



# XVIII IPOPI GLOBAL PATIENTS' MEETING

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# Defining Secondary Immunodeficiencies

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	No, Nothing to disclose
X	Yes, please specify disclosures

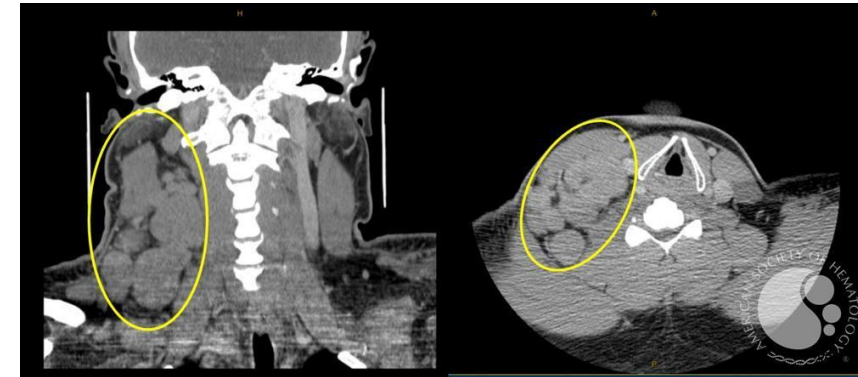
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Horizon 2020			X					
Moderna			X					

# Primary versus secondary immunodeficiency

How to differentiate?

Male, patient, 35 years of age, seen in 2014

**Reason of referral : Recurrent infections; immunodeficiency?**



Medical history:

- 2007 Lymphadenopathy cervical region; analysis inconclusive
- 2008 B-cell non Hodgkin lymphoma, extensive disease; start chemotherapy 8x, partial response
- 2009 Progressive disease, start chemotherapy, followed by Rituximab maintenance therapy
- 2010 Complete remission, continued Rituximab therapy for 2 years

# Primary versus secondary immunodeficiency

Male, patient, 35 years of age, seen in 2014

Recurrent sinopulmonary tract infections since 2012 (culture-positive, h. influenzae and s. pneumoniae)

Recurrent upper and lower respiratory tract infections since childhood?

Frequent use of antibiotics

One admission in hospital at age 21 because of pneumonia, viral or bacterial?



# Primary versus secondary immunodeficiency

## Analysis

<input type="checkbox"/> Iotaal eiwit	Bloed									g/L
<input type="checkbox"/> Albumine	Bloed									g/L
<input type="checkbox"/> IgA	Bloed				0.210					g/L
<input type="checkbox"/> IgG	Bloed				3.8					g/L
<input type="checkbox"/> IgM	Bloed				0.050					g/L
<input type="checkbox"/> CRP	Bloed				2.8					mg/L

<input type="checkbox"/> T-Cellen	Bloed			0.74						$10^9/L$
<input type="checkbox"/> CD4+T-Cellen	Bloed			0.38						$10^9/L$
<input type="checkbox"/> CD8+T-Cellen	Bloed			0.35						$10^9/L$
<input type="checkbox"/> B-Cellen	Bloed			0.00						$10^9/L$
<input type="checkbox"/> NK-cellen	Bloed			0.12						$\times 10^9/L$
<input type="checkbox"/> CD4/CD8 ratio	Bloed									

Hypogammaglobulinemia

Undetectable peripheral B lymphocytes

# Primary versus secondary immunodeficiency

Male, patient, 35 years of age, seen in 2014

Recurrent upper and lower respiratory tract infections (culture-positive, h. influenzae and s. pneumoniae)

Since use of Rituximab or since childhood?

Frequent use of antibiotics

Hypogammaglobulinemia

Undetectable peripheral B lymphocytes

# Primary versus secondary immunodeficiency

So what did we report to the General Physician?

