Nguy cơ và Phòng ngừa COVID-19 trên bệnh nhân cơ xương khớp

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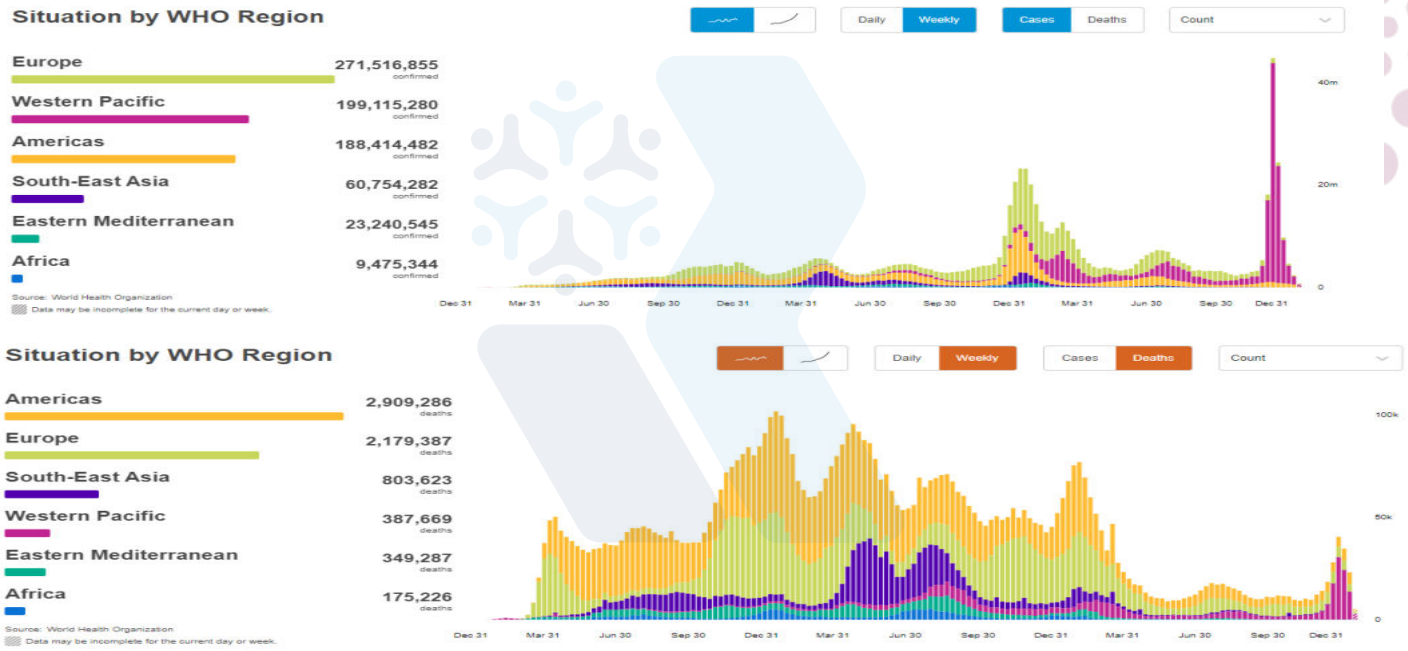
Được hỗ trợ bởi AstraZeneca vì mục đích cập nhật và giáo dục y khoa

Nội dung

- Nguy cơ nhiễm COVID-19 trên bệnh nhân cơ xương khớp
- Phòng ngừa nhiễm COVID-19 trên bệnh nhân cơ xương khớp

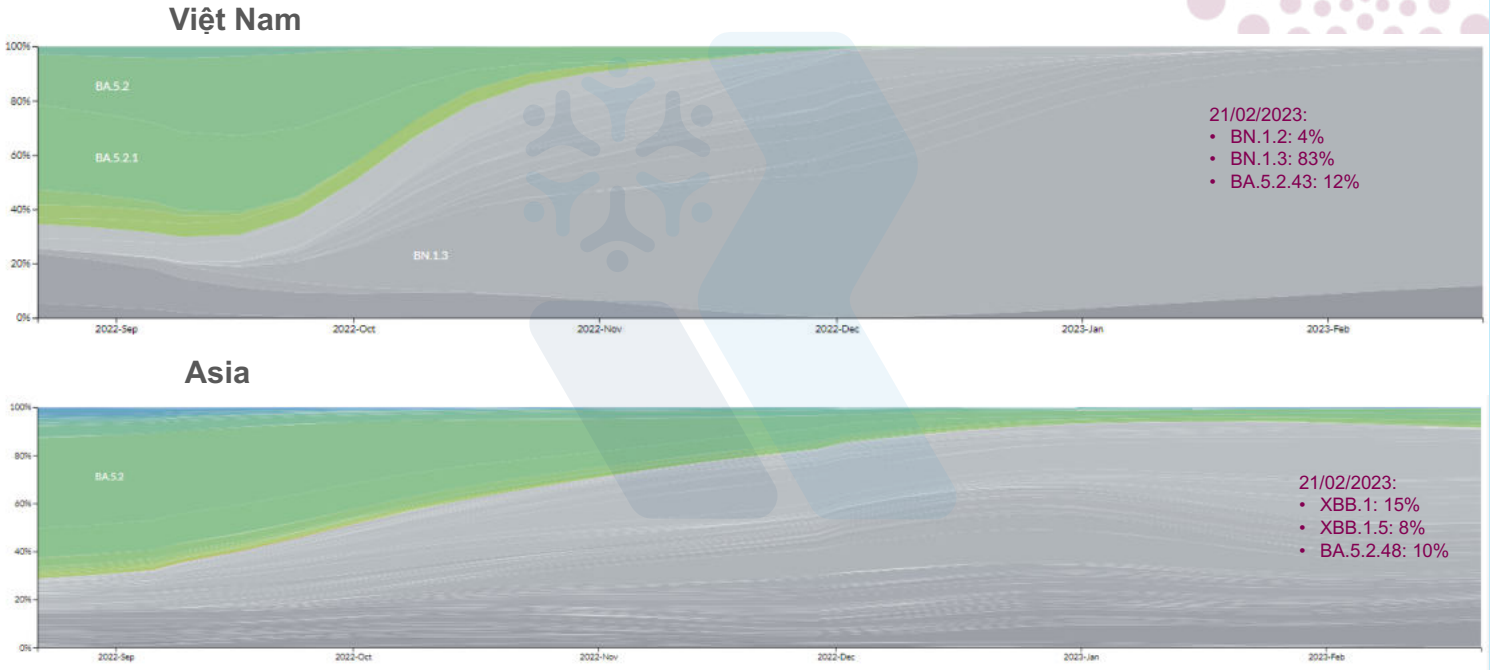
Tình hình COVID-19 trên thế giới



https://covid19.who.int/

COVID-19 chưa thực sự chấm dứt trên toàn thế giới.

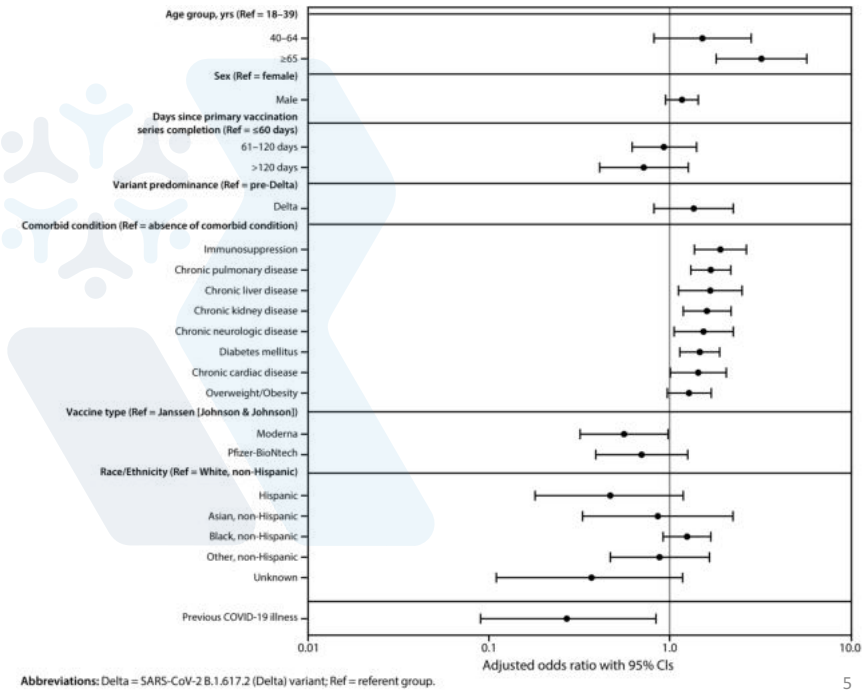
Biến thể SARs-CoV-2 tại Việt Nam và châu Á



Screenshots taken from Nextstrain.org. Genomic epidemiology of novel coronavirus – global subsampling: https://nextstrain.org/ncov/gisaid/asia?dmin=2021-03-01&tl=clade_membership. (accessed 21 Feb 2023).

