Επαναπροσδιορισμός φαρμάκων ως νέες προοπτικές στη θεραπεία της COVID-19

Μαρία Χριστοπούλου
MD,MSc,MBA
Παθολόγος –Εντατικολόγος
Medical Advisor Pharmaserve-Lilly

Drug Repurposing for COVID-19

Η de novo ανάπτυξη φαρμάκων Αργεί και Κοστίζει

Cost	Time	Success rate
>1b $	**10-15y**	**2%**

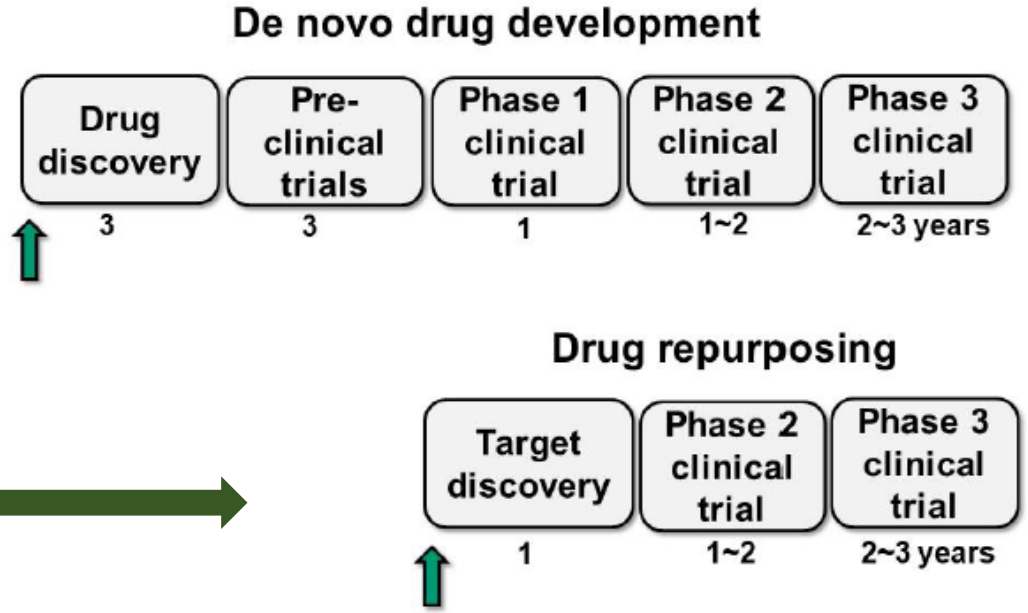
- Μόλις 5-10% την φαρμάκων που τελειώνουν τη φάση Ι τελικά εγκρίνονται
- Παρά την πρόοδο βιολογίας και τεχνολογίας ο αριθμός των νέων φαρμάκων παραμένει ο ίδιος
- Πρακτικά ανέφικτο να καλυφθούν τα 'ορφανά νοσήματα'
- Οι φαρμακευτικές εταιρείες γίνονται όλο και λιγότερο ελκυστικός στόχος για τους επενδυτές

ΠΑΡΑΜΕΝΕΙ ΜΕΓΑΛΟ ΚΕΝΟ ΜΕΤΕΞΥ ΘΕΡΑΠΕΥΤΙΚΩΝ ΑΝΑΓΚΩΝ ΚΑΙ ΔΙΑΘΕΣΙΜΩΝ ΘΕΡΑΠΕΙΩΝ

Nature Rev 2019;18:41-58

Drug Repurposing
(OR repositioning OR reprofiling OR re-tasking OR rescue)

Μια εναλλακτική προσέγγιση για να μειώσει το Development Risk



Γνωστή ΦΔ, ΦΚ,
Λιγότερο πιθανό να απορριφθεί λόγω τοξικότητας

https://doi.org/10.12793/tcp.2019.27.2.59
Nat Rev Drug Discov 2013;12:581-594.

- 30% ΤΩΝ ΦΑΡΜΑΚΩΝ ΠΟΥ ΕΓΚΡΙΝΟΝΤΑΙ ΣΗΜΕΡΑ

Μερικά μόνο παραδείγματα.....

Table 1. Examples of repositioned drugs (selected)

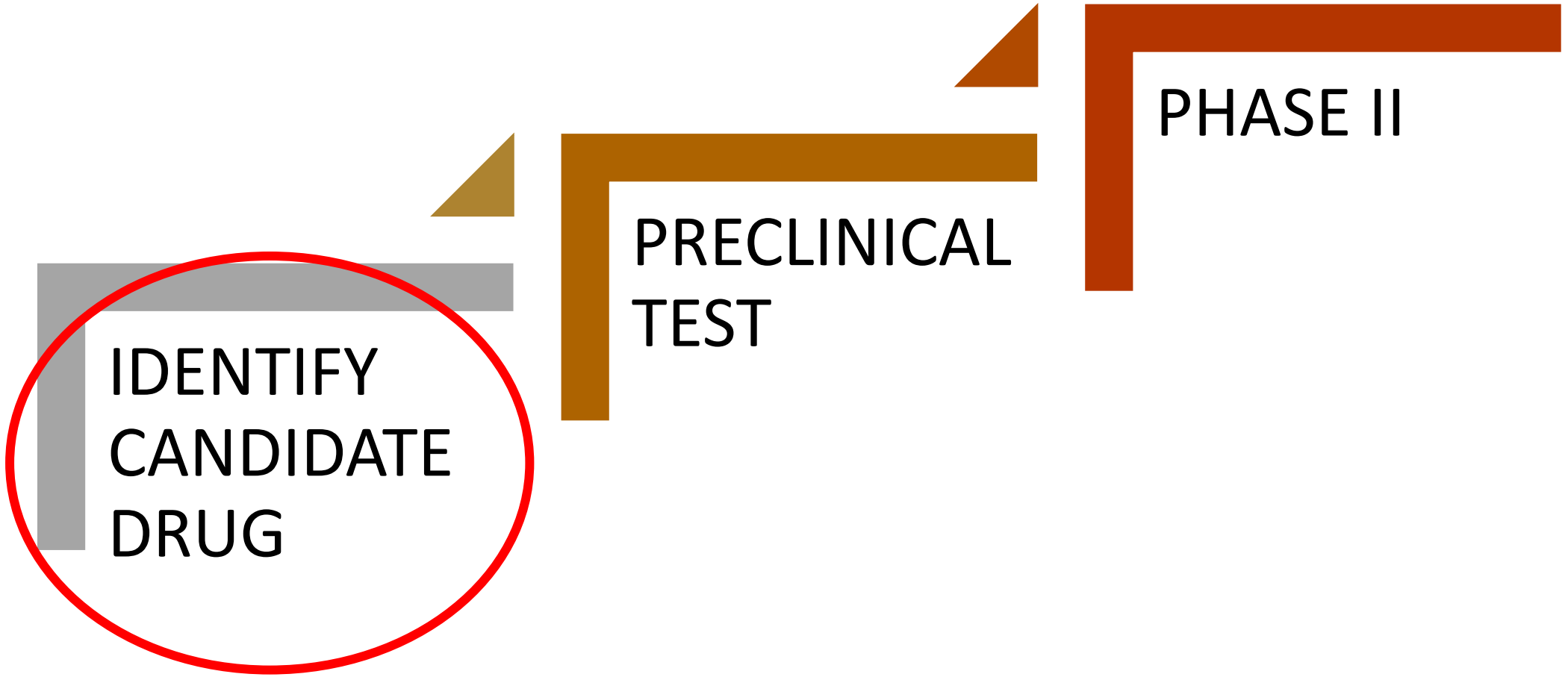
Drug	Original indication	New indication
Allopurinol	Cancer	Gout
Aspirin	Inflammation, Pain	Antiplatelet
Bromocriptine	Parkinson's disease	Diabetes mellitus
Bupropion	Depression	Smoking cessation
Duloxetine	Depression	Stress urinary incontinence
Finasteride	Benign prostatic hyperplasia	Hair loss
Gabapentin	Epilepsy	Neuropathic pain
Gemcitabine	Antiviral	Cancer
Methotrexate	Cancer	Rheumatoid arthritis
Propranolol	Hypertension	Migraine headache
Raloxifene	Osteoporosis	Breast cancer
Sildenafil	Angina	Erectile dysfunction
Thalidomide	Sedation, Morning sickness	Leprosy, Multiple myeloma
Zidovudine	Cancer	AIDS

https://doi.org/10.12793/tcp.2019.27.2.59

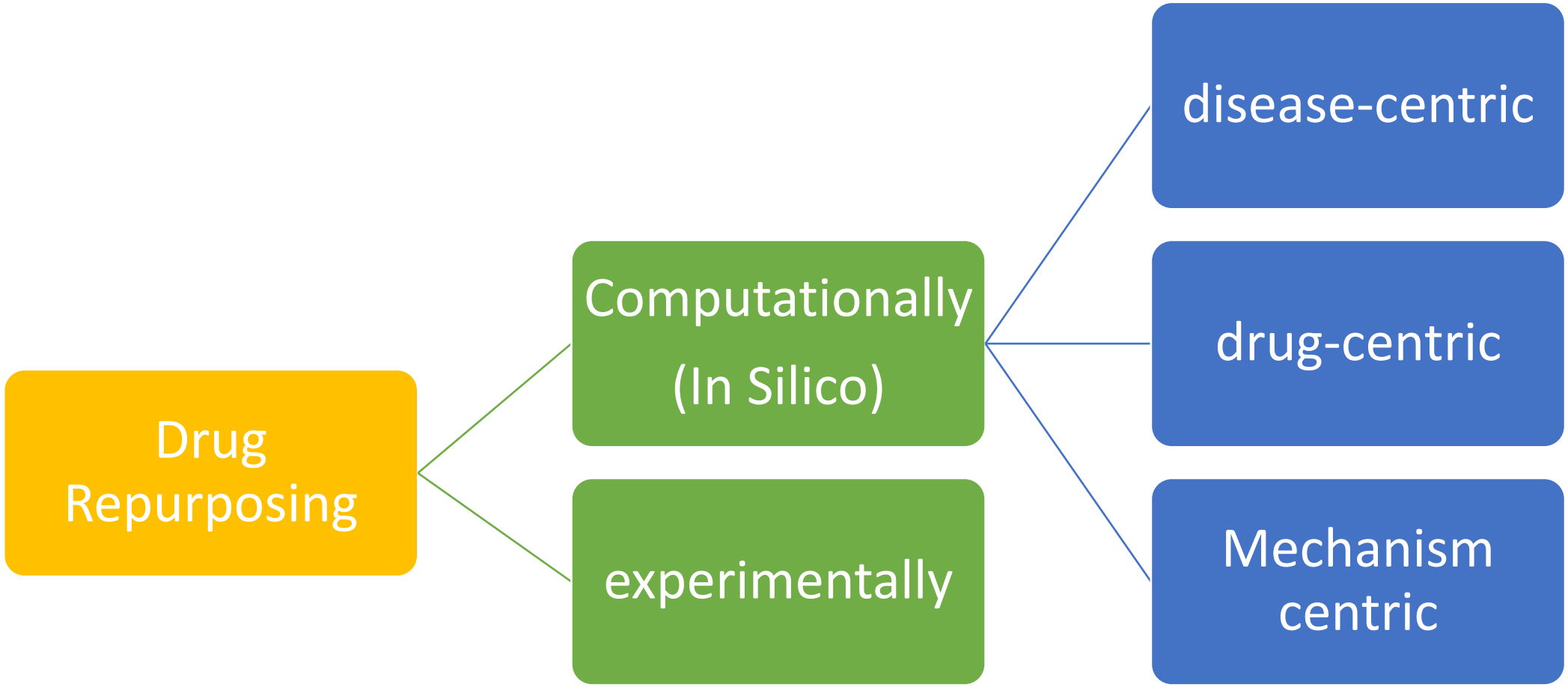
Παλαιότερα, με μη συστηματικό τρόπο

- Το παράδειγμα της Σιλδεναφίλης και της Θαλιδομίδης που ως repurposed κατέληξαν σε Revenues of billions