Conclusions/considerations

- 1) PID (CVID), with low IgG, IgA, IgM, with recurrent infections since childhood with secondary hematological malignancy
- 2) SID related to hematological malignancy
- 3) SID related to treatment for hematological malignancy (Rituximab)
- 4) Combination of the above

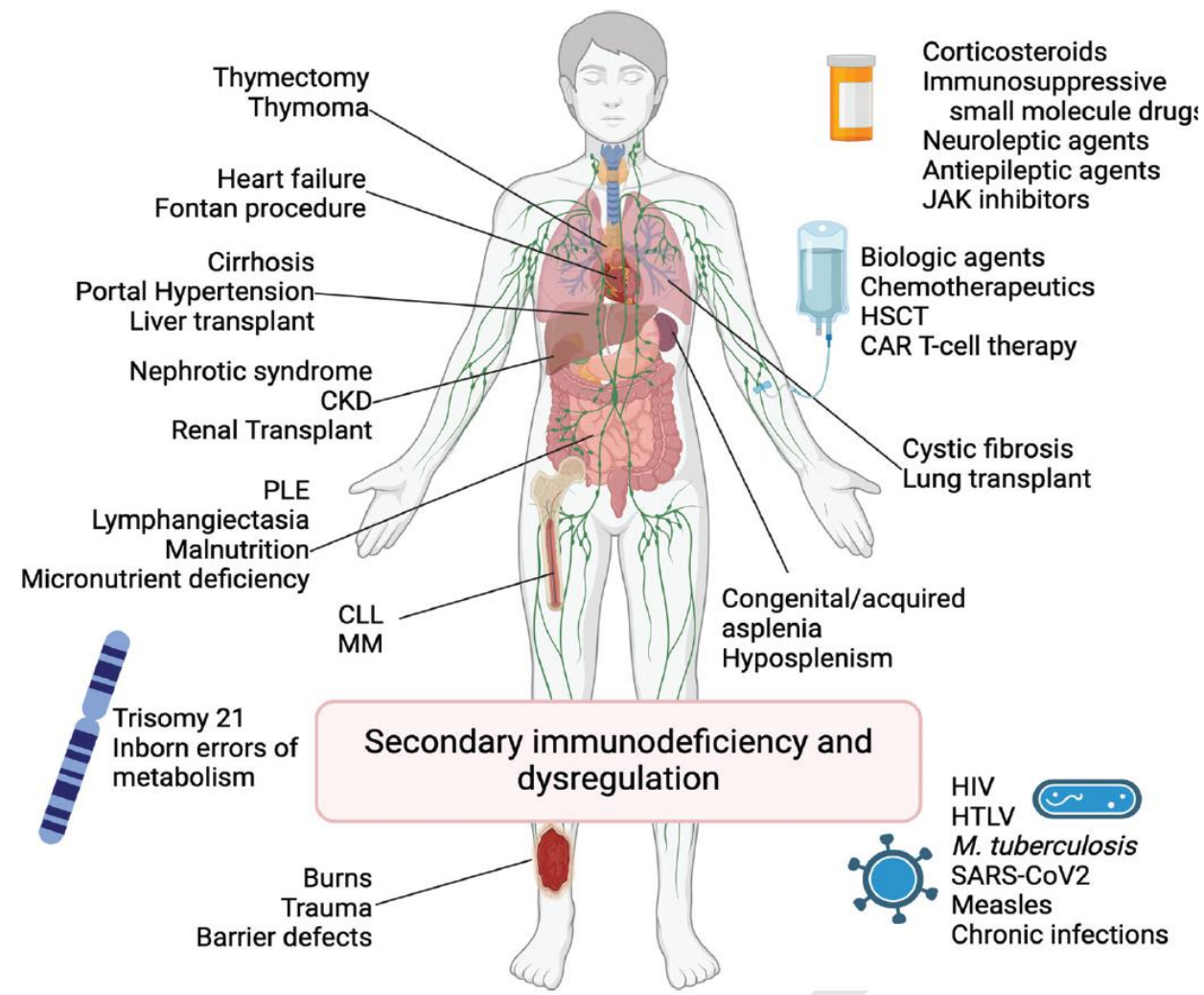


# Secondary immunodeficiencies

Acquired impairments in immune cell function and/or regulation, and may be transient, reversible, or permanent

