SCUOLA DI SPECIALIZZAZIONE IN MALATTIE INFETTIVE E TROPICALI

PANDORA ID - 22

TIME TO WEBINAR IN INFECTIOUS DISEASES

PROGETTO DI FORMAZIONE

IL RISCHIO INFETTIVO NEL PAZIENTE TRATTATO CON FARMACI BIOLOGICI

COME RIDURRE IL RISCHIO INFETTIVO NEL PAZIENTE TRATTATO CON I FARMACI BIOLOGICI? SCREENING E PROFILASSI PRIMA DELLA TERAPIA

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DIBIC

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Conflict of Interest Disclosure

I received speaker's honorarium from the following companies:

- Gilead
- VIIV
- MERCK
- MSD
- Sanofi
- Glaxo
- Novartis
- Roche

Medical specialties utilizing FDA-approved biologics

- cardiovascular disease
- neurology
- rheumatology
- nephrology
- gastroenterology
- dermatology
- ophtalmology
- oncology
- metabolic conditions
- infections
- transplant
- hematology
- pneumology

Biological and Small Molecule Targeted Immunomodulatory Therapies

- TNF- INHIBITORS
- ANTI-T LYMPHOCYTE THERAPIES
- ANTI-B LYMPHOCYTE ANTIBODIES
- COMBINATION LYMPHOCYTE-DEPLETING AGENTS
- IL-1 PATHWAY INHIBITORS
- DRUGS TARGETING IL-4
- AGENTS TARGETING IL-5 AND IgE
- IL-6-TARGETED AGENTS
- IL-12/IL-23 PATHWAY INHIBITORS IL-17-TARGETED AGENTS
- TYROSINE KINASE INHIBITOR
- JAK INHIBITORS
- BTK INHIBITORS
- PI3K INHIBITORS
- BCR-ABL INHIBITORS
- Syk INHIBITORS
- ALK INHIBITORS
- INTEGRIN INHIBITORS
- IMMUNE CHECKPOINT INHIBITORS
- COMPLEMENT PATHWAY INHIBITORS

Infectious diseases assessment

In patients candidates to immunesuppressive therapy

at diagnosis, a **baseline "infectious disease" evaluation** is recommended

This should include, at a minimum, the following:

- Personal history (childhood diseases, present or past tuberculosis contacts, travel history, personal or familiar potential sources of infection, search for possible immune deficiencies (e.g. asplenia, diabetes, etc.)
- Life style

ID card

- The initial assessment of all patients candidates to IS therapy should include immunization status and catch-up vaccination schedule, according to the National Vaccination Program
- Vaccinations to be considered for adult patients candidate to IS therapy should include the ones recommended by local regulations, except in cases of additional risk factors (travel, sexual habits, individual risk factors)
- The vaccination status of all patients candidates to IS treatment must ideally be assessed at the moment of diagnosis and always before starting immunosuppressive therapy.
- Particular safety and efficacy issues must be taken into consideration when vaccinating patients on immunosuppressants

Baseline ID assessment

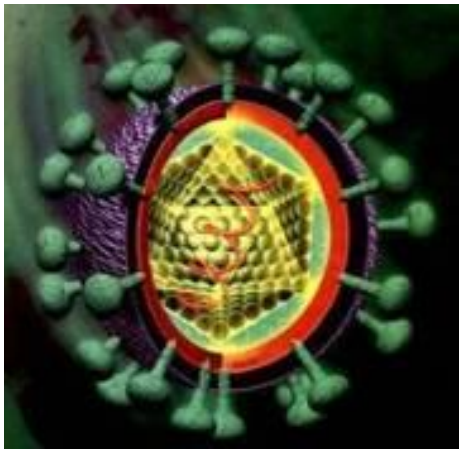
- Baseline serologic assessment
  - Toxoplasma IgG
  - Hepatitis B and C virus screening
  - Herpes simplex virus IgG
  - Varicella zoster virus IgG
  - Cytomegalovirus IgG
  - Human immunodeficiency virus
  - EBV-VCA IgG
  - JCV Screening with Stratify (for MS patients)
- Baseline screening for human papillomavirus
  - Pap smear for females + HPV PCR
  - Men? If MSM anoscopy and HPV PCR

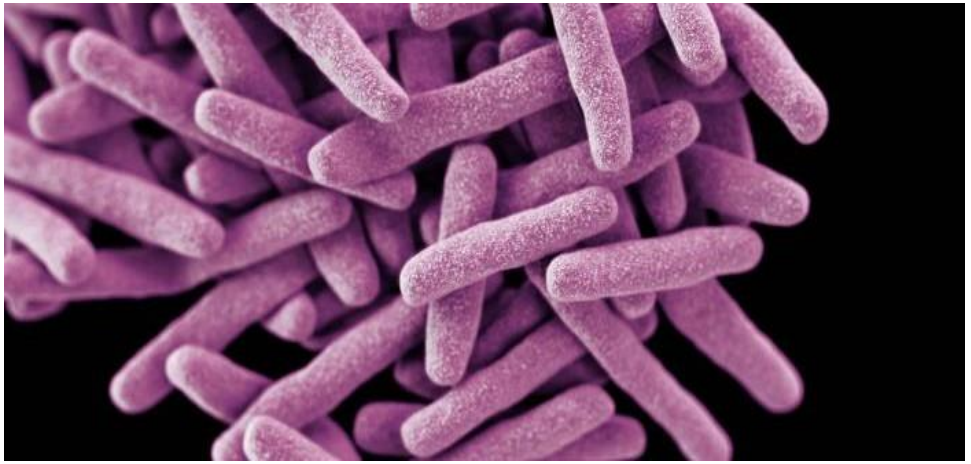
Baseline ID assessment

- TB-IGRA or PPD-IDR
  - If positive
    - Lung x-rays
    - Verify previous therapy
    - If no therap or prophylaxis, consider prophylaxis regimen before initiating immunesuppressive treatment
- Personal and familiar counseling in order to avoid future contagion
- Travel medicine counseling (for patients intending to travel)

ID prevention: general indications

- Interventions aimed at preventing HBV, HCV and TB reactivation apply to all the cases when an immunesuppressive treatment is to be administered





HBV-HCV

- All patients candidates to IS therapy should be screened for HBV/HCV infection at diagnosis and before any DMD is started.
- Screening should include: HBsAg, HBcAb, HBsAb and HCVAb.
- All patients positive for any of these markers should be referred to a specialist, with the exception of HBV vaccinated patient with isolated HBsAb reactivity

Recommendations for infectious disease screening in migrants to Western Europe with inflammatory arthropathies before starting biologic agents. Results from a multidisciplinary task force of four European societies (SIR, SER, SIMET, SEMTSI) facing the largest impact of the flow of migrants today

F. Bartalesi[1], C.A. Scirè[2], A. Requena-Méndez[3], M.A. Abad[4], D. Buonfrate[5], R. Caporali[6], F. Conti[7], F. Diaz-Gonzalez[8], C. Fernández-Espartero[9], C. Martinez-Fernandez[10], M. Mascarello[11], E. Generali[12], G. Minisola[12], A. Morrone[13], J. Muñoz[3], P. Richi[14], G. Sakellariou[6], J. Salas Coronas[14], M. Spinicci[1], F. Castelli[15], A. Bartoloni[1], Z. Bisoffi[5], F. Gimenez-Sanchez[16], S. Muñoz-Fernández[14], M. Matucci-Cerinic[17]

Clinical and Experimental Rheumatology 2017; **35**: 752-765.

