



Support PK and ADA of biologics using finger prick sampling; some real-life examples

Sanquin Diagnostic Services



Annick de Vries, PhD
Director Bioanalysis

Comparative data on venous vs. capillary blood measurement

Amsterdam UMC

infliximab in IBD-patients

Sophie Berends

Anne Strik

Ron Mateau



Reade Amsterdam

adalimumab in RA-patients

Eva Kneepkens

Gert-Jan Wolbink



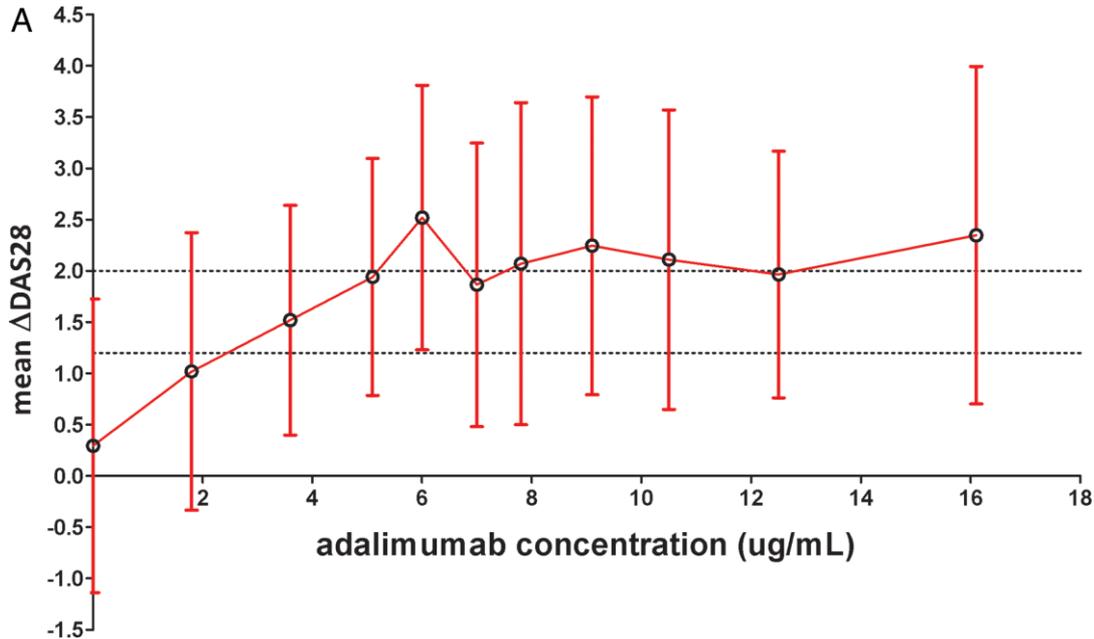
Sanquin Diagnostic Services/Sanquin Research