## Causes:

- Malignancy : hematological malignancies
- Medication : immunosuppressive therapies; anti-epileptics
- Chronic infections : HIV
- Protein losing conditions



# Examples of SID

- Hematological malignancies
  - Non-Hodgkin’s lymphoma (NHL)
  - Chronic lymphocytic leukemia (CLL)
  - Multiple myeloma (MM)

Causes of death	Cancer		General population		SMR (95% CI)
	Observed No. of deaths (%)	Mortality rates in cancer patients	Expected No. of deaths	Mortality rates in general population	
All causes	390,534 (100%)	10,399.9	NA	NA	NA
Index cancer	219,731 (56%)	5833.7	NA	NA	NA
Non-index cancer	57,631 (15%)	1534.7	NA	NA	NA
Non-cancer causes	113,172 (29%)	3004.6	45176.4	1199.4	2.51 (2.49–2.52)
Infections	19,111 (5%)	507.4	2933.4	77.9	6.51 (6.42–6.61)
Pneumonia and influenza	5748 (2%)	152.6	1609.8	42.7	3.57 (3.48–3.66)

# Chronic lymphocytic leukemia

Incidence        4.7 in 100.000

Hypogammaglobulinemia in up to 85% of patients

Infection-related deaths in 25-50% of patients

Hypogammaglobulinemia is related to stage of disease and duration of disease

# Chronic lymphocytic leukemia

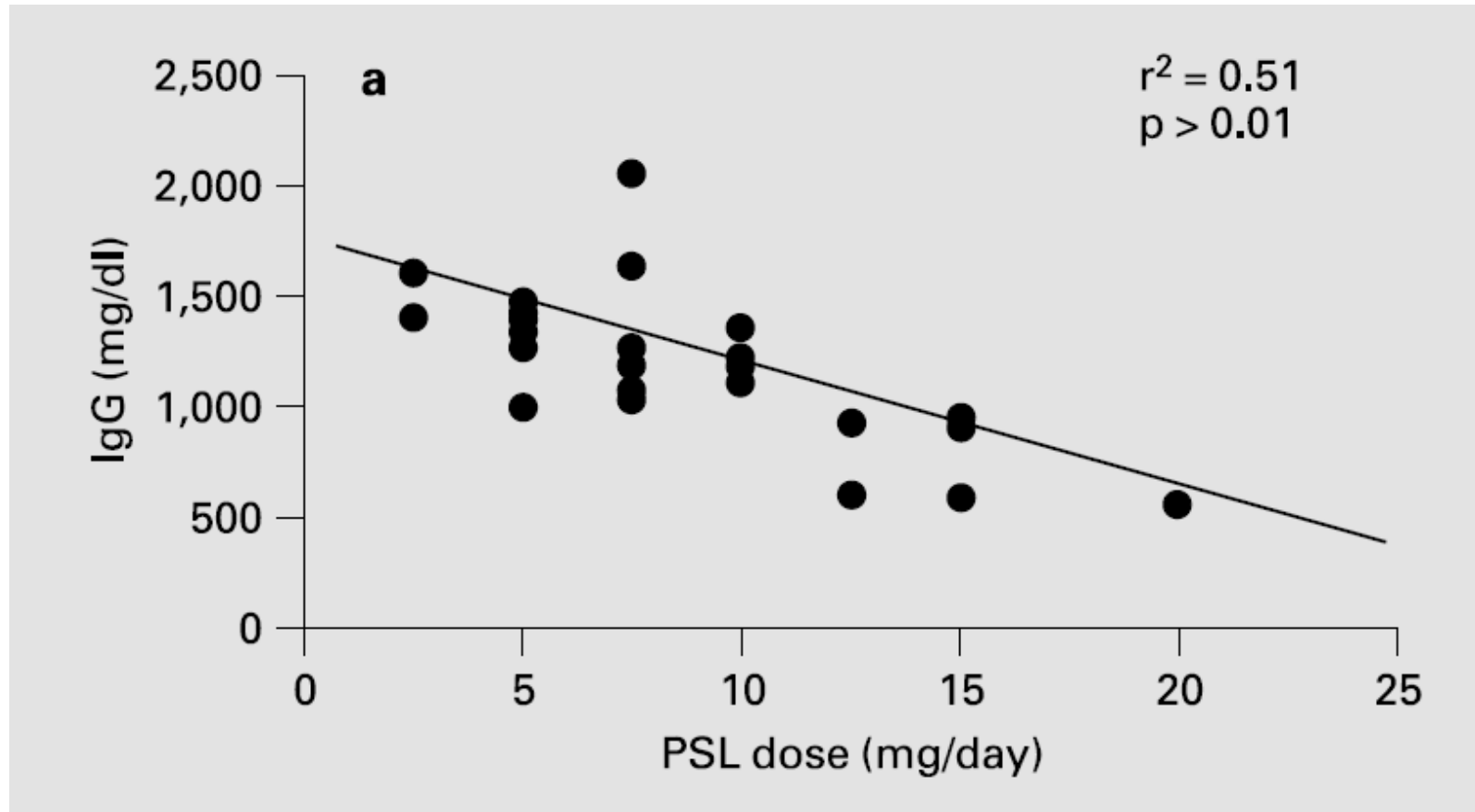
Table 1. Patient data

	Subgroup of patients with			
	No infections	Non-severe infections	Severe infections	Infection deaths
Number of patients	49 (33%)	20 (14%)	77 (53%)	42
Sex (males/females)	29/20	11/9	40/37	24/20
Age (years; mean and range);				
Males	66.6 (38–80)	69.9 (50–86)	69.6 (53–85)	66.6 (53–85)
Females	70.5 (57–82)	71.1 (56–90)	76.1 (44–90)	70.5 (56–88)
Duration of follow-up (years; mean and range)	4.6 (1–15)	4.2 (<1–13)	4.07 (<1–15)	4.9 (1–13)
S-IgG (g/l; mean±s.d.)	8.4±2.9 (n=32)	6.6±3.1 (n=11)	5.6±3.1 (n=55)	5.0±2.5 (n=30)