List of latent infection considered by the panel of expert for recommendation

Disease	Screening	Candidates for screening	Available tests
Mycobacterial diseases			
Hansen's diseases	No		None
Non-TB mycobacteria	No		None
MDR-TB	Yes	All patients[§]	TST/IGRAs
Bacterials diseases			
Brucellosis	No		Serology
Salmonellosis (typhi/paratyphi)	Yes	Patients from highly endemic areas with cholelithiasis/urinary tract defect	Stool and urine cultures
Parasitic diseases			
Leishmaniasis	No		Serology, PCR
Babesiosis	No		Blood smears, serology, PCR
Strongyloidiasis	Yes	Migrants from endemic areas and autochthonous patients with eosinophilia	Serology and stool test if available
Cysticercosis	No		Serology
Chagas disease	Yes	Patients from/whose mother was born in/blood transfused in endemic area	Serology
Viral diseases			
HEV	No		Serology, PCR
HTLV-1	No		Serology, PCR
Fungal diseases			
Histoplasmosis	Yes	Patients from endemic areas with suggestive history/radiological signs	Serology
Coccidioidomycosis	Yes	Patients from endemic areas and compatible clinical symptoms/history	Serology
Paracoccidioidomycosis	No		Serology

Prevention

Vaccinations

Tipi di vaccini

vaccini con microrganismi vivi ed attenuati	Controindicati in pazienti in terapie immunosoppressive o steroidea: febbre gialla, morbillo, rosolia, parotite, varicella, herpes zoster, tifo (orale) e poliomielite (orale Sabin), influenza (LAIV intranasale).
vaccini con microrganismi uccisi	Influenza, tifo (IM), colera, pertosse, epatite A, encefalite da zecche (TBE), encefalite giapponese, rabbia e polio (IM, Salk)
vaccini con frazioni di microrganismi	Influenza, pneumococco, meningococco ACWY, haemophilus influenzae B (HIB) e herpes zoster (a subunità, non ancora in commercio in Italia)
vaccini costituiti da anatossine o tossoidi	Tetano, difterite
vaccini da manipolazioni genetiche con la tecnica del DNA ricombinante	Epatite B, meningococco B e papilloma virus umano (HPV)

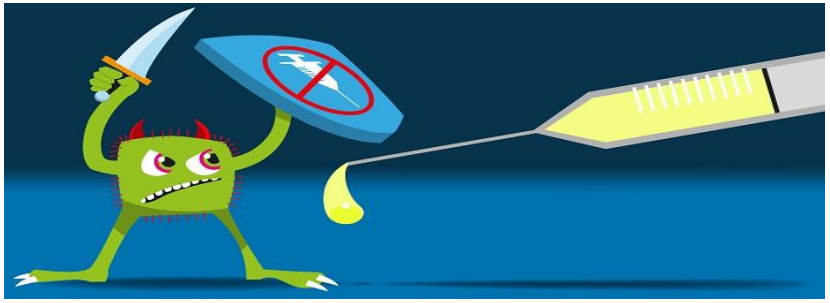
When to vaccinate?

The available literature is insufficient to answer the questions on efficacy and safety of vaccinations during IS therapy: there are few studies, with a limited range of vaccines tested (mainly influenza vaccine).

In many cases different vaccines are tested simultaneously.

The studies are usually underpowered and few RCTs are available

When to vaccinate?



Timing and schedule of vaccinations should be tailored to:

- The timing of DMD administration (past or planned)
- The time elapsed since last acute exacerbation
- The time elapsed since last corticosteroid pulse

Timing since last steroid pulse

The role of short-term pulsed steroid treatment on the immune system and its impact on response to vaccinations, in terms of safety and efficacy, warrants further research.

Experts generally agree to delay vaccination with inactivated vaccines at least 4 weeks after high-dose steroid treatment. The time for live vaccines may be longer

Inactivated vaccines

- Inactivated vaccines (either first or recall dose) should be administered at least 2 weeks before the introduction of immunosuppressive disease modifying drugs, due to efficacy concerns.
- Similarly, even though inactivated vaccines will never pose a risk of "vaccine disease" in immunosuppressed patients, their efficacy is not guaranteed until a certain time after drug interruption: this interval is not uniformly defined. In any case, such vaccines should be re-administered when initially given during a period of intense immunosuppression.
- Nonetheless, seasonal influenza vaccine is always indicated, irrespective of concomitant DMDs, on the assumption that even a reduced response might be at least partially efficacious

Live attenuated vaccines

- No study specifically addresses the effectiveness and safety of live vaccine immunizations in IS patients
- In MS one small-sized observational study on Yellow Fever vaccination suggests an increased risk of vaccine-induced MS reactivation (research on this topic is strongly needed).
- Live attenuated vaccines should be administered at least 4–6 weeks before initiation of treatment with ~~i~~immunosuppressive DMDs.
- They should never be administered to a patient on immunosuppressive drugs, or before a certain time since their interruption, the duration of which is based on expert opinion

Live attenuated vaccines: Specific recommendations on live vaccines

Health Care Delivery Sciences 2014 considered 3 months to be a safe interval for live-attenuated vaccination after an immunosuppressive steroid dosage is given.

For B-depleting therapies and both B- and T-depleting treatment, it is suggested to wait until B-cells have returned to normal levels, and no earlier than 6 months for rituximab.

Nonetheless, if administration of highly immunosuppressive DMDs is relatively urgent, decision about vaccination with live vaccines must be made on an individual basis and after consideration of the risk/benefit ratio.

Safety of live vaccines on immunosuppressive or immunomodulatory therapy—a retrospective study in three Swiss Travel Clinics

Fabienne Huber, MD[1†], Benoît Ehrensperger, MD[2†], Christoph Hatz, MD[1,3], François Chappuis, MD PhD[2], Silja Bühler, MD MSc[1*‡], and Gilles Eperon, MD[2‡]

Journal of Travel Medicine

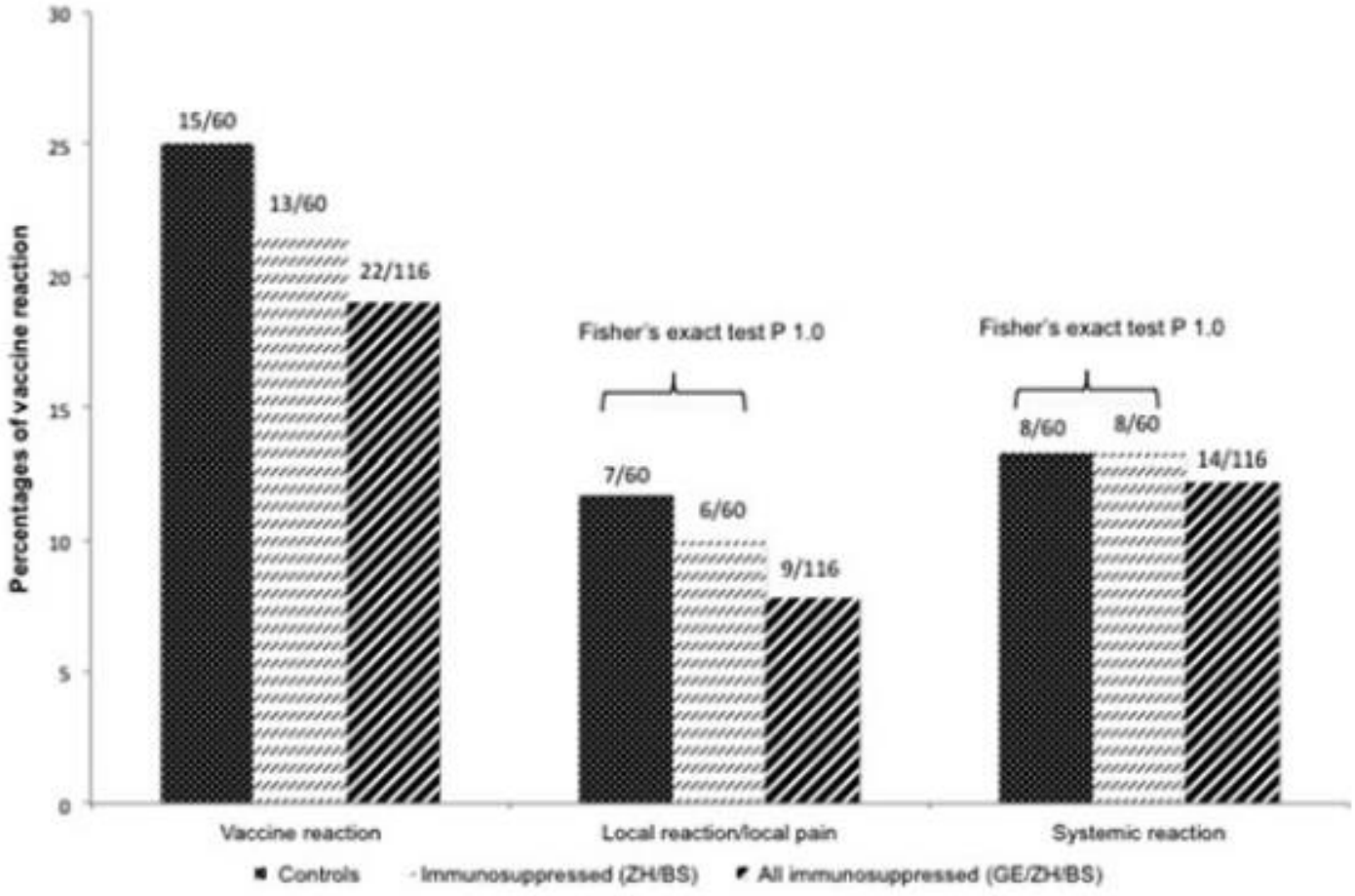
Underlying conditions in immunosuppressed patients receiving a live vaccine

