MODULE 5

PATIENT CASE STUDIES

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*We would like to acknowledge the contributions of **Ms Sarah Lane** and **Ms Megan Trewhella** who contributed to the module development, but no longer work in their previous capacity as a melanoma nurse consultant*

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OVERVIEW

In this module, you will be able to put into practice the key learning objectives you have learnt over modules 1 – 4.

This module will present five different melanoma cases, each following a similar structure:

- Patient presentation & staging/diagnosis
- Additional information on patient
- Treatment approach
- Toxicity assessment
- Patient assessment & education
- Conclusion

LEARNING OBJECTIVES

- To understand the role of a multi-disciplinary team in evaluating melanoma patients
- To describe the common adverse events in melanoma patients receiving immunotherapy or targeted therapy
- To understand the evidence-based guidelines available for monitoring and managing common adverse events
- To feel confident in educating patients on common adverse events

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CASE STUDY 1

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57-YEAR-OLD MALE PATIENT DIAGNOSED WITH STAGE IIIB *BRAF V600K* POSITIVE MELANOMA*

*Based on a real patient. Photograph has been changed for the purposes of anonymity.

PRESENTATION

1991:

- Referred by GP with new biopsy-proven primary left posterior neck nodular melanoma
- Wide local excision (WLE) completed: Breslow thickness (BT) 1.5mm, Clark level IV, mitotic rate 4, ulcerated, no extracapsular extension, no SLNB, 20 mm margin

2016:

- Self-detected local regional disease, L) neck lymph node
- Underwent lymph node dissection: 1/15 nodes positive, *BRAF V600K* mutant positive

STAGING

Staging in 2016:

- T2b: primary tumour thickness >1.0–2.0 mm with ulceration
- N1b: one clinically detected, no presence of in-transit, satellite and/or microsatellite metastases
- M0: no evidence of distant metastases; CT/PET clear of disease as well as MRI brain

T2b, N1b, M0 = Stage IIIB

SLNB, sentinel lymph node biopsy

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ADDITIONAL HISTORY

- Works as a soil tester
- Married and lives with his wife
- Smoker, occasion ETOH

Comorbidities

- Hypertension
- Dyslipidaemia

ETOH, ethanol

TREATMENT APPROACH

- Patient case discussed at MDT meeting and referred to Medical Oncology for discussion about adjuvant therapy
- Medical Oncologist discussed the options of targeted therapy vs single agent immunotherapy vs surveillance with the patient
- The patient opted for 12 months of targeted therapy with dabrafenib + trametinib; commenced in October 2019

MDT, multidisciplinary team.

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TOLERABILITY ASSESSMENT

- Dabrafenib + trametinib commenced in October 2016
- Over the first few weeks, the patient felt nauseated
  - This settled following treatment with anti-emetics taken with a large glass of water
- Two weeks later, the patient experienced rigors and fever
  - Temperature 38.0–38.5ºC
  - Intermittent ankle joint pain: score 3–4 out of 10
  - Mild nausea, no diarrhoea
  - No reported UTI or RTI signs and symptoms

Impression: targeted therapy induced pyrexia

FBC, full blood count; RTI, respiratory tract infection; UTI, urinary tract infection.

ADJUVANT MELANOMA THERAPY: TOP 5 MOST COMMON AEs WITH DABRAFENIB + TRAMETINIB

AE	Any grade (%)	Grade 3 or 4 (%)
Pyrexia	63%	5%
Fatigue	47%	4%
Nausea	40%	<1%
Headache	39%	1%
Chills	37%	1%

AEs associated with targeted therapy differ from those associated with immunotherapy

Psychosocial support is very important to ensure medication adherence

Support patient coping during therapy and managing symptoms

Please see individual Product Information for additional safety information.
AE, adverse event.
1. Long GV *et al. N Engl J Med* 2017; 377:1813-1823.

