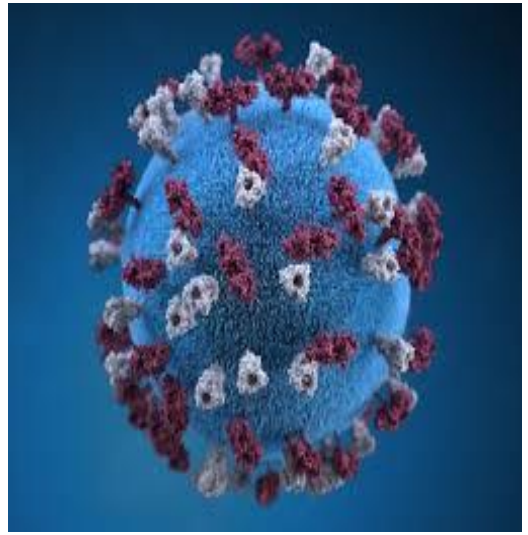
"Λοιμώξεις σε ασθενείς με ρευματικά νοσήματα - κλινική διαχείριση και πρόληψη"

COVID -19: το αποτύπωμα της πανδημίας στο ρευματολογικό ασθενή

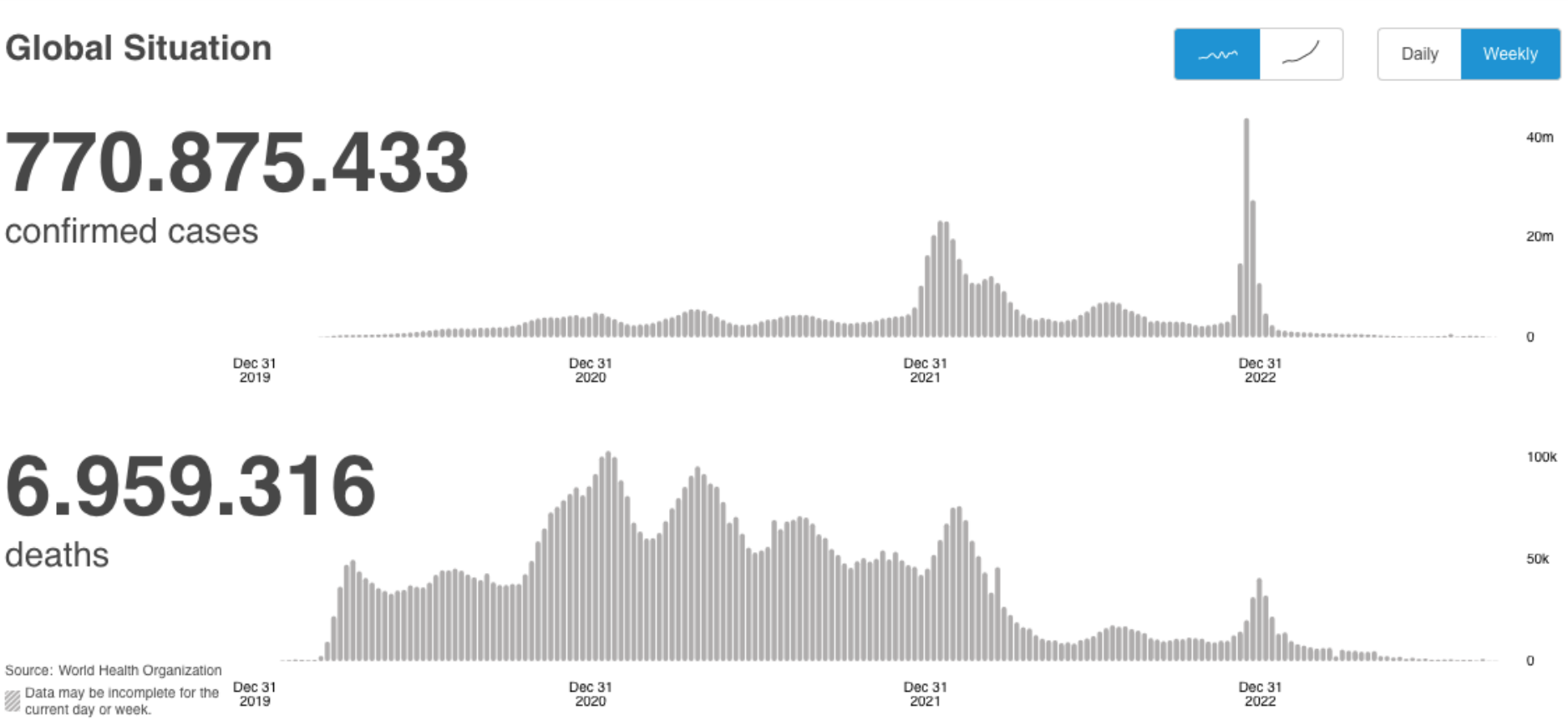


Τσίμπρης Γεώργιος, Παθολόγος- Λοιμωξιολόγος, Επιμελητής Β', Παθολογική Κλινική , Πα.Γ.Ν.Η

ΔΗΛΩΣΗ ΣΥΓΚΡΟΥΣΗΣ ΣΥΜΦΕΡΟΝΤΩΝ

Καμία

ΤΟ ΒΑΡΥ ΤΙΜΗΜΑ ΤΗΣ ΠΑΝΔΗΜΙΑΣ…



[WHO Coronavirus (COVID-19) Dashboard]

Covid is back…

ΕΘΝΙΚΟΣ ΟΡΓΑΝΙΣΜΟΣ ΔΗΜΟΣΙΑΣ ΥΓΕΙΑΣ

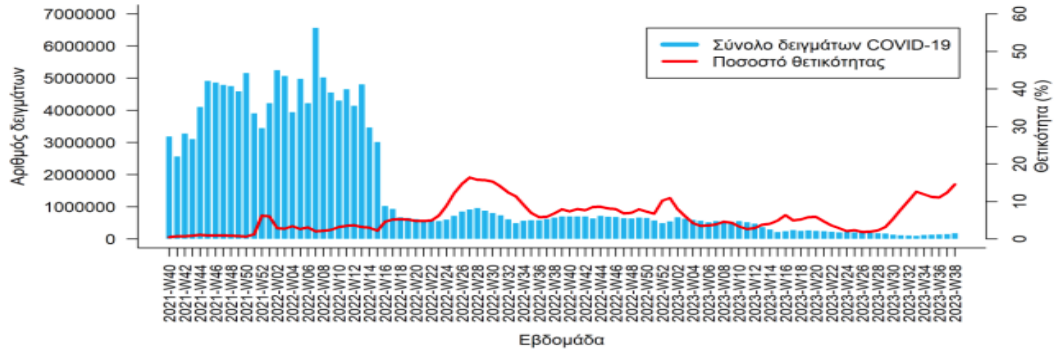
Εβδομαδιαία Έκθεση
Επιδημιολογικής Επιτήρησης Αναπνευστικών Λοιμώξεων
Εβδομάδα 38/2023 (18 Σεπτεμβρίου 2023 – 24 Σεπτεμβρίου 2023)

Σύνοψη επιδημιολογικών δεδομένων – εβδομάδα 38/2023

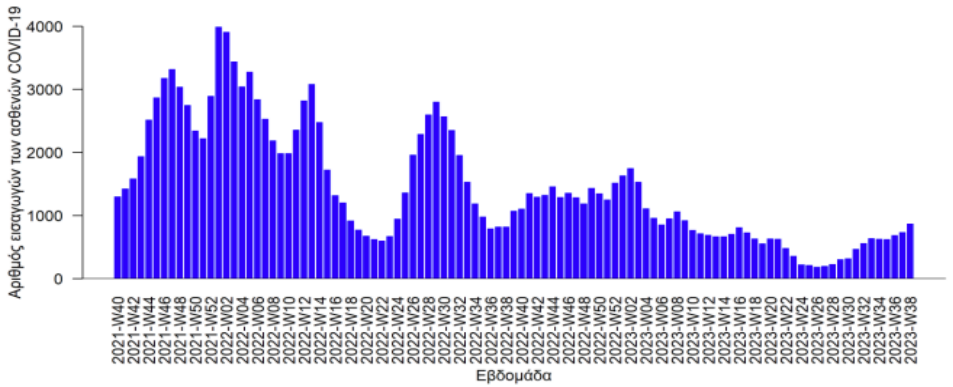
Ιός SARS-CoV2 – λοίμωξη COVID-19

- ✓ η θετικότητα στο σύνολο των ελεγχθέντων δειγμάτων παρουσίασε αύξηση σε σχέση με την προηγούμενη εβδομάδα
- ✓ ο αριθμός των εισαγωγών για COVID-19 (n=869) παρουσίασε αύξηση σε σχέση με την προηγούμενη εβδομάδα και αύξηση 30% σε σχέση με τον μέσο εβδομαδιαίο αριθμό νέων εισαγωγών κατά τις προηγούμενες 4 εβδομάδες
- ✓ ο αριθμός των νέων διασωληνώσεων (n=16) παρουσίασε αύξηση σε σχέση με την προηγούμενη εβδομάδα, καθώς και σε σχέση με τον μέσο εβδομαδιαίο αριθμό νέων διασωληνώσεων κατά τις προηγούμενες 4 εβδομάδες (n=12)
- ✓ ο αριθμός των ασθενών με λοίμωξη COVID-19 που νοσηλεύονται διασωληνωμένοι είναι 33
- ✓ καταγράφηκαν 35 θάνατοι με διάμεση ηλικία τα 86 έτη (εύρος 57-102 έτη)
- ✓ κατά τις τελευταίες εβδομάδες όλα τα αλληλουχηθέντα στελέχη ανήκαν στην υπο-παραλλαγή BA.2 της Όμικρον
- ✓ την εβδομάδα 36 η συχνότερη υπο-παραλλαγή της BA.2 ήταν η EG.5 (32%), ακολουθούμενη από την XBB.1.5 (31%) και την XBB.1.16 (29%)
- ✓ στην Ελλάδα έχουν καταγραφεί συνολικά 5 θετικά δείγματα της υπο-παραλλαγής BA.2.86, με ημερομηνίες λήψης δείγματος από 5 έως 7 Σεπτεμβρίου
- ✓ η επιτήρηση του ιικού φορτίου στα αστικά λύματα έδειξε αύξηση της κυκλοφορίας του ιού SARS-CoV-2 σε 7 από τις 9 περιοχές που ελέγχθηκαν

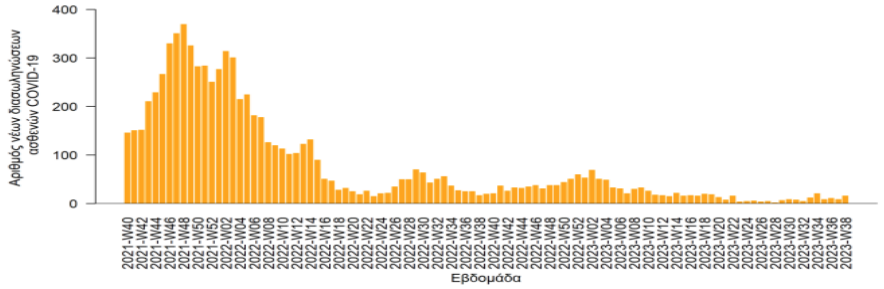
Διάγραμμα 7. Σύνολο δειγμάτων (Rapid-Ag/Rt-PCR) και ποσοστό θετικότητας με βάση το σύνολο των ελεγχθέντων δειγμάτων COVID-19, εβδομάδα 40/2021 - εβδομάδα 38/2023



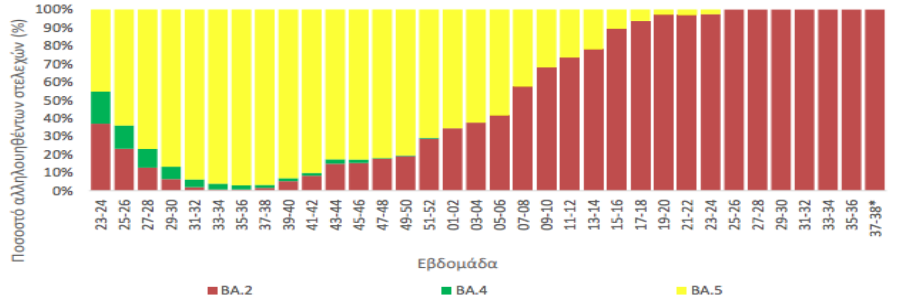
Διάγραμμα 8. Νέες εισαγωγές κρουσμάτων με λοίμωξη COVID-19 στα νοσοκομεία της επικράτειας ανά εβδομάδα, εβδομάδα 40/2021 – εβδομάδα 38/2023



