Nephrology Disease Cooperation between Canada and Germany for Applied AI (NephroCAGE)

Marcel G. Naik

20th May 2021

WP 6 & 7

Kickoff Event

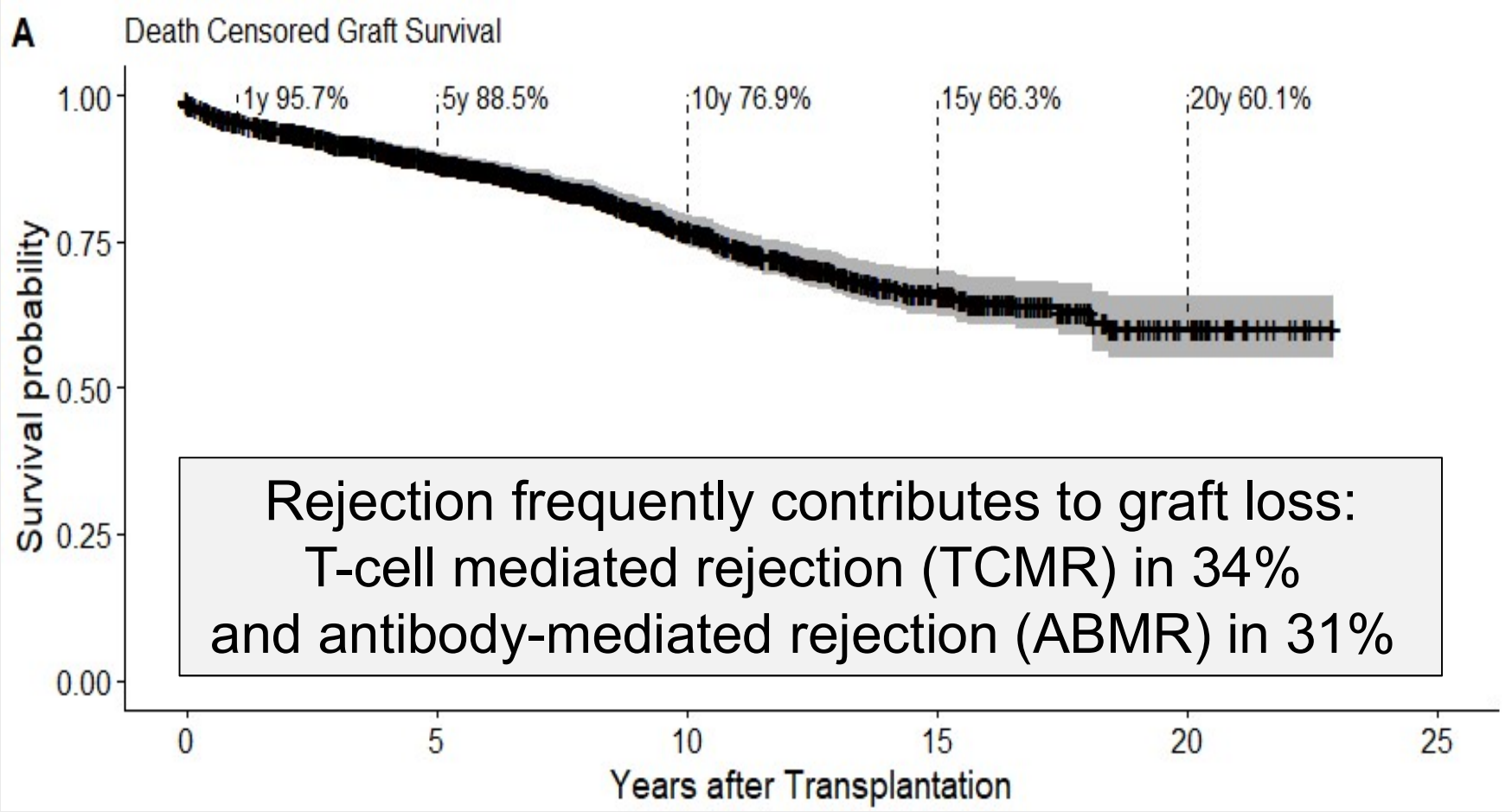
NephroCAGE

German-Canadian consortium on AI for improved kidney transplantation outcome

1st NephroCAGE Symposium, May 20, 2021

