Royal Brisbane and Women's Hospital

2023

6th Annual

CANCER PRECEPTORSHIP

FOR GENERAL PRACTITIONERS

Metro North Health

Queensland Government

Vaccinations – who and when?

Dr Cameron Curley

A/Director Department of Haematology and BMT

Royal Brisbane and Women's Hospital

Case 1

- Mrs KQ is a 66yr old patient with DLBCL who recently completed R-CHOP chemotherapy 6 months ago and remains in a complete remission. During a consultation she expresses concern regarding her weakened immune system and she wants to know what she can do to help “boost her immune system”. What would you advise?

Case 2

- Mr AB is 48yr man with metastatic melanoma currently receiving treatment with Pembrolizumab every 2 weeks. He is booked for treatment tomorrow. He requests flu vaccination today. He is planning to receive his Pfizer covid vaccine tomorrow at the hospital shortly after his immunotherapy. What would you advise?

Case 3

- Ms CV is a 70 yr old woman who is 4 and half years post allogeneic SCT for MDS. She remains well in remission with normal blood counts. She continues on tacrolimus for chronic graft versus host disease that is currently as reported by her specialist quiescent. Her sister recently had an episode of shingles and she wants to talk about the vaccine that her husband had received to help prevent this last year. What would you advise?

Why is vaccination important?

Question 1.

With regards to vaccination cancer patients may have:

a. Reduced protection from previous vaccination
b. Reduced responses to vaccines (may need extra doses)
c. An increased risk of vaccine-preventable diseases or complications
d. An increased risk of adverse events, particularly from live vaccines
e. All of the above

Know you vaccines

Vaccine	Inactivated	Live attenuated
Hep B (ENERGIX B)	+	
Diptheria, Tetanus, pertussis (DTpa - Boostrix)	+	
POLIO (IPV)	+	
Prevenar 13	+	
Pneumovax 23	+	
Fluvax	+	
Meningococcal ACWY (Menveo, Nimenrix)	+	
Meningococcal B (Bexsero)	+	
Haemophilus Influenaze (ActHiB)	+	
MMR		+
Varicella (Varilirix)		+
Zoster (Zostavax)		+
Zoster (Shingrix)	+*	
Rota (Rotarix)		+
Japanese Encephilitis B (Imojev)		+
BCG		+
Yellow Fever (Stamaril)		+
Q Fever (Q-Vax)	+*	
Rabies & Lyssa (Rapipur)	+	
HPV (Gardasil 9)	+	
Hep A	+	
Typhoid (Typhim Vi)	+	
Typhoid (Vivotif oral)		+

Know your Cancer therapies

Cancer Therapy	Degree of immunosuppression
Allogeneic SCT CAR T cell therapy Autologous SCT Fludarabine/ Bendamustine	Profound T and B cell immunodeficiency
B cell depleting or targeting (Rituximab, Obinutuzumab, Ibrutinib, Idelalisib, Venetoclax)	Marked B cell immunodeficiency (6-12mths)
Other conventional chemotherapies	Brief impaired B cell Fn (<3mth)
Immunotherapies (check-point inh, non-B cell depleting monoclonal abs)	Normal or Increased T cell responses

Post chemotherapy boosters: non SCT patients

VACCINE	6MTHS (POST THERAPY)	7MTHS
dTpa	yes	-
MMR (live)	Yes**	-
IPV	Yes	-
HepB	Yes	-
Prevenar 13	Yes	-
Pneumovax 23	-	Yes
Zostavax (live)	Yes**	-
Fluvax	Yes (annually)	

BMT vaccinations

The key differences are:

1. Need to repeat total schedule
2. Need to cover meningococcus, HiB
3. Need 3 doses Prevenar13 pre Pneumovax23
4. Leaving live vaccines till at least 2 years (must be off all immunosupression with no GVHD) – “2,1,8”

Australian Immunisation handbook 10th edition

Table 11.3 Re-vaccination schedule post Haematopoietic stem cell transplant (HSCT) in adults (irrespective of prior vaccination history) [76]

