
- PT is CEO and stakeholder of POLTREG S.A.
- Poltreg S.A. is the exclusive licensee of IP owned by Med. Univ. Gdańsk



STRATEGMED1/233368/1/NCBR/2014



LIDER/160/L-6/NCBR/2015



POIR.01.01.01-00-0769/15-01



H2020-EIC-SMEInst-2018-2020-2



Action to Focus and Accelerate Cell-based Tolerance-inducing Therapies (A FACTT)

From Academia to Company

Beginning of work at the **Medical University of Gdańsk (GUM)** on the use of T-regulatory lymphocytes (TREG) in the treatment of type 1 diabetes (DM1)

Co-financing from NCBiR (€1.5M) to increase the efficiency of the TREG multiplication process, and development of a strategy to enter the US market (GO_GLOBAL)

Horizon 2020 grant for the preparation of pivotal trial and registration granted by European Commission

GUMed gained support from the research and development program - STRATEGMED, which covered the costs of treatment of 34 patients with DM1 and 12 patients with multiple sclerosis

Grant from the EU SME Instrument Phase 2 program (€2.5M)

Phase I trial in RRMS closed and reported

Phase I trial in DM1 closed and reported



2004

2013

2014

2015

2016

2017

2018

2019

2020

2021

Grant of Polish patent for the use of the TREG method in DM1 (2014) and submission of applications in EU (2013) and USA (2014)

PoITREG established as a spin-off from the Medical University of Gdańsk (MUG)

Exclusive license from GUM for use of TREG method in DM1.

EMP granted by the EMA to the status of ATMP and the resulting Hospital Exemption procedure

Commencement of HE therapies at GUM

Filing of Pediatric investigation plan (in coop. with Parexel)

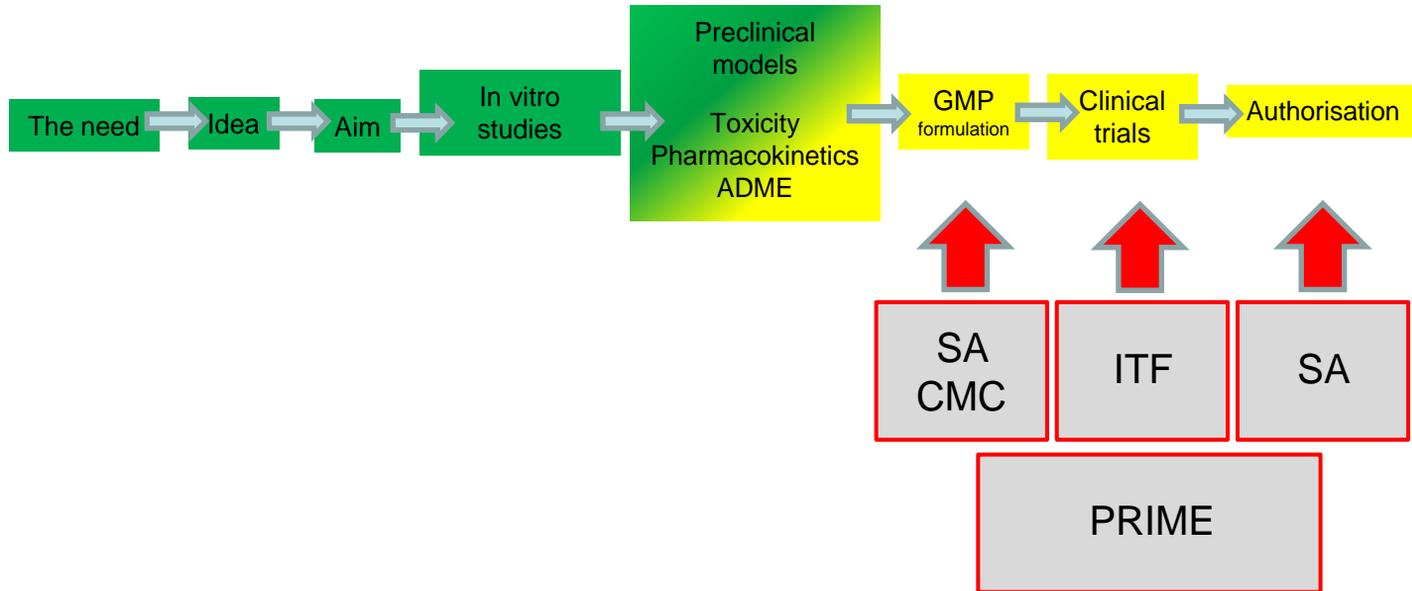
Scientific Advice EMA on further studies in DM1 received

