The immunocompromised traveller

Dr Sarah McGuinness

Infectious Diseases Physician and Head of Travel Clinic, Alfred Hospital, Melbourne, Australia

Research Fellow, School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia

Email: sarah.mcguinness@monash.edu

@drsarahmac

@drsarahmcguinness

Immunocompromised Travellers…

- Often travel while immunosuppressed[1-4]
- Often travel to high-risk destinations[1]
- Are just as likely to engage in risky behaviours[1]
- May not seek health advice prior to travel[1-4]
- May run out of their usual medications[1]

1. Bialy et al. 2015 Intern Med J 45(6):618-23
2. Boggild et al. 2004 J Travel Med 11(1):37-43
3. Roukens et al. 2007 Clin Tranplant 21(4):567-70
4. Uslan et al. 2008 Transplantation 86(3):407-12

Risks in immunocompromised

Same risks as for any traveller

PLUS RISKS OF:

- Flare/complications of underlying disease
- Opportunistic infections
- More severe manifestations of some travel-related diseases

Pre-travel preparation of immunocompromised

Same considerations as for any traveller

PLUS:

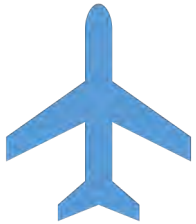
- Some vaccines may be contraindicated due to risk of adverse events or unchecked infection (e.g. live vaccines)
- Immune response to vaccines may be reduced (may need extra doses)
- Potential for medication interactions
- Availability, quality and access to medical facilities

Today's talk

Pre-travel considerations for the immunocompromised traveller

Associated risk of travel-related infection

Vaccine responses and effectiveness



Important side effects and interactions relevant to travellers

Recent cases from my clinic

Interactive: feel free to interrupt and ask questions

Case 1

Patient: 32M Australian-born software engineer with well-controlled Crohn's disease on infliximab (6-weekly infusions)

Travel plans: Travel to India for 4 weeks in Dec-Jan to visit friends and relatives in Udaipur, Rajasthan; also visiting Delhi, Agra and Jaipur

Vaccine history: up to date with routine childhood vaccines, including MMR, hepatitis B; history of childhood chickenpox. No previous travel vaccines.

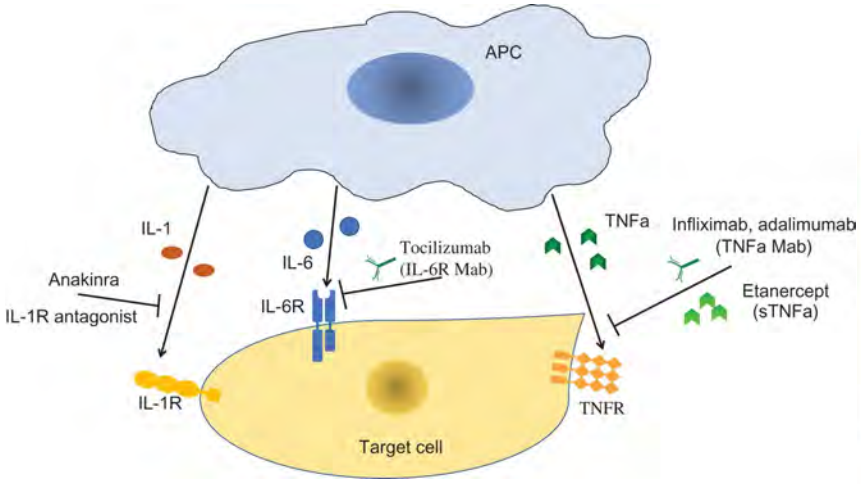
Photo credit: Unsplash

TNF-alpha inhibitors

Commonly prescribed class in autoimmune and immune mediated disorders (e.g. RA, AS, IBD, psoriasis)

Target pro-inflammatory cytokine tumour necrosis factor (TNF)

Adalimumab
Certolizumab
Golimumab
Infliximab
Etanercept



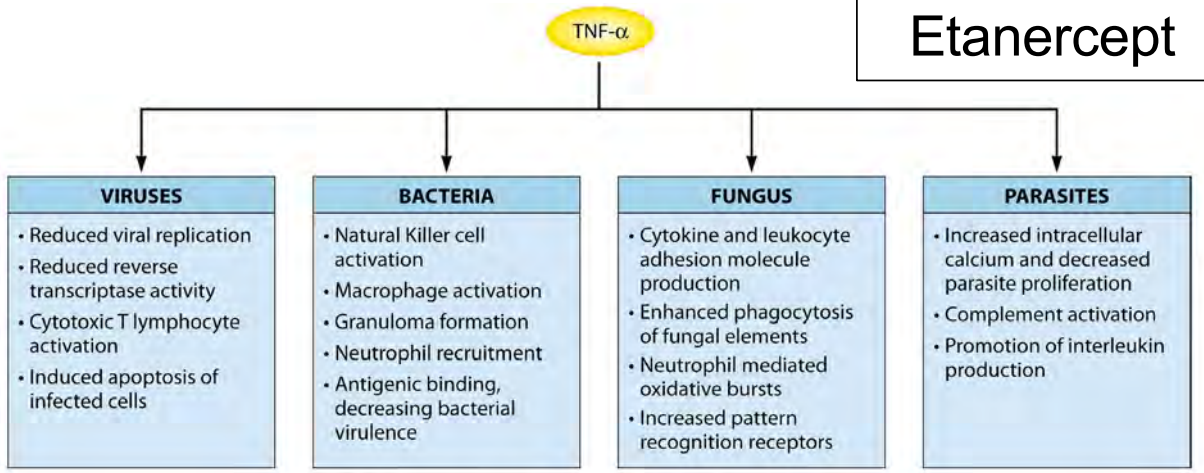


FIG 7 Tumor necrosis factor alpha action against pathogens.

Hall V et al. 2018 J Travel Med https://doi.org/10.1093/jtm/tay018;
Davis JS et al. Clin Microbiol Rev 2020; 33(3):e0035-19 https://doi.org/10.1128/cmr.00035-19

Infection risks – TNF-alpha inhibitors

Infliximab > adalimumab > etanercept

Risk of serious/disseminated bacterial infections, especially encapsulated and intracellular pathogens (e.g. *Streptococcus pneumoniae*, *Salmonella* spp., *Listeria monocytogenes*)

Risk of *M. tuberculosis* (TB) reactivation

Risk of herpes zoster & hepatitis B reactivation

Risk of invasive fungal infection (e.g. candidiasis, histoplasmosis)

Davis JS et al. Clin Microbiol Rev 2020; 33(3):e0035-19 https://doi.org/10.1128/cmr.00035-19

Case 1

32M VFR traveller with Crohn's on infliximab
Northern India for 4 weeks
Up-to-date with routine vaccines (e.g. MMR, hep B)

Risks we would consider in any traveller
Respiratory infections: **COVID-19**, **influenza**
Infections spread through food and water: **travellers' diarrhoea**, **hepatitis A**, **typhoid**
Vector-borne diseases: **dengue**, **chikungunya**, **malaria**, **Japanese encephalitis**
Environmental exposures: **rabies**, **tetanus**

Additional risks for this traveller
Respiratory: **Pneumococcal**, **tuberculosis** (TB)
Food and water: **cholera**, **listeria**
Viral reactivation: **herpes zoster** (shingles)

General advice to traveller

Food and water safety: drink bottled/treated water, eat only foods that are cooked and served hot

Hand hygiene: wash hands often with soap and water or use alcohol-based hand sanitiser

Respiratory hygiene: avoid crowded places, wear a mask

Mosquito bite prevention: insect repellent, long clothing, mosquito net

Avoid animal contact: don’t pat or feed animals

Avoid dust laden environments (e.g. construction sites), caves, areas with bats

Specific workup & interventions

Self-treatment for travellers' diarrhoea (azithromycin preferred)

Malaria chemoprophylaxis (probably not required in this case based on itinerary/season of travel despite VFR)

Baseline assessment of TB status: CXR and TST or IGRA; post-exposure follow-up with IGRA (2-3months post return) may be appropriate

Denholm JT et al. J Travel Med 2016, 23(3):taw008 https://doi.org/10.1093/jtm/taw008

Vaccine considerations: immunocompromised

Is the vaccine necessary?	Review itinerary & vaccine history
Can it be given safely?	Consider patient's medical history and medications
If given, is it likely to be immunogenic?	Consider patient's immune status

Case 1

32M with Crohn's on infliximab going to India
Up-to-date with routine vaccines

What vaccines should we consider?

