IOCN

The Immuno-Oncology Clinical Network

Consensus Statement

Baseline cardiac assessment in individuals receiving immune checkpoint inhibitors: A Joint Consensus Statement

In collaboration with the
British Cardio-Oncology Society

BRITISH CARDIO ONCOLOGY SOCIETY

Baseline cardiac assessment in individuals receiving immune checkpoint inhibitors: A Joint Consensus Statement

Table of Contents

Collaborators:

Dr Ajay Sudan	Medical Oncology Consultant	Newcastle Upon Tyne Hospitals NHS Foundation Trust
Dr Alexandra Johnson	Medical Oncology SpR	Clatterbridge Cancer Centre NHS Foundation Trust
Ms Alice Tew	Advanced Clinical Pharmacist	University Hospitals Birmingham NHS Foundation Trust
Ms Alison Hodge	Nurse Consultant & Immunotherapy Lead Nurse	University Hospitals Sussex NHS Foundation Trust
Dr Anna Olsson-Brown	Medical Oncology Consultant	University Hospitals Sussex NHS Foundation Trust
Dr Arjun Ghosh	Consultant Cardiologist	St Barts Heart Centre and University College Hospitals, London
Dr Brent O'Carrigan	Medical Oncology Consultant	Addenbrooke's Hospital, Cambridge
Prof Charlotte Manisty	Consultant Cardiologist	St Barts Heart Centre and University College Hospitals, London
Dr Chris Plummer	Consultant Cardiologist	Newcastle Upon Tyne Hospitals NHS Foundation Trust
Dr Clare Barlow	Medical Oncology Consultant	Somerset NHS Foundation Trust
Dr Heather Shaw	Medical Oncology Consultant	University College London Hospital and Mount Vernon Cancer Centre
Dr Kate Young	Medical Oncology Consultant	The Royal Marsden NHS Foundation Trust
Dr Laurence O'Toole	Consultant Cardiologist	Sheffield Teaching Hospitals NHS Foundation Trust
Dr Rebecca Dobson	Consultant Cardiologist	Liverpool Heart & Chest Hospitals NHS Foundation Trust
Dr Ricky Frazer	Medical Oncology Consultant	Velindre Cancer Centre
Prof Stuart Rosen	Consultant Cardiologist & Professor of Practice (Cardiology)	Imperial College, London
Dr Susan Ellery	Consultant Cardiologist	University Hospitals Sussex NHS Foundation Trust
Ms Trudy-Jane Guinan	Nurse Consultant & Immunotherapy Lead Nurse	Clatterbridge Cancer Centre NHS Foundation Trust

Background

The cardiovascular (CV) side effects of immune checkpoint inhibitors (ICIs) are an increasingly recognised complication of contemporary cancer treatment. So-called cardiac immune related adverse events (irAEs) include myocarditis, peri-myocarditis, arrhythmias, cardiac dysfunction and acute coronary events, and they occur collectively in 6.6-10.3% of patients treated.[1,2] Myocarditis, whilst relatively infrequent, is associated with complex immunosuppressant requirements, long treatment courses and comparatively high mortality rates. Even in the event of recovery (normalisation of troponin or resolution of myocarditis), the diagnosis of myocarditis currently leads to discontinuation of ICI treatment in the vast majority of patients.

The reported incidence of ICI-induced CV complications is likely under-reported, given the historical lack of awareness and challenges of diagnosis. Early use of ICI was predominantly in the metastatic setting, where late cardiovascular outcomes were less critical, although some patients could have a complete and durable response. However, as ICIs become increasingly utilised across multiple tumour groups in the neoadjuvant, perioperative and adjuvant settings, risk stratification, early diagnosis and treatment for CV irAE is now of significant clinical value.

The European Society for Cardiology (ESC) 2022 Cardio-Oncology guidelines have specifically reviewed the need for baseline evaluation and risk stratification prior to initiating cancer treatment. The ESC recommends an ECG, BNP or NT-proBNP, and troponin (T/I) measurements in all patients before starting ICI therapy, which has implications both in terms of service provision, and the training required to interpret the results. Patients stratified as high-risk are recommended to undergo baseline echocardiography before starting ICI therapy.

