

Immune-Related Adverse Event: Myocarditis

Myocarditis is a recognised complication of immune checkpoint inhibitors. The majority of reported cases have occurred within the first month of therapy. Approximately 1% of patients treated with checkpoint inhibitors develop cardio-toxicity. Myocarditis is associated with a high mortality rate if not treated. It is common for patients to be asymptomatic/ have minimal symptoms and abnormal cardiac tests are significant.

Mild (Grade 1)

Clinically asymptomatic or presenting with fatigue/new pedal oedema

Cardiac enzymes:

Trop T is >14 and <30 ng/L **OR** elevated above baseline by <20 ng/L (if raised at baseline)

NT-Pro-BNP is >500 <1000 ng/L

Moderate (Grade 2)

New onset of symptoms with moderate exertion (e.g. Dyspnoea, chest pain, palpitations, peripheral oedema, pre-syncope, syncope) **OR** evidence of elevated cardiac enzymes/ECG changes even in the absence of symptoms.

Cardiac Enzymes:

Trop T is >30 <100 ng/L **OR** elevated above baseline by >20 ng/L (if raised at baseline)

NT-Pro-BNP is ≥1000 <3000 ng/L **OR** increased from baseline

Severe/Life-Threatening (Grade 3 & 4)

New onset of severe symptoms at rest or with minimal exertion; intervention indicated

Cardiac Enzymes:

Trop T is ≥100 ng/L

NT-Pro-BNP is ≥3000 ng/L

Clinical Assessment

Investigations:

- ECG
- Bloods (Troponin, NT-pro-BNP, Creatinine Kinase, FBC, U&Es)
- Chest X-ray

Actions:

- Consider delay of immunotherapy
- Repeat ECG and bloods in 2 weeks
- Consider echocardiogram in the presence of pedal oedema

Clinical Assessment

As per mild (grade 1) plus

Investigations:

- Echocardiogram
- Cardiac Magnetic Resonance Scan
- Infliximab screen
- TPMT Levels
- Whilst on IV steroids for Daily ECG and repeat cardiac markers.

Treatment:

- IV Methylprednisolone 4mg/kg/day + gastric protection for 5/7. Taper to 2mg/kg/day for 3/7. Step down to Oral Prednisolone 1mg/kg. Review response and oral steroid taper (see steroid taper guidance)
- Consider ACEi +/- beta-blocker
- If evidence of overload consider diuretics.
- If evidence of cardiac impairment refer for heart failure optimisation.

Actions:

- Hold immunotherapy
- Consider hospital admission
- Consider Referral to cardio-oncologist

Clinical Assessment

As per moderate (grade 2) +

Treatment:

- IV Methylprednisolone 1g + gastric protection for 3/7. Taper to 4mg/kg/day for 3/7. Taper to 2mg/kg/day for 3/7. Step down to Oral Prednisolone 1mg/kg. Review response and oral steroid taper (see steroid taper guidance).
- Supportive therapy (inotropes, anti-arrhythmics*) and as for grade 2

Actions:

- Stop immunotherapy
- Consider whether patient requires admission to CCU/HDU and their ceilings of care
- Refer to cardio-oncologist and IO Clinician
- Consider Mycophenolate or Tacrolimus, in patients not responding optimally to high dose steroids.
- If limited response, consider biologic e.g. Infliximab, Tocilizumab or Abatacept. A further DMARD e.g. azathioprine, could also be considered.
- Consider CCC Subsequent Management Guidelines.

**If anti-arrhythmics are required amiodarone should be avoided if possible and only used on discussion with immunotherapy specialist due to the risk of pneumonitis.*

To refer a patient to Dr Dobson (Cardio-oncologist) complete the referral form and email to cardio.oncology@nhs.net. Search "cardio-oncology out-patient referral form" on CCC Intranet.

If not already done so, please complete a referral to the immunotherapy toxicity service via meditech internal referrals.

Interrupt SACT immunotherapy until discussed with Acute Oncology Team. Please contact on-call oncology/haematology team for advice. Ensure that the patient has monitoring/follow up planned with their oncology/immuno-oncology team.

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