IPO – 100mIn PLN for future development

Pipeline with clinical-stage Tregs projects

Therapeutic area	Indication	Research	Preclinical	Phase I	Phase II	Phase III	Regulatory	Next expected milestones
Type 1 Diabetes	Newly diagnosed patients (Stage 3 T1D)	PTG-007+ / rituximab CD3+CD4+CD25+CD127-FoxP3+ Tregs						Marketing authorisation
	Presymptomatic patients (Stage 2 T1D)	PTG-007 CD3+CD4+CD25+CD127-FoxP3+Tregs						Registration of the trial and regulatory steps H2'2022
Multiple Sclerosis	Relapsing-remitting	PTG-007+ / tecfidera CD3+CD4+CD25+CD127-FoxP3+Tregs						Clinical trial protocol Phase II Q3'2022
	Primary progressive	PTG-007 CD3+CD4+CD25+CD127-FoxP3+Tregs						Clinical trial protocol Phase II Q3'2022
Autoimmunity	Autoimmune diseases (T1D, MS, RA, transplantology, allergology, etc)	PTG-020 (Tregs 2.0) Antigen Specific Tregs						Validation of the product under GMP conditions, preclinical tests
		CAR-Tregs Genetically modified						

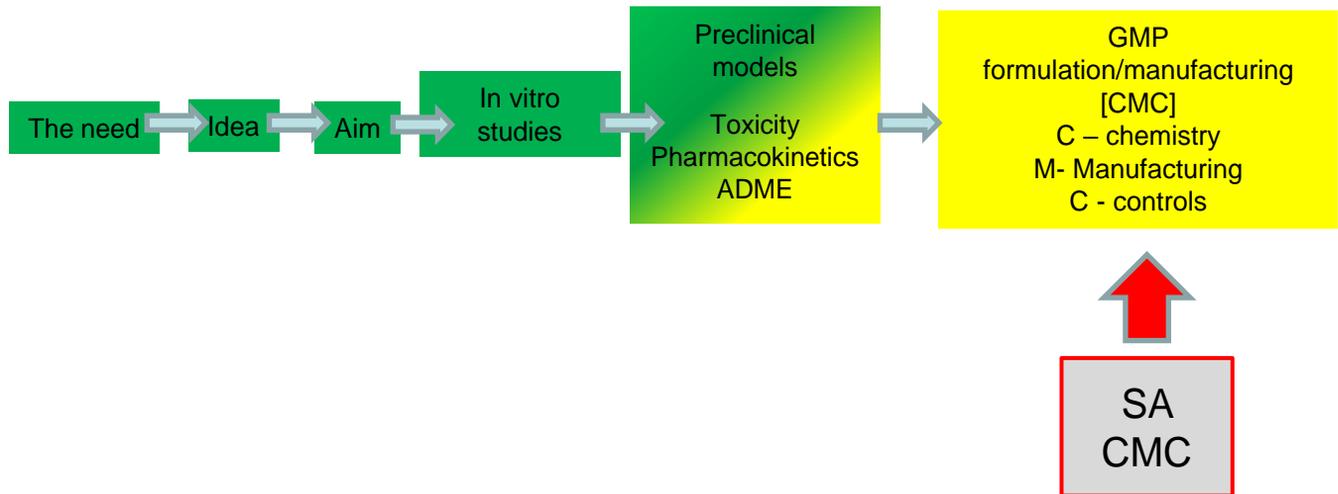
Natural history of a drug



Creating GMP formulation of the drug requires funds. Manufacturing can be 10-100 times more costly than the research-use version

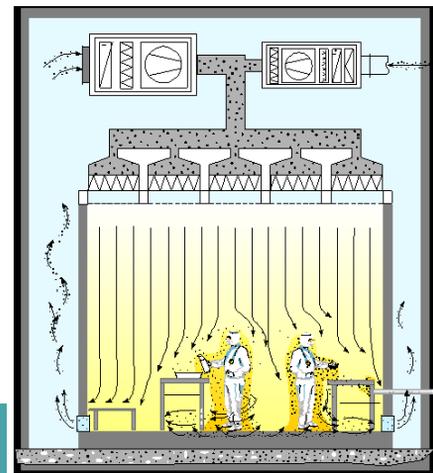
Manufacturing plant requires even more funds