Pneumococcal
COVID-19
Influenza
Zoster
Hepatitis A
Typhoid
Rabies
Japanese encephalitis
Cholera

Vaccine safety by category

Live attenuated vaccines	**Inactivated viral vaccines**	**Other non-live vaccines**
Chikungunya (Ixchiq®)* Cholera CVD 103HgR (Vaxchora®) Dengue (Dengvaxia®, Qdenga®)* Japanese encephalitis (Imojev®) MMR* Nasal influenza vaccine Oral typhoid (Ty21a) Oral poliomyelitis (OPV) Shingles (Zostavax®) Tuberculosis (BCG)* Varicella Yellow fever*	**Hepatitis A** Injectable poliomyelitis (IPV) **Injectable influenza** **Japanese encephalitis (JEspect®, Ixiaro®)** **Rabies** **Shingles (Shingrix®)**	Cholera whole-cell/recombinant (Dukoral®, Euvichol®, Shanchol™) **COVID-19 vaccines (mRNA)** DTPa (toxoid) Hepatitis B (recombinant) Meningococcal (conjugate) **Pneumococcal (conjugate)** **Pneumococcal (polysaccharide)** **Typhoid Vi (polysaccharide)**
Generally contraindicated in those on biologics	***Safe (efficacy may be reduced)***	

*Vaccines only available in live formulations

Vaccine safety by category

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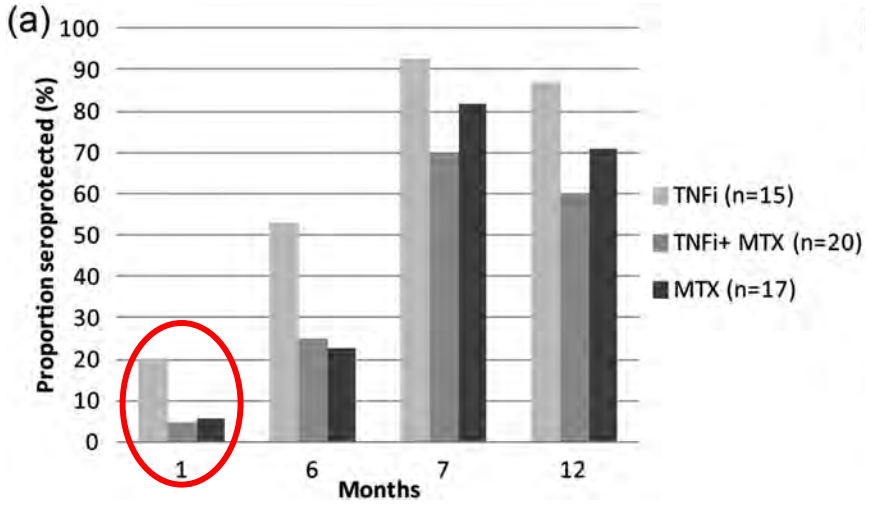
Vaccine immunogenicity

Seasonal influenza and pneumococcal vaccines most widely studied*:

- Responses adequate in patients taking anti-TNF-alpha and anti-IL-6 agents
- Responses reduced in patients taking anti-CD-20 (B-cell depletion) agents

Scarcity of evidence for most travel-related VPDs

Single dose of hepatitis A vaccine provides sub-optimal seroprotection rates in patients on anti-TNF therapy

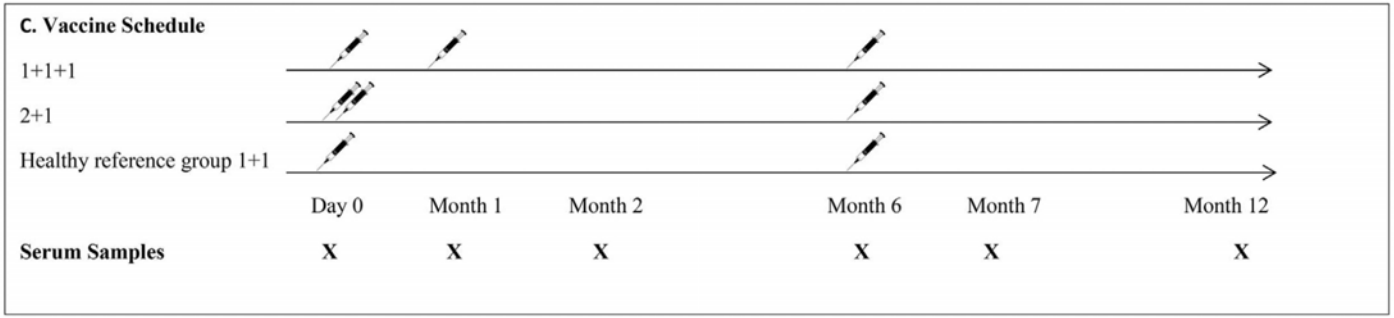


*Studies only examine immunogenicity; no data on efficacy available

Rondaan C et al. 2019 RMD Open 5:e001035; Askling HH et al. Travel Med Infect Dis. 2014 12(2); van den Bijillardt 2013 J Travel Med 20(5):278-282

Use of extra / priming doses

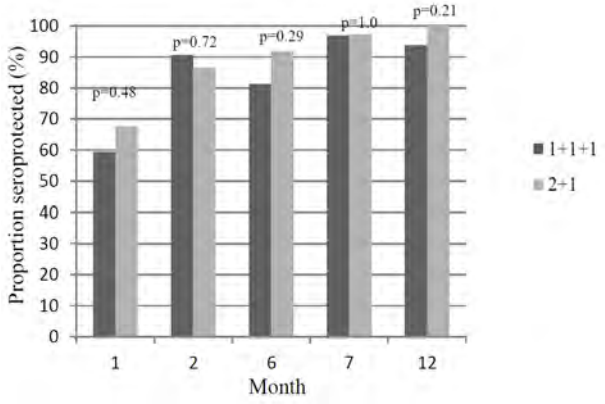
Case-control study: rheumatology patients on TNFα-inhibitors +/- methotrexate (cases) versus age-matched controls



Healthy controls: >90% seroconversion at 1 month

Cases: 60% vs 68% at 1 month; 90% vs 87% at 2m

Seroconversion rate in cases according to schedule



Rosdahl A et al. *Travel Med Infect Dis.* 2018 https://doi.org/10.1016/j.tmaid.2017.12.004

Case 2

Patient: 26F high school teacher with well-controlled rheumatoid arthritis on tocilizumab (weekly SC injection)

Travel plans: Annual trips to Uganda for a cross-cultural exchange program; Entebbe and rural village; leaving in 13 weeks

Vaccine history: up to date with routine vaccines, including MMR; history of childhood chickenpox

Concern: Aware of yellow fever (YF) risk and keen to have the yellow fever vaccine

What would you advise regarding YF?