Yếu tố nguy cơ bệnh nặng

- Yếu tố nguy cơ bệnh nặng/kết cục xấu:
  - Tuổi cao
  - Suy giảm miễn dịch
  - Bệnh nền



Abbreviations: Delta = SARS-CoV-2 B.1.617.2 (Delta) variant; Ref = referent group.

Yek, C., et al. (2022). *Morbidity and Mortality Weekly Report*, *71*(1), 19.

5

1. Nguy cơ của COVID-19 trên bệnh nhân cơ xương khớp

6

Tần suất mới mắc COVID-19

Study	Cohort	Result
Emmi et al. (33)	Italy; 458 SARD pts. (117 SLE, 37 SjS, 17 APS, 64 arthritis, 149 vasculitis, 15 familial Mediterranean fever, 9 recurrent idiopathic pericarditis, 22 others) *43% were taking TNFi, 55% glucocorticoids*	7 tested pts., 1 positive—prevalence 0.22% [0.01–1.21%], comparable to that observed in the general population of Tuscany [0.20% (0.20–0.21%)].The patient was admitted to intensive care unit.
Zen et al. (34)	Italy; 916 pts. (397 SLE, 182 ANCA associated vasculitis, 176 SSc, 111 RA, 50 idiopathic inflammatory myopathy) *36% were taking antimalarial drug*	65 tested pts; 2 (0.21%) positive, a proportion similar to that observed in the general population of the Veneto region.
Favalli et al. (36)	Italy; 955 pts. (531 RA, 203 PsA, 181 SpA, and 40 of CTD/vasculitides/autoinflammatory diseases) *55% were taking TNFi*	The incidence of confirmed COVID-19 is consistent with the general population (0.62 *vs.* 0.66%). None of the pts. developed severe respiratory involvement (three were hospitalized) or died.
Ferri et al. (39) Michelena et al. (35)	Italy; 1641 pts (695 RA, 208 PsA, 35 AS, 438 SSc, 76 SLE, 64 UCTD, 18 SjS, 19 PM/DM, 88 other) Spain; 959 SARD pts. (RA, PsA, SpA, JIA, autoinflammatory syndromes)—all pts. receiving bDMARD or tsDMARD *74% were taking TNFi*	11 confirmed COVID-19 (0.67%) significantly higher than general Italian population (0.35%) (p=0.03). Two patients developed severe COVID-19, of them one died. COVID-19 incidence rates were very similar to that of the general population [(0.48% (95% CI 0.09 to 0.87%)] and [0.58% (95% CI 0.56 to 0.60%)]. All 11 pts. recovered, 6 were admitted to hospital, one required intensive care unit.
Quartuccio et al. (37)	Italy; 1051 SARD pts. (362 RA, 275 PsA, 176 AS or non-radiograph. spondyloarthritis, 74 systemic vasculitides, 38 SLE, 19 other chronic inflammatory diseases) *59% were taking TNFi*	3.8/1000 (95% CI 1.5–9.7/1,000) pts. positive by PCR for COVID-1, compared to 2/1,000, 95% CI 1.9–2.1/1,000 in general population (p=0.33). 3/4 pts. were admitted in hospital, none to intensive care unit, all favorable outcome.
Favalli et al. (40)	Italy; 530 pts. (49% RA, 36% SpA/PsA, 10% JIA, 3% CTD, 1 patient with sarcoidosis) *53% were taking TNFi*	3 pts. confirmed COVID-19, one required hospitalization, none died; 10 pts. reported contact with COVID-19 positive-none developed infection.
Monti et al. (41)	Italy; 320 pts. (57% RA, 43% SpA) treated with bDMARD or tsDMARD; *52% treated with TNFi*	4 pts. confirmed COVID-19, four with clinical symptoms and five with contacts, but no symptoms. No death or severe COVID-19.Chronic arthritis pts. treated with bDMARDs or tsDMARDs do not seem to be at increased risk of respiratory or life-threatening complications from SARS-CoV-2 compared with the general population. No relapses of rheumatic disease observed.
Conticini et al. (42)	Italy; 859 SARD pts. (411 RA, 192 PsA, 131 AS, 54 SSc, 6 SLE, 26 vasculitides, 8 sarcoidosis, and 9 other) treated with stable and full dosage of bDMARDs or tsDMARD *41% treated with TNFi*	2 pts. diagnosed with COVID-19, one hospitalized and discharged after 3 days, other remained asymptomatic. Pts. treated with bDMARDs or tsDMARDs did not develop life-threatening complications from COVID-19.
Jovani et al. (43)	Spain; 1,037 rheumatic disease pts taking bDMARD/tsDMARD (exact diagnoses and therapy not reported)	3 pts. were hospitalized due COVID19, none required oxygen supply. 2 pts. developed acute pyelonephritis.
So et al. (38)	Hong Kong; 39,835 rheumatologic disease pts. (exact diagnoses and therapy for cohort not reported)	Incidence 0.0126% of COVID-19 confirmed in rheumatologic disease pts., compared to 0.0142% in the general population All pts. made uneventful recovery without complications or flare of underlying diseases.
Tomelleri et al. (44)	Italy; 162 large vessel vasculitis (67 Takayasu arteritis, 95 giant cell arteritis) 62% taking glucocorticoids, 32% taking tocilizumab	4 pts. confirmed COVID-19 (incidence 2.5%), 12 pts. with clinical symptoms, 2 pts. were hospitalized, oxygen not needed. None of pts experienced relapse of LVV (until April).
Bozzalla Cassione et al. (45)	Italy; 165 SLE 77% taking hydoxychloroquine, 56% taking prednisolone	2.5% Incidence higher as compared to the general population (0.76–0.47%). 4 pts. confirmed COVID-19, 8 with clinical symptoms and 7 with contacts no symptoms. 1 pt. required intensive care unit.

Lakota, K., et al (2021). *Frontiers in immunology*, *11*, 611318.

Nguy cơ nhập viện và tử vong

Study location	Rheumatic disease population (n)	Comparator population (n)	Hospitalization[a]; OR/HR/RR (95% CI)	Death[a]; OR/ HR (95% CI)	Ref.
Denmark	RA, CTD with PCR test (348 SARS-CoV-2 positive, 13,498 negative)	General population with PCR test (11,122 positive, 410,697 negative)[b]	OR 1.5 (1.1–1.9)	OR 1.1 (0.8–1.6)	31
Denmark	RA, spondyloarthritis, CTD, vasculitis (58,052)	General population (~4.5 million)[b]	HR 1.46 (1.15–1.86)	NR	32
South Korea	Inflammatory arthritis, CTD with PCR test (8,297)	General population with PCR test (133,609)[b]	NR	OR 1.69 (1.01–2.84)	18
UK	RA, systemic lupus erythematosus, psoriasis (878,475)	General population (17,278,392)[b]	NR	HR 1.19 (1.11–1.27)	33
UK	RA (5,409), gout (13,105)	General population (473,139)[b]	NR	RA OR 1.9 (1.2–3.0), gout OR 1.2 (0.8–1.7)	22
USA	Rheumatic disease (681)	COVID-19-positive general population (31,461)[b]	NR	OR 1.17 (0.85–1.60)	34
USA	Rheumatic disease (143)	Patients from same hospital without rheumatic disease (688)[c]	OR 0.87 (0.68–1.11)	OR 1.02 (0.53–1.95)	35
USA	Autoimmune rheumatic disease and COVID-19 (2,379)	Matched individuals with COVID-19 without autoimmune rheumatic disease (2,379)[c]	RR 1.14 (1.03–1.26)	RR 1.08 (0.81–1.44)	36
USA	RA (33,886)	Individuals without RA (33,886)[c]	HR 1.35 (1.10–1.66) for hospitalization or death		23

Grainger, R., et al (2022). *Nature Reviews Rheumatology*, *18*(4), 191-204.

