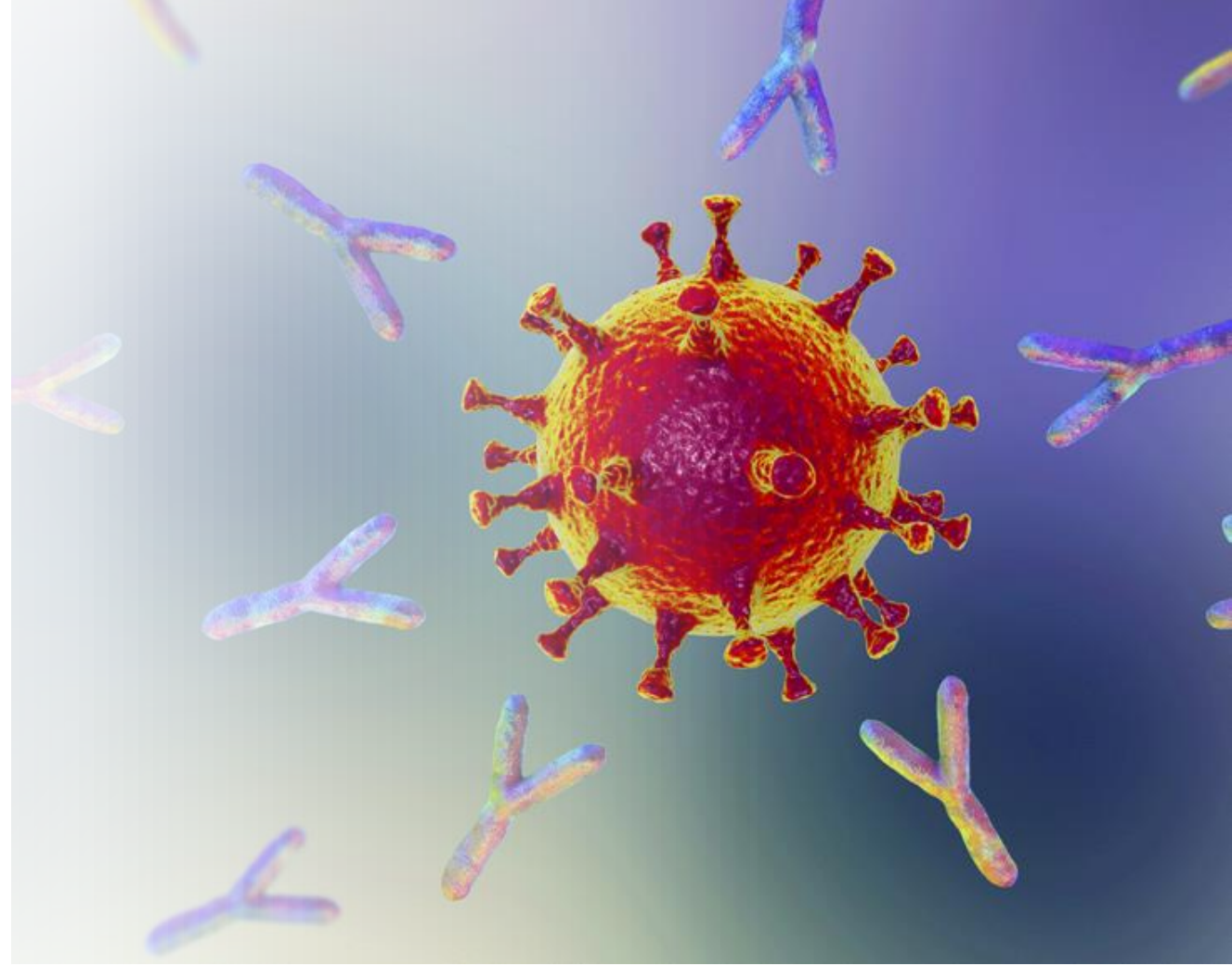


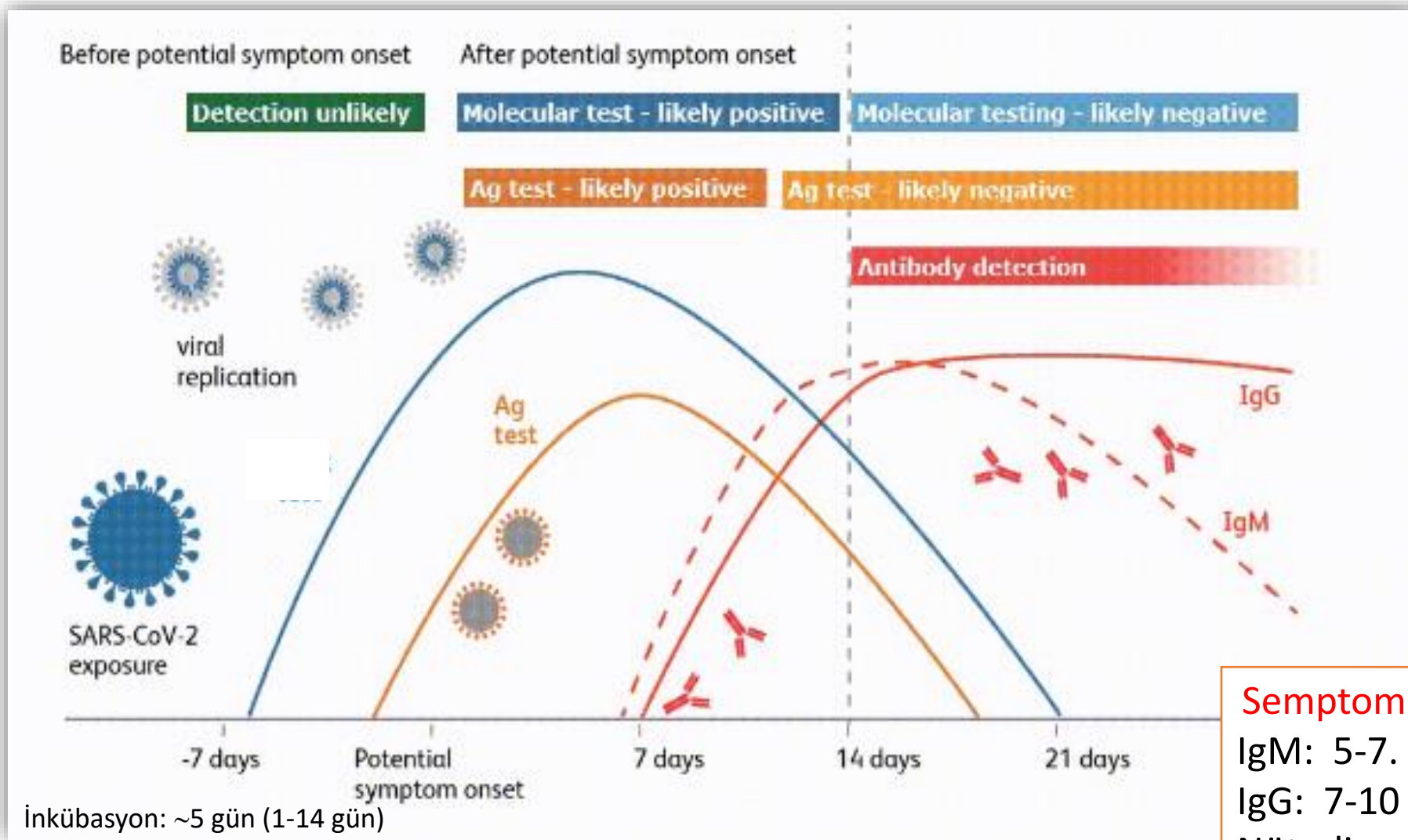
SARS-CoV-2 Antikor Testlerinde Güncel Gelişmeler

Dr. A. Arzu Sayiner

Dokuz Eylül Üniversitesi Tıp Fakültesi Tıbbi
Mikrobiyoloji AD, Tıbbi Viroloji BD

İzmir

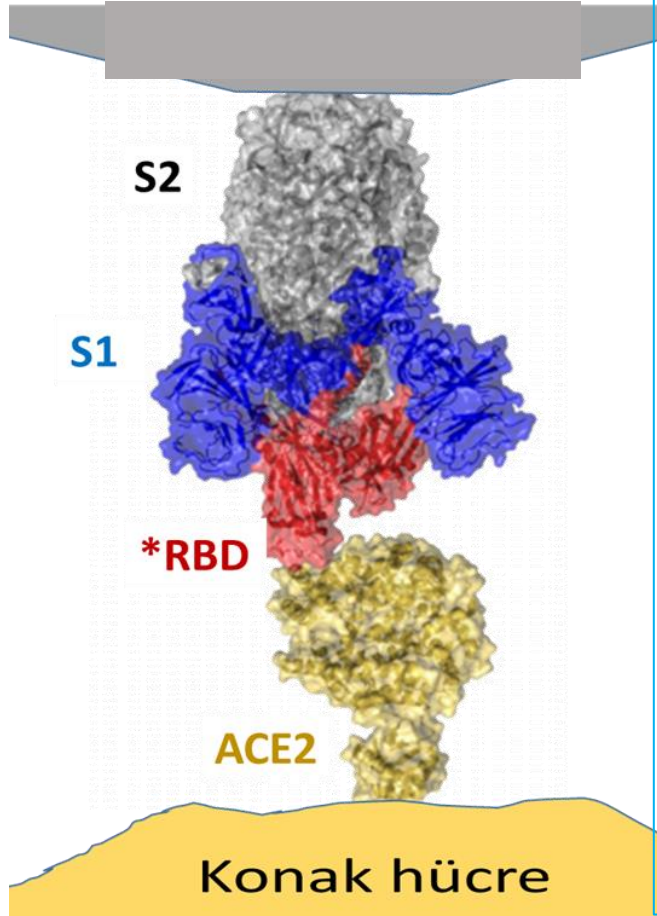




Semptomatik Hastalarda
 IgM: 5-7. günde
 IgG: 7-10 günde
 Nötralizan ab: 11 günde