There is no second chance, so it is better to ask before



Poltreg's Pharma Plant

- cGMP Lab – certified manufacturing and product
- Validated conditions



4.000 m²

And **2.100 m²** of lab space

15 automatic manufacturing lines

10 mIn Euro

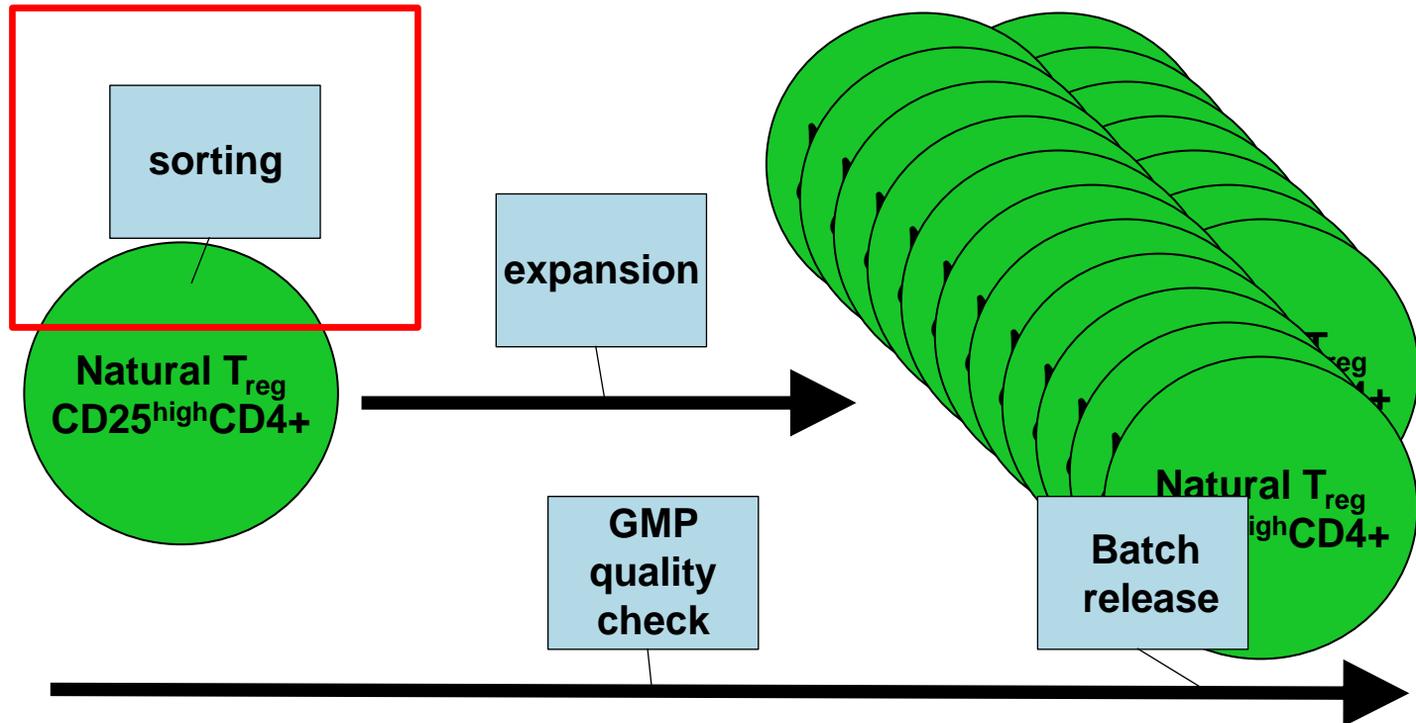


Which standard?

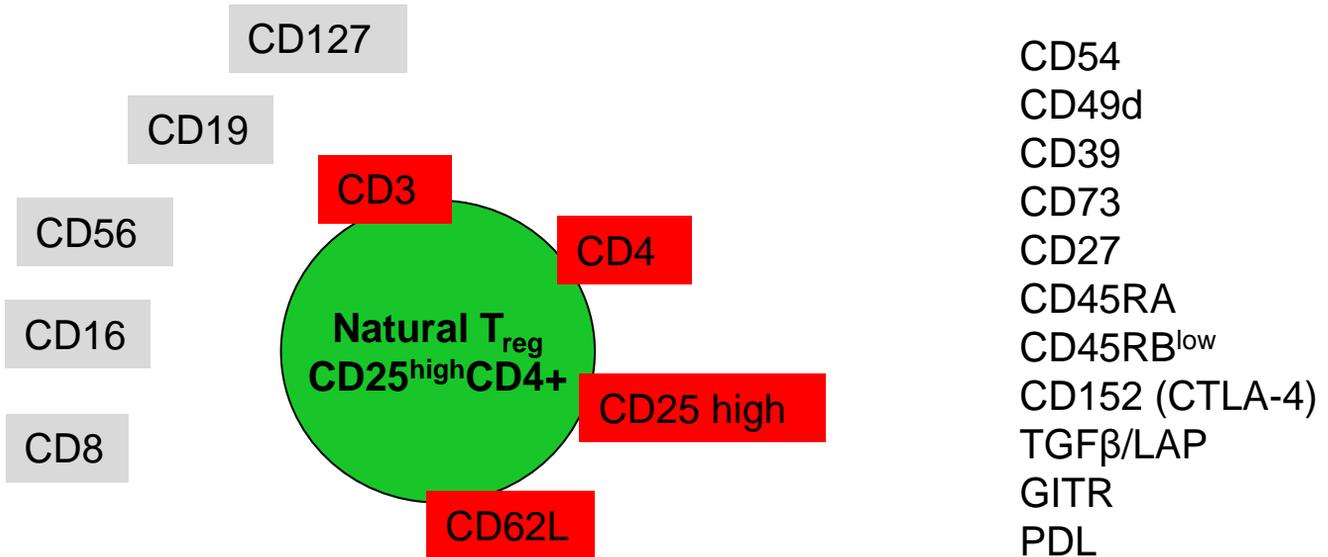
What is necessary?



ATMP- grade product with laboratory tools?