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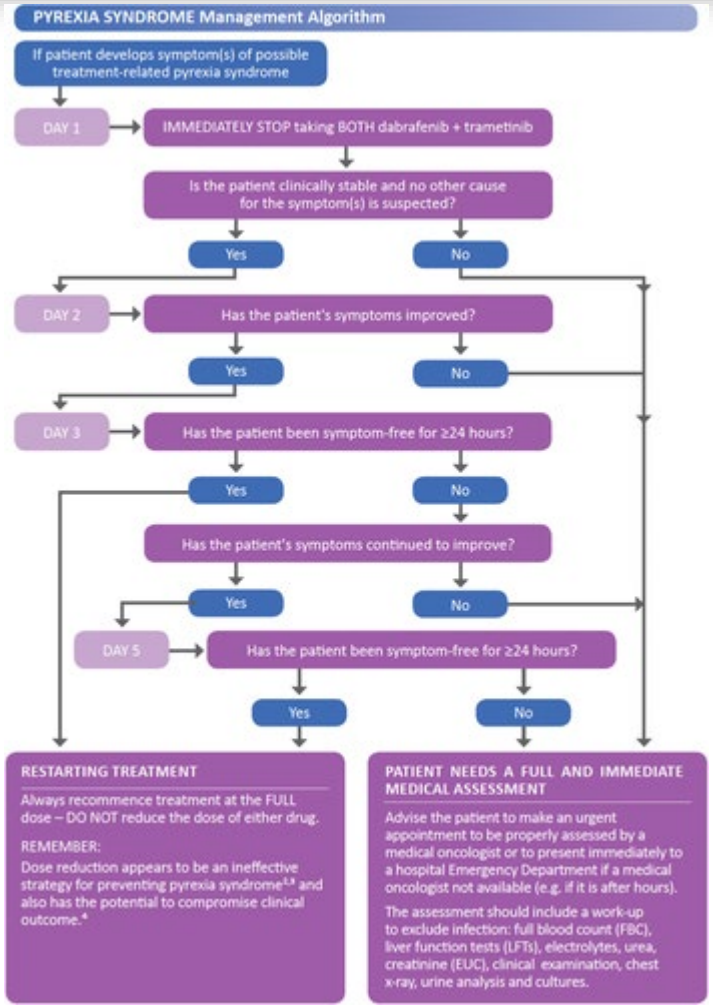
EVIDENCE-BASED MANAGEMENT APPROACH[1]

- Pyrexia is the most common adverse event in patients receiving dabrafenib + trametinib
- Non-infectious febrile events are common in patients treated with dabrafenib + trametinib at any time during the first 3 months[2]



1. Atkionson V, *e al*. *Asia-Pacific Journal of Clinical Oncology*. 2016. 30;12:5-12. eviQ. Fever and fever syndrome (BRAF MEK inhibitors only). Available at: https://www.eviq.org.au/side-effects-documents/1854-fever-and-fever-syndrome-braf-mek-inhibitors#history. Accessed January 2022.

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EVIDENCE-BASED MANAGEMENT (CONT)[1]

- There may be a "prodrome" where patients can identify the pending onset of pyrexia before temperature changes are observed
- Withhold treatment upon symptom onset. Early intervention results in prompt resolution of events, usually within 24 hours of dose interruption
- Recommencement of drug treatment can safely occur 24 hours after pyrexia resolution
- In cases of recurrent or severe pyrexia, an intermittent dosing regimen, and/or corticosteroids (prednisolone 10 to 25 mg daily) may be useful
- Unlike other toxicities such as fatigue, dose reduction does not appear to reduce the risk of pyrexia recurrence and is best avoided

1. eviQ. Fever and fever syndrome (BRAF MEK inhibitors only). Available at: https://www.eviq.org.au/side-effects-documents/1854-fever-and-fever-syndrome-braf-mek-inhibitors#history. Accessed January 2022.

PATIENT ASSESSMENT

- As per guidance, dabrafenib + trametinib withheld; regular paracetamol to help with fever and joint pain; no hospital admission required
- Dabrafenib + trametinib recommenced 24 hours after pyrexia resolved
- Recurrence of pyrexia episodes occurred after therapy restarted
- Low-dose steroids were introduced and the patient continued dabrafenib + trametinib therapy with no issues since

Ensure to:

- Exclude underlying infection (via relevant history, physical examination and investigations as appropriate)[1]
- A septic work-up is **not required** for patients with uncomplicated pyrexia and without localising infective symptoms[1]

1. eviQ. Fever and fever syndrome (BRAF MEK inhibitors only). Available at: https://www.eviq.org.au/side-effects-documents/1854-fever-and-fever-syndrome-braf-mek-inhibitors#history. Accessed January 2022.