VACCINE	Months after HSCT				
	6	8	12	24	Comments
Streptococcus pneumoniae					
13-valent pneumococcal Conjugate vaccine (13vPCV)[Prevenar13]	yes	yes	yes	not needed	
23-valent pneumococcal polysaccharide vaccine (23vPPV)[Pneumovax23]	no	no	no	yes (after 13vPCV)	
Haemophilus influenza type b					
Hib [Hiberix]	yes	yes	yes	not needed	
Diphtheria, tetanus, pertussis					
dTpa containing vaccine [Boostrix]	yes*	no	no	not needed	#1st dose dTpa followed by 2 doses of dT [ADT booster]
dT vaccine	no	yes#	yes#	not needed	
Poliomyelitis					
IPV	yes*	yes	yes	not needed	**1st dose can be given as dTpa-IPV [Boostrix-IPV]
Hepatitis B^					
Hep B vaccine	yes*	yes*	yes*	not needed	^Given by GP
Influenza^					
Two doses of inactivated influenza vaccine^ at least 4 weeks apart are recommended for all HSCT recipients with first dose at 6 months after HSCT, then single dose annually thereafter					
Neisseria meningitides					
Quadrivalent meningococcal conjugate vaccine (4vMenCV) [Menveo]	yes	yes	not needed		Consider 4CMenB [Bexsero], 2 doses 1-2 months apart avoiding co-administration with other vaccinations
Human papillomavirus					
HPV vaccine [Gardasil]	no	no	consider a 3 dose course of 4vHPV in appropriate clinical circumstances (see comment)		ie, limited sexual exposure
Measles, mumps and rubella					
MMR vaccine (live attenuated)	no	no	no	consider in non-immunosuppressed patients	ie, no active GVHD or immunosuppression with normal cell mediated immunity
Varicella					
Varicella vaccine (live attenuated VV) [Varilrix or Varivax Refrigerated]	no	no	no	Consider only in non-immunosuppressed patients whom are seronegative	ie, no active GVHD or immunosuppression with normal cell mediated immunity NB. Zoster vaccines [Zostavax] are not recommended.

COVID 19 Vaccination for cancer patients

- Established RF for death due to COVID:

1. Age (>65yrs) – 4.59 (HR)
2. Male - 1.50
3. Diabetes - 2.41
4. HTN - 2.70
5. CAD - 3.72
6. COPD - 3.53
7. Cancer - 3.04

- Case fatality rates of 21-24% in cancer patients from US and UK data (c/w 1-4% global average).
- Variable findings regarding the significance of recent vs distant therapy.
- SCT and recent therapy for Haem malignancy mortality 15-36%

Mehta V et al 2020 and Russel B et al 2020
Parohan M et al 2020

COVID vaccines

• Vaccine	• Type
BNT162b2 (Pfizer)	mRNA
ChAdOx1 nCoV-19 (Astrazeneca)	Adenoviral vectored (non-replicating)
mRNA -1237 (Moderna)	mRNA
NVX-CoV2373 (Novavax)	Protein subunit

None- “live”

Question 2

- Which cancer patients are anticipated to have impaired vaccine responses post COVID vaccination?

a. Hodgkin Lymphoma on Pembrolizumab
b. Longstanding distantly treated CLL
c. Myeloma in remission 3 years post stem cell transplantation
d. Previous CD19 CAR T cell therapy
e. All of the above
f. B and D

COVID vaccine considerations for Cancer patients

1. Type of therapy – immunotherapy versus other (away from nadir)
2. History of immediate hypersensitivity to PEG (Pfizer and Moderna) or Polysorbate 80 (Astrazeneca)
3. Impaired immune function = impaired vaccine responses
4. Better to vaccinate prior to therapy if no urgent need for cancer therapy
5. Earliest post transplant is 3mths, though after 6 mths likely to lead to better responses
6. Evusheld is no longer effective against current circulating COVID variants