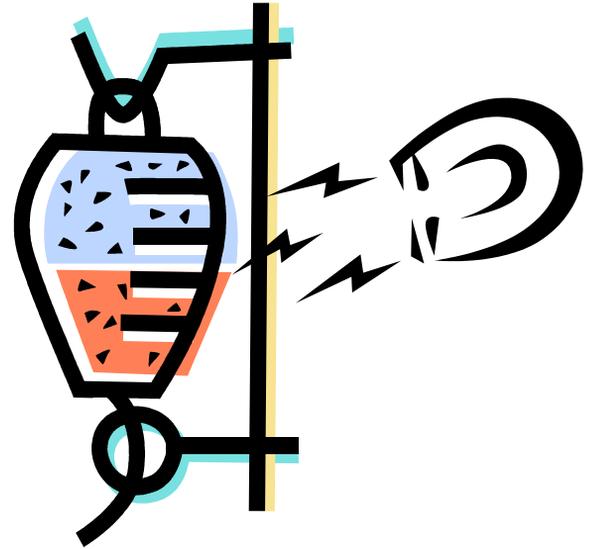
ATMP- grade product with laboratory tools?



The best found phenotype:

CD3⁺ CD4⁺ CD25^{high} CD127⁻ Lin⁻ doublet⁻

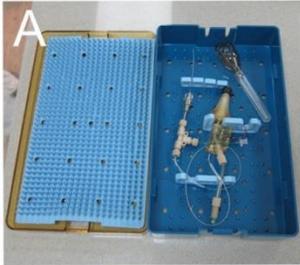
ATMP- grade product with laboratory tools?



Single-use bags

Trzonkowski P *et al.* Cytometry A 2009

FACS sorter or immunomagnetic sorting?