Karien Bloem

Theo Rispens

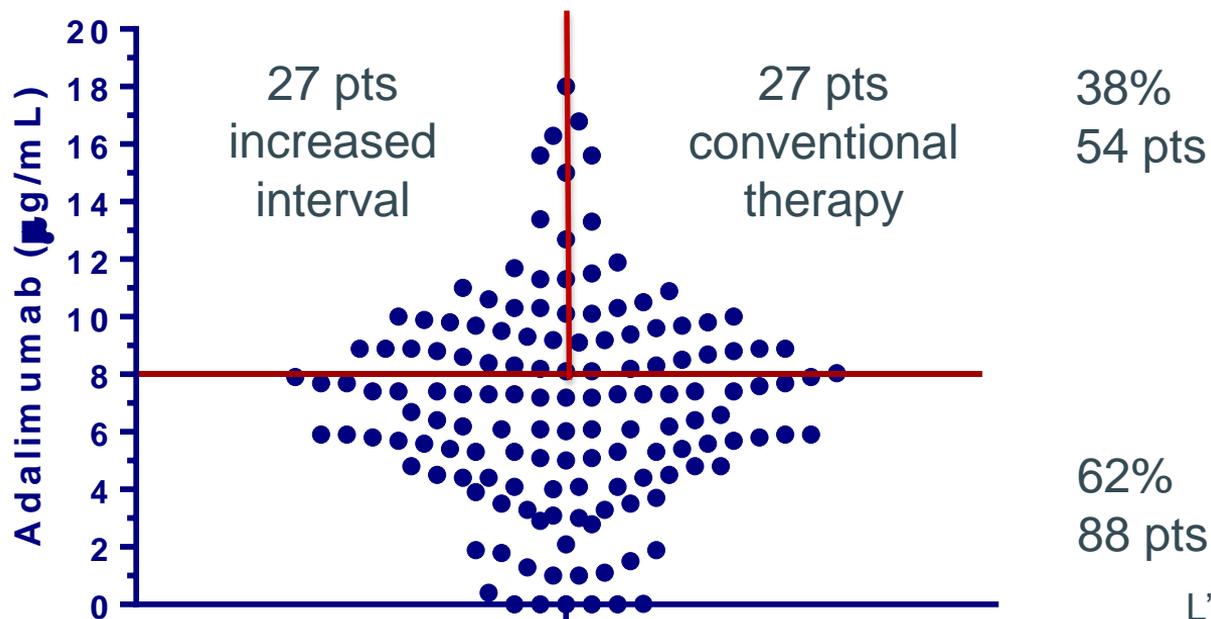
Tiny Schaap

Clinical efficacy/ serum concentration; adalimumab in RAs



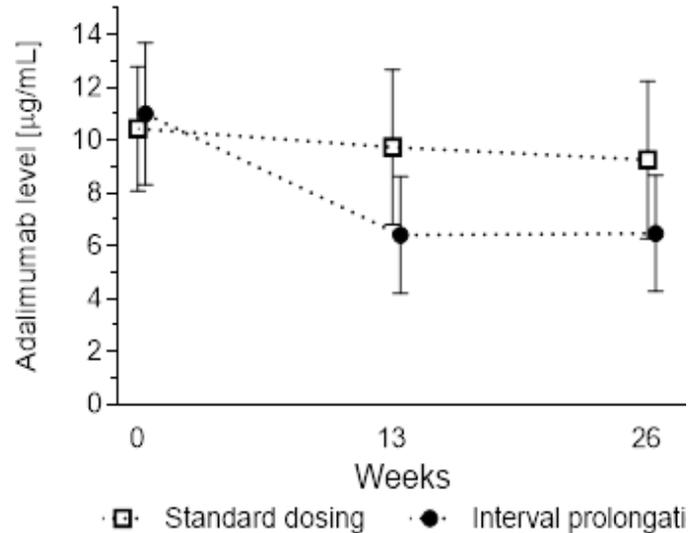
Lower dose based on serum level

Adalimumab concentration

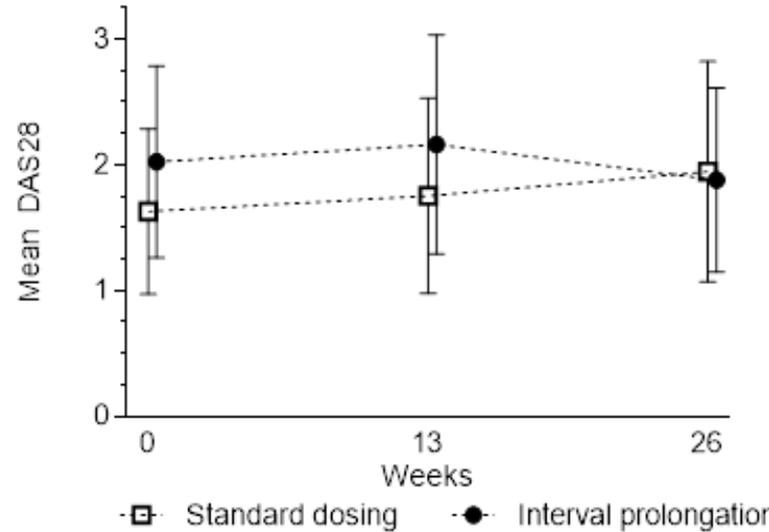


Increasing interval of administration – clinical efficacy remains

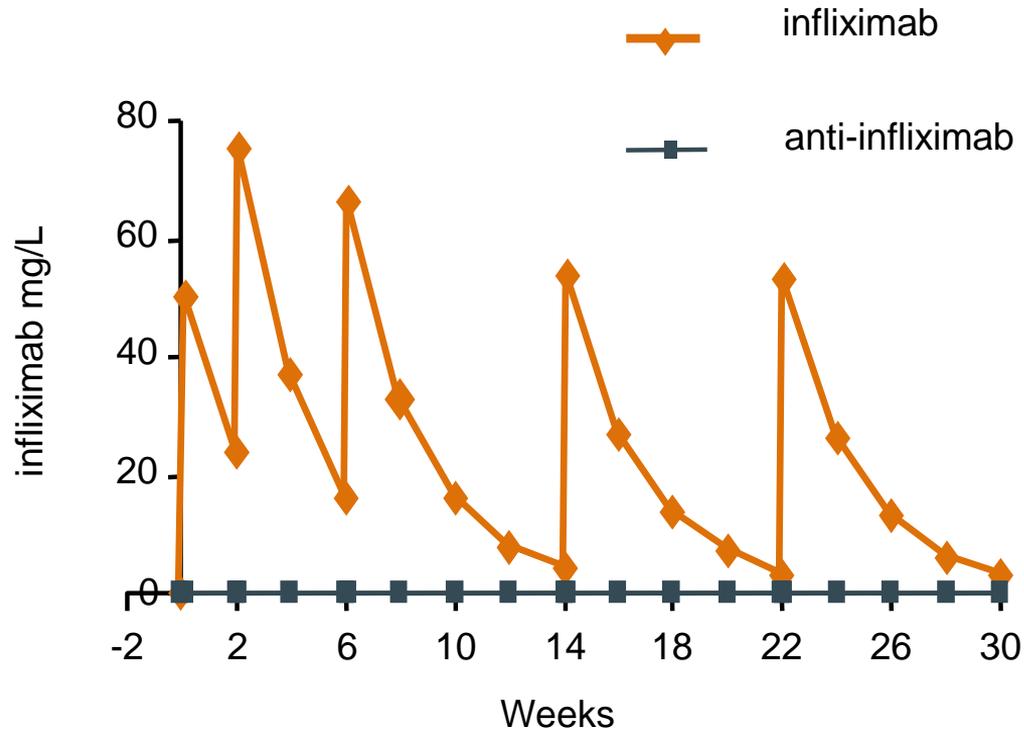
Lower serum level ADL



Clinical efficacy remains



Modelling of concentrations curves per patient



Capillary Blood sampling for biologics: A tool in Therapeutic Drug Monitoring

- Auto sampling at home
- Logistics cheap and easy
 - No need for nurse nor visit to the clinic
- Easy to sample frequently

- Clinician/ clinic receives serum concentration in advance
- Easy sampling to support PK studies
- Model concentration curve per patient
- Personal advice on dosing schedule

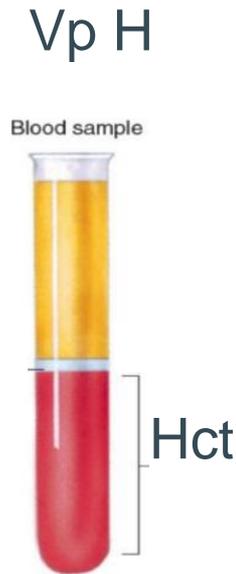


adalimumab study patients sampled in clinic

- From DBS to DBS eluate
- Measure surface of DBS
 - Scan DBS
 - Calculate surface with ImageJ
- Cut out whole DBS
- Put in 12-wells plate with 1 ml buffer
- Incubate overnight on shaker
- Take supernatant (~500 μ l)



