Module Six

Part Four – Providing care for the person receiving cancer biological and molecular targeted therapies

Overview

The aim of this module is to develop the ability of the beginning specialist cancer nurse to demonstrate competence across all domains of practice when caring for the person receiving biological or molecular targeted therapies for cancer.

Key concepts

The key concepts associated with providing care for the person receiving cancer biological and molecular targeted therapies include:

- Factors influencing selection of biological and molecular targeted therapies for treatment of cancer.
- Experience and impact of biological and molecular targeted therapies on various health domains.
- Prevention, detection, and management of common health alterations experienced by people receiving biological and molecular targeted therapies.
- Management of an adverse reaction to cancer biological and molecular targeted therapies – demonstration of competence within ICAT.

Learning activities

At times, you will have learning activities to complete. The questions will relate to the content you've just read or the video you've just watched.

Resource links

Resource links may be included throughout the module. These links lead to interesting resources, articles or websites, and are designed to encourage you to explore other available information.

Videos

You may be prompted to access EdCaN videos throughout this module.

Estimated time to complete

20 hours

Objectives

On completion of this supporting resource, you should be able to:

1. Perform a comprehensive health assessment on a person prior to, during and following biological and molecular targeted therapies.
2. Analyse clinical, psychological and social data to formulate and implement an individualised plan of care for the person having biological and molecular targeted therapies.
3. Demonstrate delivery of effective nursing care to prevent, detect and manage early and late effects associated with biological and molecular targeted therapies.
4. Demonstrate effective educational strategies in providing individualised information to the person having biological and molecular targeted therapies.
5. Demonstrate safe practice in the care of the person receiving cytotoxic agents.
6. Demonstrate competence in the administration of biological and molecular targeted therapies.

Biological and molecular targeted therapies in cancer control

Biotherapeutic agents currently approved for use in cancer treatment in Australia fall into the following broad categories:[1,2]

- cytokines
    - interferons
    - interleukins
    - haematopoietic growth factors
- monoclonal antibodies
    - unconjugated
    - armed or conjugated antibodies
- cellular therapies
    - dendritic cells
    - tumour-infiltrating lymphocytes
    - antibody-activated T cells
- vaccines
- gene therapy
- angiogenesis inhibitors.

Certain agents fall under more than one category. For example:[1]

- trastuzumab is a monoclonal antibody and also falls under the EGFR targeted therapy category
- gefitinib is an EGFR tyrosine kinase inhibitor and also has action as an angiogenesis inhibitor.

Nurses need to keep abreast of current and investigational biological and molecular targeted agents and their application in clinical practice. As knowledge of molecular processes improves, the categories and application of biotherapeutic agents will evolve. The large number of agents currently under investigation may be approved for clinical practice. Existing agents can also have application in the treatment of new diagnostic groups and in combination with antineoplastic agents.

Resource link

An overview of Biological and molecular targeted therapy agents was provided in Module 4: Cancer Treatment Principles. In the sections below, we review specific mechanisms of action of various types of agents. Completion of these sections assumes you have successfully completed the relevant learning activities in Module 4. If required, take some time to review the learning activities in Module 4 before completing this module.

Learning activities	
Completed	Activities
☐	1. Identify an example where a biological agent is being used in combination with antineoplastic agents.
☐	2. Explain the rationale for combining this biological agent with antineoplastic agents.
☐	3. Discuss some of the concerns that a person about to receive targeted therapies may have about these treatments.
☐	4. Identify a person who is to receive biological and molecular targeted therapy. Throughout this module you will complete learning activities related to the nursing management of this person throughout their treatment trajectory. • Identify their diagnosis and proposed treatment approach • Define the intent of the treatment • Review relevant clinical practice guidelines and summarise the evidence which supports this treatment approach

Categories of biological and molecular targeted therapies

Cytokines

Cytokines such as interleukin-2 (IL-2), interferon (IFN), and tumour necrosis factor (TNF) have been used with varying success in the treatment of cancer, due to their immunostimulatory effect.