Drug Repurposing



Σκεπτικό-Μέθοδοι



In Silico Repurposing

Big Data

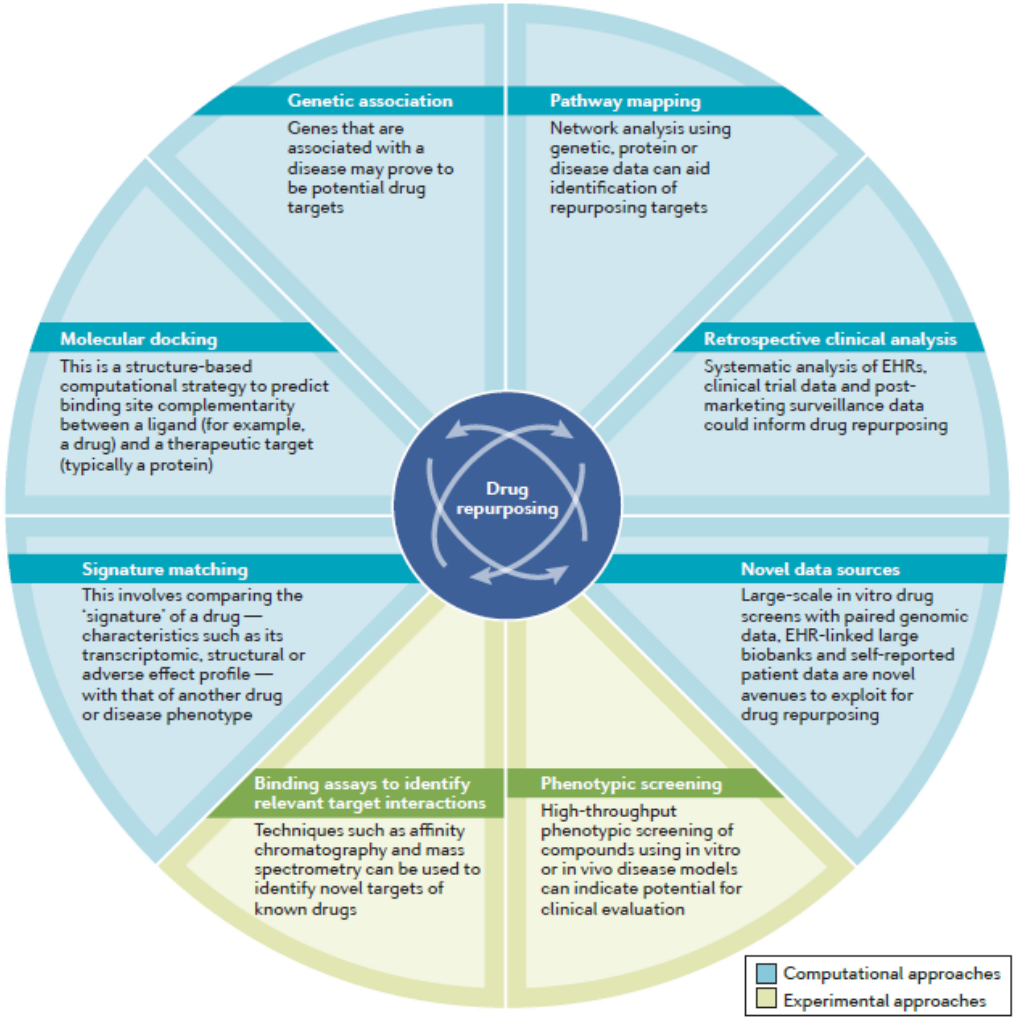
Genomics. proteomics, chemo-proteomics, phenomics, gene expression, drug-targeti nteractions, protein networks, electronic health records, clinical trial reports, drug adverse event reports etc….

Methods

- Machine Learning
- Network models
- Text mining and semantic inference

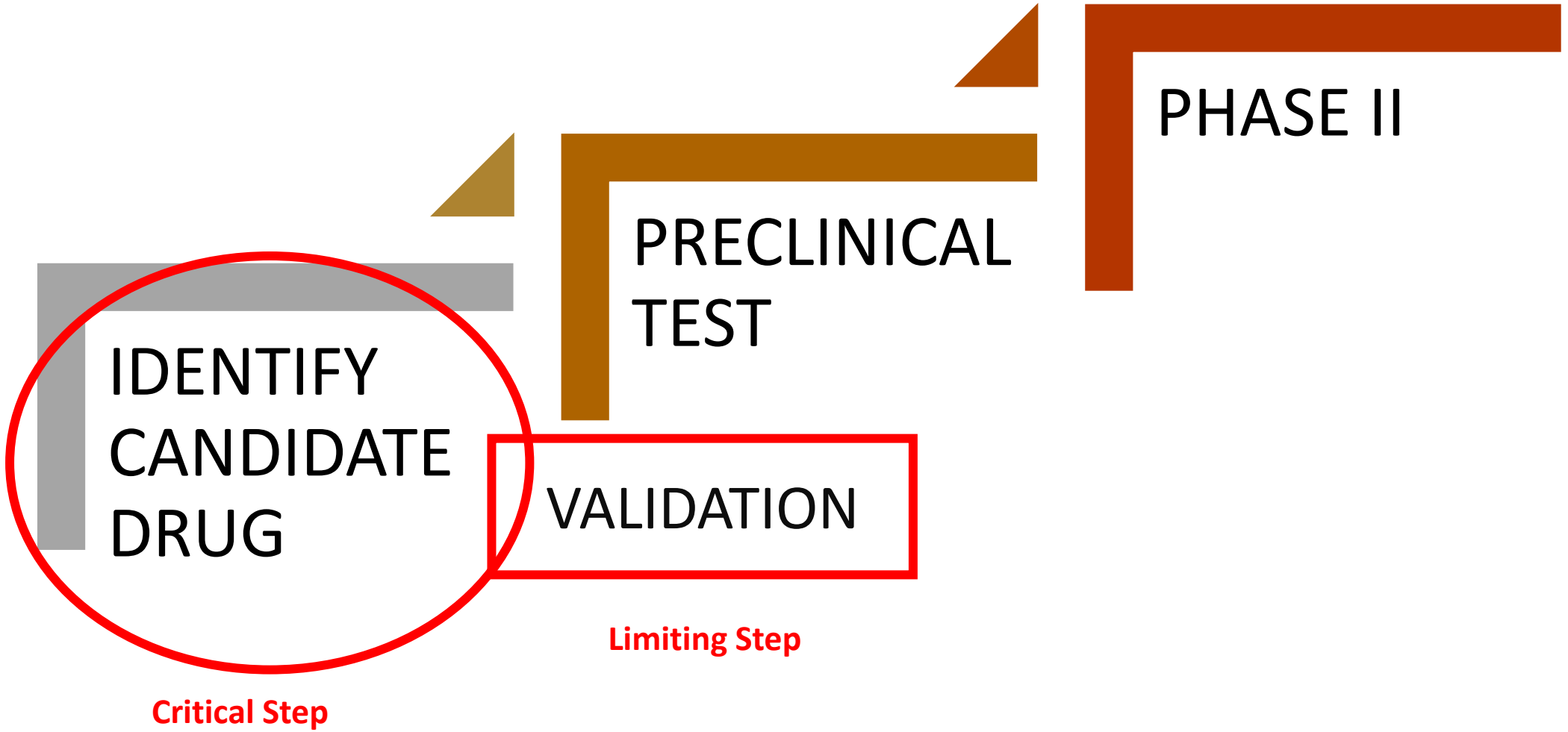
Transl Clin Pharmacol 2019;27(2):59-63

Συστηματικό Repurposing



Nature Rev 2019;18:41-58

Drug Repurposing



A bibliometric review of drug repurposing

Nancy C. Baker[1,2], Sean Ekins[3], Antony J. Williams[4] and Alexander Tropsha[1,5]

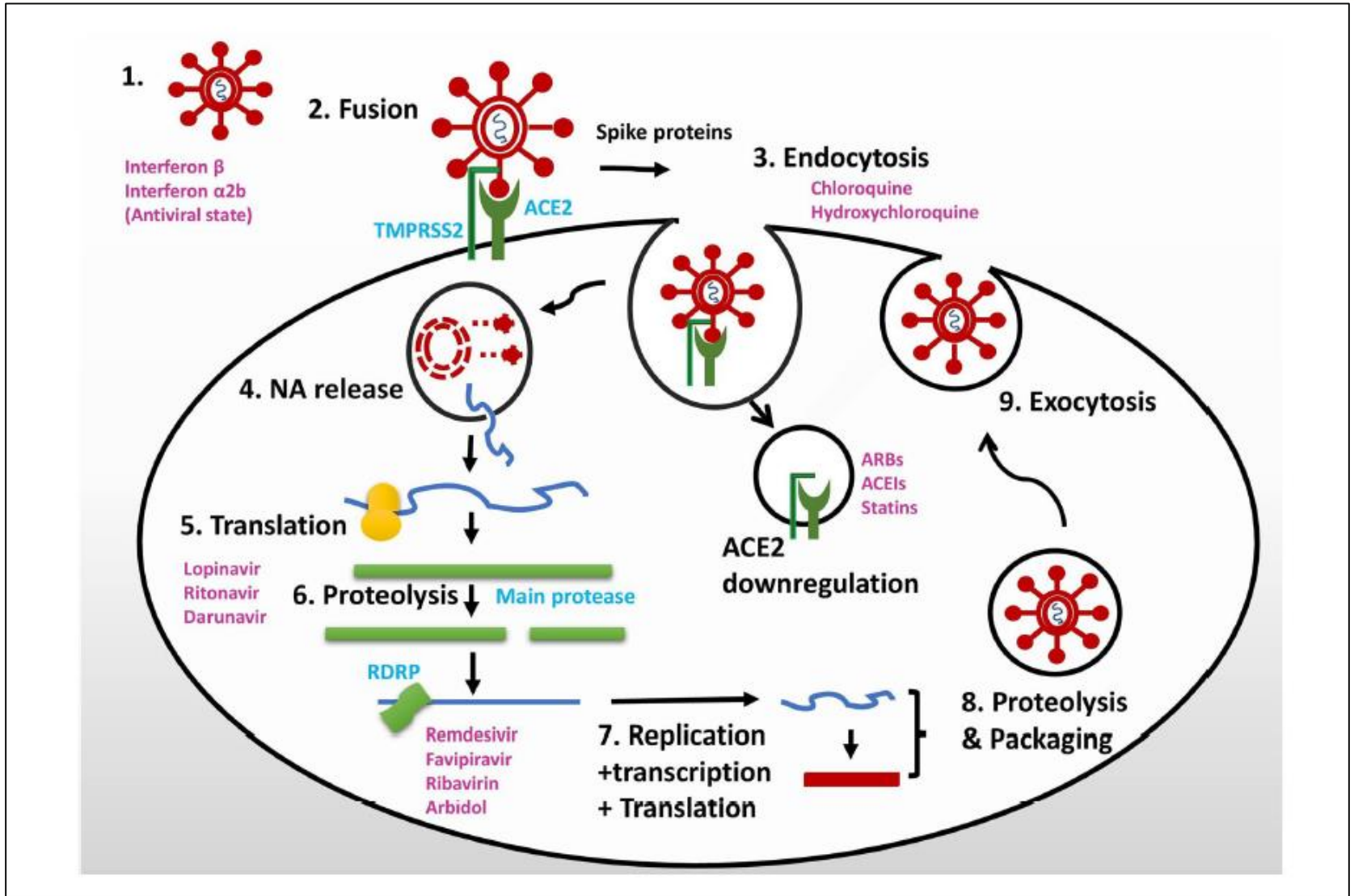
[1] Laboratory for Molecular Modeling, UNC Eshelman School of Pharmacy, UNC Chapel Hill, Chapel Hill, NC 27599, USA
[2] ParlezChem, 123 W Union Street, Hillsborough, NC 27278, USA
[3] Collaborations Pharmaceuticals, 840 Main Campus Drive, Lab 3510, Raleigh, NC 27606, USA
[4] ChemConnector, 513 Chestnut Grove Ct., Wake Forest, NC 27587, USA
[5] Kazan Federal University, Kazan 420008, Russia

We have conducted a bibliometric review of drug repurposing by scanning >25 million papers in PubMed and using text-mining methods to gather, count and analyze chemical–disease therapeutic relationships. We find that >60% of the ~35,000 drugs or drug candidates identified in our study have been tried in more than one disease, including 189 drugs that have been tried in >300 diseases each. Whereas in the majority of cases these drugs were applied in therapeutic areas close to their original use, there have been striking, and perhaps instructive, successful attempts of drug repurposing for unexpected, novel therapeutic areas.