Serum equivalents of DBS eluates Based on volumetric method



$A(\text{hct})$

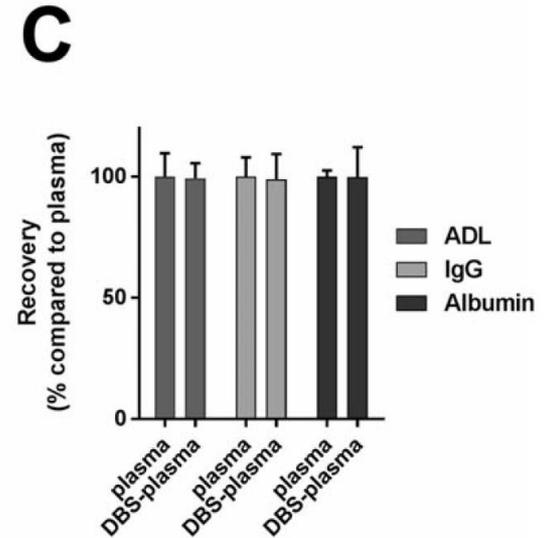
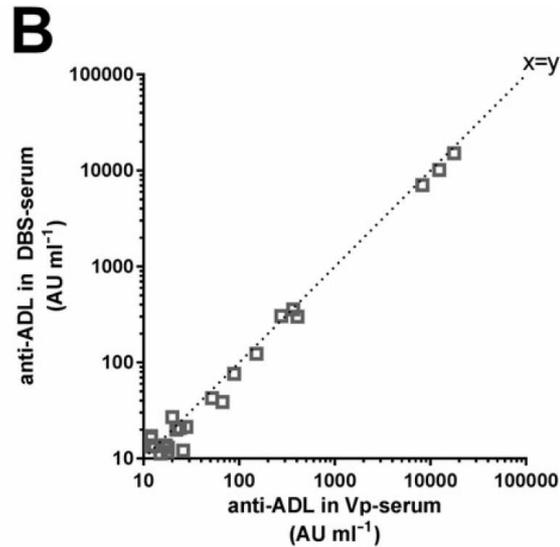
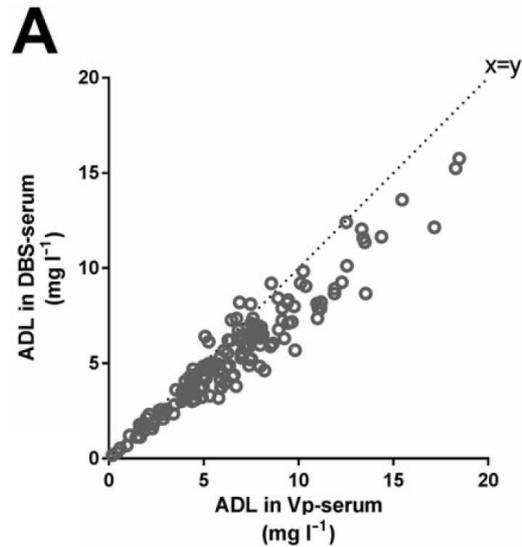
$$V_b = A(\text{hct}) \cdot v(\text{hct})$$

$$c_b = c_e \cdot \frac{V_e}{A(\text{hct}) \cdot (v_0 + v_1 \cdot \text{hct})}$$

$$c_s = \frac{c_b}{1 - \text{hct}}$$

$$c_s = c_e \cdot \frac{1}{1 - \text{hct}} \cdot \frac{V_e}{A(\text{hct}) \cdot (v_0 + v_1 \cdot \text{hct})}$$