Photo credit: Unsplash

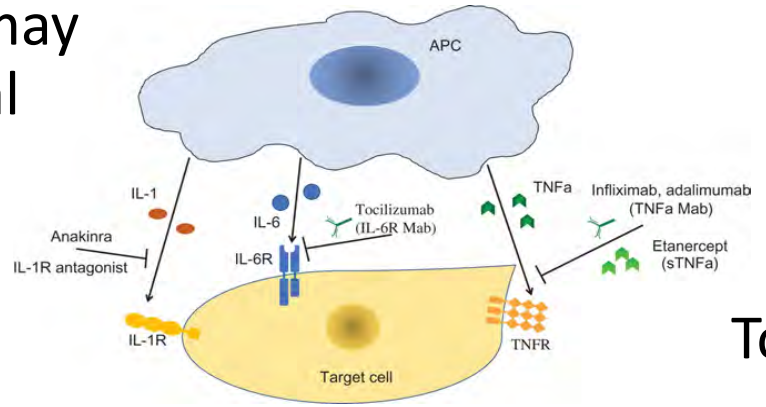
IL-6 inhibitors

Used mainly in rheumatoid arthritis (also juvenile idiopathic arthritis, giant cell arteritis and cytokine release syndrome)

Target pro-inflammatory cytokine interleukin-6 (IL-6) or its receptor

Blunts inflammatory response: fever may be low/absent and CRP may be normal

Preserved vaccine responses to pneumococcal, influenza and tetanus vaccines



Tocilizumab

Sarilumab

Siltuximab

Hall V et al. 2018 J Travel Med https://doi.org/10.1093/jtm/tay018;
Davis JS et al. Clin Microbiol Rev 2020; 33(3):e0035-19 https://doi.org/10.1128/cmr.00035-19

Infection risks – IL-6 inhibitors

Most evidence for tocilizumab (available the longest)

Increased risk of common viral infections (mainly URTIs)

Increased risk of common bacterial infections (esp. respiratory, skin)

No apparent increased risk of TB reactivation, reactivation of latent herpesvirus infections, flares of viral hepatitis, or opportunistic infections

Important to have high index of suspicion for infection given fever may be low/absent and CRP may be normal

Davis JS et al. Clin Microbiol Rev 2020; 33(3):e0035-19 https://doi.org/10.1128/cmr.00035-19

Let’s consider YF vaccine

Is the vaccine necessary?	Review itinerary & vaccine history
Can it be given safely?	Consider patient’s medical history and medications
If given, is it likely to be immunogenic?	Consider patient’s immune status

Is the vaccine necessary?

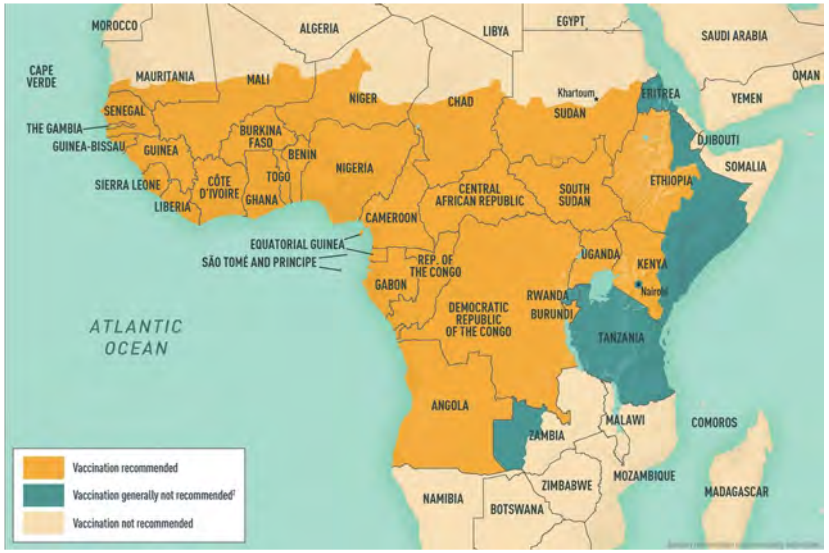
Uganda is a country with risk for YF transmission (vaccine recommended)

Estimated risk in unvaccinated traveller over a 2-week stay:

Illness: ~50 per 100,000

Death: ~10 per 100,000

This traveller is planning multiple trips



https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/yellow-fever

Is the vaccine safe?

Live attenuated vaccines	Inactivated viral vaccines	Other non-live vaccines
Chikungunya (Ixchiq®)* Cholera CVD 103HgR (Vaxchora®) Dengue (Dengvaxia®, Qdenga®)* Japanese encephalitis (Imojev®) MMR* Oral typhoid (Ty21a) Oral poliomyelitis (OPV) Shingles (Zostavax®) Tuberculosis (BCG)* Varicella **Yellow fever***	Hepatitis A Injectable poliomyelitis (IPV) Japanese encephalitis (JEspect®, Ixiaro®) Rabies Seasonal influenza (injectible) Shingles (Shingrix®)	Cholera whole-cell/recombinant (Dukoral®, Euvichol®, Shanchol™) COVID-19 vaccines (mRNA) DTPa (toxoid) Hepatitis B (recombinant) Meningococcal (conjugate) Pneumococcal (conjugate) Pneumococcal (polysaccharide) Typhoid Vi (polysaccharide)
Generally contraindicated in those on biologics	***Safe (efficacy may be reduced)***	

*Vaccines only available in live formulations

Live vaccines and alternatives

Disease	Live vaccines	Alternatives
Chikungunya	VLA1553 live attenuated (Ixchiq®)	–
Cholera	CVD 103HgR vaccine (Vaxchora®)	Whole-cell/recombinant-B-subunit vaccine (Dukoral®, Euvichol®, Shanchol™)
Dengue	CYD-TDV (DengvDengvaxia®), TAK-003 (Qdenga®)	–
Measles	Measles-mumps-rubella (MMR) vaccines	–
Poliovirus	Oral poliovirus (OPV) vaccines	Inactivated polio vaccine (IPV)
Shingles (herpes zoster)	Zoster vaccine live, ZVL (Zostavax®)	Adjuvanted recombinant (Shingrix®)
Tuberculosis	BCG vaccine	–
Typhoid	Oral Ty21a vaccine (Vivotif Oral®)	Vi polysaccharide vaccine (Typhim Vi®)
Varicella (chickenpox)	Varicella vaccines	–
Yellow fever	Yellow fever 17D-204 vaccine (Stamaril®)	–

Manual of Travel Medicine, Chapter 7 Travellers with Special Needs: https://link.springer.com/book/10.1007/978-981-13-7252-0
CDC Yellow book, Section 3: https://wwwnc.cdc.gov/travel/yellowbook/2024/additional-considerations/immunocompromised-travelers

Safety of live vaccines

Derived from “wild” viruses or bacteria attenuated (weakened) in a lab

Strike a balance between enough replication to induce strong immune response and enough attenuation to avoid symptomatic disease

Example: measles vaccine ~5% develop rash, up to 15% fever

Produce strong and durable immune response

Risk of uncontrolled replication in immunocompromised

Pollard AJ, Bijker EM *Nat Rev Immunol* 2021; 21:83–100 https://doi.org/10.1038/s41577-020-00479-7

Live vaccines & biologics

Lack of evidence of safety rather than evidence of harm (theoretical risk)

Case series / reports of inadvertent or deliberate vaccination indicate:

- **YF re-vaccination** safe & immunogenic in patients receiving TNFi (trend to lower antibody responses)
- **MMR re-vaccination** safe & immunogenic in patients receiving TNFi, IL-1 and IL-6 inhibitors

RCT of live attenuated zoster (shingles) vaccine in patients on TNF inhibitor therapy (n=617 patients, ZVL vs. placebo) – safe & well tolerated

Buhler S et al. Swiss Med Wkly. 2015;145:w14159; Curtis JR et al. 2021 Ann Intern Med 174(11); Ramirez OR 2024 Vaccine 42(26):126319; Jeyaratnam J et al. Pediatr Rheumatol 2018; 16(19)