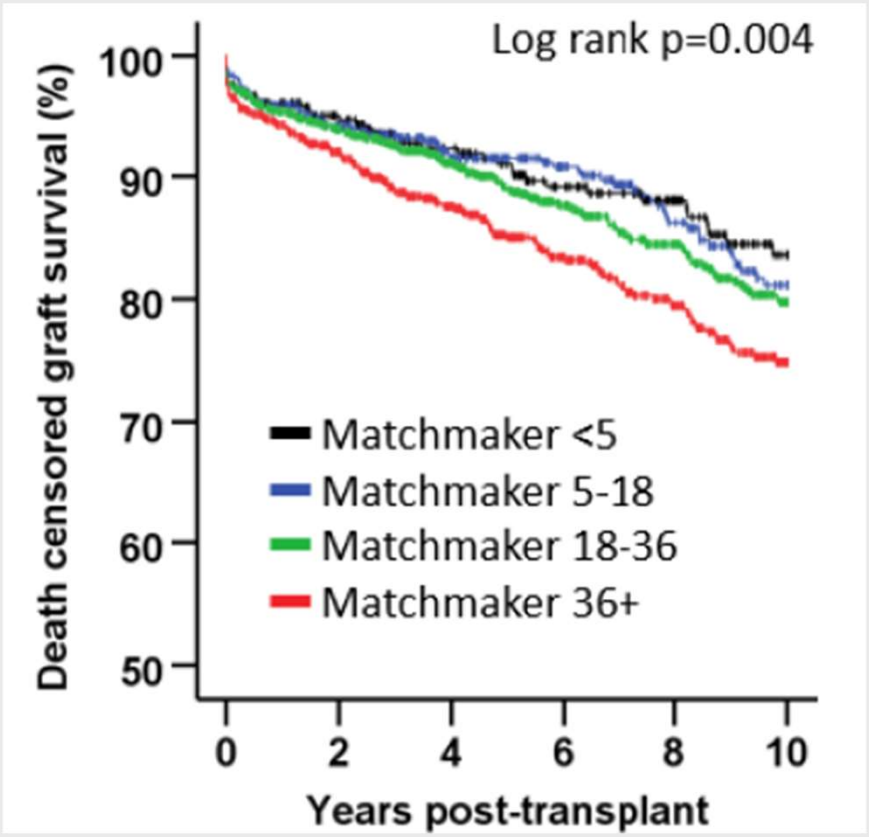
CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN

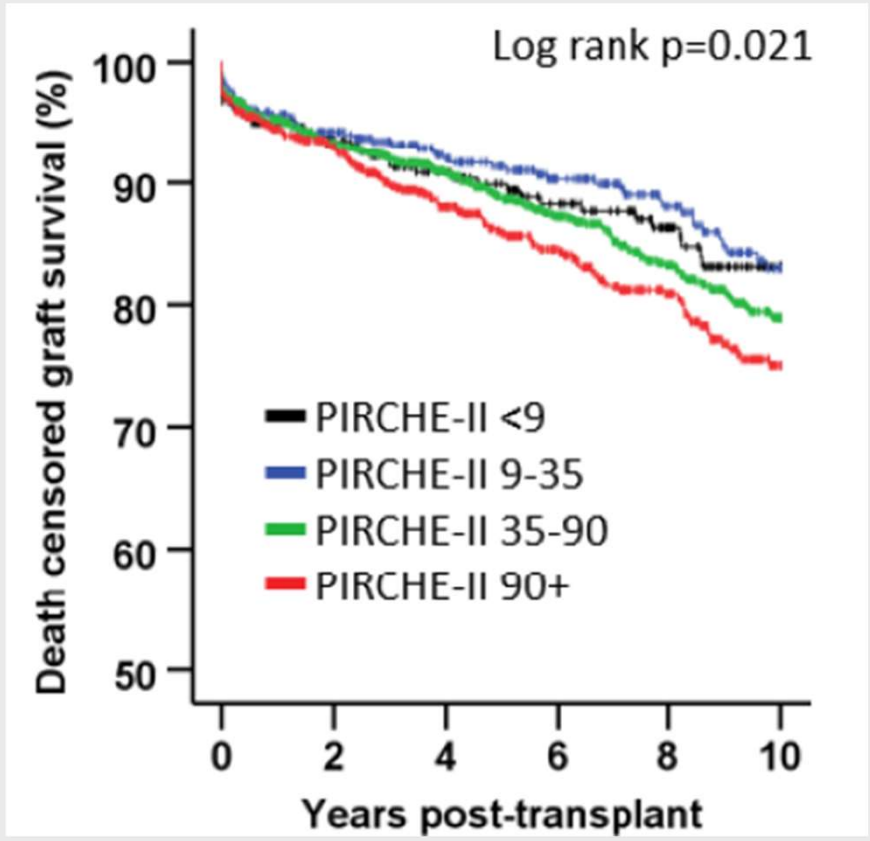
Clinical importance: graft loss over time



Exploring the complexity of Death-censored kidney allograft failure
Mayrdorfer, Liefeldt, Wu et al. JASN 32, 2021 https://doi.org/10.1681/ASN.2020081215