It is however, important to highlight that the majority of risk stratification will be performed by the treating oncologist, and oncology and cardiology services in the UK are diverse, with differing expertise and access to investigations. Additionally, the number of specialist cardio-oncology services in the UK is currently small, and the recognition and understanding of the cardiotoxicities of ICI treatment is limited. The IOCN has had significant feedback from both cardiologists and oncologists who feel uncertain how to implement baseline cardiac biomarker testing for a variety of reasons, including the potential service impact, uncertainty on who should be acting on abnormal results and what actions should be taken.

As a result, the IOCN trustees have identified a need for a UK consensus statement in collaboration with the British Cardio-Oncology Society (BCOS), and multiprofessional groups including cardiologists with an interest in cardio-oncology, oncologists and oncology nurses. This consensus statement is not intended to replace existing guidance, but to help oncologists and cardiologists navigate their implementation and delivery in the NHS.

Aims of the Consensus Statement

- To guide oncologists and cardiologists in implementing baseline testing prior to starting immune checkpoint inhibitor treatment.
- To guide oncologists and cardiologists on interpreting and acting upon the results without causing unnecessary delay in a patient's cancer treatment.
- Recommendations from the consensus should be deliverable for the majority of services across the UK, and include a comprehensive algorithm that can be applied to services with and without a specialist cardio-oncology or immunotherapy team.

This document lays out a series of generalised principles for undertaking and interpreting baseline testing. These require individual interpretation by the patient's clinical team in the context of each patient's individual risks, needs and timelines.

Development

A scoping meeting on 22nd February 2024 brought together Oncologists, Cardiologists, Cardio-Oncologists and Cancer Nurse Specialists to discuss the aims and objectives of the project.

Consensus Statement Executive Summary

It was agreed that baseline testing should be undertaken in all patients starting immune checkpoint inhibitor immunotherapy. These should include troponin T or I, NT-pro BNP or BNP and a baseline 12-lead ECG. The group recognised the need for collaboration between oncologists and cardiologists to develop a locally adapted and implemented management framework of baseline testing, derived from a national suggested framework. This framework should also minimise the potential for a single point of failure in screening (e.g. utilising immunotherapy toxicity teams, site specific cancer nurses or acute oncology teams) and highlight the importance of early screening to avoid delays in treatment.

The group also discussed and agreed with the definition of high-risk patients in the ESC guidelines. This includes patients on combination ICI-cardiotoxic therapy, dual combination ICIs or those with a history of cardiovascular disease. All patients should have a baseline assessment including biomarkers and ECG, but the use of echocardiography should be targeted to those with highest background risk or abnormal baseline biomarkers/ECG.

Alongside the importance of identifying high risk patients, baseline screening also highlights patients who would have a poorer prognosis if they were to develop CV ICI toxicity. It also provides a very important comparator to distinguish between background CV disease and cardiotoxicity, especially in patients with pre-existing CVD.

There was acknowledgement from the group that there needs to be a national roll out of baseline testing to ensure consistency of care. Local centres should be supported by oncology departments and biomedical scientists to be able to deliver the minimum biomarker evaluation for all patients commencing ICIs.

It was accepted that this carries a potential financial burden. However, compared to the cost of cardiotoxicity (occurring approx. 6.6- 10.3%)[1], early diagnosis and prompt management can avoid attendance and admission to hospital, and the use of high-cost biological therapies. Therefore, there is potentially a large cost saving associated with baseline biomarker testing and baseline ECGs.

Baseline Testing

The Utility and Importance of Baseline ECGs

ESC guidance recommends baseline clinical CV assessment, physical examination and 12-lead ECG in all cancer patients scheduled for cardiotoxic therapy. It is standard practice for many patients commencing chemotherapeutic Systemic Anti Cancer Therapy (SACT) to have a baseline ECG (e.g. 5FU and anthracyclines), therefore ECGs may be performed in SACT delivery units or outpatient departments (i.e. as part of the oncology pathway). New and evolving ECG changes are an integral component (alongside biomarkers, imaging and clinical assessment) of the diagnosis of ICI-associated cardiovascular toxicities including myocarditis. Baseline ECGs therefore provide a useful comparator if patients are admitted with concerns of cardiotoxicity. For example, AV conduction disease can be caused by ICIs in the presence or absence of myocarditis.