PATIENT EDUCATION[1-3]

- Inform the patient to contact their oncology team – a treatment break may be required
- Paracetamol +/- ibuprofen PRN
- Provide reassurance
- Stay well hydrated, and rest
- Take lukewarm showers
- Nutritional support
- Gentle exercise

Additional information can be found in the CMI.

1. TAFINLAR® (dabrafenib) Product Information, 2021. 2. MEKINIST® (trametinib) Product Information. 3. eviQ. Fever and fever syndrome (BRAF MEK inhibitors only). Available at: https://www.eviq.org.au/side-effects-documents/1854-fever-and-fever-syndrome-braf-mek-inhibitors#history. Accessed January 2022.

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PATIENT EDUCATION (CONT)[1]

- Ensure patients understand which treatment they are on, the mechanism of action and side effects profile of systemic melanoma therapies
- Discuss the possible side effects and management (teaching and coaching self-monitor)
- Ensure patients understand when and how to contact their healthcare professional (including afterhours contact) if they experience any of these symptoms
- Ensure patients understand correct dosing, administration and importance of adherence
- Offer the information pack provided by the manufacturer
- Check for drug–drug and food–drug interactions

Educate patients on identifying pyrexia-related symptoms, to immediately stop taking their tablets, and immediately contact their healthcare team

Please see individual Product Information for additional safety information.

1. Czupryn M *et al. Clin J Oncol Nurs* 2017;21(4 Suppl):11-29.

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CASE STUDY 2

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75-YEAR-OLD MALE PATIENT DIAGNOSED WITH STAGE IV *BRAF* WILD-TYPE MELANOMA*

*Based on a real patient. Photograph has been changed for the purposes of anonymity.

PRESENTATION

- Presented with 4-month history of rectal bleeding, lower abdominal pain, lethargy and loss of appetite
- No past history of melanoma
- Colonoscopy identified lesion in the rectum 1 cm above the anal sphincter
- Initial biopsy results demonstrated a poorly differentiated carcinoma
- Immunohistochemistry (IHC) showed:
  - Negative for epithelial markers AE1/AE3, CK8/18, CK7 and CK20, negative for CDX2 and SATB2
  - Strongly and diffusely positive for SOX10
  - BRAF wild-type

STAGING

- PET/CT imaging showed hepatic and pleural lesions
  - Small scattered lesions throughout the right lung, largest in RUL measuring 4 mm
- MRI brain clear of metastatic disease

Diagnosis: Stage IV Metastatic anorectal melanoma with pulmonary, hepatic and pleural metastases

ADDITIONAL INFORMATION

- Married
- Two adult children – one lives locally
- Retired, active windsurfer

Comorbidities

- Hypercholesterolemia (treated with atorvastatin 80 mg)
- Allergy to penicillin (rash)

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TREATMENT APPROACH

- April 2019: The patient underwent abdominoperineal resection with VRAM flap reconstruction plus mesh plus stoma formation
- Dyspnoea onset 1 week later
- He was admitted to hospital 3 weeks after surgery with large left pleural effusion
  - VAT pleurodesis and pleural biopsy confirmed metastatic melanoma
  - LDH was elevated
- May 2019: Ipilimumab + nivolumab commenced

LDH, lactate dehydrogenase; VAT, video-assisted thoracoscopy; VRAM, vertical rectus abdominis.

TOLERABILITY ASSESSMENT

- Prior to cycle 1, the patient presented to the rapid assessment unit with increasing dyspnoea; Concern for re-accumulation of pleural effusion
- However, pleural ultrasound demonstrated pleural metastatic disease and insufficient fluid for thoracocentesis
- Significant hepatic progression was also noted
- Patient linked with palliative care services and home O_2 was organised
  - The patient reported an improvement in breathing improved appetite and reduction in pain
  - He completed induction therapy and repeat PET demonstrated reduction in pulmonary and hepatic metastases
  - LDH was also normalising
- The patient continued with nivolumab monotherapy from the fifth cycle^

^Most patients experience at least one immune-related adverse event of any severity whilst receiving induction ipilumumab + nivolumab.