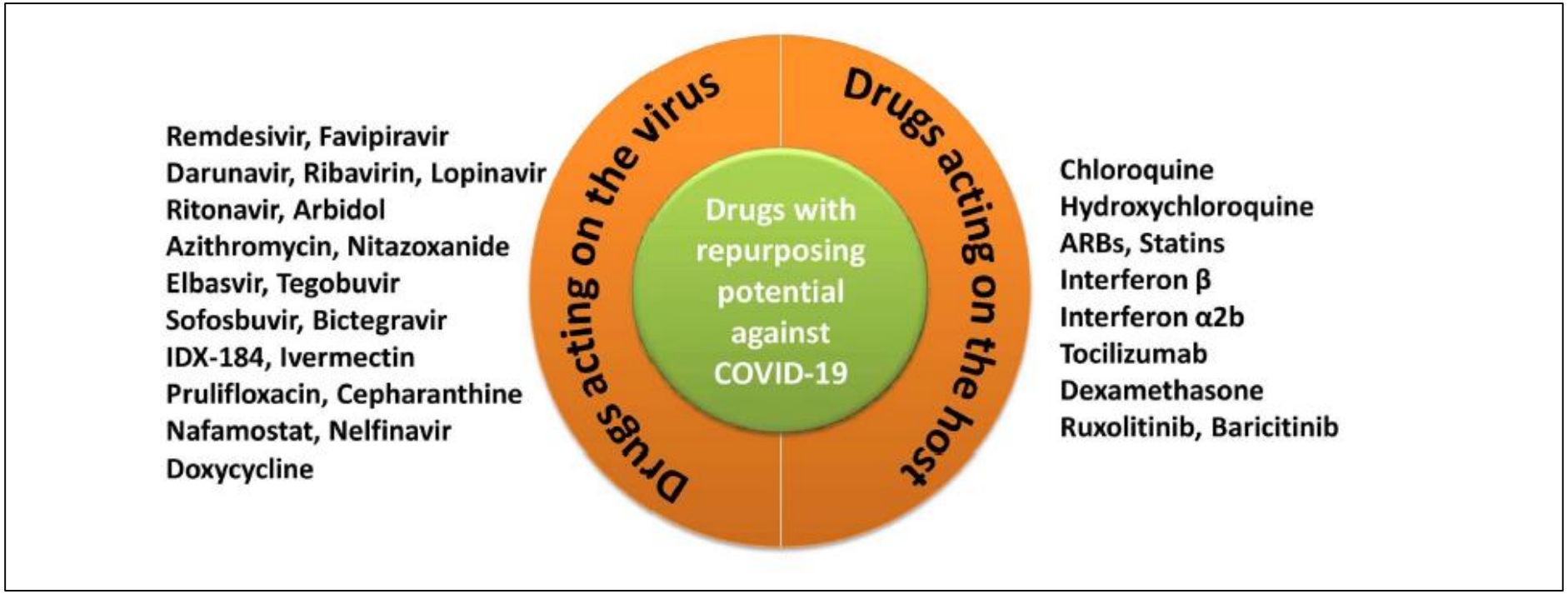
75% ΤΩΝ ΦΑΡΜΑΚΩΝ ΜΠΟΡΟΥΝ ΝΑ ΕΠΑΝΑΠΡΟΣΔΙΟΡΙΣΤΟΥΝ ΓΙΑ ΑΛΛΗ ΝΟΣΟ

Repurposing of Repurposing

Ο κύκλος του SARS-CoV2



Drug Repurposing for COVID-19



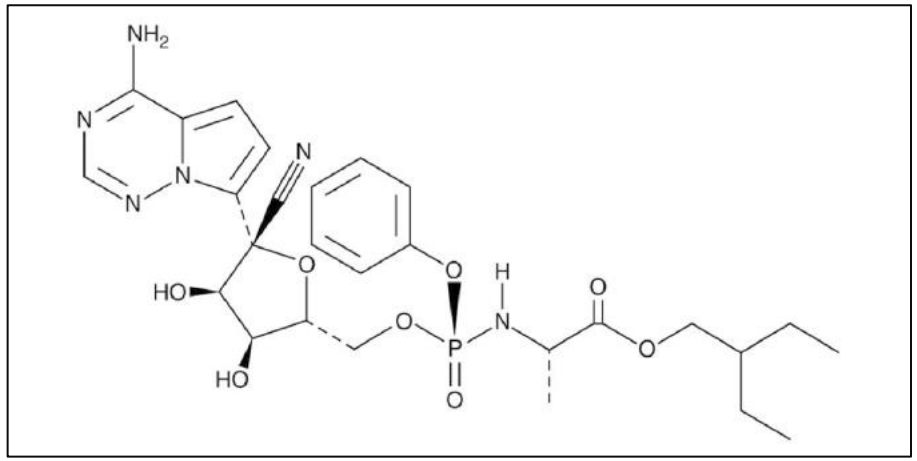
Εναντίον στόχων σχετιζόμενων με τον ιό (πχ RNA γονιδίωμα)
Εναντίον του σχηματισμού λειτουργικών πρωτεϊνών
Εναντίον της εισόδου του ιού στα επιθηλιακά κύτταρα

Ανοσολογική Απάντηση στους ιούς
Αναστολή προφλεγμονωδών κυτταροκινών

Εναντίον στόχων σχετιζόμενων με τον ιό

Remdesivir (GS-5734)

- Νουκλεοσιδικό ανάλογο
- Υπόστρωμα- Αναστολέας RdRp
- Για SARS CoV2 , EC50 = 0.77 μM



Remdesivir

Therapeutic indications (Emergency Use Authorization)

- for the treatment of coronavirus disease 2019 (COVID-19) in adults and adolescents (aged 12 years and older with body weight at least 40 kg) with pneumonia requiring supplemental oxygen


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Final Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*

2020 Oct 8;NEJMoa2007764. doi: 10.1056/NEJMoa2007764

ACTT-2

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	All (N=1062)	Remdesivir (N=541)	Placebo (N=521)
Age — yr	58.9±15.0	58.6±14.6	59.2±15.4
Male sex — no. (%)	684 (64.4)	352 (65.1)	332 (63.7)
Race or ethnic group — no. (%)†			
American Indian or Alaska Native	7 (0.7)	4 (0.7)	3 (0.6)
Asian	135 (12.7)	79 (14.6)	56 (10.7)
Black or African American	226 (21.3)	109 (20.1)	117 (22.5)
White	566 (53.3)	279 (51.6)	287 (55.1)
Hispanic or Latino — no. (%)	250 (23.5)	134 (24.8)	116 (22.3)
Median time (IQR) from symptom onset to randomization — days‡	9 (6–12)	9 (6–12)	9 (7–13)
No. of coexisting conditions — no. /total no. (%)‡			
None	194/1048 (18.5)	97/531 (18.3)	97/517 (18.8)
One	275/1048 (26.2)	138/531 (26.0)	137/517 (26.5)
Two or more	579/1048 (55.2)	296/531 (55.7)	283/517 (54.7)
Coexisting conditions — no./total no. (%)			
Type 2 diabetes	322/1051 (30.6)	164/532 (30.8)	158/519 (30.4)
Hypertension	533/1051 (50.7)	269/532 (50.6)	264/519 (50.9)
Obesity	476/1049 (45.4)	242/531 (45.6)	234/518 (45.2)
Score on ordinal scale — no. (%)			
4. Hospitalized, not requiring supplemental oxygen, requiring ongoing medical care (Covid-19–related or otherwise)	138 (13.0)	75 (13.9)	63 (12.1)
5. Hospitalized, requiring supplemental oxygen	435 (41.0)	232 (42.9)	203 (39.0)
6. Hospitalized, receiving noninvasive ventilation or high-flow oxygen devices	193 (18.2)	95 (17.6)	98 (18.8)
7. Hospitalized, receiving invasive mechanical ventilation or ECMO	285 (26.8)	131 (24.2)	154 (29.6)
Baseline score missing	11 (1.0)	8 (1.5)	3 (0.6)

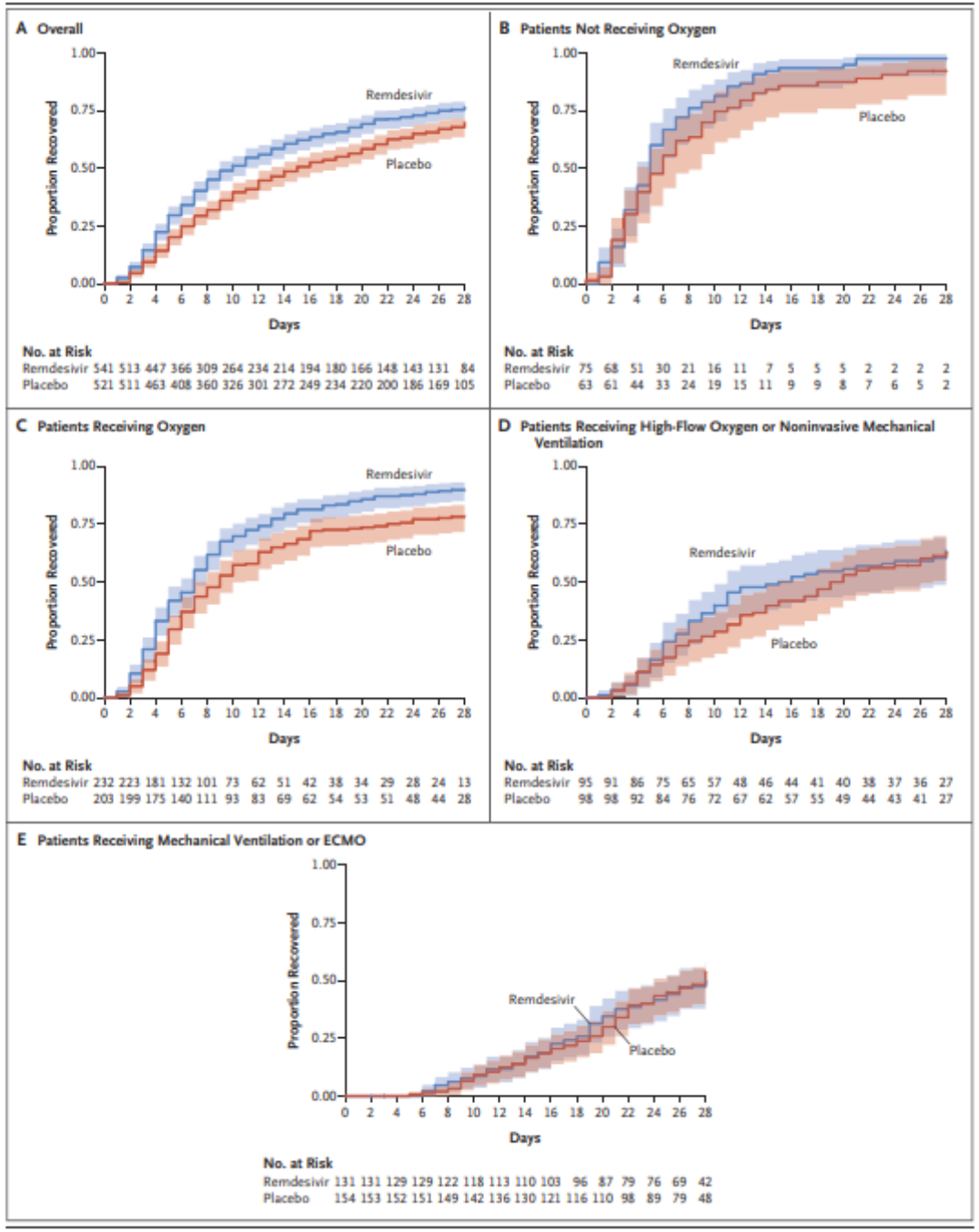
200-mg loading dose on day 1, followed by a 100-mg maintenance dose,daily on days 2 - 10

ENROLLMENT: February 21, 2020, and ended on April 19, 2020

ACTT-2 primary outcome : the time to recovery

1	not hospitalized and no limitations of activities
2	not hospitalized, with limitation of activities, home oxygen requirement, or both
3	hospitalized, not requiring supplemental oxygen and no longer requiring ongoing medical care
4	hospitalized, not requiring supplemental oxygen but requiring ongoing medical care
5	hospitalized, requiring any supplemental oxygen
6	hospitalized, requiring noninvasive ventilation or use of high-flow oxygen devices
7	hospitalized, receiving invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO)
8	Death

ACTT-2: Time to Recovery and Death Rates

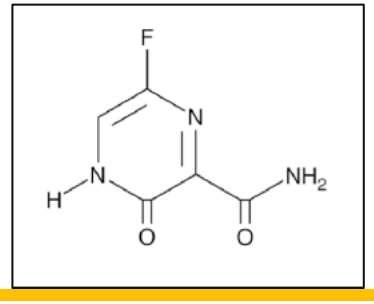


	Overall	
	Remdesivir (N=541)	Placebo (N=521)
Recovery		
No. of recoveries	399	352
Median time to recovery (95% CI) — days	10 (9–11)	15 (13–18)
Rate ratio (95% CI)†	1.29 (1.12–1.49 [P<0.001])	
Mortality through day 14‡		
Hazard ratio for data through day 15 (95% CI)	0.55 (0.36–0.83)	
No. of deaths by day 15	35	61
Kaplan–Meier estimate of mortality by day 15 — % (95% CI)	6.7 (4.8–9.2)	11.9 (9.4–15.0)
Mortality over entire study period‡		
Hazard ratio (95% CI)	0.73 (0.52–1.03)	
No. of deaths by day 29	59	77
Kaplan–Meier estimate of mortality by day 29 — % (95% CI)	11.4 (9.0–14.5)	15.2 (12.3–18.6)