Interferons were the first cytokine to be studied.[2] The interferons have a number of activities such as:[2]

- antiviral
- anti-proliferative
- immunomodulation
- inhibition of angiogenesis
- regulation of differentiation
- anti-tumour effects.

They have been used in cancer therapy in a variety of doses and schedules. Interferons can be divided into two types:[3]

- Type I (IFN-α and IFN-β) binds to the cell surface receptor of effector cells
- Type II (IFN-γ) binds to different cell surface receptors.

Interleukins are cytokines that send signals primarily between lymphocytes. They have also been found to have broader activities such as coordinating various immune cell activities and other organ systems to mount a multi level defense. [2]They do not act independently but are messengers to initiate, coordinate, and sometimes augment potent immune defense activities.[2]

There are several interleukins that have been discovered and they are identified by a number. Currently there is only one interleukin, IL-2, which has been used as an anticancer therapy at varying doses and schedules.

There are two types of TNF:

- TNF-α (cachectin) actions include increased catabolism, enhanced phagocytosis, and tumour destruction
- TNF-β (lymphotoxin) actions include cell killing and direct tumoricidal capability.

Colony stimulating factors (CSF) or haematopoietic growth factors (HGF) are naturally occurring proteins or cytokines that regulate proliferation, differentiation, and maturation of all blood cell lines.[4] Recombinant DNA technology has permitted the manufacture of large quantities of these substances.

Some HGF stimulate the growth of multiple blood cell lines such granulocyte-macrophage CSF (GM-CSF). Others stimulate production of a single cell line.

Single cell line CSF includes:

- granulocyte-CSF (G-CSF)
- macrophage-CSF
- erythropoietin (EPO)
- thrombopoietin (TPO).

Recombinant versions are used as supportive therapy and can prevent or minimise the myelosuppressive effects of cancer treatment efforts.[4]

Learning activity	
Completed ☐	Activity 1. Identify a cytokine used in cancer treatment and describe the: • indications in cancer treatment • mechanism of action • adverse effects • administration considerations

Monoclonal antibodies

Monoclonal antibody therapy includes some of the first agents that were used in the modern era of targeted therapies. Antibodies are glycoproteins produced in response to a specific antigen found in the body. Monoclonal antibodies are artificially produced proteins, from a single clone of cells sensitised to a specific antigenic protein present on the surface of a target tumour.[2]

There are four distinct types of monoclonal antibodies:

- murine
- chimeric
- humanised
- human.

Hybridoma technology was first used to produce large quantities of specific antibodies using mouse models.[5] Early challenges of this model were the immunogenic reactions involving murine antibodies. Further progress in this area with genetic engineering techniques produces monoclonal antibodies with components from both mouse and human.[5]

For monoclonal antibodies to be successful in cancer therapy, a number of key characteristics must be met:[5]

- specificity - the target antigen must be present on malignant cells only
- density - the quantity of target antigen expression directly relates to tumour response
- function - the role of target antigen in cell survival and proliferation is instrumental in cell destruction
- modulation - modulating antigens internalise the antibody / antigen complex once binding has taken place. This is required for toxin conjugated monoclonal antibodies and is less desirable when it occurs rapidly for unconjugated monoclonal antibodies.

Both unconjugated and conjugated monoclonal antibodies are approved for clinical use in cancer therapy.[2]

- *Unconjugated* monoclonal antibodies target a specific anti-tumour antigen initiating an immunologic response reliant on the host immune mechanisms to destroy the target cell. Unconjugated monoclonal antibodies include:
  - rituximab
  - trastuzumab
  - alemtuzumab.