Epitope match is associated with graft loss

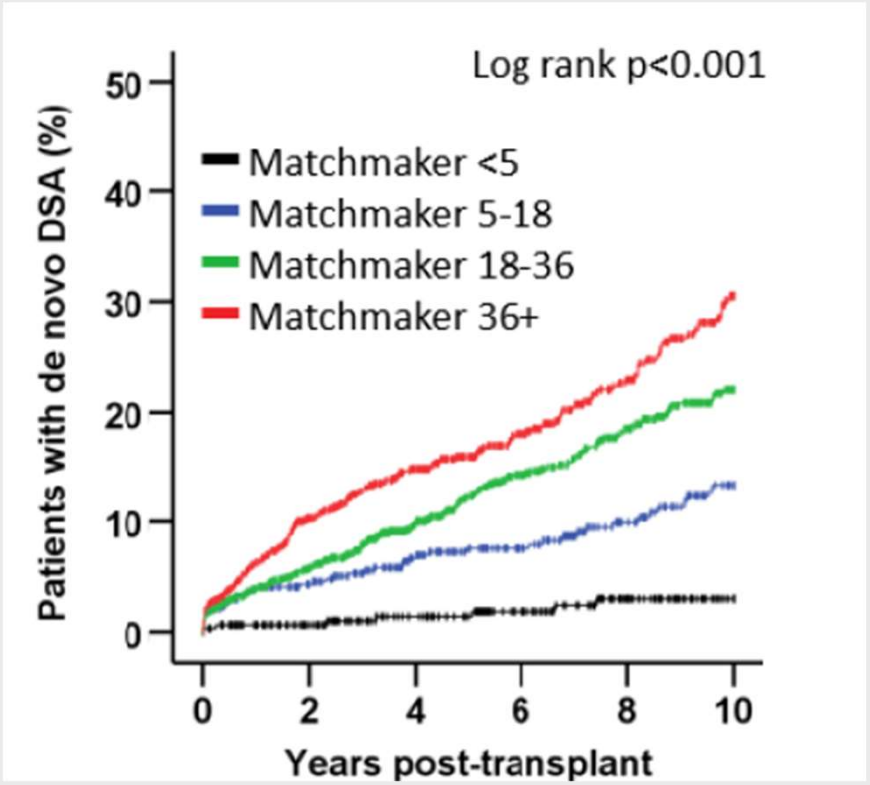


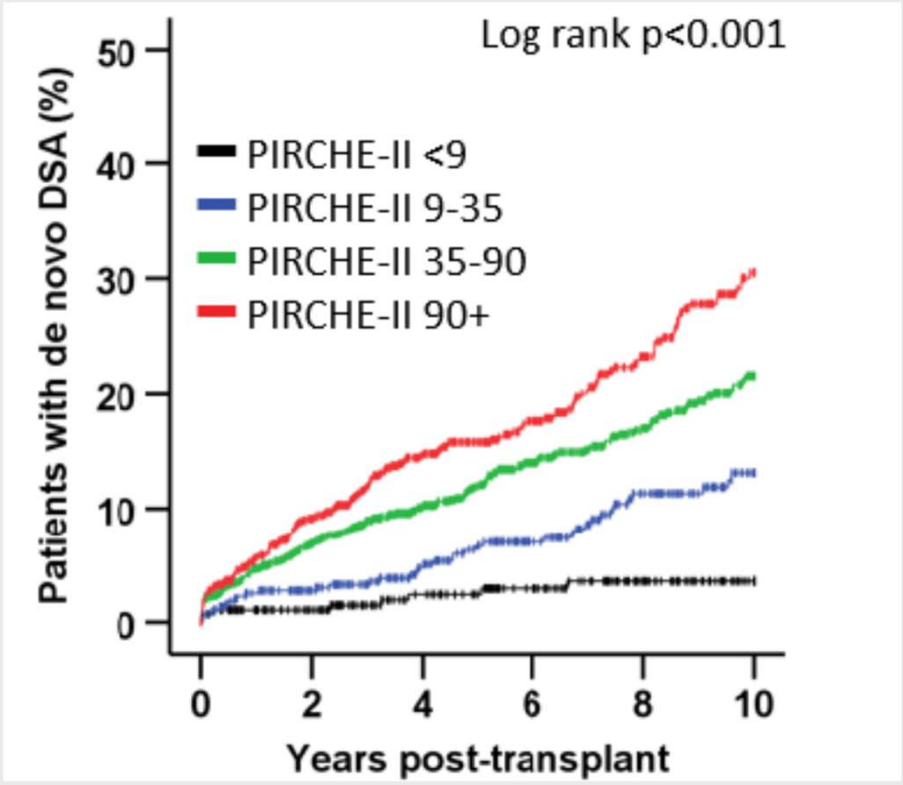


Donor–Recipient Matching Based on Predicted Indirectly Recognizable HLA Epitopes Independently Predicts the Incidence of De Novo Donor-Specific HLA Antibodies Following Renal Transplantation

Lachmann, Niemann, Reinke et al., AJT 2017; 17: 3076–3086 doi: 10.1111/ajt.14393

Epitope match is associated with development of donor specific antibodies and rejection





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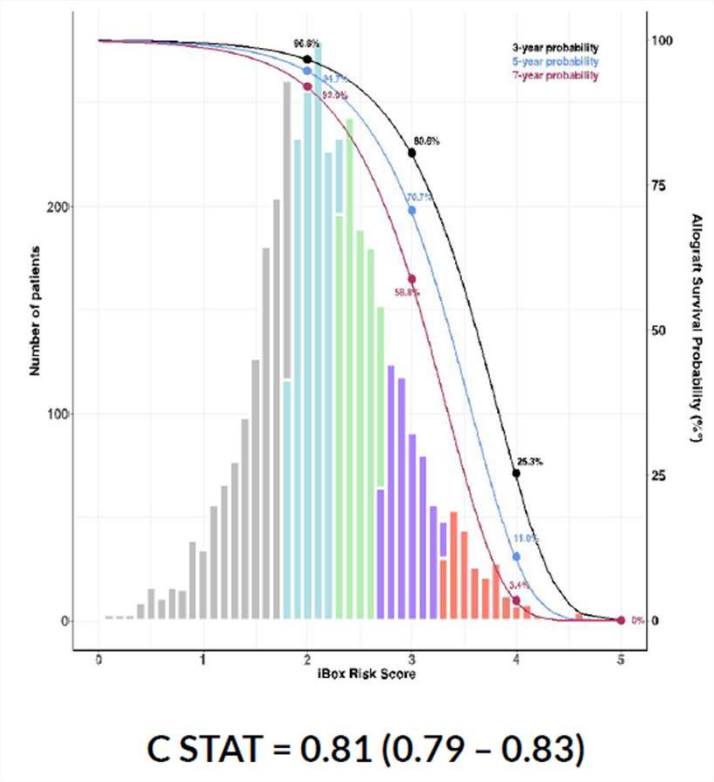
iBox – first validated prediction model