# Increasing problems of medication



# Increasing problems of medication : prednison



Higher doses of prednison  
associated with  
Lower levels of IgG

# Increasing problems of medication : prednison

Table 4. Univariable treatment predictors of pneumonia hospitalization\*

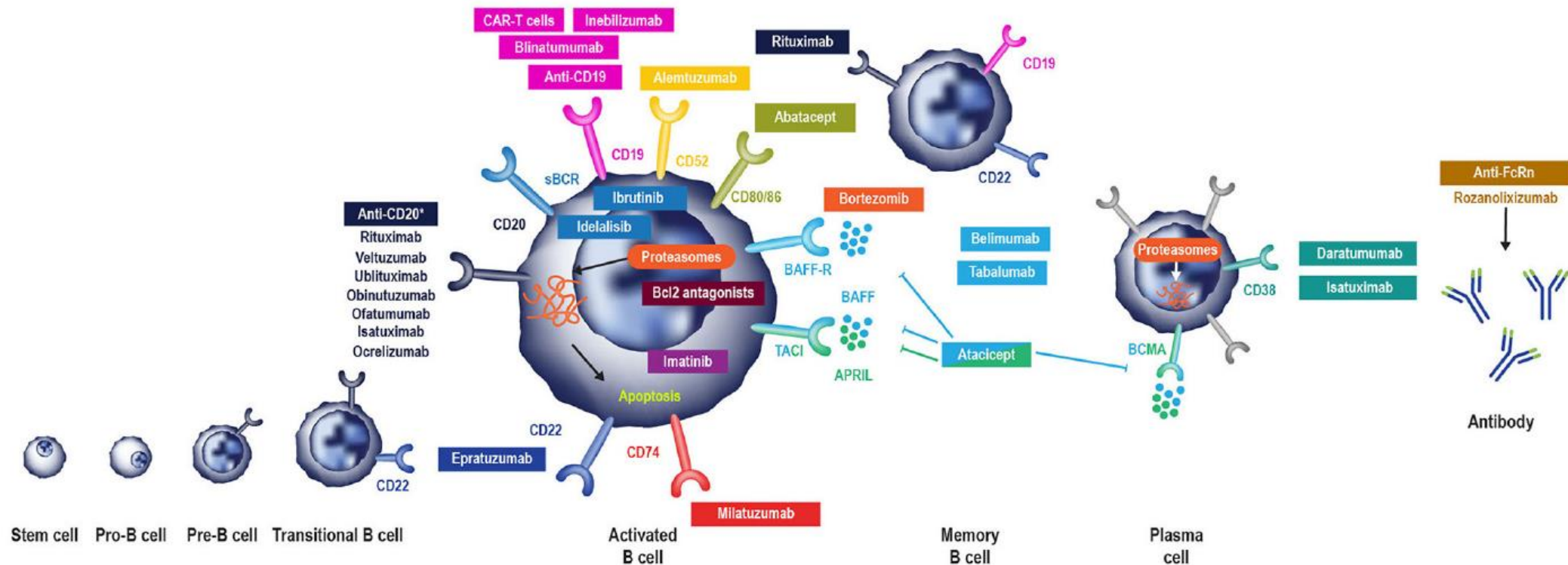
Variable	Unadjusted			Adjusted†		
	Hazard ratio	P	95% CI	Hazard ratio	P	95% CI
Prednisone, all dosages	2.3	<0.001	1.9–2.7	1.7		
No prednisone	1.0			1.0		
Prednisone ≤5 mg/day	1.7	<0.001	1.4–2.1	1.4		
Prednisone >5–10 mg/day	2.9	<0.001	2.3–2.7	2.1		