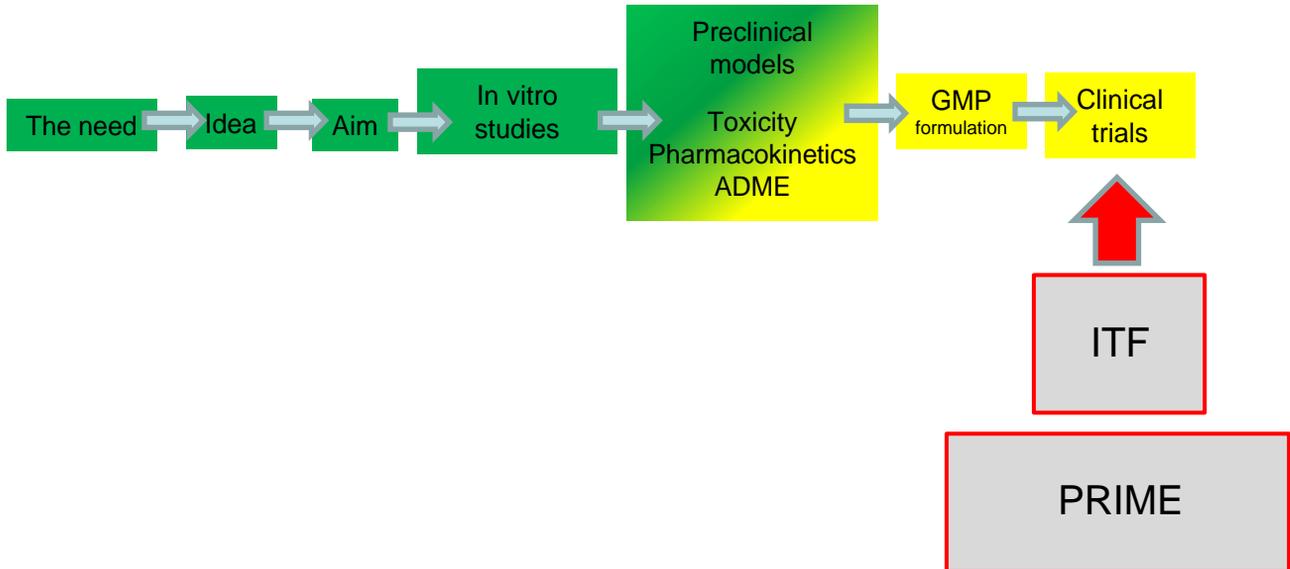
**Single-use
lines**

**HEPA
enclosure**

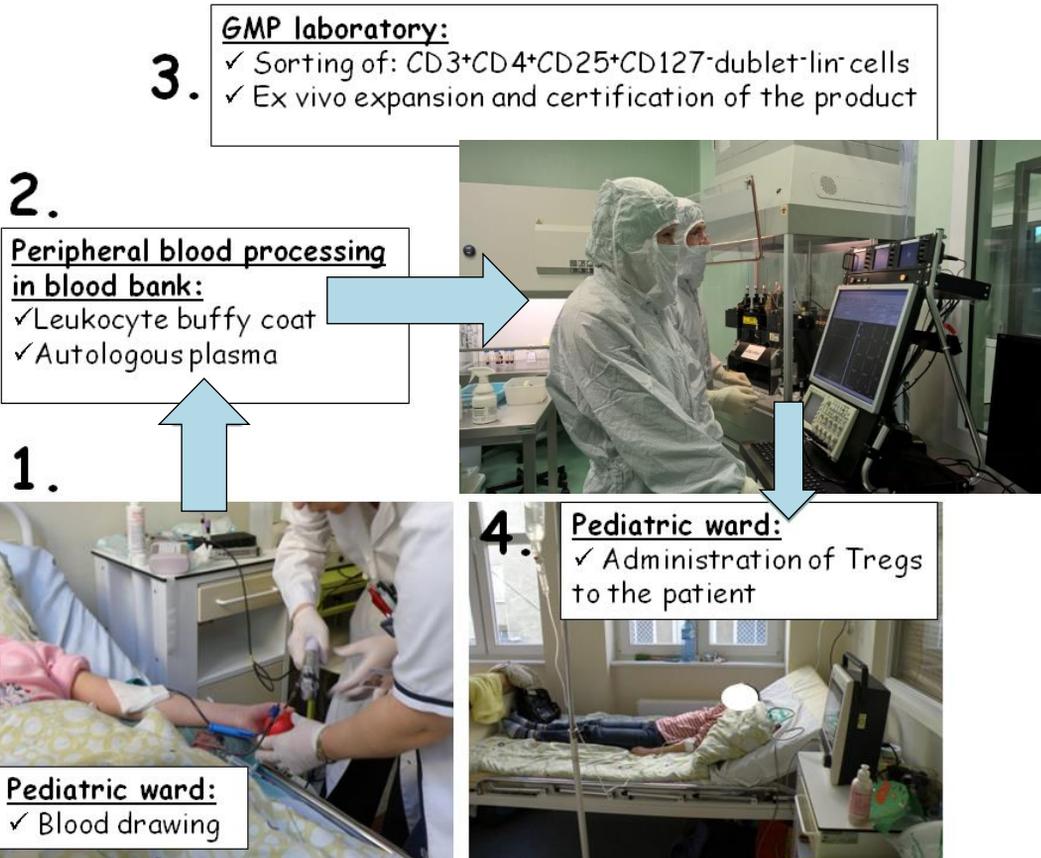


Clinical trials are long

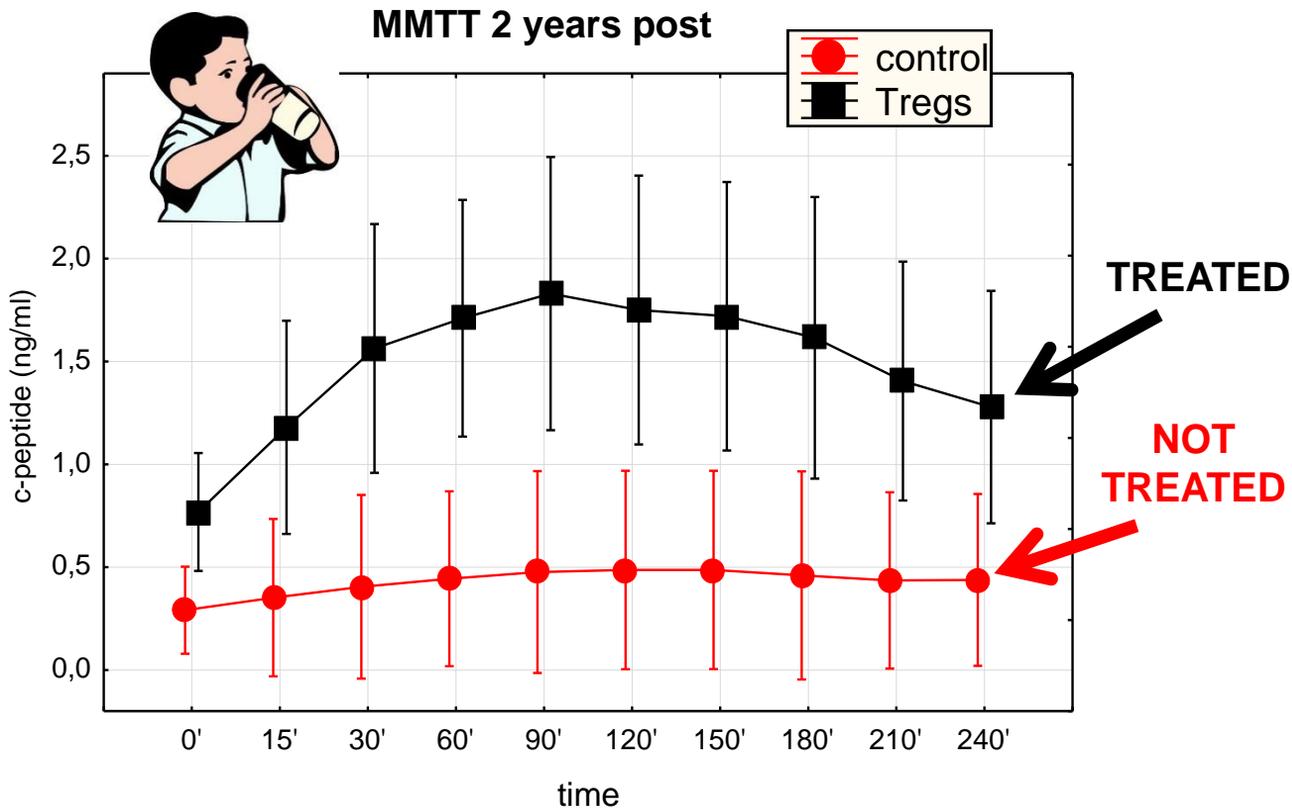
→ It is good to know where to go....Is it worth going there?