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TOLERABILITY ASSESSMENT (CONT)

Patient attended clinic for *ad hoc* assessment by Melanoma and Skin Cancer Nurse:

- Presented with grade 3 rash after cycle 5 (on single agent nivolumab)
- Erythematous papular rash, non-tender over whole torso, upper arms and thighs
- No blisters, no oral mucosal involvement
- Moderate pruritis – whole body
- Numerous seborrheic keratoses over torso with new inflammatory base
- Estimated body surface area coverage of 45% (as per ESMO immunotherapy toxicity management guidelines, 2017[1])
- Clinical photography taken; No other symptoms/suspected irAEs

ESMO, European Society for Medical Oncology; irAE, immune-related adverse event.

1. Haanen JBAG *et al. Ann Oncol* 2017 Jul 1;28(suppl_4):iv119-iv142.

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PATIENT ASSESSMENT

- Findings discussed with medical oncologist and patient commenced on:[1]
  - Diprosone dipropronate 0.05% cream BD applications
  - Oral prednisolone 50mg daily
  - Loratadine 10mg daily for itch
- Delayed cycle 5 nivolumab
- Referral to Dermatology – good response to topical and systemic corticosteroids
- Commenced on steroid-reducing regime:
  - 37.5 mg daily for 1 week, 25 mg daily for 1 week, 20 mg daily for 1 week, 15 mg daily for 1 week, 10 mg daily for 1 week, 5 mg daily for 1 week, 2. 5mg daily for 1 week then stop.
- Wet dressing regimen for rash may be utilised. Further information on technique and application can be found here – https://dermnetnz.org/topics/wet-wraps

ESMO, European Society for Medical Oncology; irAE, immune-related adverse event.

1. Haanen JBAG *et al. Ann Oncol* 2017 Jul 1;28(suppl_4):iv119-iv142.

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PATIENT ASSESSMENT (CONT)

- Continued partial response to immunotherapy, patient continued on maintenance nivolumab
- 4 weeks later – corticosteroids weaned down to 15 mg daily, and he contacted service with worsening rash over upper and lower limbs
- On assessment: patient had continued BD topical steroid applications. Noted same erythematous papular rash, no blisters, non-tender
- Patient instructed to hold steroid dose at 15 mg daily and introduce wet dressings to topical management regime and review again in 1 week
- 1 week later – rash greatly improved with wet dressing applications, continued slow reduction of oral steroid and maintained BD application of topical steroid

PATIENT EDUCATION

- Educate patients on self-identifying immune-mediated rash
  - Teach them to identify old (darker red) versus new rash (bright, angry-looking) and to report concerning features early (such as blistering, tenderness or mucosal involvement)
- Give patients confidence in self-administering topical steroid as needed[1]
  - Advise them to use only until the rash has resolved
  - Teach them about the correct amount to use with the finger-tip unit measurement (i.e. one finger-tip unit of cream is enough to treat an area the size of two adult hands)

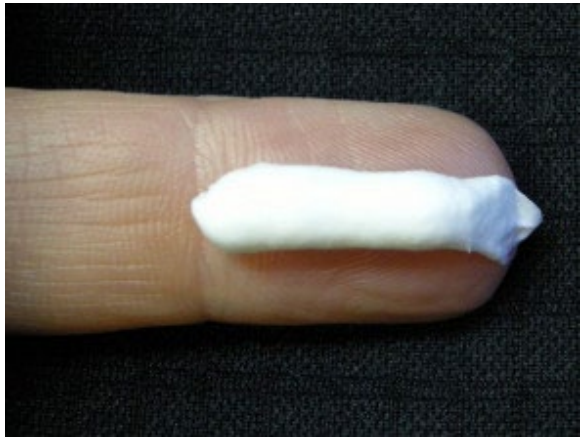

Image source: https://dermnetnz.org/topics/fingertip-unit.

1. Oakley A (2001). DermNET NZ. Finger-tip unit. Available at: https://dermnetnz.org/topics/fingertip-unit. Accessed April 2022.

CONCLUSIONS

- The patient experienced improved pain, appetite and breathing following initiation of immunotherapy
- Although the dermatitis flare negatively impacted his QoL, this was controlled with wet wraps and topical corticosteroids and his QoL has now improved
  - Once the rash resolved, he was feeling much better and could go back to windsurfing again
- He is immensely grateful that he had a great response to immunotherapy as he didn't think he was going to make it
- Occasionally, he has a dermatitis flare, but he is very aware of this now and able to confidently manage it

QoL, quality of life.

