Vaccinations – who and when?

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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?

- Cancer patients may have:

1. Reduced protection from previous vaccination
2. Reduced responses to vaccines (may need extra doses)
3. An increased risk of vaccine-preventable diseases or complications
4. An increased risk of adverse events, particularly from live vaccines

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	Profound T and B cell immunodeficiency
CAR T cell therapy	
Autologous SCT	
Fludarabine/ Bendamustine	
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) [75]

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”

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. Delay may be acceptable if weaning of IST post Allo SCT continues and community risk is low

Vaccine induced immune Thrombotic Thrombocytopenia (VITT)

- Aka – TTS, VIPIT, VATT

#Specifically described following AstraZeneca and JNJ (both Adenovirus vectored spike protein vaccines)

➢ Immune mediated prothrombotic state induced by the development of cross-reacting autoantibodies against platelet antigens (PF4) or PF4/polyanion complexes that precipitates thrombocytopenia and associated thrombosis. It can severe, rapidly progressive and fatal.

VITT

Australian data as of June 2021

Age	Risk of VITT per 1 000 000
<50yrs	31
50 - 59yrs	27
60 – 69yrs	14
70 - 79 yrs	18
80+yrs	19

Australian Case fatality rate = 3%

UK data as of July 2021

Dose of AZ	Risk of VITT per 1 000 000
1st	14.8
2nd	1.8

UK Case fatality rate = 18%

VITT

Most reported cases involve presentation with cerebral venous sinus thrombosis, other sites have also been involved (splanchnic, DVT, pulmonary embolism, arterial ischaemia).

Biologically has similarities to Heparin Induced Thrombocytopenia and Thrombosis (HITT) – with presence of +ve anti-PF4 abs on ELISA (Not Diamed) and activating antibodies on centralised functional testing.

When should I suspect VITT?

Onset days 4-42 after vaccination (AstraZeneca)

Thrombosis: predominant sites: cerebral venous sinus or splanchnic thrombosis. Other VTE and arterial ischaemia also reported

Thrombocytopenia* or falling platelet count (platelets can be normal on presentation but drop within 4-6 hours)

High D-Dimer (typically very high)

Some patients are refractory to standard anti-coagulation

Response to IVIG

How do I investigate VITT?

Clinical assessment with appropriate investigations should always be initiated based on the patient context. Do not delay the commencement of life-saving management while awaiting investigations.

Not all thrombocytopenia post vaccine is VITT. Immune thrombocytopenia post COVID-19 vaccine is also reported and SHOULD NOT be treated in the same manner.

Do not administer platelet transfusions

Do not begin heparin-based anticoagulation (IV unfractionated heparin infusions, LMWH).

How to investigate VITT

- Screen – FBC, D-Dimer, Fibrinogen :

1. PLT <150 or falling; &
2. D-Dimer >5ULN; or
3. Fibrinogen reduced

Is there thrombosis? – USS, CT or MRV, CTPA

Speak to a Haematologist if 1) thrombosis or 2) thrombocytopenia post vax

- Confirm – ELISA HIT +ve

- If yes – send for central functional confirmatory assay

How do I treat VITT?

IVIg (1-2g/kg over 2 divisions) is recommended - Haematologists may consider addition of high dose methylprednisone and/or plasma exchange in the appropriate context (e.g. signs of new/progressive thrombosis).

Anticoagulant treatment options are as per local therapeutic practice for HIT: bivalirudin, argatroban, danaparoid, fondaparinux, rivaroxaban, apixaban, dabigatran, and (after initial treatment with another agent) warfarin.

Avoid platelet transfusion

Anticoagulation duration should probably be time limited (3-6 months), with hospitalisation considered safest until there is a reduction of in vivo platelet activation and thrombin generation (increasing platelets, falling D-dimers, normal fibrinogen). Check for resolution of antibodies prior to cessation of anticoagulation.

When is AZ contraindicated?

- Prior VITT
- Prior history of HITT
- Prior history of Antiphospholipid syndrome
- Prior Cerebral venous sinus thrombosis
- Prior idiopathic splanchnic thrombosis
- Prior demonstrated anaphylaxis to PEG

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
- AZ Covid vaccine

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?

- You provide the fluvax and advise re-scheduling the the Pfizer vaccine for a weeks time.

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 only registered vaccine – Zostavax, is unsafe to administer given a risk if severe illness in an immunosuppressed state

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