- *Conjugated* monoclonal antibodies carry either radioimmunoconjugates, chemoimmunoconjugates or immunotoxins to a specific target antigen. They are capable of killing cells and do not require any host immune mechanisms. Conjugated monoclonal antibodies include:
  - gemtuzumab ozogamicin
  - Y^{90} ibritumomab tiuxetan
  - I^{131} tositimomab.

- Several other monoclonal antibodies have been developed that target specific molecular events and will be discussed later:
  - bevacizumab
  - cetuximab
  - panitumumab.

Learning activities	
Completed	Activities
☐	1. For the monoclonal antibody rituximab, identify the following: • indications in cancer treatment • mechanism of action • adverse effects • administration considerations
☐	2. You are asked by a woman who has T-cell lymphoma why she is not receiving rituximab as part of her treatment. Outline your response and identify information resources you may provide her.

Cellular therapies

Tyrosine kinase inhibitors (TKIs) are small molecule compounds that block the ATP binding site of the TK enzyme.[6] Imatinib was the first TKI to be used in humans and inhibits the protein tyrosine kinases - BCR-ABL, PDGFR, and KIT.[2, 7]

Imatinib was developed to target the fusion protein BCR-ABL present on the Philadelphia chromosome in chronic myeloid leukaemia (CML). It acts by blocking the binding site of BCR-ABL thus preventing cell proliferation. Imatinib has been found to have application in the management of other malignancies as it also inhibits two other tyrosine kinases - PDGFR and KIT. This has lead to the approval of imatinib in:[7]

- gastrointestinal stromal tumours
- chronic myelomonocytic leukaemia
- aggressive systemic mastocytosis
- hypereosinophilic syndrome / chronic eosinophilic leukaemia

- dermatofibrosarcoma protuberans.

An emerging problem of imatinib therapy is the development of resistance. Imatinib failure results when there is reactivation of BCR-ABL mutations diminishing the binding of the drug.[3] Second generation tyrosine kinases (such as dasatinib and nilotinib) have different binding characteristics. They have been found to be more potent and highly effective in the setting of imatinib failure.[3]

EGFR tyrosine kinase inhibitors

The epidermal growth factor (EGF) family of receptors comprises four closely related but distinct receptors:[2, 8]

- HER1/EGFR/ErbB-1
- HER2/ErbB-2
- HER3/ErbB-3
- HER4/ErbB-4.

The EGF family receptors are transmembrane glycoproteins that regulate cell growth, differentiation, and survival.[2, 3, 8] The EGFR-tyrosine kinase signal is strictly regulated in normal processes such as embryogenesis, organogenesis, and epithelial tissue repair. Events that can switch on EGFR-tyrosine kinase signalling extracellularly include ligand binding of EGFR and over expression of EGFR.[2]

Intracellular events can include:[2]

- over expression of EGFR
- cross communication between other receptors
- loss of regulatory mechanisms
- mutations of EGFR.

Several cancers have been identified that over express this receptor, resulting in more aggressive tumours with an increased tendency for invasion, metastases, and shortened survival.[2, 3] These cancers include:

- breast
- lung
- head and neck
- pancreatic
- colorectal
- kidney
- ovarian.

A number of monoclonal antibodies have been developed to block the extracellular domain:[1]

- EGFR-1 includes cetuximab and panitumumab in colorectal cancer
- EGFR-2 includes trastuzumab and was the first successful HER-2 targeted therapy in breast cancer.

Small molecule compounds have been developed that target the intracellular domain of EGFR. They inhibit phosphorylation of tyrosine kinase, preventing the message for cell division being sent to the nucleus.[1]

- Erlotinib inhibits EGFR-1 in lung and pancreatic cancer.
- Gefitinib inhibits a number of tyrosine kinases in lung cancer.
- Lapatinib blocks both EGFR-1 and 2 receptor kinases in breast cancer.