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CASE STUDY 3

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72-YEAR-OLD MALE PATIENT DIAGNOSED WITH *BRAF V600K* POSITIVE *STAGE IIIC* MELANOMA*

*Based on a real patient. Photograph has been changed for the purposes of anonymity.

PRESENTATION

November 2020:

- 0.9 mm SSM, non-ulcerated mid back primary, WLE

April 2021:

- GP palpated L) axillary node, referred for U/S guided core biopsy = melanoma
- PET scan: L) axilla LN, no evidence of further disease, MRI brain clear
- Lymph node dissection: 15/27 LN, focal extranodal tumour spread, largest focus 38 mm
- Extensive tumour necrosis noted and focal extranodal perineural extension of up to 2 mm is seen from 2 nodes
- *BRAF V600K* mutation positive

STAGING

Diagnosis

T1b N3b M0 = Stage IIIC

LN, lymph node; SSM, superficially spreading melanoma; U/S, ultrasound; WLE, wide local excision.

ADDITIONAL HISTORY

- Business owner: Sign writer
- Married, 2 adult children
- ECOG 0

Comorbidities

- Hypertension (treated with candesartan)
- Depression (treated with desvenlafaxine)

TREATMENT APPROACH

- Discussion with Medical Oncology and Radiotherapy regarding adjuvant options of radiotherapy, targeted therapy, immunotherapy or surveillance
- Due to extranodal extension and high risk of recurrence, the patient underwent a course of adjuvant radiotherapy (48Gy in 20 fractions)
- Targeted therapy was then commenced within 12 weeks of surgery based on potential short-term side effects versus potential long-term side effects of immunotherapy

TREATMENT APPROACH (CONT)

- Mild nausea for first week which settled without intervention
- 3 weeks after initiation, the patient developed fever (38.2°C), chills and headache
- Targeted therapy was stopped straight away and Clinical Nurse Consultant informed
- The patient took paracetamol for fever and symptoms resolved within 24 hours
- Once he was asymptomatic for another 24 hours, he was restarted on targeted therapy as per evidence-based guidelines
- No further fevers occurred, but routine bloods at 8 weeks showed Grade 2 hepatoxicity
- The patient was asymptomatic, but targeted therapy was withheld
- Patient had disease progression 3 months following cessation of targeted therapy

TREATMENT APPROACH (CONT)

- The patient was commenced on ipilimumab + nivolumab induction x4 treatments every 3 weeks
- Thyroid function at Cycle 2 showed hyperthyroidism: TSH 0.01 mIU/L and T4 37 pmol/L
- No symptoms of tachycardia, arrhythmia, palpitations, anxiety, tremor or sweating
- ECG NAD (carbimazole not considered unless patient symptomatic)
- The patient continued treatment but with weekly contact with a nurse to assess for symptoms
- The patient also experienced Grade 1 arthralgia (bilateral knee joints) treated with anti-inflammatories with good effect
- The nurse reiterated to the patient that he needed to call if he noted any changes in his condition
- Day 15 post Cycle 2, the patient phoned the Clinical Nurse Consultant with fatigue (wanted to sleep all day), nausea and headache

ECG, electrocardiogram; NAD, no apparent distress; T4, thyroxine; TSH, thyroid-stimulating hormone.

PATIENT ASSESSMENT

- The patient was asked to attend the Symptom and Urgent Review Clinic (SURC) for clinical assessment, blood test and supportive measures
- Blood test results: Cortisol 5 nmol/L; TSH now 17.6 mIU/L, T4 6.8 pmol/L
- He was then worked up for adrenal insufficiency as per endocrinology consultation (full endocrine blood panel)

Management approach

- Given IV hydrocortisone stress dosing as per hospital guidelines
- Started on 75 mg thyroxine for hypothyroidism
- IV N/Saline and anti-emetics due to Grade 1 hyponatraemia, Grade 1 hypotension and nausea
- Kept in clinic for 6 hours and reassessed; headache, hypotension and nausea resolved

ECG, electrocardiogram; NAD, no apparent distress; T4, thyroxine; TSH, thyroid-stimulating hormone.

PATIENT ASSESSMENT (CONT)

- The patient was sent home with oral hydrocortisone, at x2 maintenance dosing (stress dosing) for 2 days, then decreased back to normal maintenance dose
- Phone review with the Clinical Nurse Consultant occurred on the following day with future Endocrine and Oncology clinic appointments
- He was given an adrenal insufficiency advice plan/letter and education by the Clinical Nurse Consultant for times of illness or other stress to the body where risk for adrenal crisis is increased

Once the patient was asymptomatic,
he completed cycles 3 and 4 of ipilimumab + nivolumab

CONCLUSIONS

- The patient was concerned about stopping treatment before having four doses* of combination immunotherapy so was relieved when his endocrine toxicity did not prevent him from continuing treatment
- The patient didn’t realise how unwell he had been until he felt better!
- He had stopped his daily exercise routine due to lack of energy and is now back walking and cycling again
- He no longer feels nauseated, fatigued or has headaches. His low mood has improved since he has been able to get back to his normal daily activates

*In clinical practice, it is not uncommon for patients to discontinue immunotherapy treatment, or to not complete combination therapy induction therapy due to toxicities. Always discuss with the treating medical oncologist on the best course for your patient

CASE STUDY 4

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55-YEAR-OLD FEMALE PATIENT DIAGNOSED WITH *BRAF V600K* POSITIVE *STAGE III* MELANOMA*

*Based on a real patient. Photograph has been changed for the purposes of anonymity.

PRESENTATION

January 2020

- Self-detected axillary mass – no primary melanoma
- Left axillary dissection after PET/CT demonstrated no systemic disease
- Lymph node dissection: 6/31 nodes involved. With extracapsular spread
- *BRAF V600K* mutation positive

STAGING

Diagnosis

Lack of M staging, and presence of clinically detected nodal involvement confirmed stage III. However, as no T stage was provided, specific stage III sub-category is unknown.

LN, lymph node; SSM, superficially spreading melanoma; U/S, ultrasound; WLE, wide local excision.

ADDITIONAL HISTORY

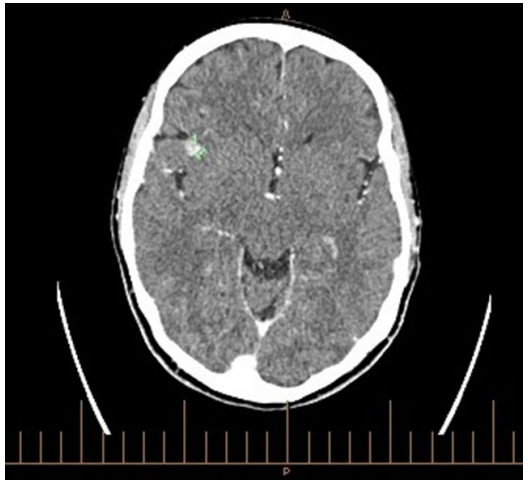
- Highschool teacher
- Married, with 3 children

Comorbidities

- No other medical history of note
- Occasional hayfever symptoms

TREATMENT APPROACH

- In March 2020, discussion with Medical Oncology and Radiotherapy regarding adjuvant options of targeted therapy or immunotherapy
- Proceeded to receive nivolumab
- MRI brain conducted prior to adjuvant nivolumab was clear, however routine scan after 3 cycles revealed brain metastasis



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TREATMENT APPROACH (CONT)

- Started on dabrafenib/trametinib with plan for interval MRI brain and consider Gamma knife
- Admitted in hospital for pyrexia syndrome, which was managed with treatment interruption. Frequent episodes following initial admission led to intermittent dosing, as per evidence-based guidelines
- Switched to encorafenib/binimetinib due to frequent pyrexia syndrome

CR: complete response

TOXICITY ASSESSMENT

- Patient maintained CR at next 3 month scan and continued on encorafenib/binimetinib
- Continued to experience frequent grade 1 fevers, managed with intermittent encorafenib/binimetinib treatment
- One month after commencing treatment, self-reported blurry vision and seeing "dark spots"
- Referral for ophthalmologist - diagnosed with targeted therapy induced central serous retinopathy

CR: complete response

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PATIENT ASSESSMENT

- According to eviQ guidelines, treatment was withheld and referral to ophthalmic review was performed
- Dose reduction to 300mg/30mg bd 2 days on and 5 days off due to poor tolerance of full-dose

The patient is continuing to respond clinically to encorafenib/binimetinib, yet still experiences intermittent fevers