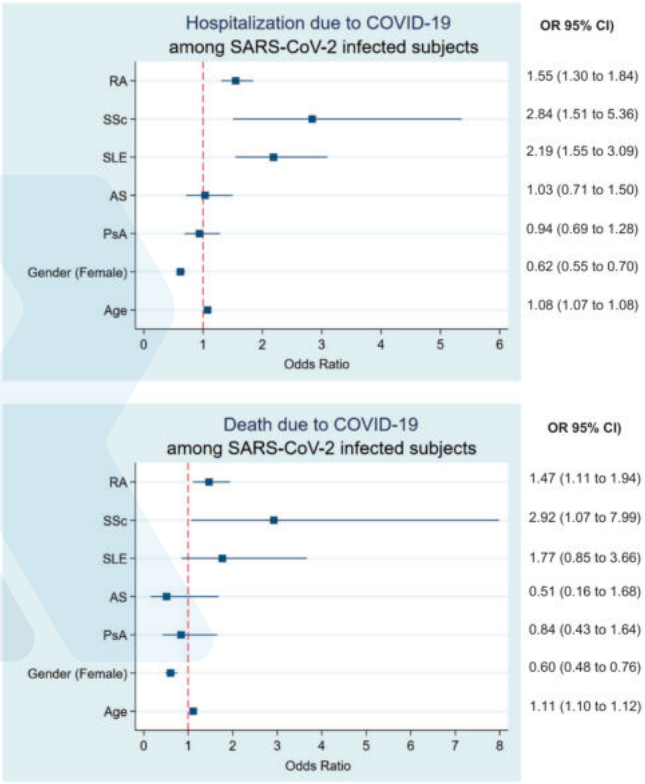
COVID-19 Outcomes in Patients with Systemic Autoimmune Rheumatic Diseases (SARDs) Compared to the General Population: A US Multi-Center Comparative Cohort Study

	Unmatched			Exposure Score-Matched*			Extended Exposure Score-Matched†		
	SARD Events, n (%)	Non-SARD Comparator Events, n (%)	Relative Risk (95% CI)	SARD Events, n (%)	Non-SARD Comparator Events, n (%)	Relative Risk (95% CI)	SARD Events, n (%)	Non-SARD Comparator Events, n (%)	Relative Risk (95% CI)
Hospitalization	620 (26)	21,501 (15)	**1.73 (1.62, 1.85)**	620 (26)	546 (23)	**1.14 (1.03, 1.26)**	616 (26)	579 (24)	1.06 (0.96, 1.17)
ICU Admission	142 (6)	4,615 (3)	**1.85 (1.57, 2.17)**	142 (6)	108 (5)	**1.32 (1.03, 1.68)**	141 (6)	134 (6)	1.05 (0.84, 1.32)
Mechanical Ventilation	78 (3)	2,938 (2)	**1.59 (1.28, 1.99)**	78 (3)	74 (3)	1.05 (0.77, 1.44)	77 (3)	85 (4)	0.91 (0.67, 1.23)
ARF requiring RRT	38 (2)	737 (1)	**3.09 (2.24, 4.28)**	38 (2)	21 (1)	**1.81 (1.07, 3.07)**	38 (2)	41 (2)	0.93 (0.60, 1.44)
Ischemic Stroke	42 (2)	833 (1)	**3.03 (2.23, 4.11)**	42 (2)	28 (1)	1.50 (0.93, 2.41)	42 (2)	39 (2)	1.08 (0.70, 1.66)
VTE	85 (4)	1,721 (1)	**2.96 (2.39, 3.67)**	85 (4)	49 (2)	**1.74 (1.23, 2.45)**	85 (4)	53 (2)	**1.60 (1.14, 2.25)**
Death	94 (4)	2,962 (2)	**1.90 (1.56, 2.33)**	94 (4)	87 (4)	1.08 (0.81, 1.44)	93 (4)	79 (3)	1.18 (0.88, 1.58)
Composite outcome‡	213 (9)	7,069 (5)	**1.81 (1.59, 2.06)**	213 (9)	179 (8)	1.19 (0.98, 1.44)	212 (9)	191 (8)	1.11 (0.92, 1.34)

D'Silva, K. M., et al (2021). *Arthritis & rheumatology*, *73*(6), 914-920.

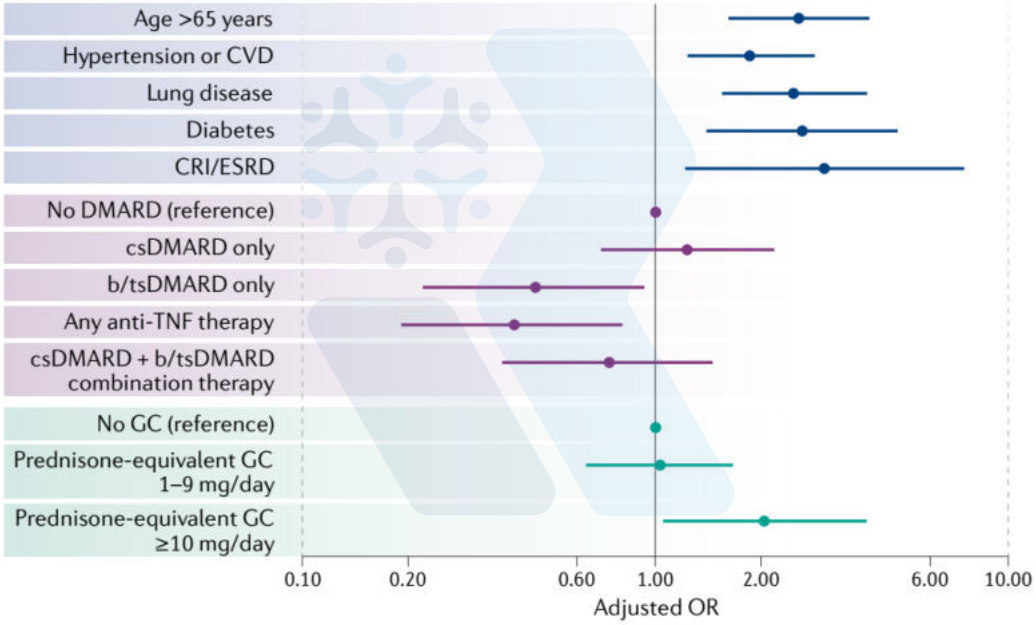
Nguy cơ COVID-19

- Tỉ lệ nhập viện và tử vong thay đổi tùy theo bệnh lý
- VKDT, Lupus ban đỏ và xơ cứng bì có nguy cơ nhập viện cao hơn so với dân số chung
- VKDT có nguy cơ tử vong cao hơn



Bournia, V. K., Fragoulis, G. E., Mitrou, P., Mathioudakis, K., Tsolakidis, A., Konstantonis, G., ... & Sfikakis, P. P. (2022). Different COVID-19 outcomes among systemic rheumatic diseases: a nation-wide cohort study. *medRxiv*, 2022-03.

Yếu tố nguy cơ liên quan với nhập viện



Hyrich, K. L., & Machado, P. M. (2021). *Nature Reviews Rheumatology*, *17*(2), 71-72.