ACTT-2: Εξέλιξη της λοίμωξης

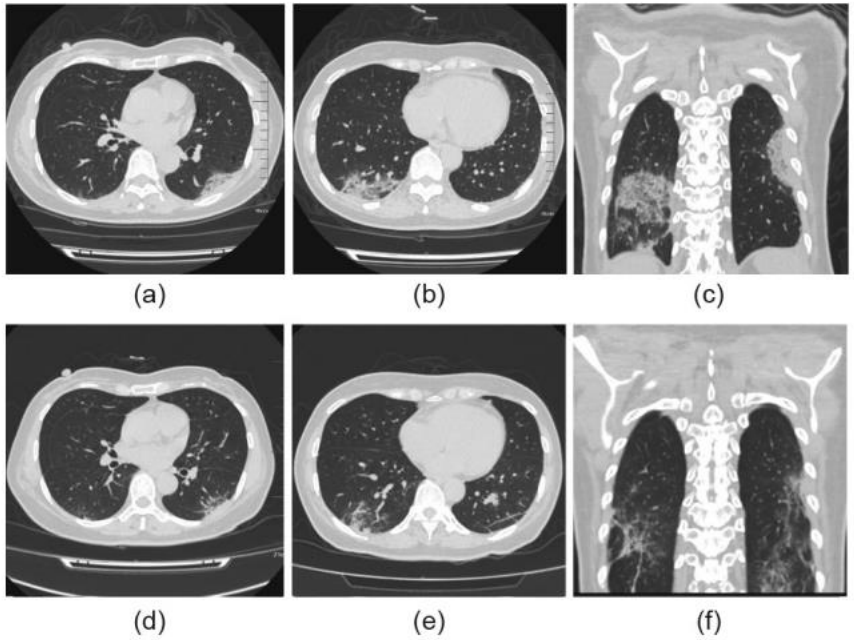
- 52 vs 82 ασθενείς έναρξη μηχανικού αερισμού
- 52 vs 64 ασθενείς έναρξη αερισμού υψηλής ροής
- 17 vs 20 ημέρες μέση διάρκεια μηχανικού αερισμού αν είχε ήδη εφαρμοστεί κατά την είσοδο στη μελέτη
- 47 vs 80 αναπνευστικά SAEs συμπεριλαμβανομένων των ARDS/διασωληνώσεων (8.8 vs 15.5%)

Favipiravir



- Αναστολέας RdRps

day 1: 1600 X2. /days 2–14: 600 mg X2 per os



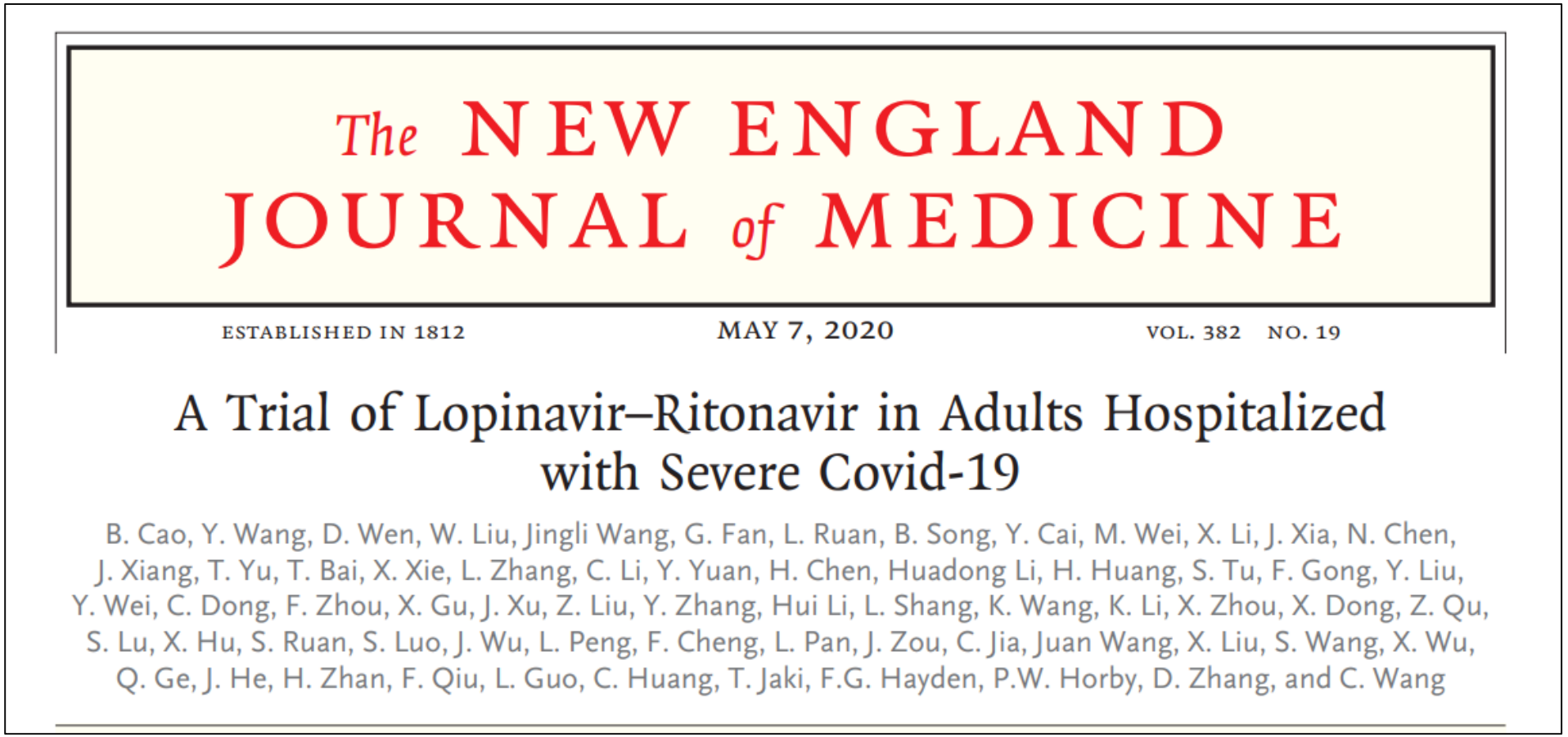
Preliminary Open label data
F+Inhaled IFNa Vs lopinavir-ritonavir +Inhaled IFNa

- recovery time median, 4 days vs 11 days $p < 0.001$).
- Chest imaging improvement 91.43% vs 62.22% on D14 of the treatment

https://doi.org/10.1016/j.eng.2020.03.007.

Εναντίον του σχηματισμού λειτουργικών πρωτεϊνών

Lopinavir-Ritonavir



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 7, 2020 VOL. 382 NO. 19

A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19

B. Cao, Y. Wang, D. Wen, W. Liu, Jingli Wang, G. Fan, L. Ruan, B. Song, Y. Cai, M. Wei, X. Li, J. Xia, N. Chen, J. Xiang, T. Yu, T. Bai, X. Xie, L. Zhang, C. Li, Y. Yuan, H. Chen, Huadong Li, H. Huang, S. Tu, F. Gong, Y. Liu, Y. Wei, C. Dong, F. Zhou, X. Gu, J. Xu, Z. Liu, Y. Zhang, Hui Li, L. Shang, K. Wang, K. Li, X. Zhou, X. Dong, Z. Qu, S. Lu, X. Hu, S. Ruan, S. Luo, J. Wu, L. Peng, F. Cheng, L. Pan, J. Zou, C. Jia, Juan Wang, X. Liu, S. Wang, X. Wu, Q. Ge, J. He, H. Zhan, F. Qiu, L. Guo, C. Huang, T. Jaki, F.G. Hayden, P.W. Horby, D. Zhang, and C. Wang

Lopinavir-Ritonavir

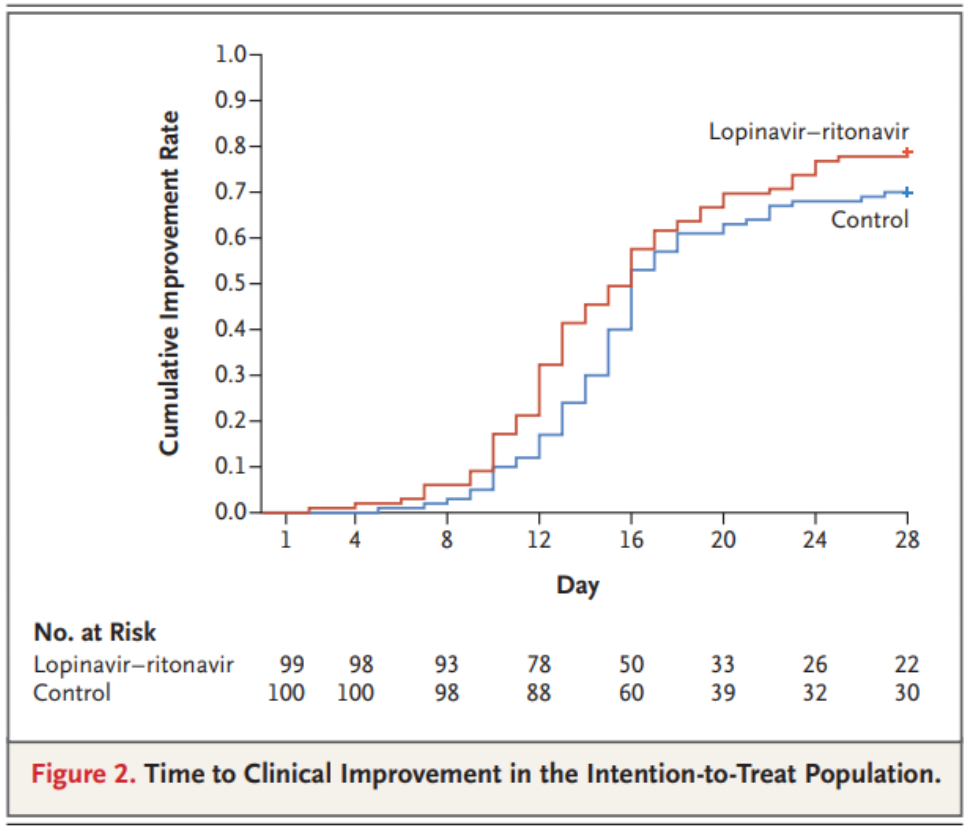
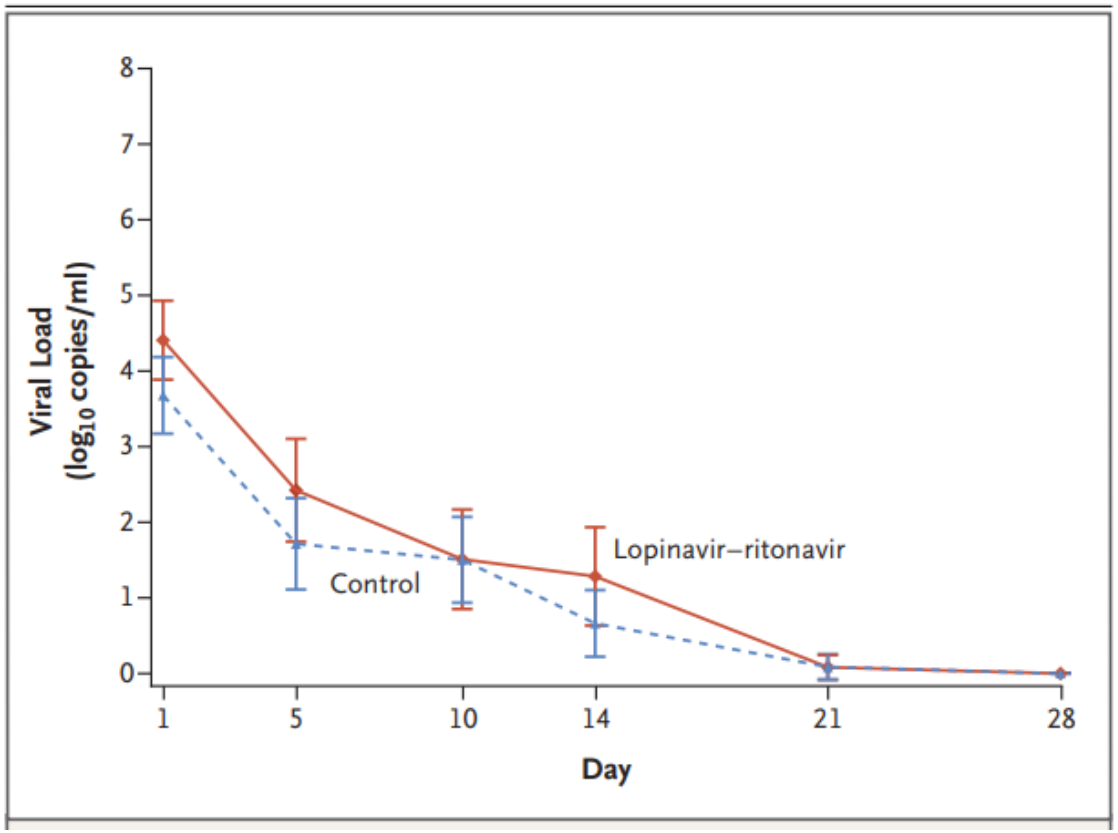


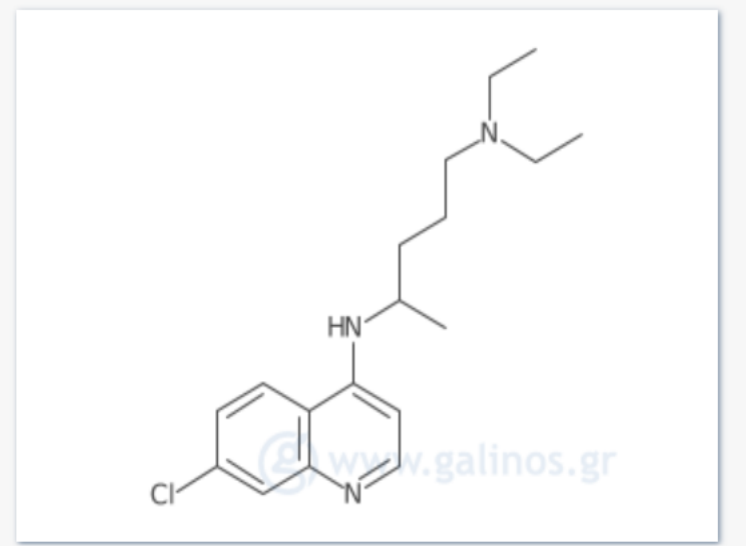
Figure 2. Time to Clinical Improvement in the Intention-to-Treat Population.



N Engl J Med 2020;382:1787-99

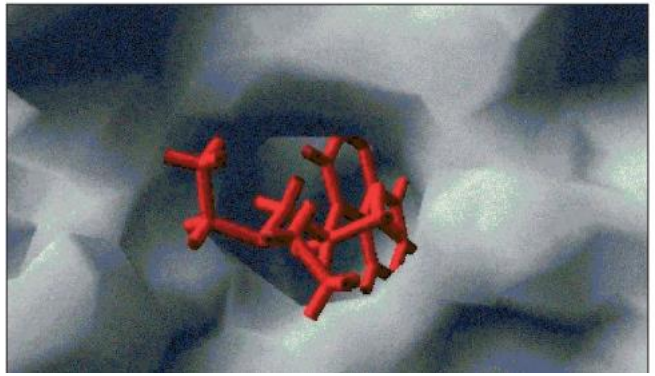
Εναντίον της εισόδου του ιού στα επιθηλιακά κύτταρα

Χλωροκίνη



- Ανεβάζει το pH του ενδοσώματος με το οποίο εισέρχεται ο ιός στο κύτταρο
- Ψευδο-γλυκοζυλίωση του ACE2

LEVEL OF EVIDENCE : Προκλινικά δεδομένα και αναφορές

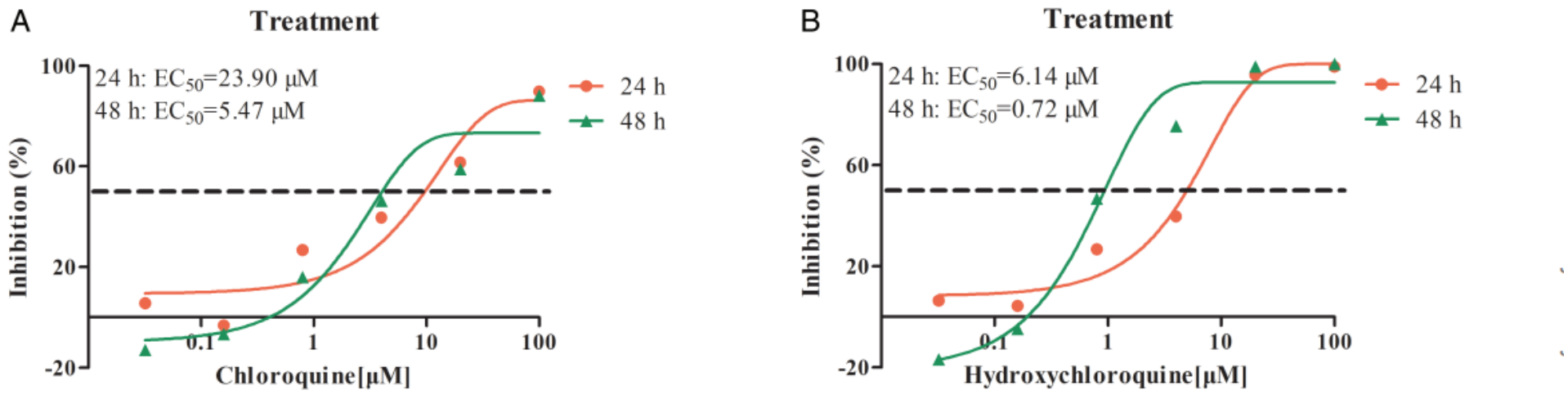


1000 mg PO on day 1, then 500 mg
PO once daily for 4 to 7 days

Lancet Infect Dis. 2006 Feb; 6(2): 67–69.

Υδροξυχλωροκίνη

- Πιο ισχυρή vs χλωροκίνης (EC50 0.72 και 5.47 μM αντίστοιχα)για COVID-19
- Λιγότερες αλληλεπιδράσεις με άλλα φάρμακα (παράταση QT)

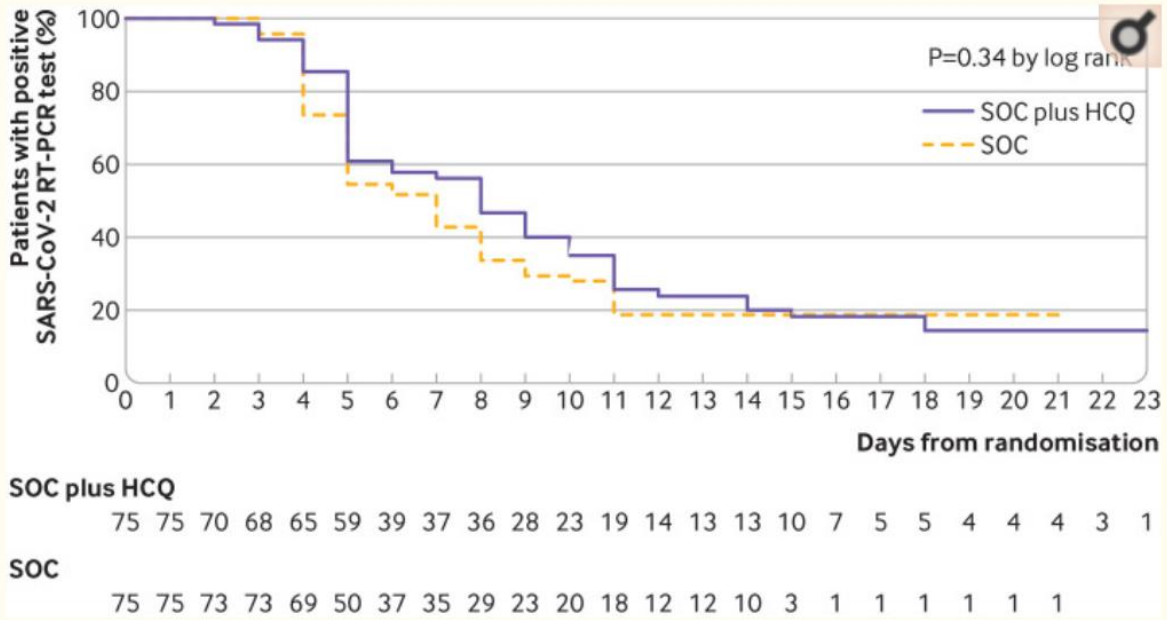


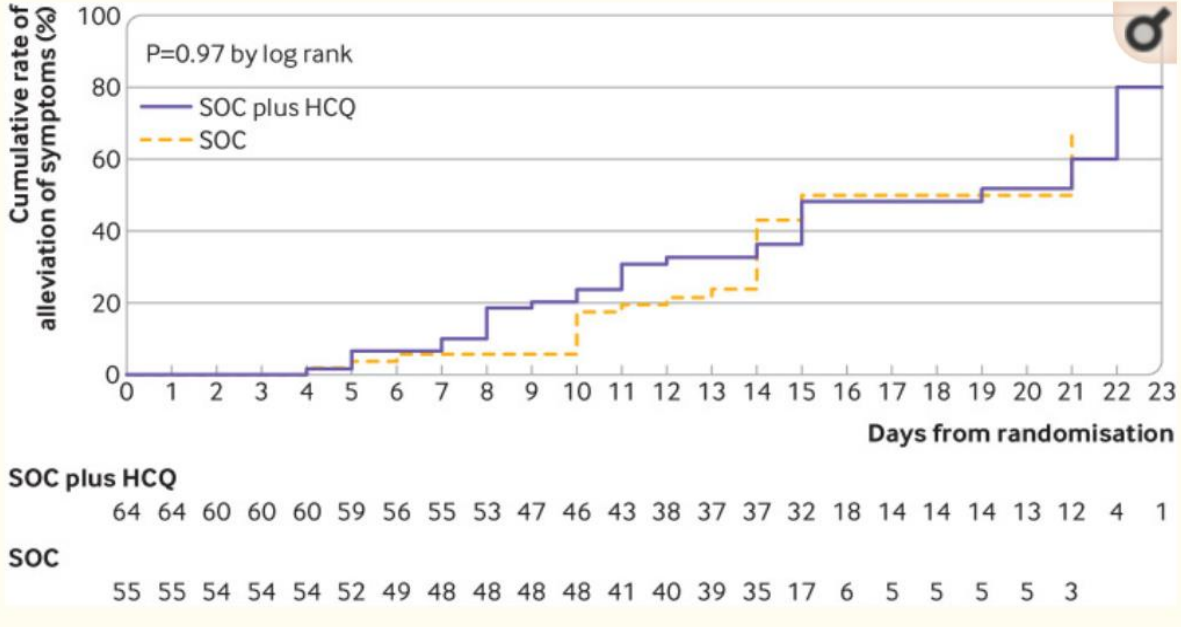
lin Infect Dis. 2020;71(15):732–9

loading dose of
400 mg twice daily, followed by a maintenance dose of 200 mg twice daily for 4 days

BMJ. 2020; 369: m1849.
Published online 2020 May 14. doi: 10.1136/bmj.m1849
PMCID: PMC7221473
PMID: 32409561

Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial





https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7221473/

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19

Joshua Geleris, M.D., Yifei Sun, Ph.D., Jonathan Platt, Ph.D., Jason Zucker, M.D., Matthew Baldwin, M.D., George Hripcsak, M.D., Angelena Labella, M.D., Daniel K. Manson, M.D., Christine Kubin, Pharm.D., R. Graham Barr, M.D., Dr.P.H., Magdalena E. Sobieszczyk, M.D., M.P.H., and Neil W. Schluger, M.D.

N Engl J Med. 2020;382(25):2411–8.

