Government of Western Australia
South Metropolitan Health Service
Fiona Stanley Fremantle Hospitals Group

# The Rapidly Evolving Landscape of Antibody Drug Conjugates and Bispecific Antibodies in Haematology and Oncology

## Implications for Nursing Care

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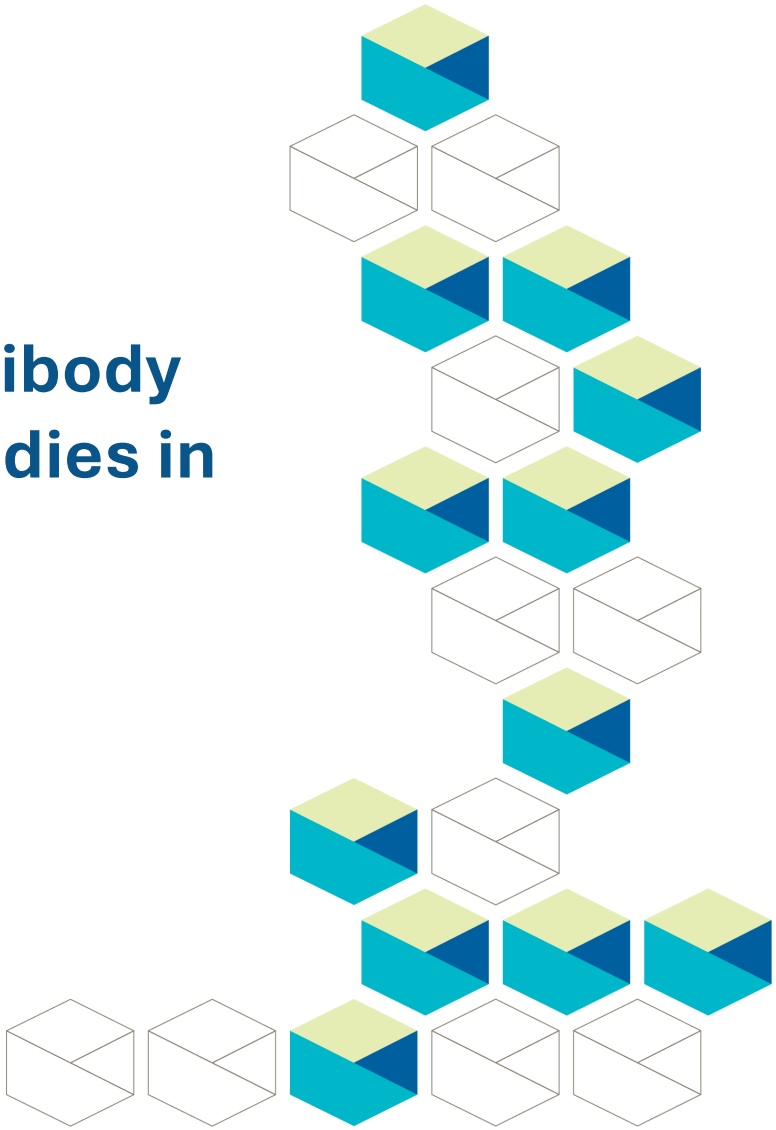


# Objectives

- Describe the mechanisms of action of antibody drug conjugates (ADCs) and bispecific antibodies.
- Recognise approved and emerging therapies in haematology and oncology in Australia
- Identify unique toxicity profiles associated with these agents.
- Discuss the pivotal role of nurses in patient assessment, education and toxicity management.
- Explore future directions and survivorship implications.

# Evolution of Targeted Cancer Therapy

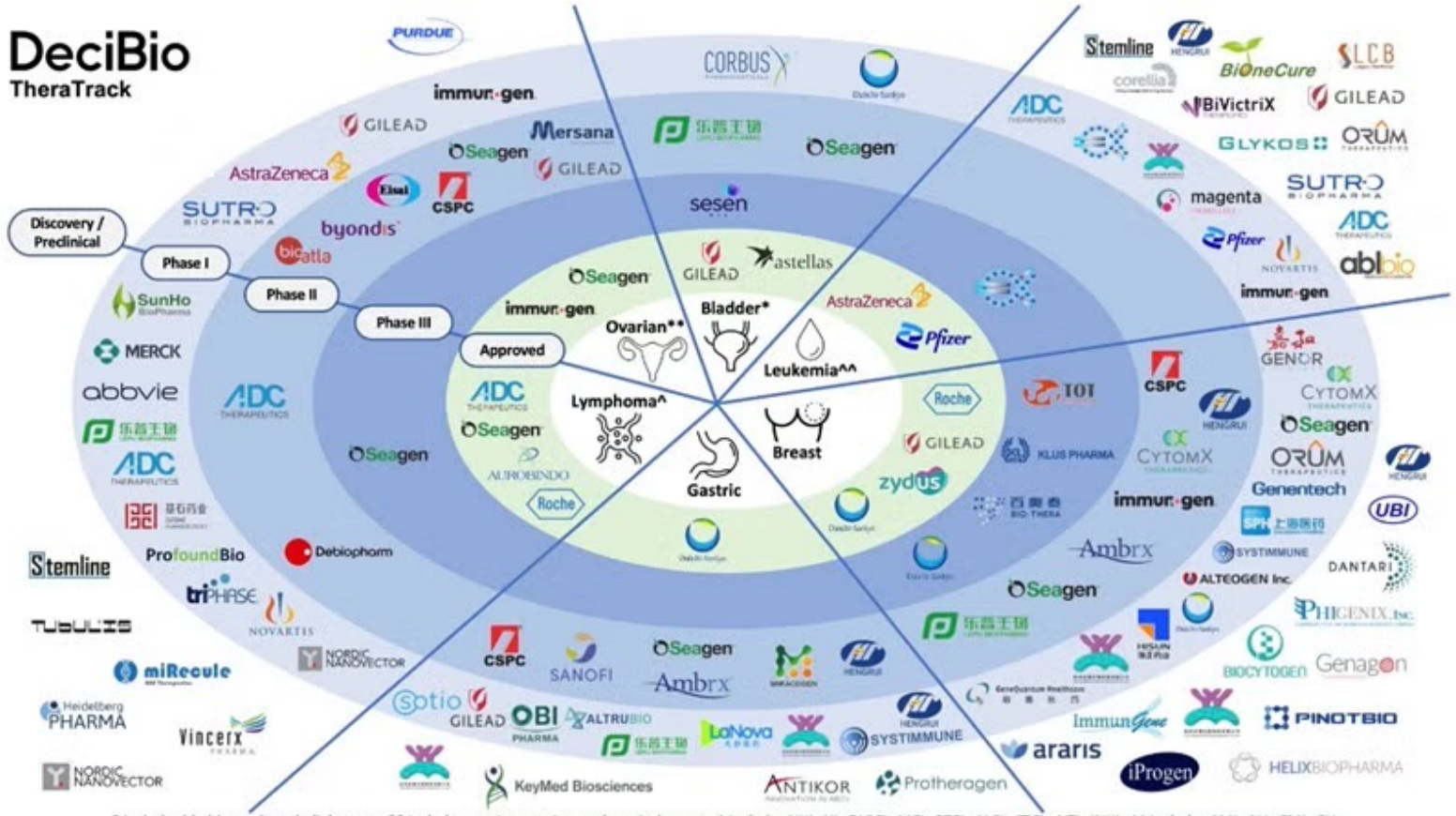
- Chemotherapy
- Monoclonal Antibodies
- Checkpoint Inhibitors
- Antibody Drug Conjugates
- Bispecific Antibodies
- Cellular Therapies

# EDUCATION  Why does this matter?

**New Therapy**
**Haematology / Oncology / Radiation Oncology / Cellular Therapy**

- **Mechanism of Action**
- **Side Effect Profile**
- **NURSES – How can we support the patient?**

# Antibody Drug Conjugates – Clinical Pipeline




* Includes bladder and urothelial cancer; ** Includes ovarian, uterine, and cervical cancer; ^ Includes NHL, HL, DLBCL, MCL, PTCL, ALCL, CTCL, AITL, INHL; ^^ Includes AML, ALL, CML, CLL
Note: Not an exhaustive list and does not include companies with assets in development for general solid or hematologic tumors; Some companies have multiple assets per phase / stage;
Not all preclinical / discovery programs are disclosed; Graphic shows the most advanced phase of unique assets in each indication