PCR ve Antijen testleri → Aktif enfeksiyonu saptar
 Antikor testleri → Karşılaşmayı / bağışık yanıtı saptar

Antikor testleri - Antijenler

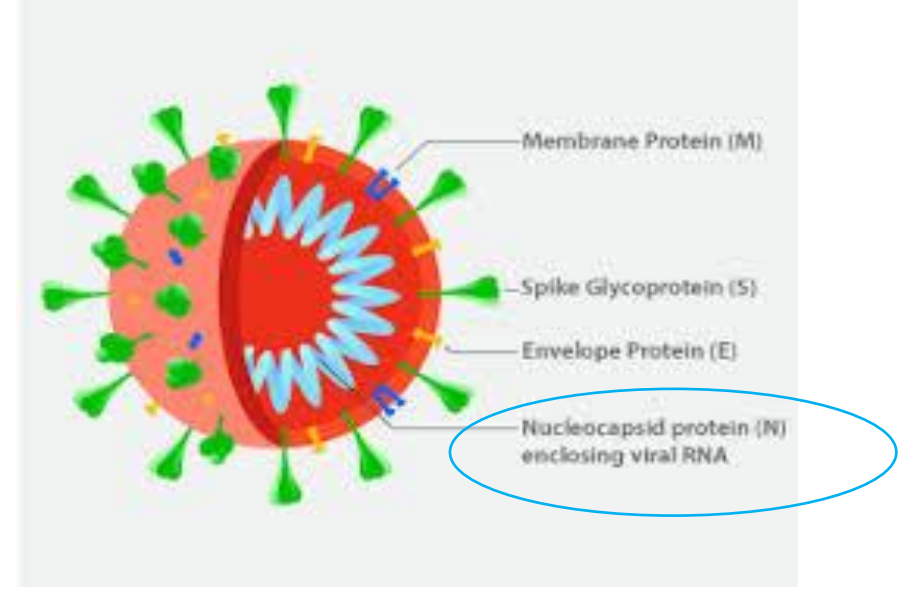


Spike pr

- Büyük: 1273 aa
 - S2: Füzyon
 - S1: Reseptöre tutunma
 - RBD: Nötralizan antikor
- Daha deęişken – özgül
- Kompleks yapı
- Glikolize bölgeleri ve konformasyonel yapı
 - Bu özellikleri taşımayan rekombinant ag – yalancı negatiflik riski

Nükleokapsid pr

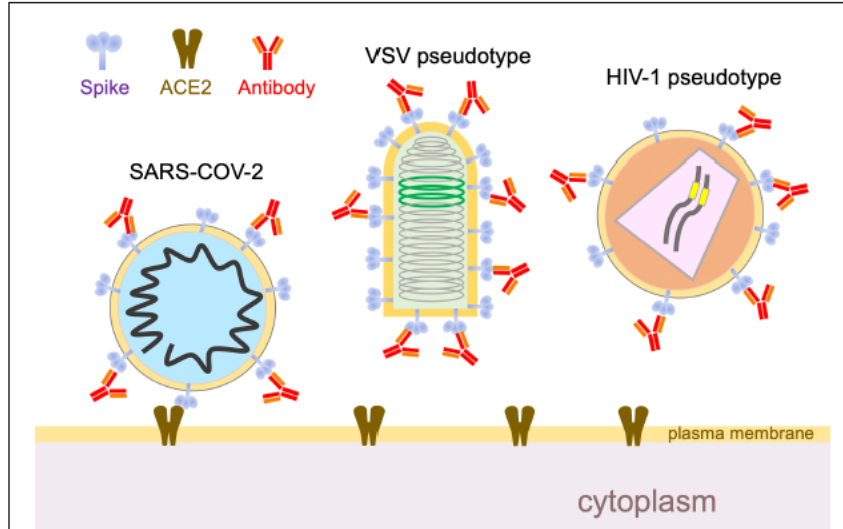
- Küçük
- Glikolize deęil
- Korunmuş bölge
 - Çapraz reaksiyon



Antikor testleri

Bağlanan antikor saptama

- IgM, IgA, IgG, total
- IgA = mukozal immünite
- Yöntem
 - Lateral flow
 - ELISA
 - CIA



Poeschla. eLife 2020;9:e64496.

KLİMUD, 9.05.2021

Nötralizan antikor saptama

- Virüs nötralizasyon testi
 - Plak redüksiyon, mikronötralizasyon
 - Virüs izolatu
 - Pseudovirüs nötralizasyon testi
 - SARS-CoV-2 S pr ekspres eden rekombinant virüs (lentivirus vb)
- ### Yarışmalı nötralizasyon testi
- Antikorların, işaretli RBD ile ACE-2 arasındaki bağlanmayı nötralize etme kapasitesini kalitatif olarak değerlendirir.
 - Canlı virüs gerektirmez
 - Bir adet FDA-hızlı onay almış test



Antikor testleri Seenekler & performansları



Because diagnosis matters

COVID-19

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The list below was compiled from information submitted voluntarily by test suppliers and is not independently verified. If you have any queries or wish for us to make updates in the pipeline, please [contact us](#).

To know more about the FIND evaluations of submitted SARS-CoV-2 tests, click here. [ONGOING TEST EVALUATIONS](#)

SHOW ALL	IMMUNOASSAYS	MOLECULAR ASSAYS	SAMPLE COLLECTION / INACTIVATION	DIGITAL SOLUTIONS	OTHER DIAGNOSTICS
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Status	Test format	Antibody	Regulatory	FILTER	EXPORT TO XLS
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442 RESULT(S)

- [AAZ-LMB](#) COVID-PRESTO@ (CE-IVD) [Contact](#)
- [AB Dianostic Systems GmbH](#) abia SARS-CoV-2 IgG/IgM (CE-IVD) [Contact](#)
- [Abace Biotechnology](#) COVID-19 IgG / IgM Antibody Test Kit (CE-IVD) [Contact](#)
- [Abbott Diagnostics](#) Panbio™ COVID-19 IgG/IgM Rapid Test Device (CE-IVD)
- [Abbott Laboratories](#) Abbott Architect SARS-CoV-2 IgG (US FDA EUA - Singapore HSA - Health Canada - CE-IVD) [Contact 1](#) [Contact 2](#)
- [Abbott Laboratories](#) SARS-CoV-2 IgM Kit (Australia TGA)
- [Abbott Laboratories](#) AdviseDx SARS-CoV-2 IgM (US FDA EUA)
- [Absea Biotechnology Ltd](#) The non-invasive MEGA test of SARS-CoV-2 (mucosal swabs) (In development) [Contact 1](#) [Contact 2](#)
- [Academia Sinica](#) Anti-SARS-CoV-2 nucleocapsid protein human IgM/IgG rapid detection kit (In development) [Contact](#)
- [Access Bio, Inc.](#) CareStart™ COVID-19 IgM/IgG (US FDA EUA - RUO) [Contact](#)
- [AccuBioTech Co. Ltd](#) Accu-Tell COVID-19 IgG/IgM Rapid Test Cassette (CE-IVD) [Contact](#)



COVID-19

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Home > FIND evaluation of SARS-CoV-2 antibody (Ab) detection tests

SARS-CoV-2-specific antibodies are part of the immune response to infection, and may be detected during the early, late, convalescent, and post-recovery phases of disease. They are most useful for identifying recent or prior infection.

In March 2020, FIND launched an expression of interest (EOI) process for test developers interested in having their immunoassays for the detection of SARS-CoV-2 antibodies evaluated using standardized, independent protocols. [Thirty-five RDTs and 16 manual ELISA tests were selected for inclusion in the studies.](#)

In collaboration with partners, FIND conducted multicentre diagnostic evaluation studies from Q2 2020-Q1 2021 of the selected COVID-19 antibody assays using archived, frozen serum/plasma. In addition to clinical samples, we also performed a limited cross-reactivity assessment for the RDTs using samples from individuals confirmed to have had malaria/and or dengue infection. Finally, all tests (RDTs and ELISAs) were tested using a working reference panel developed by the National Institute for Biological Standards and Control (NIBSC). All evaluations are now complete, and results are available.

ANTIBODY TEST EVALUATION PROTOCOL SUMMARY

ANTIBODY EVALUATION METHODOLOGY OVERVIEW

Results for the evaluation of 35 Antibody RDTs:

- The clinical performance estimates for the 35 RDTs which were evaluated can be accessed [here](#).
- The limited cross-reactivity assessment for the RDTs can be accessed [here](#).

Results for the evaluation of 16 Antibody ELISAs

- The overall sensitivity and specificity estimates can be accessed [here](#).
- A sub-analysis on the performance of manual ELISAs according to days post symptom onset can be found [here](#).