Underlying condition	Number (%)
Rheumatic disorders	
Rheumatoid arthritis	21 (18.1)
Polymyalgia rheumatica	8 (6.9)
Psoriasis/psoriatic arthritis	7 (6.0)
MCTD	2 (1.7)
Spondylarthritis	1 (0.9)
Behçet's disease	1 (0.9)
Inflammatory bowel disease	
Ulcerative colitis	20 (17.2)
Crohn's disease	12 (10.3)
IBD of unknown origin	1 (0.9)
Neurological condition	
Multiple sclerosis	7 (6.0)
Allergy/asthma	7 (6.0)
Sarcoidosis	3 (2.6)
Chronic myeloid leukaemia	2 (1.7)
Addison's disease	2 (1.7)
Hypopituitarism	1 (0.9)
Solid organ transplant	1 (0.9)
Other	11 (9.5)
Unclear	9 (7.8)
Total	116 (100)

Administered live vaccination according to immunosuppressive/ immunomodulatory medication

Adalimumab	3	2	1	0	6 (6)
Azathioprine	0	1	0	2	3 (3)
Budesonide	1	1	0	0	2 (2)
Etanercept	1	0	0	0	1 (1)
Dimethyl fumarate	1	0	0	0	1 (1)
Glatiramer acetate	3	0	0	0	3 (3)
Imatinib	2	0	0	0	2 (2)
Infliximab	1	0	0	0	1 (1)
Interferon beta	2	1	0	0	3 (3)
6-Mercaptopurine	1	0	0	1	2 (1)
Mesalazine	17	11	0	1	29 (29)
Methotrexate	16	4	0	1	21 (18)
Mycophenolic acid	2	0	0	0	2 (2)
Natalizumab	1	0	0	0	1 (1)
Omalizumab	1	0	0	0	1 (1)
Corticosteroids (<2 weeks)[b]	6	0	1	0	7 (7)
Corticosteroids (≥2 weeks)[b]	34	0	3	0	37 (37)
Sulfasalazine	3	1	1	0	5 (5)
Tacrolimus	1	0	0	0	1 (1)
Ustekimumab	1	0	0	0	1 (0)
Total *n* of vaccinations	92	21	6	4	

Vaccine reactions in vaccinated immunosuppressed patients and controls



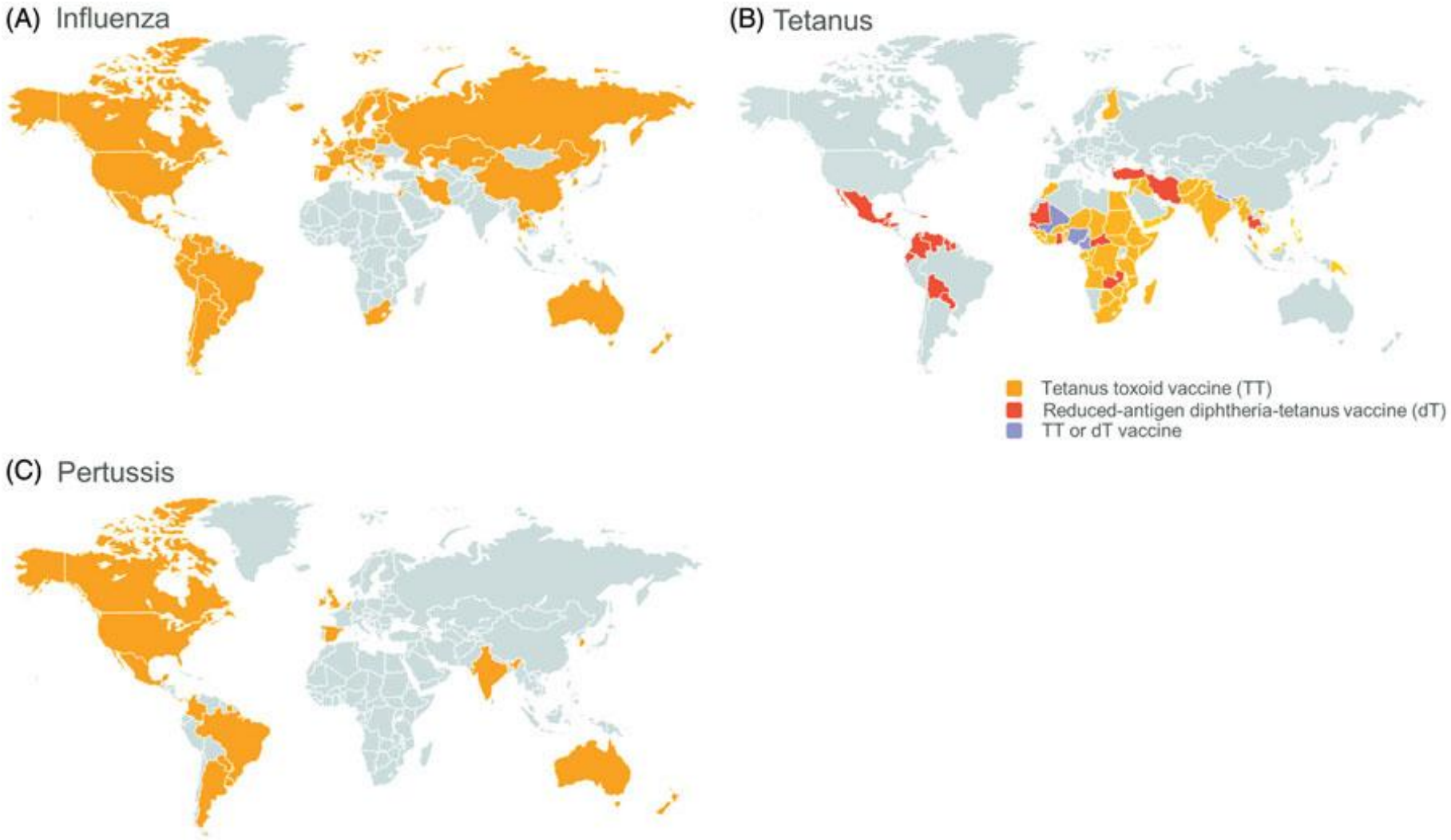
What vaccines?

- Seasonal influenza every year for all patients
- Tetanus/diphtheria/pertussis acellular if never received (TD recall if needed)
- Hib if never received
- Pneumococcal conjugate vaccine (PCV13) followed by PPV23 after >2 months
- Inactivated polio vaccine if never received and planning to travel in endemic countries

What vaccines?

- Hepatitis B vaccine if HBcAb negative and HBsAb negative
- Hepatitis A vaccine if hepatitis A virus IgG negative and traveler, men who have sex with men, raw seafood eater
- MCV4 and MenB
- HPV9 for women and men <45 years old?
- Varicella (VAR) vaccine for those VZV IgG negative
- Zoster vaccination

Recommendations for maternal immunization worldwide



How to vaccinate?

Influenza vaccine effectiveness in older subjects

- There is evidence that seasonal influenza vaccine effectiveness is lower in adults over the age of 65 than in healthy adults 18–64 years old
- Recent meta-analysis estimated VE against influenza in older adults at about 49% (95% CI 33,62) while effectiveness was closer to 59% (95% CI 51, 67) for healthy younger adults
- This reduction in influenza VE may be partially explained by a reduction in immune response to influenza immunization as adults age

Immunogenicity and safety of high-dose versus standard-dose inactivated influenza vaccine in rheumatoid arthritis patients: a randomised, double-blind, active-comparator trial

Inés Colmegna, Mariana L Useche, Katherine Rodriguez, Deirdre McCormack, Giuliana Alfonso, Aakash Patel, Agnihotram V Ramanakumar, Elham Rahme, Sasha Bernatsky, Marie Hudson, and Brian J Ward

Baseline characteristics of study participants included in the intention-to-treat analysis

	HD-TIV (n=138)	SD-QIV (n=136)
Sex		
Female	109 (79%)	109 (80%)
Male	29 (21%)	27 (20%)
Age*, years	59·7 (13·9)	61·9 (11·8)
Ethnic origin		
White	110 (80%)	106 (78%)
African American	6 (4%)	7 (5%)
Asian	13 (9%)	14 (10%)
Hispanic	1 (1%)	4 (3%)
Other	8 (6%)	5 (4%)
Comorbidities		
Diabetes	16 (12%)	9 (7%)
Cancer	11 (8%)	24 (18%)
Angina or myocardial infarction	5 (4%)	5 (4%)
Congestive heart failure	2 (1%)	0
Asthma, COPD, or emphysema	16 (12%)	22 (16%)
RAPID3 score	2·2 (2)	2·3 (2·1)
RADAI-5 score	2·9 (2·2)	3·3 (2·2)
Current rheumatoid arthritis treatment		
Steroids	30 (22%)	28 (21%)
Dose, mg/day	8·2 (9·0)	8·6 (6·0)
Methotrexate	70 (51%)	69 (51%)
Dose, mg/week	18·1 (5·5)	18·0 (4·6)
Biologics	59 (43%)	65 (48%)
Etanercept	22 (16%)	18 (13%)
Adalimumab	8 (6%)	20 (15%)
Certolizumab pegol	5 (4%)	1 (1%)
Golimumab	3 (2%)	2 (1%)
Infliximab	1 (1%)	2 (1%)
Tocilizumab	4 (3%)	6 (4%)
Sarilumab	1 (1%)	0
Abatacept	9 (7%)	9 (7%)
Rituximab	6 (4%)	7 (5%)
JAK inhibitors	10 (7%)	7 (5%)