Baseline ECG Pathway and Interpretation

A good quality baseline 12-lead ECG should be performed and interpreted by an appropriate clinician. It is recommended that all oncology services have a formalised pathway for ECG review by a clinician in a timely manner prior to patients starting treatment. However, the experience and availability of oncologists to interpret ECGs is variable. Some centres may therefore feel it reasonable for this to be an oncology delivered service, while others may consider a baseline ECG being conducted in a cardiology department, and others may elect to develop a formal review process with cardiology clinicians (e.g. heart rhythm nurse specialist). There is a common perception that ECG machines tend to over- rather than under-report abnormalities, but studies show evidence of both false positives and false negatives[3]. Consideration of the local mechanisms for ECG acquisition and interpretation should be embedded into a local pathway to support consistency.

Baseline ECGs should be accessible wherever a patient receives clinical care, hence digital ECG storage is preferable to paper copies. It must be available in the patients' clinical records. These should be shared with other clinicians through a Health Information Exchange (e.g. The Great North Care Record (https://www.greatnorthcarerecord.org.uk/, One London https://www.onelondon.online/) and a copy of the ECG should be offered to the patient.

Recording a baseline ECG should not delay cancer treatment, but any significant abnormality which needs urgent cardiology input must be identified and acted upon by an appropriate clinician. Whilst minor findings are unlikely to require urgent intervention, recognition of highly concerning features that need immediate action is important. Concerning features on an ECG should also prompt a cardiovascular history and physical examination including auscultation for significant murmurs or fluid retention.

Baseline Testing

The following findings on a baseline ECG should warrant urgent review and the patient should not proceed with ICI therapy:

- Acute Ischaemia on ECG (to be reviewed in clinical context)
- Undiagnosed non-sinus tachycardia
- 2nd or 3rd degree AV block
- Widespread deep T wave inversion in keeping with cardiomyopathy

The consensus statement group recommend cardiology or cardio-oncology advice and accompanying referral for patients where there are cardiovascular concerns or ECG abnormalities including:

- 3 or more ventricular ectopic beats on a standard ECG
- Q waves consistent with previous MI
- Abnormal T wave inversion consistent with cardiomyopathy
- PR interval >200ms (5mm) or any non-conducted P waves
- Any atrial or ventricular arrhythmia
- Left bundle branch block (to confirm if new or old correlate with previous ECGs or joined up care system if able)

Atrial fibrillation or flutter are common and should be communicated to the patient's GP, if not previously diagnosed, to consider anticoagulation. They do not need immediate action unless they are causing symptoms or there are rate concerns e.g. AF with a fast (HR >110) or slow (HR <60) ventricular response.

Regular ECG interpretation and monitoring is important in patients with suspected myocarditis to identify patients at risk of cardiac arrhythmias, inform the clinical trajectory and help guide immunosuppressant management. A series of protocols and suggested guidelines to inform clinicians on ECG changes and monitoring can be found via:

https://www.ioclinicalnetwork.co.uk/clinical-support/io-cardiac-complications.

There is also an intention from the consensus group to develop a myocarditis consensus statement in the near future.

Cardiac Biomarkers

Baseline cardiac blood biomarkers provide an indicator of underlying cardiac dysfunction and serve as an important baseline comparator as part of the clinical assessment of patients with potential cardiotoxicity, including for diagnosis and prognosis of ICI-associated myocarditis. The utility and importance of baseline biomarker testing is reflected in a number of guidelines and studies.[4,5,6] This consensus group strongly recommends baseline biomarker testing in all patients starting ICI treatment.