VACCINE EFFECTIVENESS IN CANCER PATIENTS

Seroconversion Rates Following COVID-19 Vaccination Among Cancer Patients

N = 242 Subjects
Prospectively Enrolled, Anti-Spike IgG Tested Post Vaccination

- 32% Hematological Malignancy
- 67% Active Anti-Cancer therapy

Table 3. Association of anti-spike IgG with disease characteristics

Type of malignancy	Positive anti-SARS-CoV-2 spike IgG patients, n (%)	Negative anti-SARS-CoV-2 spike IgG patients, n (%)	p value
Solid malignancy	131 (98%)	3 (2%)	0.001053*
Hematologic malignancy	56 (85%)	10 (15%)	
Type of cancer therapy			
Anti-CD20	16 (70%)	7 (30%)	0.0001168**
Stem cell transplant	19 (73%)	7 (27%)	0.0002866**
CAR-T cell therapy	0 (0%)	3 (100%)	0.0002178**
Hormonal therapy	47 (100%)	0 (0%)	0.04129**
Immune checkpoint inhibitor therapy	30 (97%)	1 (3%)	0.6962

*Statistically significant when compared with each other.
**Statistically significant when compared with overall cohort.

Thakker, Cancer Cell, 2021

SEROCONVERSION IN SPECIFIC HAEMATOLOGICAL SUBTYPES

Table S1. Patient characteristics

	Negative (N=357)	Positive (N=1,088)	All Patients (N=1,445)	P value
Age (yrs)	68 (28, 85)	66 (16, 110)	66 (16, 110)	<0.001
Gender				<0.001
Male	184 (32.1%)	390 (67.9%)	574 (100.0%)	
Female	172 (19.8%)	696 (80.2%)	868 (100.0%)	
Cancer Diagnosis				<0.001
Acute lymphoblastic leukemia (ALL)	2 (11.8%)	15 (88.2%)	17 (100.0%)	
Acute myeloid leukemia (AML)	3 (8.8%)	31 (91.2%)	34 (100.0%)	
Blastic plasmacytoid dendritic cell neoplasm (BPDCN)	1 (100.0%)	0 (0.0%)	1 (100.0%)	
Burkitt lymphoma (BL)	0 (0.0%)	1 (100.0%)	1 (100.0%)	
Chronic lymphocytic leukemia (CLL)	233 (35.8%)	417 (64.2%)	650 (100.0%)	
Chronic myeloid leukemia (CML)	1 (2.9%)	33 (97.1%)	34 (100.0%)	
Diffuse large B cell lymphoma (DLBCL)	11 (21.2%)	41 (78.8%)	52 (100.0%)	
Follicular lymphoma (FL)	22 (22.4%)	76 (77.6%)	98 (100.0%)	
Hairy cell leukemia (HCL)	0 (0.0%)	7 (100.0%)	7 (100.0%)	
Hodgkin lymphoma (HL)	1 (1.5%)	64 (98.5%)	65 (100.0%)	
Mantle cell lymphoma (MCL)	15 (55.6%)	12 (44.4%)	27 (100.0%)	
Marginal zone lymphoma (MZL)	13 (38.2%)	21 (61.8%)	34 (100.0%)	
Myelodysplastic syndrome / myeloproliferative neoplasm	1 (2.9%)	34 (97.1%)	35 (100.0%)	
Multiple myeloma (MM)	9 (4.9%)	175 (95.1%)	184 (100.0%)	
Non-Hodgkin lymphoma no specified	10 (20.8%)	38 (79.2%)	48 (100.0%)	
Primary amyloidosis	0 (0.0%)	2 (100.0%)	2 (100.0%)	
Primary central nervous system lymphoma (PCNSL)	1 (50.0%)	1 (50.0%)	2 (100.0%)	
Primary mediastinal (thymic) large B cell lymphoma	0 (0.0%)	4 (100.0%)	4 (100.0%)	
Smoldering multiple myeloma	0 (0.0%)	29 (100.0%)	29 (100.0%)	
T cell lymphoma	2 (15.4%)	11 (84.6%)	13 (100.0%)	
Waldenstrom macroglobulinemia (WM)	25 (25.8%)	72 (74.2%)	97 (100.0%)	
COVID-19 Vaccination Type				0.084
BNT162b2 (Pfizer)	210 (26.5%)	583 (73.5%)	793 (100.0%)	
mRNA-1273 (Moderna)	147 (22.5%)	505 (77.5%)	652 (100.0%)	