Learning activity	
Completed ☐	Activity 1. Identify a molecular targeted therapy used in cancer treatment, and describe the: • indications in cancer treatment • mechanism of action • adverse effects • administration considerations

Cancer vaccines

Cancer vaccines are a type of active specific immunotherapy. Antigens are administered and then presented to the immune system in a way that will activate or enhance a cell mediated anti-tumour response, attacking existing cancer cells.[2, 9]

Different approaches are being used to develop cancer vaccines and most vaccines remain in clinical trial settings. One that has been approved is the quadrivalent human papilloma virus (HPV) vaccine (Gardasil) for the prevention of infection from HPV types 6, 11, 16 and 18. The vaccine works by mediating the development of humoral immune responses. Induction of anti-papilloma virus antibodies results in protection against infection.[10] The vaccine is indicated in females for prevention of the following:[10]

- infection by HPV types 6, 11, 16, 18
- genital warts
- precancerous or dysplastic lesions of cervix, vulva, and vagina
- cervical, vulvar, and vaginal cancer.

Learning activity	
Completed ☐	Activity 1. Access current guidelines and t*he fact sheet What are Cancer Vaccines* and: • summarise the differences between preventive vaccines and therapeutic vaccines in cancer control

Angiogenesis inhibitors

Anti-angiogenic agents work by targeting the neovasculature of tumours, halting their growth, preventing tumour invasion, and precluding metastatic diffusion.[12] Anti-angiogenic agents ideally should be used with other cancer therapies. More than one agent may be required to target different steps in the angiogenesis process.[13]

Angiogenesis inhibitors can have either a direct or indirect effect.[2]

- *Direct* anti-angiogenesis agents prevent vascular endothelial cells from proliferating, migrating, or avoiding cell death. They are not as likely to induce drug resistance.
- *Indirect* anti-angiogenesis agents prevent the expression of a tumour protein that activates angiogenesis or blocks the expression of its endothelial cell receptor.

Anti-angiogenesis agents that target the extracellular domain include bevacizumab. This therapy potently neutralises the biologic activities of human VEGF, preventing VEGF from binding to VEGFR-2. It has applications in:[2]

- colorectal cancer
- breast cancer
- lung cancer
- ovarian cancer.

Anti-angiogenic agents that target the intracellular domain include sunitinib and sorafinib. These multi targeted tyrosine kinase inhibitors block the message in the endothelial cell that has been initiated by VEGFR-2. They have applications in renal cell carcinoma and GIST. [2]

Anti-angiogenic and immunomodulatory properties have also been identified in thalidomide. This drug is hypothesised to modulate VEGF inhibiting neovasculature. Another example of these agents is lenalidomide, although its exact mechanism is unknown.[2]

Learning activity	
Completed ☐	Activity 1. Identify an anti-angiogenic agent used in cancer treatment, and describe the: • indications in cancer treatment • mechanism of action • adverse effects • administration considerations

Miscellaneous agents

Bortezomib is an inhibitor of the 26S proteasome. This proteasome normally regulates the intracellular concentration of specific proteins that are required for controlling homeostasis. Disruption to this pathway results in disruption to multiple signalling pathways encouraging cell death. Its current application is in multiple myeloma.[3]

Denileukin difitox is a fusion protein that contains diphtheria toxin fragments fused to IL-2. It targets cells that have IL-2 receptors containing the CD25 component. The IL-2 portion of the protein binds to IL-2 receptors, the diphtheria toxin fragments are transferred into the cell and ultimately inhibit protein synthesis, resulting in cell death. Its application has been in individuals with:[2]

- cutaneous T-cell lymphoma
- CLL
- Hodgkin and non-Hodgkin's lymphoma.

Temsirolimus is an inhibitor of the mammalian target of rapamycin (mTOR). mTOR is a kinase enzyme inside the cell. When activated it is involved in the control of cell proliferation and angiogenesis.[14, 15] Temsirolimus interferes with the synthesis of proteins that regulate proliferation, growth, and survival, leading to cell cycle arrest in G1.[3] It also inhibits angiogenesis by reducing synthesis of VEGF.

Tretinoin or all-*trans*-retinoic acid (ATRA) is a vitamin A derivative used to treat acute promyelocytic leukaemia (APML). The chromosomal abnormality in APML produces an oncogenic protein that blocks cellular differentiation and maturation of promyelocytes. Tretinoin functions as a differentiating agent allowing the leukemic cells to grow into mature granulocytes.[16]

Learning activities	
Completed	Activities
☐	1. Identify a miscellaneous agent used in cancer treatment, and describe the: • indications in cancer treatment • mechanism of action • adverse effects • administration considerations
☐	2. Define 'ATRA Syndrome' and outline the nursing and medical approaches to its prevention and management.

Principles of administering biological and molecular targeted therapies

Biological and molecular targeted therapies represent new classes of drugs. There is limited data on the effects of biological and molecular targeted agents and their potential occupational health risks,[1] so further hazard assessments are required.[3, 6] Until adequate information to the contrary becomes available, biological and molecular targeted therapies used in clinical practice and those still in the investigational setting should be handled as hazardous drugs.[3]

Most biological agents do not affect DNA and therefore do not cause genetic changes. One agent that is considered a hazardous agent is interferon.[17] Nurses involved in administering these agents need to ensure local policy and procedures relevant to these agents are updated in light of current evidence, and promote safe practice.

Biopharmaceuticals are inherently different to other drugs and the following principles guiding their storage, preparation, and handling should be followed:[1, 2]

- biopharmaceuticals are protein-based agents and refrigeration is often required
- biopharmaceuticals cannot tolerate extremes in temperature when transported such as car boots and airplane baggage holds
- use safe handling precautions for biopharmaceuticals that are considered hazardous (e.g. IFN)
- wear gloves when biopharmaceuticals are irritating to the skin (e.g. rituximab)
- when lyophilised product is reconstituted the vial should not be shaken, and the solution should be directed down the side of the vial and not onto powder
- do not shake as this may cause foaming and can denature the protein
- not all biopharmaceuticals are compatible with all plastic syringes and intravenous tubing.

For the nurse, educating individuals receiving these therapies presents a challenge to ensure compliance. The cancer nurse will need to acquire the necessary knowledge to understand the complex processes underlying biological and targeted therapies. Developing an education plan, communicating it effectively, and evaluating an individual's comprehension of this topic is essential. Many of these agents are oral, making them a convenient long term therapy that can be administered in the home setting when supported by effective education and information provision.[2, 6]

Learning activities	
Completed	Activities
☐	1. Review the proposed treatment protocol for the individual assessed earlier receiving a targeted therapy: • Summarise the pharmacodynamic properties of the agent • Outline the adverse effects • Identify any administration considerations
☐	2. Access the following resources: Local policy and procedures related to safe handling and administration on biological and targeted therapies *Guidelines for the Safe Prescribing, Supply and Administration of Cancer Chemotherapy*[18] • Discuss the major considerations that designate a drug as hazardous. • Discuss the extent to which current local policies and procedures are consistent with the principles of safe handling and administration of biological and molecular targeted therapies.
☐	3. Demonstrate safe handling, preparation and administration of a biological and targeted therapy.
☐	4. Many targeted therapy agents are administered orally requiring increased participation of the individual in their care. Access the *Clinical Guidelines for the Administration of Oral Chemotherapy Agents in the Community Setting*[19], and discuss: • factors that promote compliance to treatment • factors that contribute to non-compliance • the role of the cancer nurse in education of the individual receiving oral agents in the community

Care of people receiving biological and molecular targeted therapies

Biological and molecular targeted therapies have been established into standard clinical practice in the last 10 years, and many more are in development in clinical trials. This has resulted in an evolving profile of effects as agents are administered to a wider group of individuals with a specific cancer, and expanded to other cancer groups. Nurses need to recognise the unique side effect profile these therapies present from traditional antineoplastic agents.

Adverse effects are usually mild to moderate, and with astute assessment can be controlled through prompt intervention and management. Some agents have effects similar to antineoplastic agents, such as nausea and vomiting, myelosuppression, and diarrhoea.

More unique effects are emerging such as:[1, 2]

- cytokine release syndrome with monoclonal antibodies
- dermatological changes with EGFR inhibitors
- hypertension from VEGF inhibitors
- thromboembolic events with anti angiogenesis inhibitors.

Specific agents are being identified with rare but serious complications when used alone or in combination with other antineoplastic agents, such as:[1]

- profound lymphopenia with alemtuzumab
- cardiovascular toxicity with trastuzumab, bevacizumab, and sunitinib
- haemorrhage and gastrointestinal perforations with bevacizumab.

To effectively manage individuals receiving biological and molecular targeted therapies the cancer nurse needs to:[1, 2]

- promote participation of individuals in clinical trials to identify the benefits and risks of a specific agent
- review knowledge, adverse effect profile, and risk factors of the agent to be administered
- educate individuals and their carers on how agents work, what effects they may have, how to manage these at home, and when to report effects to health care professionals
- initiate measures such as premedications to prevent infusion related side effects
- monitor and document effects following administration of biological and molecular targeted agents.

Learning activities	
Completed	Activities
☐	1. For the person you assessed previously: • Outline their potential and actual supportive care needs related to their unique circumstances and proposed treatment approach. • Document a nursing care plan to meet these needs.
☐	2. Access pp. 12-14 of the *Guidelines for the Safe Prescribing, Supply and Administration of Cancer Chemotherapy*[18], and document a detailed education plan for the person you have assessed based on their circumstances, preferences and treatment approach.
☐	3. Provide a pre treatment education session with the person assessed previously. Reflect on the session to identify how effective you were in providing information and how you could improve your skills in this area.
☐	4. Discuss your responsibilities as a cancer nurse with respect to the process of reporting adverse effects of biological and molecular targeted agents.

Management of responses to biological and molecular targeted therapies

Infusion related effects

A potentially serious cluster of symptoms known as cytokine release syndrome has been observed as an effect of monoclonal antibodies.[20]

Cytokines, which are naturally occurring proteins, are produced and secreted by most cells of the human body. They include interleukin, interferons, and tumour necrosis factor.[20] Cells targeted by the monoclonal antibody, along with immune effector cells that have been recruited, release cytokines. This results in the occurrence of the following symptoms, which are usually mild to moderate in severity:[20]

- fever, nausea, chills
- hypotension, tachycardia
- asthenia, headache, rash
- scratchy throat, tongue and throat swelling, dyspnoea

Cytokine release syndrome is usually related to the first infusion. Effects appear more severe in those individuals who have not received prior antineoplastic agents. Symptoms subside with subsequent infusions as target cells have been rapidly cleared with the first infusion, resulting in decreased tumour burden and therefore decreased cytokine release.[20]

Cytokine release syndrome is more commonly seen in individuals with haematologic malignancies. It can also occur in individuals with solid tumours.

Management principles include:[20]

- assess need for premedication and administer as required
- always administer via an infusion pump
- the first infusion should be administered slowly and subsequent infusions can be administered more rapidly
- intravenous access should be maintained with normal saline in the event of a reaction
- monitor vital signs frequently and observe individuals closely for reactions
- individuals at high risk may require additional precautions such as:
    - inpatient monitoring and frequent assessment of renal function
    - allopurinol and hydration to prevent renal damage
- individuals experiencing severe reactions require additional precautions such as:
    - supplemental oxygen, bronchodilators, and emergency medications
- monitor for thrombocytopenia and electrolyte abnormalities and replace as required

Learning activities	
Completed	Activities
☐	1. Outline the information and supportive care that may be provided to a person who is to receive rituximab for the first time.
☐	2. List nursing observations that would be undertaken for a person receiving a monoclonal antibody infusion.
☐	3. Outline the immediate nursing responses for a person who is experiencing a severe reaction to a targeted therapy.