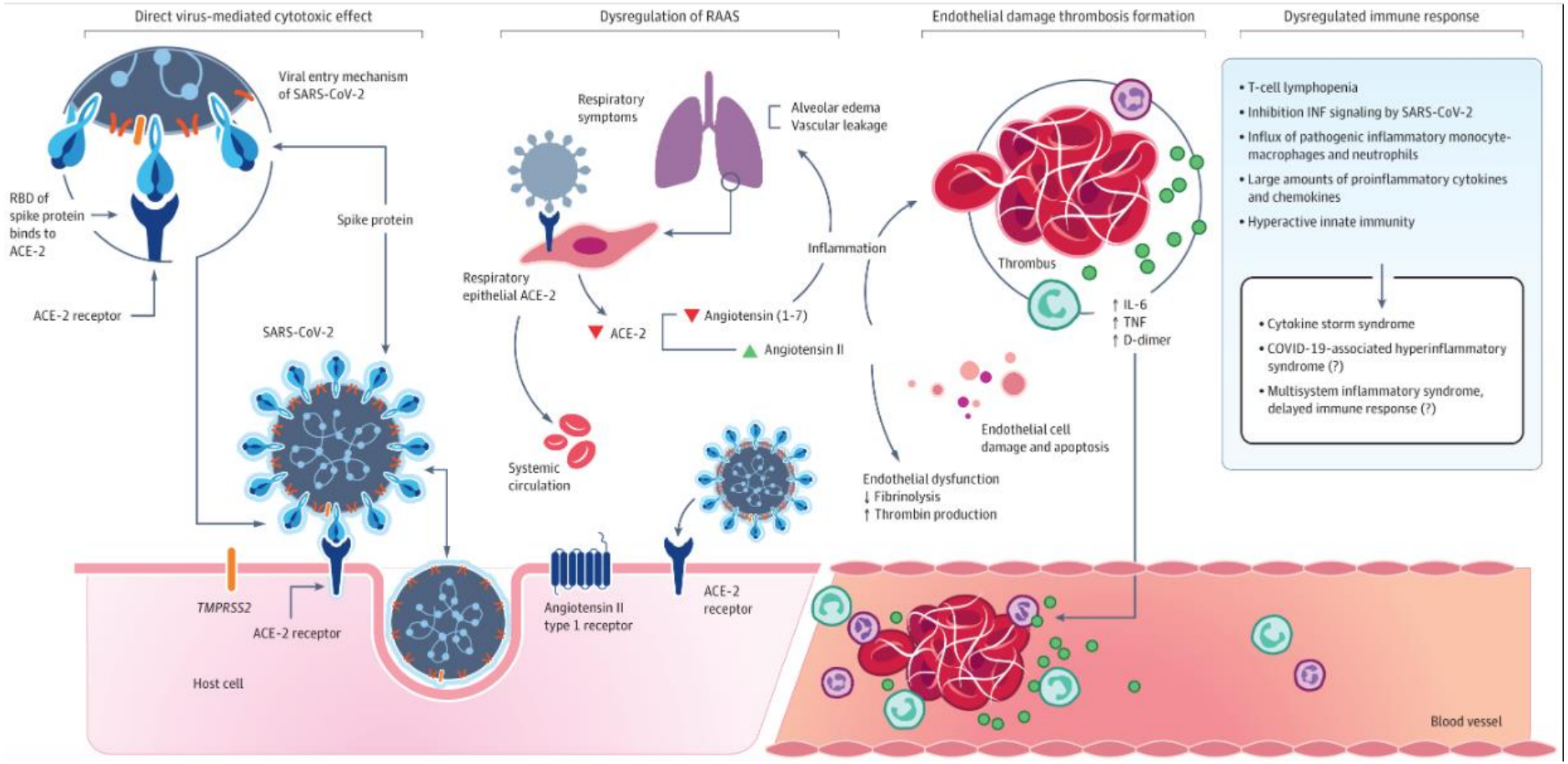
Διάγραμμα 9. Εβδομαδιαίος αριθμός νέων διασωληνώσεων ασθενών COVID-19, σύνολο χώρας, εβδομάδα 40/2021 – εβδομάδα 38/2023



Διάγραμμα 16. Ποσοστό αλληλουχηθέντων δειγμάτων από τυχαία δειγματοληψία με απομονωθέν στέλεχος B.1.1.529 (Όμικρον) ανά βασική υπο-παραλλαγή, ανά 15νθήμερο, έως 14/09/2023, σύνολο χώρας

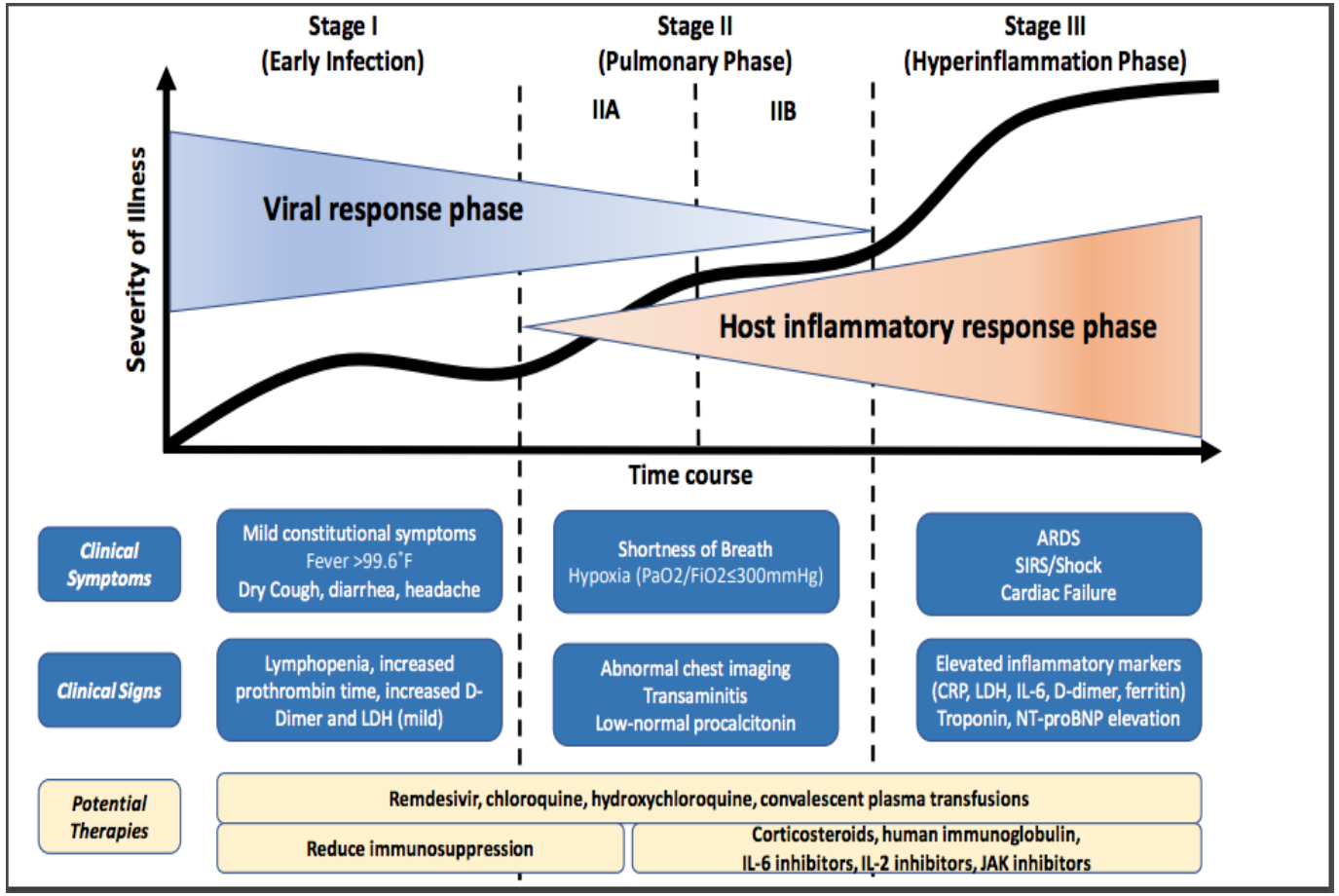


ΠΑΘΟΦΥΣΙΟΛΟΓΙΑ



COVID -19 ΚΑΙ ΡΕΥΜΑΤΙΚΑ ΝΟΣΗΜΑΤΑ: ‘’ΚΟΙΝΟΙ ΓΝΩΣΤΟΙ’’

- Παθογένεια –Υπερφλεγμονή, ενεργοποιηση μακροφάγων(κυτταροκινες IL-1, IL-6, TNF)
- Κλινικοεργαστηριακή εικόνα (έξαρση νόσου Vs λοίμωξη)
- Κοινή θεραπευτική(βιολογικοί παράγοντες , ανοσοκατασταλτικά)
- Ανοσολογικές επιπλοκές Covid (HLH, MIS-C,A) -Post covid condition ,επαγωγή αυτοανοσίας



J Heart Lung Transplant. 2020 May; 39(5): 405–407

ΠΑΡΑΓΟΝΤΕΣ ΚΙΝΔΥΝΟΥ ΓΙΑ ΕΚΔΗΛΩΣΗ ΝΟΣΟΥ

- ΣΥΝΝΟΣΗΡΟΤΗΤΕΣ(ηλικία, ΣΝ , ΧΑΠ, ΚΑ, ΑΥ, ΧΝΝ, ΣΔ, παχυσαρκία
- ΡΕΥΜΑΤΙΚΟ ΝΟΣΗΜΑ και η τρέχουσα κατάσταση – ενεργότητα (Connective tissue disease, προσβολή πνεύμονα)
- ΕΙΔΟΣ ΘΕΡΑΠΕΙΑΣ (high dose κορτικοειδη , rituximab, CYC, MYC)

Annals of the
Rheumatic Diseases

Article Text

Article info

Epidemiology

Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry

PDF

Abstract

Objectives COVID-19 outcomes in people with rheumatic diseases remain poorly understood. The aim was to examine demographic and clinical factors associated with COVID-19 hospitalisation status in people with rheumatic disease.

Methods Case series of individuals with rheumatic disease and COVID-19 from the COVID-19 Global Rheumatology Alliance registry: 24 March 2020 to 20 April 2020. Multivariable logistic regression was used to estimate ORs and 95% CIs of hospitalisation. Age, sex, smoking status, rheumatic disease diagnosis, comorbidities and rheumatic disease medications taken immediately prior to infection were analysed.

Results A total of 600 cases from 40 countries were included. Nearly half of the cases were hospitalised (277, 46%) and 55 (9%) died. In multivariable-adjusted models, prednisone dose ≥10 mg/day was associated with higher odds of hospitalisation (OR 2.05, 95% CI 1.06 to 3.96). Use of conventional disease-modifying antirheumatic drug (DMARD) alone or in combination with biologics/Janus Kinase inhibitors was not associated with hospitalisation (OR 1.23, 95% CI 0.70 to 2.17 and OR 0.74, 95% CI 0.37 to 1.46, respectively). Non-steroidal anti-inflammatory drug (NSAID) use was not associated with hospitalisation status (OR 0.64, 95% CI 0.39 to 1.06). Tumour necrosis factor inhibitor (anti-TNF) use was associated with a reduced odds of hospitalisation (OR 0.40, 95% CI 0.19 to 0.81), while no association with antimalarial use (OR 0.94, 95% CI 0.57 to 1.57) was observed.

Conclusions We found that glucocorticoid exposure of ≥10 mg/day is associated with a higher odds of hospitalisation and anti-TNF with a decreased odds of hospitalisation in patients with rheumatic disease. Neither exposure to DMARDs nor NSAIDs were associated with increased odds of hospitalisation.

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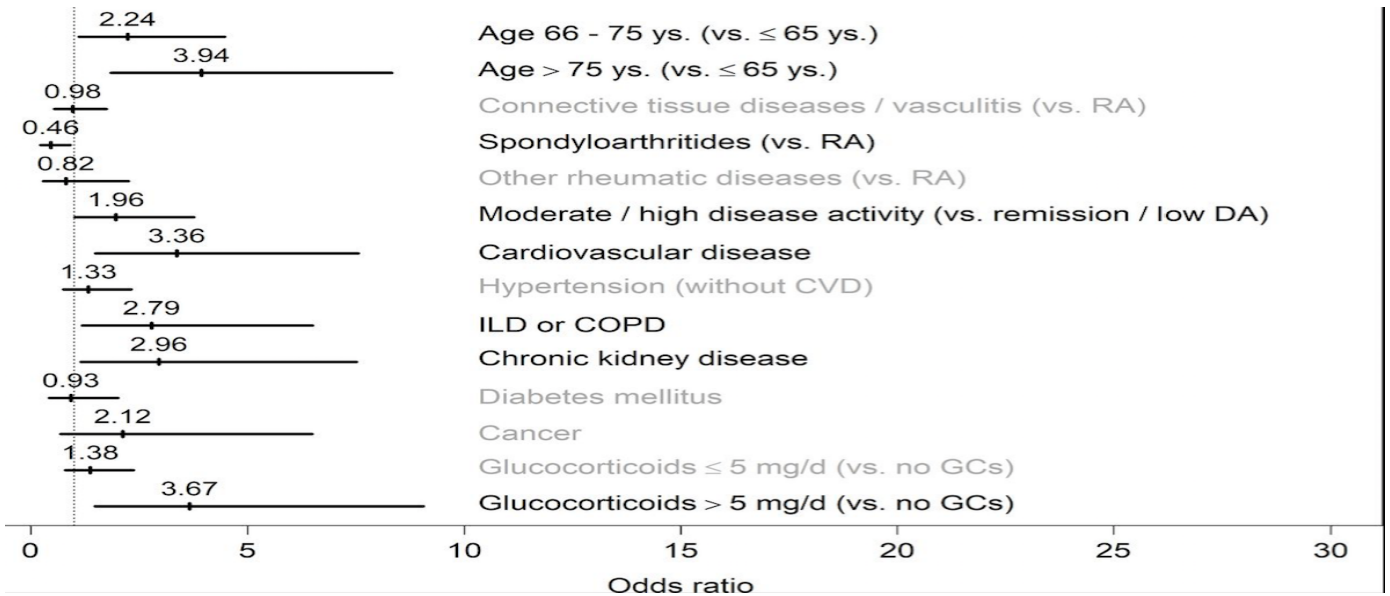
Older age, comorbidity, glucocorticoid use and disease activity are risk factors for COVID-19 hospitalisation in patients with inflammatory rheumatic and musculoskeletal diseases

Rebecca Hasseli [1], Ulf Mueller-Ladner [1], Bimba F Hoyer [2], Andreas Krause [3], Hanns-Martin Lorenz [4], Alexander Pfeil [5], Jutta Richter [6], Martin Schäfer [7], Tim Schmeiser [8], Anja Strangfeld [7], Hendrik Schulze-Koops [9], Reinhard E Voll [10], Christof Specker [11] and Anne Constanze Regierer [7]
Correspondence to Dr Anne Constanze Regierer; Anne.Regierer@drfz.de

PDF



Rheumatoid arthritis

Associations of baseline use of biologic or targeted synthetic DMARDs with COVID-19 severity in rheumatoid arthritis: Results from the COVID-19 Global Rheumatology Alliance physician registry

Abstract

Objective To investigate baseline use of biologic or targeted synthetic (b/ts) disease-modifying antirheumatic drugs (DMARDs) and COVID-19 outcomes in rheumatoid arthritis (RA).