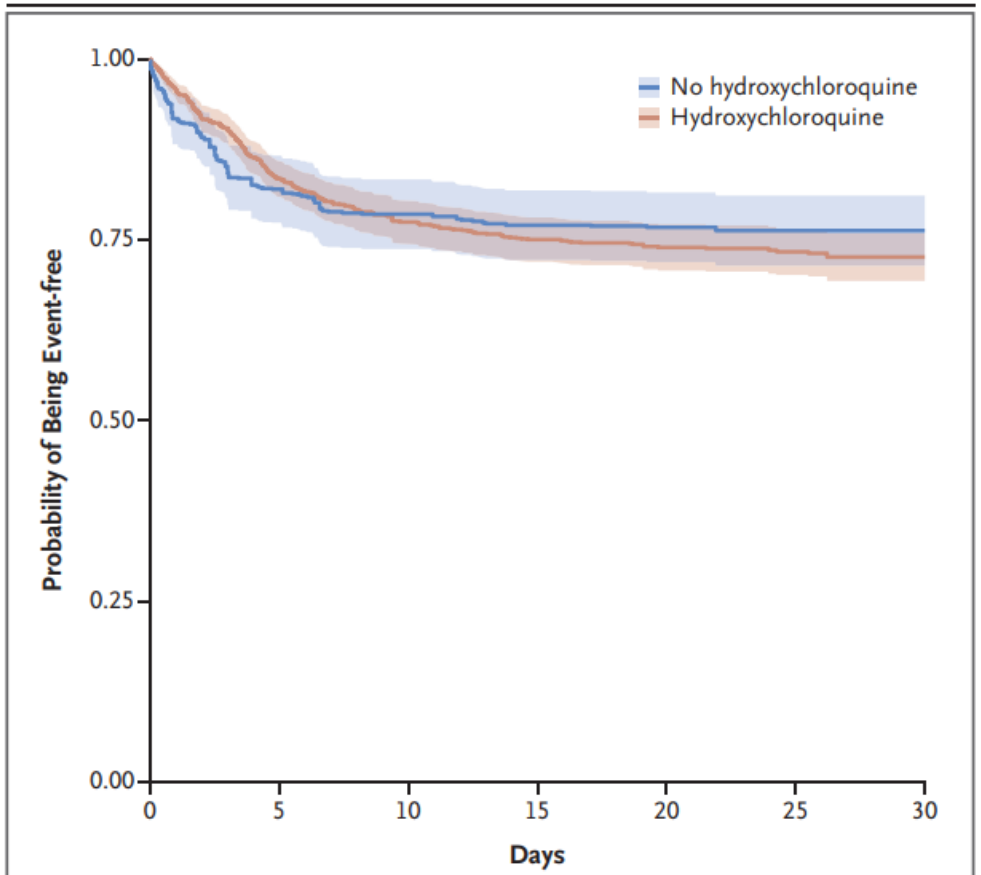
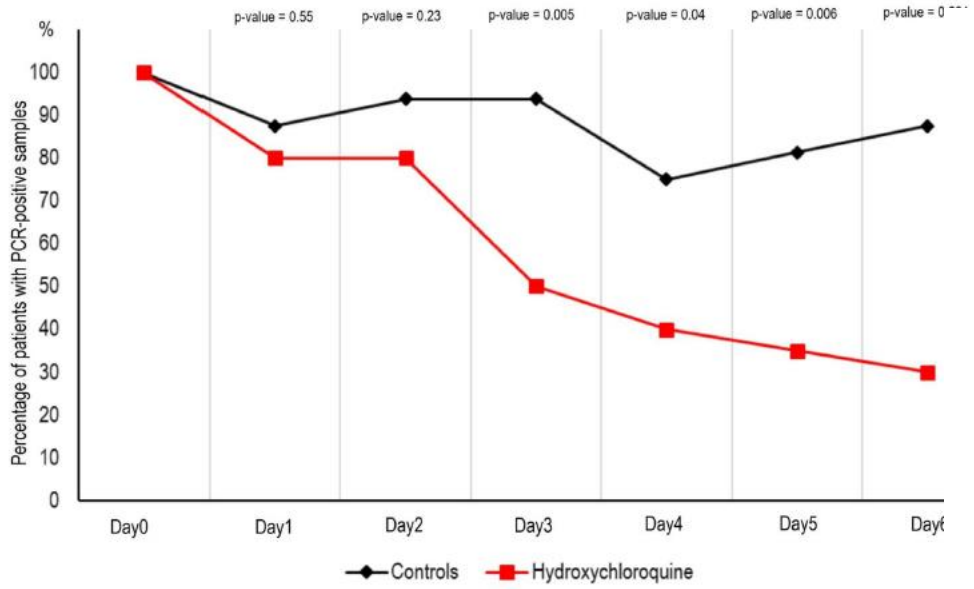
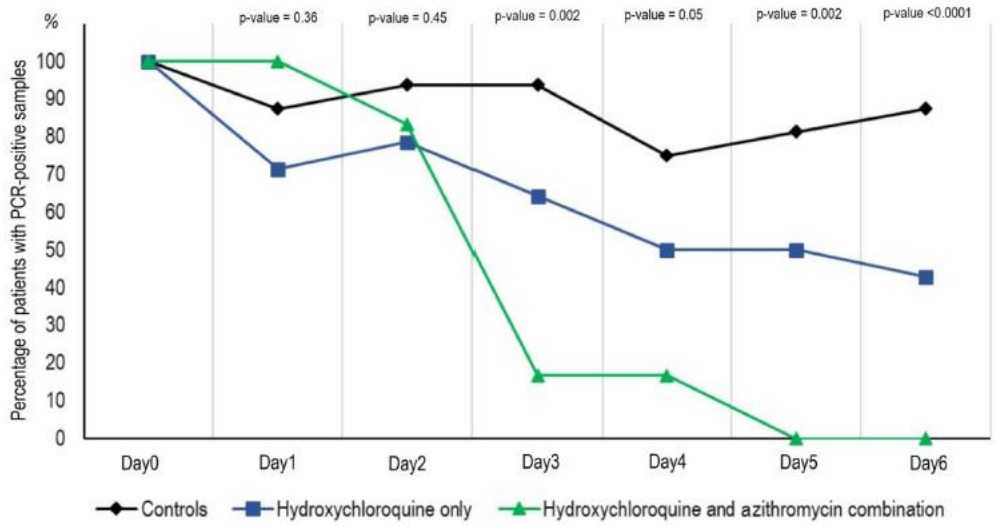


Figure 2. Freedom from Composite End Point of Intubation or Death.
The shaded areas represent pointwise 95% confidence intervals.

Υδροξυχλωροκινη+ Αζιθρομυκινη





Int J Antimicrob Agents. 2020;56:105949

Treatments for COVID-19: Canadian Arm of the SOLIDARITY Trial (CATCO)

NCT04330690

Detailed Description:

This study is an adaptive, randomized, open-label, controlled clinical trial, in collaboration with countries around the world through the World Health Organization.

Subjects will be randomized to receive either standard-of-care products or the study medication plus standard of care, while being hospitalized for COVID-19.

Participants will be randomized to one of the following groups:

1. Lopinavir/ritonavir 400mg/100mg PO BID for 14 day plus optimized supportive care, OR
2. Hydroxychloroquine 800mg BID for 1 day then 400mg BID for 10 days plus optimized supportive care, OR
3. Remdesivir 200mg IV on day 1, followed by 100 mg IV daily infusion for 9 days plus optimized supportive care, OR
4. Optimized support care all or until discharge from hospital, whichever occurs first

Primary end point : All cause mortality

Ανοσολογική Απάντηση στους ιούς

Ιντερφερόνες

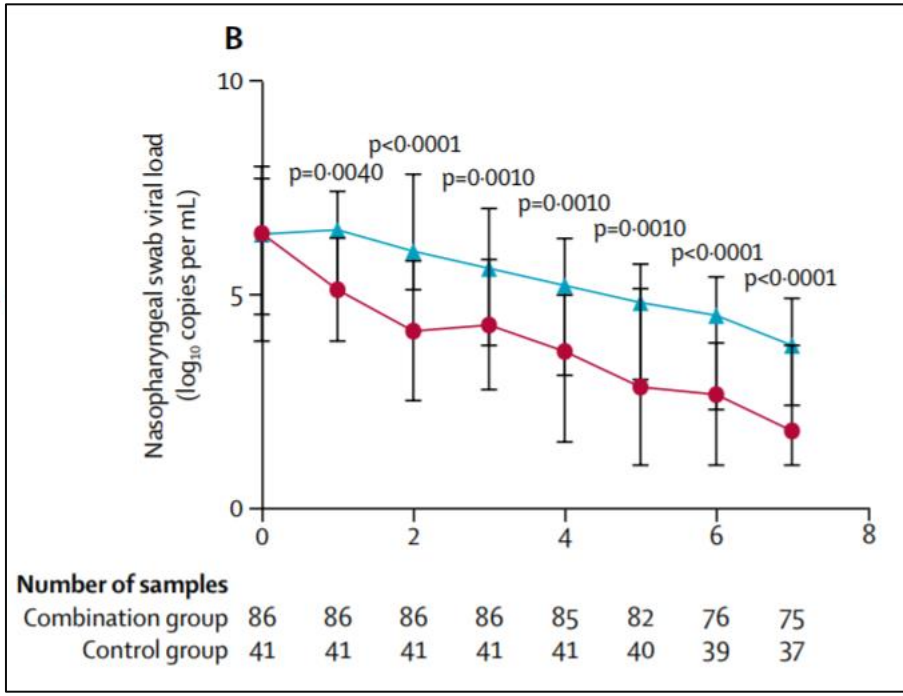
Triple combination of interferon beta-1b, lopinavir–ritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19: an open-label, randomised, phase 2 trial

Ivan Fan-Ngai Hung, Kwok-Cheung Lung, Eugene Yuk-Keung Tso, Raymond Liu, Tom Wai-Hin Chung, Man-Yee Chu, Yuk-Yung Ng, Jenny Lo, Jacky Chan, Anthony Raymond Tam, Hoi-Ping Shum, Veronica Chan, Alan Ka-Lun Wu, Kit-Man Sin, Wai-Shing Leung, Wai-Lam Law, David Christopher Lung, Simon Sin, Pauline Yeung, Cyril Chik-Yan Yip, Ricky Ruiqi Zhang, Agnes Yim-Fong Fung, Erica Yuen-Wing Yan, Kit-Hang Leung, Jonathan Daniel Ip, Allen Wing-Ho Chu, Wan-Mui Chan, Anthony Chin-Ki Ng, Rodney Lee, Kitty Fung, Alwin Yeung, Tak-Chiu Wu, Johnny Wai-Man Chan, Wing-Wah Yan, Wai-Ming Chan, Jasper Fuk-Woo Chan, Albert Kwok-Wai Lie, Owen Tak-Yin Tsang, Vincent Chi-Chung Cheng, Tak-Lun Que, Chak-Sing Lau , Kwok-Hung Chan, Kelvin Kai-Wang To, Kwok-Yung Yuen

Summary

Background Effective antiviral therapy is important for tackling the coronavirus disease 2019 (COVID-19) pandemic.

Lancet 2020; 395: 1695–704



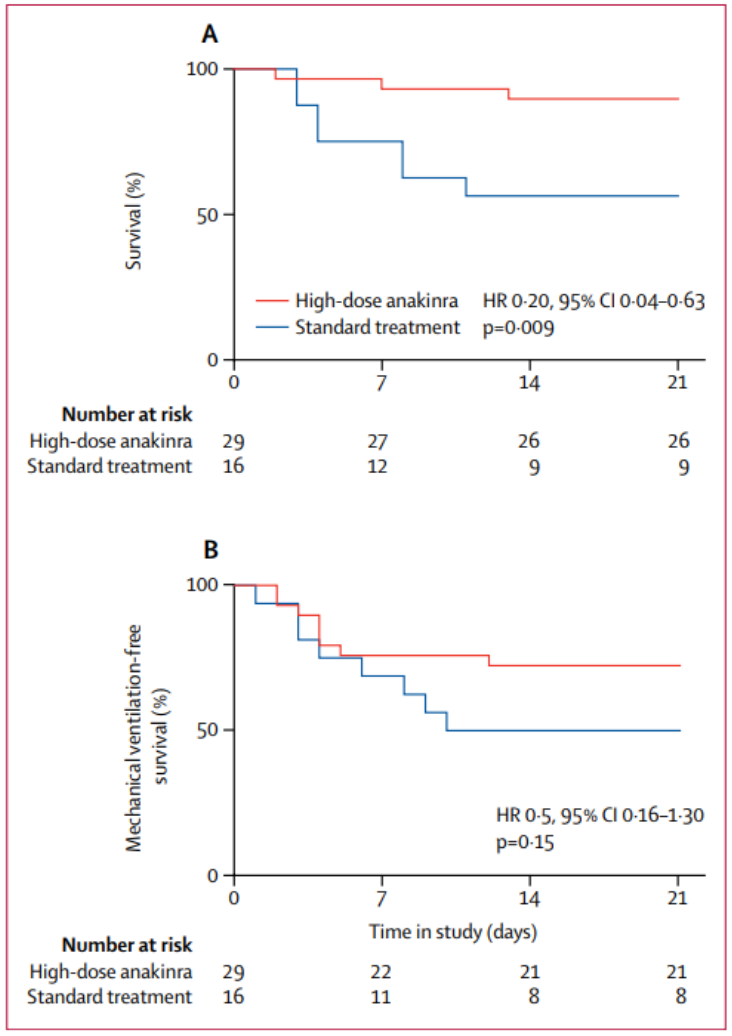
Biosci Trends. 2020;14:69–71.
https://doi.org/10.1007/s12519-020-00344-6