Prednisone >10 mg/day	3.1	<0.001	2.2–4.3	2.3		

Higher doses of prednison  
associated with  
Increased risk of infections

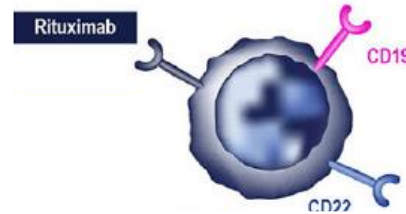


16788 patiens with rheumatoid arthritis

# Increasing problems of medication : more therapies



# Increasing problems of medication : Rituximab



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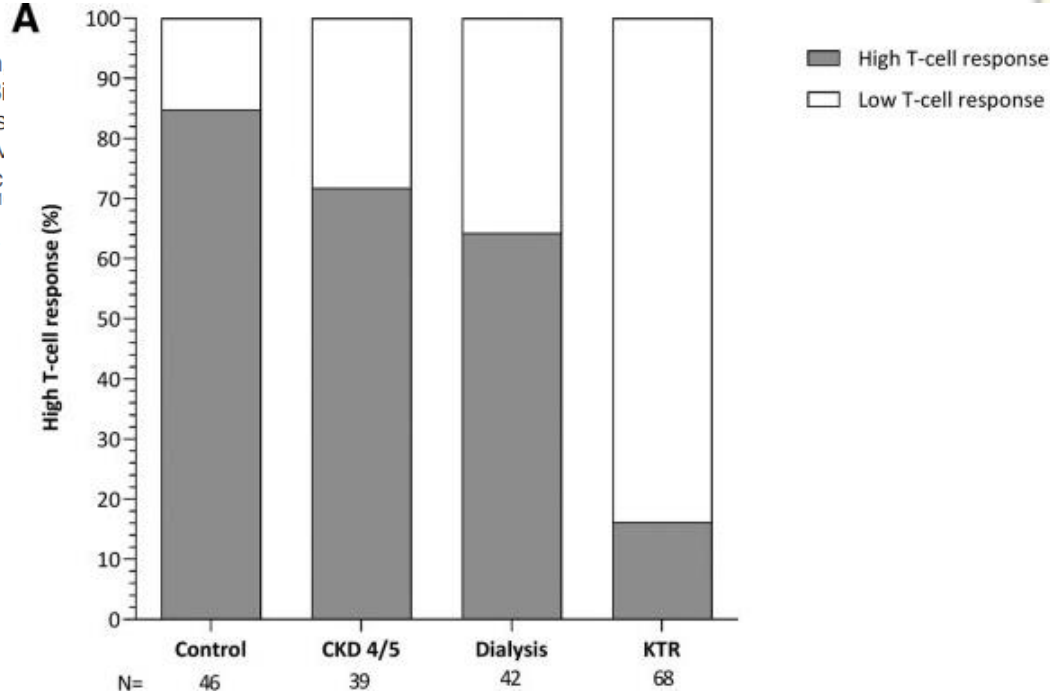
## Association of Immunoglobulin Levels, Infectious Risk, and Mortality With Rituximab and Hypogammaglobulinemia