Methods We analysed the COVID-19 Global Rheumatology Alliance physician registry (from 24 March 2020 to 12 April 2021). We investigated b/tsDMARD use for RA at the clinical onset of COVID-19 (baseline): abatacept (ABA), rituximab (RTX), Janus kinase inhibitors (JAKi), interleukin 6 inhibitors (IL-6i) or tumour necrosis factor inhibitors (TNFi, reference group). The ordinal COVID-19 severity outcome was (1) no hospitalisation, (2) hospitalisation without oxygen, (3) hospitalisation with oxygen/ventilation or (4) death. We used ordinal logistic regression to estimate the OR (odds of being one level higher on the ordinal outcome) for each drug class compared with TNFi, adjusting for potential baseline confounders.

Results Of 2869 people with RA (mean age 56.7 years, 80.8% female) on b/tsDMARD at the onset of COVID-19, there were 237 on ABA, 364 on RTX, 317 on IL-6i, 563 on JAKi and 1388 on TNFi. Overall, 613 (21%) were hospitalised and 157 (5.5%) died. RTX (OR 4.15, 95% CI 3.16 to 5.44) and JAKi (OR 2.06, 95% CI 1.60 to 2.65) were each associated with worse COVID-19 severity compared with TNFi. There were no associations between ABA or IL6i and COVID-19 severity.

Conclusions People with RA treated with RTX or JAKi had worse COVID-19 severity than those on TNFi. The strong association of RTX and JAKi use with poor COVID-19 outcomes highlights prioritisation of risk mitigation strategies for these people.

Epidemiology

Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry

Anja Strangfeld [1], Martin Schäfer [1], Milena A Gianfrancesco [2], Saskia Lawson-Tovey [3,4], Jean W Liew [5], Lotta Ljung [6,7], Elsa F Mateus [8,9], Christophe Richez [10], Maria J Santos [11,12,13], Gabriela Schmajuk [2], Carlo A Scirè [14], Emily Sirotich [15,16], Jeffrey A Sparks [17], Paul Sufka [18], Thierry Thomas [19,20,21], Laura Trupin [2], Zachary S Wallace [22], Sarah Al-Adely [4,23], Javier Bachiller-Corral [24,25], Suleman Bhana [26], Patrice Cacoub [27,28,29], Loreto Carmona [30], Ruth Costello [23], Wendy Costello [31], Laure Gossec [32,33], Rebecca Grainger [34], Eric Hachulla [35], Rebecca Hasseli [36], Jonathan S Hausmann [37,38], Kimme L Hyrich [4,23], Zara Izadi [2], Lindsay Jacobsohn [2], Patricia Katz [2], Lianne Kearsley-Fleet [23], Philip C Robinson [39,40], Jinoos Yazdany [2], Pedro M Machado [41,42,43] COVID-19 Global Rheumatology Alliance

Correspondence to Dr Pedro M Machado, Centre for Rheumatology, UCL Division of Medicine, University College London, London WC1E 6JF, UK; p.machado@ucl.ac.uk

Disease groups and diseases included

Inflammatory Joint Diseases (IJD)
- Rheumatoid arthritis (RA)
- Axial and peripheral spondyloarthritis (SpA)
- Psoriatic arthritis (PsA)
- Oligoarticular/polyarticular juvenile idiopathic arthritis (JIA)
- Other inflammatory arthritis

Connective Tissue Diseases (CTD)/Vasculitis
- Systemic lupus erythematosus (SLE)
- Sjögren's syndrome
- Systemic sclerosis
- Inflammatory myopathy (dermatomyositis, polymyositis)
- Mixed CTD
- Undifferentiated CTD
- ANCA-associated vasculitis
- Giant cell arteritis
- Behcet's disease
- Polymyalgia rheumatica
- Kawasaki disease
- Other vasculitis

Other (neither IJD nor CTD/vasculitis)
- Gout
- Ocular inflammation
- Auto-inflammatory syndromes
- IgG4-related disease
- Systemic JIA
- Calcium pyrophosphate deposition disease
- Other non-specified rheumatic diseases

Medication groups and medications included

Conventional synthetic DMARDs (csDMARDs)
- Methotrexate
- Leflunomide
- Sulfasalazine
- Antimalarials (chloroquine, hydroxychloroquine)

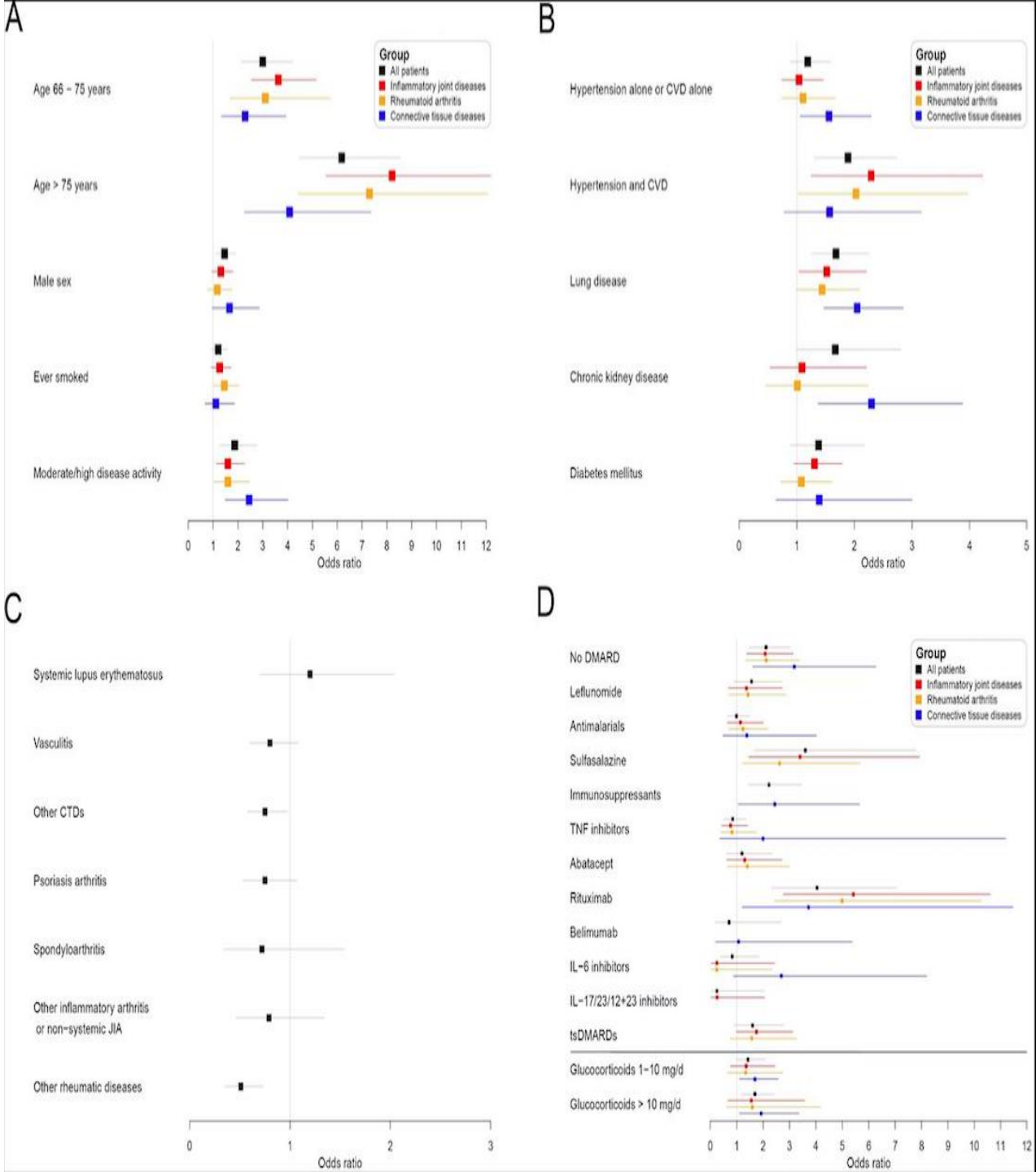
Biological DMARDs (bDMARDs)
- Abatacept
- IL-1 inhibitors
- IL-6 inhibitors
- IL-12/23, IL-17 or IL-23 inhibitors
- TNF inhibitors
- Belimumab
- Rituximab

Targeted synthetic DMARDs (tsDMARDs)
- Apremilast
- JAK inhibitors

Immunosuppressants (except glucocorticoids)
- Azathioprine
- Cyclophosphamide
- Cyclosporine
- Mycophenolate mofetil/mycophenolic acid
- Tacrolimus

Glucocorticoids
- Prednisolone-equivalent dose

Disease-specific factors, namely, moderate/high disease activity and certain medications (rituximab, sulfasalazine and immunosuppressants (as opposed to immunomodulators like disease-modifying anti-rheumatic drugs (DMARDs)) were also associated with COVID-19-related death.



ΚΛΙΝΙΚΗ ΠΕΡΙΠΤΩΣΗ

- Άνδρας 65 ετών, οροαρνητική longstanding διαβρωτική P.A, χρόνια ουρικη αρθρίτιδα υπο prezolon 5mg , λεφλουνομίδη ,rituximab από 2ετίας,ανα 6μηνο(τελευταία προ 5μηνου) σε μερική ύφεση,ΧΑΠ υπο NIMV, ΚΜ, ΚΑ mrEF, ,ΑΥ, ΔΛΔ, ΧΝΝ σταδιου 3Α, περιφερική αξονική νευροπάθεια,αλκοόλ, κάπνισμα 140 pack-years
- Διάγνωση covid προ 2μηνου(πλήρως εμβολιασμένος+ booster δόση) , άρνηση λήψης pre-exposure prophylaxis με mAb
- Εμπύρετο , διάρροιες , έμετοι , δύσπνοια προσπαθείας, rapid+ pcr covid αρνητικό, ΑΠ:100/65, 100 bpm, Spo2=91%, RR:23/min, GCS:15/15
- Τελοεισπνευστικοι τρίζοντες αμφω, ήπια ενεργή αρθρίτιδα, σταθερή νευροπάθεια
- Hb: 8 g/dL, MCV : 86, MCH: 27WBC : 3700(N :2500, L:700) , PLT: 90000, ALB=2,5 mg/dL, AST 60 IU/L,Cr: 1,9 ,CRP 9mg/L ,ΤΚΕ =110,Fer: 5000, Tg :380, trop:250 , IgG=360
- CT ΘΩΡΑΚΟΣ : εκτεταμένα ground glass περιφερικά άμφω, CT ΚΟΙΛΙΑΣ: σπληνομεγαλια,
- Δ/Δ :Έξαρση νόσου(DAH, πνευμονίτιδα), κοινή ή ευκαιριακη λοιμωξη (PCP,Legionella , TB , ατυπο μυκοβακτηριδιο, Leishmania, aspergillus, Cryptococcus, CMV, RSV, Nocardia)
- Εμπειρική αντιμικροβιακή αγωγη (ceftaroline , levofloxacin), συνέχιση κορτιζόνης
- HLH(MAS?)
- ΟΜΒ :αιμοφαγοκυττάρωση , Leishmania(-), λεμφουπερπλαστικό-), ΒΡΟΓΧΟΣΚΟΠΗΣΗ :PCR BAL + Sars COV-2(ct value =14), αιμοσιδηροφαγα ιστιοκύτταρα(+), λοιπός έλεγχος αρνητικός
- 5/8 classic ctiteria . HScore :243, >99% πιθανότητα HLH,MIS-A?
- Remdesivir , Dexaton ,IVIG, ANAKINRA
- ΣΗΠΤΙΚΗ ΚΑΤΑΠΛΗΞΙΑ , ΘΑΝΑΤΟΣ την 26^{η} μέρα νοσηλείας

HLH -MAS

Diagnostic Criteria (Must Fulfill 5 of 8 Parameters)	
Fever	≥38.5C
Splenomegaly	---
Hypertriglyceridemia and/or Hypofibrinogenemia	Fasting Triglycerides ≥300mg/dL or Fibrinogen <150mg/dL
Hyperferritinemia	≥500ug/L
Low or Absent NK Cell Activity	---
Hemophagocytosis	Evidence of Phagocytosis on Bone Marrow, Lymph Node Biopsy, or CSF
Cytopenias	2 or More Cell Lines; Anemia and Thrombocytopenia Most Common
Elevated Soluble IL2 Receptor (CD 25)	≥2400U/mL or 2 Standard Deviations Above Reference Value

H-Score

Metric	Result	Score
Known underlying immunosuppression (HIV positive or receiving long-term immunosuppressive therapy, i.e. glucocorticoids, ciclosporin, azathioprine)	No	0
	Yes	18
Temperature (°C)	<38.4	0
	38.4-39.4	33
	>39.4	49
Organomegaly	No	0
	Hepatomegaly or Splenomegaly	23
	Hepatomegaly and Splenomegaly	38
Number of Cytopenias (Haemoglobin <92g/l, White Cell Count ≤5.0x10⁹/l, Platelets ≤110x10⁹/l)	1	0
	2	24
	3	34
Ferritin (ug/l)	<2000	0
	2000-6000	35
	>6000	50
Triglyceride (mmol/l)	<1.5	0
	1.5-4	44
	>4	64
Fibrinogen (g/l)	>2.5	0
	≤2.5	30
AST (U/l)	<30	0
	≥30	19
Heamophagocytosis features on bone marrow aspirate	No	0
	Yes	35

Multisystem Inflammatory Syndrome in Adults (MIS-A) Case Definition and Information for Healthcare Providers

CDC Case Definition for MIS-A

This definition was developed in 2021 through expert opinion and is intended to assist in identification and reporting of MIS-A cases to CDC passive surveillance.