Adalimumab in venous vs capillary blood correlates well

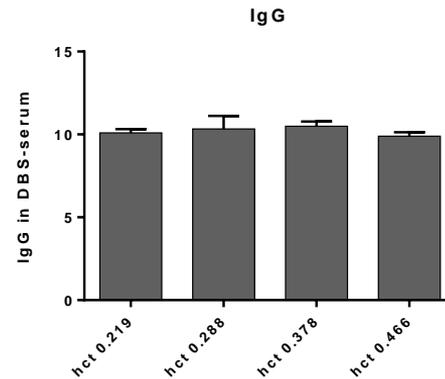
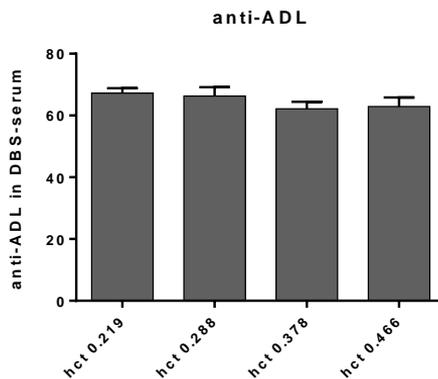
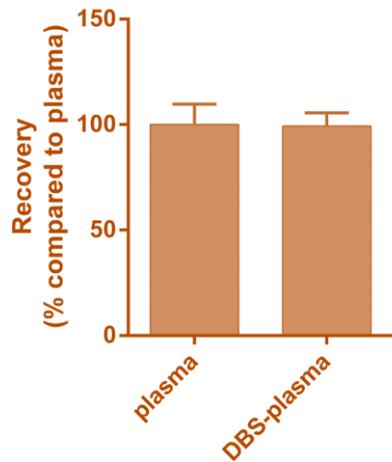