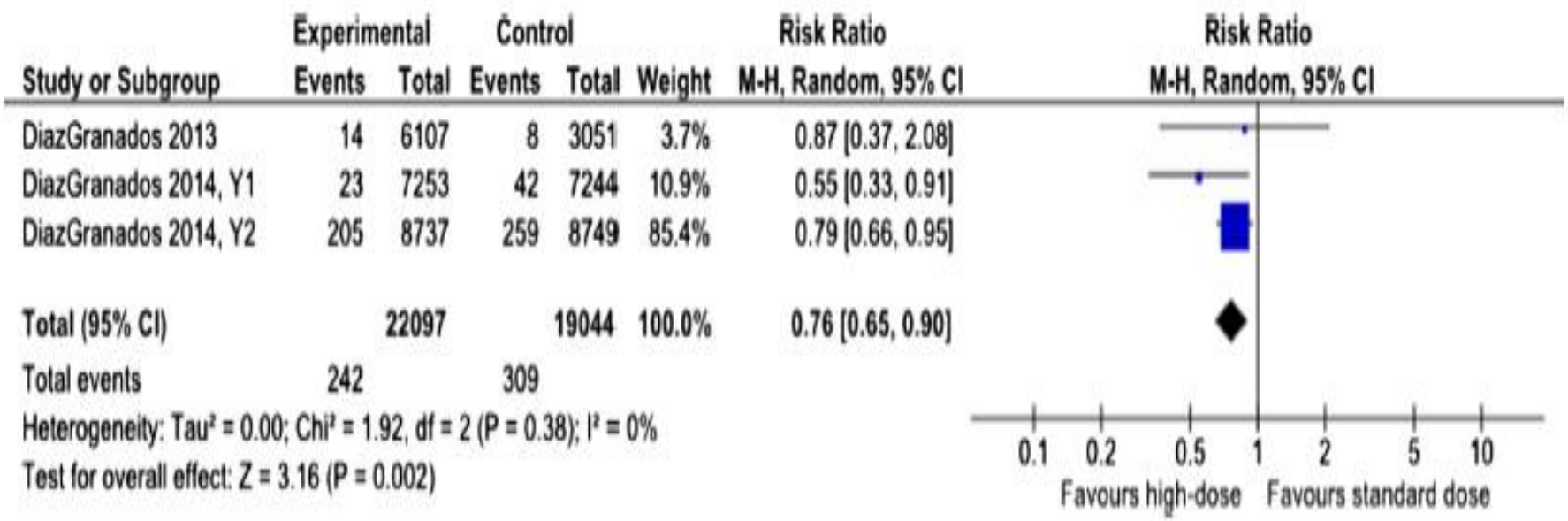
Seroconversion in the modified intention-to-treat population at day 28

	Seroconversion, HD-TIV group	Seroconversion, SD-QIV group	Unadjusted odds ratio (95% CI), HD-TIV *vs* SD-QIV
Haemagglutination-inhibition antibodies			
A/Hong Kong/4801/2014*	31/138 (22%)	12/136 (9%)	2·99 (1·46–6·11)
B/Brisbane/60/2008†	62/138 (45%)	40/136 (29%)	1·95 (1·19–3·22)
A/California/7/2009‡ (year 1)	36/69 (52%)	18/71 (25%)	3·21 (1·57–6·56)
A/Michigan/45/2015‡ (year2)	32/69 (46%)	17/65 (26%)	2·44 (1·18–5·06)
Microneutralisation antibodies			
A/Hong Kong/4801/2014	61/138 (44%)	45/136 (33%)	1·60 (0·98–2·62)
B/Brisbane/60/2008†	58/138 (42%)	26/136 (19%)	3·07 (1·78–5·28)
A/California/7/2009‡ (year 1)	37/69 (54%)	20/71 (28%)	2·95 (1·46–5·94)
A/Michigan/45/2015‡ (year2)	42/69 (61%)	26/65 (40%)	2·33 (1·17–4·66)

Adverse events in the modified intention-to-treat population

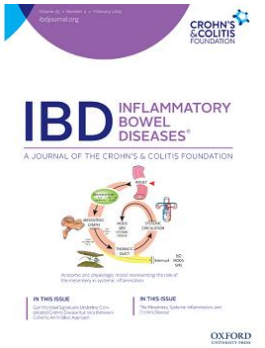
	HD-TIV group	SD-QIV group	Odds ratio (95% CI)
All SAEs	2	1	1·97 (0·10–117·11)
Days 0–28	0	0	NA
Days 28–186	2	1	1·97 (0·10–117·11)
Solicited adverse events, days 0–7	206	238	0·85 (0·62–1·16)
Redness at injection site	18	19	0·93 (0·44–1·97)
Swelling at injection site	19	16	1·17 (0·54–2·54)
Fever (≥ 37·9°C)	0	0	NA
Chills	21	26	0·79 (0·40–1·55)
Headache	28	32	0·86 (0·47–1·57)
Tiredness	23	33	0·67 (0·36–1·28)
Nausea	13	16	0·80 (0·34–1·85)
Vomiting	0	1	NA
Diarrhoea	13	12	1·07 (0·43–2·65)
Myalgia	46	46	0·98 (0·60–1·62)
Red eyes	5	5	0·99 (0·22–4·38)
Arthralgia	11	11	0·98 (0·37–5·59)
Joint swelling	5	9	0·54 (0·14–1·87)
Morning stiffness	4	12	0·32 (0·07–1·12)
Unsolicited adverse events	52	49	1·05 (0·64–1·69)
Days 0–28	20	19	1·04 (0·50–2·15)
Respiratory illness*	6	7	0·84 (0·23–3·02)
Musculoskeletal†	6	3	1·97 (0·41–12·39)
Days 28–186	32	30	1·05 (0·58–1·90)
Respiratory illness*	14	19	0·73 (0·32–1·60)
Musculoskeletal†	1	3	0·33 (0·07–4·16)

Laboratory-confirmed influenza infection in patients randomized to high-dose influenza vaccine versus standard-dose influenza vaccine

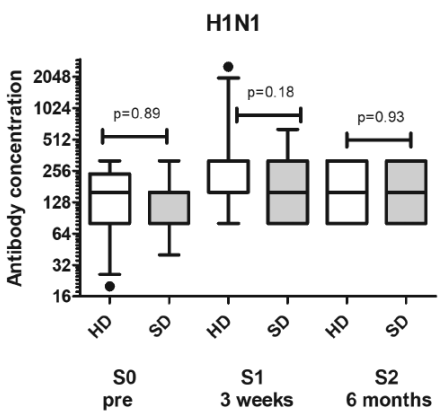


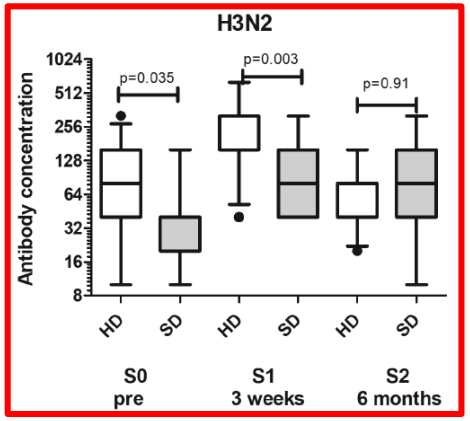
Immunogenicity of High Dose Influenza Vaccine for Patients with Inflammatory Bowel Disease on Anti-TNF Monotherapy: A Randomized Clinical Trial

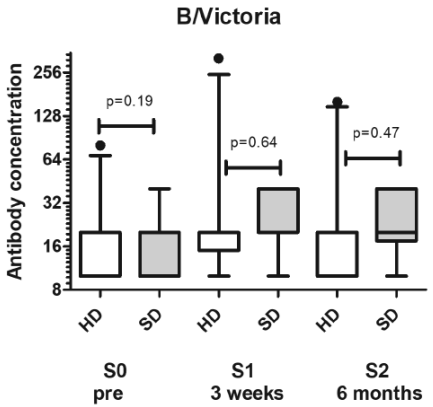
Freddy Caldera, DO, MS, Luke Hillman, MD,* Sumona Saha, MD, MS,* Arnold Wald, MD,* Ian Grimes, MD,* Youqi Zhang,† Abigail R. Sharpe, BS,† Mark Reichelderfer, MD,* and Mary S. Hayney, PharmD, MPH†*



Antibody concentrations between study groups



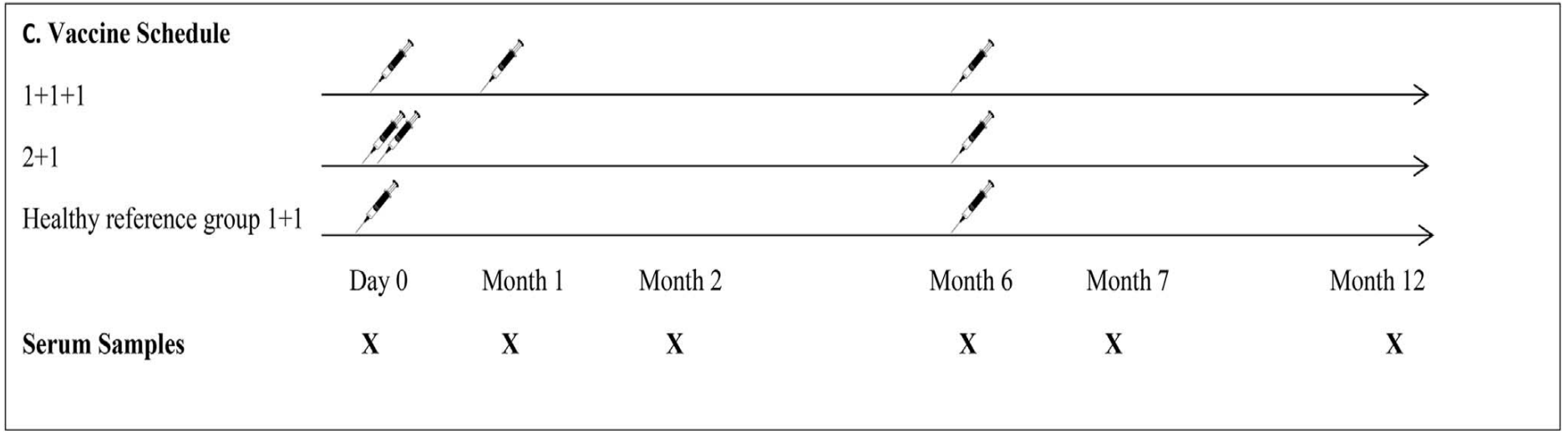




High dose influenza vaccine induced higher post-immunization H3N2 antibody concentrations compared with standard dose influenza vaccine. High dose influenza vaccine did not induce higher antibody concentrations 3 weeks post to H1N1 or B/Victoria compared. Antibody concentrations were similar between the 2 groups for each vaccine virus at 6 months post-immunization

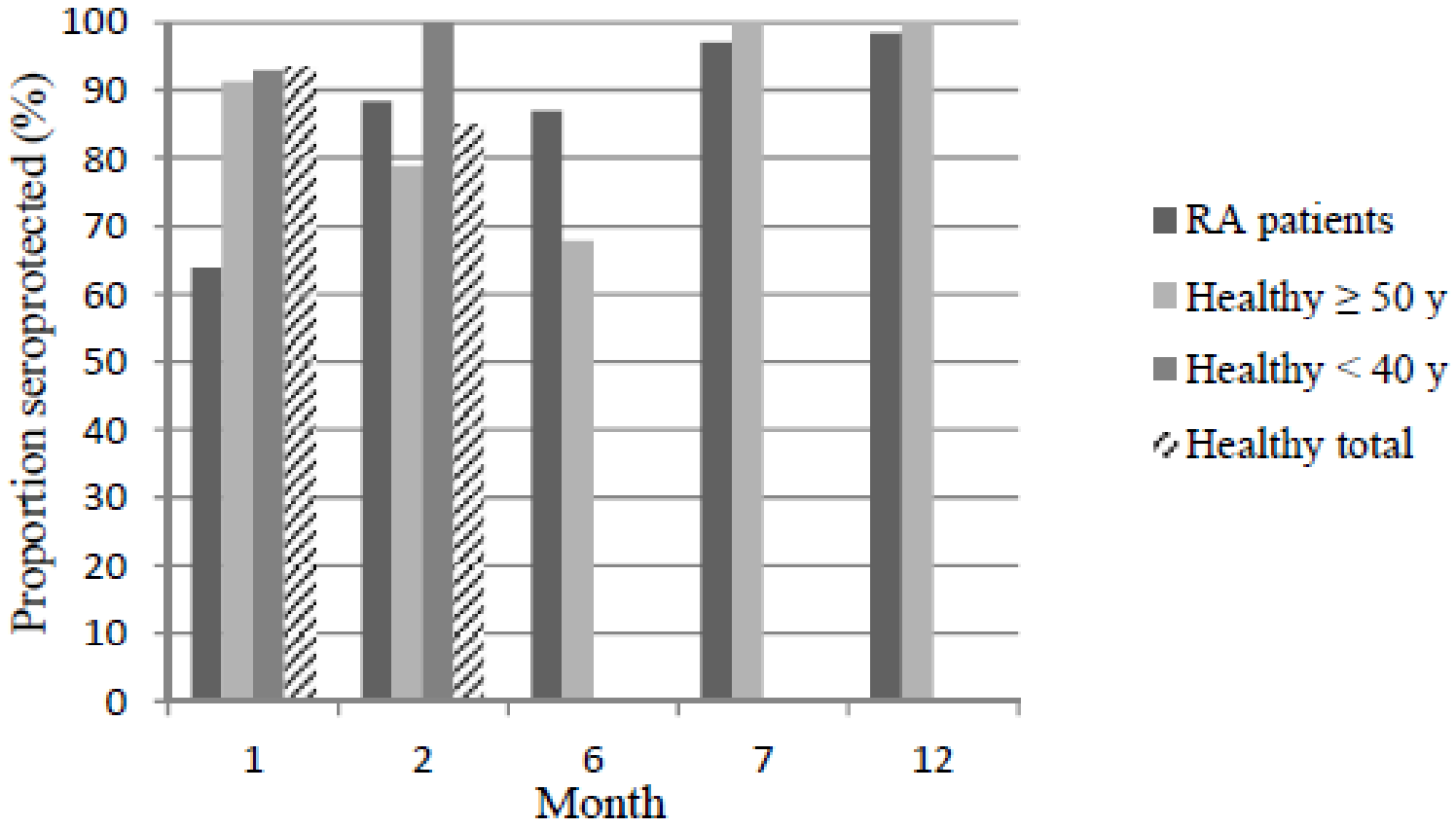
An extra priming dose of hepatitis A vaccine to adult patients with rheumatoid arthritis and drug induced immunosuppression – A prospective, open-label, multi-center study

Anja Rosdahl[a,b,*], Christian Herzog[c,d], Gert Frösner[e], Torbjörn Norén[a,f], Lars Rombo[g], Helena H. Askling[h,i]



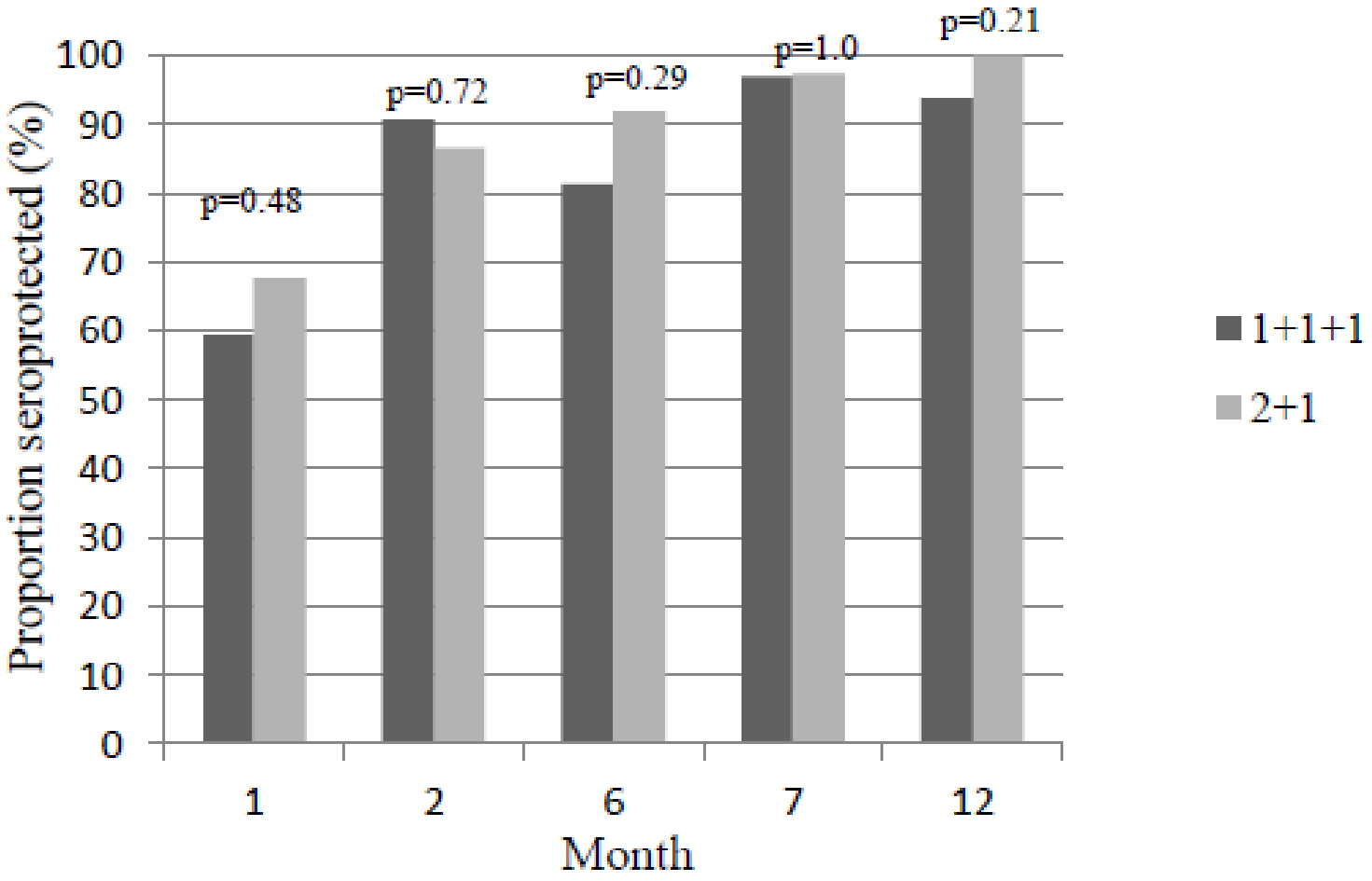
Previous studies have indicated that a pre-travel single dose of hepatitis A vaccine is not sufficient as protection against hepatitis A in immunocompromised travelers

An extra priming dose of hepatitis A vaccine to adult patients with rheumatoid arthritis and drug induced immunosuppression



Seroconversion rate in RA patients and healthy subjects

Seroconversion rate according to vaccination schedule



Sequential administrations of PCV-13–PPV-23 among immunocompromised adults based on ACIP recommendation

Pneumococcal vaccine-naive immunocompromised* adult persons				
First vaccine	Interval between two vaccines		Second vaccine	
PCV-13	≥8 weeks		PPV-23	
Previously PPV-vaccinated immunocompromised adult persons ≥65 years				
First vaccine	Interval between two vaccines		Second vaccine	
PPV-23	≥1 year		PCV-13	
Previously received PPV-23 in immunocompromised adults, when aged <65 years				
First vaccine before age 65	Interval between first PPV-23 and PCV-13	Second vaccine	Interval between PCV-13 and second PPV-23	Third vaccine
PPV-23	≥1 year	PCV-13	≥8 weeks	PPV-23
Interval between first and second PPV-23 vaccine: ≥5 years				

Vaccination uptake

- Vaccination rates of RA patients have been shown to be lower than in the general population
  - failure of the physician to recommend vaccination
  - misinterpretation of the current state of immunosuppression as a contraindication for vaccination
  - fear of vaccine-related side effects

Marco Krasselt Rheumatol Int 2017

A retrospective cohort study confirms that prophylactic vaccination is underused in patients on tumor necrosis factor inhibitors

Vaccination rate of patients on biologic therapy from 2014 to 2016

Vaccination	Vaccine received	Number	% of total
Influenza vaccination	In 2014	31,117	34.92
	In 2015	32,854	36.87
	In 2016	35,344	39.67
Zoster vaccination	In 2014-2016	2963	3.33
Pneumococcal	In 2014-2016	9406	10.56

Variable	Vaccinated, %	Unvaccinated, %	χ^2 test	*P* value	OR	95% CI	*P* value
Infections							
Influenza	0.44	7.37	3291.90	<.00001	17.83	15.5999-20.3789	<.0001
Zoster	1.11	1.73	6.5526	.010473	1.5672	1.1078-2.2171	.0111
Pneumococcal pneumonia	2.32	3.71	47.7092	<.00001	1.6258	1.4145-1.8688	<.0001
Hospitalization for							
Those infected	12.09	13.45	0.7311	.39252	1.1301	0.8536-1.4962	.3928
All individuals on TNFi	0.09	0.47	192.8935	<.00001	5.2889	4.0654-6.8806	<.0001

Inflection rates and hospitalizations based on vaccination status from 2014-2016

Vaccine coverage and reasons for non-vaccination

Studies	Population	Vaccine coverage	Reasons for non-vaccination
Bridges et al., 2003 [40]	129 RA patients on DMARDs No biotherapy	Influenza vaccine: 57%	Vaccine not recommended: 42% Side effects: 19%
Sowden et al., 2007 [41]	101 patients including 71 with RA on DMARDs and/or TNFα antagonists	Influenza vaccine: 53% Pneumococcal vaccine: 28%	Increase ++ in vaccine coverage if comorbidities
Pradeep et al., 2007 [42]	64 RA patients on DMARDs and/or TNFα antagonists ($n = 10$)	Influenza vaccine: 62% Pneumococcal vaccine: 43%	Vaccine not recommended ++
Lanternier et al., 2008 [43]	137 patients with systemic disease on immunosuppressants and/or GC	Influenza vaccine: 28%	Vaccine not recommended: 58% Fear of side effects: 35%
Koutsogeorgopoulou et al., 2008 [44]	131 RA patients on DMARDs and/or TNFα antagonists (4%)	Influenza vaccine: 36%	Vaccine not recommended: 62%
Mc Carthy et al., 2011 [45]	100 patients with inflammatory joint disease	Influenza vaccine: 42% Pneumococcal vaccine: 19%	No clearly defined immunization schedule for these patients
Desai et al., 2011 [46]	2763 patients with joint disease treated with immunosuppressants	Pneumococcal vaccine: 54%	Follow-up duration: if < 10 years, 72%; if > 10 years, 52%
Haroon et al., 2011 [47]	110 patients treated with immunosuppressants	Influenza vaccine: 34% Pneumococcal vaccine: =11%, both: 11%	Vaccine not recommended: 80% Vaccine considered useless: 12%
Feuchtenberger et al., 2012 [48]	125 RA patients on DMARDs (group 1), 117 on TNFα antagonists (group 2), and 59 on rituximab (group 3)	Vaccines against influenza/pneumococcus: 64.5%/20.2% group 1, 69.2%/36.8% group 2, 59.3%/39.0% group 3	Patients and primary-care physicians insufficiently knowledgeable about the pneumococcal vaccine

Vaccination in Inflammatory Bowel Disease Patients: Attitudes, Knowledge, and Uptake

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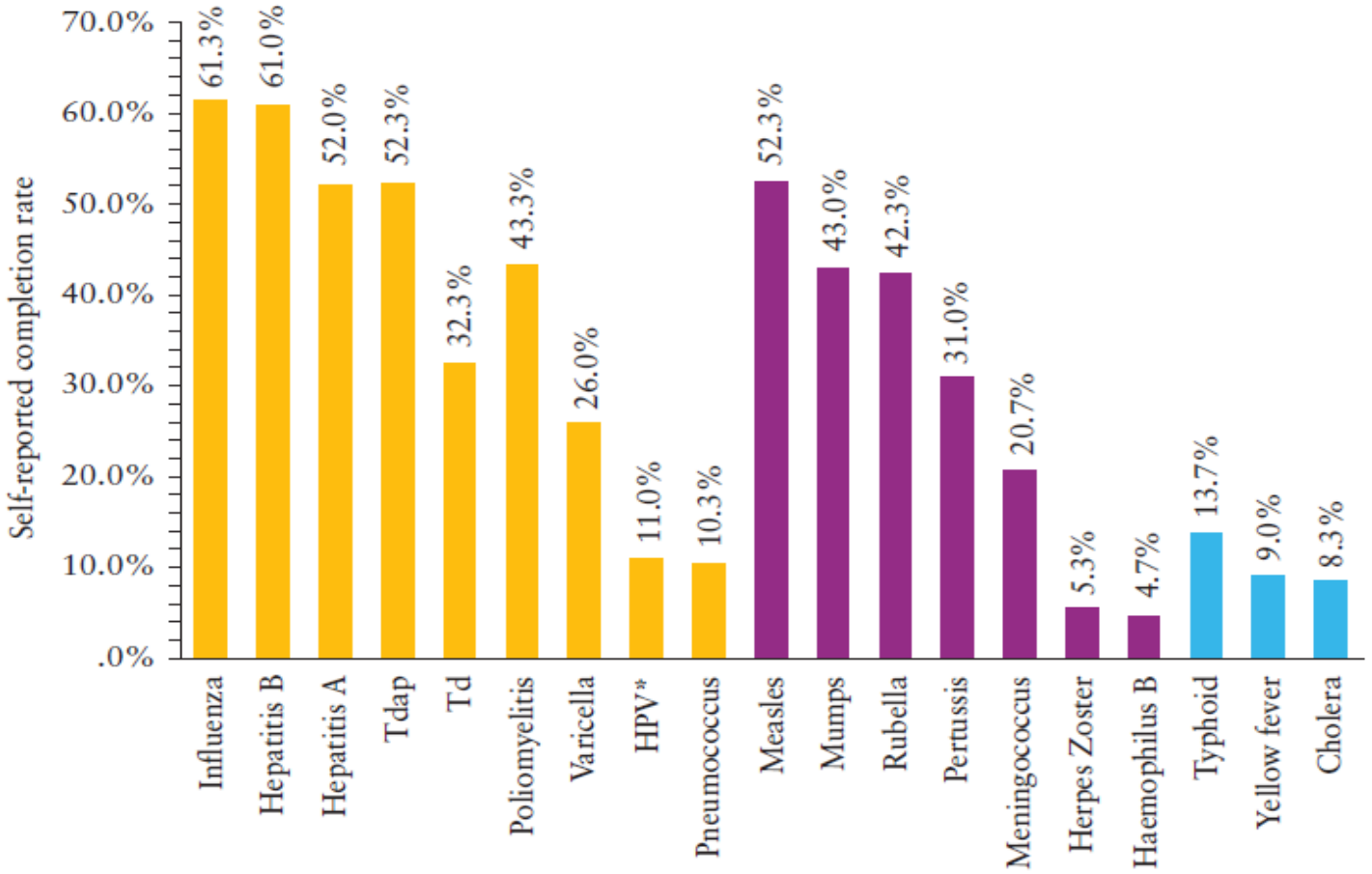

Self-reported uptake of recommended adult, childhood, and travel vaccinations

Vaccination coverage and attitude in MS patients

Patients 210	DTP	Men B	Men ACWY	Pneumo	Flu	Zoster	MPR
Vaccinated	20 (9.5%) 10 aa	2 (0.95%)	19 9.0%	29 (13.8%)	31 (14.7%)	0	ND
Not vaccinated	190 (90.5%)	208 (99.05%)	191 (91%)	181 (86.2%)	179 (86.3%)	0	ND
Subsequent Adhesion to vaccination	180 (94.7%)	181 (87%)	168 (87.9%)	169 (93.4%)	210 (100%)	NA	NA
Subsequent refusal of vaccination	10 (5.3%)	27 (13%)	23 (12.1%)	12 (6.6%)	0 (0%)	NA	NA

Vaccine implementation

- Scientific formation of the specialists
- Identification of susceptible subjects needing vaccination
- Grant proactive vaccine offer
- Free vaccinations
- Easy access to vaccination
- Infectivologist consultation
- Involvement of general practitioners

Open Forum Infectious Diseases

REVIEW ARTICLE

Risk Factors for Herpes Zoster Infection: A Meta-Analysis

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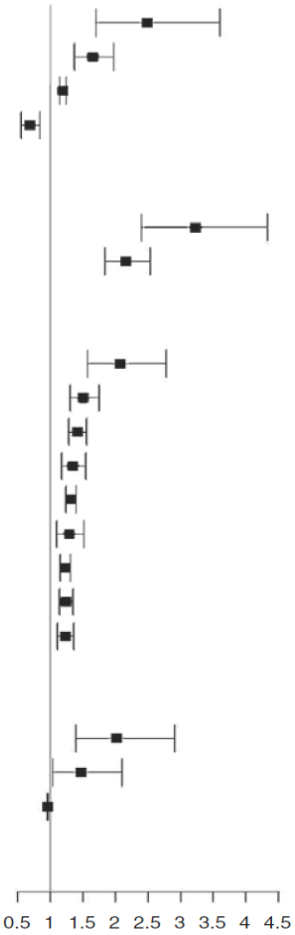
Risk Factor	No. of Studies	Effect Estimate	Pooled Effect Estimate with 95% CI	I^2	*P* Value
Innate Characteristics					
Family History	9		OR: 2.48 (1.70–3.60)	94.40%	<0.0001
Age	39		RR: 1.65 (1.37–1.97)	100.00%	<0.0001
Sex (Women)	56*		RR: 1.19 (1.14–1.24)	99.40%	<0.0001
Race (Black)	17*		RR: 0.69 (0.56–0.85)	97.90%	<0.0001
Immunosuppression					
HIV/AIDS	16*		RR: 3.22 (2.40–4.33)	98.10%	<0.0001
Malignancies	40*		RR: 2.17 (1.86–2.53)	99.60%	<0.0001
Co-morbidities					
Systemic Lupus Erythematosus	13		RR: 2.08 (1.56–2.78)	98.00%	<0.0001
Rheumatoid Arthritis	12		RR: 1.51 (1.31–1.75)	99.10%	<0.0001
Chronic Obstructive Pulmonary Disease	12		RR: 1.41 (1.28–1.55)	99.10%	<0.0001
Cardiovascular conditions	16		RR: 1.34 (1.17–1.54)	97.50%	<0.0001
Inflammatory Bowel Disoder	8		RR: 1.32 (1.24–1.40)	83.00%	<0.0001
Chronic Renal Disease	18		RR: 1.29 (1.10–1.51)	99.50%	<0.0001
Asthma	12*		RR: 1.24 (1.16–1.31)	97.30%	<0.0001
Diabetes	32*		RR: 1.24 (1.14–1.35)	99.50%	<0.0001
Depression	14*		RR: 1.23 (1.11–1.36)	98.40%	<0.0001
Other Studies					
Physical Trauma	6		RR: 2.01 (1.39–2.91)	92.50%	<0.0001
Psychological Stress	8*		RR: 1.47 (1.03–2.10)	99.50%	<0.0001
Smoking	8		RR: 0.96 (0.95–0.97)	36.40%	0.0057



Pooled analysis of the risk of herpes zoster

What can we learn from Covid 19 pandemic and vaccination in patients on immunesuppressive therapies?

- Some IS therapies affect vaccine response
- We do not know if IS reduces the vaccine efficacy time length
- We know very little about vaccine efficacy in patients on IS therapy

Correlation between antibody responses to similar antigens in the same vaccine (such as different serotypes of a bacteria or virus), as well as responses to antigens conjugated to similar carrier proteins, are strong.

In contrast, correlation between responses to other vaccines are weak.

Measuring antibody responses to one or a few vaccine antigens therefore does not offer a reliable surrogate marker of responses to unrelated vaccines.

Where do we go from here?

- Vaccinate patients candidate to IS before starting DMDs if possible
- Check vaccine response and persistence of protection
- Vaccinate friends and family
- Design and perform vaccination trials in patients on immunesuppressive drugs
- Explore new vaccination strategies if needed
- Inform and educate specialists and family doctors in regard to vaccination opportunities for iatrogenic IS patients

Use of oral antivirals for COVID-19

Three oral antivirals have so far been authorised in Italy for the treatment of coronavirus disease 2019 (COVID-19) in adults who do not need supplemental oxygen and who are at high risk of progressing to severe COVID-19:

- Nilmetravir/ritonavir
- Molnupiravir
- Remdesivir

The prescription of antivirals for the treatment of COVID-19 is subject to a monitoring register and envisages the use of a sheet for medicinal products subject to monitoring.