Thuốc điều trị và nguy cơ COVID-19

			Univariate		Multivariable	
	Controls (405 597)	Cases (44 020)	Rate ratio (95% CI)	p	Rate ratio (95% CI)	p
Conventional synthetic DMARDs						
Methotrexate	3010 (1%)	531 (1%)	1.66 (1.51, 1.82)	2×10^{-26}	1.29 (1.15, 1.45)	1×10^{-5}
Hydroxychloroquine	1898 (0%)	361 (1%)	1.80 (1.61, 2.02)	4×10^{-24}	1.17 (1.02, 1.35)	0.02
Sulfasalazine	1661 (0%)	420 (1%)	2.41 (2.16, 2.68)	5×10^{-57}	2.09 (1.83, 2.38)	1×10^{-27}
Leflunomide	265 (0%)	52 (0%)	1.86 (1.38, 2.50)	5×10^{-5}	1.21 (0.86, 1.71)	0.3
Glucocorticoids (prednisolone equivalent mg daily)						
0	403 211 (99%)	43 214 (98%)		–		–
> 0 to 5	1574 (0%)	467 (1%)	2.78 (2.50, 3.08)	2×10^{-81}	2.53 (2.24, 2.86)	3×10^{-51}
> 5 to 10	566 (0%)	201 (0%)	3.33 (2.83, 3.92)	7×10^{-48}	2.73 (2.26, 3.30)	3×10^{-25}
> 10	246 (0%)	138 (0%)	5.4 (4.4, 6.7)	9×10^{-56}	5.2 (4.1, 6.6)	1×10^{-40}
Targeted DMARDs						
TNF inhibitors	164 (0%)	34 (0%)	2.00 (1.38, 2.90)	2×10^{-4}	1.44 (0.94, 2.20)	0.09
B-cell depletion	25 (0%)	15 (0%)	5.9 (3.1, 11.4)	7×10^{-8}	3.61 (1.68, 7.77)	0.001
IL-6 inhibitors	21 (0%)	9 (0%)	4.07 (1.86, 8.90)	4×10^{-4}	3.04 (1.23, 7.51)	0.02
IL-17 inhibitors	24 (0%)	5 (0%)	1.79 (0.66, 4.83)	0.2	0.99 (0.30, 3.22)	1
JAK inhibitors	27 (0%)	12 (0%)	4.37 (2.20, 8.68)	2×10^{-5}	2.30 (1.04, 5.07)	0.04

McKeigue, P. M., et al (2022). *Scandinavian Journal of Rheumatology*, 1-6.

JAMA Internal Medicine | Original Investigation

Association Between Immune Dysfunction and COVID-19 Breakthrough Infection After SARS-CoV-2 Vaccination in the US

Table 2. COVID-19 Breakthrough Infection Among Patients With Immune Dysfunction

Patient group	Pre-Delta variant period			Post-Delta variant period		
	Total person-months	No. of breakthrough infection cases	Incidence rate per 1000 person-months (95% CI)[a]	Total person-months	No. of breakthrough infection cases	Incidence rate per 1000 person-months (95% CI)[a]
Partial vaccination						
Overall	553 478	2165	2.9 (2.9-2.9)	218 443	1562	9.6 (9.5-9.7)
No immune dysfunction	524 821	2007	2.8 (2.8-2.9)	205 139	1433	9.3 (9.2-9.4)
HIV infection	7010	37	3.6 (3.6-3.7)	3354	26	11.9 (11.4-12.4)
MS	2418	<20[b]	3.5 (3.5-3.6)	954	<20[b]	11.6 (10.8-12.4)
RA	10 718	46	3.7 (3.7-3.8)	4003	27	12.2 (11.8-12.6)
SOT	7007	66	6.3 (6.2-6.4)	4164	55	20.6 (19.4-21.8)
BMT	1503	<20[b]	3.4 (3.3-3.5)	829	<20[b]	11.2 (10.3-12.2)
Full vaccination						
Overall	1 501 418	2808	2.2 (2.2-2.2)	2 162 800	16 382	7.3 (7.3-7.4)
No immune dysfunction	1 423 568	2484	2.2 (2.2-2.2)	2 053 050	15 255	7.1 (7.1-7.2)
HIV infection	17 336	45	2.8 (2.8-2.8)	26 844	250	9.1 (8.8-9.4)
MS	6568	<20[b]	2.7 (2.7-2.8)	9644	85	8.9 (8.4-9.3)
RA	32 847	103	2.8 (2.8-2.9)	43 044	408	9.3 (9.1-9.6)
SOT	17 314	137	4.8 (4.7-4.9)	24 647	343	15.7 (15.1-16.4)
BMT	3786	21	2.6 (2.6-2.7)	5581	41	8.6 (8.0-9.1)

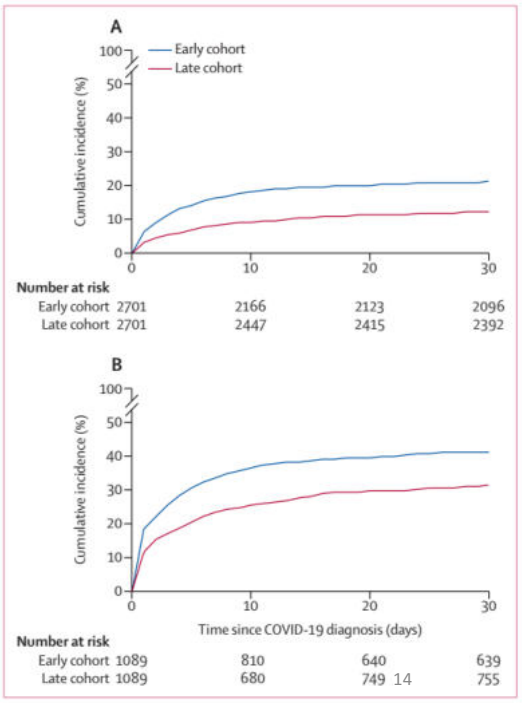
Sun, J., et al. (2022). *JAMA internal medicine*, *182*(2), 153-162.

Xu hướng điều trị

	Unmatched cohorts			Exposure score matched cohorts		
	Early cohort events (n=2811)	Late cohort events (n=5729)	RR (95% CI)	Early cohort events (n=2701)	Late cohort events (n=2701)	RR (95% CI)
Hospitalisation	1309 (46·6%)	1658 (28·9%)	0·62 (0·59–0·66)	1227 (45·4%)	874 (32·4%)	0·71 (0·67–0·76)
Intensive care unit admission	417 (14·8%)	370 (6·5%)	0·44 (0·38–0·50)	385 (14·3%)	214 (7·9%)	0·56 (0·47–0·65)
Mechanical ventilation	257 (9·1%)	171 (3·0%)	0·33 (0·27–0·39)	247 (9·1%)	96 (3·6%)	0·39 (0·31–0·49)
Acute kidney injury	601 (21·4%)	672 (11·7%)	0·55 (0·50–0·61)	560 (20·7%)	372 (13·8%)	0·66 (0·59–0·75)
Renal replacement therapy	34 (1·2%)	38 (0·7%)	0·54 (0·34–0·86)	32 (1·2%)	17 (0·6%)	0·53 (0·30–0·96)
Death	273 (9·7%)	209 (3·6%)	0·38 (0·32–0·45)	252 (9·3%)	122 (4·5%)	0·48 (0·39–0·60)
Composite outcome*	647 (23·0%)	544 (9·5%)	0·41 (0·37–0·46)	605 (22·4%)	309 (11·4%)	0·51 (0·45–0·58)

Data are n (%), unless otherwise indicated. RR=relative risk. *Death, intensive care unit admission, or mechanical ventilation. Exposure score includes all covariates in table 1.

Table 2: 30-day outcomes after COVID-19 diagnosis among patients with rheumatic and musculoskeletal diseases



Jorge, A., et al (2021). *The Lancet Rheumatology*, *3*(2), e131-e137.

