Good Practice Guidance for

Immuno-Oncology Medicines

About the UK Systemic Anti-Cancer Therapy Board

The UK Systemic Anti-Cancer Therapy (SACT) Board provides guidance, oversight and support for the continuing development of SACT services in the UK. Its core membership comprises representatives of the Royal College of Radiologists (RCR), the Royal College of Physicians (RCP), the Association of Cancer Physicians (ACP), the British Oncology Pharmacy Association (BOPA) and the UK Oncology Nursing Society (UKONS). The Board also has representation from the four UK nations and from other organisations closely involved in SACT services, including the Royal College of Pathologists.

About the Immuno-Oncology Clinical Network

The Immuno-Oncology Clinical Network (IOCN) received charitable status and was launched in 2023 to support healthcare professionals manage the complexities of immuno-oncology treatments, including the inflammatory and immune mediated side effects. The IOCN aim is to improve patient care through clinical support, education, service development, governance and research activities.

Summary

Good practice guidance for immuno-oncology medicines was first produced by the UK SACT Board in 2018 in response to concerns that patients presenting with serious side effects from immuno-oncology medicines may be triaged to staff who are unfamiliar with the management of these adverse events. The guidance has now been updated jointly by the UK SACT Board and IOCN and recognises that the identification and management of immuno-oncology specific side effects has become more complex, given that these medicines are now commonly used in combination with cytotoxic chemotherapy, targeted therapy, hormonal therapy and radiotherapy. The guidance provides recommendations for services to ensure patients are managed safely: it is *not* a clinical protocol for the management of immune-related adverse events but links to useful clinical protocols are provided within this document.

Introduction

Immuno-oncology medicines are now embedded into clinical practice, with an ever-increasing number of approvals for multiple agents across a broad range of tumour types. Outcomes for many patients have significantly improved with the use of immuno-oncology agents.

Education for all healthcare professionals involved in immuno-oncology treatment, as well as patients and carers, is critical to the safe use of these treatments, so that immune-related adverse events (IrAEs) are recognised early and managed promptly.

The immuno-oncology landscape continues to evolve rapidly with many new medicines being investigated and approved for use, including checkpoint inhibitors, oncolytic vaccines. T-cell bispecifics, chimeric antigen receptor T (CAR-T) cell therapy and vaccines. The focus of this guideline remains the use of checkpoint inhibitors alone or in combination with other treatments.

Immuno-oncology medicines have a different side effect profile from traditional cytotoxic and targeted therapies. Immune-related reactions can affect any organ or system. Side effects may be subtle and therefore easily over-looked. They can occur at any time during treatment and for a long time (potentially years) after completion of treatment and may leave patients with a life-long related disease. Patients can develop multiple toxicities simultaneously and some toxicities can occur as a well-recognised collection in an overlapping manner.

IrAEs include but are not limited to:

- Endocrinopathies (including adrenal crisis, hypophysitis, thyroid dysfunction, diabetes)
- Skin toxicities
- Diarrhoea and colitis
- Hepatotoxicity
- Arthralgia/myalgia
- Pneumonitis
- Renal toxicities
- Neurological toxicities
- Cardiac toxicities

Scope of this document

This document is designed to give a practical framework for the safe introduction and ongoing use of immuno-oncology in existing SACT services. This guidance is relevant to both solid tumour oncology and haemato-oncology. The guidance does *not* cover the use of CAR-T Cell therapy or vaccines. Although developed for NHS providers, the guidance is equally applicable to private sector providers.

This document does not seek to give clinical guidance on recognition and management of the side effects of immuno-oncology medicines as such guidance is comprehensively addressed in a number of local, regional and national guidelines. Links to these guidelines can be found at the end of this document. These and other additional useful resources are also available via the IOCN website.

Recommendations for providers

Services providing immuno-oncology treatment should ensure that the following recommendations are met:

1. **Education:**

   This should include administration of immuno-oncology treatments, recognition and management of acute and long term side effects, appropriate referral pathways and information provided to patients

   - **SACT delivery service staff:**

     Education should be provided to all staff involved in the delivery of immuno-oncology medicines, including but not limited to: medical and non-medical prescribers, SACT-administering staff, Ward Staff, Clinical Nurse Specialists, Clinical Pharmacists, SACT screening technicians and Research Nurses.

   - **Acute Haemato-Oncology/24-hour helpline staff:**

     Staff who provide acute haemato-oncology services and/or cover a 24-hour helpline should have had the same education in recognition and management of IrAEs as SACT delivery staff. The provider should ensure that 24-hour advice is available for patients receiving immuno -oncology treatment and that appropriate triage is in place to identify potential immuno-oncology side effects, such as that recommended in the UKONS triage tool.

- **Emergency Care Staff:**

All hospital staff who could come into contact with immuno-oncology patients via an emergency presentation should be informed and signposted to appropriate training packages. This includes, but is not limited to, Emergency Department, Same Day Emergency Care (SDEC) and Acute Medical Unit staff. Providers should ensure that their own emergency care staff are aware of the different side effect profile of immuno-oncology agents and know where to find clinical guidance (both policy and local expert) on management of IrAEs.

- **Patients and carers:**

Immuno-oncology specific education should be provided to all patients and carers or family members before the start of treatment. This should include advice on how to recognise side effects, how to access acute haemato-oncology services and when to present to hospital. Preliminary information, including educational videos on SACT needs to include specific immuno-oncology information for patients who are receiving this treatment, alone or in combination with other forms of SACT.

2. **Regimen-specific Consent Forms:**

Trusts and Health Boards should use regimen specific consent forms for immuno-oncology medicines. National standardised SACT regimen-specific consent forms which have been developed under the auspices of the UK SACT Board are provided on the Cancer Research UK (CRUK) website.

3. **Patient-Held Alert Card:**

Patients must be given a drug or therapeutic class-specific alert card warning that they are receiving immuno-oncology treatment and may develop IrAEs. Patients should be instructed to carry this with them at all times and present it to a healthcare professional if they become unwell. Trusts/Health Boards may have developed their own alert cards for local use. Alternatively, most companies have produced drug-specific alert cards which are comprehensive. A Macmillan alert card is also available and includes the option to provide alerts for immuno-oncology and chemotherapy when used in combination. If local alerts are used for patients on combination therapy, separate alerts for immuno-oncology and other SACT should both be supplied and the patient must know to present both in an emergency setting.

4. **Patient-Held Treatment Record:**

Patients should be given a patient-held record with specific information on recognising and dealing with IrAEs, including out-of-hours contact to the SACT/Acute Haemato-oncology team. Patients should be instructed to show this to other healthcare providers, including hospital teams in the Emergency Department, assessment units or in primary care if they attend for advice or treatment. Specific information signposting hospital teams to contacts for advice should be included.

5. **Treatment details to Primary Care Physician:**

Providers should ensure that the patient's primary care physician is provided with details of the treatment the patient is about to receive, the intent of treatment, specific details of IrAEs and advice about who to contact for further information. This could be sent as a companion letter alongside the letter detailing the patients specific information and treatment plan.

With the rapid expansion of immuno-oncology and targeted treatments it may be difficult for primary care teams to differentiate between different types of therapy and specific information is therefore highly valuable. Initial triage in Primary Care may help identify side effects. This can be done using the UKONS and Macmillan primary care risk assessment tool for oncology and haematology patients.

6. **Patient Pathway:**

Immuno-oncology services should have a clear pathway for managing acute side effects 24/7 so that staff and patients know who to contact for advice, at all times.

7. **Baseline Investigations:**

Real-world practice has identified that baseline investigations are highly valuable for comparison when toxicities occur. Where it is feasible, it is recommended that providers consider, following locoregional discussion where relevant, undertaking the following baseline investigations before initiation of any immuno-oncology treatment:

- FBC
- U+E and LFTs
- Bone profile
- TFTs

- Random cortisol
- Random glucose and also consider HbA1c
- Hepatitis B (surface antigen and core antibody), also consider CMV, Hepatitis C, HIV in high prevalence areas
- Hormone profile as appropriate eg testosterone in male patients
- Amylase
- Troponin and BNP
- ECG
- Consideration of echocardiogram if significant cardiac history and/or significantly elevated baseline troponin/BNP
- Prior exposure to TB testing (eg TB Quantiferon or T-spot) should be considered as a baseline investigation for patients receiving combination therapy with ipilimumab and nivolumab, given the significant risk of grade 3/4 toxicity requiring escalation to the use of biologics (eg infliximab, vedolizumab). Consideration of testing is also recommended for patients presenting with G2 non-resolving toxicity (if not carried out at baseline) as escalation to biologics may also be required.

8. **Organisational Clinical Policy for management of IrAEs:**

Providers should ensure they have protocols and pathways in place for the management of IrAEs which are easily accessible electronically to all clinical staff who may come into contact with immuno-oncology patients. It is recommended that providers adopt the UKONS *Acute Oncology Initial Management Guidelines* or develop similar comprehensive guidance. Pharmacy departments should work with clinical teams to ensure there are no barriers to rapid access of emergency supportive care medications, including outside of normal pharmacy opening hours.

Oncology teams should also identify the internal governance processes by which policies and procedures are going to be developed, reviewed and implemented. Alongside this the establishment of a clinical support network of oncologists experienced in the management of irAEs should be considered

9. **Establishment of links to related clinical specialties for symptom and disease management:**

Close collaboration between the SACT and clinical specialist teams is critical to optimal management of IrAEs. SACT services should ensure that all relevant clinical specialist teams are aware that there are patients within their locality receiving

immuno-oncology medicines who may present with IrAEs which may require their specialist input. This should include endocrinologists, gastroenterologists, hepatologists, dermatologists, renal physicians, respiratory physicians, neurologists, cardiologists and ophthalmologists. Providers without on-site access to these specialties should ensure they have pathways in place to access both telephone and face-to-face advice/input. It is recommended that advice for local clinical teams with limited experience of IrAEs is sought from specialists with a specific interest (details via the IOCN website)

10. **Assessment of disease response:**

Providers should ensure all radiologists involved in the assessment of radiological response to immuno-oncology treatments are aware of the mechanism of action of these agents, the irRECIST criteria and the potential side effects that may be radiologically evident and important such as pneumonitis, colitis and sarcoidosis. It is also important to ensure radiologists are aware of the potential for pseudo-progression and late responses to immuno-oncology treatments.

11. **Mandatory Data Submission:**

NHS providers in England must ensure data on patients receiving immuno-oncology treatment is provided to the SACT Team within the National Disease Registration Service (NDRS).

12. **Morbidity and Mortality Review:**

Providers should ensure all patients who die within 30 days of receiving immuno-oncology treatment are discussed at an appropriate meeting such as the department mortality and morbidity meeting or audit meeting. Providers should consider adopting a standardised review process such as that developed by the UK SACT Board. For patients who die beyond 30 days, but the death is considered to be related to toxicity, this should still be reported and discussed as a treatment-related death.

13. **Pharmacovigilance**

Monitoring of Adverse Drug Reactions is particularly crucial for drug safety in the rapidly developing field of immuno-oncology, especially as the true incidence of ADRs may not yet be known, new ADRs may emerge and long-term effects are also as yet unknown. Reporting via the MHRA yellow card scheme and collaborative sharing of experience through the IOCN will facilitate accurate reporting and increase national awareness.

Useful resources

Below is a list of resources that may be useful to providers in implementing these good practice guidelines. This list is not exhaustive and additional resources can be found via the IOCN website www.IOclinicalnetwork.co.uk

UKONS toxicity guidelines

ukons_ao_initial_management_guidelines_final_version_2023.pdf

ESMO toxicity guidelines
Management of toxicities from immunotherapy: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up

ASCO toxicity guidelines
Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: ASCO Guideline Update

CRUK Consent forms
Consent forms for SACT (Systemic Anti-Cancer Therapy) | Cancer Research UK

UK Chemotherapy Board> Morbidity and Mortality within 30 days of Systemic Anti-Cancer Therapy (SACT): Review of Current Practice suggested Standardised Review Process. May 2016
Clinical_Radiology_Specialty_Training_Board_Minutes_27_01_2012 (rcr.ac.uk)

Home :: UK Acute Oncology Society

Recommendations for further research

These recommendations are based on pragmatic agreement by healthcare professionals on the best way to manage the pathway for safe management of patients who have potential to develop serious IrAEs. It is important to acknowledge that evidence for effectiveness of some of these interventions is lacking and is an area for further research.

Providers are encouraged to put systems in place to monitor toxicities and outcomes and to actively engage in local/regional/national audit, data collection and research. The IOCN website www.IOclinicalnetwork.co.uk will be a useful resource for identifying such activities.

Acknowledgements

These guidelines were originally developed by Mr Steve Williamson (representing the British Oncology Pharmacy Association), Professor Ruth Board (representing the Royal College of Physicians) and Dr Jeanette Dickson (representing The Royal College of Radiologists), on behalf of the UK Chemotherapy Board. The update has been carried out by Dr Clare Barlow (IOCN representative, UK SACT Board) and Professor Ruth Board (Royal College of Physicians ’representative, UK SACT Board) in consultation with UK SACT Board members and IOCN Board of Trustees.