Blood sample



Hct

100% recovery of spiked proteins in spotted DBS eluates



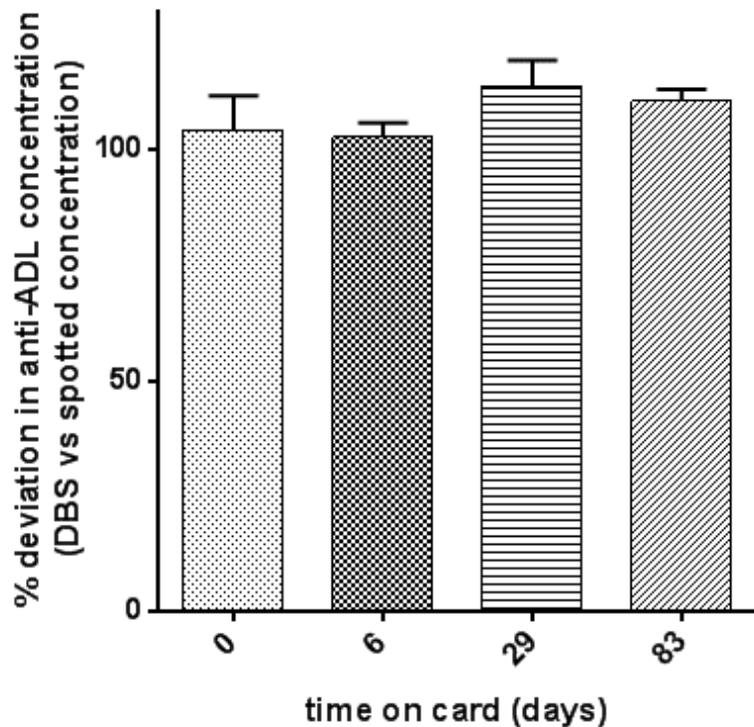
Blood sample



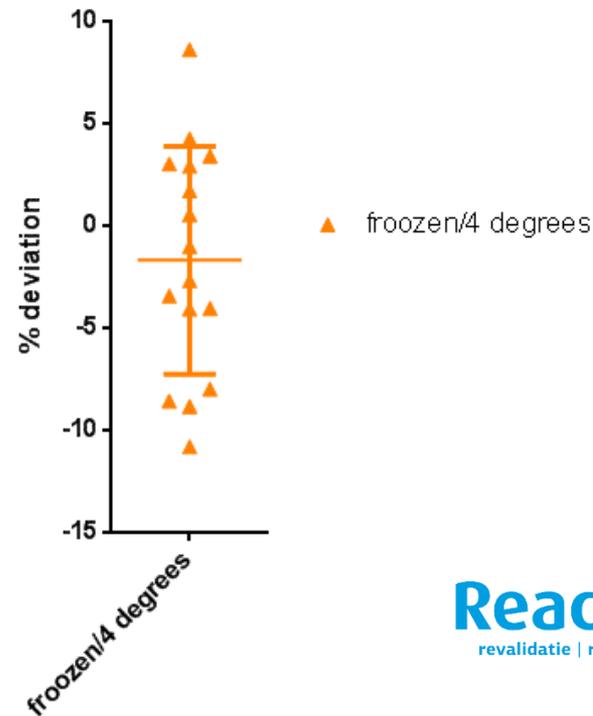
Independent of Hct level

Hct

DBS are stable on filter cards for 3 months



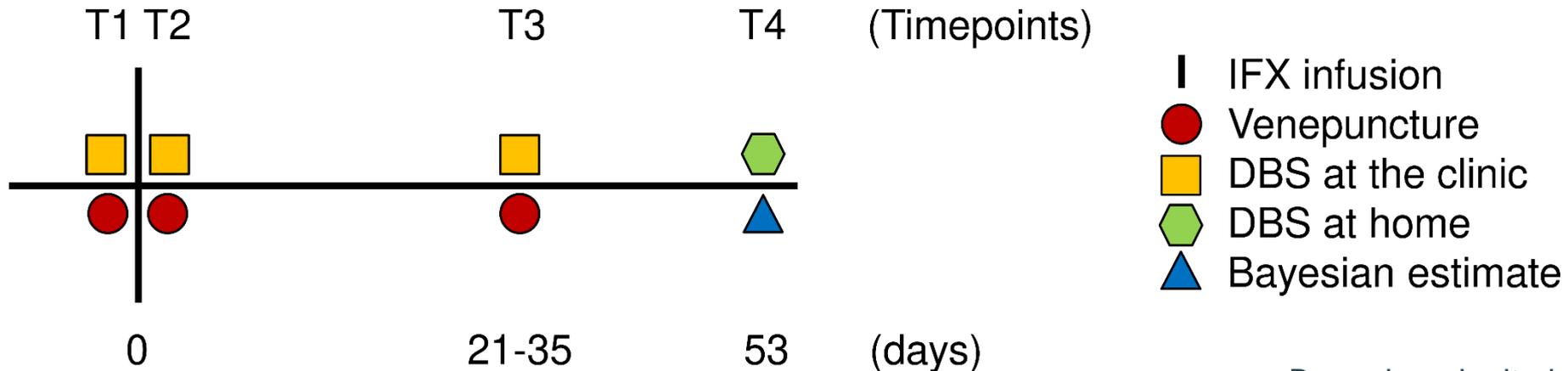
eluates frozen





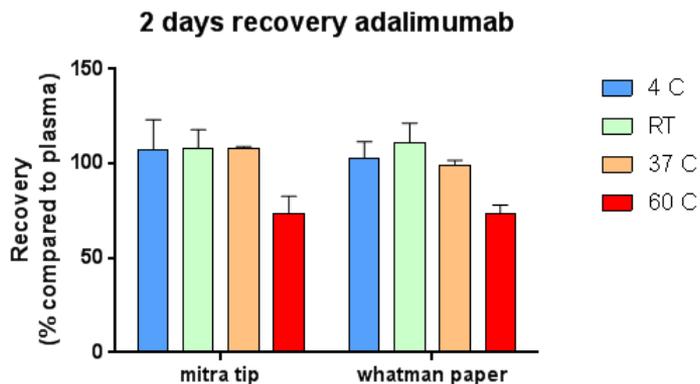
How well does home-sampling work for DBS?

infliximab study; real-life data
simultaneous venous/finger prick and home sampling



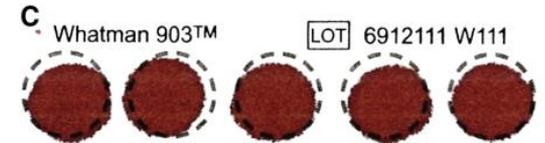
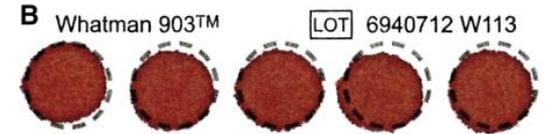
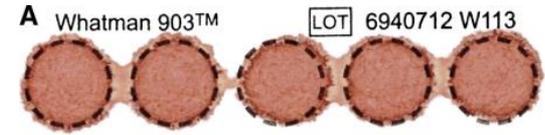
infliximab study