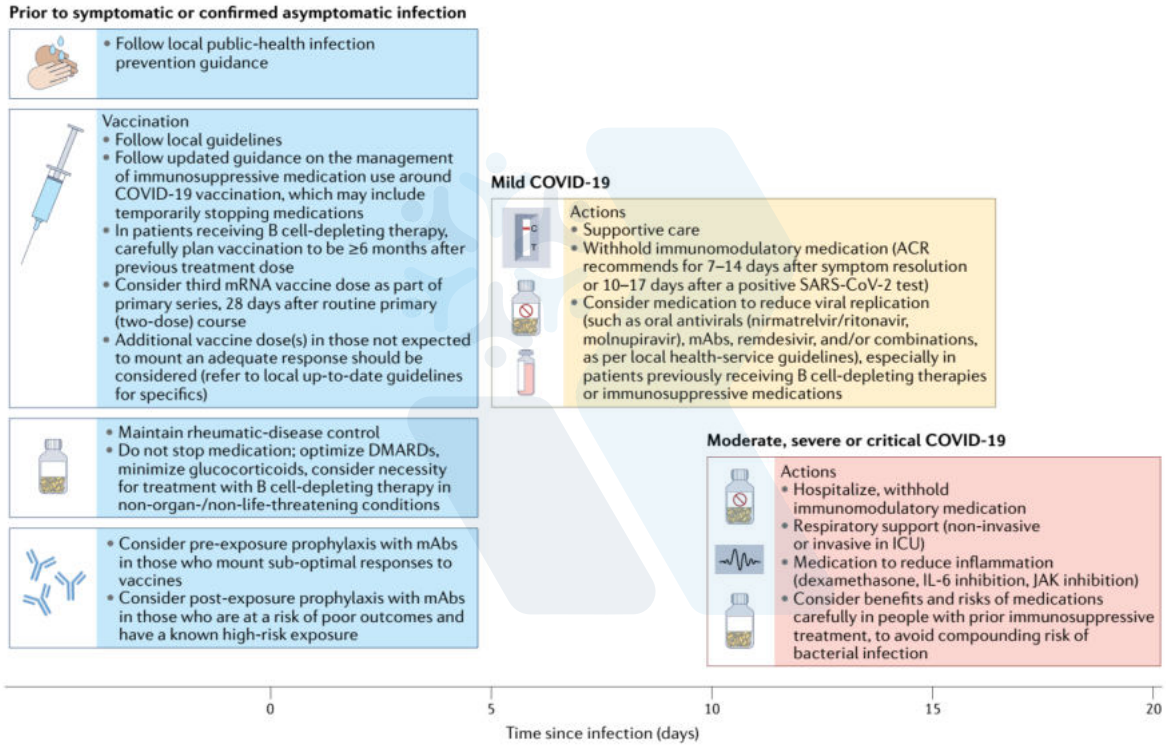
Nguy cơ COVID-19 ở BN cơ xương khớp

- Nguy cơ nhiễm cao hơn so với dân số chung
- Nguy cơ diễn tiến nặng, kết cục xấu
- Liên quan với các yếu tố khác: tuổi, bệnh đồng mắc, điều trị
- Nguy cơ có thể khác nhau giữa các bệnh lý và điều trị

→ Phòng ngừa là cần thiết!!!

Curtis, J. R., et al. (2023). *Arthritis & Rheumatology*, *75*(1), E1-E16.

2. Phòng ngừa COVID-19 trên bệnh nhân cơ xương khớp



Grainger, R., et al. (2022). *Nature Reviews Rheumatology*, *18*(4), 191-204.

Khuyến cáo lâm sàng

Statement domain	Guidance statement	Level of task force consensus
Clinical practice	RMD and AIIRD patients should receive COVID-19 vaccination, consistent with the age restriction of the EUA and/or FDA approval.†	Strong
Clinical practice	RMD patients without an AIIRD who are receiving immunomodulatory therapy should be vaccinated in a similar manner as described in this guidance as AIIRD patients receiving those same treatments.	Moderate
Vaccine effectiveness/ safety	For AIIRD patients who are not yet vaccinated, either of the mRNA vaccines is recommended over the Johnson & Johnson vaccine. There is no recommendation for one mRNA vaccine over another.†	Moderate
Vaccine effectiveness	For a multidose primary vaccine, AIIRD patients should receive the second dose of the same vaccine, even if there are nonserious adverse events associated with receipt of the first dose, consistent with timing described in CDC guidelines (32).	Strong
Clinical practice	**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**
Clinical practice	For patients who previously completed the mRNA COVID-19 vaccine series an mRNA vaccine supplemental dose of either type (Pfizer or Moderna) is preferred.	Moderate
Clinical practice	**Primary vaccination, supplemental dosing, and booster doses should be given regardless of whether patients have experienced natural COVID-19 infection.**	**Strong**
Clinical practice	Health care providers should not routinely order any laboratory testing (e.g., antibody tests for IgM and/or IgG to spike or nucleocapsid proteins) to assess immunity to COVID-19 postvaccination, nor to assess the need for vaccination in an as-yet-unvaccinated person.§	Strong
Public health	Following COVID-19 vaccination, RMD patients should continue to follow all public health guidelines regarding physical distancing and other preventive measures.¶	Strong
Clinical practice	**For high-risk AIIRD patients, pre-exposure prophylaxis monoclonal antibody treatment is recommended when available, if licensed or approved under FDA EUA.#**	**Moderate**
Clinical practice/public health	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.	Moderate
Vaccine effectiveness/ disease-related	While vaccination would ideally occur in the setting of well-controlled AIIRD, except for AIIRD patients with life-threatening disease (e.g., in the ICU for any reason), COVID-19 vaccination should occur as soon as possible for those for whom it is being recommended, irrespective of disease activity and severity.	Strong

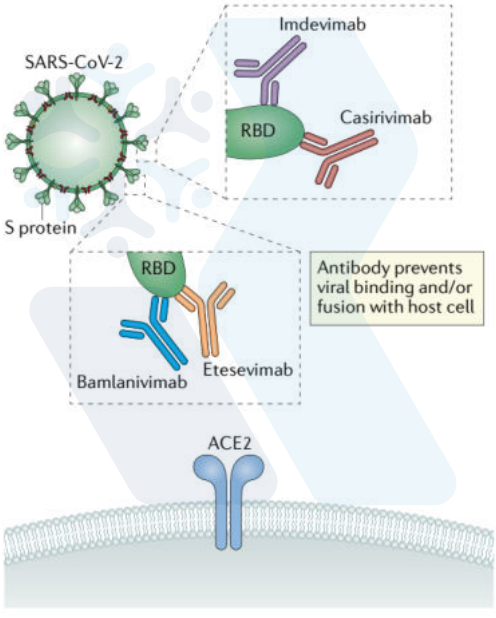
Curtis, J. R., et al (2023). *Arthritis & Rheumatology*, *75*(1), E1-E16.

Điều chỉnh thuốc theo tiêm vaccin

Medication(s)	Timing considerations for immunomodulatory therapy and vaccination	Level of task force consensus
Abatacept (IV)	Time vaccination to occur 1 week prior to the next dose of abatacept (IV).	Moderate
Abatacept (SC)	Withhold for 1–2 weeks (as disease activity allows) after each COVID-19 vaccine dose.	Moderate
Acetaminophen, NSAIDs	Assuming that disease is stable, withhold for 24 hours prior to vaccination. No restrictions on use post vaccination to once symptoms develop.	Moderate
Belimumab (SC)	Withhold for 1–2 weeks (as disease activity allows) after each COVID-19 vaccine dose.	Moderate
TNFi, IL-6R, IL-1R, IL-17, IL-12/23, IL-23, and other cytokine inhibitors†	The task force failed to reach consensus on whether or not to temporarily interrupt these following each COVID-19 vaccine dose, including both primary vaccination and supplemental/booster dosing.	Moderate
Cyclophosphamide (IV)	Time cyclophosphamide administration so that it will occur ~1 week after each vaccine dose, when feasible.	Moderate
HcQ, **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 rheumatology provider before proceeding.‡	Moderate
All other conventional and targeted immunomodulatory or immunosuppressive medications (e.g., JAK inhibitors, MMF) except for those listed above§	Withhold for 1–2 weeks (as disease activity allows) after each COVID-19 vaccine dose.	Moderate

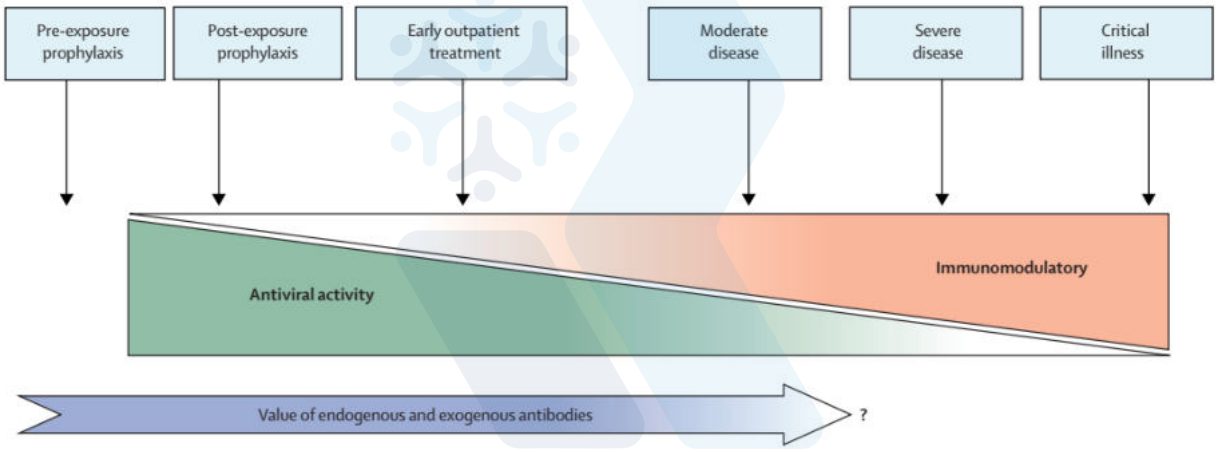
Curtis, J. R., et al (2023). *Arthritis & Rheumatology*, *75*(1), E1-E16.