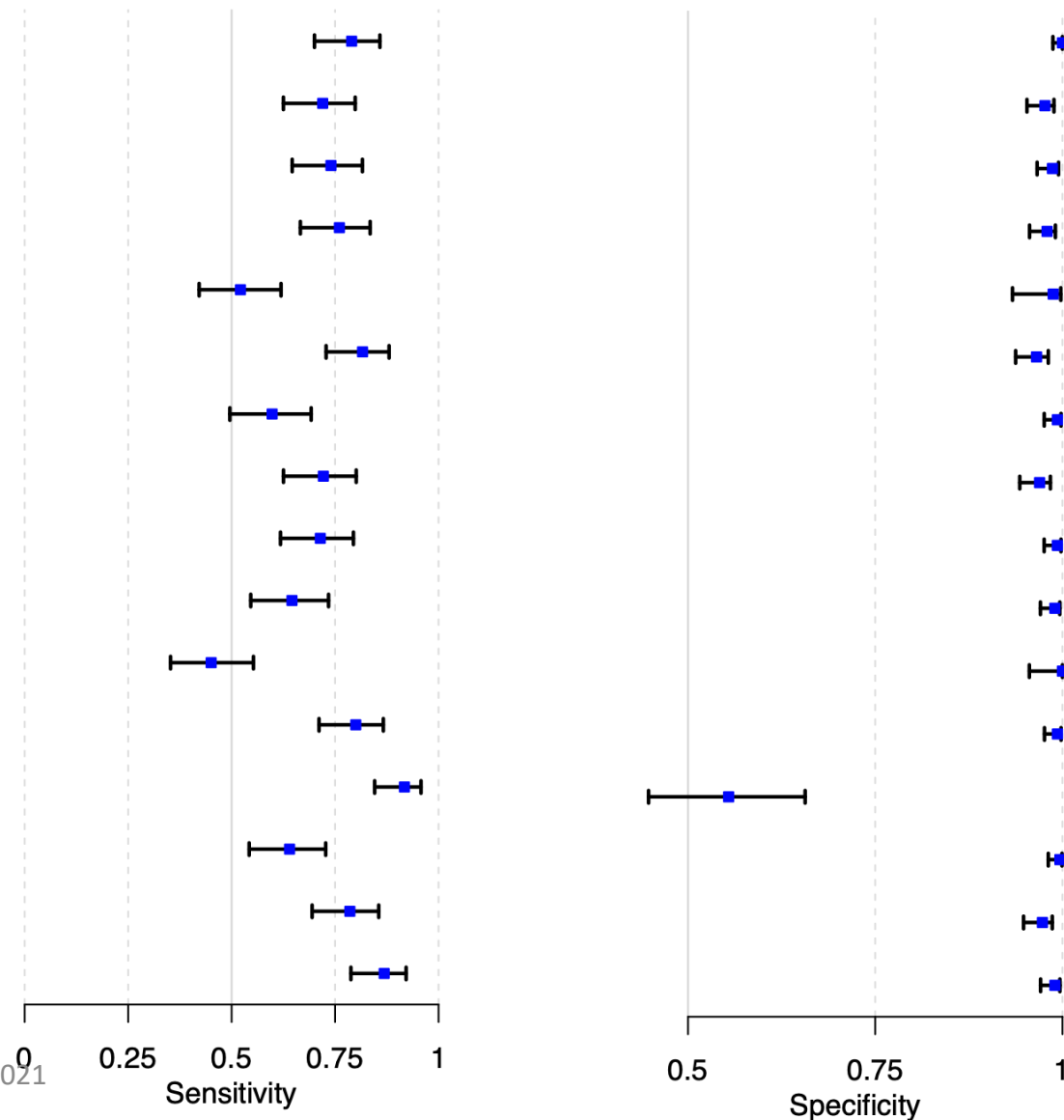
Reactivity of all assays evaluated (RDTs + ELISA) according to the NIBSC panels can be found [here](#).

KLIMOD, 9.05.2021

Group Test N TP FP TN FN Sensitivity [95% CI] Specificity [95% CI]

All

Bio-Rad Total Ab	398	79	0	298	21	0.79 [0.70–0.86]	1.00 [0.99–1.00]
Darui IgG	400	72	7	293	28	0.72 [0.63–0.80]	0.98 [0.95–0.99]
Darui IgM	400	74	4	296	26	0.74 [0.65–0.82]	0.99 [0.97–0.99]
Epitope Dx IgG	389	73	6	287	23	0.76 [0.67–0.83]	0.98 [0.96–0.99]
Epitope Dx IgM*	175	49	1	80	45	0.52 [0.42–0.62]	0.99 [0.93–1.00]
EuroImmune IgA-S	387	80	10	279	18	0.82 [0.73–0.88]	0.97 [0.94–0.98]
EuroImmune IgG-S	388	55	2	294	37	0.60 [0.50–0.69]	0.99 [0.98–1.00]
EuroImmune IgG-N	392	70	9	286	27	0.72 [0.63–0.80]	0.97 [0.94–0.98]
NovaTec IgA	393	70	2	293	28	0.71 [0.62–0.79]	0.99 [0.98–1.00]
NovaTec IgG	392	62	3	293	34	0.65 [0.55–0.73]	0.99 [0.97–1.00]
NovaTec IgM*	174	41	0	83	50	0.45 [0.35–0.55]	1.00 [0.96–1.00]
SD Bio Total Ab	400	80	2	298	20	0.80 [0.71–0.87]	0.99 [0.98–1.00]
Teco IgG*	180	89	37	46	8	0.92 [0.85–0.96]	0.55 [0.45–0.66]
Teco IgM	396	64	1	295	36	0.64 [0.54–0.73]	1.00 [0.98–1.00]
Wantai IgM	397	77	8	291	21	0.79 [0.69–0.86]	0.97 [0.95–0.99]
Wantai Total Ab	397	86	3	295	13	0.87 [0.79–0.92]	0.99 [0.97–1.00]



* did not pass to full panel.

FDA

The screenshot shows the FDA website page titled "EUA Authorized Serology Test Performance". The page includes a navigation bar with the FDA logo and "U.S. FOOD & DRUG ADMINISTRATION". Below the navigation bar, there is a breadcrumb trail: "Home / Medical Devices / Medical Device Safety / Emergency Situations (Medical Devices) / Emergency Use Authorizations for Medical Devices / Coronavirus Disease 2019 (COVID-19) Emergency Use Authorizations for Medical Devices / EUA Authorized Serology Test Performance". The main heading is "EUA Authorized Serology Test Performance". Below the heading, there are social media sharing options for Facebook, Twitter, LinkedIn, Email, and Print. The page content is divided into three columns. The left column contains a sidebar with "Coronavirus Disease 2019 (COVID-19) Emergency Use Authorizations for Medical Devices" and several sub-links: "Blood Purification Devices EUAs", "Continuous Renal Replacement Therapy and Hemodialysis Devices EUAs", "Decontamination System EUAs for Personal Protective Equipment", "In Vitro Diagnostics EUAs", "Infusion Pump EUAs", and "Personal Protective Equipment EUAs". The middle column is titled "About this Page" and contains a paragraph: "Serology tests detect the presence of antibodies in the blood from the body's adaptive immune response to an infection, like COVID-19. They do not detect the virus itself. In the early days of an infection when the body's adaptive immune response is still building, antibodies may not be detected. This limits the test's effectiveness for diagnosing current COVID-19 and is one reason serology tests should not be used to diagnose or exclude acute COVID-19 infection. Serology tests play a role in the fight against COVID-19 by helping health care professionals identify individuals who may have developed an adaptive immune response to SARS-CoV-2. However, to use serology tests properly, it is important to understand their performance characteristics and limitations. Moreover, studies are underway to address questions that will better inform the appropriate use of these tests, such as which antibodies may indicate a level of protection that would prevent or reduce the severity of infection or re-infection as well as the duration for which this protection may last." Below this paragraph, it states: "The performance of these tests is described by their 'sensitivity,' or their ability to identify those with antibodies to SARS-CoV-2 (true positive rate), and their 'specificity,' or their ability to identify those without antibodies to SARS-CoV-2 (true negative rate). A test's sensitivity can be estimated by determining whether or not it is able to detect antibodies in". The right column contains "Content current as of: 04/28/2021", "Regulated Product(s): Medical Devices", and "Health Topic(s): Coronavirus".

The screenshot shows the FDA website page for the "Roche Elecsys Anti-SARS-CoV-2" test. The page title is "Roche Elecsys Anti-SARS-CoV-2". Below the title, it lists: "Developer: Roche", "Test: Elecsys Anti-SARS-CoV-2", "Technology: High Throughput ECLIA", and "Target: Nucleocapsid". Below this information, there are two tables. The first table is titled "Antibody", "Performance Measure", "Estimate of Performance", and "95% Confidence Interval". It contains two rows: "Pan-Ig Sensitivity (PPA) 100% (29/29) (88.3%; 100%)" and "Pan-Ig Specificity (NPA) 99.8% (5262/5272) (99.7%; 99.9%)". The second table is titled "Prevalence Assumption", "Estimate of PPV", and "Estimate of NPV". It contains 11 rows for prevalence assumptions from 5.0% to 50.0%. Below the tables, there is a "Test Facts:" section. A "Top" button is visible in the bottom right corner.