- From DBS to DBS eluate
- 2x20ul sampled by fixed-volume device
- Elute overnight on shaker in tube
- Take supernatant (~500 μ l)



Finger prick sampling paper or fixed volume sampling

- Stability:
 - Good stability
 - At room temperature
 - both eluate and filter paper
- Easy to use
 - For patient
 - For lab
- Easy to implement GxP
- Tips with fixed volume
 - Facilitates quantitative serum measurement



Bioanalysis of Biologics

Assays	Inhibitor PK/ADA tests
TNF inhibitors	adalimumab, infliximab, etanercept, certolizumab, golimumab
B-cell and T-cell inhibitors	vedolizumab, rituximab, natalizumab, abatacept
Other cytokine inhibitors	ustekinumab, tocilizumab, mepolizumab, reslizumab, guselkumab, dupilumab
Glycoprotein Iib/IIIa receptor antagonist	abciximab
HER2 inhibitor	trastuzumab
IgE inhibitor	omalizumab
PD1 inhibitor	nivolumab/pembrolizumab



Drug-tolerant biotin/FLAG-label based homogeneous bridging ELISA for the detection of anti-ustekinumab antibodies



www.sanquin.org/biologics

Annick.deVries@sanquin.nl

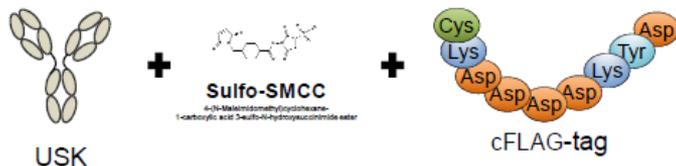
Annick de Vries¹, Floris Loeff², Margreet Hart², Lisanne Dijk², Pleuni Ooijevaar-de Heer², Karien Bloem¹ and Theo Rispens²

¹ *Biologics Laboratory, Sanquin Diagnostics, Amsterdam, The Netherlands.*

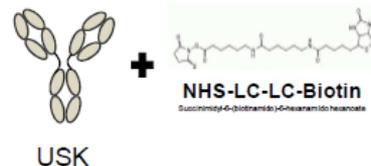
² *Department of Immunopathology, Sanquin Research, Amsterdam, The Netherlands.*

Reagents

1 cFLAG-tagging ustekinumab

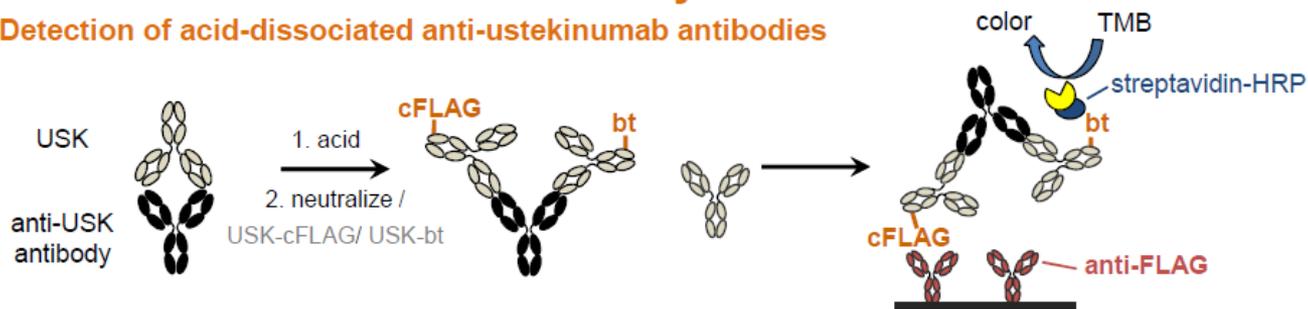


2 Biotin-tagging ustekinumab



Assay

3 Detection of acid-dissociated anti-ustekinumab antibodies





Questions?

Annick.deVries@sanquin.nl

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