The choice of troponin assay, and choice of BNP or NT-pro BNP utilised by the oncology or SACT departments will ultimately be determined by local availability, and it does not matter which is undertaken.[7] However, it is important to note that it is difficult to compare Troponin T vs Troponin I, or BNP versus NT pro-BNP as they are not interchangeable. Whilst there is only one troponin T assay. There are multiple different troponin I assays The assays used for baseline testing should therefore be the same as those used during treatment, with communication and agreement between specialist cancer and cardiology units where feasible.[8]

Baseline biomarker testing will incur a cost to the oncology or SACT department. However, it is important that ICI treatments are prescribed as safely as possible to help identify patients at high risk of cardiovascular toxicities, and those who will tolerate cardiac toxicity poorly. ICI-induced myocarditis also incurs high costs associated with acute admission and complex treatment and remains associated with a significant mortality rate.

Interpretation of baseline values

It is expected that the majority of patients will have baseline biomarker results within acceptable limits not requiring intervention and thus services will not be overwhelmed by abnormal results.[9]

Raised baseline biomarker values should always be interpreted in the clinical context but may require further investigation and discussion with local cardiology or cardio-oncology teams. Elevated values should not be an automatic bar to initiation of ICI therapy but may require additional investigations and increased monitoring during ICI treatment. Abnormal baseline values should be interpreted on a clinical risk of ICI induced CV complications vs the treatment benefit or options available. For example, some tumour groups have no other 1st line treatment options other than immunotherapy vs other tumour sites with alternative non ICI options.

Some oncology centres may not have easy or timely access to cardiology or cardio-oncology review, investigations or advice. Therefore the decision to continue with ICI treatment prior to cardiology may need to be made on a risk vs benefit decision by the treating oncologist prior to further investigation.

Raised baseline biomarkers should not be assumed to be due to metastatic disease as there does not appear to be a different baseline biomarker value set for patients with metastatic cancer vs the normal population.

Biomarker Interpretation Pathway

The following pathway has been formulated to help clinicians interpret and act pragmatically on baseline results:

Baseline results normal
TnT < 14ng/L
TnI < 50ng/L
(check local normal range)
and
NT Pro-BNP/ BNP <400ng/L
(check local normal range)

→ **No action required.**

Baseline results mildly elevated
TnT 14-50ng/L or TnI >50-200ng/L
(check local normal range)
and/or
NT Pro-BNP/BNP = 400-1000ng/L
(check local normal range)

→ **Consider signs, symptoms and history of acute coronary syndrome and/or heart failure**

- **Review baseline ECG**
- **Request echocardiogram**

Consider discussion with local cardiologist / cardio-oncologist
– patients do not necessarily need to wait for this prior to starting ICI treatment if the treating oncologist regards this as a low risk.

Baseline results elevated
TnT >50ng/L or TnI >200 ng/L
and/or
NT Pro-BNP/ BNP > 1000 ng/l
** Unless biomarkers can be explained in clinical context or that cardiology advise in keeping with pre-existing cardiac conditions e.g. rate controlled AF***

