UK Chemotherapy Board

Good Practice Guideline for Immuno-Oncology Medicines

About the UK Chemotherapy Board

The UK Chemotherapy Board provides guidance, oversight and support for the continuing development of chemotherapy 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 Royal College of Pathologists (RCPath), 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 chemotherapy services, including the NHS England Chemotherapy Clinical Reference Group and the Chemotherapy Clinical Information Group of Public Health England (PHE).

Summary

This guidance has been produced by the UK Chemotherapy Board in response to concerns that patients may not be correctly triaged when presenting with serious side effects from immuno-oncology medicines to staff who are unfamiliar with the management of these adverse events. This guidance concerns the systems for ensuring patients are managed safely; it is *not* a clinical protocol for the management of immune-related adverse events.

Introduction

Immuno-oncology medicines are innovative therapies that have moved into day-to-day practice in the majority of systemic anti-cancer therapy (SACT) services in UK hospitals following approvals for use of immune checkpoint inhibitors for various common cancers.[1,2,3,]

Immuno-oncology medicines are relatively new treatments which, for many patients, can achieve excellent outcomes. Immuno-oncology medicines are associated with immune-related adverse events (IrAEs) that can be unfamiliar to staff in SACT services.

It is these new and often serious side effects that are cause for concern; education of staff and patients in recognition and management of these side effects is critical for the safe use of immuno-oncology.

The immuno-oncology landscape is evolving rapidly, with many new medicines and therapies being investigated and approved for use - e.g. checkpoint inhibitor, chimeric antigen receptor T (CAR-T) cell therapy (not included in this guideline) and vaccines.

Scope of this Document

This document is designed to give a practical framework for the safe introduction and ongoing use of immunotherapy in existing SACT services. Although developed for NHS providers, the guidance is equally applicable to private sector providers.

Clinical management of patients with IrAEs are comprehensively addressed in a number of local, regional and national documents.[4,5,6]

This document does not seek to give clinical guidance on recognition and management of these side effects of immuno-oncology medicines. Instead it outlines the practical steps for safe use of these medicines that must be in place before they are used in chemotherapy services. It does **not** cover the use of CAR-T cell therapy.

The advice given in this good practice guideline is intended primarily for NHS providers of chemotherapy services. Private sector providers are encouraged to adopt these guidelines.

Summary of Safety Risk

Unlike traditional cytotoxic medicines and targeted therapies used for SACT treatment, immuno–oncology medicines have a different side effect profile in which immune–related reactions can occur. These include:

- pneumonitis
- rash
- adrenal insufficiency
- nephritis or renal dysfunction
- diarrhoea or colitis
- diabetes
- hepatitis
- hypothyroidism
- hyperthyroidism
- hypophysitis
- uveitis

Recommendations for Providers

All SACT services that deliver immuno–oncology medicines to their patients must ensure that, before these medicines are used in their service, the following actions have been taken:

1. **Education of chemotherapy delivery service staff:** Education must be provided to prescribers, nurses and pharmacists involved in the use of all immuno-oncology medicines.
2. **Education of Acute Oncology/24-hour helpline staff:** Staff who provide acute oncology services and/or cover on-call a 24-hour helpline must have had the same education in recognition and management of IrAEs as chemotherapy delivery service staff. The provider should ensure that 24-hour advice is available for patients receiving immunotherapy and that appropriate triage is in place to identify potential immuno-oncology side effects such as that recommended in the UKONS triage tool.[7]

   Note:

   Education for SACT teams and acute oncology/helpline staff should cover both general information on immuno-oncology and drug-specific information for each new regimen. It should include administration, management of patients, understanding of education to be provided to patients and management of IrAEs.
3. **Emergency care staff education**: When an immuno–oncology service is set up, all hospital staff who could potentially come into contact with patients via an emergency presentation should be informed and signposted to appropriate training packages. Providers must ensure that their own emergency care staff are aware of the different side-effect profile of immuno–oncology and where to find clinical guidance (both policy and local expert) on management of IrAEs. This may be incorporated into acute oncology training and a register of training should be kept, with new starters identified and trained as soon as possible.

4. **Patient education**: Immuno-oncology-specific education must be provided to all patients and carers or family members where appropriate before the start of treatment on the recognition of side effects, how to seek advice and when to present to hospital.[8] It should be emphasised that traditional chemotherapy pre-assessments including educational DVDs focus on cytotoxic chemotherapies and providers should ensure they adopt or develop specific immunotherapy information[9] for patients.

5. **Trusts and Health Boards should use regimen-specific consent forms for immuno–oncology medicines:** National standardised SACT regimen-specific consent forms which were developed in conjunction with the UK Chemotherapy Board (UKCB) are provided on the Cancer Research UK (CRUK) website.[9]

6. **Patient-Held Alert Card:** Patients must be given a drug or therapeutic class-specific alert card warning that they are receiving immuno–oncology and may be prone to IrAEs. Patients must be instructed to carry this with them at all times and present it to a healthcare professional if they become unwell.

7. **Patient-Held Treatment Record**: Patients must be given a patient-held record book with specific information on recognising and dealing with IrAEs, including out-of-hours contact to the SACT/acute 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.

8. **Treatment details to primary care physician:** Providers should provide the patient's primary care physician 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.

9. **Patient pathway**: The immuno–oncology patient pathway must be defined so staff and patients are aware of arrangements for out-of-hours support from SACT and/or acute oncology teams.

10. **Organisational clinical policy for management of IrAEs:** Providers should ensure they have protocols and pathways in place for the management of IrAEs. These protocols should be easily accessible for all clinical staff. It is recommended that providers adopt the UKONS *Acute Oncology Initial Management Guidelines*[13] or develop similar comprehensive guidance, made available electronically to all staff that may come into contact with these patients. Pharmacy departments must work with clinical teams to ensure there are no barriers to rapid access of emergency supportive care medication, including outside of normal pharmacy opening hours.

11. **Establish links to related clinical specialities for symptom and disease management**: The chemotherapy service should ensure that each of the related clinical specialties is aware that patients in the organisation are receiving immuno–oncology medicines and may present with IrAEs which need their specialist input.

    This should include endocrinologists, hepatologists, dermatologists, renal physicians, respiratory medicine, neurology, gastroenterologists and ophthalmology. Providers without on-site access to these specialities should ensure they have pathways in place to access both telephone and face-to-face advice and input.

12. **Assessment of disease response:** Providers should ensure all radiologists involved in the assessment of radiological response to immunotherapy are aware of the mechanism of action of immunotherapies, irRECIST criteria and potential side effects that may be radiologically evident and important such as pneumonitis, colitis and sarcoidosis.

13. **Mandatory data submission:** NHS providers in England must ensure data on patients receiving immunotherapy is provided to PHE and NHS England via submissions to the SACT dataset.

14. **Morbidity and Mortality Review**: Providers should ensure all patients who die within 30 days of receiving immunotherapy 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 Chemotherapy Board [10]

Adoption of Safety Standards

The UK Chemotherapy Board will discuss with the relevant national statutory bodies in all four home nations (e.g. NHS England Quality Surveillance Team) how these good practice guidelines can be incorporated into existing self-assessment standards.

Useful Resources

Below is a list of selected resources that may be useful to providers in implementing these good practice guidelines. This list is not exhaustive. The resources below are examples. Further details are provided in the references on pages 4 and 5.

- UKONS triage toolkit[7]
- CRUK national standardised regimen specific SACT consent forms[9]
- Lancashire Teaching Hospitals NHS Foundation Trust: Immunotherapy Video[11]
- European Society for Medical Oncology (ESMO) guidance for IrAEs management[6]
- The Clatterbridge Cancer Centre: Acute Oncology Guidance[12]
- UKONS Acute Oncology Initial Management Guidelines[13]

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. Evidence for the effectiveness of some of these interventions is lacking and is an area for further research.

Conclusions

Providers can ensure that immuno-oncology is used with minimal risk if their staff and patients are well educated in how to manage potential immune-related adverse events. Patients must be provided with alert cards, with patient-held treatment records and understand the requirement to show these to healthcare staff if they become unwell. Providers must ensure that they support patients by providing appropriate materials and education to patients, and ensure their staff are aware of how to access guidance not safety standards. Providers must also ensure their staff are educated in the management of serious immune-related adverse events in patients receiving immuno-oncology medicines.

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