>90%

Vaccine Efficacy

MPN/MDS/AML

Myeloma

Hodgkin's Lymphoma

<90%

Vaccine Efficacy

CLL

Indolent Lymphoma

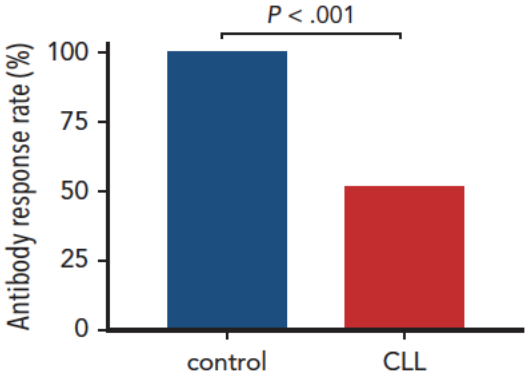
PTCL

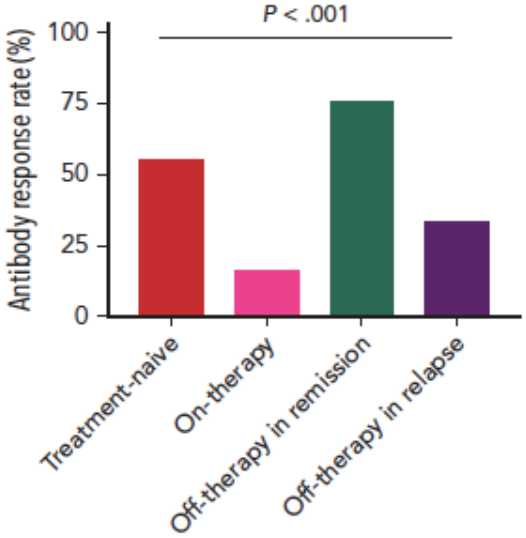
DLBCL

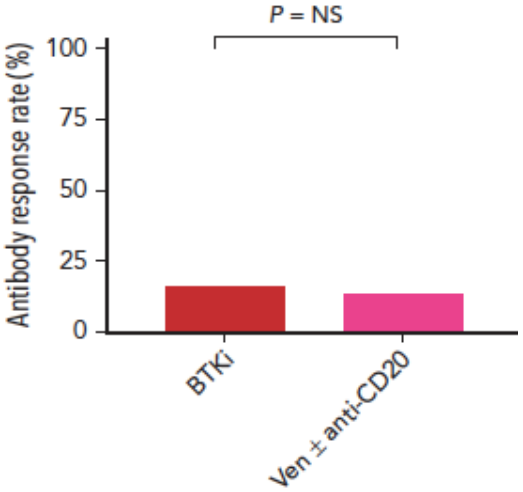
Moderna > Pfizer seroconversion rates
(OR = 1.50; 1.12–2.00; p = 0.007)