Not all live vaccines are created equal

Table 4: Replication capacity and complication risk of live vaccines.		
	Systemic replication capacity*	**Theoretical risk of complication†**
Yellow fever	++++	++
Mumps, measles, rubella	++	+
Varicella and herpes zoster	+	(+)
Oral typhoid vaccine	(+)	–
The replication capacity, relative risks of different live vaccines as well as the availability of an antiviral agent, immunoglobulin or antibiotic treatment must be considered when deciding on whether a person under immunosuppressive treatment can be vaccinated. * ++++ very strong systemic replication capacity, +++ strong systemic replication capacity, ++ moderate systemic replication capacity, + weak systemic replication capacity, (+) very weak systemic replication capacity † ++++ very strong risk of complication, +++ strong risk of complication, ++ moderate risk of complication, + weak risk of complication, (+) very weak risk of complication		

Consider:

Replication capacity of vaccine

Potential severity of complications

Primary vs. re-vaccination

YF vaccine:

Very high systemic replication capacity & potentially fatal adverse events

Buhler S et al Swiss Med Wkly. 2015;145:w14159 https://doi.org/10.4414/smw.2015.14159

YF vaccine side effects

Common: tiredness, low-grade fever, headache, myalgias (10-30%)

Immediate hypersensitivity reactions, including anaphylaxis: ~1.8 per 100,000 doses

Vaccine-associated viscerotropic adverse events (YEL-AVD)

Vaccine-associated neurotropic adverse events (YEL-AND)

	<60 years	≥60 years
Overall serious events	3·0/100 000	8·0/100 000
Neurotropic disease	0·8/100 000	2·2/100 000
Viscerotropic disease	0·3/100 000	1·2/100 000

Number of adverse events recorded per 100 000 vaccine administrations by disease process and age at the time of vaccination.

Table: **Adverse events associated with yellow fever vaccination**

Among all age groups in France, 2012-2022:

- YEL-AND: 0.5 per 100,000 doses
- YEL-AVD: 0.1 per 100,000 doses

Reno E et al. 2020 Lancet Infect Dis 20(6): E129-E137 https://doi.org/10.1016/S1473-3099(20)30170-5
Le Hir A et al. J Travel Med 2023, 31(2) https://doi.org/10.1093/jtm/taad160

YFV contraindications and precautions

CONTRAINDICATIONS

- Anaphylaxis to vaccine component/previous dose
- Age <6 months
- Symptomatic HIV infection or CD4 T-lymphocytes <200/mm^3 (<15% of total in children <6 years)[1]
- History of thymus disorder OR thymectomy
- Primary immunodeficiencies
- Malignant neoplasms
- Transplantation
- Immunosuppressive and immunomodulatory therapies
- Severe egg allergy*
- First degree family history of YEL-AVD or YEL-AND

PRECAUTIONS

- Age 6–8 months
- Age ≥60 years
- Low-dose steroids or non-biological oral immune modulating drugs
- Individuals living with HIV with CD-4 200–499/mm^3 (or 15%–24% in children aged <6 years)
- Pregnancy
- Breastfeeding

https://travelhealthpro.org.uk/factsheet/87/yellow-fever-pre-vaccination-checklist

Specialist vaccination/immunology clinics are potentially able to offer a graded challenge under medical supervision to egg-allergic individuals. See Sharma et al 2020 Pediatric Infectious Disease Journal 39(6):p e76-e78, https://doi.org/10.1097/INF.0000000000002625

YF vaccine & biologics

Data on primary yellow fever vaccination limited to case reports / series

Patients either vaccinated inadvertently or after carefully weighing risks of vaccine vs. risks of disease

Single case report of YEL-AND in 67M patient on TNFi therapy – survived

No other serious adverse events (YEL-AVD) or deaths that I'm aware of

Long-term immune responses to vaccine similar to healthy individuals

Nash ER et al *J Travel Med* 2015;22(4):279-81; Wieten RW et al. J Infect 2016;72(6):713-22; Huber F et al. *J Travel Med* 2018;25(1); Le Hir A et al. J Travel Med 2023, 31(2); Lagos L et al J Travel Med 2023 30(2):taac095

Case 2

26F teacher with RA on tocilizumab (IL-6i)
Annual trips to Uganda with school group
Up-to-date with routine vaccines (e.g. MMR, hep B)

What are our options regarding Yellow fever?

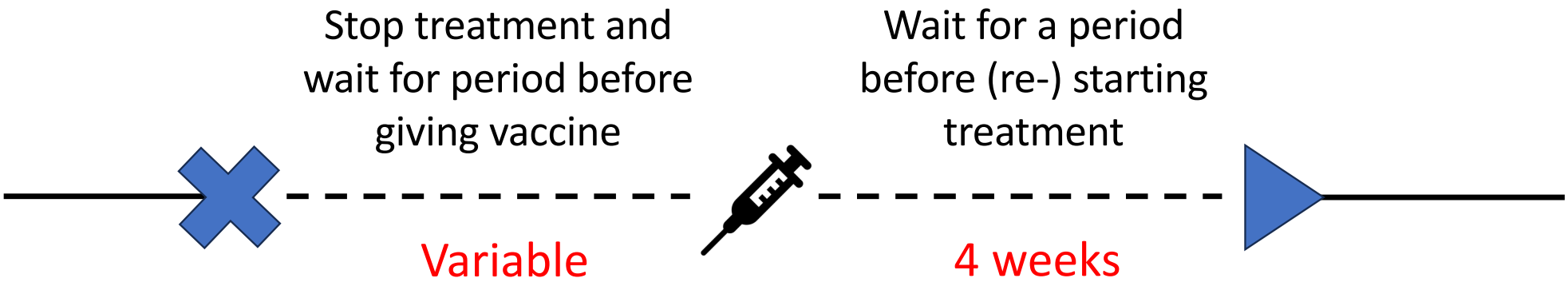
Alternatives: South Africa, Botswana, Namibia, Zimbabwe

Option 1: **Don't travel** or **modify travel itinerary**

Option 2: **Disease avoidance measures & exemption letter** – only advised if risks of vaccination outweigh benefits

Option 3: **Treatment interruption to facilitate vaccination** – decision to be made in consultation with treating specialist

Treatment interruption



Recommendations vary by agent and advisory group (based on expert opinion)

Longer periods (6-12 months) advised for B-cell depleting agents, abatacept

Bass AR et al Arthritis Care & Research 2023; https://doi.org/10.1002/acr.25045
Buhler S et al Swiss Med Wkly. 2015;145:w14159 https://doi.org/10.4414/smw.2015.14159

Variability in recommendations

Time between stopping treatment and administering live vaccine (wait at least)

Agent	**American College of Rheumatology Guideline**	**Swiss Vaccine Recommendations**
IL-6 pathway inhibitors	1 dosing interval*	3 months
IL-1 inhibitors	1 dosing interval*	3 months
TNF-alpha inhibitors	1 dosing interval*	Etanercept: 1 month Others: 3 months
Rituximab (CD-20)	6 months	12 months

*Use longest recommended dosing interval

Bass AR et al Arthritis Care & Research 2023; https://doi.org/10.1002/acr.25045
Buhler S et al Swiss Med Wkly. 2015;145:w14159 https://doi.org/10.4414/smw.2015.14159

Case 2

26F teacher with RA on weekly S/C tocilizumab
Leaving in 13 weeks
Up to date with routine vaccinations

Consulted with rheumatologist, stopped tocilizumab & requested serology for measles, mumps, rubella, VZV and hepatitis B

Pragmatic decision to vaccinate after 10 weeks (5 half lives)

Serology results: measles & mumps IgG negative; rubella & VZV IgG positive

Co-administered MMR, YF, dTpa-IPV and Meningococcal ACWY vaccines; given atovaquone/proguanil for malaria chemoprophylaxis

Co-administration of live vaccines

Yellow fever and other live vaccines can be given either on **same day** OR **at least four weeks apart**

Limited evidence suggests lower seroconversion rates when YF and MMR vaccines are co-administered (studies in children/primary dose)