Kháng thể đơn dòng



Taylor, P. C., et al (2021). *Nature Reviews Immunology*, *21*(6), 382-393.

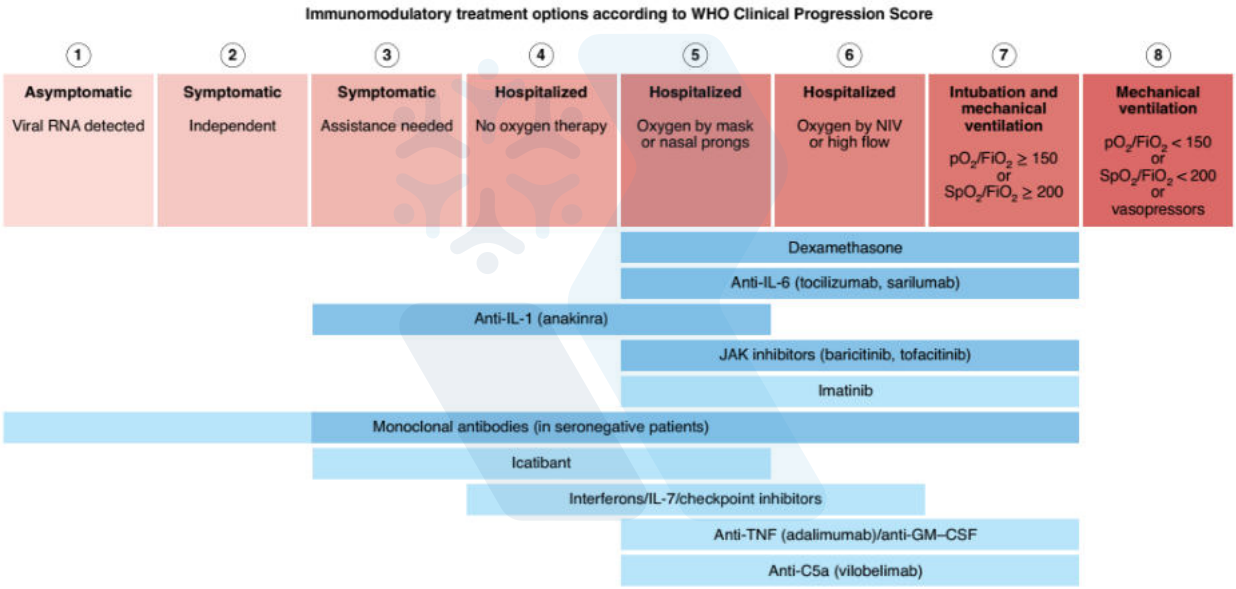
Vai trò của kháng thể trong COVID-19



21

Shapiro, A. E., & Ignacio, R. A. B. (2022). *The Lancet Infectious Diseases*, *22*(5), 567-569.

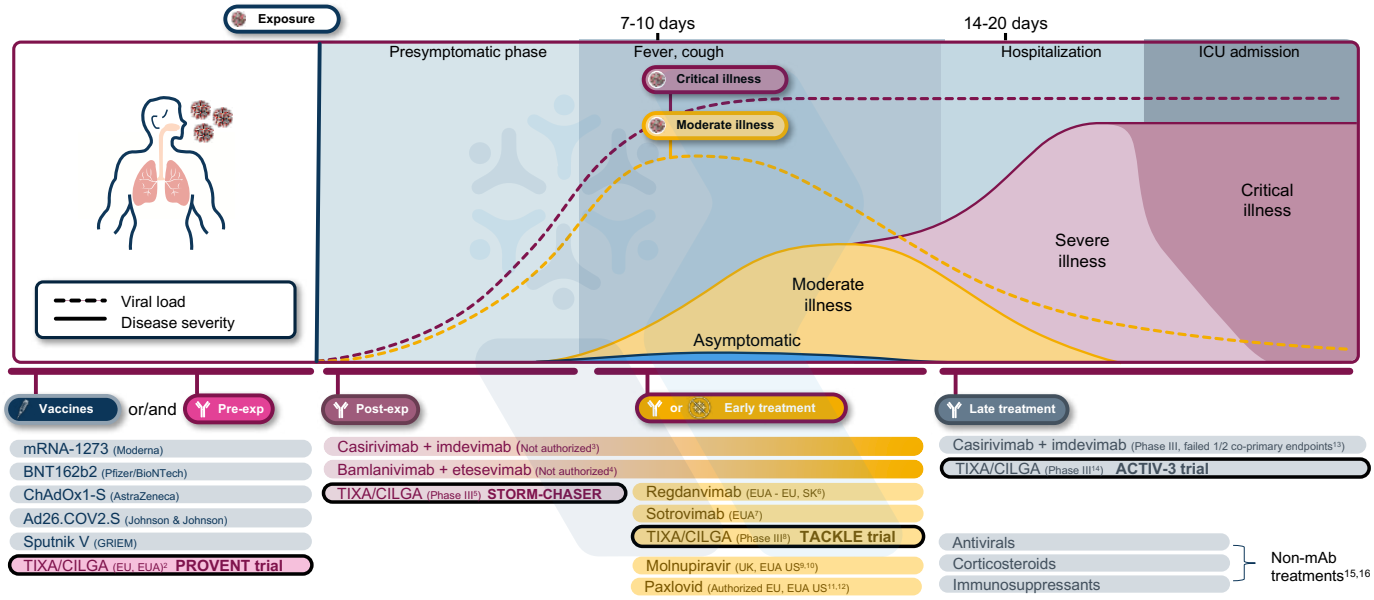
Tổng quan về điều trị COVID-19



22

van de Veerdonk, F. L., et al (2022). *Nature Medicine*, *28*(1), 39-50.

Nghiên cứu phát triển các giải pháp kiểm soát bệnh COVID-19



Some of the information provided is based off a preprint research paper that has not been peer reviewed.
COVID-19 = coronavirus disease 2019; EUA = Emergency Use Authorization; EU = European Union; exp = exposure; ICU = intensive care unit; mAb = monoclonal antibody; mRNA = messenger ribonucleic acid; SK = South Korea; TIXA/CILGA = tixagevimab/cilgavimab; UK = United Kingdom; US = United States; VAB = virtual advisory board. 1. Corti D et al. *Cell*. 2021;184:3086-3108; 2. Fact sheet for healthcare providers. Emergency Use Authorization (EUA) of EVUSHELD™ (tixagevimab co-packaged with cilgavimab). 2022; 3. Regeneron Pharmaceuticals Inc. Casirivimab and imdevimab; 4. Lilly. Bamlanivimab and etesevimab Emergency Use Authorization; 5. Study NCT04625972. ClinicalTrials.gov website; 6. Celltrion Healthcare press release. Published November 14, 2021; 7. GlaxoSmithKline. Sotrovimab: Emergency Use Authorization (EUA) information for healthcare providers; 8. AstraZeneca Pharmaceuticals LP press release. Published November 18, 2021; 9. Merck & Co., Inc. Molnupiravir: information for healthcare providers; 10. Medicines and Healthcare products Regulatory Agency press release. Published August 20, 2021; 11. European Medicines Agency press release. Published January 27, 2022; 12. U.S. Food and Drug Administration. Fact sheet for healthcare providers: Emergency Use Authorization for nirmatrelvir and ritonavir. https://www.fda.gov/media/155050/download; 13. RECOVERY Collaborative Group. *Lancet*. 2022;399:665-676; 14. Holland TL et al. Preprint published online. *Lancet*. 2022; 15. World Health Organization. https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2022.2. Accessed March 5, 2022; 16. National Institutes of Health. Therapeutic management of hospitalized adults with COVID-19. https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/hospitalized-adults--therapeutic-management/.