C STAT = 0.81 (0.79 – 0.83)

Prediction system for risk of allograft loss in patients receiving kidney transplants: international derivation and validation study

Loupy, Aubert, Orandi, et al., *BMJ* 2019;366:l4923
http://dx.doi.org/10.1136/bmj.l4923

iBox – first validated prediction model

Data input		Output
Mandatory	Additional	
• Time from transplant • eGFR (mL/Min/1.73m2) • Proteinuria (g/g)	• Banff lesions grading: g,i,t,ptc,cg,IFTA • Histology diagnoses • Anti HLA DSA (MFI)	• Individual patient prediction of allograft survival 3, 5 and 7 years after evaluation time

Prediction system for risk of allograft loss in patients receiving kidney transplants: international derivation and validation study

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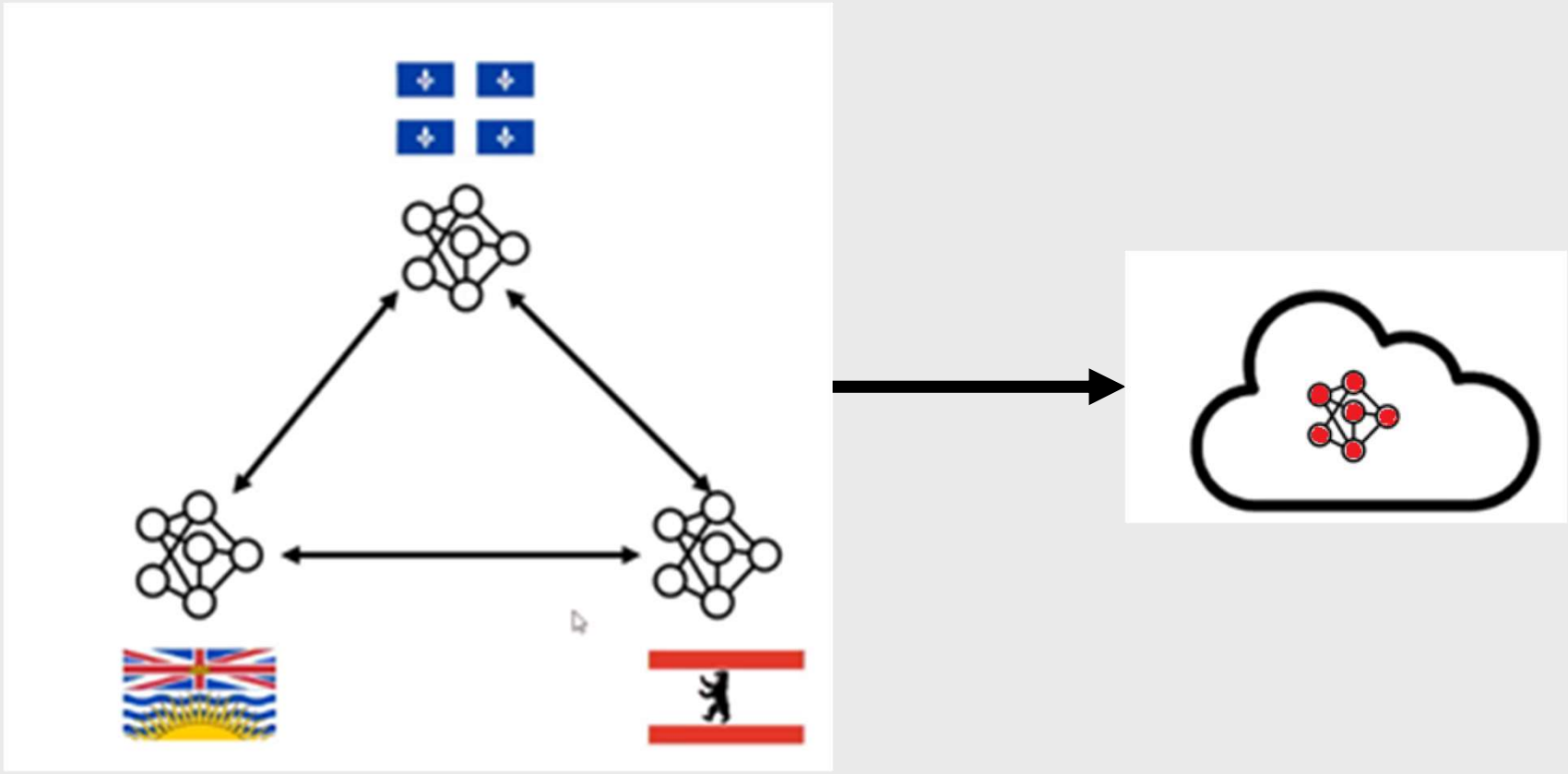
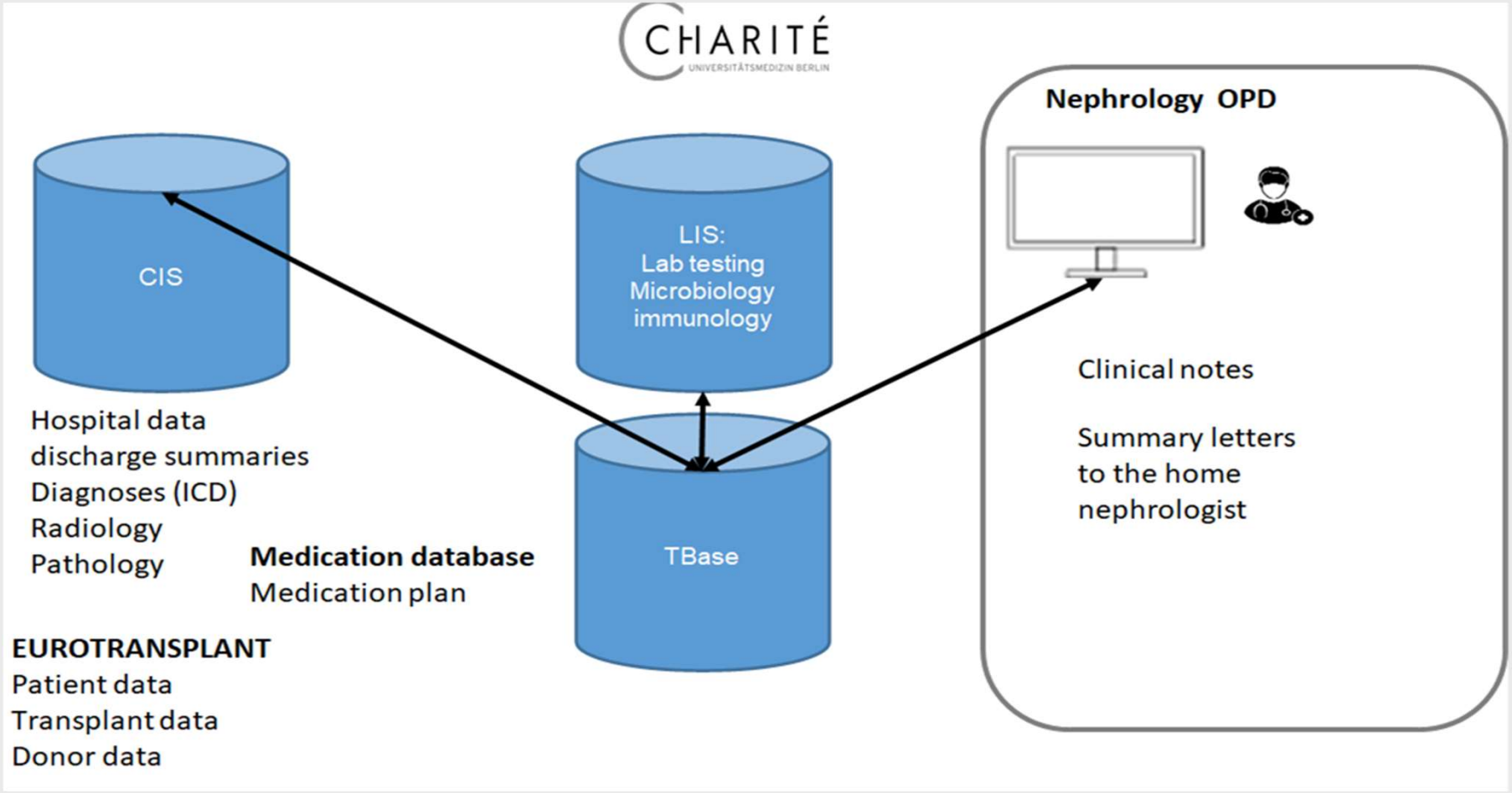
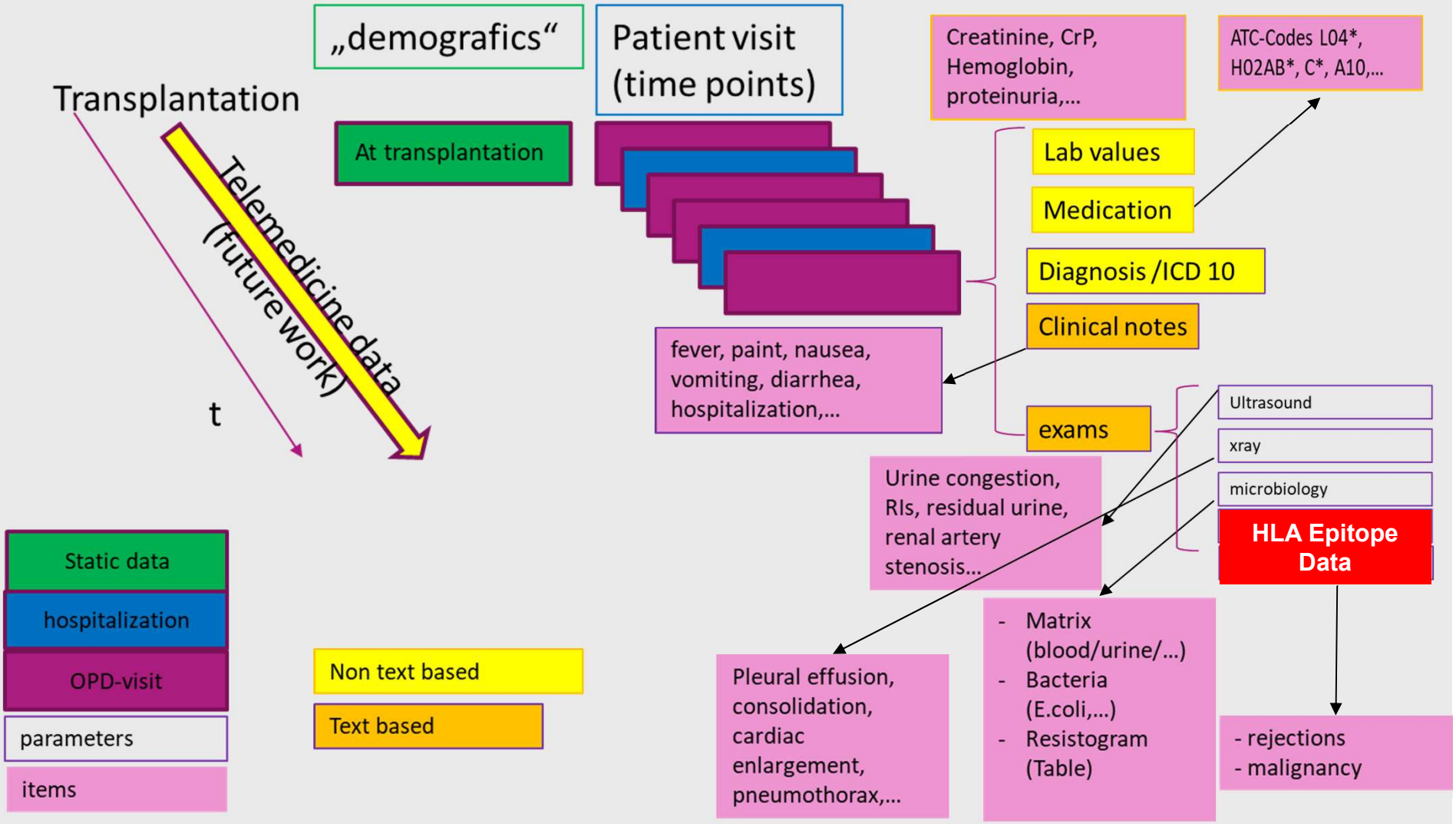
Aim: Development of an advanced prediction model including epitope match through federated learning