# What Are Antibody Drug Conjugates (ADC's)?

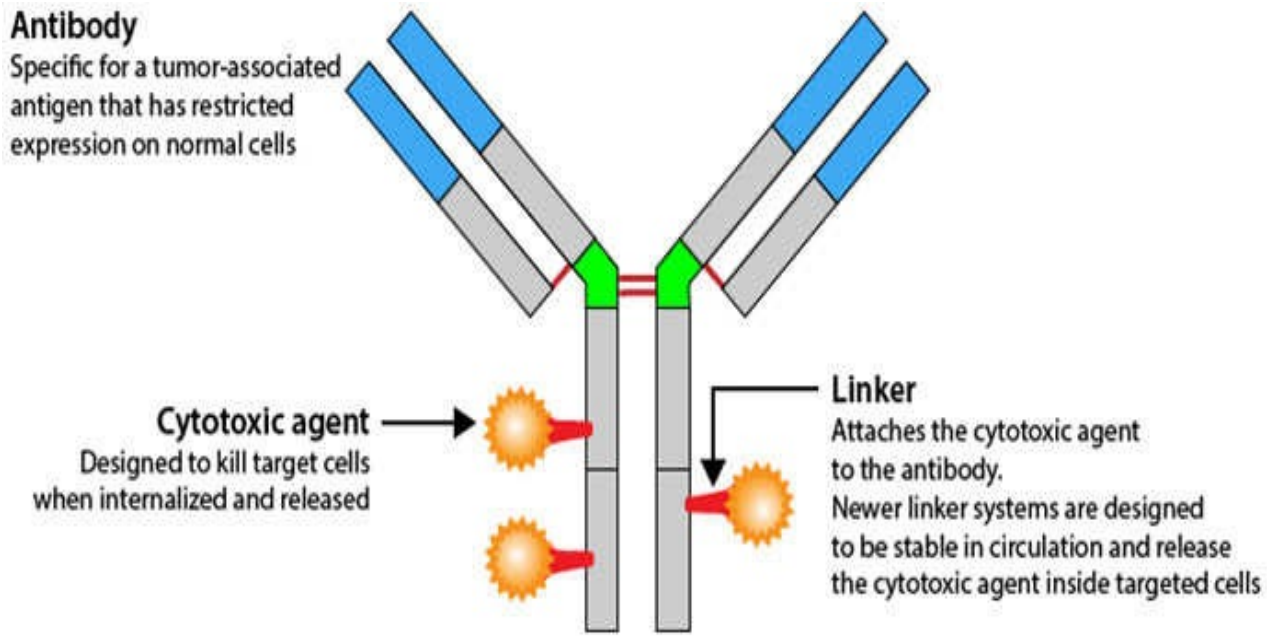
- **ADCs combine:**

- Monoclonal antibody
- Linker
- Cytotoxic payload

- **Goal:**

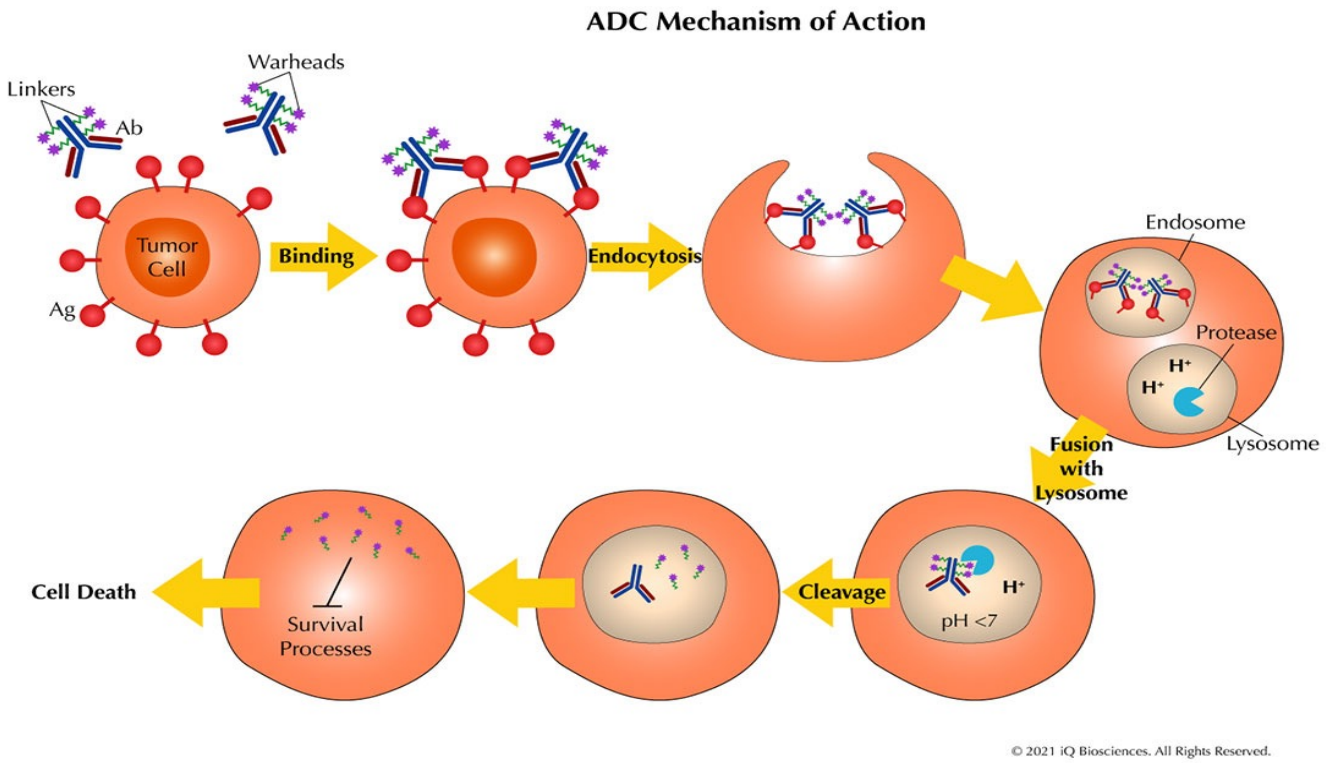
- Maximise tumour killing

- Minimise systemic toxicity




BOCscience https://www.bocsci.com/blog/types-of-adc-linkers/

# How ADCs Work




IQ Biosciences https://iqbiosciences.com/blog/the-abcs-of-adcs-an-introduction-to-antibody-drug-conjugates/

# Why do ADC's cause Toxicity ?

- **Mechanism based toxicity**
- On TARGET off TUMOR effects
- Payload toxicity
- Bystander effect
- Linker instability

# ONCOLOGY ADC’s, Trials, Response Rates and Toxicities

*References List

# HAEMATOLOGY ADC's, Trials, Response Rates and Toxicities

Ansell et al 2022 Overall Survival with Brentuximab Vedotin in Stage III or IV Hodgkin's Lymphoma NEJM
Tilly et al 2021 Polatuzumab Vedotin in Previously Untreated Diffuse Large B-Cell Lymphoma NEJM
Kantarjian et al 2016 Inotuzumab Ozogamicin versus Standard Therapy for Acute Lymphoblastic Leukemia NEJM
Hungria et al 2024 Belantamab Mafodotin, Bortezomib, and Dexamethasone for Multiple Myeloma NEJM