Flu like symptoms

Flu like symptoms are commonly associated with the anti-cytokine therapies such as the interleukins and interferons. Symptoms can be more severe when higher doses are administered.[1, 2] Flu like symptoms have also been associated with monoclonal antibodies.

A phenomenon of tachyphylaxis can develop where the body adapts to certain flu like symptoms (fever, chills, and rigors) and the severity and occurrence decreases with repeated doses of the agent. Other symptoms such as malaise and fatigue are cumulative and dose limiting.

Flu like symptoms include:[1]

- fever
  - rapid onset for interferons and monoclonal antibodies
  - delayed onset in IL-2
  - low grade fevers may occur with colony stimulating factors such as G-CSF
- chills and rigors
  - occur prior to temperature spikes with interferons, interleukins, and monoclonal antibodies
- myalgia or arthralgia, headache, malaise, and fatigue
  - occur commonly with the interferons and interleukins
  - monoclonal antibodies commonly cause arthralgia and malaise, while headache is uncommon and fatigue is rare.

Resource link

Putting Evidence into practice: evidence-based interventions for fatigue during and following cancer and its treatment[21].

Learning activities	
Completed	Activities
☐	1. Identify resources and information you can provide to individuals regarding fatigue management.
☐	2. Access *Putting Evidence into practice: evidence-based interventions for fatigue during and following cancer and its treatment*[21], and summarise current evidence based strategies to prevent and manage fatigue.

Dermatologic effects

EGFR inhibitors bind to receptors on normal epidermal cells found in human skin and the gastrointestinal lining.[2, 22, 23] Although the exact biology is not fully understood it is thought that different mechanisms occur to interfere with keratinocyte growth and survival, cell differentiation and attachment, and migration from basal to stratum corneum.[22, 23] The results are inflammation and dryness of the skin, leading to hyperkeratosis, folliculitis, and finally a papulopustular rash that usually occurs within the first three weeks of treatment.[22, 23]

The spectrum of skin toxicities can vary in severity. Most commonly reported reactions include a mild to moderate skin rash that occurs on the face, upper chest, back, and dorsal arms (sun exposed areas).[22, 23] There can be an increased incidence of the inflammatory reactions and sensitivity to sun exposure. Other changes can include xerosis / pruritus, periungual or nail alterations, hair loss, and eye or eyelash abnormalities.[23] The effects appear to be specific to the EGFR targeted therapies.

The cancer nurse needs to be proactive in the management of skin toxicities and provide information and support.[22, 23]

Learning activity	
Completed	Activity
☐	1. Access the Oncology Nursing Society webpage *Skin Reactions*[24], and identify interventions to prevent, minimise, and/or manage skin toxicities associated with targeted therapies.

Cardiotoxicity

Angiogenesis inhibitors exert their effect by either neutralising VEGF (bevacizumab) or blocking signalling within the endothelial cell (sunitinib or sorafinib).[3] This results in a unique group of cardiac effects such as:[25]

- hypertension
- reduced left ventricular ejection fraction (LVEF)
- cardiovascular events including:
- myocardial ischemia
- myocardial infarction
- congestive heart failure
- arrhythmia.

Although the exact mechanism is unknown, theories that have been proposed include:

- blockade of nitric oxide, which is required for the walls of arterioles and other resistance vessels to relax[3]
- direct toxicity to cardiomyocytes[25]

Cardiac toxicity associated with trastuzumab can range from an asymptomatic reduced LVEF to congestive heart failure.[2, 25] Although the exact mechanism of cardiotoxicity is unknown, the damage has been described as a type II chemotherapy-related cardiac dysfunction (CRCD), which appears mostly reversible with improvement on discontinuation of therapy.[25]

The risk of cardiotoxicity increases with the concomitant administration of antineoplastic agents such as anthracyclines and paclitaxel. The two most significant risk factors have been identified as age and combination of trastuzumab and anthracycline therapy. The two agents should therefore should not be given together.[25] A feature of trastuzumab cardiotoxicity is its reversible nature, which may allow therapy to be reintroduced in certain individuals after improvement in LVEF.