→ **Referral to local cardiologist/ cardio-oncologist**
Request echocardiogram

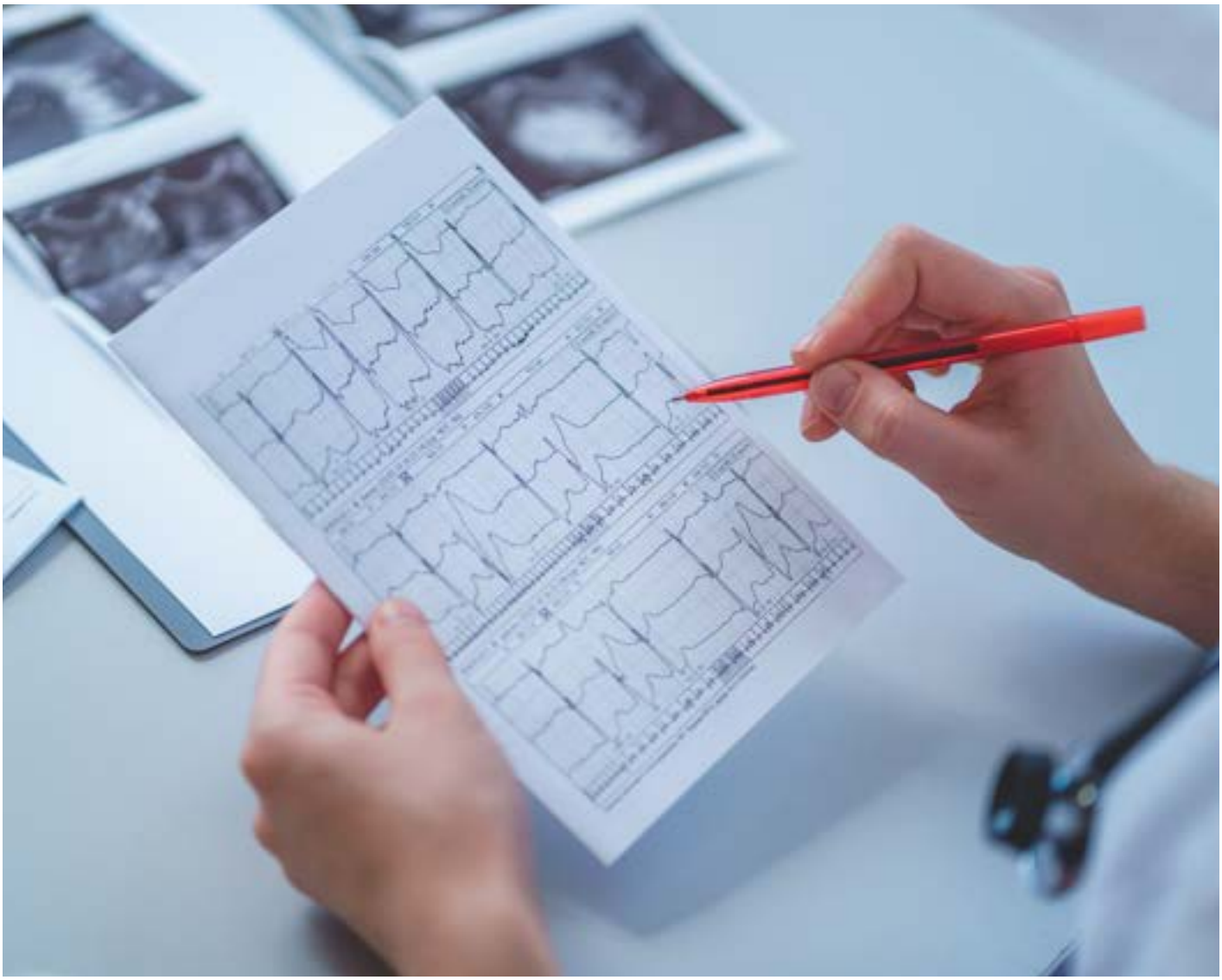
NOTE – Symptomatic patients or any conerns from treating oncologist need urgent referral to cardiology prior to starting ICI (unless the balance of risk vs benefit is felt to warrant treatment prior to review). Asymptomatic patients do not necessarily need to wait for cardiology review prior to starting ICI if no concerns from treating oncologist.

In some patients identified by the clinical team, pre-cycle monitoring may be required for those with significant risk factors and/or raised baseline cardiac markers.

Patients with abnormal baseline biomarkers and pre-existing cardiac disease

There is increasing evidence that patients with pre-existing cardiovascular disease are at increased risk of developing ICI induced myocarditis.[10,11,12] Although a personalised risk is very difficult to quantify at present, patients with abnormal baseline biomarkers who have been identified to have pre-existing cardiac disease need to be appropriately counselled about the increased risk of myocarditis, and the implications of this vs the benefit of treatment.

Some patients with abnormal baseline biomarkers and identified cardiac disease should be considered for pre-cycle monitoring or repeated imaging, as illustrated in the ESC guidelines.[13] However, in a UK study of 400 patients the clinical utility of pre-cycle screening has not demonstrated enhanced or earlier detection of myocarditis compared to clinical assessment and represents an area of potential.[14]



Cardiovascular Imaging

Utility and importance of baseline imaging

Cardiovascular imaging is of value prior to ICI in selected high-risk patients. This is both to aid risk stratification in patients with known or suspected cardiovascular disease, and to provide a baseline assessment for subsequent comparison during treatment in patients at high risk of cardiovascular events during treatment.[13] Although there is no strong evidence linking conventional cardiovascular risk factors or pre-existing cardiovascular disease with subsequent incidence of immune-related myocarditis, patients with lower cardiovascular reserve at baseline are likely to tolerate complications less well. Detection of cardiovascular disease at baseline gives an opportunity to optimise risk factors and start evidence-based treatment prior to ICI exposure.