1. Cancer Institute NSW, Melanoma metastatic biNIMEtinib and encorafenib (2022) Available at: https://www.eviq.org.au/medical-oncology/melanoma/metastatic/3600-melanoma-metastatic-binimetinib-and-encorafen#dose-modifications. Accessed December 2022

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CONCLUSIONS

- The patient was concerned about switching targeted therapies, however they were reassured that efficacy is similar
- The patient tolerated encorafenib/binimetinib poorly, and it did not improve pyrexia issues
- Still having ongoing ophthalmologic examinations; unfortunately the ocular toxicity has significantly impacted their work as a teacher and dose titrations and still being trialled.

CASE STUDY 5

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45-YEAR-OLD MALE PATIENT DIAGNOSED WITH *BRAF V600E* POSITIVE *STAGE IIIB* MELANOMA*

*Based on a real patient. Photograph has been changed for the purposes of anonymity.

PRESENTATION

September 2018

- 0.6mm SSM, mid-upper back, WLE
- Lymphatic mapping and U/S revealed
  two sentinel nodes in right axilla, and three in the left axilla

October 2019:

- Right axillary mass was clinically detected
- PET scan: confirmed metastatic melanoma in right axillary LN
- Bi-lateral lymph node dissection: R) 2/14 positive, 45mm and L) 1/18 positive, 25mm. Both with extracapsular spread
- *BRAF V600E* mutation positive

STAGING

Diagnosis

T1a N2b M0 = Stage IIIB

LN, lymph node; SSM, superficially spreading melanoma; U/S, ultrasound; WLE, wide local excision.

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ADDITIONAL HISTORY

- Lawyer
- Single (recently divorced) with 1 teenager
- ECOG 0

Comorbidities

- Mild vitiligo (not managed with any treatment)
- Depression (managed with therapy and counselling)

TREATMENT APPROACH

- Discussion with Medical Oncology and Radiotherapy regarding adjuvant options of targeted therapy and immunotherapy
- Due to extranodal extension, high risk of recurrence and young age, the patient started to receive pembrolizumab Q3W
- Pembrolizumab was started as the patient preferred not to take daily tablets

TOLERABILITY ASSESSMENT

- Mild nausea for first week which settled without intervention
- 3 weeks after initiation, the patient developed grade 2 diarrhoea
- The Clinical Nurse Consultant discussed with the patient at next infusion cycle and informed the Medical Oncologist
- The patient started taking prednisolone 25mg/day for one week, weaning by 5mg weekly

CONCLUSIONS

- The patient was concerned about the frequent colitis as it significantly impacted his day-to-day activities, and made him feel very embarrassed
- Steroid use has significantly helped the patient
- Review with gastroenterologist has been organised.
- The patient has changed his diet and meal times to avoid any nausea episodes, which was inconvenient at first but he is now used to it
- Upon completing 12 months of pembrolizumab, the patient has continued to have slightly watery diarrhea for an additional 6 months

PRACTICE POINTS

- Individualise your patient's education to suit their needs and build a good rapport with them
- Use the eVIQ Immunotherapy patient assessment tool to help assess all symptoms[1]
- Consult with your medical team for advice and support
- Frequent communication between the patient, their carers and the MDT is important in symptom management
- Provide education materials that patients can use as a reference at home
  - For patients on targeted therapy, patient booklets/diaries can help track and monitor how the patient is feeling
  - For patients on immunotherapy, ensure patients can identify immune-related AEs and are aware that some AEs may be permanent
- Emphasise to your patients that the earlier your medical team is informed of a symptom, the greater the potential that it will be treated and resolved quickly

MDT, multidisciplinary team.

1. eVIQ. Available at: https://www.eviq.org.au/clinical-resources/assessment-tools/3533-immunotherapy-patient-assessment-tool. Accessed February 2022.

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FOR **PRESCRIBING INFORMATION**, PLEASE CLICK:

Dabrafenib | Trametinib | Vemurafenib | Cobimetinib | Encorafenib
Binimetinib | Nivolumab | Ipilimumab | Pembrolizumab

FOR **PBS INFORMATION,** PLEASE CLICK:

Dabrafenib | Trametinib | Vemurafenib | Cobimetinib | Encorafenib
Binimetinib | Nivolumab | Ipilimumab | Pembrolizumab

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