TregVac 1.0



TregVAC1.0 - Safe and efficacious



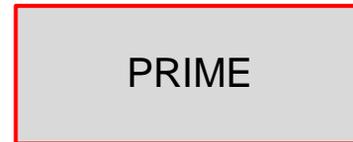
Marek-Trzonkowska P *et al.* J Transl Med. 2016

Two years follow-up?

- Too short
- Too few patients

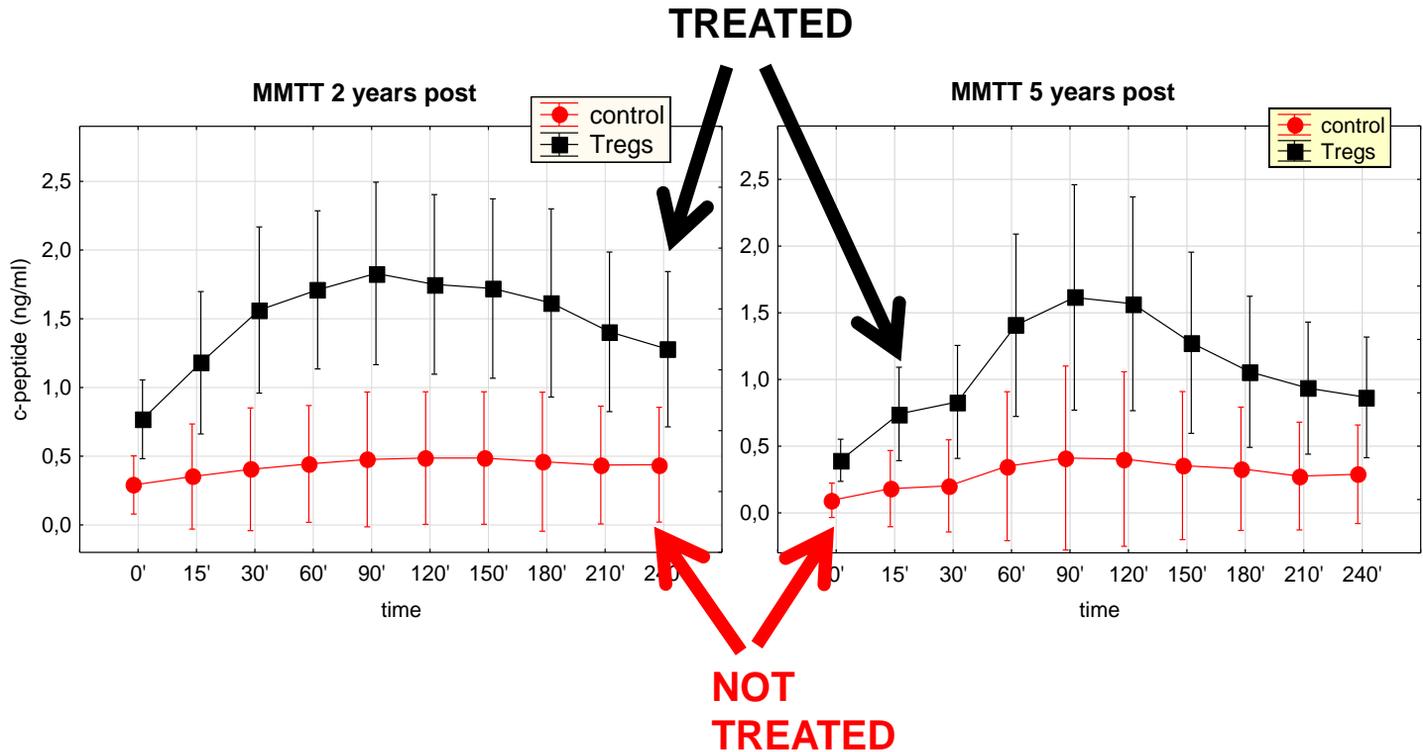
A gray rectangular box with a red border containing the text "ITF".

