Improving Cardiovascular Care for Patients Receiving Immunotherapy for Cancer in North London

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BACKGROUND

The role of immune checkpoint inhibitors (ICI) in the treatment of cancer is increasing. Since 2020, ICI are approved as first- or second-line therapy in over 50 malignancies and 43% of patients will have cancers eligible for an ICI.(1) This has led to an expansion in the number of patients receiving ICIs and the associated complications.

Cardiovascular immune-related adverse events (CV irAE) include myocarditis in 1.8% of patients.(2) Early recognition, aggressive immunosuppression, potential advanced heart failure therapies and management by a multidisciplinary team are required as the mortality is up to 50%.(3)

ICI are associated with a 3-fold increased risk of atherosclerotic cardiovascular events and ≥3-fold higher rate of aortic plaque progression.(4) Appropriate primary and secondary prevention for cardiovascular disease (CVD) are required.

The cardio-oncology service at Barts Heart Centre has experience of managing ICI-related myocarditis and has an established pathway for shared inpatient care with oncologists. Currently other hospitals refer patients on a case-by-case basis for specialist advice and transfer of care.

OBJECTIVES:

1. To improve the baseline CV risk assessment, primary and secondary CVD prevention management for patients receiving ICI;

2. To develop regional expertise in the identification and management of CV irAE;

3. To develop a specialist referral pathway for patients with CV irAE.

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METHODS:

A multi-professional working group was created consisting of cardiologists, oncologists and a cardio-oncology specialist nurse. The project schedule is illustrated (Figure 1).

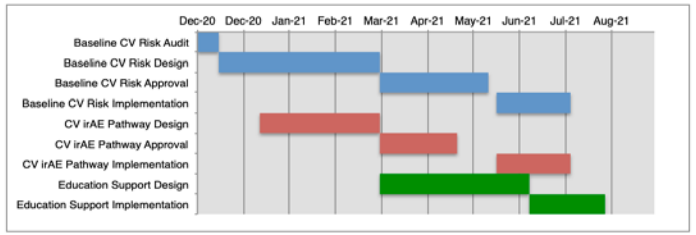
An audit of 20 consecutive patients commencing adjuvant ICI for malignant melanoma at St Bartholomew's Hospital in 2019-2020 was performed using data from GP and hospital electronic patient records. A QRISK®3 was calculated for all patients without established CVD.

Current patient pathways were reviewed. A GP guidance letter was developed, reviewed by a GP representative and submitted to Mount Vernon Cancer Centre, University College Hospital and St Bartholomew's Hospital Cancer Directorates for local approval. The proposed referral pathway for CV irAE was approved by the Cancer Directorate at St Bartholomew's Hospital: Five district general hospitals (DGH) with cardiology services were included as pilot sites for implementation.

RESULTS:

Audit: Two patients (10%) had a QRISK®3 calculated by their GP within 3 months prior to ICI. One patient (5%) had established CVD. The QRISK®3 was calculated for the remaining 19 patients. Nine patients (45%) had QRISK®3 ≥10%; two were already treated with a statin, whilst the remaining seven patients were untreated. **Baseline CV risk assessment is currently not performed for the majority of patients prior to commencing ICI.**

Figure 1. Gantt chart of the project schedule



RESULTS:

1. Baseline CV Risk Assessment: A letter to the GP recommending a baseline CV risk assessment, including QRISK®3, and guidance for primary prevention based on NICE guidance* was developed. Oncologists agreed to take the required blood tests in clinic and make the results available for the GP. A patient information leaflet was developed, which directs patients towards the Macmillan Cancer Support Heart Health and Cancer Treatment booklet.

2. Developing Regional Expertise: A local cardiologist was appointed in each DGH to be a local champion for patients with CV irAE. A programme of educational material for GPs, Cardiologists and Oncologists is being developed.

3. Referral Pathway for CV irAE: A proposed management pathway was developed (Figure 2). It provides guidance on the assessment and management of patients with CV irAE, including when and how to access specialist advice and when to consider transfer to the specialist centre based on the severity of myocarditis.

*Recommendations taken from NICE Guidance. Cardiovascular disease: risk assessment and reduction, including lipid modification [CG181]; Hypertension in adults: diagnosis and management [NG136]; Type 2 diabetes in adults: management [NG28]

Figure 2. Proposed CV immune-related adverse events management pathway

Consider cardiac immune-related adverse event in any patient on immunotherapy presenting with:
Chest pain, shortness of breath, palpitations, syncope, incidental cardiac biomarker rise / abnormal ECG, myocardial infarction, arrhythmias, heart failure, suspected pericarditis/ myocarditis, vasculitis, impaired LV function
High-risk patients: coronary artery disease, autoimmune disorders, combination immunotherapy, other IRAEs

Assessment:
History (inc. systems review for other IRAEs), Examination inc. weight
Bloods inc. Troponin, NT-proBNP or BNP, CK
ECG, CXR, Echo

If symptoms and assessment consistent with cardiac IRAE:
Urgently refer to the Acute Oncology Service (AOS)/oncology team.
If patient on a clinical trial, urgently contact their trial team
Stop the immunotherapy Treat cardiac presentation with usual treatment. Early cardiology review.

For all grades: Urgently contact AOS/oncology team.
Advice: Local cardiologist/AOS/oncology team can seek advice from Dr Ghosh/Dr Manisty at UCLH/St Bartholomew's Hospital (SBH) Cardio-oncology service.
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Grade 1 (Asymptomatic. Abnormal biomarkers/ECG)	AOS/oncology team to consider referral to local cardiologist.
Grade 2 (Mild symptoms. Abnormal tests)	Admit to local hospital with cardiac beds. Daily troponin & ECG
Grade 3 (Moderate symptoms. Abnormal tests)	Admit to local hospital with cardiac beds. Liaise with AG/CM. Aim to transfer to SBH. Daily troponin & ECG. If worsening despite 48 hours of steroid, for transfer to SBH.
Grade 4 (Severe symptoms. Requiring IV treatment of procedure)	Within hours, liaise with AG/CM. Out-of-hours, liaise with the Heart Failure on-call registrar at SBH (Tel: 07825 976924). Transfer to SBH. N.B. if requires emergency pacing, temporary permanent system preferable as AV block may be reversible once immunotherapy stopped

CONCLUSION:

Through collaboration with a multi-professional team and engagement with different institutions we have developed cross-site pathways to improve the baseline CV risk assessment and management of CV immune-related adverse events in patients receiving immune-checkpoint inhibitors. The effect of this project will be evaluated in a re-audit.

We aim to expand the network of hospitals involved in these pathways.

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