Recommended Imaging Modality

Transthoracic echocardiography is recommended as the first-line imaging modality in this context, and comprehensive UK guidelines for echocardiography in cancer patients have been previously published.[15] Protocols should include 3D ejection fraction and global longitudinal strain measurement where feasible, and blood pressure should be recorded to document haemodynamic conditions at the time of the scan. Initiation of immunotherapy need not be delayed in asymptomatic patients, although echocardiography should be performed prior to administration of the second cycle.

Patients with cardiac symptoms suggestive of angina at baseline may require further investigation with angiography (CT or invasive) or functional imaging (stress echocardiography, nuclear perfusion or perfusion CMR) following review by cardiology or cardio-oncology before ICI initiation.

For patients being re-challenged following a cardiotoxic event on ICI, CMR including full tissue characterisation with parametric (T1, T2 and ECV) mapping and late enhancement imaging should be performed to assess for residual myocardial oedema, and provide a comparator in case of subsequent cardiac complications.

The high coronary event rate in patients receiving immunotherapy means that baseline cardiovascular risk factor optimisation is recommended. Patients with a history of a previous cardiovascular event should have appropriate secondary prevention treatment. This optimization can either be done in primary care (in the vast majority of patients as part of their cardiovascular risk profile), by their treating oncologist or by a cardiologist if this is felt inappropriate. Those with a QRISK®[3] score of >10 over 10-years should be offered atorvastatin 20mg daily (https://qrisk.org/). Coronary artery calcium (CAC) scoring may further stratify atherosclerotic risk, and although non-ECG gated, assessing coronary calcium from standard thoracic CT images is feasible and recommended by radiology guidelines.[16] As most patients starting ICI will have undergone CT for diagnosis and/or staging, image review for coronary calcium and subsequent administration of statins for those at high risk with high calcium burden should be considered.[17,18]

Cardiovascular Imaging

Recommendations

- Transthoracic echocardiography is recommended for patients with:
  - Known cardiovascular disease (coronary artery disease, moderate or greater valvular heart disease, heart failure, arrhythmias, prior myocarditis).
  - Previous exposure to cardiotoxic therapies (anthracyclines, targeted therapies including HER2 agents, prior immunotherapy) ECG and biomarker measurements abnormalities at baseline.
  - Cardiac symptoms (chest pain compatible with angina, exertional shortness of breath, palpitations interfering with activities of daily living).
  - On re-challenge following prior suspected or diagnosed IO cardiotoxicity.

- Echocardiography protocols should include GLS and 3D measurements where available (as per BSE/BCOS guidelines) including blood pressure recording.

- For patients where significant abnormalities are detected (LVEF <50%, moderate or greater pericardial effusion, intracardiac mass or thrombus, moderate or greater valvular heart disease, elevated pulmonary pressures), discussion with local cardiology is recommended.

- Pathways should be agreed with partner hospitals where echocardiography is not available on-site to ensure streamlined referral, with timely scan scheduling and transfer of reports back to the referring cancer centre.

- For patients with symptoms at baseline (e.g. chest pain compatible with angina) further imaging, including stress echocardiography, may be required.

- For patients being re-challenged following prior IO myocarditis, cardiovascular MRI (CMR) including full tissue characterisation is recommended.

Education and Training

Education and training in the interpretation of baseline values needs to be delivered on a local level between oncologists and cardiologists. The consensus group recognises that not all hospitals have a cardiologist with experience in cardio-oncology that can provide this. The IOCN and BCOS aim to provide educational tools and resources that can be used in oncology and cardiology departments.