Antibody	Performance Measure	Estimate of Performance	95% Confidence Interval
Pan-Ig	Sensitivity (PPA)	100% (29/29)	(88.3%; 100%)
Pan-Ig	Specificity (NPA)	99.8% (5262/5272)	(99.7%; 99.9%)

Prevalence Assumption	Estimate of PPV	Estimate of NPV
5.0%	96.5% (95% CI: 93.0%; 98.1%)	100% (95% CI: 99.4%; 100%)
10.0%	98.3% (95% CI: 96.6%; 99.1%)	100% (95% CI: 98.7%; 100%)
15.0%	98.9% (95% CI: 97.8%; 99.4%)	100% (95% CI: 98.0%; 100%)
20.0%	99.2% (95% CI: 98.4%; 99.6%)	100% (95% CI: 97.1%; 100%)
25.0%	99.4% (95% CI: 98.8%; 99.7%)	100% (95% CI: 96.2%; 100%)
30.0%	99.6% (95% CI: 99.1%; 99.8%)	100% (95% CI: 95.2%; 100%)
35.0%	99.6% (95% CI: 99.3%; 99.8%)	100% (95% CI: 94.1%; 100%)
40.0%	99.7% (95% CI: 99.4%; 99.8%)	100% (95% CI: 92.7%; 100%)
45.0%	99.8% (95% CI: 99.5%; 99.9%)	100% (95% CI: 91.2%; 100%)
50.0%	99.8% (95% CI: 99.6%; 99.9%)	100% (95% CI: 89.5%; 100%)

FDA - Üretici bilgileri + bağımsız değerlendirme
65 EUA onaylı test (Ocak 2021)

Duyarlılık ve özgüllük:

İngiltere : $\geq 98\%$

FDA Duyarlılık: $\geq 90\%$ Özgüllük: 95%

<https://open.fda.gov/apis/device/covid19serology/>



AMERICAN
SOCIETY FOR
MICROBIOLOGY

Journal of
Clinical Microbiology®

JCM 2021; 59

Comparison of 16 Serological SARS-CoV-2 Immunoassays in 16 Clinical Laboratories

- Danimarka ulusal değerlendirme çalışması
- 15 ticari, 1 lab yapımı test
 - 6 total ab, 7 IgG, 3 IgM
- 150 örnek ile duyarlılık; >586 örnek ile özgüllük

- Ag farkının test performansına etkisi yok.
- Hastalığın şiddeti ve semptom başlangıcına göre geçen süre ab yanıtını etkiliyor
 - Testlerin duyarlılık farkları, semptom başlangıcına göre ≤ 3 hft olan örneklerde daha fazla
- 4 olguda tüm testler ile ab yok (3'ü hafif enf)

Duyarlılık
%96.7 – 95.9

%81

%95.9 – 87.0

%82.7-26.4

Total-Ab assays

Wantai ELISA
In-house CUH-NOVO ELISA
Ortho CD Vitros
Siemens Atellica
Roche Elecsys

Siemens Vista

IgG assays

YHLO iFlash
Ortho CD Vitros
Abbott Architect
Abbott Alinity

Euroimmun ELISA
Snibe Maglumi

DiaSorin Liaison XL

IgM assays

Wantai ELISA
YHLO iFlash
Snibe Maglumi

Özgüllük
 ≥ 99

%97.2

%99 – 96.3

Comparison of 16 Serological SARS-CoV-2 Immunoassays in 16 Clinical Laboratories

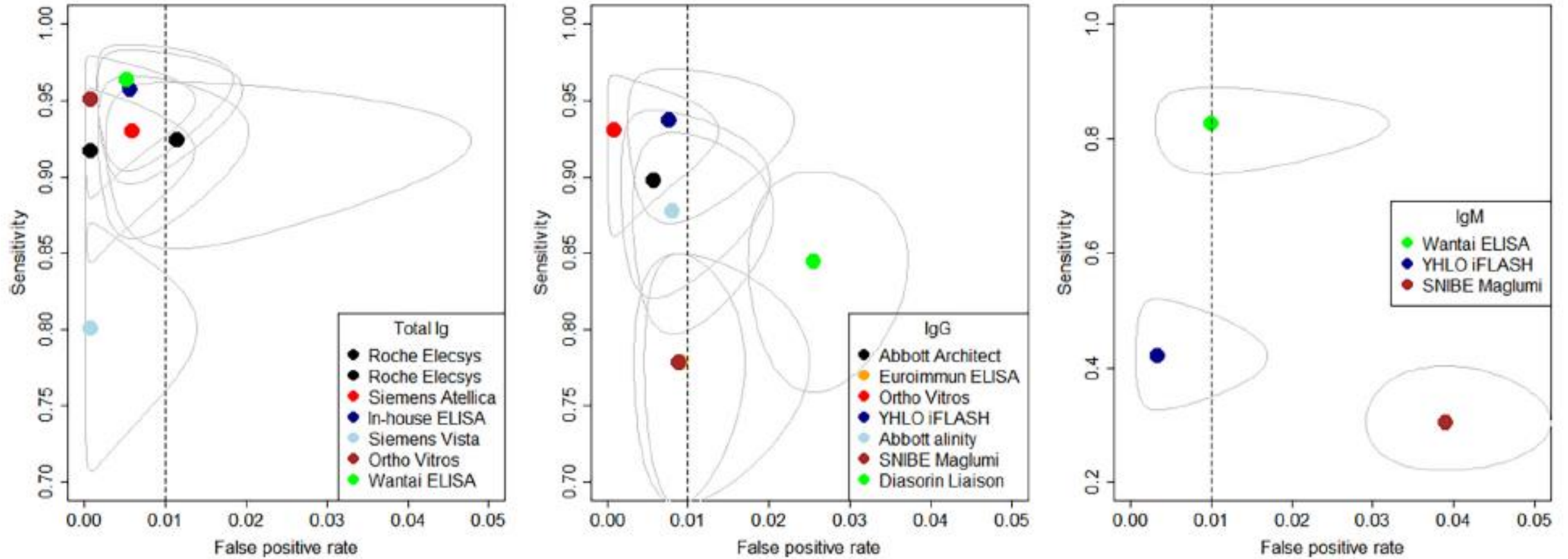
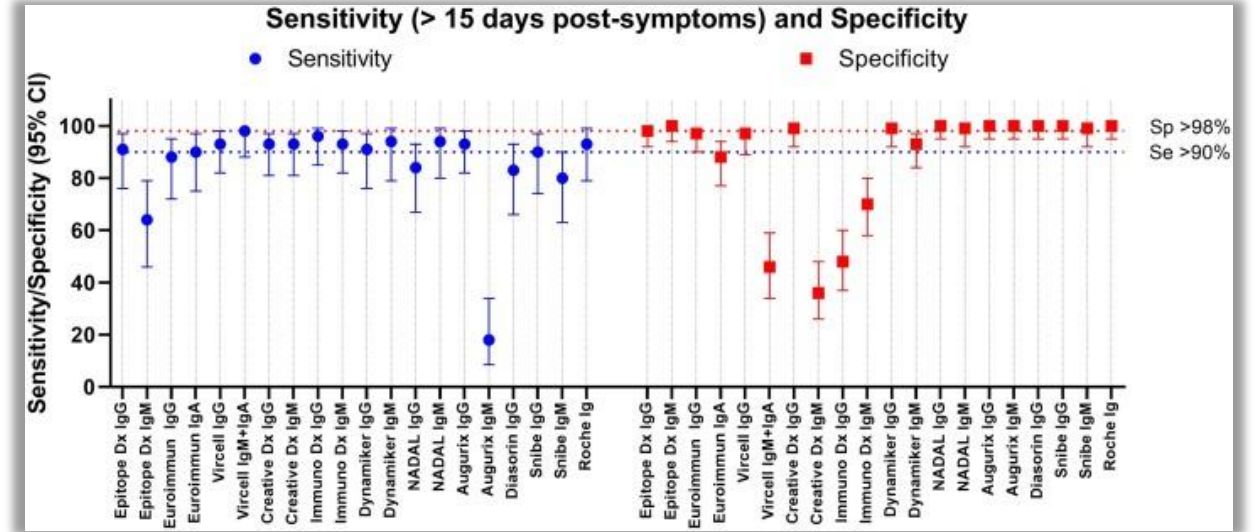


FIG 1 Summary ROC plot of sensitivity and false-positive rate with elliptic 95% bivariate confidence regions corresponding to the data in Table 3 for assays with total Ig, IgG, and IgM, respectively.

Comparison of SARS-CoV-2 serological tests with different antigen targets

J Clin Virol 2021;134:104690

- 17 test
 - 10 ELISA, 3 LFA, 3 CLIA, 1 ECLIA
 - IgG, IgM, IgA, IgM+IgA, IgM+IgG, total
- Özgüllük, duyarlılık, zaman ile ilişki
- 8 adet total / IgG testleri arasında
 - 5 tanesi = >%90 duyarlılık, >%98 özgüllük
- 6 IgM/IgA testleri arasında
 - 1 tanesi duyarlılık >%80, özgüllük >%99
- LFA
 - 1 tanesi başarılı

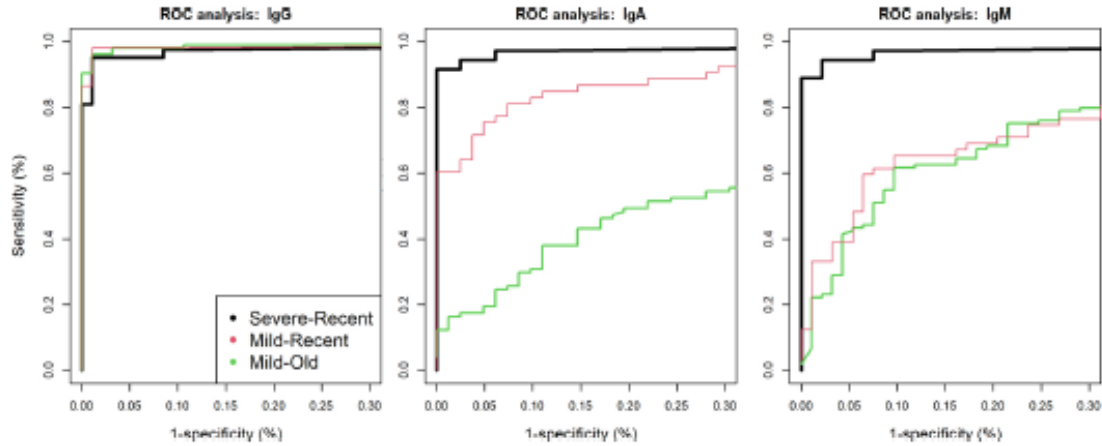


- Bazı hastalarda geç ab yanıtı (>25 gün post-semptom)
- N ve S ab arası zaman farkı yok
- M ve G birlikte saptanıyor.

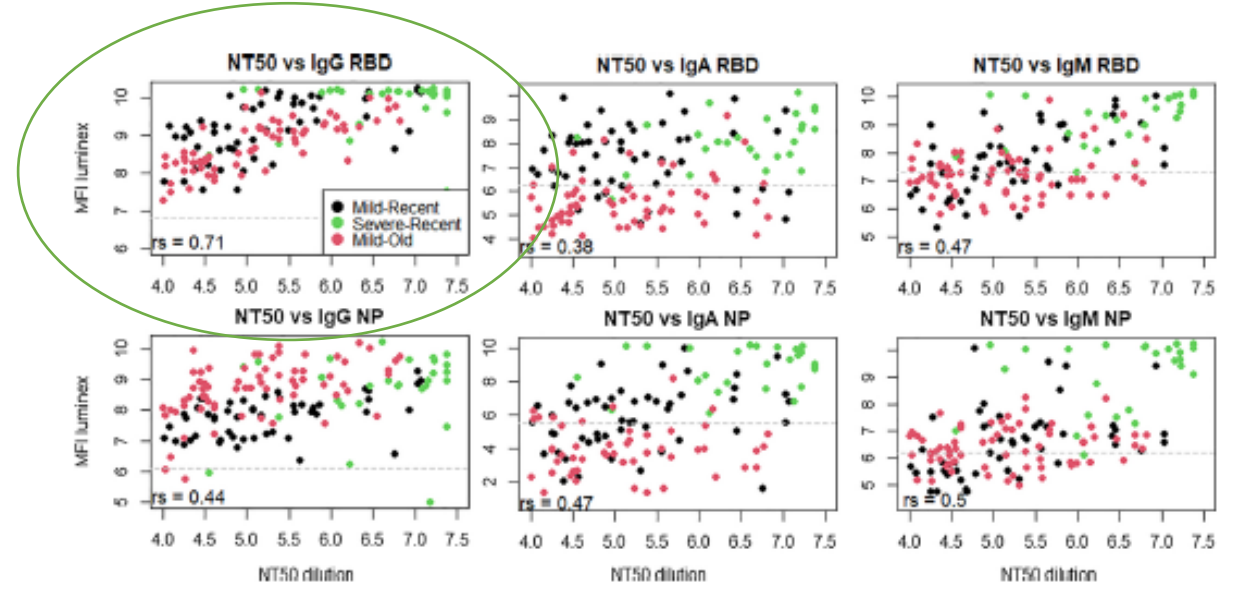
Evaluating SARS-CoV-2 spike and nucleocapsid proteins as targets for antibody detection in severe and mild COVID-19 cases using a Luminex bead-based assay

J Virol Methods 2021;288:114025

- 296 serum
- RBD, S1, S1S2, N
- IgG, IgM, IgA



IgG tüm dönemlerde ve farklı klinik tablolarında anlamlı
IgM ve IgA ciddi enfeksiyonda erken dönemde anlamlı



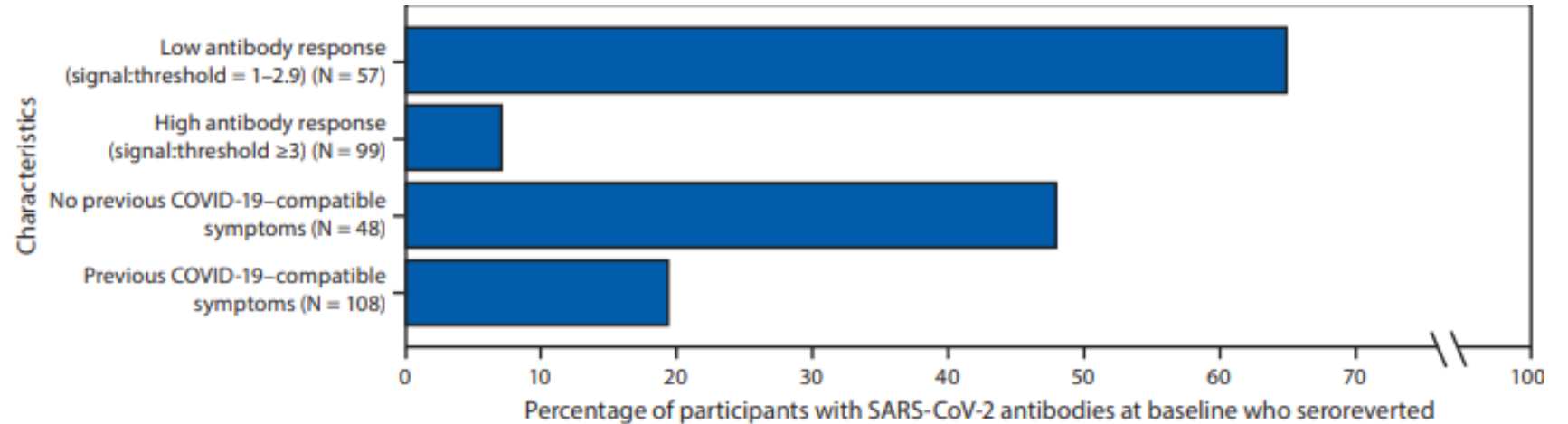
Nötralizan antikorlar RBD-IgG ile korele
Nötralizan ab en az 5 ay kalıcı ancak titre enf. şiddeti ile ilişkili
RBD özgül, N duyarlı → birlikte kullanımı başarılı

Antikorların saptanma süreleri nedir?

Decline in SARS-CoV-2 Antibodies After Mild Infection Among Frontline Health Care Personnel in a Multistate Hospital Network — 12 States, April–August 2020

- 194 antikor pozitif SÇ → anti-S total ab, CDC
- 60 gün sonra %93.6'sında ab düzeyinde azalma
 - 44 kişi (%28) seronegatif
 - Başlangıç ab düzeyi düşük olanların (S/CO 1.0-2.9) %65'i
 - Semptomsuzlar

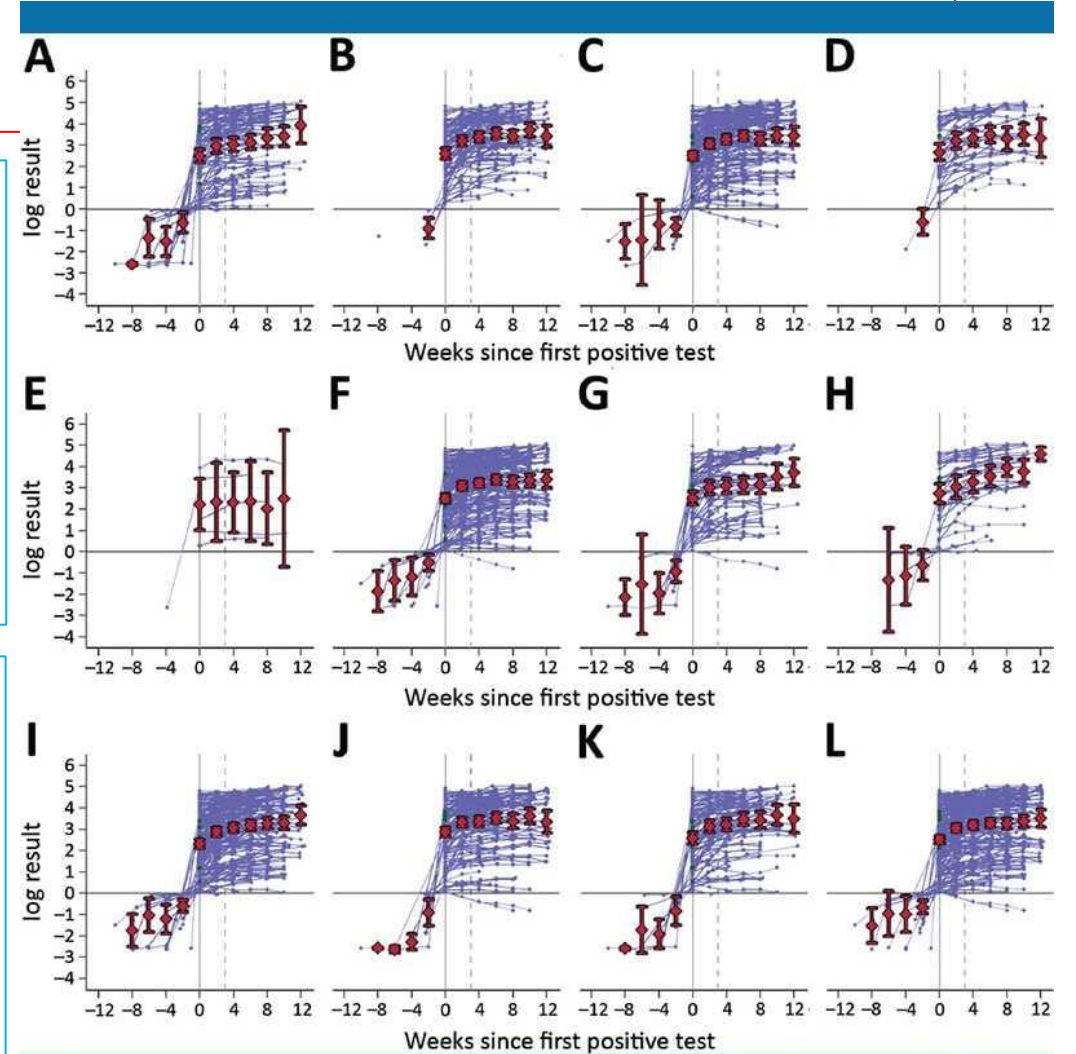
- Seroprevalans çalışmalarında ve geçirilmiş enfeksiyonu belirlemede sorun
- Klinik anlamı ?



Persistence of SARS-CoV-2 N-Antibody Response in Healthcare Workers, London, UK

Emerging Infectious Diseases 2021;27:1155

- 1069 SÇ → Mart - Temmuz 2020
 - 14 günde bir kan alımı
 - 312 (%29) birden çok örnek
 - 181 (%58) ≥ 8 örnek
 - 42 (%13) ≥ 12 örnek
 - Elecsys total antikor (N ab)
-
- %30 Ab (+)
 - Seronegatifleşme 4 kişide
 - Seropozitifleşme 33 kişide
 - **Log titre stabil**, hafif artış (haftalık %4 artış)
 - N ab → enfeksiyon sürveyansı için daha uygun



Medscape

Klinik, görev yeri, yaşa göre alt gruplar

SARS-CoV-2 antibodies remain detectable 12 months after infection and antibody magnitude is associated with age and COVID-19 severity

medRxiv preprint, May 2, 2021

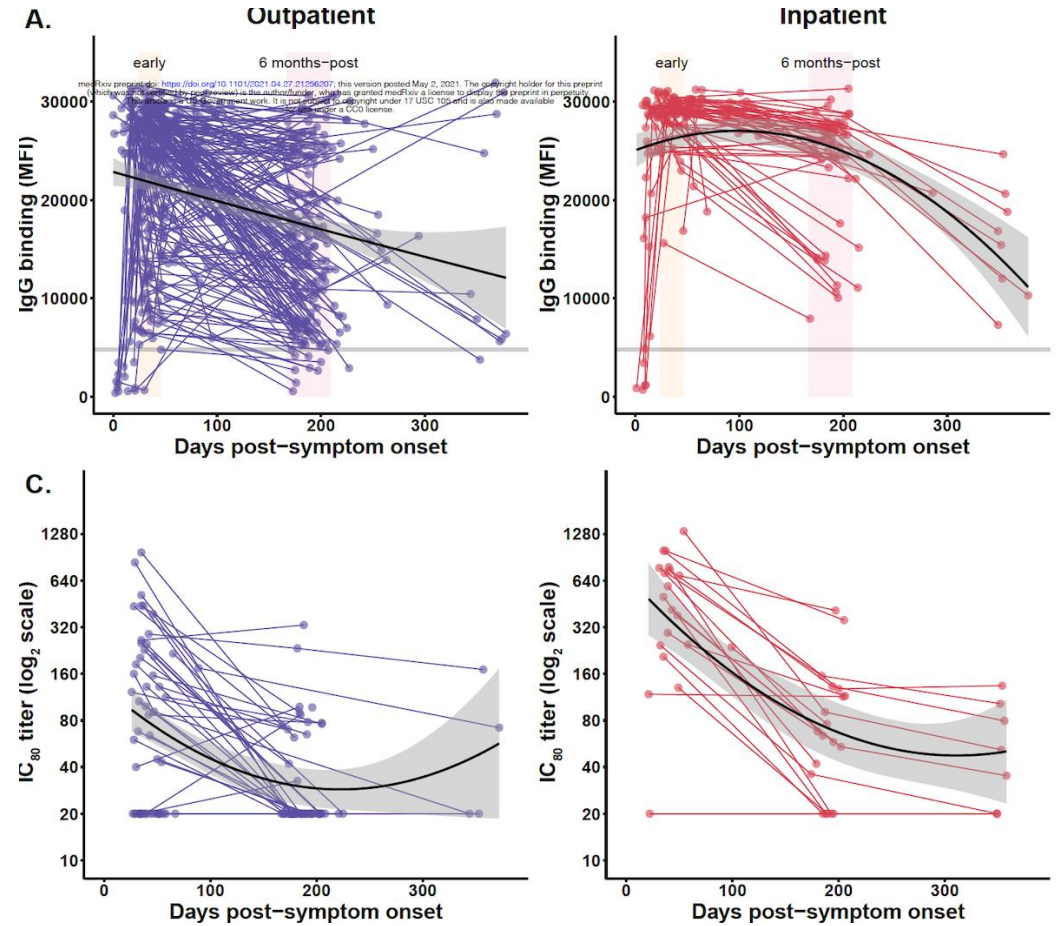
- Mart 2020-Mart 2021
- 192 ayakta, 58 yatan hasta
 - 12. ay kontrol: 11 ayakta, 8 yatan
- Yöntem:
 - Lab yapımı anti-S IgG & Nötralizan ab

IgG

- Ayaktan hastalarda
 - 6. ayda tümü pozitif
 - 6-10 ayda %5 negatifleşme (n: 192)
 - 12. ayda %18 negatifleşme (n: 11)
- Yatan hastalarda
 - 6. ve 12. ayda tümü pozitif

Ab kaybı:

- <65 yaş ve ayakta hst
- Nötralizan ab:
 - Yatan hst. da ↑
 - >44 yaş hst. da ↑



Saptanan antikorlar enfeksiyona karşı
koruyucu mu?

SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study (SIREN) *Lancet 2021;397:1459–69*

25 661 kişi
PCR ve antikor testi (her 2-4 haftada bir)
Sorgulama (her 2 haftada bir)

Haziran 2020 – Ocak 2021 arası veri
Enfeksiyon kanıtı = PCR (+)

SONUÇ

- Enfeksiyonu geçirenlerde, enfekte olma riski %84 daha düşük.
- Koruyucu süre en az 7 ay

POZİTİF KOHORT

8278 kişi

155 re-enfeksiyon

İnsidans

7.6 / 100 000 kişi-gün

İlk enfeksiyon ile re-enfeksiyon arası >200 gün

NEGATİF KOHORT

17 383 kişi

1704 enfeksiyon

İnsidans

57.3 / 100 000 kişi-gün

Association of SARS-CoV-2 Seropositive Antibody Test With Risk of Future Infection

- 3 257 478 kişi – kohort
 - %11.6 antikor (+)
 - %18.4 seronegatifleşme
 - %88.3 antikor (-)

Seropozitif/seronegatif PCR (+) riski

0-30 gün 2.85 (virüs saçımı)

31-60 gün 0.67

61-90 gün 0.29

>90 gün 0.10

Seropozitiflik enfeksiyondan korunmada etkili

SARS-CoV-2 seropositivity and subsequent infection risk in healthy young adults: a prospective cohort study

Lancet Respir Med, 2021

- 3076 asker – 6 hafta
 - 189 ab (+) → %10 enfeksiyon
 - Viral yük düşük
 - Başlangıç anti-S IgG titresini düşük olmak risk faktörü
 - 2247 ab (-) → %48 enfeksiyon

Seropozitiflerin enfeksiyon riski, seronegatiflere göre 1/5



Antikorlar büyük oranda koruyucu ancak nötralizan etki garantisiz

Antikor testlerinde standardizasyon ve koruyuculuk eşik değeri belirlenmesi

WHO

National Institute for Biological Standards and Control (NIBSC)

Standart adı	NIBSC kod numarası
First WHO International Standard for anti-SARS-CoV-2 immunoglobulin, human	20/136
First WHO International Reference Panel for anti-SARS-CoV-2 immunoglobulin, human	20/268
Anti-SARS-CoV-Verification Panel for Serology Assays	20/B770
Anti-SARS-CoV-2 Antibody Diagnostic Calibrant	20/162
External Quality Control reagent for anti-SARS-CoV-2 antibody	20/B764
Research reagent for anti-SARS-CoV-2 Ab	20/130

WHO International Standard for anti-SARS-CoV-2 immunoglobulin

Lancet 2021;397:1347-8

- CEPI, NIBSC, WHO işbirliği
- Uluslararası standart
 - 44 lab – 15 ülke
 - Lab arası varyasyonlarda
 - Nötralizasyon testleri için 50 kat,
 - ELISA testleri için 2000 kat azalma
- Tüm çalışmalarda IU ve/veya BAU kullanılması
 - Aşı, seroprevalans, terapötik antikor, antikorların varyantlar üzerindeki etkinliği, vb
 - Tüm kuruluşlara ve dergi editörlerine çağrı

WHO Reference Panel
First WHO International Reference Panel for anti-SARS-CoV-2
immunoglobulin
NIBSC code: 20/268

	High 20/150	Mid 20/148	low S, high N 20/144	Low 20/140	
Neut Ab	1473	210	95	44	IU/mL
anti-RBD IgG	817	205	66	45	BAU/mL
anti-S1 IgG	788	246	50	46	BAU/mL
anti-Spike IgG	832	241	86	53	BAU/mL
anti-N IgG	713	295	146	12	BAU/mL

Data Sheet
Research reagent for
anti-SARS-CoV-2 Ab
NIBSC code 20/130
(Version 2, Dated 17/01/2021)

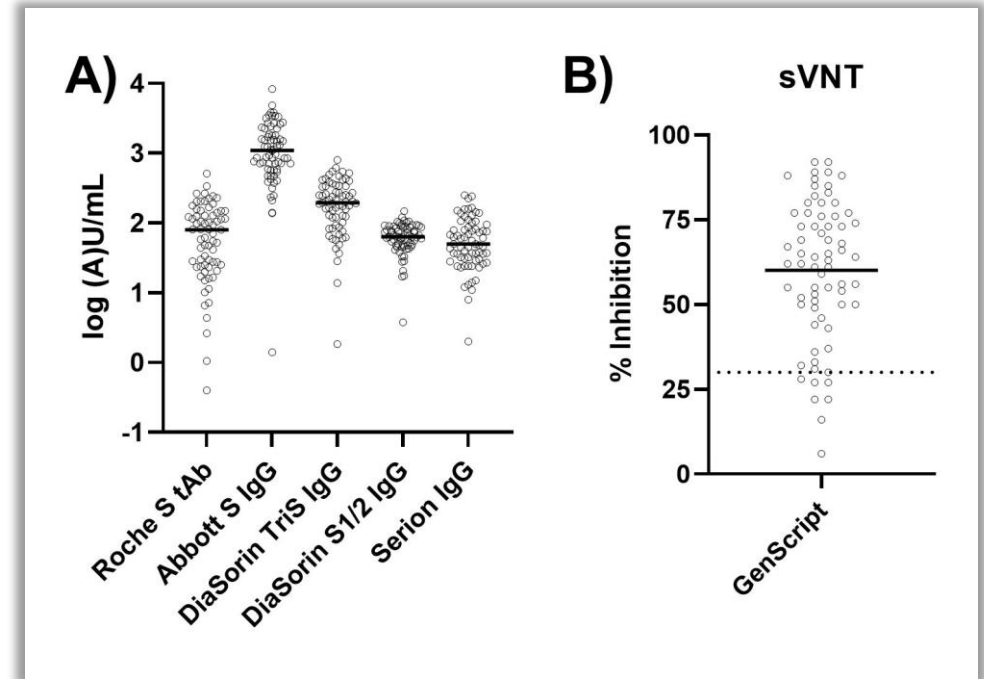
	GM	95% CI	
Neut Ab	1300	981-1719	IU/mL
anti-RBD IgG	502	382-660	BAU/mL
anti-S1 IgG	588	398-870	BAU/mL
anti-Spike IgG	476	418-542	BAU/mL
anti-N IgG	747	214-2606	BAU/mL

Anti-spike protein assays to determine post-vaccination antibody levels: a head-to-head comparison of five quantitative assays

MedRxiv Mar 8, 2021

- 69 kişi - 1 doz Biontech aşı 21 ± 1 gün sonrası
- 5 kit arası uyum $p=0.80-0.94$
 - BAU/ml çevrimi ile sonuç değişmiyor
- 7 (%10) kişide sVNT negatif (<%30 inhib)

Test	Ab	Ag	Range	CO	BAU
Roche Elecsys	RBD	total	0.4 – 2500 U/ml	0.8	X 1
Abbott Quant	RBD	IgG	21 – 40 000 AU/ml	50	X 1/7
DiaSorin trimeric	TriS	IgG	1.63 – 800 AU/ml	13	X 2.6
DiaSorin Liaison	S1/2	IgG	3.8– 400 AU/ml	15 GZ	-
Virion Serion	S	IgG	3 – 250 U/ml	15 GZ	X 2.1



Prognosis

Oxford Starts First Study to Reinfect Recovered Covid Patients

By [Todd Gillespie](#)

April 19, 2021, 2:01 AM GMT+3

- ▶ Researchers seek 64 healthy, previously infected volunteers
- ▶ Challenge trials hold advantages for studying viral activity

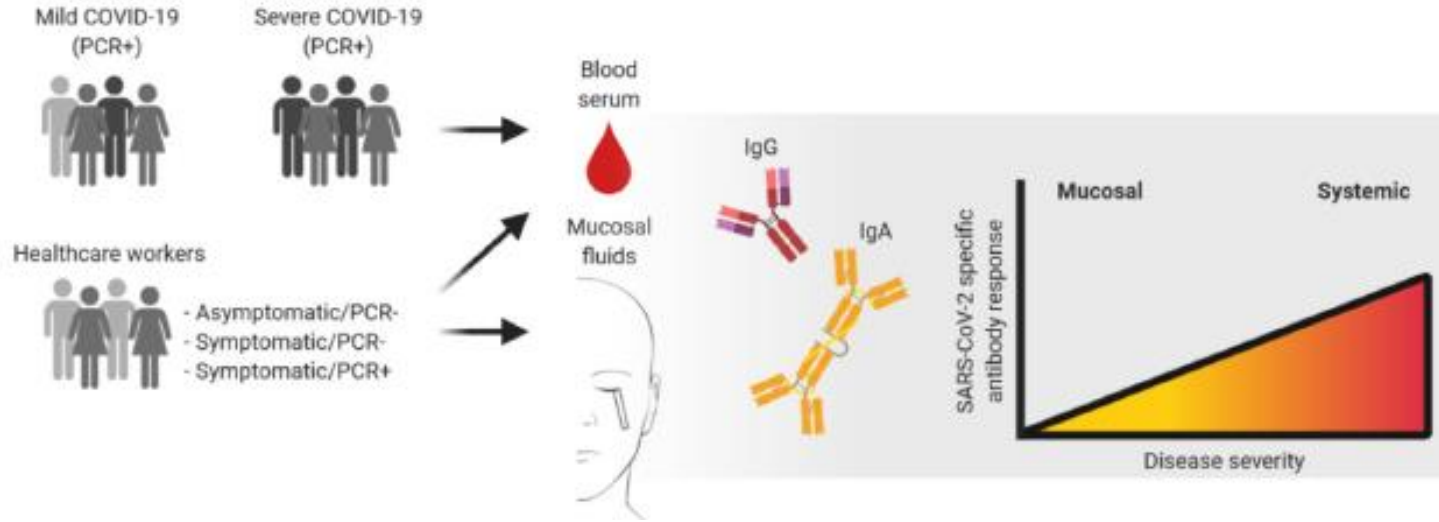
- 18-30 yaş arası, daha önce COVID-19 geçirmiş sağlıklı gönüllüler (64 kişi)
- Enfeksiyon gelişirse terapötik ab (REGEN-COV™ (casirivimab + imdevimab, Regeneron))

Koruyucu antikor miktarı nedir?

- Aşıllılarda / enfeksiyon geçirenlerde koruyuculuk süresini belirleme
- Hangi tür immün yanıt(lar)ın korunmada rol oynadığını belirleme
- Yeni aşıllarda etkinliği öngörebilme
- Rapel gerekliliğini ve zamanını belirleme

Systemic and mucosal antibody responses specific to SARS-CoV-2 during mild versus severe COVID-19

J Allergy Clin Immunol
2021; 147:545



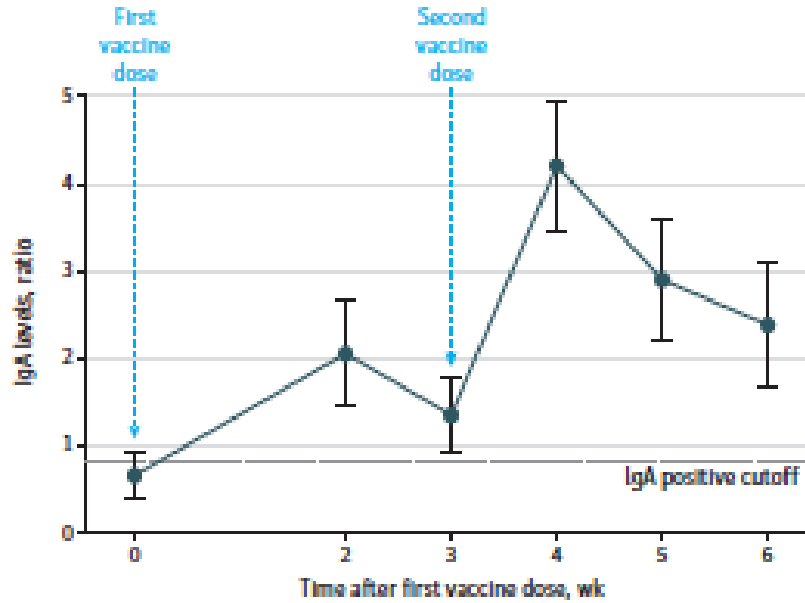
- Hafif enf
 - Serum IgG negatif veya >12 günde (+)
 - Serum IgA geçici (+)
- Ciddi enf: Serum IgG ve IgA ↑
- Serum Ab negatif
 - Mukozalarda spesifik IgA (+)
 - Nötralizan etki (+)

Yöntem: Euroimmun anti-S IgA, Elecsys total ab ve nötralizasyon testi

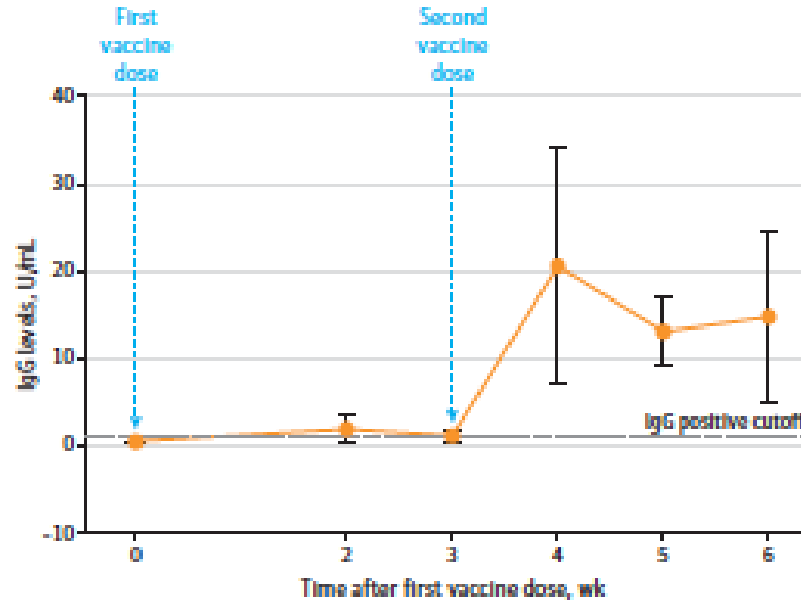
SARS-CoV-2-Specific Antibodies in Breast Milk After COVID-19 Vaccination of Breastfeeding Women

JAMA, March 30, 2021

A IgA levels



B IgG levels



- Aşı öncesi ve Biontech aşı sonrası 6 hafta süresince haftalık izlem
 - Elecsys anti-S kantitatif ve Euroimmun anti-S IgA
- İlk dozdan 2 hft sonra IgA, 2. dozdan bir hafta sonra (4. hafta) IgG artışı

Nötralizan antikorlar

COVID-19 Convalescent Plasma (CCP) Under Emergency Use Authorization

- Enfeksiyonun erken döneminde uygulama(2-3 gün)
- Yüksek titreli plazma tek ünite olarak uygulanması önerilir.
- Donör kriteri:
Ciddi enfeksiyon geçirmek veya enfeksiyon + aşı

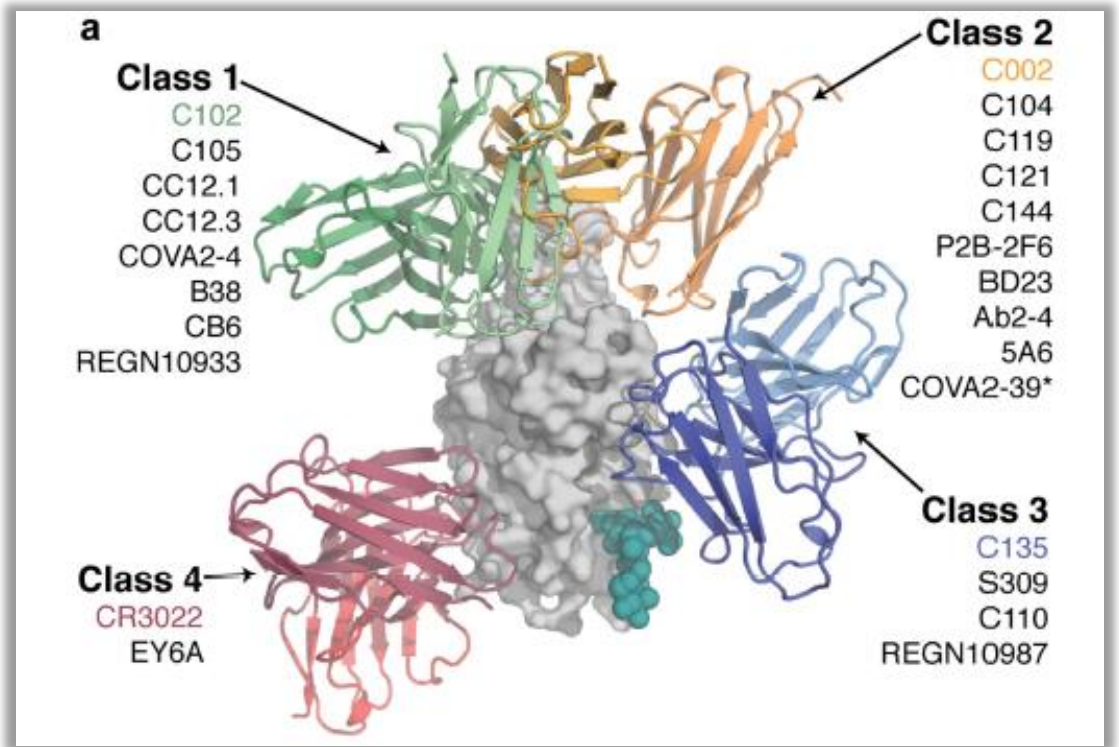
https://www.aabb.org/docs/default-source/default-document-library/regulatory/toolkit-for-ccp-under-eua.pdf?sfvrsn=741be857_18

Manufacturer	Assay	Result
Abbott	SARS-CoV-2 IgG Architect & Alinity	Index (S/C) \geq 4.5
	AdviseDx SARS-CoV-2 IgG II	\geq 840 AU/ml
Beckman Coulter	Access SARS-CoV-2 IgG	S/C \geq 3.3
Euroimmun	Anti-SARS CoV 2 ELISA IgG	Ratio \geq 3.5
GenScript	cPass SARS-CoV-2 Neutralization Ab detection kit	Inhibition \geq 68%
Kantaro	COVID- SeroKlir, Kantaro Semi-Quantitati ve SARS- CoV-2 IgG Antibody Kit	Spike ELISA $>$ 47 AU/mL
Mount Sinai	COVID-19 ELISA IgG	Spike ELISA titer \geq 1:2880
Ortho	VITROS Anti- SARS- CoV-2 IgG	S/C \geq 9.5
Roche	Elecsys Anti- SARS- CoV-2	COI \geq 109
	Elecsys Anti-SARS-CoV-2 S	\geq 132 U/ml
Siemens	ADVIA Centaur SARS- CoV-2 IgG (COV2G)	Index \geq 4.8

SARS-CoV-2 neutralizing antibody structures inform therapeutic strategies

Nature 2020; 588

- ACE-2 ve RBD bağlanma özelliklerine göre 4 farklı nötralizan ab
- Bir grubu bloke eden mutasyonların diğer gruba etkisi yok.
- Kombine kullanım önerilir



b

C144 VH3-53/VL2-14 Class 2				C002 VH3-30/VK1-39 Class 2			
RBD	k_a (10^5) ($M^{-1}s^{-1}$)	k_d (10^{-3}) (s^{-1})	K_D (nM)	RBD	k_a (10^5) ($M^{-1}s^{-1}$)	k_d (10^{-3}) (s^{-1})	K_D (nM)
wt	2.3	4.1	18	wt	8.3	9.0	11
R346S	1.1	5.6	52	R346S	3.2	8.6	27
N439K	1.2	3.6	29	N439K	6.0	9.7	16
N440K	1.4	5.8	40	N440K	3.3	8.1	24
A475V	2.3	53	228	A475V	2.1	6.3	31
V483A	1.3	4.1	32	V483A	2.7	2.9	11
E484K	n.b.	n.b.	n.b.	E484K	n.b.	n.b.	n.b.
Q493R	n.b.	n.b.	n.b.	Q493R	1.8	106	596

Sonuç

Enfeksiyon sonrası antikorlar

- Enfeksiyon sonrası S ve N antikorları en az 7 (12 ?) ay kalır.
 - Klinik ne kadar ciddi ise ab miktarı ve kalış süresi o kadar fazla
 - IgG daha stabil
 - Antikor kitine bağlı farklılıklar
- %5-10 hastada serumda IgG saptanmayabilir.
- Seronegatifleşme
 - Hafif klinik ile ilişkili
- Nötralizan ab → RBD karşı gelişir.
 - Nötralizan ab ve anti-RBD bağlanan ab testleri arası korelasyon var
- Re-enfeksiyon
 - Ab (+) olanlarda daha nadir.
 - %80-96 daha az
- Ab gelişmesi ile solunum sistemindeki virüs miktarı azalıyor.

Ab testlerinin kullanımı ve yorumlanması

- Akut enfeksiyon tanısında NAT/ag testleri yerine kullanılamaz.
 - Uygun koşullarda akut enfeksiyon tanısını destekleyebilir.
 - Multisistem enflamatuvar sendrom gibi komplikasyonların tanısında kullanılabilir.
- IgG (+): Enf zamanı söylenemez
- IgG (-): Enfeksiyonu dışlayamaz
- Seroepidemiolojik çalışmalar
 - Salgının izlenmesi
 - Kararların alınması
- MIS-C tanısı
- Konvelesan plazma donörlerinin belirlenmesi
- S/N ab farkı ile enfeksiyon/aşı (S aşısı) ayrımı
- Nötralizan ab belirlemede yardımcı
 - Aşı çalışmaları
 - Varyantlara etki

<https://www.idsociety.org/practice-guideline/covid-19-guideline-serology/>

<https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html>



Teşekkür ederim