Greenburger, Cancer Cell, 2021

THERAPY AND SEROCONVERSION





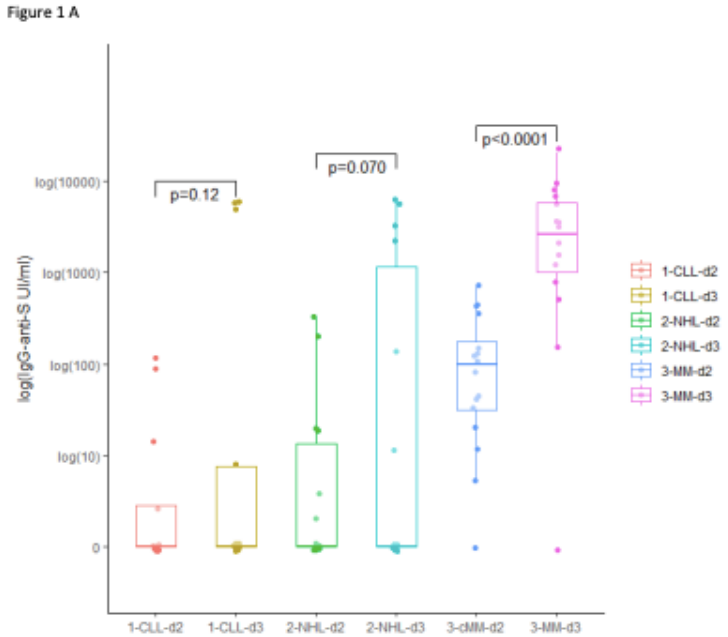


Addit: CD20 mAb
< 12 mo 0.0%
> 12 mon 54%

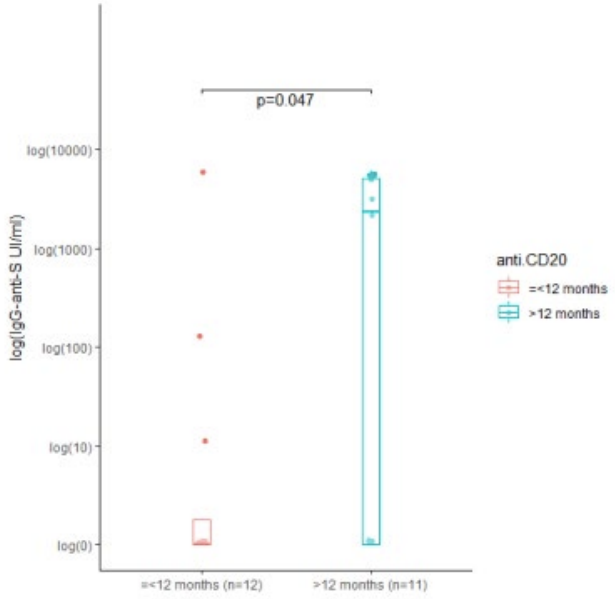
Herishanu, Blood Adv, 2021

EFFICACY OF THIRD DOSE IN HAEMATOLOGY PATIENTS

Humoral quantitative IgG after 2nd & 3rd Dose of the vaccine in 43 patients with lymphoid malignancy



Humoral quantitative IgG after 3rd Dose of the vaccine in 23 patients pre-treated with an anti-CD20 mAb