Sara Barmettler, MD; Mei-Sing Ong, PhD; Jocelyn R. Farmer, MD, PhD; Hyon Choi, MD, DrPH; Jolan Walter, MD, PhD

# Increasing problems of medication : not only B-cells

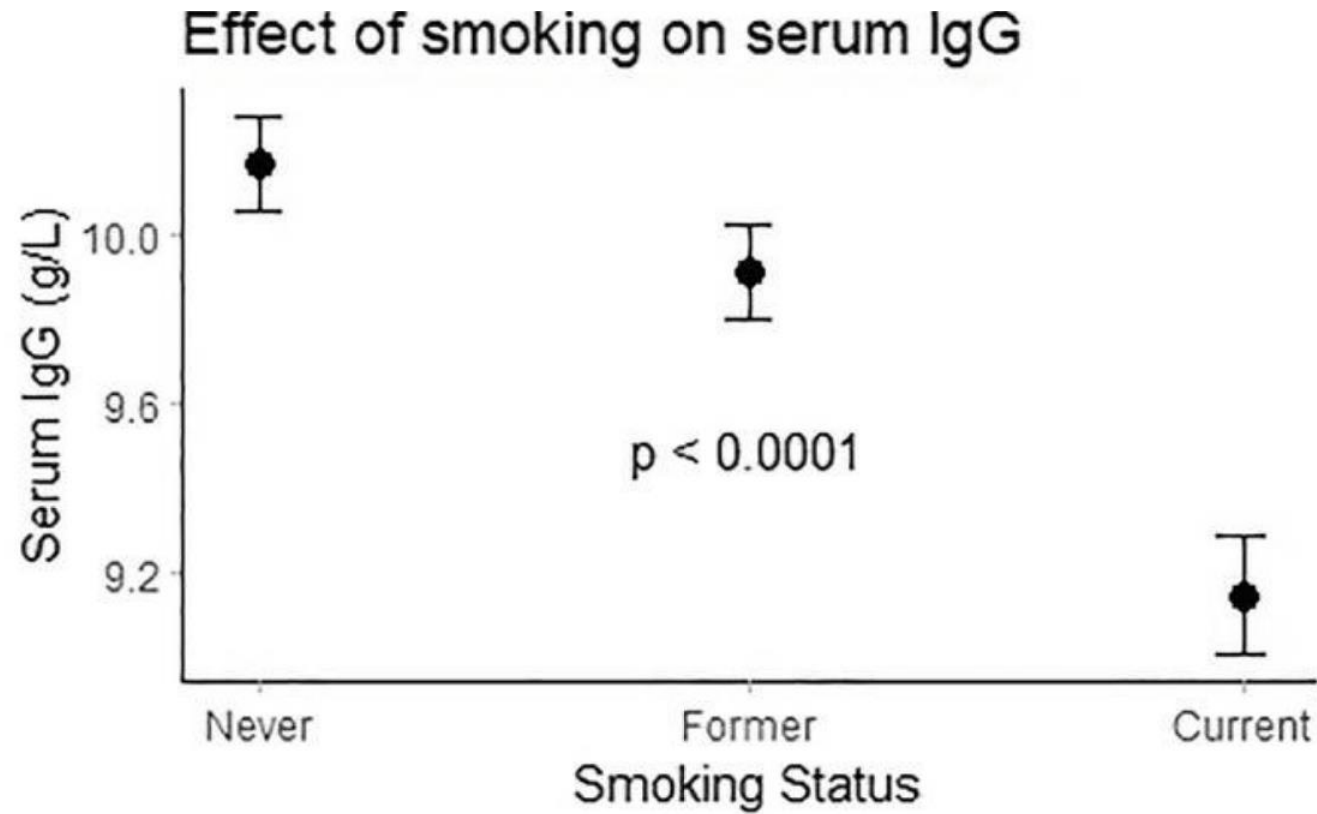
## The RECOVAC Immune-response Study: The Immunogenicity, Tolerability, and Safety of COVID-19 Vaccination in Patients With Chronic Kidney Disease, on Dialysis, or Living With a Kidney Transplant

Jan-Stephan F. Sanders, MD, PhD,<sup>1</sup> Frederike J. Bemelman  
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Marieke van der Heiden, PhD,<sup>4</sup> Celine Imhof, MD,<sup>1,4</sup> Marcia N  
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Djenolan van Mourik, BSc,<sup>8</sup> Ester B.M. Remmerswaal, PhD,<sup>1</sup>  
Rory D. de Vries, PhD,<sup>8</sup> Ron T. Gansevoort, MD, PhD,<sup>1</sup> Luuk  
Reinders, MD, PhD<sup>3</sup>; RECOVAC Collaborators\*



In kidney transplant patients the use of immunosuppressive treatments results in disturbed T-cell function

# Don't forget smoking





# Evaluation for SID

Not so different from PID

Medical history, chart review, use of medication

Leukocyte count including lymphocyte subsets

Albumin and protein levels

Immunoglobulins

HIV

Functional tests including responses to immunization?

# Treatment of SIDs

Remove the underlying cause if possible

Antibiotics / prophylaxis

Immunoglobulin replacement therapy

Immunization

# Treatment of SIDs

## Economic impact of immunoglobulin replacement therapy in secondary immunodeficiency to hematological cancer: a single center observational study

Luciana del Campo Guerola<sup>1,2</sup>, Ana Andrea García Sacristán<sup>3</sup>, Antonio Portolés<sup>4</sup>, Maricruz Jasso<sup>1</sup>, Teresa Guerra-Galán<sup>1,2</sup>, Eduardo de la Fuente-Munoz<sup>1,2</sup>, María Palacios-Ortega<sup>1,2</sup>, Miguel Fernández-Arquero<sup>1,2</sup>, Cristina Cuesta-Mínguez<sup>5</sup>, Aránzazu Rodríguez-Sanz<sup>5</sup>, Ascensión Peña-Cortijo<sup>6</sup>, Marta Polo<sup>6</sup>, Marta Mateo Morales<sup>6</sup>, Eduardo Anguita-Mandly<sup>6,7</sup>, Teresa Benítez Jiménez<sup>3</sup>, Celina Benavente Cuesta<sup>6,7</sup> and Silvia Sánchez-Ramón<sup>1,2\*</sup>

# Conclusions

Secondary immunodeficiencies much more prevalent than primary immunodeficiencies

From few symptoms to severe disease

Various causes, including malignancies and use of medication

Treatment : remove the underlying cause; comparable to primary immunodeficiencies?

Bigger problems ahead?

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# Thank you for your attention

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