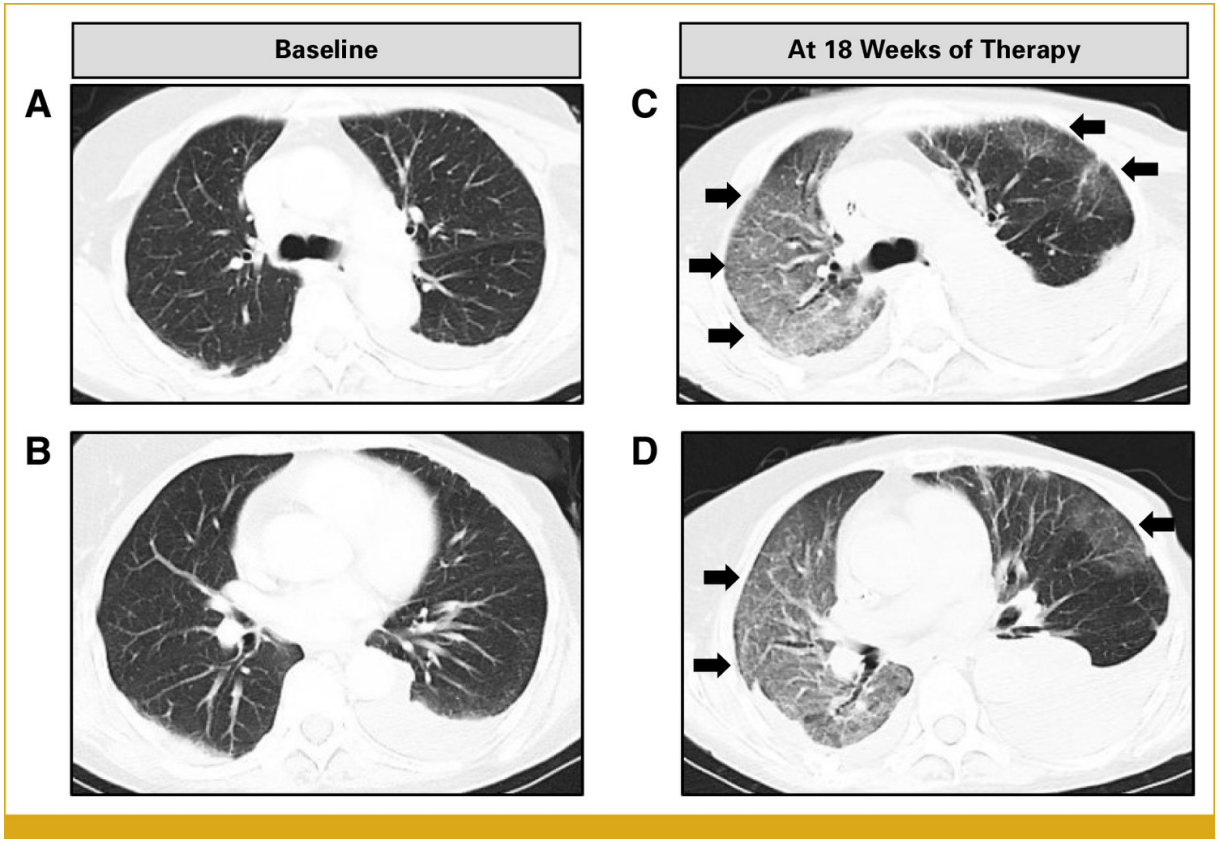
# Nursing Assessment Interstitial Lung Disease - ILD Pneumonitis

## MONITOR

- New Cough
- Dyspnoea
- Reduced Oxygen Saturation

## MANAGEMENT

- Hold treatment
- CT Chest
- Respiratory review
- Corticosteroids

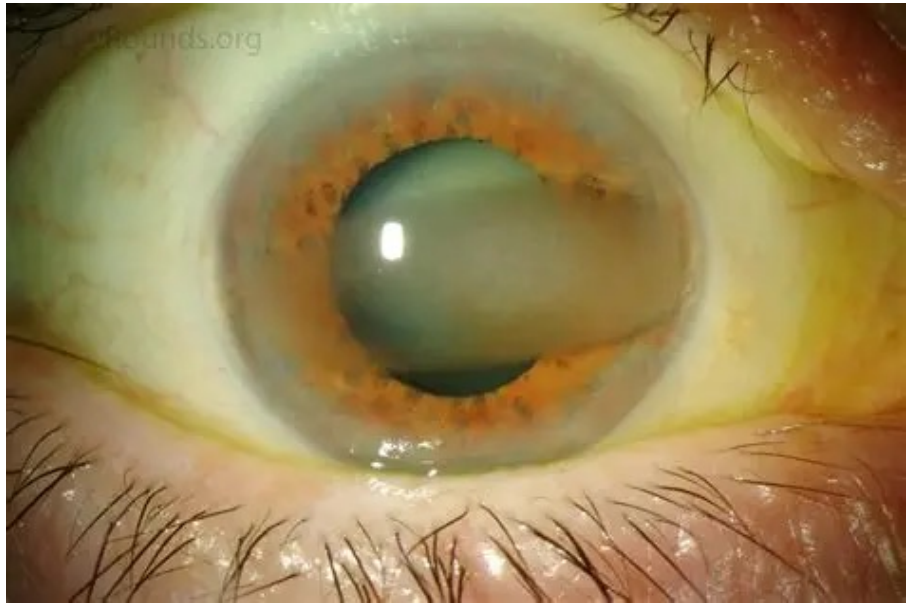



Modi et al 2022 Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer NEJM
Image - https://ascopubs.org/cms/10.1200/PO.23.00391/asset/9f173085-78c5-4d8a-8e06-bed9a1667134/assets/images/large/po.23.00391f4.jpg

# Nursing Considerations
# Ocular Toxicity – Keratopathy

**Antibody Drug Conjugate**

- **Belantamab – Payload MMAF (microtubule inhibitor)**
- **Corneal cells lack BCMA Target -**
- **Non- specific cellular uptake MACROPINOCYTOSIS**
- **MMAF – released inside corneal cells – Apoptosis**
- **DREAMM-7 79% DREAMM-8 89%**



**MONITOR**

- Vision changes
- Dry eyes
- Eye Pain
- Photophobia
- Increased risk with underlying eye conditions

**MANAGEMENT**

- Baseline Ophthalmology review
- Lubricating eye drops
- Dose modifications / Hold treatment
- Coordinate ophthalmology appointments (reviews every 2 months for 1st 6 months)

# Nursing Considerations – Hepatotoxicity and VOD

- Hepatotoxicity - raised liver enzymes
- Veno-Occlusive Disease VOD / Sinusoidal Obstruction Syndrome (SOS)
- Damage to sinusoidal endothelial cells and hepatocytes

## ONSET

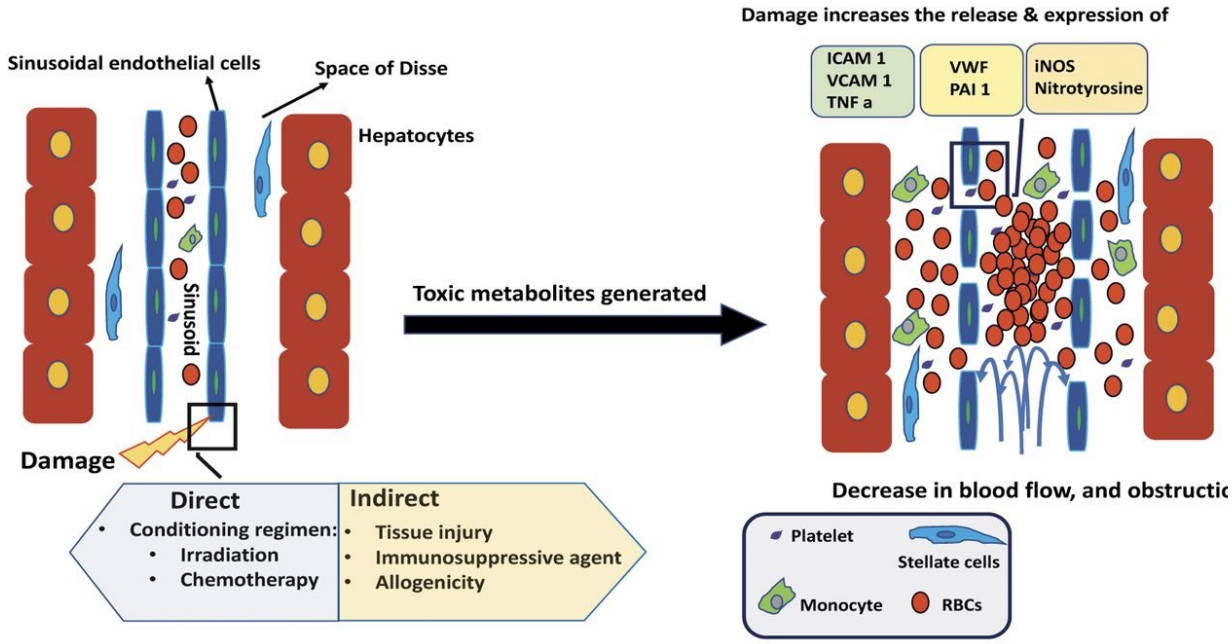
Can present up to 56 days post last dose of treatment

## PRESENTATION

- Rapid weight gain from fluid retention
- Painful hepatomegaly
- Jaundice and elevated bilirubin
- Ascites and peripheral edema
- Severe cases may progress to hypoxia, encephalopathy, pleural effusions, renal insufficiency, and multi-organ failure

## MANAGEMENT

- Monitor LFT's
- Dose reduction – elevated liver enzymes
- Permanent discontinuation – if VOD develops
- For patients proceeding to HSCT limit 2 cycles of Inotuzumab – reduce risk VOD/SOS




Nassereddine et al 2018. Sinusoidal Obstruction Syndrome (Veno-occlusive Disease) Following Hematopoietic Stem Cell Transplant: Insights and Therapeutic Advances. Anticancer Research