Preferred timing: space out by at least 4 weeks apart if possible

If rapid protection is required or window of opportunity for vaccination is limited, the two vaccines can be given at the same visit

Nascimento Silva JR et al. Vaccine 2011;29:6237-34;
Vizzoti C et al. BMC Infect Dis 2023; 23:165

Stefano I et al Vaccine 1999; 17(9):1042-1046;

Travelling with biologics

Sensitive to heat: keep at recommended temp range

Patients may discontinue treatment during travel due to concerns about storing or transporting meds

Cooler or insulated med bag for portable refrigeration

Original packaging + script or letter from treating clinician

May be option to time trips between doses / have IV infusion

Szabados F et al 2020 Eur J Rheumatol: 7(4):158-163 https://doi.org/10.5152/eurjrheum.2020.19190

Case 3

Patient: 40M Australian-born lawyer with HIV well controlled on daily bictegravir/tenofovir/emtricitabine (Biktarvy): VL undetectable, CD4+ 450

Travel plans: Honeymoon with 38M HIV- husband to East Africa (Kenya, Uganda): Nairobi (2N), Masai Mara (3N), Lake Naivasha (2N), Amboseli (1N), Entebbe (1N), Lake Mutanda / Bwindi (3N), Nairobi (1N)

Vaccine history: up to date with routine childhood vaccines; COVID-19 and flu boosters (May 2024); Mpox (2 doses Oct-Nov 2023), hepatitis A (2 doses) and meningococcal ACWY (2022), history of childhood chickenpox. No past YF or typhoid vaccines

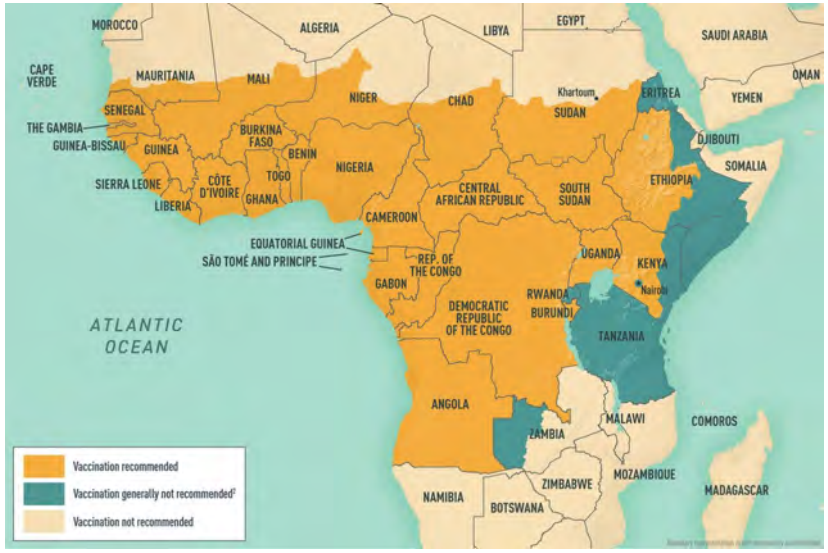
Case 3

What would be your advice re: yellow fever?

A. Provide the yellow fever vaccine

B. Provide a yellow fever waiver

C. Advise against travel



https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/yellow-fever

Can it be given safely?

Live attenuated vaccines	**Inactivated viral vaccines**	**Other vaccines**
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Generally contraindicated in immunocompromised	***Safe (efficacy may be reduced in immunocompromised)***	

*Vaccines only available in live formulations

Live vaccine recommendations

Contraindicated	Case by case	Safe
▪ Acute leukaemia / lymphoma ▪ Severe immunodeficiencies (e.g. primary T/B-cell) ▪ Solid organ transplant (SOT) on immunosuppression ▪ High-dose chemotherapy ▪ HSCT <2 years post-transplant or with GVHD ▪ HIV with CD4 <200 or <15% or symptomatic HIV/AIDS ▪ Most biologic therapies (e.g. TNF-alpha, CD-20 inhibitors)	▪ HIV with CD4 >200 or >15% ▪ >2 years post HSCT + no GVHD + off immunosuppression ▪ Post-chemo cancer patients in remission (3+ months) ▪ Post-immunosuppressive therapy (3-12 months, depending on agent) ▪ Chronic granulomatous disease	▪ Isolated complement deficiencies ▪ Asplenia ▪ Chronic kidney disease/ dialysis ▪ Chronic liver disease/cirrhosis ▪ Diabetes mellitus

*Based on Australian Immunisation Handbook, CDC Pink Book, Rubin et al 2013

**BCG and Ty21a *Salmonella typhi* vaccines contraindicated in these patients; live viral vaccines only

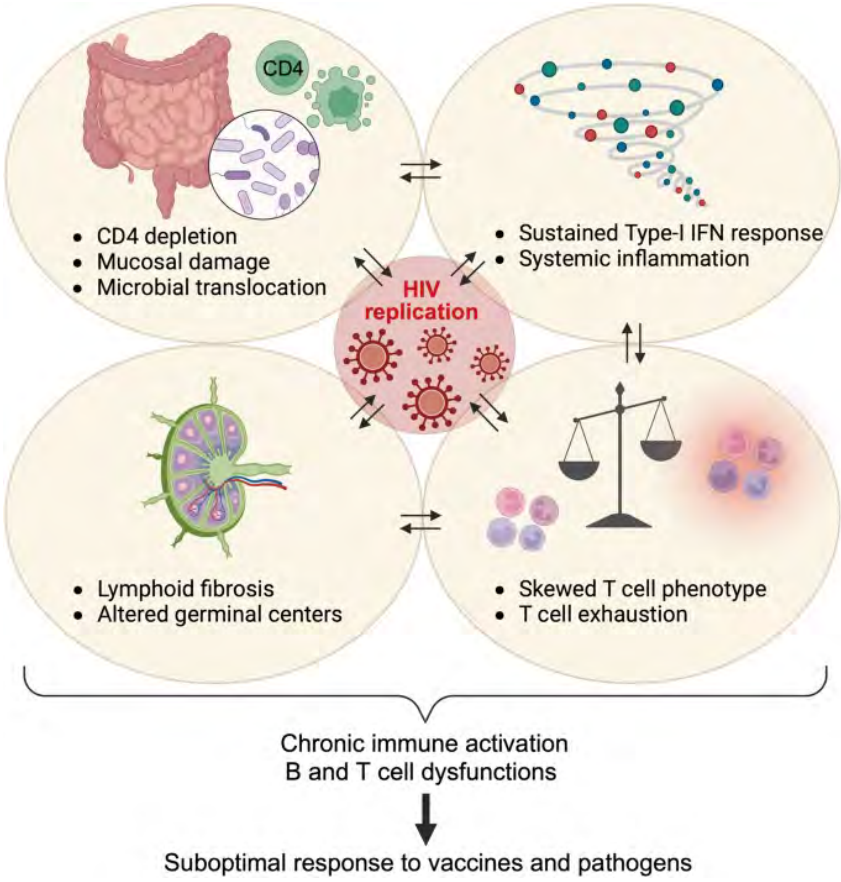
HIV and immune responses

HIV impairs immune system's ability to respond effectively to pathogens and vaccines

Affects formation of long-lived plasma cells and memory B cell proliferation

Results in suboptimal vaccine responses

Vaccine-induced antibodies may wane faster



Hoft MA et al. 2024 Cellular Mol Immunol; 21(2):184-196 https://doi.org/10.1038%2Fs41423-023-01087-w

Yellow fever vaccine in PLHIV

Considered safe if CD4 >200 cells/mm & viral load controlled

Risk: One case of fatal YEL-AVD in 53yo patient with unrecognised HIV (CD4 108)[1]

Immunogenicity and duration of protection:[2]

- **Seroconversion:** ~98% if HIV RNA controlled (n=561, 10 studies)
- **Seropersistence:** ~72% had neutralising antibodies 1-10y after YFV (n=315, 6 studies); titres declined rapidly

