



Nabespreking HIM-SKML

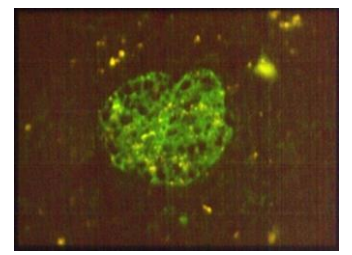
Rondzending Diabetes

Manou Batstra, medisch immunoloog
16 februari 2023

Systematiek van de Rondzending

- 9 samples
- 3 antistoffen:
 - GAD
 - IA2
 - ICA
 - ZnT8?
- In principe wordt consensus uitkomst gehanteerd, expert lab kan “overrulen”

ICA door de jaren

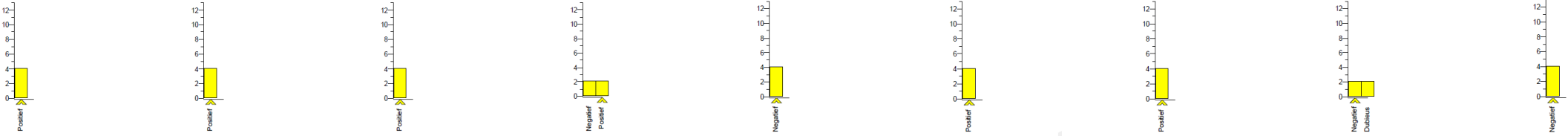


2018

N=4

Technieken: IFA

Leveranciers: 3 - homemade (humaan), INOVA, menarini (primaat)

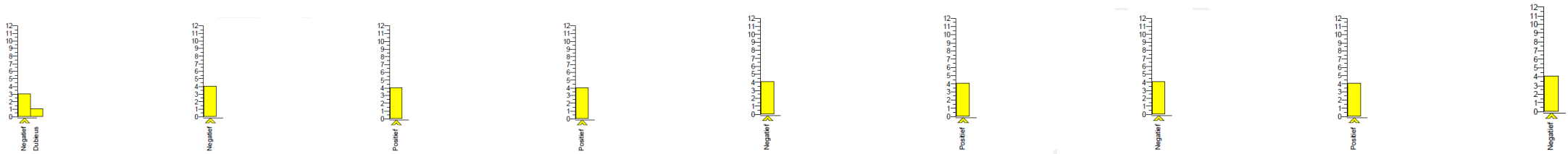


2020

N=4

Technieken: IFA

Leveranciers: 3 - homemade (humaan), INOVA, menarini (primaat)

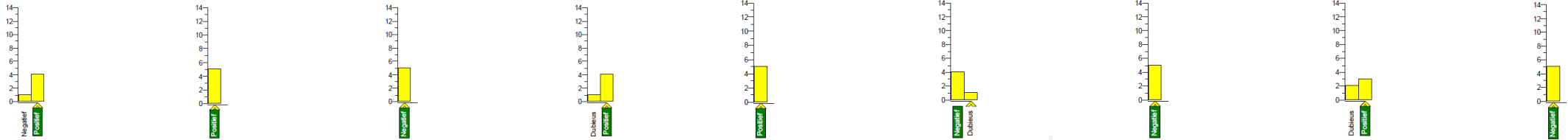


2022

N=5

Technieken: IFA

Leveranciers: 5 - homemade humaan, overigen, menarini, INOVA



ICA in 2022

- Monster A: 1 lab negatief (Menarini)
- Monster D: 1 lab dubieus (Menarini)

- Monster H:
 - ICA+ 64JDFU (sterk positief)
GAD antistoffen (170 – 220 IU/ml)
 - 2 labs ICA dubieus (overigen en Menarini)

- Jongen 8 jaar. Insuline afhankelijk. Uitgeboekt als T1 DM
(2 of meer antistoffen duidelijk positief)