Αναστολή προφλεγμονωδών κυτταροκινών

JAK inhibitors : Baricitinib,Ruxolitinib

Clinical, laboratory, respiratory parameters	Baricitinib-treated				Standard therapy				Baricitinib vs Standard therapy
	Baseline	Week 1	Week 2	P value Baseline values vs Week 1* or vs Week 2† values	Baseline	Week 1	Week 2	P value Baseline values vs Week 1* or vs Week 2† values	P value Week 1* comparisons or Week 2† comparisons
Cough N (%)	10 (83)	8 (66)	0	0.640 * **0.000** †	12 (100)	10 (83)	9 (75)	0.478 * 0.217 †	0.640 * **0.000** †
Dyspnea N (%)	10 (83)	1 (8)	0	**0.001** * **0.000** †	9 (75)	8 (67)	8 (67)	1.000 * 1.000 †	0.001 * 0.001 †
Sputum production N (%)	4 (33)	1 (8)	1 (8)	0.317 * 0.317 †	3 (25)	3 (25)	3 (25)	1.000 * 1.000 †	0.590 * 0.217 †
Headache N (%)	5 (42)	0	0	0.037 * 0.037 †	4 (33)	2 (17)	3 (25)	0.640 * 1.000 †	0.478 * 0.217 †
Diarrhea N (%)	2 (17)	0	0	0.478 * 0.478 †	1 (8)	1 (8)	0	1.000 * 1.000 †	1.000 * NA †
Ageusia/Anosmia N (%)	6 (50)	3 (25)	2 (17)	0.400 * 0.193 †	5 (42)	4 (33)	3 (25)	1.000 * 0.667 †	1.000 * 1.000 †
Fever, °C median (IQR)	38 (37.4–38.2)	36.1 (36–36.4)	36 (36–36.1)	**0.001** * **0.001** †	38.1 (37.7–38.7)	37.7 (37.1–38.2)	37.8 (37.4–38.1)	0.123 * 0.285 †	**0.000** * **0.000** †
Breath, N/min median (IQR)	23 (19.5–24.2)	18 (14–20.2)	16 (16–18)	**0•004** * **0.010** †	22 (19.7–24)	19 (17.5–21.7)	18 (16–22.7)	0.063 * 0.885 †	0.603 * 0.094 †
SpO2,% median (IQR)	91 (90–92.5)	96 (96–98.2)	97 (95.7–98)	**0.000** * **0.002** †	92 (91.2–93)	93.6 (90.8–94.1)	93.1 (86.5–94.2)	0.289 * 0.544 †	**0.000** * **0.000** †
PaO2/FiO2 value median (IQR)	290 (199.2–292.2)	410 (315.7–452)	421.5 (308.6–456)	**0•000** * **0.001** †	268.6 (264.4–295)	302.2 (240.1–405.7)	267.6 (144.2–350.5)	0.106 * 0.862 †	0.237 * **0.017** †
Pulse rate, N/minute median (IQR)	82 (73–88.3)	70 (68–76)	67 (63.2–71.7)	**0•050** * 0.077 †	90 (87.2–94.5)	85.5 (77.5–93.5)	89 (84.5–104.5)	0.433 * 1.000 †	**0.002** * **0.000** †
WBC, x10^9/L median (IQR)	7.8 (5.8–10.8)	7.3 (6.2–9)	7.2 (6.3–9.3)	0•581 * 0.122 †	8.2 (7.3–8.8)	6.9 (6.5–7.4)	8 (7.4–8.3)	0.013 * 0.931 †	0.389 * 0.634 †
Neutrophils, x10^9/L median (IQR)	6.5 (4.5–7.7)	5.2 (4.8–6.9)	4.8 (4–7.1)	0•351 * 0.201 †	6.9 (6.4–7.6)	5.9 (5.2–6.4)	6.8 (6.1–7.2)	0.026 * 1.000 †	0.436 * 0.201 †

Αναστολή IL1



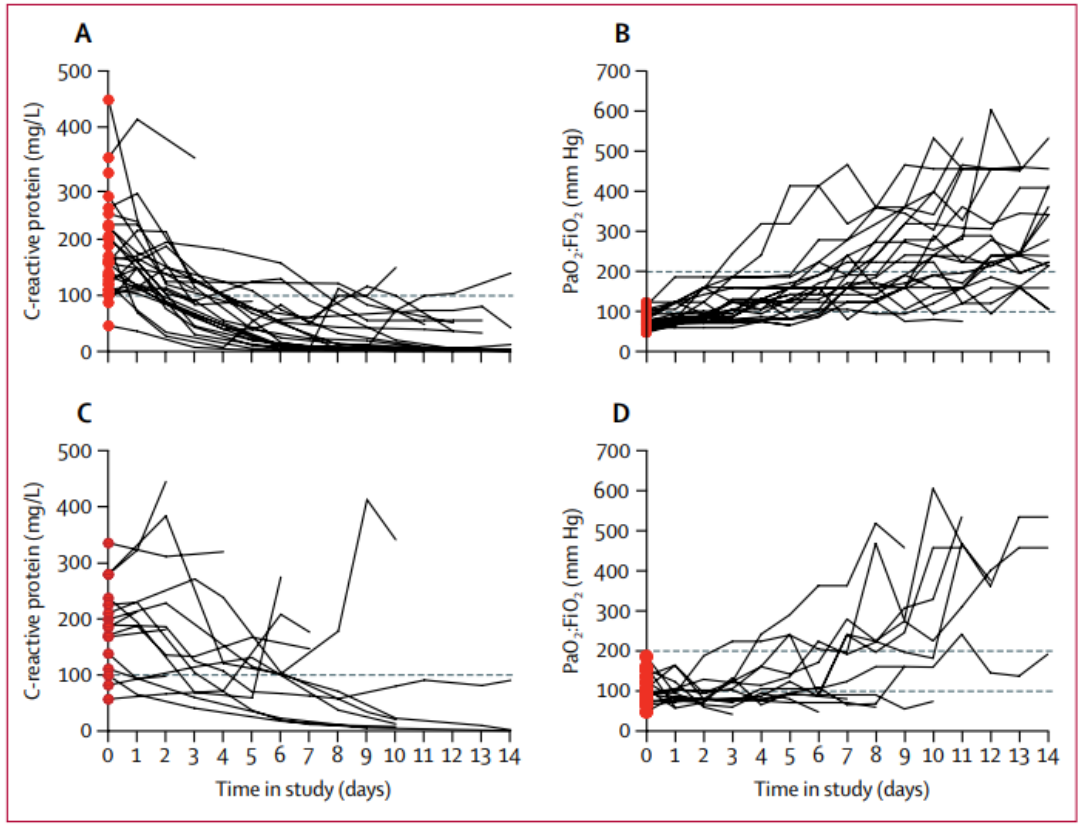
Interleukin-1 blockade with high-dose anakinra in patients with COVID-19, acute respiratory distress syndrome, and hyperinflammation: a retrospective cohort study

Giulio Cavalli, Giacomo De Luca, Corrado Campochiaro, Emanuel Della-Torre, Marco Ripa, Diana Canetti, Chiara Oltolini, Barbara Castiglioni, Chiara Tassan Din, Nicola Boffini, Alessandro Tomelleri, Nicola Farina, Annalisa Ruggeri, Patrizia Rovere-Querini, Giuseppe Di Lucca, Sabina Martinenghi, Raffaella Scotti, Moreno Tresoldi, Fabio Ciceri, Giovanni Landoni, Alberto Zangrillo, Paolo Scarpellini, Lorenzo Dagna

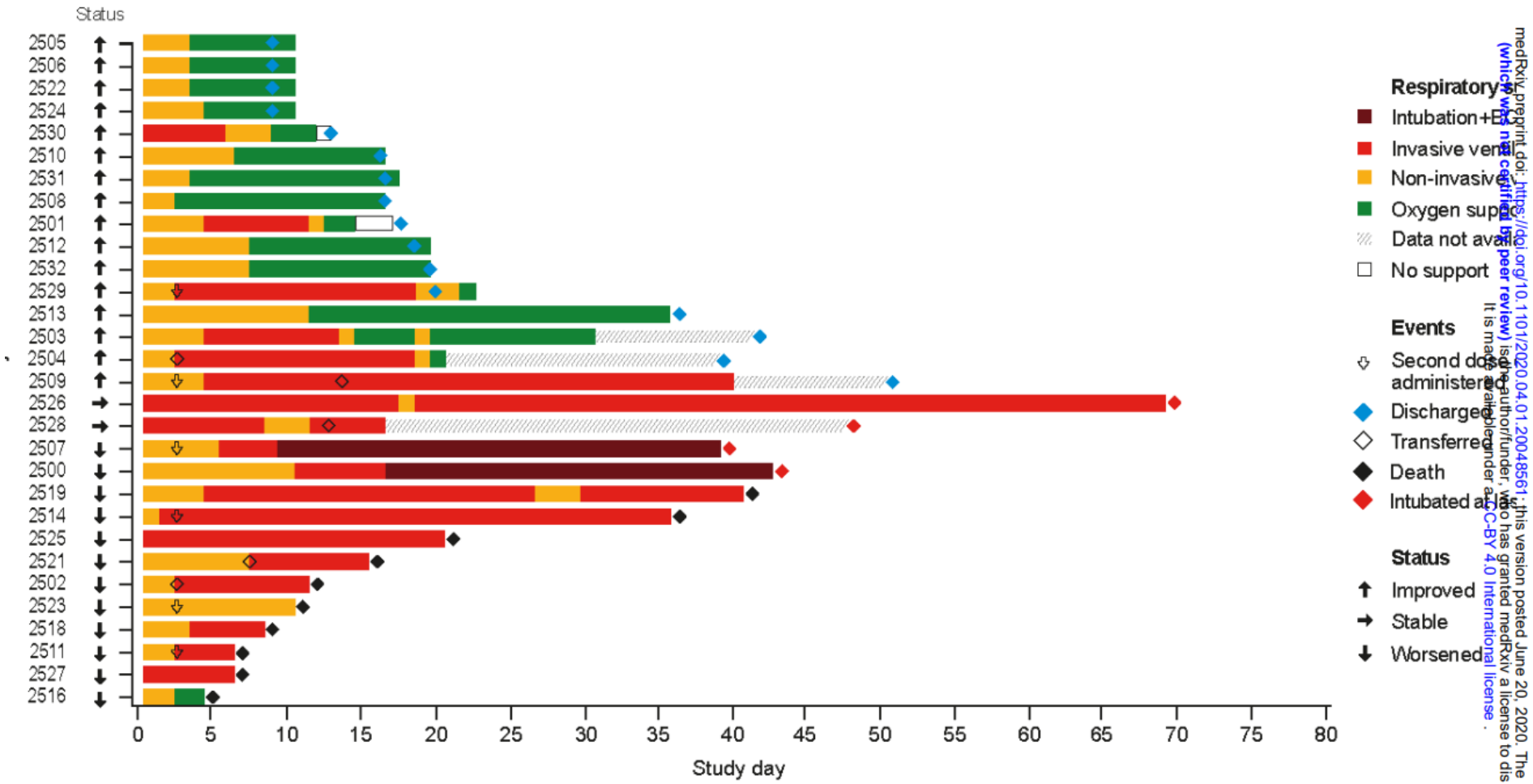
Summary

Background Mortality of patients with coronavirus disease 2019 (COVID-19), acute respiratory distress syndrome

Lancet Rheumatol 2020;



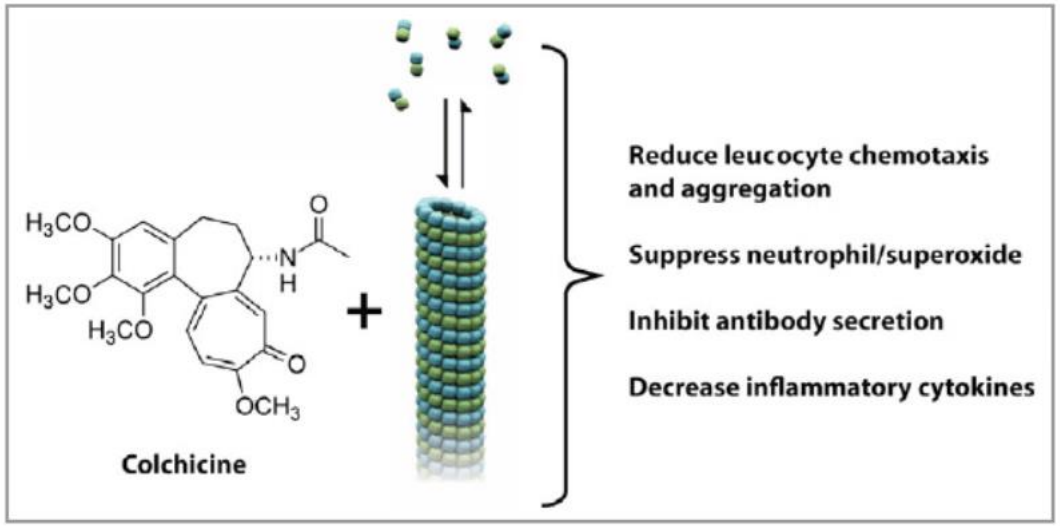
Αναστολή IL 6: Siltuximab Tocilizumab,Sarilumab



https://doi.org/10.1101/2020.04.01.20048561.