Booster doses recommended (every 10y)

Small number of studies and patients

Almost all in non-endemic areas

Heterogeneity in lab techniques and antibody cut-offs

[1]Kengsakul K et al J Med Assoc Thai 2002;85(1):131-4
[2]Martin C et al. Clin Microbiol Infect. 2021; 27(7):958-967 https://doi.org/10.1016/j.cmi.2021.03.004

Back to the question

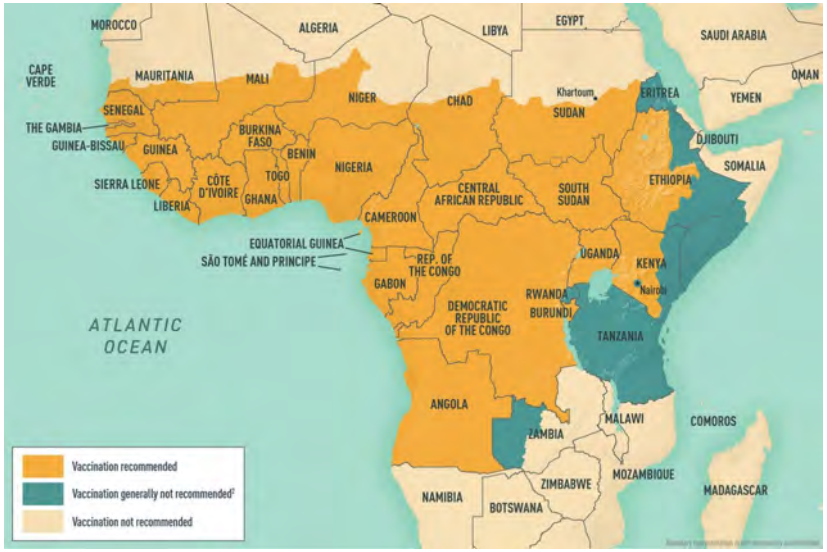
35yo male living with HIV

What would be your advice re: yellow fever?

A. Provide the yellow fever vaccine

B. Provide a yellow fever waiver

C. Advise against travel



Advise that booster doses may be required if travelling to risk areas in future

https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/yellow-fever

Case 3

What about malaria chemoprophylaxis?

UGANDA

Malaria Recommendations

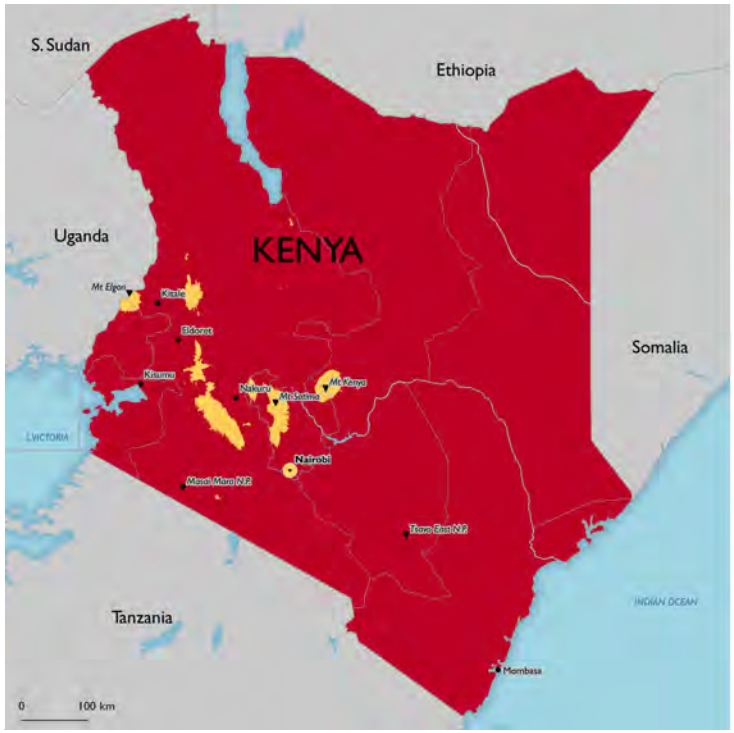
There is a high risk of malaria in Uganda

Antimalarials recommended: atovaquone-proguanil or doxycycline or mefloquine

Other countries

This map is intended as a guide. It should be used with the recommendations in the risk section

Capital
City
Point of interest



KENYA

Malaria Recommendations

There is a high risk of malaria in Kenya
Antimalarials recommended: atovaquone-proguanil or doxycycline or mefloquine

There is very low risk in the city of Nairobi and above 2,500m
Awareness and bite avoidance recommended

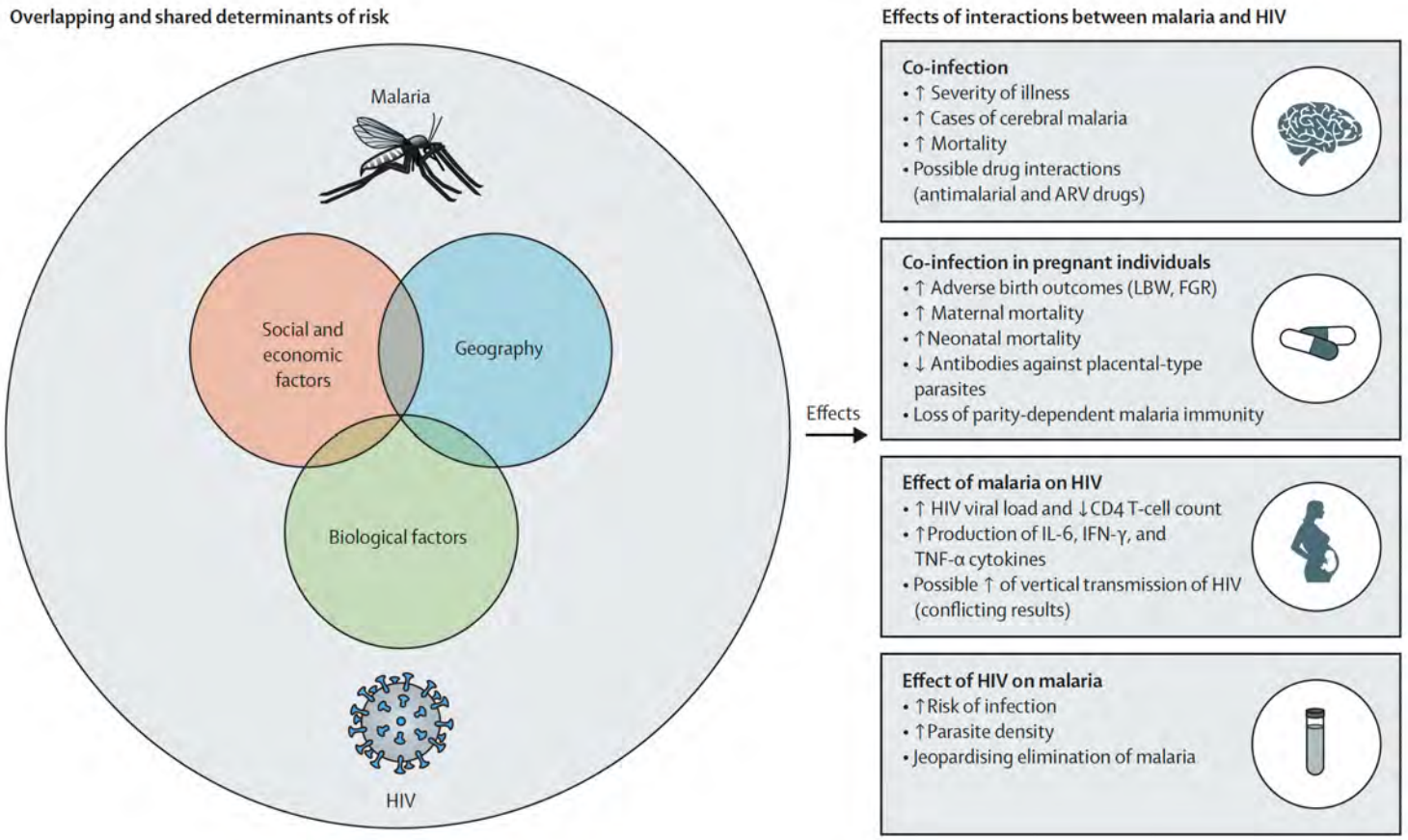
Other countries

This map is intended as a guide. It should be used with the recommendations in the risk section