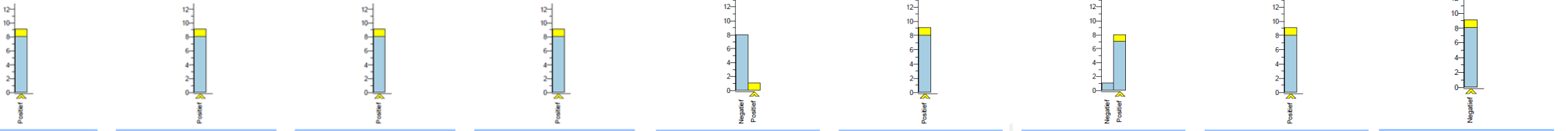
IA2 antistoffendoor de jaren

N= 9

Technieken: ELISA / RIA

Leveranciers: 4 - medipan, euroimmuun, menarini, overig

2018

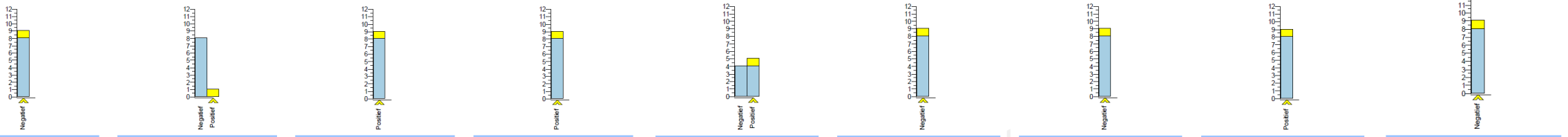


N= 9

Technieken: ELISA / RIA

Leveranciers: 5 - Euroimmuun, ITK, Medipan, Menarini, Overig

2020

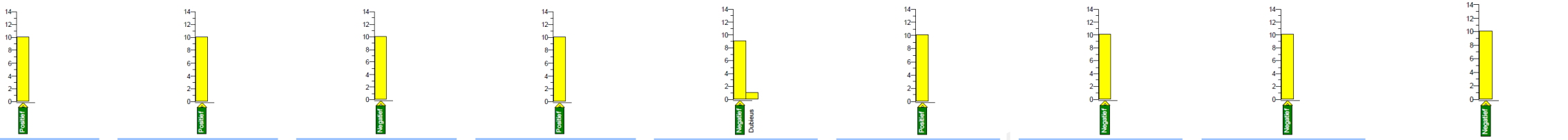


N= 10

Technieken: ELISA

Leveranciers: 4 - ITK, euroimmuun, medipan, overig

2022



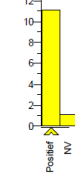
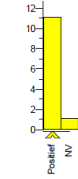
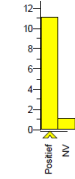
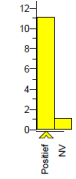
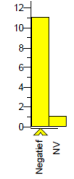
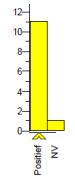
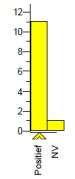
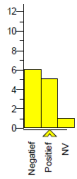
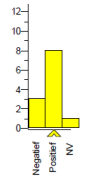
GAD antistoffen door de jaren

2018

N=12

Technieken: ELISA

Leveranciers: 4 - euroimmuun, mediphos, medipan, overig

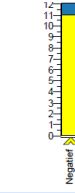
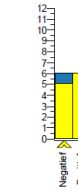
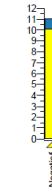
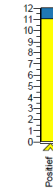
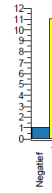
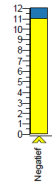
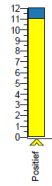
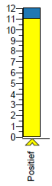
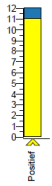


2020

N=12

Technieken: ELISA / RIA

Leveranciers: 5 – euroimmuun, ITK, medipan, mediphos, overig

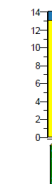
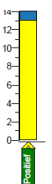
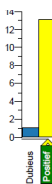
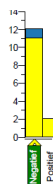
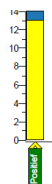
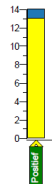
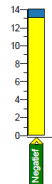
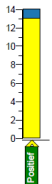
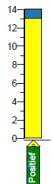