Conclusion

The consensus statement group strongly recommends the implementation of baseline cardiac biomarkers and a baseline ECG for all patients starting ICI treatment as well as appropriate imaging in selected patients as outlined in this document. Although the implementation may be complex to deliver the guidance above provides cardiologists and oncology teams with a pragmatic approach to interpretating and acting on baseline biomarkers.

Collaboration between oncologists and cardiologists is essential, as is the development of a locally adapted and implemented management framework of baseline testing derived from the national suggested framework outlined in this document. Local centres should be supported by oncology departments and biomedical scientists to be able to deliver the minimum biomarker evaluation for all patients commencing ICIs, which has a favourable cost benefit when compared to the financial toxicity of myocarditis.

For more information please visit www.ioclinicalnetwork.co.uk

References

1. D'Souza M, Nielsen D, Svane IM, Iversen K, Rasmussen PV, Madelaire C, et al. The risk of cardiac events in patients receiving immune checkpoint inhibitors: a nationwide Danish study. Eur Heart J. 2021; 42:1621–1631.
2. Laenens D, Yu Y, Santens B, Jacobs J, Beuselinck B, Bechter O, et al. Incidence of cardiovascular events in patients treated with immune checkpoint inhibitors. J Clin Oncol. 2022; 40: 3430–3438.
3. Schläpfer J, Wellens HJ. Computer-Interpreted Electrocardiograms: Benefits and Limitations. J Am Coll Cardiol. 2017 Aug; 29;70(9):1183-1192.
4. Lyon AR, Yousaf N, Battisti NML, Moslehi J, Larkin J. Immune checkpoint inhibitors and cardiovascular toxicity. Lancet Oncol. 19 (9) (2018) e447–e458.
5. Lyon AR, Dent S, Stanway S, et al. Baseline cardiovascular risk assessment in cancer patients scheduled to receive cardiotoxic cancer therapies: a position statement and new risk assessment tools from the Cardio-Oncology Study Group of the Heart Failure Association of the European Society of Cardiology in collaboration with the International Cardio-Oncology Society. Eur. J. Heart Fail. 22 (11) (2020) 1945–1960.
6. Pudil R, Mueller C, Celutkien˙ J, et al. Role of serum biomarkers in cancer patients receiving cardiotoxic cancer therapies: a position statement from the Cardio-Oncology Study Group of the Heart Failure Association and the Cardio-Oncology Council of the European Society of Cardiology. Eur. J. Heart Fail. 22 (11) 2020) 1966–1983.
7. Talukder S, Ghose A, Chakraborty T, et al. Evolving cardiac biomarkers for immune checkpoint inhibitor related myocarditis in cancer patients. Int J Cardiol Heart Vasc. 2023 Oct 8;49:101278.
8. Barac A, Wadlow RC, Deeken JF, deFilippi C. Cardiac Troponin I and T in ICI Myocarditis Screening, Diagnosis, and Prognosis, JACC: CardioOncology, 2024,ISSN 2666-0873.
9. Waliany S, Neal JW, Reddy S, Wakelee H, shah SA, Srinivas S et al. Myocarditis Surveillance with high sensitivity troponin I during cancer treatment with immune checkpoint inhibitors. JACC CardioOncology (2024); 3: 137-9.
10. Oren O, Yang EH, Molina JR, Bailey KR, Blumenthal RS, Kopecky SL. Cardiovascular Health and Outcomes in Cancer Patients Receiving Immune Checkpoint Inhibitors. Am J Cardiol. 2020 Jun 15;125(12): 1920-1926. doi: 10.1016/j.amjcard.2020.02.016. Epub 2020 Mar 5. PMID: 32312493.
11. Rubio-Infante N, Ramírez-Flores YA, Castillo EC, Lozano O, García-Rivas G, Torre-Amione G. Cardiotoxicity associated with immune checkpoint inhibitor therapy: a meta-analysis. Eur J Heart Fail. 2021 Oct;23(10):1739-1747. doi: 10.1002/ejhf.2289. Epub 2021 Jul 29. PMID: 34196077.
12. Noseda R, Ruinelli L, Gaag LCV, Ceschi A. Pre-Existing Cardiovascular Conditions as Clinical Predictors of Myocarditis Reporting with Immune Checkpoint Inhibitors: A VigiBase Study. Cancers (Basel). 2020 Nov 23;12(11):3480. doi: 10.3390/cancers12113480. PMID: 33238481; PMCID: PMC7700285.
13. Lyon et al. ESC Scientific Document Group. 2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). Eur Heart J. 2022 Nov 1;43(41):4229-4361.
14. Johnson A, Pickering S, Garbutt N, Guinan T, Dobson R, Olsson-Brown A. 2035P Routine biomarker monitoring does not replace comprehensive clinical assessment in the detection of immunotherapy induced myocarditis. Annals of Oncology. Oct 23. Volume 34, Supplement 2, S1080.
15. Dobson R, Ghosh AK, Ky B, Marwick T, Stout M, Harkness A, et al: British Society of Echocardiography (BSE) and the British Society of Cardio-Oncology (BCOS). BSE and BCOS Guideline for Transthoracic Echocardiographic Assessment of Adult Cancer Patients Receiving Anthracyclines and/or Trastuzumab. JACC CardioOncol. 2021 Mar 16;3(1):1-16.
16. Williams MC, Newby DE, Nicol ED. Coronary atherosclerosis imaging by CT to improve clinical outcomes. J Cardiovasc Comput Tomogr. 2019;13:281.
17. Schiffer WB, Deych E, Lenihan DJ, Zhang KW. Coronary and aortic calcification are associated with cardiovascular events on immune checkpoint inhibitor therapy. Int J Cardiol. 2021;322:177–182.
18. Lopez-Mattei J, Yang EH, Baldassarre LA, et al. Cardiac computed tomographic imaging in cardio-oncology: An expert consensus document of the Society of Cardiovascular Computed Tomography (SCCT). Endorsed by the International Cardio-Oncology Society (ICOS). J Cardiovasc Comput Tomogr. 2023;17:66–83.