# “How the payload predicts the Toxicity”

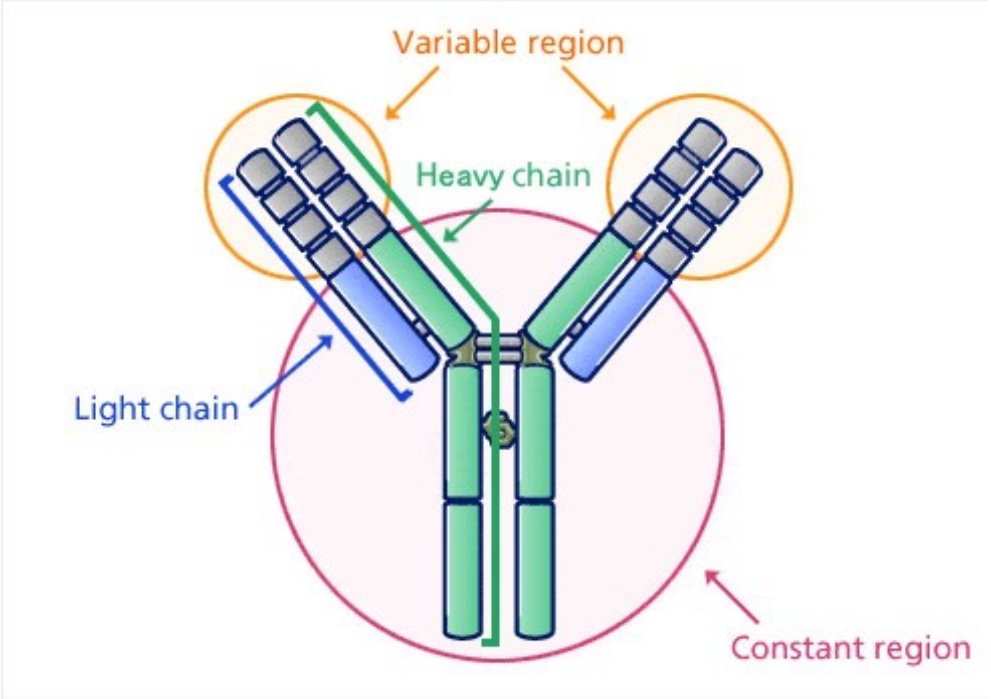
| Payload | Mechanism Cell Death | Cell Permeability | Antibody Drug Conjugate Examples | Toxicity |
|---|---|---|---|---|
| Monomethyl Auristatin E<br>MMAE | Mitotic Inhibitor<br>Micro tubulin inhibitor | Highly cell permeable | Brentuxumab, Polatuzumab, Enfortumab | Peripheral Neuropathy |
| Monomethyl Auristatin F<br>MMAF | Mitotic Inhibitor<br>Micro tubulin inhibitor | Low cell permeability<br>Reduced off target toxicities. | Belantamab | Ocular Toxicity (keratopathy) |
| Deruxtecan<br>Topoisomerase Inhibitor | Interrupts DNA Replication | Membrane permeable | Transtuzumab Deruxtecan T-DxT<br>Datopotamab Deruxtecan | Interstitial Lung Disease<br>Pneumonitis |
| SN-38<br>Active metabolite Irinotecan<br>Topoisomerase Inhibitor | Interrupts DNA Replication | Membrane permeable | Sacituzumab Govitecan | Diarrhoea and Neutropenia |
| Calichemicin | Direct double DNA Strand breaks | Low “bystander effect”<br>Low volume of drug as so potent | Inotuzumab Ozogamicin | Hepatotoxicity and VOD |
| Derivative of Maytansine 1<br>DM1 | Mitotic Inhibitor<br>Micro tubulin inhibitor | Low cell permeability | Trastuzumab emtansine | Thrombocytopenia and Hepatotoxicity |

# Antibody Constructs

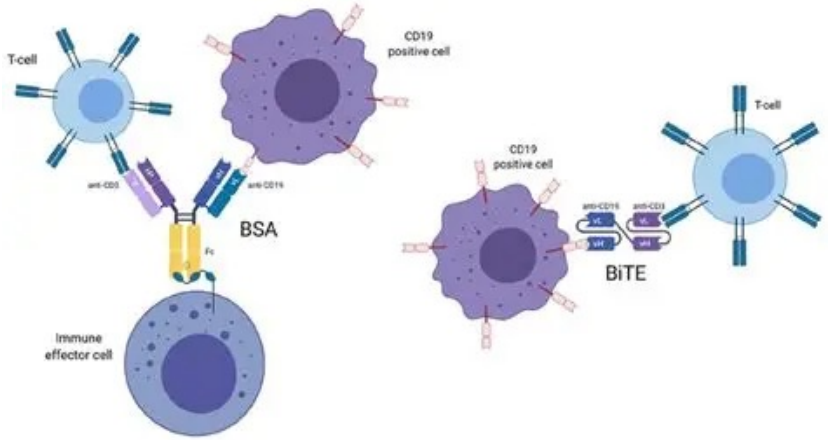
- **Monoclonal = 1 Target**
- eg CD20
- Rituxumab

- **Bispecific Antibodies = 2** Targets (Tumor)
- Eg EGFR + MET
- Amivantamab (NSCLC)

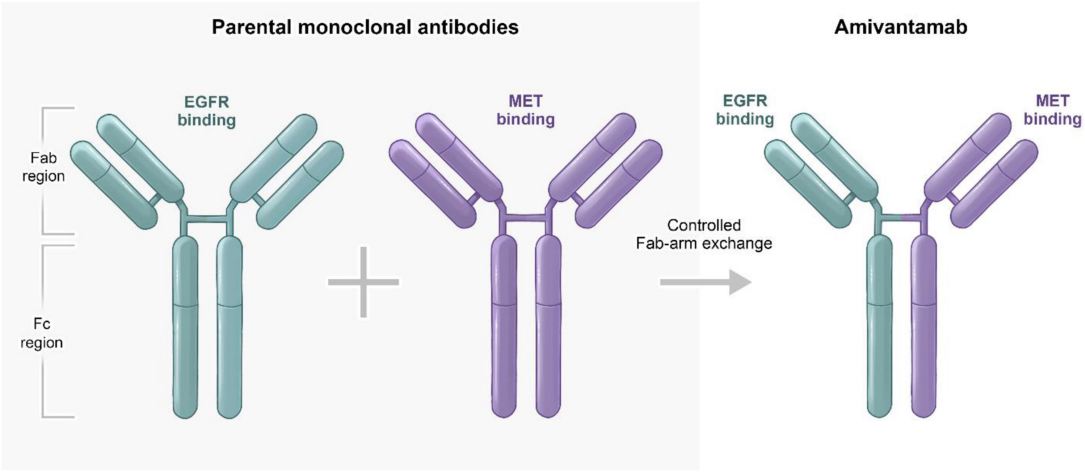
- **Bispecific T Cell Engagers**
- = 2 Targets
- GPRC5D + T Cell
- **CRS and ICANS**




# Bispecific Antibodies




Bispecific Antibody - T Cell Engager

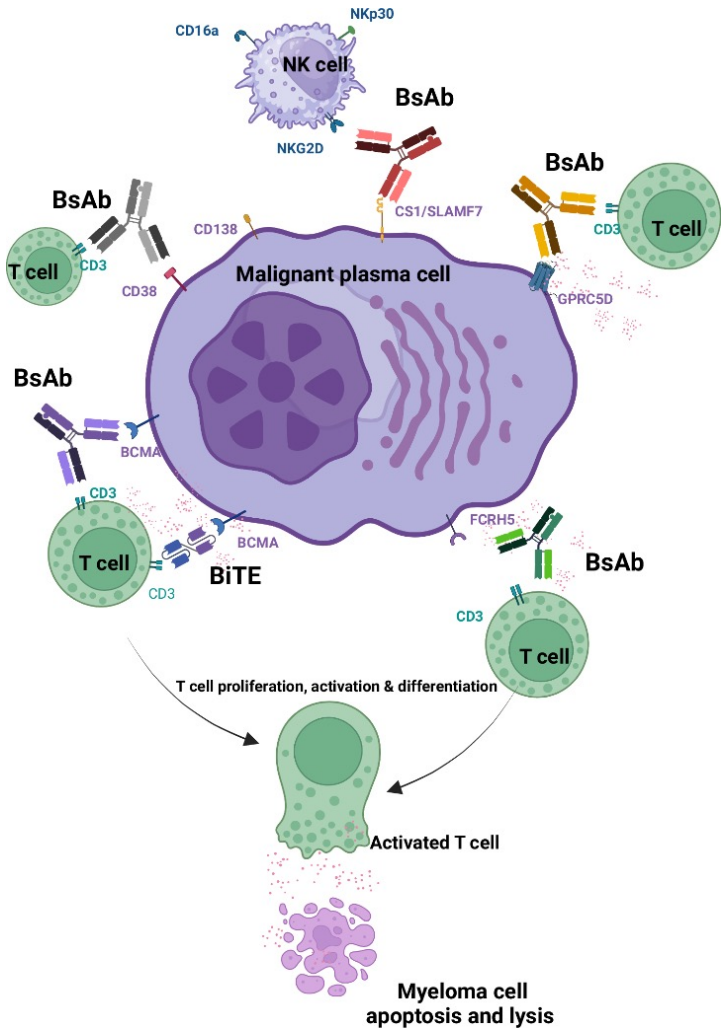



Bispecific Antibody - Tumor Targeting

# What are Bispecific T Cell Engagers ?

How do activated T cells work?