2022

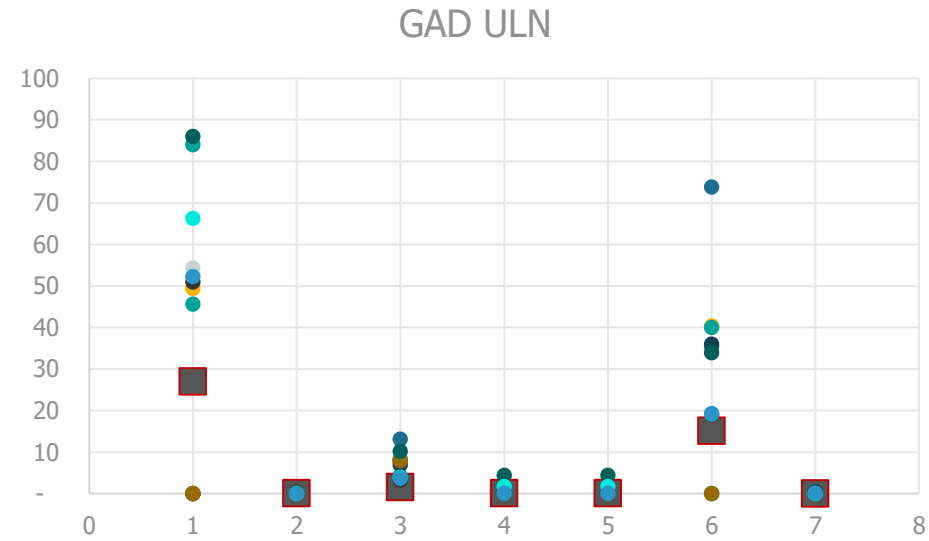
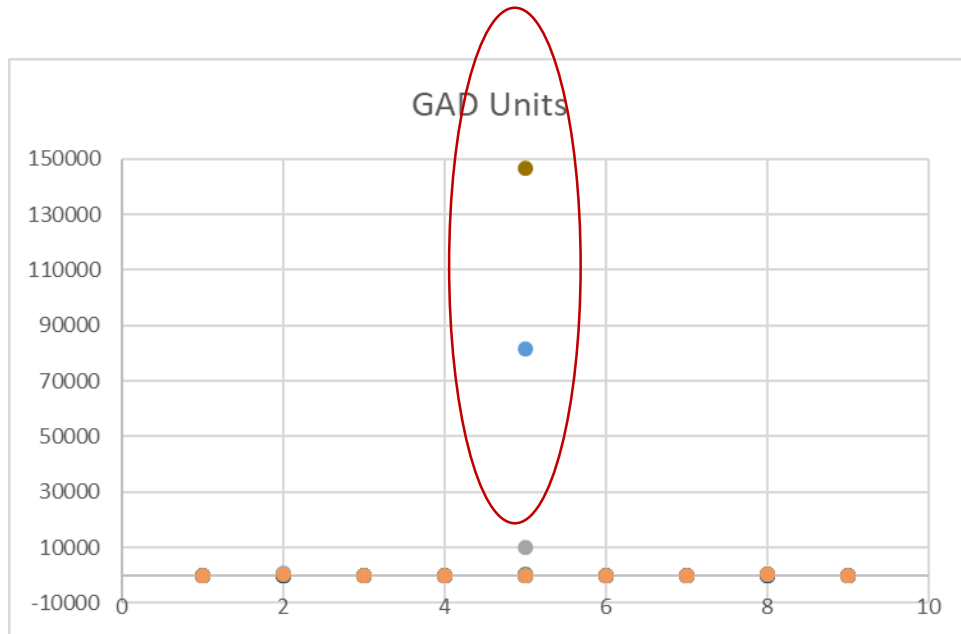
N=14