EVUSHELD (tixagevimab-cilgavimab) profilassi COVID-19

Profilassi pre-esposizione dell'infezione da SARS-CoV-2 in soggetti adulti ed adolescenti di età pari o superiore a 12 anni e con peso corporeo di almeno 40kg, che presentano almeno uno dei seguenti fattori di rischio:

Pazienti che abbiano assunto nell'ultimo anno terapie che comportano deplezione dei linfociti B (ad es. rituximab, ocrelizumab, ofatumumab, alemtuzumab)

Pazienti in trattamento con inibitori della tirosin-chinasi Bruton

Pazienti trattati con CarT

Pazienti trapiantati di cellule ematopoietiche che hanno una malattia di rigetto o che stanno assumendo farmaci immunosoppressori

Pazienti con malattia onco-ematologica in fase attiva

Pazienti trapiantati di polmone

Pazienti trapiantati di organo solido (diverso dal trapianto di polmone) entro 1 anno dal trapianto

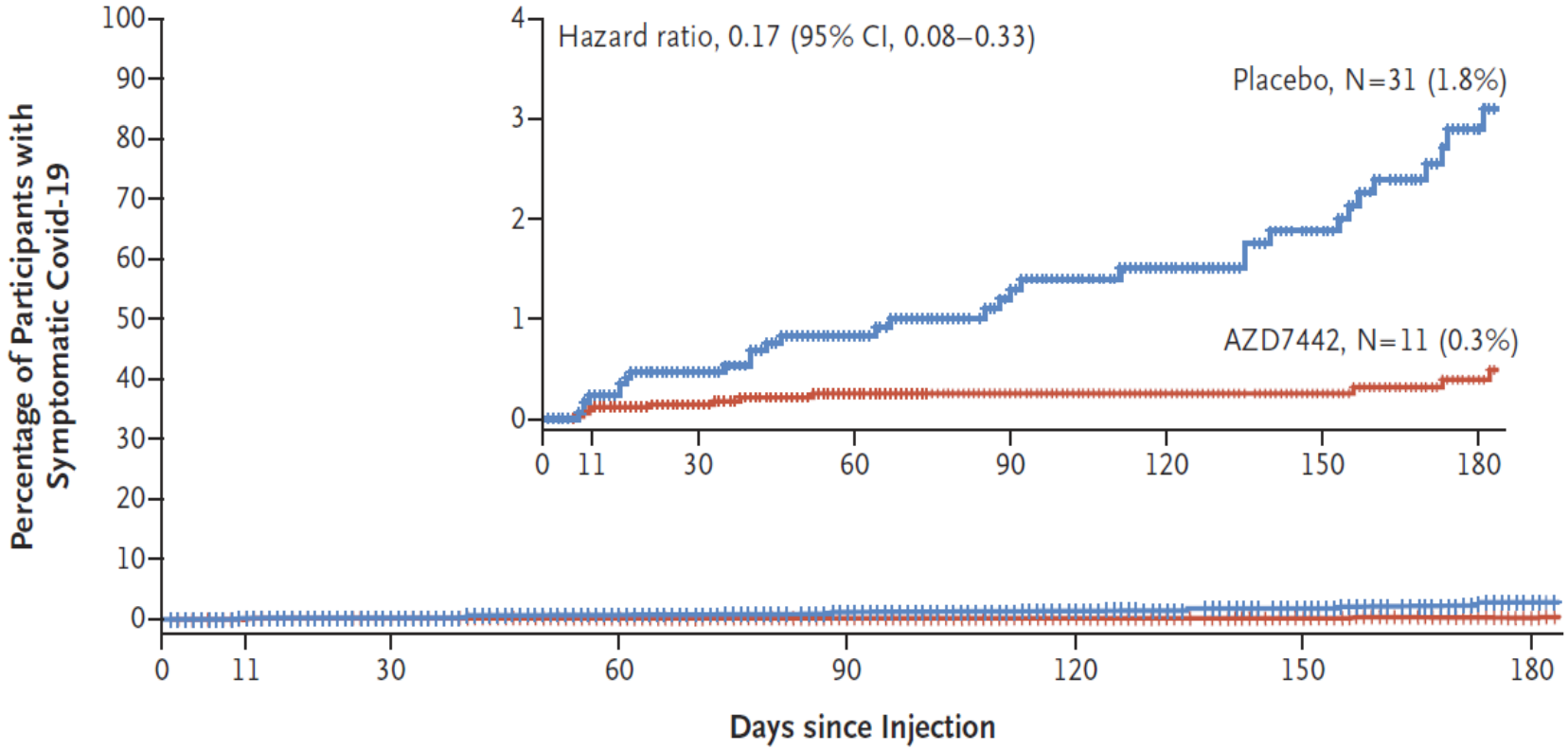
Pazienti trapiantati di organi solidi con recente trattamento per rigetto acuto con agenti che riducono le cellule T o B

Pazienti con immunodeficienze combinate gravi

Pazienti con infezione da HIV non in trattamento e una conta dei linfociti T CD4 <50 cellule/mm3

Pazienti con altra compromissione del sistema immunitario che ha determinato mancata sieroconversione

Time to First SARS-CoV-2 RT-PCR–Positive Symptomatic Illness

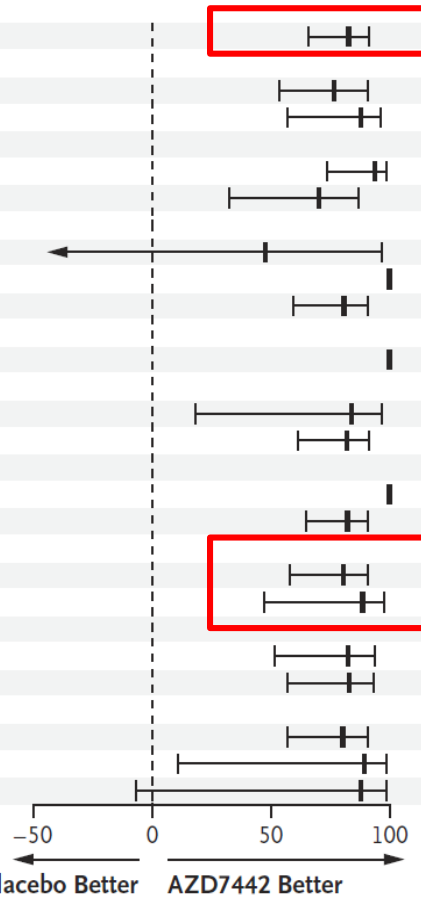


No. at Risk								
Placebo	1731	1680	1483	1177	991	856	774	472
AZD7442	3441	3323	2957	2393	2054	1815	1667	1044

Relative Risk Reduction in the Incidence of the First SARS-CoV-2 RT-PCR–Positive Symptomatic Illness with AZD7442 as Compared with Placebo, at a Median 6-Month Follow-up

A

Subgroup According to Baseline Characteristics	AZD7442	Placebo	Relative Risk Reduction (95% CI)
	no. of participants with event (%)		
Overall	11/3441 (0.3)	31/1731 (1.8)	82.8 (65.8 to 91.4)
Age			
<60 yr	8/1945 (0.4)	19/976 (1.9)	79.6 (53.5 to 91.1)
≥60 yr	3/1496 (0.2)	12/755 (1.6)	87.8 (56.9 to 96.6)
Sex			
Male	2/1856 (0.1)	16/934 (1.7)	93.9 (73.7 to 98.6)
Female	9/1585 (0.6)	15/797 (1.9)	70.3 (32.4 to 87.0)
Race or ethnic group			
Asian	1/109 (0.9)	1/60 (2)	48.0 (–743.4 to 96.8)
Black	0/593	4/302 (1.3)	100
White	10/2533 (0.4)	24/1243 (1.9)	80.8 (59.9 to 90.8)
American Indian or Alaska Native	0/18	0/10	
Native Hawaiian or other Pacific Islander	0/4	1/4 (25)	100
Hispanic or Latinx ethnic group			
Yes	2/531 (0.4)	5/215 (2.3)	84.1 (18.1 to 96.9)
No	9/2721 (0.3)	25/1406 (1.8)	82.1 (61.7 to 91.6)
Resident in long-term care facility			
Yes	0/13	1/12 (8)	100
No	11/3428 (0.3)	30/1719 (1.7)	82.3 (64.7 to 91.1)
Increased risk of inadequate response to Covid-19 vaccination			
Yes	9/2536 (0.4)	22/1260 (1.7)	80.7 (58.0 to 91.1)
No	2/905 (0.2)	9/471 (1.9)	88.6 (47.4 to 97.5)
Increased risk of exposure to SARS-CoV-2			
Yes	5/1806 (0.3)	14/905 (1.5)	82.6 (51.8 to 93.7)
No	6/1635 (0.4)	17/826 (2.1)	83.1 (57.2 to 93.3)
Geographic region			
North America	9/2470 (0.4)	22/1228 (1.8)	80.3 (57.2 to 90.9)
United Kingdom	1/611 (0.2)	5/311 (1.6)	89.6 (11.1 to 98.8)
European Union	1/360 (0.3)	4/192 (2.1)	88.1 (–6.3 to 98.7)



“Si devono temere soltanto quelle cose che hanno il potere di fare male agli altri; le altre no, poiché non sono paurose.”

Andrea del Castagno (1448)