ITF

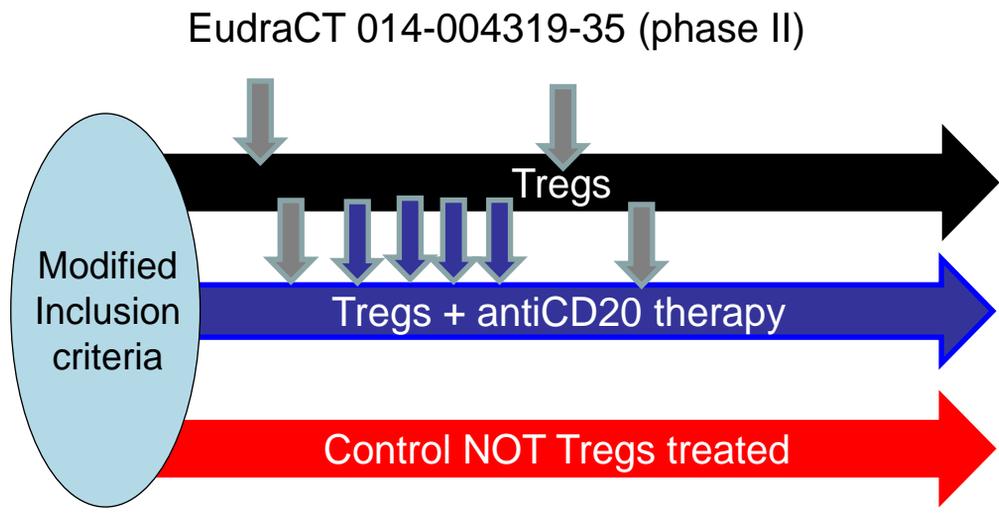
A gray rectangular box with a red border containing the text "PRIME".