A patient aged ≥21 years hospitalized for ≥24 hours, or with an illness resulting in death, who meets the following clinical and laboratory criteria. The patient should not have a more likely alternative diagnosis for the illness (e.g., bacterial sepsis, exacerbation of a chronic medical condition).

I. Clinical Criteria
Subjective fever or documented fever (≥38.0 C) for ≥24 hours prior to hospitalization or within the first THREE days of hospitalization* and at least THREE of the following clinical criteria occurring prior to hospitalization or within the first THREE days of hospitalization*. At least ONE must be a primary clinical criterion.

A. Primary clinical criteria

1. Severe cardiac illness *Includes myocarditis, pericarditis, coronary artery dilatation/aneurysm, or new-onset right or left ventricular dysfunction (LVEF<50%), 2nd/3rd degree A-V block, or ventricular tachycardia. (Note: cardiac arrest alone does not meet this criterion)*
2. Rash AND non-purulent conjunctivitis

B. Secondary clinical criteria

1. New-onset neurologic signs and symptoms *Includes encephalopathy in a patient without prior cognitive impairment, seizures, meningeal signs, or peripheral neuropathy (including Guillain-Barré syndrome)*
2. Shock or hypotension not attributable to medical therapy (e.g., sedation, renal replacement therapy)
3. Abdominal pain, vomiting, or diarrhea
4. Thrombocytopenia (platelet count <150,000/ microliter)

II. Laboratory evidence
The presence of laboratory evidence of inflammation AND SARS-CoV-2 infection.

A. Elevated levels of at least TWO of the following: C-reactive protein, ferritin, IL-6, erythrocyte sedimentation rate, procalcitonin

B. A positive SARS-CoV-2 test for current or recent infection by RT-PCR, serology, or antigen detection

CDC

GUIDELINES COVID-19- Update

IDSA Guidelines on the Treatment and Management of Patients with COVID-19

Published by IDSA, 5/27/2021. Last updated, 6/26/2023

June 26, 2023

Version 11.0.0 has been released and includes the following:

- **Convalescent Plasma:** A new recommendation was developed against the routine use of convalescent plasma among immunocompromised patients hospitalized with COVID-19. Additionally, this section includes updated remarks for the existing recommendation on the use of convalescent plasma for ambulatory patients with mild-to-moderate COVID-19 at high risk for progression to severe disease who have no other treatment options.
- **Anakinra**: This section has been added and includes a new recommendation against the routine use of anakinra among hospitalized patients with severe COVID-19.
- **Nirmatrelvir/Ritonavir**: This section includes updated remarks for the existing recommendation on the use of nirmatrelvir/ritonavir for ambulatory patients with mild-to-moderate COVID-19 at high risk for progression to severe disease.

Table 37. COVID-19 therapies by disease severity and care location

Care location and COVID-19 severity	Pharmacologic treatments available in the United States
Ambulatory mild-to-moderate disease (not hypoxemic) *with high risk for progression to severe disease*, hospitalization or death *(see individual drug section for specific considerations for each of these agents)* Can be considered in patients with mild-moderate COVID-19 hospitalized for other reasons	• Nirmatrelvir/ritonavir X 5 days (oral) • Remdesivir x 3 days (intravenous) • Anti-SARS-CoV-2 monoclonal antibodies if regional circulating SARS Cov-2 variants are susceptible to available agents [a] • If other treatment options are not available then consider Molnupiravir x 5 days (oral) or, if immunocompromised, high-titer convalescent plasma with activity against circulating variant (intravenous). • Systemic steroids have no demonstrated benefit and may harm. • No benefit demonstrated for hydroxychloroquine, azithromycin, lopinavir/ritonavir, or ivermectin.
Hospitalized for mild-to-moderate COVID-19 (not hypoxemic)	• If at high risk for progression and within 7 days of symptom onset, remdesivir x 3 days. • Systemic steroids have no demonstrated benefit and may harm. • No benefit demonstrated in RCTs for convalescent plasma, hydroxychloroquine, azithromycin, lopinavir/ritonavir, or ivermectin.
Hospitalized for severe, but not critical COVID-19 (hypoxemic needing low flow supplemental oxygen)	• Corticosteroids (dexamethasone 6 mg/d x 10 days or until discharge or an equivalent dose of another agent). • Remdesivir x 5 days • Tocilizumab or Sarilumab in progressive disease with elevated inflammatory makers. or • Baricitinib or tofacitinib in patients with elevated inflammatory markers. • No benefit demonstrated in RCTs for convalescent plasma, hydroxychloroquine, azithromycin, lopinavir/ritonavir, or ivermectin.
Hospitalized for critically ill COVID-19, needing non-invasive ventilation or Hi flow oxygen	Corticosteroids (dexamethasone 6 mg/d x 10 days or until discharge or an equivalent dose of hydrocortisone or methylprednisolone). • Tocilizumab or Sarilumab in patients with elevated inflammatory makers • Baricitinib or tofacitinib in patients with elevated inflammatory markers • No benefit demonstrated in RCTs for remdesivir, convalescent plasma, hydroxychloroquine, azithromycin, lopinavir/ritonavir, or ivermectin.
Hospitalized for critically ill COVID-19, needing invasive mechanical ventilation or ECMO	• Corticosteroids (dexamethasone 6 mg/d x 10 days or until discharge or an equivalent dose of hydrocortisone or methylprednisolone). • Tocilizumab or sarilumab in patients with elevated inflammatory makers • Baricitinib or tofacitinib in patients with elevated inflammatory markers • No benefit demonstrated in RCTs for remdesivir, convalescent plasma, hydroxychloroquine, azithromycin, lopinavir/ritonavir, or ivermectin.

IDSA, 6/2023

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2/2021

COVID-19 Clinical Guidance for Adult Patients with Rheumatic Diseases

Recommendations

General statements for patients with rheumatic disease:

- The risk of poor outcomes from COVID-19 appears to be related primarily to general risk factors such as age and comorbidity (H).
- Patients should be counseled on general preventive measures, e.g., social distancing and hand hygiene (H).
- As part of a shared decision-making process between patients and rheumatology providers, select measures to reduce healthcare encounters and potential exposure to SARS-CoV-2 (beyond general preventive measures) may be reasonable, e.g., reduced frequency of lab monitoring, optimal use of telehealth, increased dosing intervals between intravenous medications) (M/H).
- If indicated, glucocorticoids should be used at the lowest dose possible to control rheumatic disease, regardless of exposure or infection status (M/H).
- Glucocorticoids should not be abruptly stopped, regardless of exposure or infection status (H).
- If indicated, angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) should be continued in full doses or initiated (M/H).

Ongoing treatment of stable patients in the absence of infection or SARS-CoV-2 exposure:

- Hydroxychloroquine or chloroquine (HCQ/CQ), sulfasalazine (SSZ), methotrexate (MTX), leflunomide (LEF), immunosuppressants (e.g., tacrolimus, cyclosporine, mycophenolate mofetil, azathioprine), biologics, Janus kinase (JAK) inhibitors and non-steroidal anti-inflammatory drugs (NSAIDs) may be continued (this includes patients with giant cell arteritis with an indication, in whom IL-6 inhibitors should be continued, if available) (M/H).
- Denosumab may still be given, extending dosing intervals to no longer than every 8 months, if necessary to minimize healthcare encounters (M).
- For patients with a history of vital organ-threatening rheumatic disease, immunosuppressants should not be dose-reduced (M).

In patients with SLE:

- In newly diagnosed disease, HCQ/CQ should be started at full dose, when available (H).
- In pregnant women with SLE, HCQ/CQ should be continued at the same dose, when available (H).
- If indicated, belimumab may be initiated (M).

Ongoing treatment of stable patients following SARS-CoV-2 exposure (without symptoms related to COVID-19):

- SSZ and NSAIDs may be continued (M/H).
- HCQ/CQ, immunosuppressants, non-IL-6 biologics, and JAK inhibitors should be stopped temporarily, pending 2 weeks of symptom-free observation (M). The panel noted uncertainty re: temporarily stopping MTX or LEF in this situation.
- In select circumstances, as part of a shared decision-making process, IL-6 inhibitors may be continued (M).

Rheumatic disease treatment in the context of documented or presumptive COVID-19 infection:

- Regardless of COVID-19 severity, anti-malarial therapies (HCQ/CQ), SSZ, MTX, LEF, immunosuppressants, non-IL-6 biologics, and JAK inhibitors should be stopped or held (M/H).
- For patients with severe respiratory symptoms, NSAIDS should be stopped (M). The panel demonstrated low consensus with regards to stopping NSAIDs in the absence of severe symptoms.
- In select circumstances, as part of a shared decision-making process, IL-6 inhibitors may be continued (M).

Reinitiating Treatment Following COVID-19:

- For patients with uncomplicated COVID-19 infections (characterized by mild or no pneumonia and treated in the ambulatory setting or via self-quarantine), consideration may be given to re-starting rheumatic disease treatments (e.g., DMARDs, immunosuppressants, biologics and JAK inhibitors) within 7 to 14 days of symptom resolution. For patients who have a positive PCR test for SARS-CoV-2, but are (and remain) asymptomatic, consideration may be given to re-starting rheumatic disease treatments (e.g., DMARDs, immunosuppressants, biologics and JAK inhibitors) 10 to 17 days after the PCR test is reported as positive (H).
- Decisions regarding the timing of reinitiating rheumatic disease therapies in patients recovering from more severe COVID-19-related illness should be made on a case-by-case basis (H).

RITUXIMAB AND COVID

- Παράγοντας κινδύνου για σοβαρή , εμμένουσα λοίμωξη, αυξημένη θνητότητα
- Ανθεκτική υπογαμμασφαιριναιμία(B-Cell depletion)
- Convalescent plasma ως αντιμετώπιση persistent infection (ΕΛΛΗΝΙΚΗ ΜΕΛΕΤΗ)
- Εμβολιασμός 2-4 weeks πριν την επόμενη χορήγηση , μειωμενη ανοσολογικη απαντηση(αντισωματική), διατήρηση κυτταρικης απόκρισης- breakthrough infection

Lancet Rheumatol. 2021 Jun; 3(6): e419–e426.
Published online 2021 Mar 25. doi: 10.1016/S2665-9913(21)00059-X
PMCID: PMC7993930
PMID: 33786454

COVID-19 outcomes in patients with inflammatory rheumatic and musculoskeletal diseases treated with rituximab: a cohort study

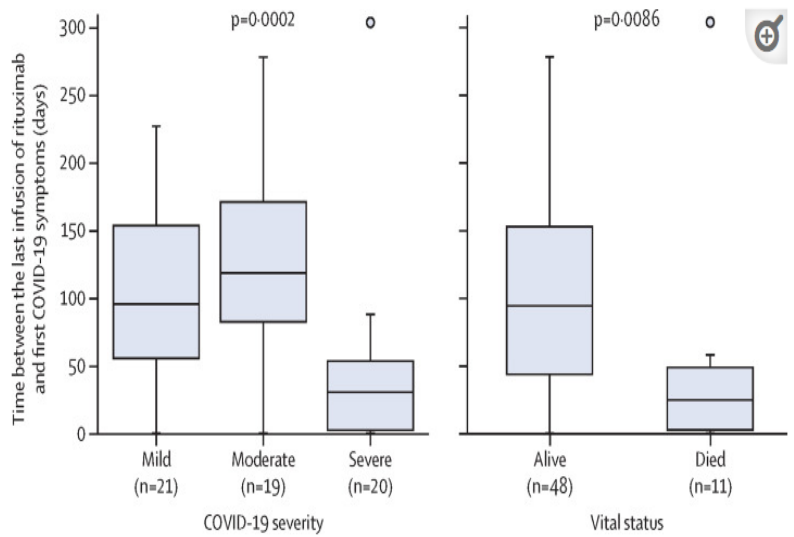
Jérôme Avouac, Prof, MD,[a,*] Elodie Drumez, PhD,[b] Eric Hachulla, Prof, MD,[c] Raphaèle Seror, Prof, MD,[d] Sophie Georgin-Lavialle, Prof, MD,[e] Soumaya El Mahou, MD,[f] Edouard Pertuiset, Prof, MD,[g] Thao Pham, Prof, MD,[h] Hubert Marotte, Prof, MD,[i,j,k] Amélie Servettaz, Prof, MD,[l] Fanny Domont, MD,[m] Pascal Chazerain, MD,[n] Mathilde Devaux, MD,[o] Pascal Claudepierre, Prof, MD,[p] Vincent Langlois, MD,[q] Arsène Mekinian, Prof, MD,[r] Alexandre Thibault Jacques Maria, MD,[s] Béatrice Banneville, MD,[t] Bruno Fautrel, Prof, MD,[t] Jacques Pouchot, Prof, MD,[u] Thierry Thomas, Prof, MD,[v] René-Marc Flipo, Prof, MD,[w] Christophe Richez, Prof, MD,[x] and FAIR/SFR/SNFMI/SOFREMIP/CRI/IMIDIATE consortium and contributors, on behalf of the

Table 2

Comparison in outcomes between rituximab and non-rituximab treated patients in inverse probability of treatment weighting propensity score analyses