Charité infrastructure

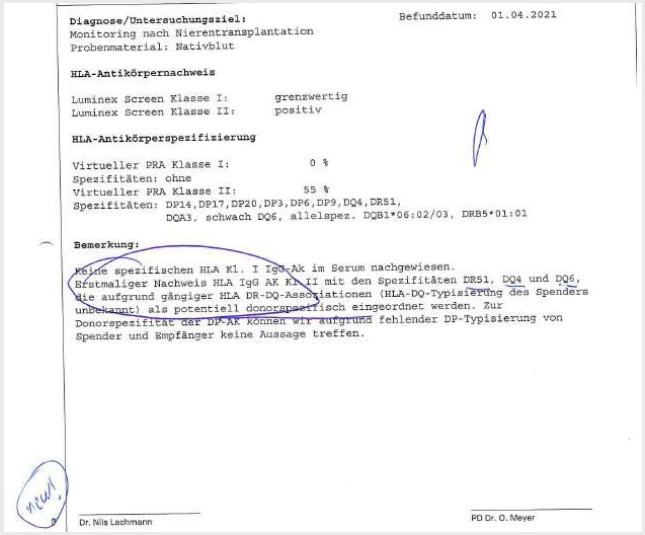


Potential model outline



HLA Data flow

HLA-Lab
Tissue typing
HLA-screening
Epitope Scores



Diagnose/Untersuchungsziel: Befunddatum: 01.04.2021
Monitoring nach Nierentransplantation
Probenmaterial: Nativblut

HLA-Antikörpernachweis

Luminex Screen Klasse I: grenzwertig
Luminex Screen Klasse II: positiv

HLA-Antikörperspezifizierung

Virtueller PRA Klasse I: 0 %
Spezifitäten: ohne
Virtueller PRA Klasse II: 55 %
Spezifitäten: DP14,DP17,DP20,DP3,DP6,DP9,DQ4,DR51,
DQA3, schwach DQ6, allelspez. DQB1*06:02/03, DRB5*01:01

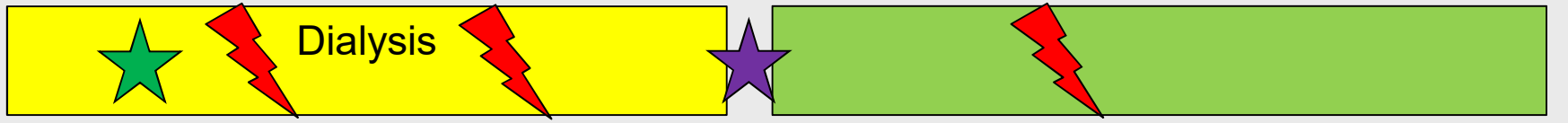
Bemerkung:

Viele spezifischen HLA Kl. I IgG-AK im Serum nachgewiesen.
Erstmaliger Nachweis HLA IgG AK Kl. II mit den Spezifitäten DR51, DQ4 und DQ6, die aufgrund gängiger HLA DR-DQ-Assoziationen (HLA-DQ-Typisierung des Spenders unbekannt) als potentiell donorspezifisch eingeordnet werden. Zur Donorspezifität der DP-AK können wir aufgrund fehlender DP-Typisierung von Spender und Empfänger keine Aussage treffen.