PRIME

Results – long-term efficacy

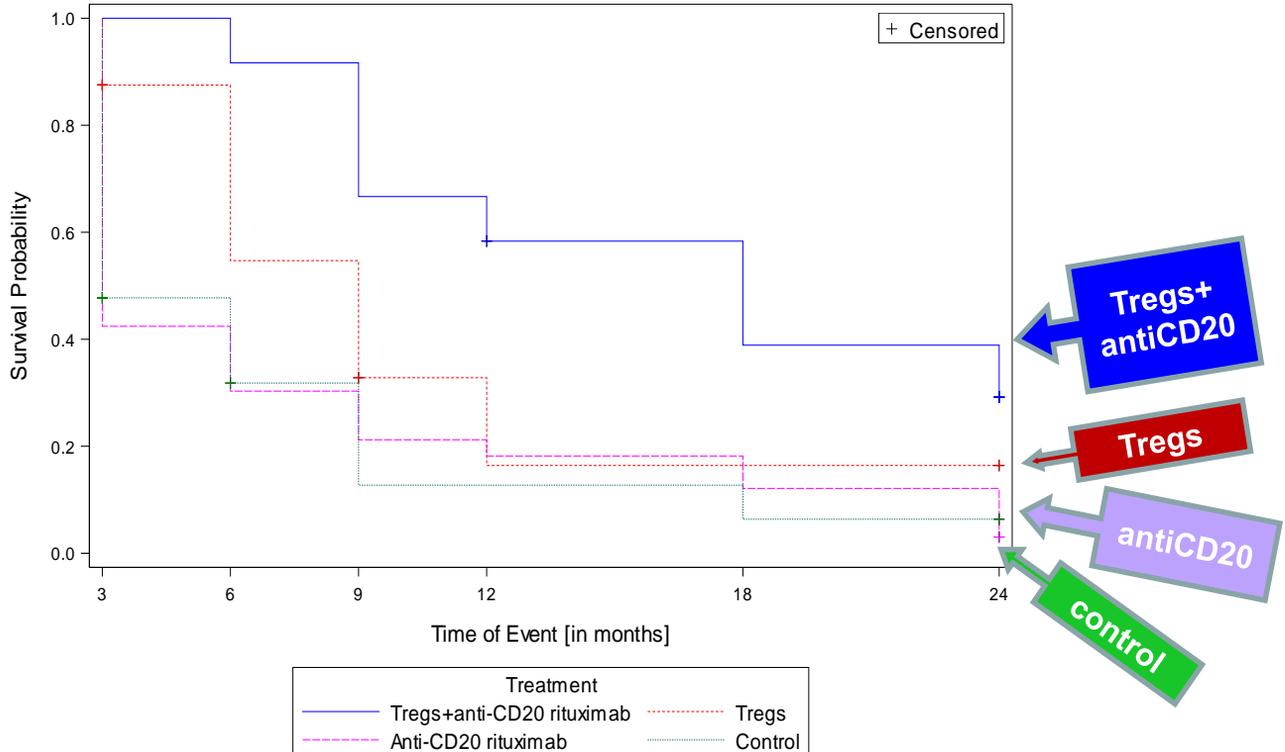


TregVac 2.0



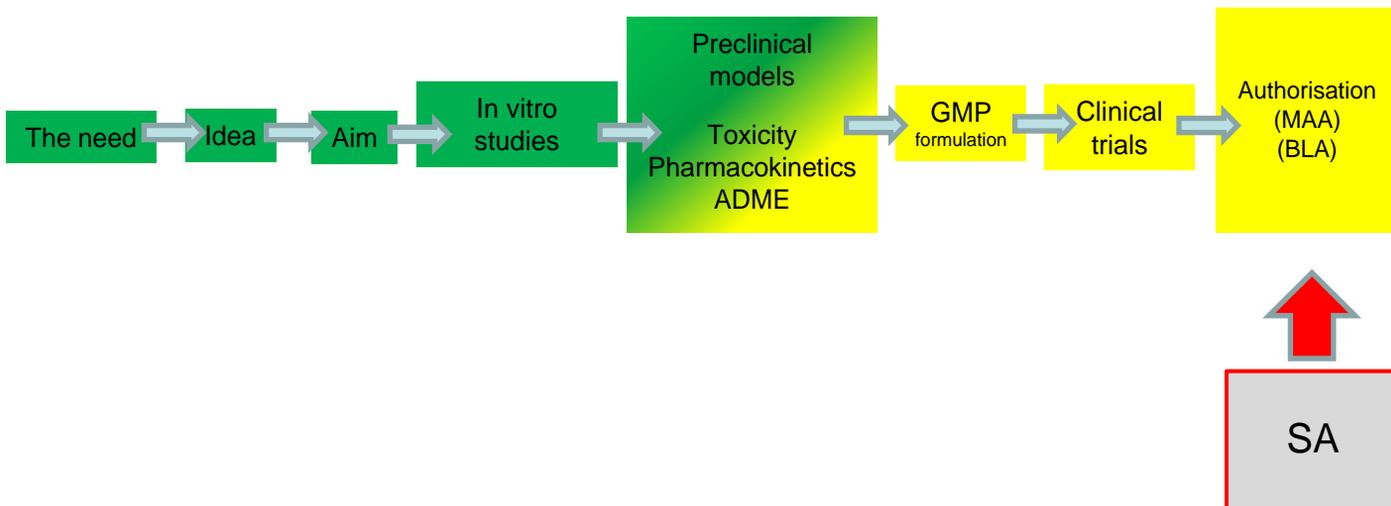
Remission

Kaplan-Meier Plot of First Loss of Remission

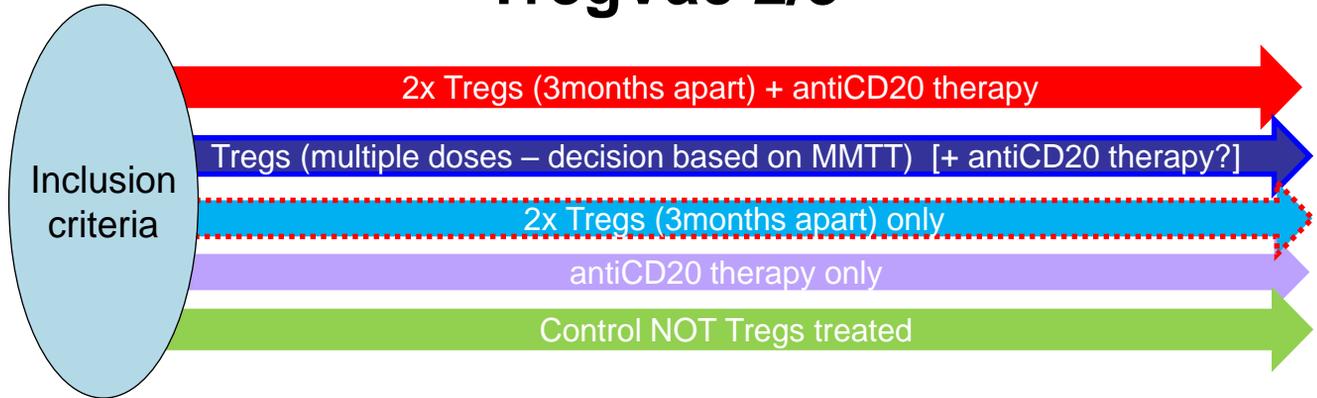


Zielinski *et al.* DOM 2022

- Is my drug safe for my patients?
- Is my drug efficacious?
- Will my patients buy my drug (health technology assessment)?



TregVac 2/3



- **Inclusion criteria** allows including only the patients in a very early phase of type 1 diabetes, mainly: **fasting c-peptide above 0.8ng/ml** and at least **100% increase** in c-peptide levels after the challenge **in MMTT**
- **Five arms:**
 - **ARM 1** – two doses of TREGS 3 months apart (2 x 30x10⁶ Tregs per kg b.w.) and four doses of anti-CD20 (rituximab) in between (375 mg/m² at days: +14, +22, +29 and +36)
 - **ARM 2** – multiple doses of TREGS (30x10⁶ Tregs per kg b.w. per dose) – decision based on MMTT (?) and four doses of anti-CD20 (rituximab) in between (375 mg/m² at days: +14, +22, +29 and +36) – add antiCD20?
 - **ARM 3a** – two doses of TREGS 3 months apart (2 x 30x10⁶ Tregs per kg b.w.)
 - **ARM 3b** – four doses of anti-CD20 (rituximab) (375 mg/m² at days: +14, +22, +29 and +36)
 - **ARM 4** – control group treated with insulin only

5
years
follow
up

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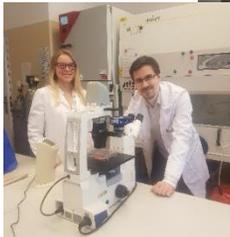
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Thank you - Dziękuję