Capital
City
Point of interest

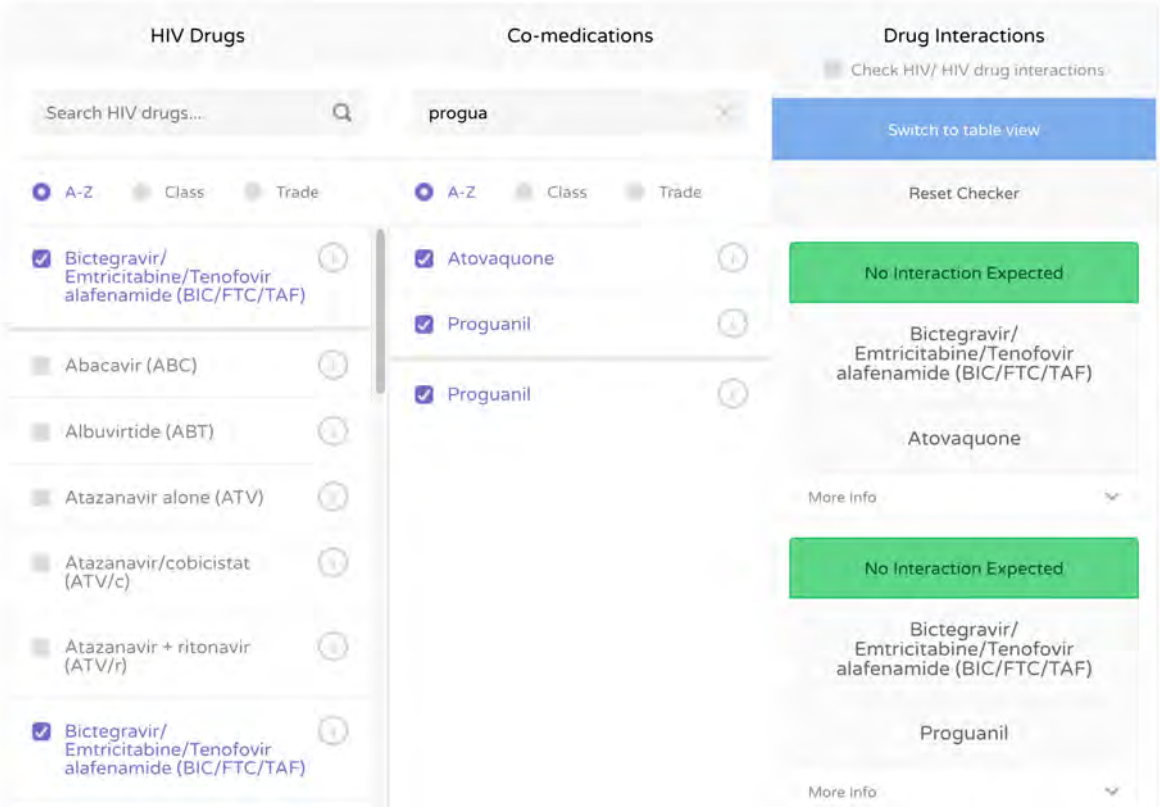
Maps from Travel Health Pro: https://travelhealthpro.org.uk/country/117/kenya#Malaria

Interactions between malaria and HIV



Figueroa-Romero et al. 2024 Lancet HIV. 11(4):E255-267 https://doi.org/10.1016/S2352-3018(24)00035-3

PLHIV: medication interactions



Liverpool HIV Drug Interactions checker: https://www.hiv-druginteractions.org/checker

Case 4

Patient: 28F newly diagnosed multiple sclerosis being worked up for immunosuppression (likely with ocrelizumab – anti-CD20 agent)

Travel plans: Travel to Bali, Indonesia in January for a friend's wedding (2 weeks)

Vaccine history: up to date with routine vaccines

Concern: Wants to optimise vaccine coverage prior to starting immunosuppression

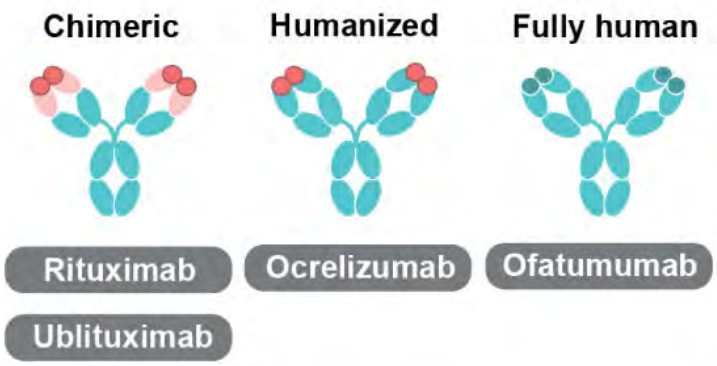
What would you advise?

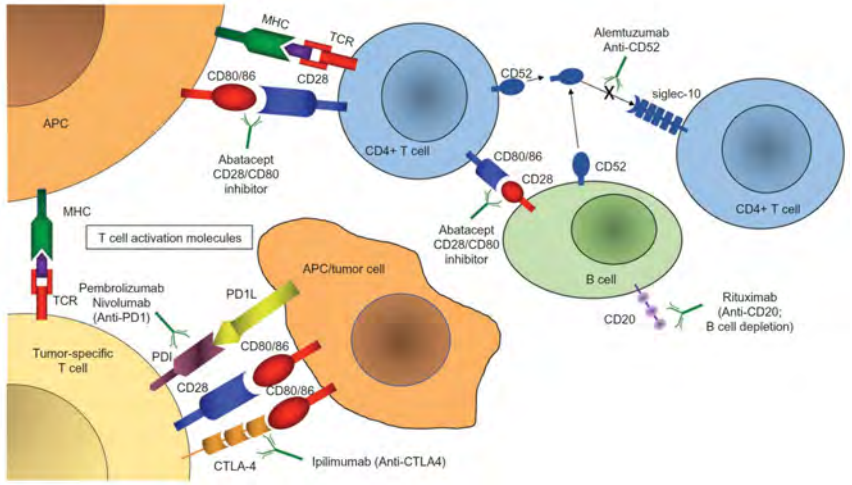
Photo credit: Unsplash

Anti-CD-20 therapies

Used in patients with autoimmune disease (RA, MS, ITP, granulomatosis with polyangiitis) and haematological malignancies (e.g. lymphoma, CLL)

Monoclonal antibodies that deplete CD20+ B cells (decreased B-cell numbers for at least 6-9 months with reduced/absent Ab production)





Hall V et al. 2018 J Travel Med https://doi.org/10.1093/jtm/tay018;
De Seze J et al. 2023 Front Immunol https://doi.org/10.3389/fimmu.2023.1004795

Infection risks – Anti-CD-20

Most data available for rituximab (available the longest)

Serious infections (bacterial & viral) more common in patients with haematological malignancies cf. autoimmune dx

Risk of hepatitis B reactivation (black box warning)