Άλλα

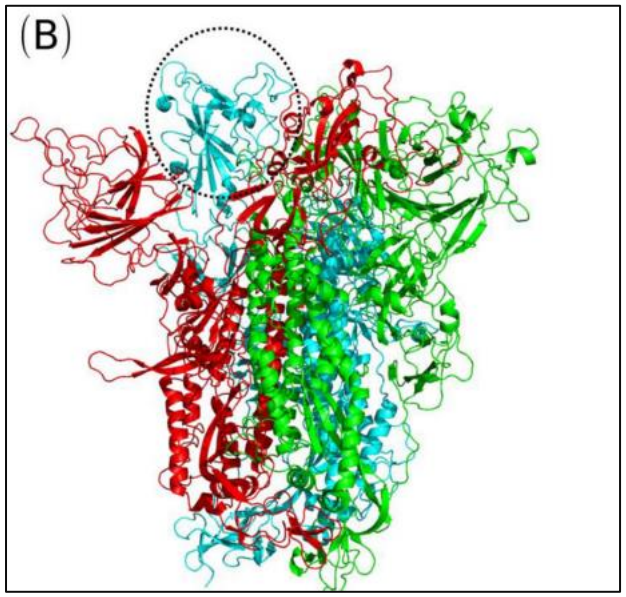
Κολχικίνη



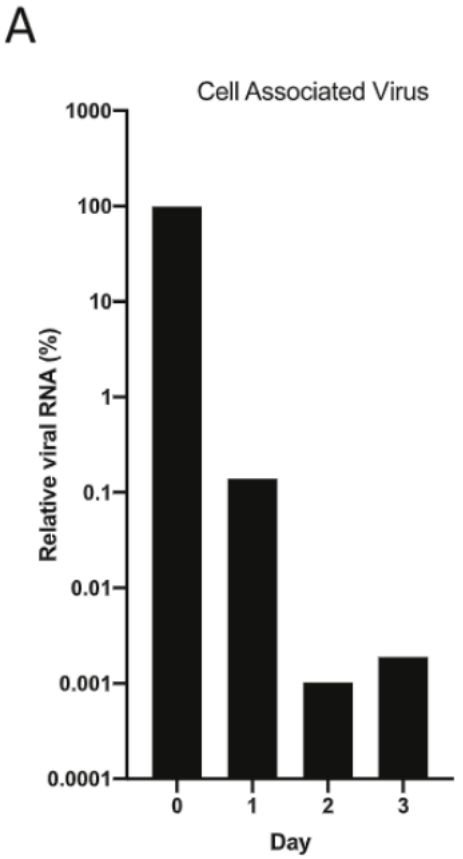
Έχει αντ-ιϊική και αντιφλεγμονώδη δράση και έχει συσχετιστεί με μικρότερη επίπτωση πνευμονίας μετά ΟΕΜ

Br J Dermatol. 2018;178(2):350–6.

Ivermectin



RBD region

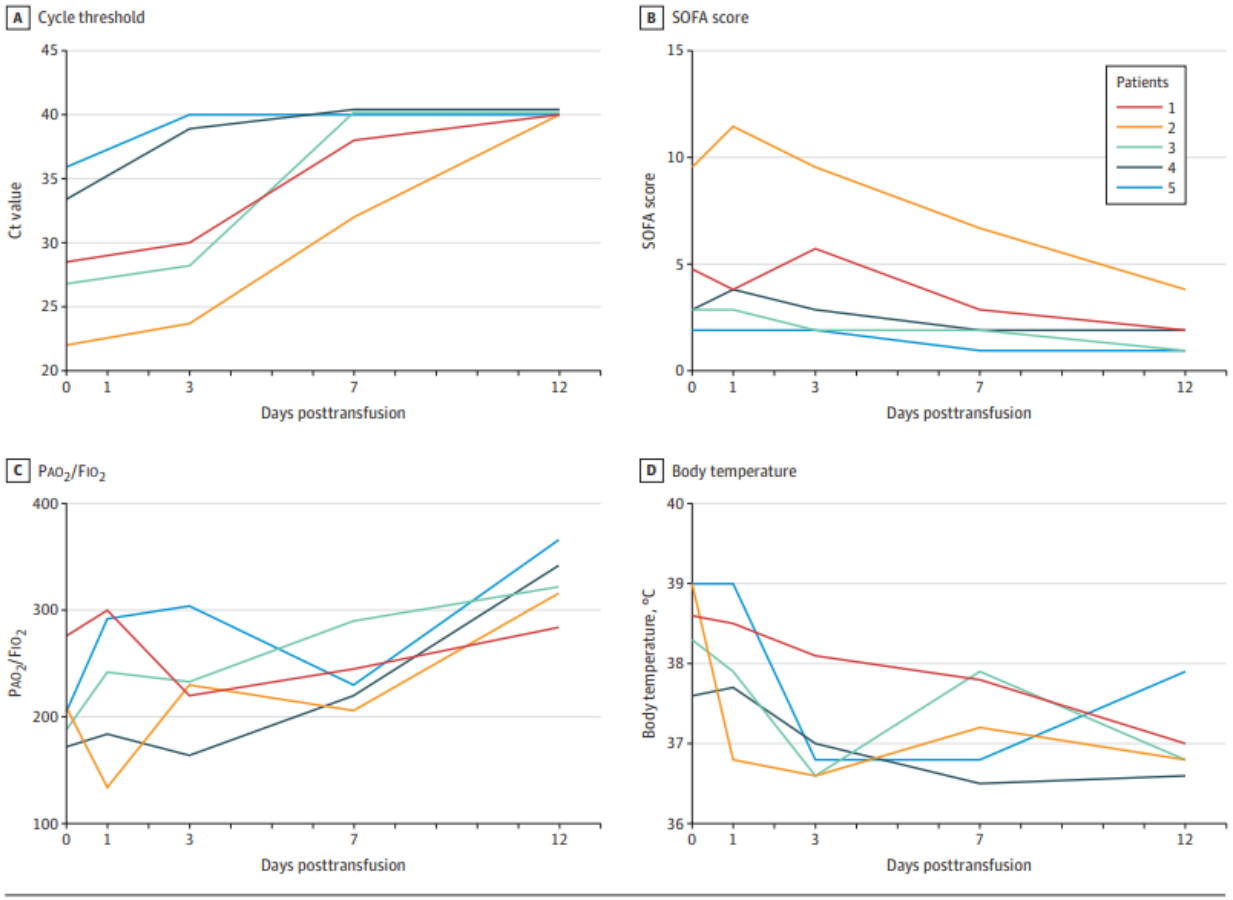


Antivir Res. 2020;178:104787.

Υερδοσολογια
Πιθανή δραση στο ΚΝΣ

Παράγωγα πλάσματος αναρρωνυόντων

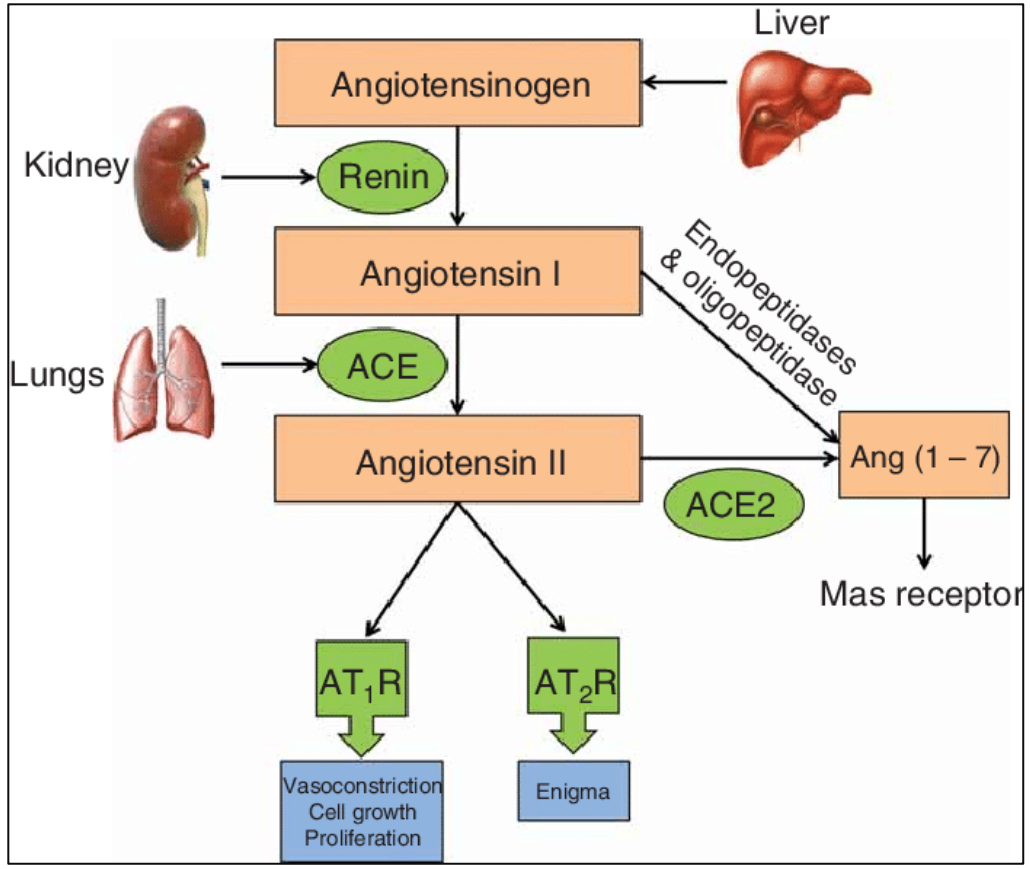
Figure 1. Temporal Changes of Cycle Threshold Value, PaO_2/FiO_2, SOFA Score, and Body Temperature in Patients Receiving Convalescent Plasma Transfusion



JAMA. 2020;323(16):1582–9

ACE Αναστολείς-Στατίνες

- Ο ιός χρησιμοποιεί το ACE2 των μεμβρανών των κυττάρων στόχων.
- Μετά την είσοδό του, ακολουθεί downregulation των ACE2
- Upregulation των ACE2 οδηγεί σε καλύτερη άμυνα στον πνεύμονα
- Υποστροφή των ACE2 είναι στοιχείο της χρονολογικής γήρανσης
- Η θεραπεία με ACE inhibitors οδηγεί σε υπερέκφραση του υποδοχέα και απότομη απόσυρση μπορεί να προκαλέσει απότομο downregulation
- Αναδρομικές παρατηρήσεις για την έκβαση της COVID 19 μεταξύ ατόμων που λάμβαναν ACEinh ή όχι, δεν ανέδειξαν
- Οι στατίνες



https://doi.org/10.1007/s43440-020-00155-6

Συμπεράσματα

- Το φάσμα των δυνατοτήτων των τεχνικών του Drug Repurposing, σε ελάχιστο βαθμό έχει συνεισφέρει πρακτικά στην Covid-19, πιθανόν λόγω των ταχύτατων εξελίξεων
- Χαμηλό Level of Evidence για τα περισσότερα προτεινόμενα φαρμακα, συνεπάγεται ιδιαίτερη δυσκολία στη γενίκευση κατευθυντήριων οδηγιών
- Παραμένουν ερωτηματικά για την ίδια δραστικότητα του κάθε φαρμάκου και για τον ενδεδειγμένο χρόνο χορήγησης
- Δεν έχουν ελεγχθεί επαρκώς υποομάδες
- Ακάλυπτο το ζήτημα της πρόληψης
- Για τα περισσότερα φάρμακα, σημαντικά AEs και φαρμακευτικές αλληλεπιδράσεις, και μερικά επικινδυνα στην εγκυμοσύνη

Ευχαριστώ πολύ!