- Release specialised toxic proteins
- Perforin “punch holes”
- Granzymes enter the cell and trigger programmed cell death.




Devasia et al. (2024) Bispecific Antibodies in the treatment on multiple myeloma. BC

# Bispecific Antibodies T-cell Engagers - Haematology

| Drug | Targets | Indication | Landmark pivotal trial | ORR (approx.) | Main toxicities with incidences (approx.) | Key nursing considerations |
|---|---|---|---|---|---|---|
| **Blinatumomab** | CD19 × CD3 | R/R Ph- B-ALL | TOWER | CR/CRh ~44% | CRS: ~5% any grade, ~2% grade ≥3. **Neurologic events (ICANS-like): any grade ~50%,** grade ≥3 ~9–15%. Infections: ~40–50%. **SHORT HALF LIFE** | CRS: close vitals, early escalation for fever, hypotension, hypoxia. Neurotoxicity: frequent neuro obs, seizure precautions, educate on confusion, speech changes, seizures. Continuous IV: pump checks, line security, clear instructions for alarms. |
| **Epcoritamab** | CD20 × CD3 | R/R DLBCL after ≥2 lines | EPCORE NHL-1 | ORR ~63%, CR ~39% | **CRS: ~50% any grade,** ~3% grade ≥3. ICANS: ~6% any grade, ≤1–2% grade ≥3. Neutropenia: ~25–30%. Infections: ~40–50%. | Step-up dosing: ensure correct schedule and premeds. CRS/ICANS monitoring: frequent obs during early doses; clear escalation plan. Infection risk: FBC monitoring, prompt review of fevers, patient education on when to present. |
| **Glofitamab** | CD20 × CD3 | R/R DLBCL after ≥2 lines | NP30179 | ORR ~52%, CR ~39% | **CRS: ~60–65% any grade**, ~3–4% grade ≥3. ICANS: ~3% any grade. Neutropenia: ~25–30%. Infections: ~40–50%. | Obinutuzumab pre-treatment: confirm given to debulk B-cells and reduce CRS. CRS vigilance: highest risk with first few doses—close monitoring and rapid access to tocilizumab/steroids per protocol. TLS risk: monitor labs, hydration, urate-lowering in bulky disease. |
| **Mosunetuzumab** | CD20 × CD3 | R/R follicular lymphoma (G1–3a) | GO29781 | ORR ~80%, CR ~60% | **CRS: ~40–45% a**ny grade, ~2% grade ≥3. Neutropenia: ~25–30%. Infections: ~40–45%. Hypogammaglobulinaemia: common. | Outpatient step-up dosing: ensure patients understand early-cycle monitoring requirements. CRS: educate on fever and flu-like symptoms; clear instructions for after-hours contact. Immune suppression: monitor IgG, consider IVIG per local policy; reinforce infection-prevention behaviours. |
| **Teclistamab** | BCMA × CD3 | R/R MM, triple-class exposed | MajesTEC-1 | ORR ~63% | CRS: ~70–72% any grade, ~1% grade ≥3. ICANS: ~3–5% any grade, ≤1% grade ≥3. **Neutropenia: ~65–70%. Infections: ~75–80% (grade ≥3 ~40–45%).** | Inpatient/close-monitor step-up: vitals protocol for first doses. High infection burden: strict infection screening, vaccination where appropriate, prophylaxis (HSV/PCP) per protocol, early antibiotics. Neuro checks: orientation, handwriting, speech; low threshold to escalate. |
| **Talquetamab** | GPRC5D × CD3 | R/R MM after ≥3 lines | MonumenTAL-1 | ORR ~73% | CRS: ~75–79% any grade, ~1–2% grade ≥3. **Skin/nail disorders: ~60–70%. Dysgeusia/ageusia & oral AEs: ~50–60%.** Infections: ~50–55%. Neutropenia: ~30–40%. | CRS: same step-up and monitoring principles as other TCEs. Skin/nail care: moisturisers, nail protection, pain management; body-image support if needed. Taste changes & oral issues: dietitian referral, soft/energy-dense foods, oral hygiene, manage weight loss and reduced intake |
| **Elranatamab** | BCMA × CD3 | R/R MM after ≥3 lines | MagnetisMM-3 | ORR ~61% | CRS: ~55–60% any grade, ~1% grade ≥3. ICANS: ~3% any grade. Infections: ~65–70% (grade ≥3 ~40%). Neutropenia: ~40–45%. Anaemia/thrombocytopenia: ~30–40%. | Step-up dosing and observation: similar CRS/ICANS precautions as teclistamab. Cytopenias: monitor FBC, transfusion support, bleeding precautions, fatigueA1:G8 management. Infection vigilance: patient education on fever, cough, urinary symptoms; rapid access pathways for review. |

# Toxicities of Bispecific Antibodies – T Cell Engagers

1. Cytokine Release Syndrome (CRS)
2. Neurotoxicity (ICANS)
3. Infections
4. Cytopenias
5. Hypogammaglobulinaemia
6. Target-specific toxicities

- Most toxicities occur early during step-up dosing.

# 1. Cytokine Release Syndrome

**ONSET**

Most common early toxicity.

- Within the first few doses
- During step-up dosing

**PRESENTATION**

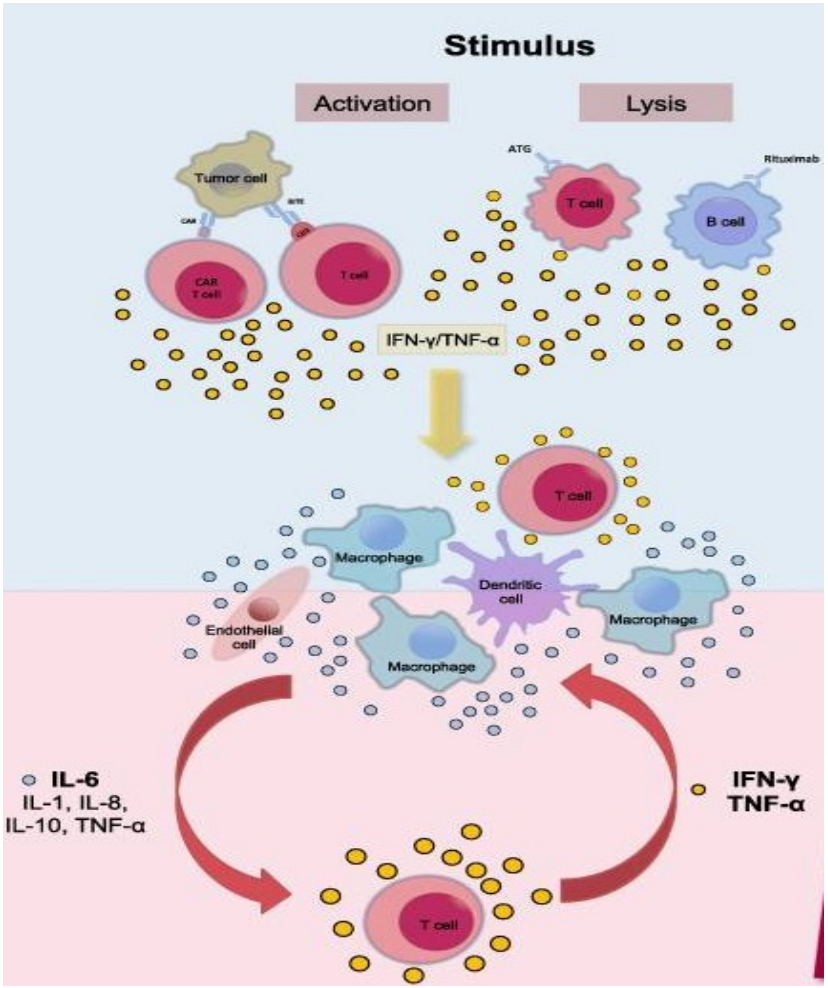
- Fever
- Hypotension
- Tachycardia
- Hypoxia

**Incidence**

- Predominantly Grade 1–2
- Severe CRS uncommon

**Management:**

- Supportive care
- Tocilizumab
- Corticosteroids when required



# Flash card: BsAB or TsAB Recipient Cytokine Release Syndrome (CRS) Management

If your patient is experiencing the following **post** Bispecific Antibody (BsAB) **OR** Trispecific Antibody (TsAB) therapy:

- Febrile (temperature ≥ 38°C)
- Hypotension (systolic BP ≤ 90mmHg)
- ↑ $O_2$ requirement to maintain $SpO_2$ ≥ 90%

## → Initiate CRS management and call Haem registrar

| Grade | Description | Management |
|---|---|---|
| **1** | Temp ≥ 38°C | Initiate **Febrile Neutropenia Management pathway**<br>Daily bloods, minimum 4/24 vital sign observations<br>Hold therapy until resolution of CRS<br>**Administer Tocilizumab**<br>**Dexamethasone:** 10mg IV to 20 mg per day can be initiated |
| **2** | Temp ≥ 38°C<br>SBP ≤ 90mmHg<br>Or requires $O_2$ via mask or nasal prongs **≤ 6L/min** | Hold therapy until resolution of CRS<br>Grade 1 CRS management **and** 1 litre normal saline as bolus<br>Early ICU consult<br>**Administer Tocilizumab**<br>**Dexamethasone:** 10mg IV to 20 mg per day can be initiated , dose can be increased as needed. |
| **3** | Temp ≥ 38°C<br>Hypotension requiring single vasopressor<br>or<br>$O_2$ via mask or high-flow nasal prongs **>6L/min** | Hold therapy until resolution of CRS<br>Grade 1 CRS management **and** ICU admission<br>Vasopressor and high-flow $O_2$ as per ICU<br>**Administer Tocilizumab**<br>**Dexamethasone:** 10mg IV 6 hourly<br>Consider **Anakinra 100mg SC** daily if no improvement after Tocilizumab. |
| **4** | Temp ≥ 38°C<br>Hypotension requiring **2+** vasopressors<br>or<br>Positive pressure $O_2$ (BiPAP, | Consider permanent therapy discontinuation a per protocol .<br>Grade 1 CRS management **and** ICU admission<br>Vasopressor and high-flow $O_2$ therapy as per ICU<br>**Administer Tocilizumab**<br>**Give methylprednisolone**<br>Consider **Anakinra 100mg SC** daily if no improvement |

**Fiona Stanley Clinical Haematology Key Contacts**
**Haematology registrar (ward):** via helpdesk
**Haematologists (Hasib Sidiqi, Allison Barraclough):** via helpdesk
**After hours (haematologist on-call):** via helpdesk

## Tocilizumab (Consult haem registrar and haematologist)

**Dose:** 8mg/kg (Max dose 800mg)
**Frequency:** TDS every 8 hours*, max 3 times/24H, max 4 doses*
*Some patients may receive prophylactic tocilizumab, ensure 8hrs between all doses of tocilizumab. Max doses not inclusive of pre-tocilizumab doses.
**Administration:** Intravenously over 1 hour
**Compatibility:** 0.9% normal saline

| | |
|---|---|
| Weekday, time **before** 18:00 | Call Clinical Pharm haem/ Onc 6152 7743 |
| Weekday, time **after** 18:00 | Call Compounding Oncall pharmacist 0466315102 |
| Saturday, time **before** 16:00 | Call Compounding staff onsite 6152 5048 |
| Saturday, time **after** 16:00 | Call Compounding Oncall pharmacist 0466315102 |
| Sunday, time **before** 14:00 | Call Compounding staff onsite 6152 5048 |
| Sunday, time **after** 14:00 | Call Compounding Oncall pharmacist 0466315102 |

- **Maximum timeframe** from call to administration = **1 hour**
- Tocilizumab has a **24-hour expiry** once made
- PPE as per standard cytotoxic precautions

### Corticosteroid

**Dexamethasone:** 10mg IV 6 hourly, if no response to Tocilizumab after 12 – 18 hours

**Methylprednisolone:** IV 1000mg IV daily for 3 days then taper.

Lee et al 2019

# 2. Neurotoxicity (ICANS)

## ONSET

- 2-4 days (median onset)
- Step up dosing and first full dose

## PRESENTATION

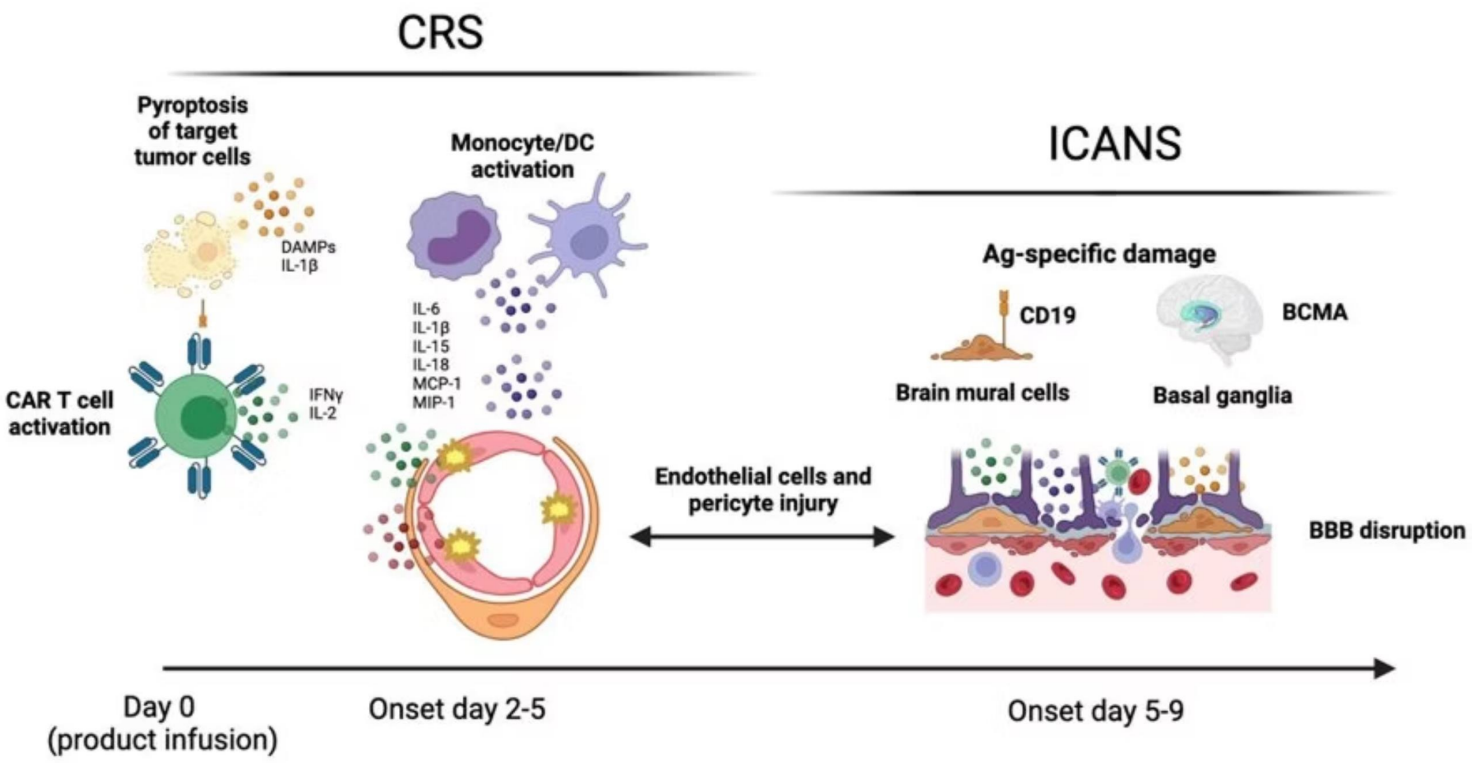
- Confusion
- Word-finding difficulties - Dysphasia
- Tremor
- Altered consciousness

## INCIDENCE

- Less common and generally less severe than CAR-T associated neurotoxicity

## MANAGEMENT

- Early recognition
- Corticosteroids
- Neurological monitoring



# Flash card: BsAB or TsAB Recipient Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS) Management

If your patient is experiencing the following **post** Bispecific Antibody (BsAB) **OR** Trispecific Antibody (TsAB) therapy:

- Decreased ICE score
- Seizure, motor weakness
- Raised intracranial pressure

→ **ICANS management, use ICE assessment tool and call Haem registrar**

**Fiona Stanley Clinical Haematology Key Contacts**
**Haematology registrar (ward):** via helpdesk
**Haematologists (Hasib Sidiqi, Allison Barraclough):** via helpdesk
**After hours (haematologist on-call):** via helpdesk

| Grade | Description | Management |
|---|---|---|
| 1 | ICE score: 7-9<br>Awakens spontaneously | Hold therapy until resolution of event.<br>Keep NBM until medical and speech path review<br>Medications review for risk of CNS depression<br>Switch to IV meds and hydration<br>Consult with Neurology, Consider EEG, MRI scan (CT if MRI unavailable)<br>Consider seizure prophylaxis (e.g. leviteracetam)<br>**Dexamethasone:** 10mg IV/12h |
| 2 | ICE score: 3-6<br>Awakens to **voice** | Hold therapy until resolution of event.<br>Grade 1 ICANS management **and** Consider ICU admission<br>**If no concurrent CRS, give dexamethasone (10mg IV every 6 hours until ICANS ≤ grade 1)**<br>**If concurrent CRS, administer dexamethasone 10mg IV 6 hourly first and discuss Tocilizumab for CRS management with Consultant** |
| 3 | ICE score: 0-2<br>Awakens to **tactile stimulus**<br>Focal/local/non-convulsive seizures<br>Focal/local cerebral oedema | Hold therapy until resolution of event.<br>Grade 1 ICANS management **and ICU admission**<br>Consider repeated neuroimaging every 2-3 days<br>**Give dexamethasone (dose and duration as above)**<br>**If concurrent grade 2 or greater CRS, give Tocilizumab per CRS management in addition to corticosteroids.**<br>Consider **Anakinra 100mg SC** daily if no improvement after Tocilizumab. |
| 4 | **Unrousable**: stupor/coma<br>Repetitive seizures ≥ 5mins<br>Diffuse cerebral oedema<br>Decerebrate/decorticate | Consider permanent therapy discontinuation a per protocol .<br>Grade 1 ICANS management **and ICU admission** for airway protection<br>**Give methylprednisolone 1000mg IV daily for 3 days then taper**<br>**If concurrent grade 2 or greater CRS, give Tocilizumab per CRS management in addition to corticosteroids** |

## Immune effector Cell-associated Encephalopathy (ICE) Assessment Tool

| | |
|---|---|
| **Orientations (4 points)** | Orientation to year, month, city, hospital |
| **Naming (3 points)** | Name 3 objects (point to clock, pen, button) |
| **Following commands (1 point)** | Show 2 fingers, or<br>Close your eyes and stick out your tongue |
| **Writing (1 point)** | Ability to write a standard sentence<br>"Our national animal is the Emu" |
| **Attention (1 point)** | Count backwards from 100 by ten |

**ICE Score**

**10:** No impairment
**7-9:** Grade 1 ICANS
**3-6:** Grade 2 ICANS
**0-2:** Grade 3 ICANS
**0:** Grade 4 ICANS – Unrousable & unable to perform ICE assessment

Lee et al 2019

# 3. Infection Risk: The Major Long-Term Challenge

## ONSET

- T-cell exhaustion
- Plasma cell depletion
- Hypogammaglobulinaemia

## COMMON INFECTIONS

- Respiratory viral infections
- Bacterial infections
- Opportunistic infections

## INCIDENCE

- Teclistamab 76%
- Elranatamab 69.9%
- Talquetamab 58.7%, 66.2%, and 72.5%

## MANAGEMENT

- IVIG replacement
- Antimicrobial prophylaxis
- Vaccination strategies
- Close surveillance

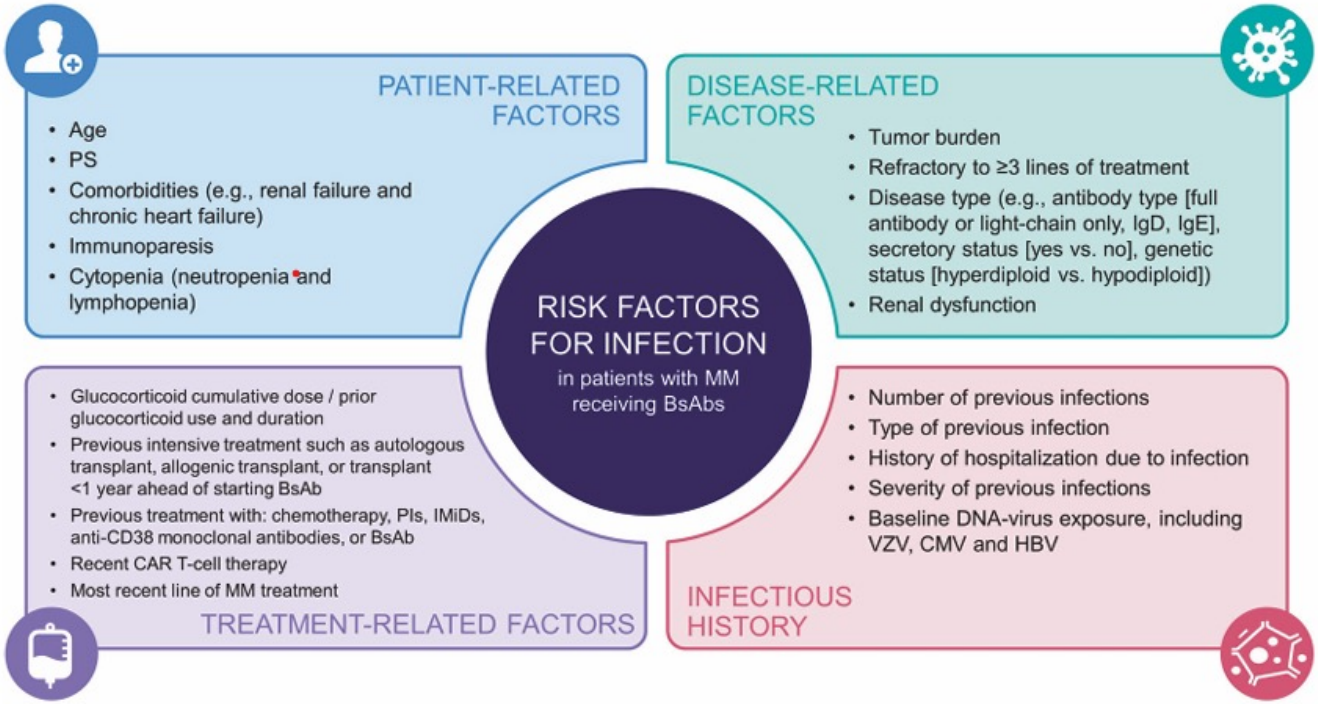



Fig. 1 Risk factors for infection in patients with MM receiving BsAbs. BsAb bispecific antibody, CAR-T chimeric antigen receptor T-cell, CMV cytomegalovirus, HBV hepatitis B virus, IMiD immunomodulatory drug, MM multiple myeloma, PI proteasome inhibitors, PS propensity score, VZV varicella zoster virus.

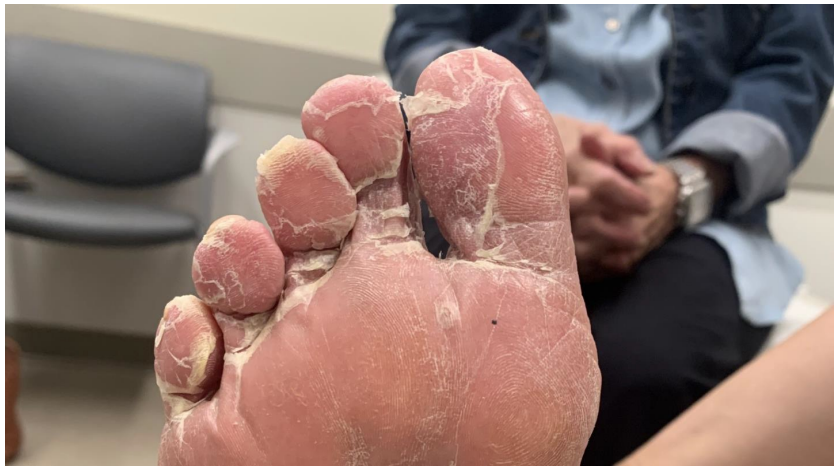
Schnike et al 2025 Infections and parameters of humoral immunity with talquetamab in relapsed/refractory multiple myeloma in MonumenTAL-1Blood Advances
Raje et al 2023 Monitoring, prophylaxis, and treatment of infections in patients with MM receiving bispecific antibody therapy:

# 6. Target Specific Toxicities
# GPRC5D – Skin Toxicities

Skin Toxicities
Palmoplantar keratoderma
Skin related event 67% Grade 3 0%

## Management

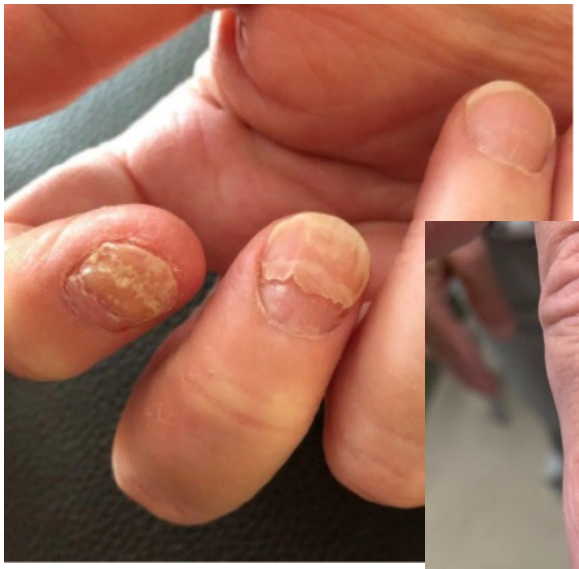
- Emollients (Cera-Ve, Cetaphil) within minutes of getting out of shower
- Topical steroids, e.g. Triamcinolone or Fluocinonide or Clobetasol
- Vaseline to hands, feet or areas with significant dryness
- Wear cotton gloves/socks at least 15-30 minutes to maximize absorption(overnight is best)

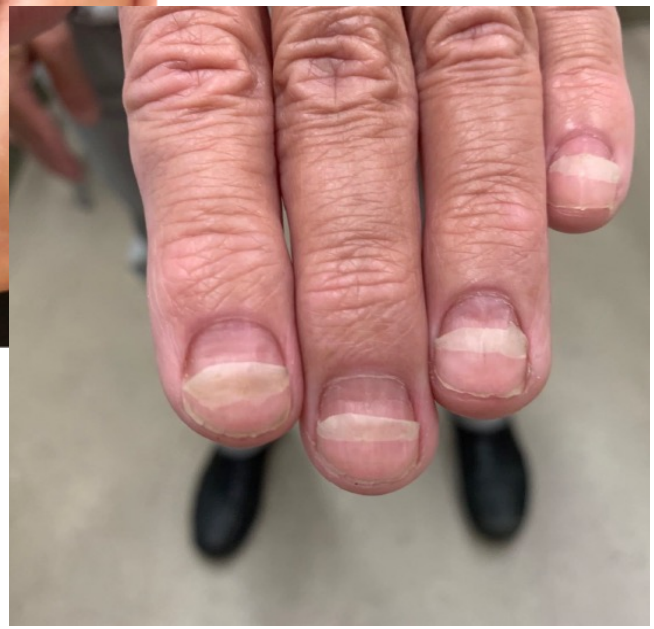


Samantha Shenoy, MSN, ACNP-BC UCSF, Medical Center, San Francisco, CA Presentation MM Bispecific antibody
Schinke CD, et al. ASCO 2023. Poster 8036; Catamero et al, IMS 2023
Chari et al 2025 Safety and activity of talquetamab in patients with relapsed or refractory multiple myeloma (MonumenTAL-1): a multicentre, open-label, phase 1–2 study. Lancet
Onychomadesis and palmoplantar keratoderma associated with talquetamab therapy for relapsed and refractory multiple myeloma - PMC

# 6. Target Specific Toxicities
# GPRC5D – Nail Toxicities

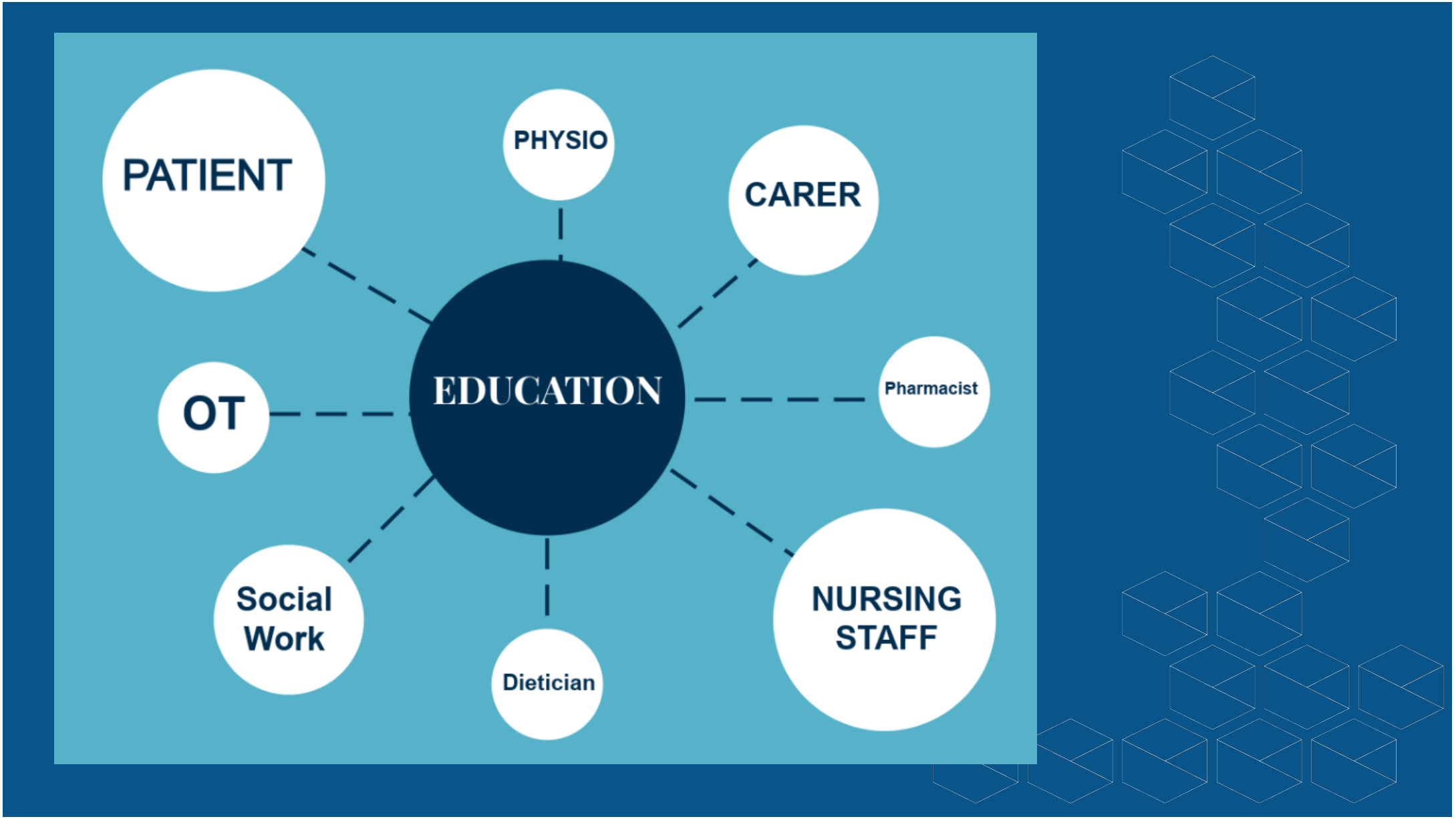
- Nail related event – 57% ≥ Grade 3 0%
- * Onycholysis
- * Onychomadesis
- * Ridging
- * Discoloration
- * Onychoclasis
- * Dystrophy
- Onset - Cycle 2-3 Median onset 69 days
- Median Duration 74 – 89 days
- 26-33% events resolve mostly Grade 1 – 2
- No Patients discontinued treatment due to nail toxicities





- **Management strategies**
- Avoid frequent/long durations of water immersion
- Frequent application of emollients - Vaseline
- File to smooth the edges
- Clear nail polish or nail hardeners
- Cuticle oil/Vit E oil to keep cuticles from drying out
- Avoid tight shoes; wear soft socks
- Monitor for any nail fold inflammation or paronychia (they are at increased risk of infection)

Samantha Shenoy, MSN, ACNP-BC UCSF, Medical Center, San Francisco, CA
Presentation MM Bispecific antibody
Chari et al 2025 Safety and activity of talquetamab in patients with relapsed or refractory multiple myeloma (MonumenTAL-1): a multicentre, open-label, phase 1–2 study. Lancet
https://myeloma.blog/talquetamab-nail-problems/


PATIENT
PHYSIO
CARER
EDUCATION
OT
Pharmacist
Social Work
Dietician
NURSING STAFF

# KEY TAKE HOME MESSAGES

**New Therapy**
**Haematology / Oncology / Radiation Oncology / Cellular Therapy**

- **EDUCATION**
- **Mechanism of Action**
- **Side Effect Profile**
- **NURSES – How can we support the patient?**

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Neurology
Medical Imaging
Occupational Therapy
Physiotherapy
Social Work

The patients and their families

# Questions?

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