Primary analysis

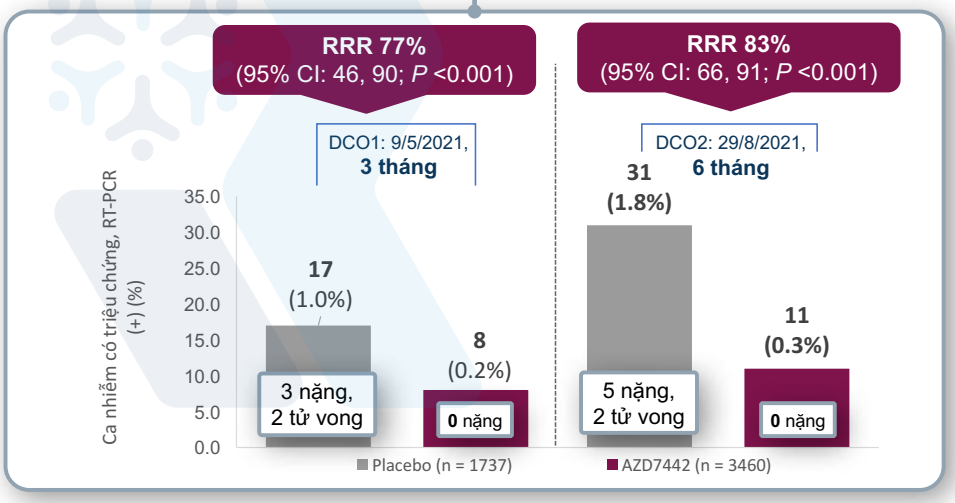
Nghiên cứu **PROVENT**: nghiên cứu pha 3, mù đôi, có đối chứng (giả dược) về khả năng dự phòng trước phơi nhiễm của AZD7442 trên 5197 đối tượng [1,2]

ClinicalTrials.gov identifier: NCT04625725
Actual start date: 21 November 2020
Actual primary completion: 5 May 2021
(estimated study completion: 22 June 2022)

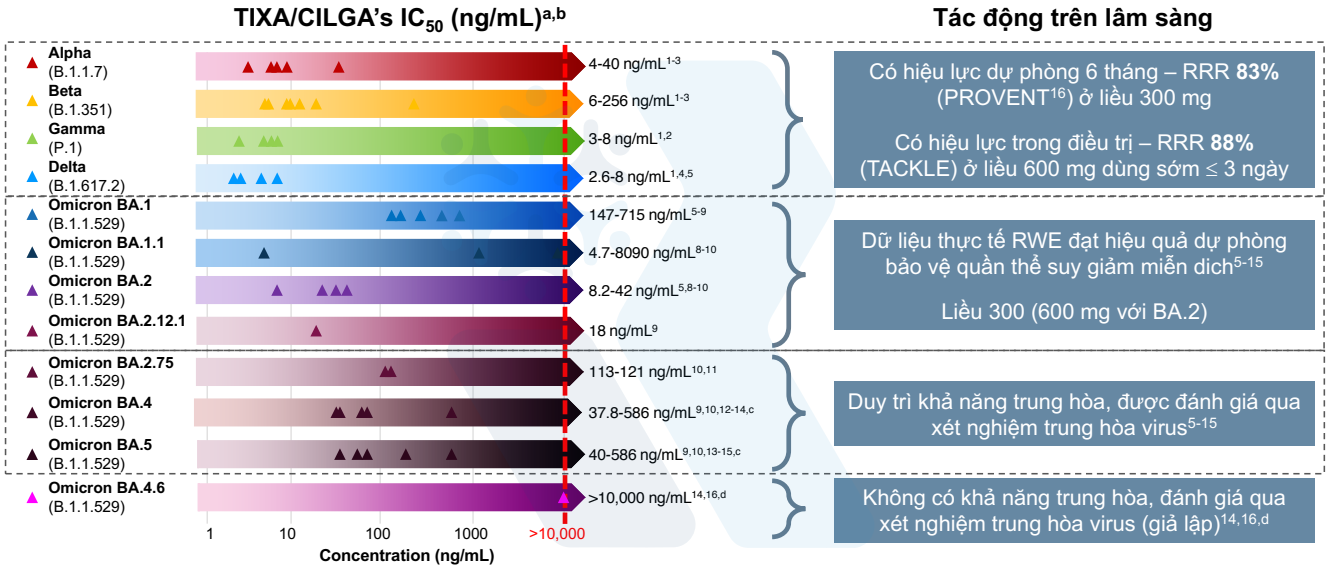
Tiêu chí hiệu lực chính

- Tần suất ca nhiễm SARS-CoV-2 RT-PCR dương tính có triệu chứng trước ngày 183
- Tính an toàn và dung nạp của TIXA/CILGA (tỉ lệ xuất hiện AEs, SAEs, MAAEs, AESIs)

Giảm có ý nghĩa tần suất các ca nhiễm COVID-19 có triệu chứng mới mắc giữa nhóm AZD7442 so với nhóm giả dược



Khả năng trung hòa của Tixa/Cilga đối với các biến thể SARS-CoV-2[1-15]



[a]IC_{50} is the concentration of an inhibitory substance or antagonist that reduces a given biological process or biological component by 50%[17]; [b]Some data points presented are EC_{50} values, which represent the concentration of a drug that produces 50% of the maximum possible effect[8,15,17]; [c]For neutralization assays that used pseudoviruses harboring the BA.4/5 spike protein, IC_{50} data points were included on both the BA.4 and BA.5 rows[8,10,14]; [d]Omicron BA.4.6 showed reduced susceptibility to tixagevimab (>1,000-fold) and to cilgavimab (>1,000-fold) such that tixagevimab and cilgavimab together are unlikely to be active against this variant.[16] Some of the information provided is based off preprint research papers that have not been peer reviewed. [e]Day of earliest documented samples (BA.4.6 in Jul 2022).

EC_{50} = half-maximal effective concentration; IC_{50} = half-maximal inhibitory concentration; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; TIXA/CILGA = tixagevimab/cilgavimab; VOCs = variants of concern.

1. National Center for Advancing Translational Sciences. Evusheld: tixagevimab (tixagevimab) and cilgavimab (cilgavimab) mAbs for SARS-CoV-2 antiviral resistance information (version 5); 2. Dejnirattisai W et al. *Cell.* 2021;184(11):2939-2954.e9; 3. Chen RE et al. *Nat Med.* 2021;27(4):717-726; 4. Liu C et al. *Cell.* 2021;184(16):4220-4236.e13; 5. Bruel T et al. *Nat Med.* 2022;28(6):1297-1302; 6. Dejnirattisai W et al. *Cell.* 2022;185(3):467-484.e15; 7. VanBlargan LA et al. *Nat Med.* 2022;28(3):490-495; 8. Case JB et al. Pre-print. *bioRxiv.* 2022;
9. Cao Y et al. *Nature.* 2022;608(7923):593-602; 10. Yamasoba D et al. Pre-print. *bioRxiv.* 2022; 11. Cao Y et al. Pre-print. *bioRxiv.* 2022; 12. Tuekprakhon A et al. Article and supplementary material; pre-print. *bioRxiv.* 2022; 13. Takashita E et al. Letter. *N Engl J Med.* 2022;387(5):468-470; 14. Wang Q et al. Article and supplementary material; pre-print. *bioRxiv.* 2022; 15. Touret F et al. *Sci Rep.* 2022;12(1):12609; 16. Fact sheet for healthcare providers. Emergency Use Authorization (EUA) of EVUSHELD™ (tixagevimab co-packaged with cilgavimab). 2022; 17. Neubig RR et al. *Pharmacol Rev.* 2003;55(4):597-606.

Những điểm lưu ý khi dùng kháng thể đơn dòng để dự phòng COVID-19

Cần được bác sĩ khám và chỉ định

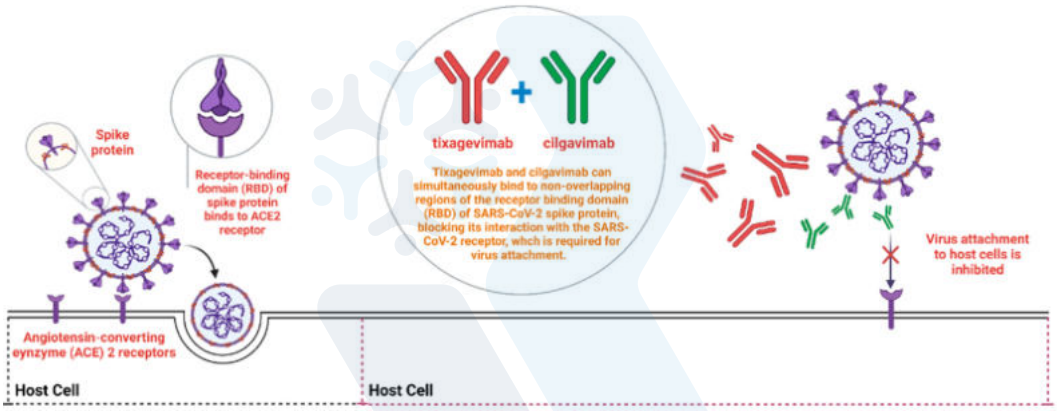
Kháng thể được dùng qua đường tiêm (bắp)

Nếu tiêm bắp, ưu tiên cơ vùng mông

- Cần theo dõi sau tiêm trong thời gian tối thiểu 1 giờ.
- **Không cần trì hoãn tiêm ngừa vaccine COVID-19** sau khi sử dụng kháng thể đơn dòng hay huyết tương của người đã khỏi bệnh[2]
- Ở người đã tiêm ngừa vaccine COVID-19 trước đó cần dự phòng thêm, nên tiêm kháng thể đơn dòng tối thiểu sau 2 tuần[2]

1. US EUA Fact Sheet: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-new-long-acting-monoclonal-antibodies-pre-exposure (posted Jun 2022). 2. Centers for Disease Control and Prevention. Interim clinical considerations for use of COVID-19 vaccines currently approved or authorized in the United States. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#:~:text=COVID-19 vaccination is recommended for all people aged 12,persons aged ≥12 years.

Kháng thể đơn dòng



- Giảm tử vong, nhập viện, nhập ICU, giảm độ nặng – triệu chứng, an toàn

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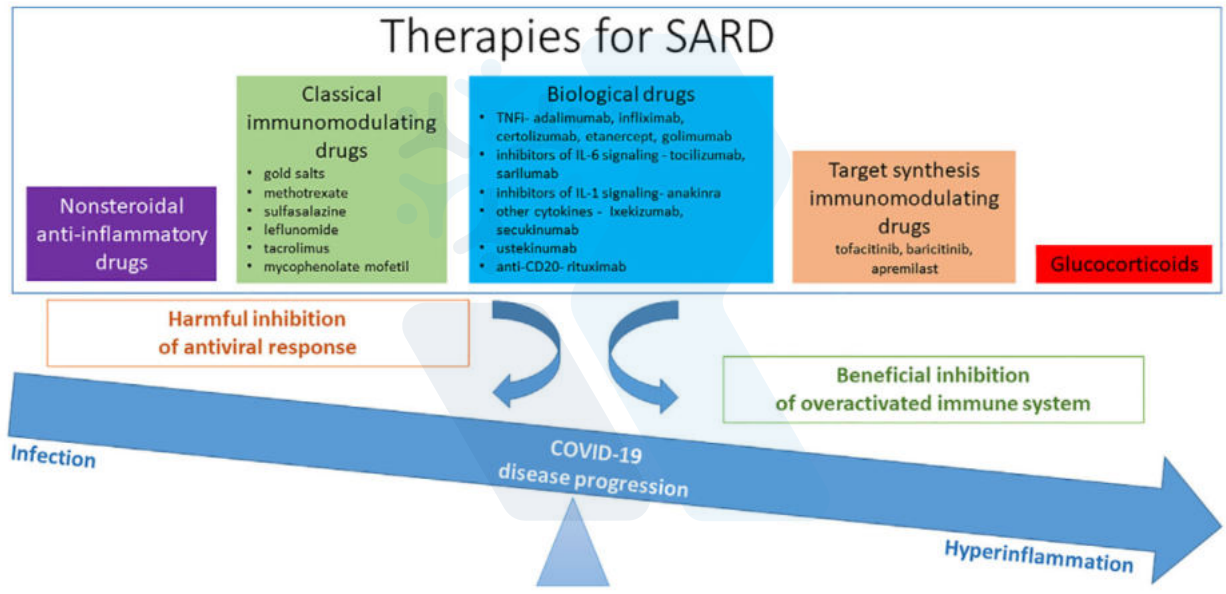
Taylor, P. C., et al (2021). *Nature Reviews Immunology*, *21*(6), 382-393.

COVID-19 và Bệnh cơ xương khớp



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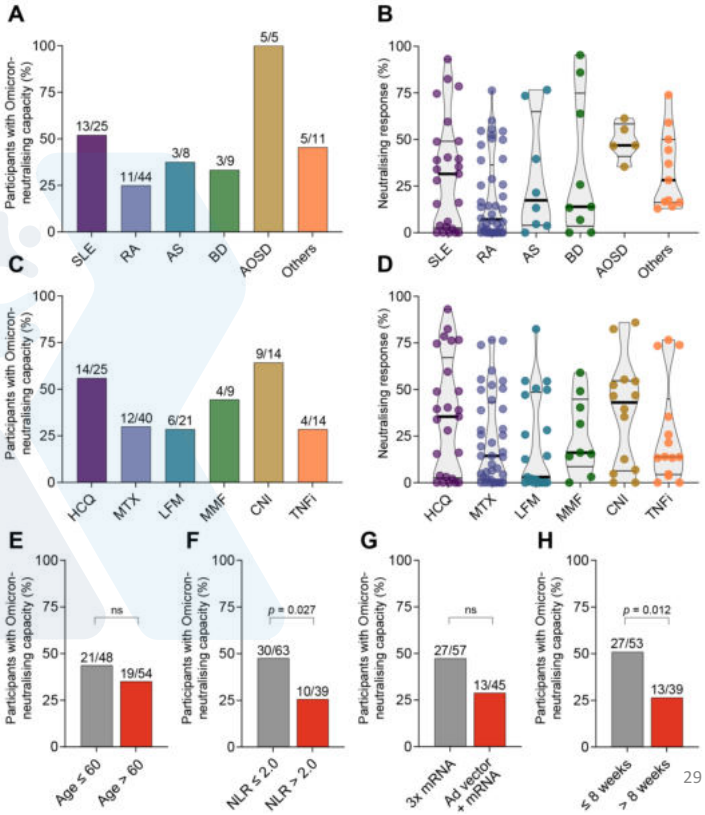
Lakota, K., et al (2021). *Frontiers in immunology*, *11*, 611318.

EPIDEMIOLOGICAL SCIENCE

SARS-CoV-2 Omicron escapes mRNA vaccine booster-induced antibody neutralisation in patients with autoimmune rheumatic diseases: an observational cohort study

Woo-Joong Kim [1], Seong-Ho Choi [2], Ji Young Park [3], Jung Soo Song [4], Jin-Won Chung [2], Sang Tae Choi [4]



Kim, W. J., et al (2022). *Annals of the Rheumatic Diseases, 81*(11), 1585-1593.

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Tóm tắt

- Cần lưu ý nguy cơ nhiễm COVID-19 ở bệnh nhân cơ xương khớp
- Nhiễm COVID-19 làm tăng tử vong và các biến cố xấu
- Phòng ngừa là biện pháp quan trọng
- Cần phối hợp nhiều biện pháp phòng ngừa
- Cá thể hóa tùy theo từng trường hợp

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hAnK yo