		Rituximab group (n=63)	No rituximab group (n=1027)	Effect size (95% CI)[1]	p value
Severity		..	..	..	0·0018
	Mild	21 (33%)	645 (63%)	1 (ref)	..
	Moderate	20 (32%)	267 (26%)	1·98 (1·08–3·63)‡	0·026
	Severe	22 (35%)	115 (11%)	3·26 (1·66–6·40)‡	0·0006
Duration of hospital stay, days		13 (7–not reached)	9 (4–17)	0·62 (0·46–0·85)‡	0·0024
Death		13 (21%)	76 (7%)	1·32 (0·55–3·19)‡	0·53

Figure



CONVALESCENT PLASMA AND B-CELL DEPLETING mAbs

viruses MDPI

Viruses. 2023 Mar; 15(3): 756.
Published online 2023 Mar 15. doi: 10.3390/v15030756

PMCID: PMC10059055
PMID: 36992465

Convalescent Plasma Treatment of Patients Previously Treated with B-Cell-Depleting Monoclonal Antibodies Suffering COVID-19 Is Associated with Reduced Re-Admission Rates

Petros Ioannou, Methodology, Software, Validation, Formal analysis, Data curation, Writing – original draft, Visualization,[1,2,*] Athanasios Katsigiannis, Investigation, Writing – review & editing,[2] Ioanna Papakitsou, Software, Investigation, Writing – review & editing,[2] Ioannis Kopidakis, Investigation, Writing – review & editing,[1] Eirini Makraki, Investigation, Writing – review & editing,[1] Dimitris Milonas, Methodology, Investigation, Writing – review & editing,[2] Theodosios D. Filippatos, Methodology, Writing – review & editing,[1,2] George Sourvinos, Methodology, Writing – review & editing,[3] Marina Papadogiannaki, Methodology, Writing – review & editing,[4] Evaggelia Lydaki, Methodology, Writing – review & editing, Supervision,[4] Georgios Chamilos, Methodology, Writing – review & editing, Supervision,[1,5] and Diamantis P. Kofteridis, Conceptualization, Resources, Writing – review & editing, Supervision, Project administration[1,2,*]

Karolina Akinosoglou, Academic Editor, George T. Dimopoulos, Academic Editor, and Wei Xu, Academic Editor

Table 1

Patients' characteristics in total and in regard to whether they received treatment with plasma.

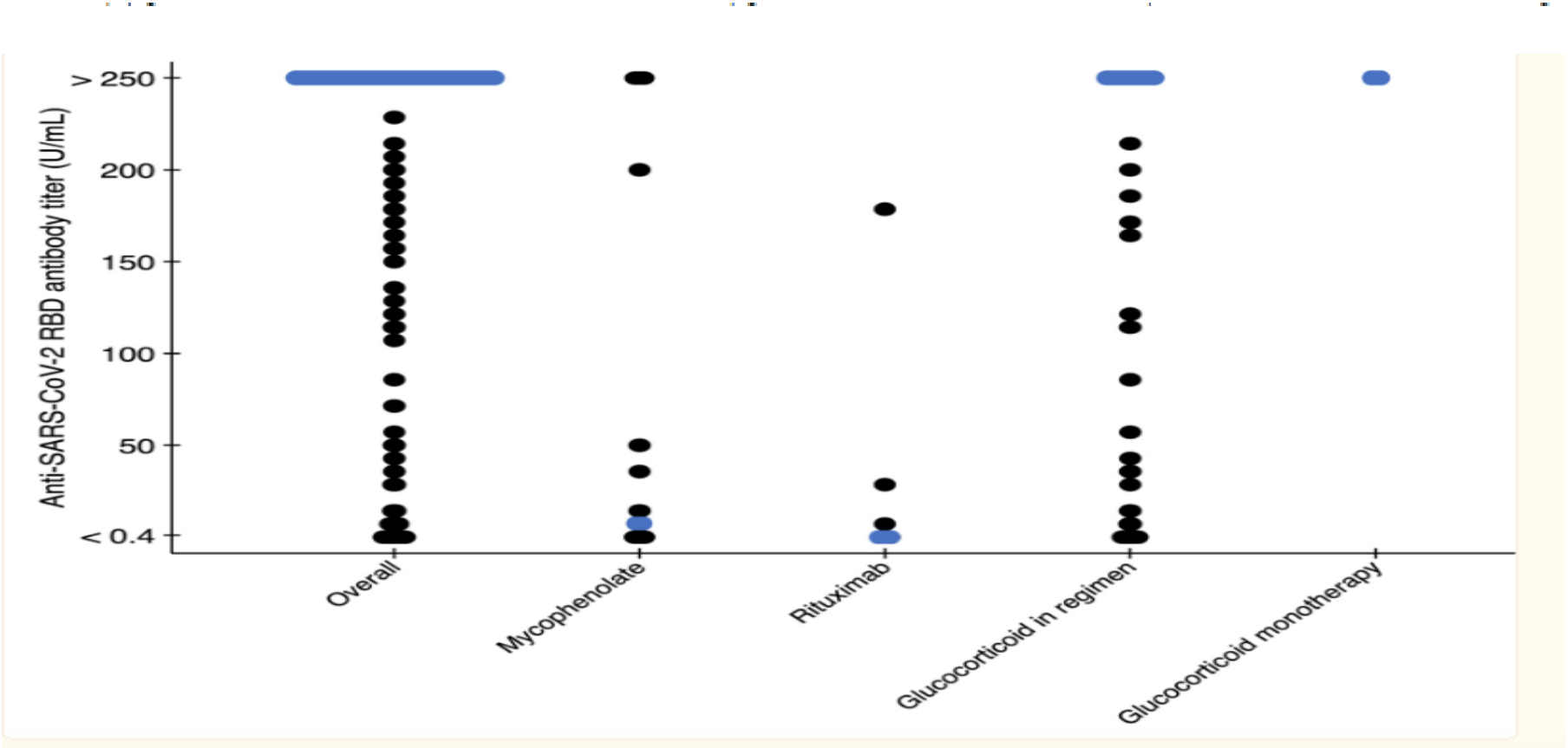
Characteristic	All Patients (n = 39)	Received Plasma (n = 21)	Did Not Receive Plasma (n = 18)	*p*
Age, years, mean (SD)	66.3 (12.8)	68.5 (13.5)	63.7 (11.8)	0.2461
Male gender, n (%)	20 (51.3)	10 (47.6)	10 (55.6)	0.7512
Diagnosed until December 2021 *	17 (43.6)	9 (42.9)	8 (44.4)	1
Diagnosed after December 2021 **	22 (56.4)	12 (57.1)	10 (55.6)	1
Respiratory failure on presentation, n (%) ***	10 (27)	5 (26.3)	4 (22.2)	1
Fever, n (%)	26 (66.7)	11 (52.4)	15 (83.3)	0.0508
Infiltrates in chest X-ray, n (%)	24 (61.5)	12 (57.1)	12 (66.7)	0.7424
IgG levels, mg/dL, median (IQR)	551.5 (468.3–662.3)	584 (471–706.5)	534 (421–734.5)	0.7228
Lymphocytes, cells/μL, median (IQR)	600 (400–1000)	700 (450–1050)	600 (400–1025)	0.6394
Hematological disease, n (%)	22 (56.4)	13 (61.9)	9 (50)	0.5279
Rheumatological disease, n (%)	15 (38.5)	7 (33.3)	8 (44.4)	0.5254
Number of plasma units used, median (IQR)	NA	3 (2.5–3.5)	NA	NA
Remdesivir, n (%)	35 (89.7)	18 (85.7)	17 (94.4)	0.6094
Corticosteroids, n (%)	37 (94.9)	20 (95.2)	17 (94.4)	1
Antibiotics, n (%)	35 (89.7)	19 (90.5)	16 (88.9)	1
Co-infection, n (%)	4 (10.3)	2 (9.5)	2 (11.1)	1
ICU stay, n (%)	6 (15.4)	1 (4.8)	5 (27.8)	0.0775
Duration of stay, days, median (IQR)	9.5 (5–16.3)	9 (5-14.5)	12 (5.5–28)	0.3164
In-hospital mortality, n (%)	6 (15.4)	3 (14.3)	3 (16.7)	1

5. Conclusions

Go to: ▸

Patients with previous treatment with B-cell-depleting monoclonal antibodies hospitalized for COVID-19 have a similar mortality as patients in the general population. Patients who died had a longer duration of hospitalization as confirmed by a multivariate logistic regression analysis. Treatment with CP in this patient population may be associated with lower rates for readmission for COVID-19, even though this was not identified to be independently associated with a lower likelihood for readmission in our multivariate logistic regression analysis model. Further studies should be performed to identify the role of CP in patients with treatment with B-cell-depleting monoclonal antibodies suffering from COVID-19.

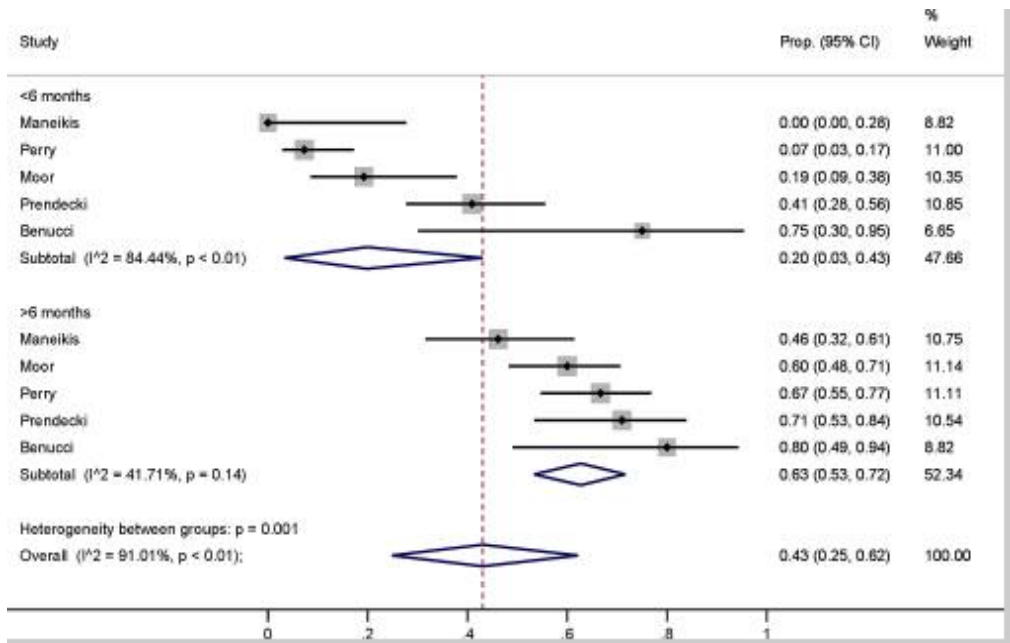
High Antibody Response to Two-Dose SARS-CoV-2 Messenger RNA Vaccination in Patients with Rheumatic and Musculoskeletal Diseases

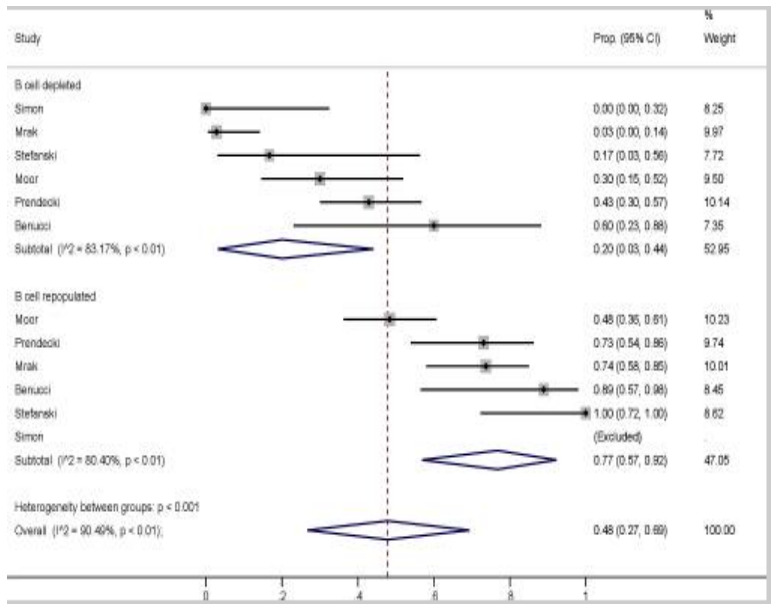


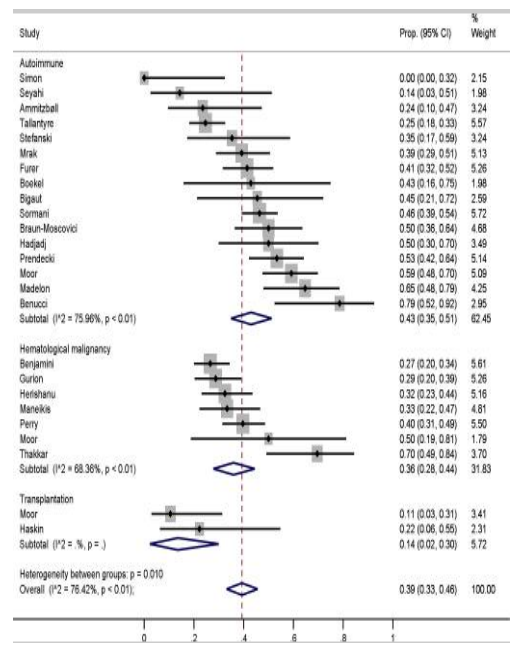
Ann Rheum Dis. 2021 Oct; 80(10): 1351–1352.

Humoral and cellular immune responses on SARS-CoV-2 vaccines in patients with anti-CD20 therapies: a systematic review and meta-analysis of 1342 patients

Simeon Schietzel,[1] Manuel Anderegg,[1,2] Andreas Limacher,[3] Alexander Born,[1] Michael P Horn,[4] Britta Maurer,[5] Cedric Hirzel,[6] Daniel Sidler,[1] and Matthias B Moor[1]







RMD Open. 2022; 8(1): e002036.

ΠΡΟΛΗΨΗ

- Εμβολιασμός
- Μάσκες, υγιεινή χεριών
- Κοινωνική αποστασιοποίηση
- Τηλειατρική(?)- αραίωση επισκέψεων ,θεραπείας σε σταθερούς ασθενείς
- Pre exposure - post exposure prophylaxis(mAbs)? .
- Πρώιμη θεραπεια(early remdesivir ,nirmaltrevir/ritonavir, molnupinavir ,convalescent plasma, monoclonal Abs ?)

ΣΥΣΤΑΣΗ ΓΙΑ ΕΜΒΟΛΙΑΣΜΟ

Συστήνεται η χορήγηση αναμνηστικής δόσης με τα επικαιροποιημένα διδύναμα εμβόλια έναντι του κορωνοϊού που περιλαμβάνουν και την παραλλαγή Όμικρον (BA.1, BA.4/BA.5) σε χρονικό διάστημα τουλάχιστον 3 μηνών μετά την τελευταία δόση του εμβολίου ή τη νόσηση από κορωνοϊό σε:

- όλα τα άτομα ηλικίας 60 ετών και άνω
- άτομα ηλικίας 12-59 ετών που ανήκουν σε ομάδες αυξημένου κινδύνου (βλ. Πίνακες 1 και 2) σύμφωνα με τις οδηγίες του θεράποντα ιατρού
- διαμένοντες και εργαζόμενους σε μονάδες φροντίδας ηλικιωμένων ή άλλες μονάδες φροντίδας χρονίως πασχόντων
- επαγγελματίες υγείας
- διαβιούντες με άτομα σε ανοσοκαταστολή ή άλλο υποκείμενο νόσημα (βλ. Πίνακες 1 και 2)
- φροντιστές ατόμων που πάσχουν από νοσήματα που αυξάνουν τον κίνδυνο επιπλοκών από κορωνοϊό

ΠΑΡΑΡΤΗΜΑ 2.

Ιατρικές καταστάσεις ή θεραπείες που προκαλούν σοβαρή ανοσοκαταστολή και μη επαρκή ανοσιακή απόκριση στον εμβολιασμό για την COVID-19 (ενδεικτικά):

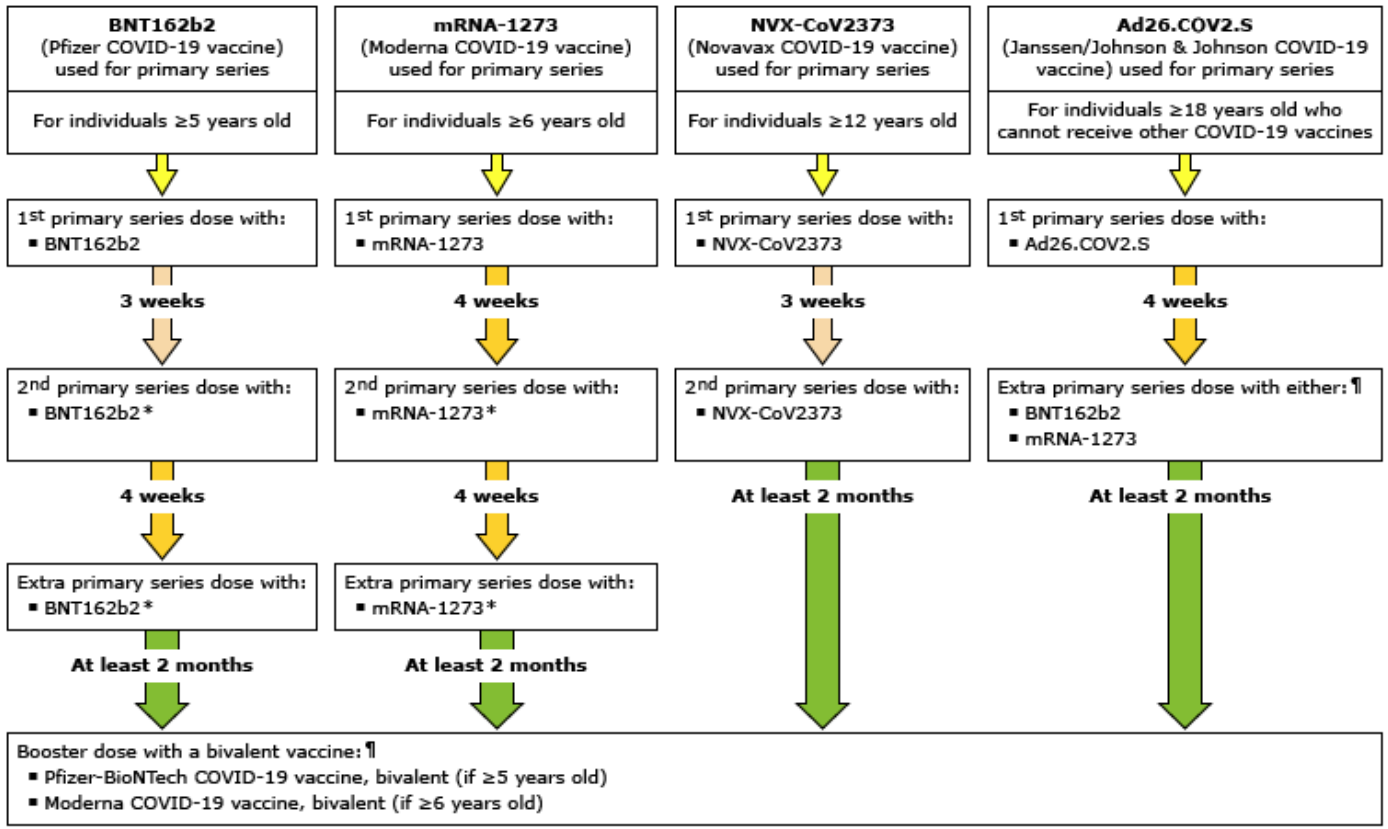
- Θεραπεία με CAR-T cells ή άμεσα προγραμματισμένη θεραπεία με CAR-T cells
- Μεταμόσχευση αιμοποιητικών κυττάρων (την τελευταία διετία ή με λήψη ανοσοκατασταλτικής αγωγής ή με ενεργό GvHD) ή προς άμεση μεταμόσχευση αιμοποιητικών κυττάρων
- Αιματολογική κακοήθεια υπό ενεργό θεραπεία και κατά προτεραιότητα κακοήθη νοσήματα του β-λεμφοκυττάρου (όπως πολλαπλούν μυέλωμα, B-cell λεμφώματα, ΧΛΛ)
- Μεταμόσχευση συμπαγούς οργάνου και λήψη ανοσοκατασταλτικής αγωγής
- Λήψη θεραπείας με βιολογικό παράγοντα που στρέφεται έναντι β-κυττάρων (anti-CD20 -rituximab. ocrelizumab, ofatumumab, veltuzumab, κ.α.)
- Πρωτοπαθείς ανοσοανεπάρκειες (π.χ. σύνδρομο DiGeorge, σύνδρομο Wiskott-Aldrich, κοινή ποικίλη ανοσοανεπάρκεια)

Φάρμακα ανοσοκατασταλτικής/ανοσοτροποποιητικής αγωγής που η λήψη τους συνιστά ένδειξη για τη χορήγηση αναμνηστικής δόσης
Γλυκοκορτικοειδή
Πρεδνιζολόνη, Μεθυλπρεδνιζολόνη (pos/IV)[3]
Μη βιολογικοί παράγοντες
Azathioprine (AZA)
Cyclophosphamide (CYC)
Cyclosporine (CsA)
Leflunomide (LEF)
Methotrexate (MTX)
6-mercaptopurine (6-MP)
Mycophenolate acid (MPA)
Mycophenolate mofetil (MMF)
Tacrolimus
Βιολογικοί παράγοντες
Abatacept
Anti-IL1 (Anakinra, Canakinumab)
Anti-IL6 (Tocilizumab)
Anti-IL12/23 (Ustekinumab)
Anti-IL17 (Brodalumab, Secukinumab)
Anti-TNFs (Adalimumab, Certolizumab pegol, Etanercept, Golimumab, Infliximab)
Belimumab
Anti-B cell (Rituximab)
Στοχευμένοι συνθετικοί παράγοντες
Apremilast
Αναστολείς JAK (Tofacitinib)

[3] Πρεδνιζολόνη >20mg ημερησίως για διάστημα >30 ημερών ή 700mg συνολικής δόσεως σε 2 μήνες.

ΠΛΑΝΟ ΕΜΒΟΛΙΑΣΜΟΥ

COVID-19 vaccine schedule for adults, adolescents, and children ≥5 years old with moderately to severely immunocompromising conditions



Safety of vaccination against SARS-CoV-2 in people with rheumatic and musculoskeletal diseases: results from the EULAR Coronavirus Vaccine (COVAX) physician-reported registry

Results The study included 5121 participants from 30 countries, 90% with I-RMDs (n=4604, 68% female, mean age 60.5 years) and 10% with NI-RMDs (n=517, 77% female, mean age 71.4). Inflammatory joint diseases (58%), connective tissue diseases (18%) and vasculitis (12%) were the most frequent diagnostic groups; 54% received conventional synthetic disease-modifying antirheumatic drugs (DMARDs), 42% biological DMARDs and 35% immunosuppressants. Most patients received the Pfizer/BioNTech vaccine (70%), 17% AstraZeneca/Oxford and 8% Moderna. In fully vaccinated cases, breakthrough infections were reported in 0.7% of I-RMD patients and 1.1% of NI-RMD patients. I-RMD flares were reported in 4.4% of cases (0.6% severe), 1.5% resulting in medication changes. AEs were reported in 37% of cases (37% I-RMD, 40% NI-RMD), serious AEs in 0.5% (0.4% I-RMD, 1.9% NI-RMD).

Conclusion The safety profiles of SARS-CoV-2 vaccines in patients with I-RMD was reassuring and comparable with patients with NI-RMDs. The majority of patients tolerated their vaccination well with rare reports of I-RMD flare and very rare reports of serious AEs. These findings should provide reassurance to rheumatologists and vaccine recipients and promote confidence in SARS-CoV-2 vaccine safety in I-RMD patients.

Immunogenicity and safety of the BNT162b2 mRNA COVID-19 vaccine in adult patients with autoimmune inflammatory rheumatic diseases and in the general population: a multicentre study

Abstract

Introduction Vaccination represents a cornerstone in mastering the COVID-19 pandemic. Data on immunogenicity and safety of messenger RNA (mRNA) vaccines in patients with autoimmune inflammatory rheumatic diseases (AIIRD) are limited.

Methods A multicentre observational study evaluated the immunogenicity and safety of the two-dose regimen BNT162b2 mRNA vaccine in adult patients with AIIRD (n=686) compared with the general population (n=121). Serum IgG antibody levels against SARS-CoV-2 spike S1/S2 proteins were measured 2–6 weeks after the second vaccine dose. Seropositivity was defined as IgG ≥15 binding antibody units (BAU)/mL. Vaccination efficacy, safety, and disease activity were assessed within 6 weeks after the second vaccine dose.

Results Following vaccination, the seropositivity rate and S1/S2 IgG levels were significantly lower among patients with AIIRD versus controls (86% (n=590) vs 100%, p<0.0001 and 132.9±91.7 vs 218.6±82.06 BAU/mL, p<0.0001, respectively). Risk factors for reduced immunogenicity included older age and treatment with glucocorticoids, rituximab, mycophenolate mofetil (MMF), and abatacept. Rituximab was the main cause of a seronegative response (39% seropositivity). There were no postvaccination symptomatic cases of COVID-19 among patients with AIIRD and one mild case in the control group. Major adverse events in patients with AIIRD included death (n=2) several weeks after the second vaccine dose, non-disseminated herpes zoster (n=6), uveitis (n=2), and pericarditis (n=1). Postvaccination disease activity remained stable in the majority of patients.

Conclusion mRNA BNTb262 vaccine was immunogenic in the majority of patients with AIIRD, with an acceptable safety profile. Treatment with glucocorticoids, rituximab, MMF, and abatacept was associated with a significantly reduced BNT162b2-induced immunogenicity.

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COVID-19 Vaccine Clinical Guidance Summary for Patients with Rheumatic and Musculoskeletal Diseases

Developed by the ACR COVID-19 Vaccine Clinical Guidance Task Force

Version 5
Revised August 12, 2022

Recommendations

Table 1: General Considerations Related to COVID-19 Vaccination in Rheumatic and Musculoskeletal Disease Patients

	Guidance Statement	Level of Task Force consensus
	The rheumatology healthcare provider is responsible for engaging the RMD patient in a discussion to assess COVID-19 vaccination status and engage in a shared decision-making process to discuss receiving the COVID-19 vaccine.	Strong-Moderate
	Acknowledging heterogeneity due to disease- and treatment-related factors, and after considering the influence of age and sex, AIIRD patients are at higher risk for hospitalized COVID-19 and worse outcomes compared to the general population.	Moderate
	Based on their risk for COVID-19, AIIRD patients should be prioritized for vaccination before the non-prioritized general population of similar age and sex.	Moderate
	Beyond known allergies to vaccine components, there are no known additional contraindications to COVID-19 vaccination for AIIRD patients.	Moderate
	The expected response to COVID-19 vaccination for many AIIRD patients on systemic immunomodulatory therapies is blunted in its magnitude and duration compared to the general population.	Moderate
	A theoretical risk exists for AIIRD flare or disease worsening following COVID-19 vaccination. However, the benefit of COVID-19 vaccination for RMD patients outweighs the potential risk for new onset autoimmunity.	Moderate

RMD = rheumatic and musculoskeletal disease; AIIRD=autoimmune and inflammatory rheumatic disease

Table 2: Recommendations for Primary and Supplemental Dosing of the COVID-19 Vaccine in RMD Patients*

Guidance Statement	Level of Task Force consensus
RMD and AIIRD patients should receive COVID-19 vaccination, consistent with the age restriction of the EUA and/or FDA approval.†	Moderate
RMD patients without an AIIRD who are on immunomodulatory therapy should be vaccinated in a similar fashion as described in this guidance for AIIRD patients receiving those same treatments.	Moderate
For AIIRD patients not yet vaccinated, either of the mRNA vaccines is recommended over the J&J vaccine. There is no recommendation for one mRNA vaccine over another.	Moderate
For a multi-dose primary vaccine, AIIRD patients should receive the second and third dose of the same vaccine, even if there are non-serious adverse events associated with receipt of the first dose, consistent with timing described in CDC guidelines.	**Strong**
RMD and AIIRD patients who completed the primary COVID vaccine series of 3 doses and are expected to have mounted an inadequate vaccine response should receive supplemental doses (e.g., ≥ 2 additional boosters, for a total of 5 doses) as recommended by the CDC for immunocompromised individuals.‡	Strong
For patients who previously completed the mRNA COVID-19 vaccine series, an mRNA vaccine dose of either type (Pfizer or Moderna) is preferred.	Moderate
Primary vaccination, supplemental dosing, and booster doses should be given regardless of whether patients have experienced natural COVID-19 infection.	**Strong**
Healthcare providers should not routinely order any lab testing (e.g., antibody tests for IgM and/or IgG to spike or nucleocapsid proteins) to assess immunity to COVID-19 post-vaccination, nor to assess the need for vaccination in a yet-unvaccinated person. §	Strong
Following COVID-19 vaccination, RMD patients should continue to follow all public health guidelines regarding physical distancing and other preventive measures.¶	Strong
For high-risk AIIRD patients, pre-exposure prophylaxis monoclonal antibody treatment is recommended when available, if licensed or approved under FDA EUA.#	Moderate
AIIRD patients at high risk for poor outcomes related to COVID should receive monoclonal antibody therapy, either as prevention (i.e., post-exposure prophylaxis for asymptomatic, recently exposed patients) or as treatment for newly symptomatic patients, if licensed or approved under FDA EUA.#	Moderate
Household members and other frequent, close contacts of AIIRD patients should undergo COVID-19 vaccination when available to them to facilitate a 'cocooning effect' that may help protect the AIIRD patient. No priority for early vaccination is recommended for household members.	Moderate
While vaccination would ideally occur in the setting of well-controlled AIIRD, except for those patients with life-threatening illness (e.g., in the ICU for any reason), COVID vaccination should occur as soon as possible for those for whom it is being recommended, irrespective of disease activity and severity.	Strong-Moderate

* RMD = rheumatic and musculoskeletal disease; AIIRD=autoimmune and inflammatory rheumatic disease; EUA = Emergency Use Authorization; FDA = US Food and Drug Administration; mRNA = messenger RNA; CDC = Centers for Disease Control and Prevention; ICU = intensive care unit

Table 3: Guidance Related to the Use and Timing of Vaccine Dosing and Immunomodulatory Therapy in Relation to COVID-19 Vaccination in RMD Patients*

Medication	Timing Considerations for Immunomodulatory Therapy and Vaccination (applies to both primary vaccination and supplemental [booster] dosing)	Level of Task Force Consensus
Abatacept IV	Time vaccination so that it occurs one week prior to the next dose of IV abatacept	Moderate
Abatacept SQ	Hold for one to two weeks (as disease activity allows) after each COVID vaccine dose	Moderate
Acetaminophen, NSAIDs	Assuming that disease is stable, hold for 24 hours prior to vaccination. No restrictions on use post vaccination once symptoms develop.	Moderate
Belimumab SQ	Hold for one to two weeks (as disease activity allows) after each COVID vaccine dose	Moderate
TNFi, IL-6R, IL-1R, IL-17, IL12/23, IL-23, and other cytokine inhibitors†	The Task Force failed to reach consensus on whether or not to temporarily interrupt these following each COVID vaccine dose, including both primary vaccination and supplemental (booster) dosing	Moderate
Cyclophosphamide IV	Time CYC administration so that it will occur approximately 1 week after each vaccine dose, when feasible	Moderate
Hydroxychloroquine, **IVIG**	**No modifications to either immunomodulatory therapy or vaccination timing**	Strong (HCQ), **Moderate (IVIG)**
Rituximab or other anti-CD20 B-cell depleting agents	Discuss the optimal timing of dosing and vaccination with the rheumatology provider before proceeding‡	Moderate
All other conventional and targeted immunomodulatory or immunosuppressive medications (e.g., JAKi, MMF) except those listed above§	Hold for one to two weeks (as disease activity allows) after each COVID vaccine dose	Moderate

* RMD = rheumatic and musculoskeletal disease; IVIG = intravenous immunoglobulin; TNFi = tumor necrosis factor inhibitor; IL = interleukin; JAKi = janus kinase inhibitor; CYC = cyclophosphamide; RTX = rituximab; IV = intravenous; SQ = subcutaneous; NSAID = non-steroidal anti-inflammatory drugs; MMF = mycophenolate mofetil; ***JAKi = baricitinib, tofacitinib, upadacitinib***

† Examples of specific cytokine inhibitors are as follows: IL-6R = sarilumab; tocilizumab; IL-1R = anakinra, canakinumab; IL-17 = ixekizumab, secukinumab; IL-12/23 = ustekinumab; IL-23 = guselkumab, rizankizumab

‡ Some practitioners measure CD19 B cells as a tool with which to time the booster and subsequent rituximab dosing. For those who elect to dose without such information, or for whom such measurement is not available or feasible, provide a supplemental dose 2-4 weeks before next anticipated rituximab dose (e.g., at month 5.0 or 5.5 for patients on an every 6 month rituximab dosing schedule)

§ Includes apremilast; azathioprine; calcineurin inhibitors; cyclophosphamide (oral); IVIG; leflunomide; methotrexate, janus kinase inhibitors [JAKi] (baricitinib, tofacitinib, upadacitinib), mycophenolate; sulfasalazine

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PMC COVID-19 Collection

COVID-19 vaccine safety and nocebo-prone associated hesitancy in patients with systemic rheumatic diseases: a cross-sectional study

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Comorbidities and behavioural patterns of patients enrolled in our study

Characteristics	Vaccinated, $n = 437$	Non-vaccinated, $N = 120$	p value
Arterial hypertension, n (%)	139 (31.8)	29 (24.2)	0.144
Coronary heart disease, n (%)	27 (6.2)	5 (4.2)	0.510
Congestive heart failure, n (%)	5 (1.1)	2 (1.7)	0.645
Diabetes mellitus, n (%)	36 (8.2)	3 (2.5)	**0.027**
Chronic kidney disease, n (%)	31 (7.1)	8 (6.7)	1.000
Chronic obstructive pulmonary disease, n (%)	19 (4.3)	0 (0.0)	**0.019**
Missed appointment (during last year), n (%)	169 (38.7)	54 (45.0)	0.207
Treatment discontinuation amid first COVID-19 wave, n (%)	6/250 (2.4)	2/73 (2.7)	1.000
Nocebo behaviour, n (%)[a]	23/352 (6.5)	18/65 (27.7)	**0.0001**
Negative vaccination behaviour, n (%)[a]	30 (6.9)	47 (39.2)	**0.0001**

Comparison between vaccinated and unvaccinated patients

Paxlovid – αλληλεπιδράσεις με αντι-ρευματικούς παράγοντες

Immuno-suppressants	Nirmatrelvir/ritonavir (5 days)
Abatacept	◆
Abrocitinib	◆
Adalimumab	◆
Anti-thymocyte globulin	◆
Apremilast	◆
Azathioprine	◆
Basiliximab	◆
Belatacept	◆
Belimumab	◆
Certolizumab pegol	◆
Ciclosporin (Cyclosporine)	●
Dimethyl fumarate	◆
Etanercept	◆
Everolimus	●
Filgotinib	◆
Golimumab	◆
Ixekizumab	◆
Leflunomide	◆
Methotrexate (rheumatoid arthritis)	◆
Mycophenolate	▲
Pirfenidone	▲
Risankizumab	◆
Secukinumab	◆
Sirolimus	●
Tacrolimus	●
Tofacitinib	▬
Upadacitinib	▬
Ustekinumab	◆
Vedolizumab	◆
Voclosporin	●

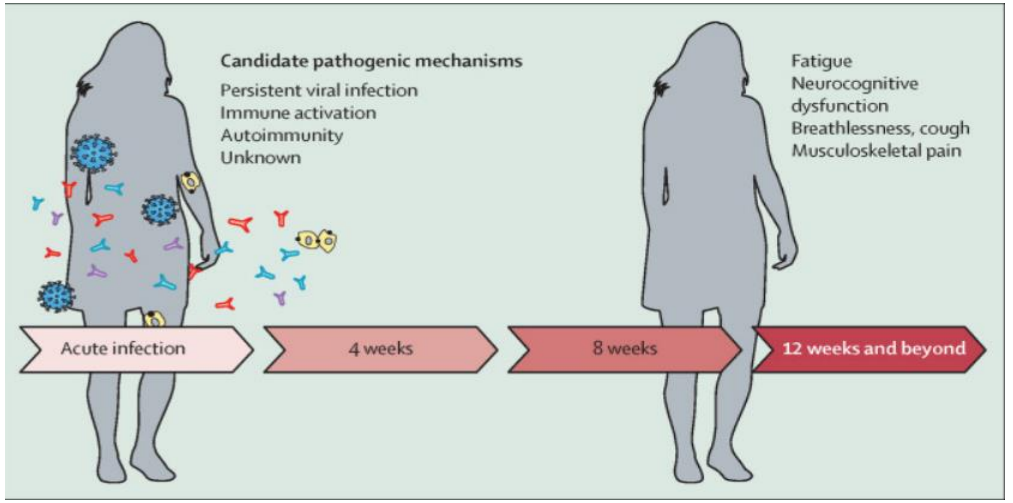
● Do Not Coadminister ▬ Potential Interaction ▲ Potential Weak Interaction ◆ No Interaction Expected

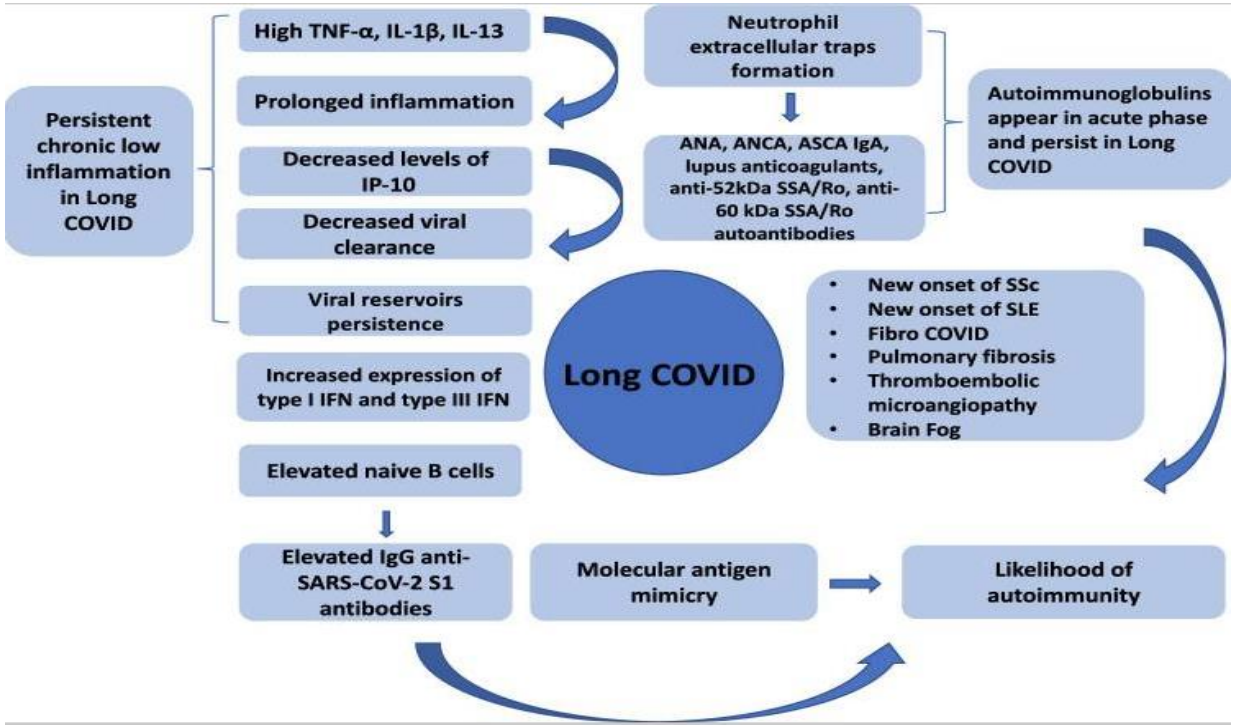
LIVERPOOL DRUG INTERACTIONS

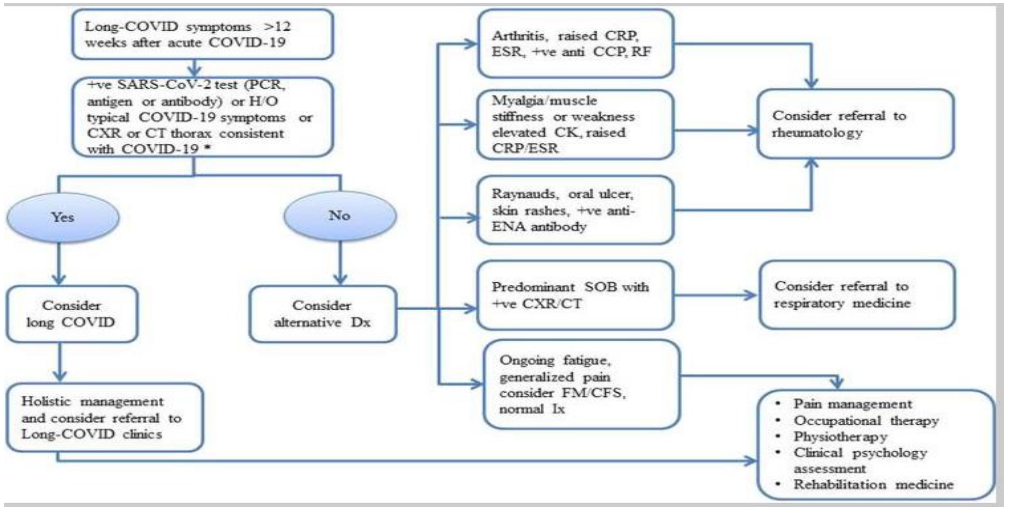
POST—COVID CONDITION

•**Acute COVID-19** - Symptoms of COVID-19, up to four weeks following the onset of illness.

•**Post-COVID condition** - Broad range of symptoms (physical and mental) and symptom clusters that develop during or after COVID-19, continue for ≥2 months (ie, three months from the onset of illness), have an impact on the patient's life, and are not explained by an alternative diagnosis.







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Lancet Rheumatol. 2022 Dec; 4(12): e812–e814.

ΣΥΜΠΕΡΑΣΜΑΤΑ

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Understanding immunopathological fallout of human coronavirus infections including COVID-19: Will they cross the path of rheumatologists?

Jayakanthan Kabeerdoss [1] and Debashish Danda [1]

- ΑΛΛΗΛΕΠΙΔΡΑΣΗ Covid-19 –Ρευματικών νοσημάτων (πολυεπίπεδο (ανοσο)αποτύπωμα
- ΠΑΡΑΓΟΝΤΕΣ ΚΙΝΔΥΝΟΥ (συννοσηρότητες , ενεργότητα νόσου, anti –CD20 –θεραπεία)
- ΚΛΙΝΙΚΗ ΔΙΑΧΕΙΡΙΣΗ (έγκαιρη διάγνωση,’’επιθετικό΄ work up για αποκλεισμό άλλων ευκαιριακών λοιμώξεων , έξαρση νόσου, τοξικότητα θεραπείας)
- ΠΡΟΛΗΨΗ (πρώιμη θεραπεία για αποτροπή εξέλιξης σε σοβαρή νόσο, εμβόλια, μη φαρμακευτικές παρεμβάσεις)

ΕΥΧΑΡΙΣΤΩ ΠΟΛΥ!

ΠΑΡΑΡΤΗΜΑ 2.

Ιατρικές καταστάσεις ή θεραπείες που προκαλούν σοβαρή ανοσοκαταστολή και μη επαρκή ανοσιακή απόκριση στον εμβολιασμό για την COVID-19 (ενδεικτικά):

- Θεραπεία με CAR-T cells ή άμεσα προγραμματισμένη θεραπεία με CAR-T cells
- Μεταμόσχευση αιμοποιητικών κυττάρων (την τελευταία διετία ή με λήψη ανοσοκατασταλτικής αγωγής ή με ενεργό GvHD) ή προς άμεση μεταμόσχευση αιμοποιητικών κυττάρων
- Αιματολογική κακοήθεια υπό ενεργό θεραπεία και κατά προτεραιότητα κακοήθη νοσήματα του β-λεμφοκυττάρου (όπως πολλαπλούν μυέλωμα, B-cell λεμφώματα, ΧΛΛ)
- Μεταμόσχευση συμπαγούς οργάνου και λήψη ανοσοκατασταλτικής αγωγής
- Λήψη θεραπείας με βιολογικό παράγοντα που στρέφεται έναντι β-κυττάρων (anti-CD20 -rituximab. ocrelizumab, ofatumumab, veltuzumab, κ.α.)
- Πρωτοπαθείς ανοσοανεπάρκειες (π.χ. σύνδρομο DiGeorge, σύνδρομο Wiskott-Aldrich, κοινή ποικίλη ανοσοανεπάρκεια)

Σοβαρότητα Νόσου	Θεραπευτική παρέμβαση*
Εξω-νοσοκομειακός ασθενής με ήπια προς μέτρια νόσο (κορεσμός οξυγόνου >94% σε αέρα δωματίου), που δεν έχει παράγοντες κινδύνου (Βλ. **Παράρτημα 1**) για σοβαρή νόσο[1]	Δεν χορηγείται ειδική φαρμακευτική αγωγή Ο ασθενής παρακολουθεί την θερμοκρασία του και τον κορεσμό οξυγόνου με οξύμετρο τουλάχιστον δύο φορές την ημέρα. Προτείνεται καλή ενυδάτωση, λήψη αντιπυρετικών και κλινοστατισμός μέχρι την πλήρη υποχώρηση του πυρετού. Επί ενδείξεων Χορηγούνται αντιβιοτικά[2] επί κλινικών, απεικονιστικών ή εργαστηριακών ενδείξεων συλλοίμωξης με βακτηριακή πνευμονία, σύμφωνα με τις οδηγίες της Ελληνικής Εταιρείας Λοιμώξεων για την πνευμονία της κοινότητας
Εξω-νοσοκομειακός ασθενής με ήπια προς μέτρια νόσο (κορεσμός οξυγόνου >94% σε αέρα δωματίου), που έχει παράγοντες κινδύνου (Βλ. **Παράρτημα 1**) για σοβαρή νόσο[1]	Ο ασθενής παρακολουθεί την θερμοκρασία του και τον κορεσμό οξυγόνου με οξύμετρο τουλάχιστον δύο φορές την ημέρα. Προτείνεται καλή ενυδάτωση, λήψη αντιπυρετικών και κλινοστατισμός μέχρι την πλήρη υποχώρηση του πυρετού. Επί ενδείξεων Χορηγούνται αντιβιοτικά[2] επί κλινικών, απεικονιστικών ή εργαστηριακών ενδείξεων συλλοίμωξης με βακτηριακή πνευμονία, σύμφωνα με τις οδηγίες της Ελληνικής Εταιρείας Λοιμώξεων για την πνευμονία της κοινότητας **Πρώιμη θεραπεία για την αποφυγή της προόδου σε σοβαρή νόσο[3]** *Υπάρχουν οι παρακάτω επιλογές (για προτεραιοποίηση βλ. **Παράρτημα 3**)* 1. **Νιρματρελβίρη / Ριτοναβίρη[4]** από του στόματος για 5 ημέρες 2. **Ρεμδεσιβίρη[5] IV** για 3 ημέρες 3. **Tixagevimab / cilgavimab[6],** ενδομυϊκά, εφάπαξ (Σημείωση: το φάρμακο χορηγείται κατά απόλυτη προτεραιότητα ως προφύλαξη πριν την έκθεση, όπως περιγράφεται παρακάτω) 4. **Μολνουπιραβίρη[6]** από του στόματος για 5 ημέρες (Προσωρινή σύσταση. Εκκρεμεί αίτημα για έγκριση από τον EMA)
Εξω-νοσοκομειακός ασθενής με ήπια προς μέτρια νόσο (κορεσμός οξυγόνου >94% σε αέρα δωματίου), είτε έχει είτε δεν έχει παράγοντες κινδύνου (Βλ. **Παράρτημα 1**) για σοβαρή νόσο[2]	ΔΕΝ ΠΡΕΠΕΙ να χορηγούνται τα παρακάτω σκευάσματα σε ασθενείς με COVID-19 που δεν νοσηλεύονται o Ιβερμεκτίνη o Δεξαμεθαζόνη ή άλλα κορτικοειδή o Εισπνεόμενα φάρμακα εκτός αν ο ασθενής έχει ΧΑΠ ή/και άσθμα. o Αζιθρομυκίνη ή Κλαριθρομυκίνη ή κινολόνες o Ηπαρίνη ή άλλα αντιπηκτικά φάρμακα[7] o Χλωροκίνη / Υδροξυχλωροκίνη o Κολχικίνη

Νοσηλευόμενος ασθενής με ήπια νόσο που δεν χρήζει παροχής	• Σε ασθενείς άνευ παραγόντων κινδύνου για επιδείνωση[1] : **δεν χορηγείται ειδική φαρμακευτική αγωγή**

Νοσηλευόμενος ασθενής με ήπια νόσο που δεν χρήζει παροχής συμπληρωματικού οξυγόνου	• Σε ασθενείς άνευ παραγόντων κινδύνου για επιδείνωση[1] : **δεν χορηγείται ειδική φαρμακευτική αγωγή** • Σε ασθενείς με παράγοντες κινδύνου για επιδείνωση χορηγείται μέσα στο νοσοκομείο **πρώιμη θεραπεία για την αποφυγή της προόδου σε σοβαρή νόσο[1] .** Για τις θεραπευτικές επιλογές και την προτεραιοποίηση βλ. τον θεραπευτικό αλγόριθμο των μη-νοσηλευόμενων ασθενών
Νοσηλευόμενος ασθενής που λαμβάνει συμπληρωματικό οξυγόνο χωρίς συμπτώματα και σημεία σοβαρής νόσου[2]	• **Ρεμδεσιβίρη[4]** ενδοφλέβια. • Σε ασθενείς με **αυξανόμενες ανάγκες σε συμπληρωματικό οξυγόνο: ρεμδεσιβίρη[4] και δεξαμεθαζόνη[5]** ενδοφλέβια. • Σε ασθενείς με **πνευμονία** και σοβαρό κίνδυνο για αναπνευστική ανεπάρκεια, όπως καθορίζεται από τα επίπεδα ορού της πρωτεΐνης soluble urokinase plasminogen activator receptor **(suPAR) ≥ 6 ng/ml προστίθεται anakinra[8]** • Σε όλους τους ασθενείς χορηγείται **ηπαρίνη χαμηλού μοριακού βάρους σε προφυλακτική δόση[6]** **Επί ενδείξεων** Χορηγούνται αντιβιοτικά μόνο επί κλινικής/απεικονιστικής/εργαστηριακής τεκμηρίωσης ή υποψίας βακτηριακής πνευμονίας, σύμφωνα με τις οδηγίες της Ελληνικής Εταιρείας Λοιμώξεων για την πνευμονία της κοινότητας[7]
Νοσηλευόμενος ασθενής σε υψηλή παροχή οξυγόνου (high-flow) ή σε μη-μηχανική υποστήριξη της αναπνοής ή/και με συμπτώματα και σημεία σοβαρής νόσου[2]	• **Ρεμδεσιβίρη[4] και δεξαμεθαζόνη[5]** ενδοφλέβια. • Σε **μη βελτιούμενους ασθενείς με αυξημένους δείκτες φλεγμονής προστίθεται baricitinib[9] ή tocilizumab[10]. ***** • Σε ασθενείς με **πνευμονία** που λαμβάνουν συμπληρωματικό οξυγόνο υψηλής παροχής και σοβαρό κίνδυνο για αναπνευστική ανεπάρκεια, όπως καθορίζεται από τα επίπεδα ορού της πρωτεΐνης soluble urokinase plasminogen activator receptor **(suPAR) ≥ 6 ng/ml μπορεί να χρησιμοποιηθεί anakinra[8]** • Σε όλους τους ασθενείς χορηγείται **ηπαρίνη χαμηλού μοριακού βάρους σε προφυλακτική δόση[6]** **Ο ασθενής τοποθετείται σε πρηνή θέση** **Επί ενδείξεων** Χορηγούνται αντιβιοτικά μόνο επί κλινικής/απεικονιστικής/εργαστηριακής τεκμηρίωσης ή υποψίας συνυπάρχουσας βακτηριακής πνευμονίας, σύμφωνα με τις οδηγίες της Ελληνικής Εταιρείας Λοιμώξεων για την πνευμονία της κοινότητας ή την

Νοσηλευόμενος ασθενής σε μηχανικό αερισμό ή ECMO[3]	**Το πρώτο 24ωρο από την εισαγωγή στη ΜΕΘ** • **Δεξαμεθαζόνη[5]** εφόσον δεν έχει ήδη χορηγηθεί ή δεν έχουν συμπληρωθεί 10 ημέρες χορήγησης του φαρμάκου **σε συνδυασμό με tocilizumab[11]** εφόσον δεν έχει ήδη χορηγηθεί και δεν υπάρχουν αντενδείξεις (λοίμωξη). • **Ρεμδεσιβίρη** χορηγείται μόνον εφόσον πρόκειται για συνέχιση θεραπείας και μέχρι τη συμπλήρωση του πενθήμερου σχήματος. • Σε όλους τους ασθενείς χορηγείται **ηπαρίνη χαμηλού μοριακού βάρους** σε **προφυλακτική δόση[6]** **Επί ενδείξεων** Χορηγούνται αντιβιοτικά μόνο επί κλινικής/απεικονιστικής/εργαστηριακής τεκμηρίωσης ή υποψίας συνυπάρχουσας βακτηριακής πνευμονίας, σύμφωνα με τις οδηγίες της Ελληνικής Εταιρείας Λοιμώξεων για την πνευμονία της κοινότητας ή την νοσοκομειακή πνευμονία[7]