Technieken: ELISA / RIA

Leveranciers: 5 – ITK, medipan, euroimmuun, mediphos, overig



Samenvatting 2022 - GAD



Monster E:

- Zeer hoge GAD antistof titers (hoogste 146000 IU/ml)



GAD en neurologische ziekten

Baekkeskov et al (1990)

- In 1986 werd voor de zeldzame ziekte **Stiff Person Syndrome (SPS)** de aanwezigheid van antistoffen tegen een eiwit van 65kD beschreven: GAD65
- Associatie van SPS met diabetische ketoacidose
- 1990: De antistoffen tegen een 64kD eiwit bij diabetes patienten bleken ook gericht tegen GAD65
- **SPS:**
lineaire epitopen (western) blot
- **Diabetes type-1:**
conformationele epitopen (RIA, tegenwoordig ELISA)

> [Nature](#). 1990 Sep 13;347(6289):151-6. doi: 10.1038/347151a0.

Identification of the 64K autoantigen in insulin-dependent diabetes as the GABA-synthesizing enzyme glutamic acid decarboxylase

S Baekkeskov ¹, H J Aanstoot, S Christgau, A Reetz, M Solimena, M Cascalho, F Folli, H Richter-Olesen, P De Camilli

Munoz Lopetegi et al (2020):

- 56 patienten met enig neurologisch symptoom en GAD-antistoffen
- 36 patienten met GAD Ab > 10.00 IU/ml
- 34 (94%) specifieke neurologische symptomen passend bij
 - stiff-person syndrome (7)
 - cerebellar ataxia (3)
 - chronic epilepsy (9)
 - limbic encephalitis (9)
 - or an overlap of 2 or more of the former (6)
- **Conclusie: >90% van de patienten met GAD-antistoffen > 10.000 IU/ml heeft GAD gemedieerde neurologische ziekte**

Neurologic syndromes related to anti-GAD65

Clinical and serologic response to treatment

Amaia Muñoz-Lopetegi, MD, Marienke A.A.M. de Bruijn, MD, Sanae Boukhrissi, BSc, Anna E.M. Bastiaansen, MD, Mariska M.P. Nagtzaam, BSc, Esther S.P. Hulsenboom, BSc, Agnita J.W. Boon, MD, PhD, Rinze F. Neuteboom, MD, PhD, Juna M. de Vries, MD, PhD, Peter A.E. Sillevius Smitt, MD, PhD, Marco W.J. Schreurs, PhD, and Maarten J. Titulaer, MD, PhD

Neuro Immunol Neuroinflamm 2020;7:e696. doi:10.1212/NXI.0000000000000696

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Dr. Titulaer
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Reinier de Graaf Gasthuis

Eén internist:

- 3 patiënten met refractaire epilepsie
GAD antistoffen > 25000
GAD blot positief

- **Vraag: hoe vaak komt dit voor in de perifere praktijk?**

219 monsters van nieuwe diabetes patiënten van onze polikliniek interne

- 62 positieven 28%
 - 33 >250 53% (15% van totaal)
 - 9 > 25.000 12% (4% van totaal)
- (waaronder de 3 bekende patiënten)

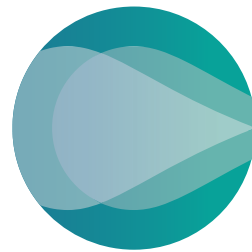
Conclusies

- Aantal deelnemers SKML-HIM diabetes is licht gegroeid
- Gerapporteerde kwantitatieve en kwalitatieve waarden voor GAD- en IA2-antistoffen komen steeds dichterbij elkaar toe
- Voor de ICA blijft een grotere variatie tussen de labs bestaan.
- Meerwaarde titratie GAD antistoffen?
- Behoefte aan ZnT8 antistoffen in rondzending?



Bedankt voor uw aandacht!

Vragen?



Heeft u een goed monster voor de rondzending?
Wij helpen graag met informeren van patient over de extra afname zonder kosten!
Mail: I.bakker@reinier-mdc.nl