Dr. Nils Lachmann PD Dr. O. Meyer

dialysis unit
Regular dialysis and visits
Referring for transplant
updating examination status

Transplant center
Evaluation
Listing at EUROTRANSPLANT
Follow Up care



time

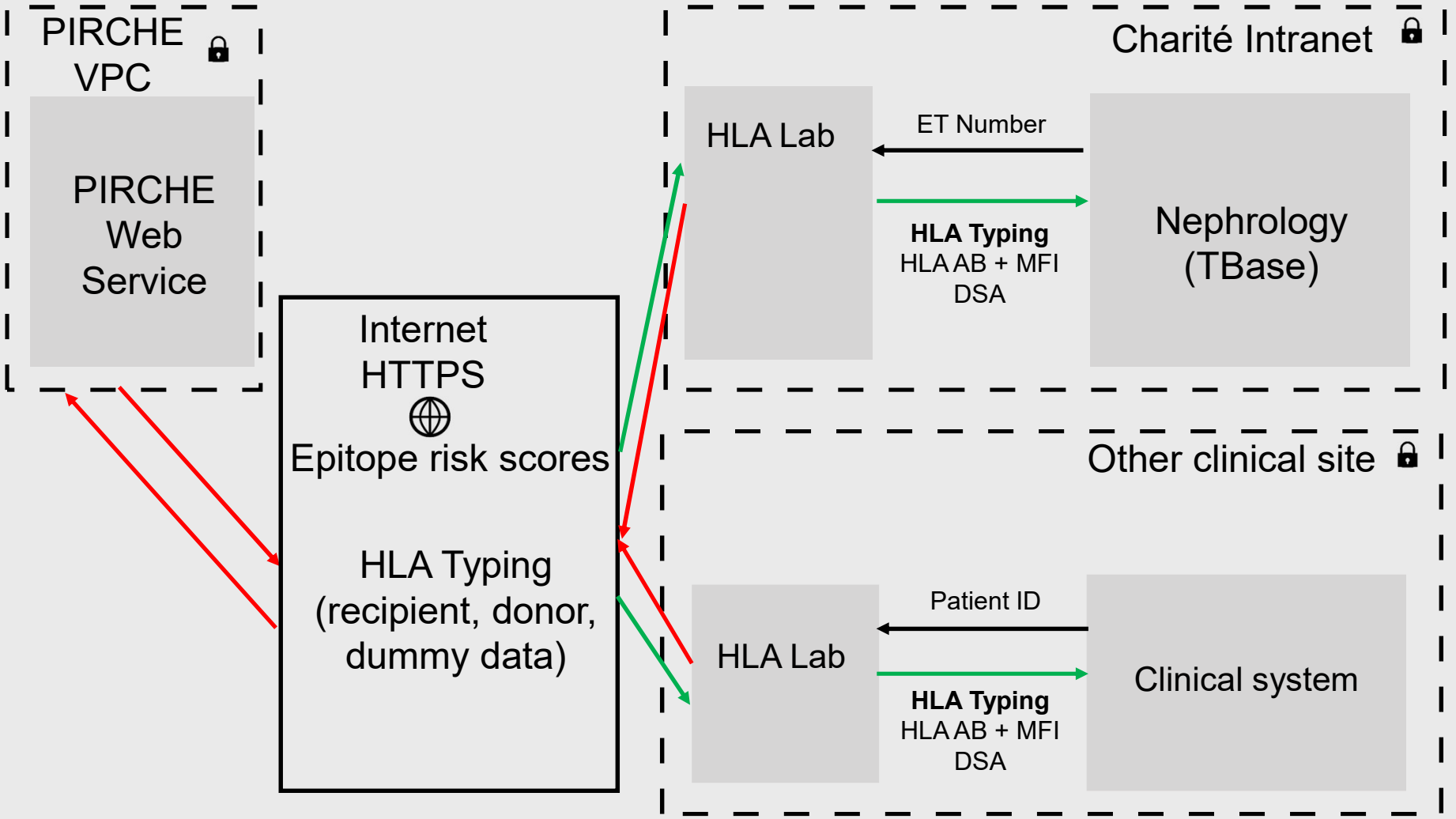
WP6 Approach

- Training of HLA laboratory staff
- Recalibration of clinical prediction model (CPM) for use on local clinical sites
- Integration of CPM into current clinical workflow
- Test and Validation of CPM outcomes
- User feedback for development of clinical demonstrator
- Training for users and support staff