The significance of the cardiotoxic related events has led to warnings with regards to the use of these agents in individuals with a history of cardiovascular events and exposure to other cardiotoxic agents.[25]

Learning activity	
Completed ☐	Activity 1. Outline the evidence based information and supportive care strategies to prevent and manage cardiac toxicity in the individual receiving targeted therapies.

Immunosuppression

Alemtuzumab is a monoclonal antibody targeting the CD52 antigen expressed on the surface of both normal and malignant T and B lymphocytes, natural killer cells and cells of the myeloid lineage.[16, 26]

Alemtuzumab therapy results in bone marrow suppression and a profound lymphopaenia. This puts individuals at increased risk of developing serious bacterial, fungal, viral and protozoan infections.[16]

Management strategies include:[16, 26]

- prophylaxis for pneumocystis pneumonia with trimethoprim / sulfamethoxazole, dapsone or pentamidine
- prophylaxis for varicella zoster and herpes simplex infections with acyclovir or valacyclovir
- antifungal therapy as required
- monitoring for signs and symptoms of cytomegalovirus (CMV) infection during therapy and for 2 months post completion
- CMV surveillance, CT scans, and bronchoscopy

Other effects

Fluid retention is common and presents as periorbital and lower extremity oedema in at least 50-60% of individuals treated with imatinib.[16, 27] Serious effects of fluid retention include:

- pleural effusion
- ascites
- rapid weight gain
- pulmonary oedema.

Fluid retention and oedema has also been reported in the second generation TKI dasatinib. Management includes monitoring for signs of fluid retention and oedema during therapy. Individuals need to be educated to weigh themselves daily at home and to report weight gains of 1 kg in one week and symptoms of dyspnoea.[3] Symptom management strategies include diuretics for periorbital and lower extremity oedema and ice packs or haemorrhoid preparations for periorbital oedema.[27]

A group of rare but significant side effects has been associated with the use of bevacuzumab including:[2, 3, 25]

- development of potentially fatal gastrointestinal perforations
- complicated wound healing and tissue repair such as wound dehiscence, tracheoesophageal fistula, and perforation of nasal septum
- haemorrhage - epistaxis, hematemesis, hemoptysis, bleeding at tumour sites, subarachnoid, and haemorrhagic stroke.

This has led to black box warnings being listed with the use of this agent. Although rare, at times these serious adverse events can be fatal and requires nurses to develop skills in assessing for alterations and educating individuals on the importance of reporting symptoms early. The following management strategies should be considered:[3, 25]

- assess baseline bowel and skin integrity and signs of delayed wound healing each visit
- assess for conditions that place the individual at risk for bleeding
- assess baseline mental status and neurological signs and monitor during therapy for CNS haemorrhage, reversible posterior leukoencephalopathy and fatal encephalopathy
- educate individuals on signs to report immediately - wound dehiscence, bleeding tendencies such as epistaxis, hematemesis, and hemoptysis, abdominal pain associated with nausea, vomiting and constipation
- treatment should be interrupted prior to surgical procedures, although the exact time interval required is not known.

Learning activities	
Completed	Activities
☐	1. For the person you have assessed: • identify the short term effects they are at risk of or experience • summarise current evidence based strategies to prevent and manage these effects • document a nursing care plan to meet their needs
☐	2. Provide an education session with an individual prior discharge to prevent or manage at least two treatment related effects in the community. Reflect on the session to identify how effective you were in providing information and how you could improve your skills in this area.

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