Quick Reference Guide

Baseline testing should be rolled out nationally and be undertaken in all patients starting immune checkpoint inhibitor immunotherapy. Baselines tests should include Troponin T or I, NT-proBNP or BNP and a baseline 12-lead ECG. The use of echocardiography should be targeted to those with highest background risk or abnormal baseline biomarkers/ECG. Collaboration between oncologists and cardiologists is essential, as is the development of a locally adapted and implemented management framework of baseline testing derived from this national suggested framework (outlined below). Local centres should be supported by oncology departements and biomedical scientists to be able to deliver the minimum biomarker evaluation for all patients commencing ICIs which has a favourable cost benefit when compared to the financial toxicity of myocarditis.

Baseline results normal **TnT < 14ng/L** **TnI < 50ng/L** (check local normal range) and **NT Pro-BNP/ BNP <400ng/L** (check local normal range)	**No action required.**
Baseline results mildly elevated **TnT 14-50ng/L or TnI >50-200ng/L** (check local normal range) and/or **NT Pro-BNP/BNP = 400-1000ng/L** (check local normal range)	**Consider signs, symptoms and history of acute coronary syndrome and/or heart failure** • **Review baseline ECG** • **Request echocardiogram** **Consider discussion with local cardiologist / cardio-oncologist** – patients do not necessarily need to wait for this prior to starting ICI treatment if the treating oncologist regards this as a low risk.
Baseline results elevated **TnT >50ng/L or TnI >200 ng/L** and/or **NT Pro-BNP/ BNP > 1000 ng/l** ** Unless biomarkers can be explained in clinical context or that cardiology advise in keeping with pre-existing cardiac conditions e.g. rate controlled AF***	**Referral to local cardiologist/ cardio-oncologist** **Request echocardiogram** **NOTE –** Symptomatic patients or any conerns from treating oncologist need urgent referral to cardiology prior to starting ICI (unless the balance of risk vs benefit is felt to warrant treatment prior to review). Asymptomatic patients do not necessarily need to wait for cardiology review prior to starting ICI if no concerns from treating oncologist.

In some patients identified by the clinical team, pre-cycle monitoring may be required for those with significant risk factors and/or raised baseline cardiac markers.


IOCN
The Immuno-Oncology Clinical Network