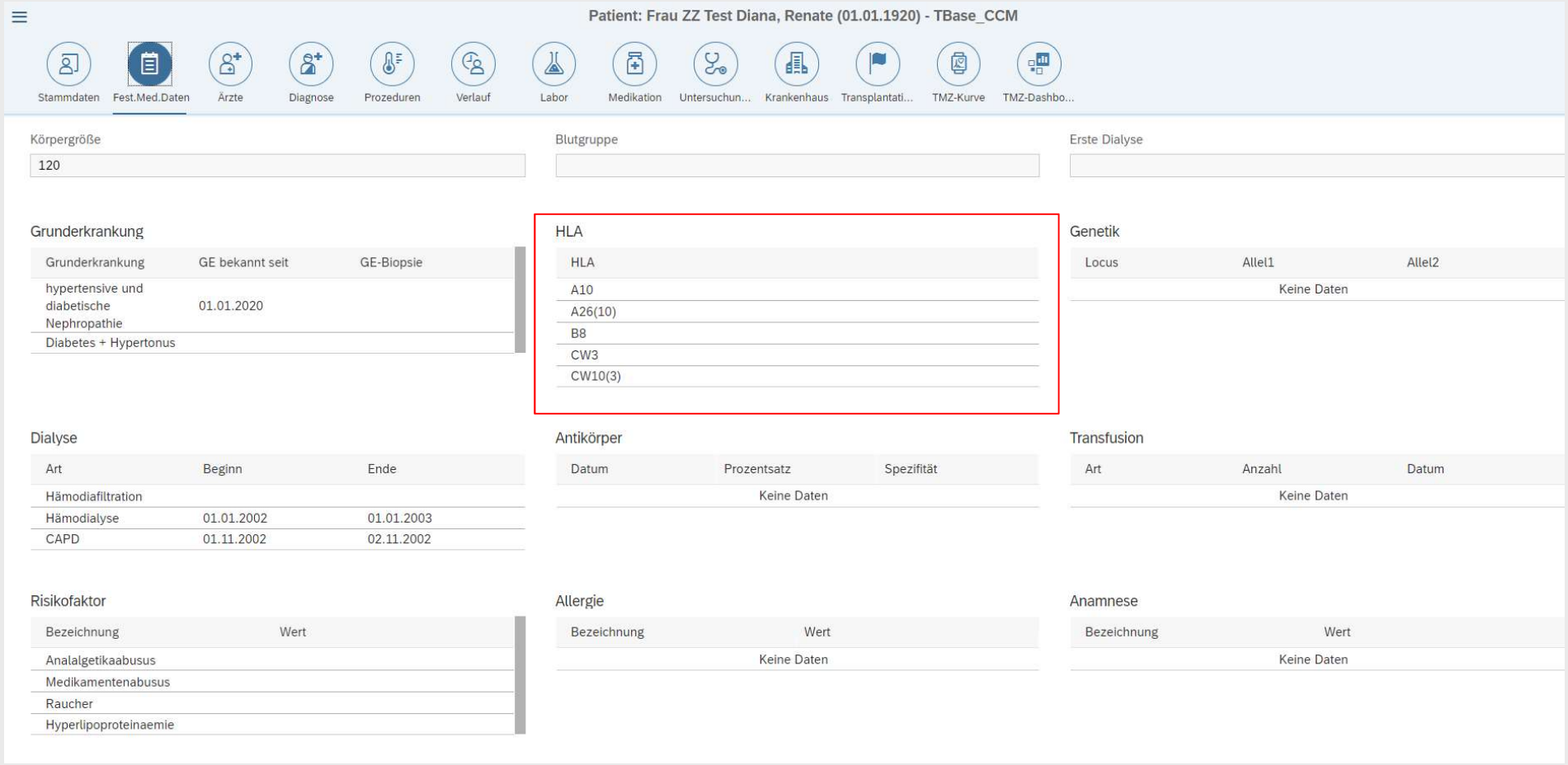
WP6 Output

- At the end of this work package, the Clinical prediction model is deployed to all clinical sites, recalibrated, and configured for regular learning

WP7 web application for demonstrator



Potential demonstrator: Recipient HLA-Data



Potential demonstrator: Donor HLA-Data

Geschlecht	Alter		Vermittlung	
Männlich	19			
Entnahmedatum	**Zentrum**		**Art des Spenders**	
	GLUTP		Hirntot	
Blutgruppe	**Hypotensive Phasen**	**Herzstillstand**	**Todesursache**	**Arterienzahl**
0+			T_CAPI: Trauma: Schädel	2
Perfusionsbeginn	**Perfusionslösung**	**Perfusionsvolumen**	**Arteriosklerose (Spender)**	
	HTK	8000		

› Laborwerte

⌄ HLA

Bezeichnung
A3
A19
A33(19)
B14
B15
B62(15)
B64(14)
CW3
CW8
DQ1
DQ3
DR1
DR8

Körpergrösse in cm	Körpergewicht in kg	Dauer des Intensivaufenthaltes in Tagen	Dauer Beatmung in Tagen
180	80		
Diurese letzte Stunde in ml	**Diurese in ml / h**	**Organqualität**	
	4960 / 13		

Potential demonstrator integrated in database

Gain from this project

- Better HLA data display locally
- Novel comprehensive web-based kidney graft loss risk calculator
- First transcontinental federated learning approach in transplant medicine
- Improved risk assessment including HLA epitopes
  - may pave the road for better outcomes
  - basis for personalized immunosuppression
  - doctors and patient education
  - starting point for interventional studies

Thank you

NephroCAGE
German-Canadian consortium on AI for improved kidney transplantation outcome
1st NephroCAGE Symposium, May 20, 2021
Hasso Plattner Institut
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THE UNIVERSITY OF BRITISH COLUMBIA
Université de Montréal
POLYTECHNIQUE MONTRÉAL
GenomeQuébec
PIRCHE
CHARITÉ
Centre universitaire de santé McGill
McGill University Health Centre
CHUM
GenomeCanada
Genome BritishColumbia