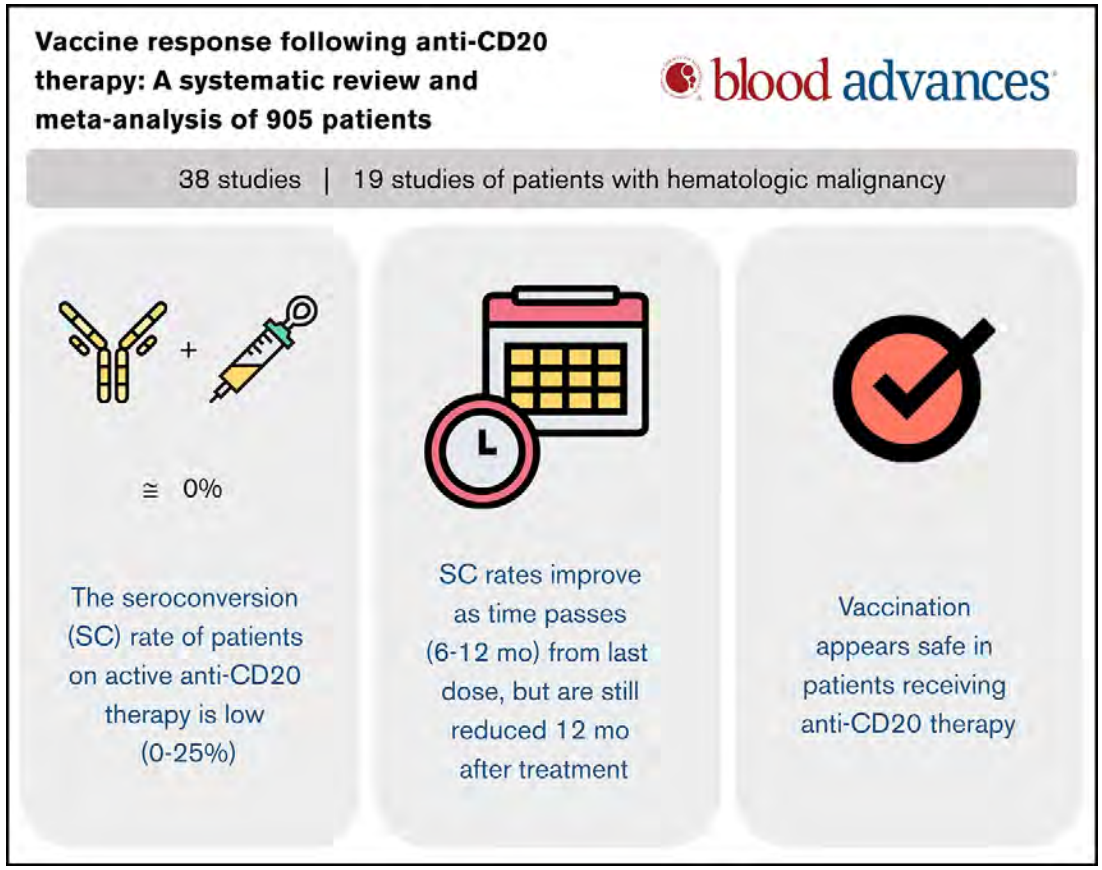
Risk of herpes zoster reactivation (lymphoma > autoimmune dx)

Cases of progressive multifocal leukoencephalopathy (PML) 1 in 25,000

TB reactivation appears to be rare

Davis JS et al. Clin Microbiol Rev 2020; 33(3):e0035-19 https://doi.org/10.1128/cmr.00035-19

Vaccine responses – Anti-CD-20



Impaired vaccine responses to influenza and pneumococcal vaccines

Partly restored immunogenicity 6-8 months post-therapy

Vijenthira A et al. 2021 *Blood Advances* https://doi.org/10.1182/bloodadvances.2021004629

Case 4

28F newly diagnosed multiple sclerosis being worked up for immunosuppression

Pre-immunosuppression work-up

- Review vaccination and infection history

Evaluate future travel plans

Consider relevant occupational and lifestyle factors

Optimise vaccine coverage

Pre-immunosuppression workup

- Varicella zoster serology (IgG)
- Measles serology (IgG)
- Mumps serology (IgG)
- Rubella serology (IgG)
- Hepatitis A (IgG), B (sAb, sAg, cAb) and C serology
- Human immunodeficiency virus (HIV) serology
- Syphilis serology
- JC virus serology
- *Mycobacterium tuberculosis* interferon-gamma release assay (IGRA)
- Travel vaccine workup if clinically appropriate
- Vaccination and infection history

Nesbitt C et al. Med J Aust 2021; 214(8):350-354; Davis JS et al. Clin Microbiol Rev 2020; 33(3):e0035-19

Key considerations for all patient groups

1. Risk assessment
2. Risk communication
3. General preparation
4. Vaccinations (+/- serological testing)
5. Drugs (e.g. chemoprophylaxis / drug-drug-interactions)

1. Risk Assessment

Stage and stability of underlying condition

Degree of immunocompromise

Availability of medical services along the planned trip

Traveler-specific and destination-specific health risks

“Worst case” scenario

2. Risk communication

Issues around vaccine safety & immunogenicity

Challenging to get insurance covering pre-existing conditions

Travel is "safer" if:

- Period of stable disease +/- relatively immunocompetent
- Access to high quality medical facilities at destination
- Trip is shorter duration
- Insurance cover available / destination with reciprocal health agreement

Travel should be avoided during

- Periods of heavy immunosuppression (e.g. first 12 months after SOT / HSCT)
- Periods where disease is unstable

3. General preparations

Providing medical documentation (e.g. doctor’s letter)

Advice re: medications & devices

Management plan for illness

Finding trustworthy healthcare centres

4. Vaccinations and serology

Consider for each vaccine:

- Is the vaccine necessary?
- Can the vaccine be given safely?
- If given, is the vaccine likely to be immunogenic?

Additional considerations:

- Immune protection from previous vaccinations may be diminished: consider serological testing
- Additional booster doses may be required

5. Drugs

Special considerations for chemoprophylaxis (e.g. malaria) or self-treatment (e.g. travellers' diarrhoea)

Always evaluate for drug-drug interactions

Various tools available, such as:

- Drugs.com: https://www.drugs.com/drug_interactions.html - FREE
- Liverpool COVID-19 interaction checker: https://covid19-druginteractions.org/checker (also HIV, hepatitis drugs) - FREE
- UpToDate Lexidrug: https://online.lexi.com/lco/action/login - SUBSCRIPTION

Take home messages

Immunocompromised travellers are an increasingly important group who face a range of potential infection risks

Practical considerations regarding transport and storage of meds

Inactivated vaccines are safe, but immunogenicity may be reduced

Live vaccines generally contraindicated:

- Vaccinate pre-immunosuppression where possible
- Consider treatment interruption to allow vaccination in select cases

Pre-immunosuppression planning should include vaccine optimisation

Further reading

- Aung AK et al. Travel risk assessment, advice and vaccinations in immunocompromised travellers (HIV, solid organ transplant and haematopoeitic stem cell transplant recipients): A review. Travel Med Infect Dis 2015, 13(1):31-47 https://doi.org/10.1016/j.tmaid.2014.12.007
- Chang L et al. Travel vaccination recommendations and infection risk in HIV-positive travellers J Travel Med 2019 26(6):taz034, https://doi.org/10.1093/jtm/taz034
- Hall V, Johnson D, Torresi J. Travel and biologic therapy: travel-related infection risk, vaccine response and recommendations. *J Travel Med* 2018;25(1) doi: 10.1093/jtm/tay018 [published Online First: 2018/04/11]
- Kotton CN, Mileno MD. The Immunocompromised traveller. In: Travel Medicine (fourth edition) https://doi.org/10.1016/B978-0-323-54696-6.00027-6
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- Rubin LG, Levin MJ, Ljungman P et al. 2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host. Clin Infect Dis 2014; 58(3):e44–e100. https://doi.org/10.1093/cid/cit684
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- Trubiano JA et al. Travel vaccination recommendations and endemic infection risks in solid organ transplantation recipients. J Travel Med 2016; 23(6): taw058, https://doi.org/10.1093/jtm/taw058
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