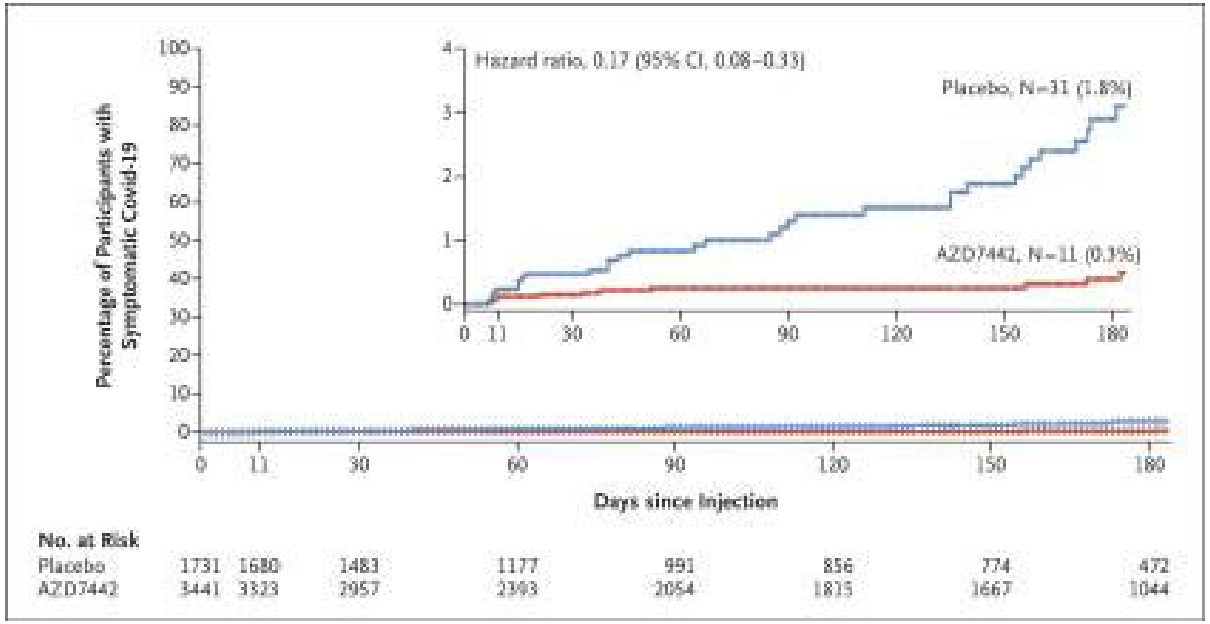


Re, Medrxiv, 2021

3rd primary dose of COVID-19 Vaccine

1. Patients with active haematological malignancy
2. Non-haematological malignancy receiving chemoradiotherapy (excluding immunotherapy or hormonal)
3. Solid organ transplant recipient
4. HSCT or CAR T recipients (note pts need 3 additional doses if previously vaccinated – starting from 3mths post)
5. Patients on immunosuppressive therapies (long list)
6. Primary immunodeficiency
7. Advanced HIV
8. Dialysis patients

Evusheld – pre-exposure prophylaxis



82% relative risk reduction of Symptomatic COVID at 6mths

All severe COVID in the placebo arm

All deaths in the placebo arm

However, ineffective with current variants (XBB.1.5, XB1.16 etc)

Case 1

- Mrs KQ is a 66yr old patient with DLBCL who recently completed R-CHOP chemotherapy 6 months ago and remains in a complete remission. During a consultation she expresses concern regarding her weakened immune system and she wants to know what she can do to help “boost her immune system”. What would you advise?

- You recommend

- booster vaccines: Boostrix-IPV, Energix B, Prevenar-13, MMR, Zostavax

- Fluvax

- COVID-19 Vaccination – booster (mRNA or Novavax)

Case 2

- Mr AB is 48yr man with metastatic melanoma currently receiving treatment with Pembrolizumab every 2 weeks. He is booked for treatment tomorrow. He requests flu vaccination today. He is planning to receive his 3rd primary Pfizer covid vaccine tomorrow at the hospital shortly after his immunotherapy. What would you advise?

- You provide the fluvax and advise re-scheduling the the Pfizer vaccine for a weeks time (note 3rd dose will be considered a booster)

Case 3

- Ms CV is a 70 yr old woman who is 4 and half years post allogeneic SCT for MDS. She remains well in remission with normal blood counts. She continues on tacrolimus for chronic graft versus host disease that is currently as reported by her specialist quiescent. Her sister recently had an episode of shingles and she wants to talk about the vaccine that her husband had received to help prevent this last year. What would you advise?

- You advise that the funded vaccine – Zostavax, is contraindicated to administer given a risk if severe illness in an immunosuppressed state.
- Shingrix (adjuvanted recombinant varicella zoster virus glycoprotein E (gE) subunit, non-live vaccine) is safe and efficacious – funding anticipated for those 70yrs+ and immunosuppressed patients from ~ Sept/Oct 2023

References

- Parohan M, Yaghoubi S, Seraji A, et al, Risk Factors for Mortality in patients with COVID-19 infection: a systematic review and meta-analysis of observational studies. The aging male 2020; 23(5): 1416-1424.
- Mehta, V., et al., *Case Fatality Rate of Cancer Patients with COVID-19 in a New York Hospital System.* Cancer Discov, 2020. **10**(7): p. 935-941.
- Russell, B., et al., *Factors Affecting COVID-19 Outcomes in Cancer Patients: A First Report From Guy's Cancer Center in London.* Front Oncol, 2020. **10**: p. 1279.
- Australian Technical Advisory Group on Immunisation (ATAGI). Australian Immunisation Handbook, Australian Government Department of Health, Canberra, 2018, immunisationhandbook.health.gov.au.
- https://www.moga.org.au/all-position-statements/covid-19-vaccination-in-patients-with-solid-tumours
- https://anztct.org.au/covid-19-updates-resources/
- https://www.thanz.org.au/documents/item/591
- *Haematology Society of Australia and New Zealand. COVID-19 Vaccination in Haematology Patients: An Australia and New Zealand Consensus Position Statement*. 2021 2 Feb 2021 [cited 2021 Feb 28];
- Baden, L.R., et al., *Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine.* N Engl J Med, 2020. **384**(5): p. 403-416.
- Polack, F.P., et al., *Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine.* N Engl J Med, 2020. **383**(27): p. 2603-2615.
- Voysey, M., et al., *Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK.* Lancet, 2021. **397**(10269): p. 99-111.
- https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting