Targeted Therapies and Immunotherapy: General Principles (Oncology) – CE

ALERT
Don appropriate personal protective equipment (PPE) based on the patient’s signs and symptoms and indications for isolation precautions.

Refer to Oncology Nursing Society (ONS) interim guidelines for PPE recommendations during an emergent shortage of PPE (e.g., pandemic).

Hypersensitivity reactions, such as anaphylaxis, may occur with targeted therapy and immunotherapy; therefore, frequent assessments and monitoring are required.

Only qualified physicians, physician assistants, advanced practice registered nurses (APRNs), or nurses with demonstrated competency administer antineoplastic therapies. Refer to the professional’s regulatory scope of practice and the organization’s practice.

Take steps to eliminate interruptions and distractions during medication preparation.

OVERVIEW
Normal cell reproduction, growth, and apoptosis are controlled by complex signaling pathways at the extracellular and intracellular levels. Malfunctioning of these pathways occurs in malignancies, leading to increased proliferation, tissue invasion, metastases, and apoptosis inhibition.

Development of targeted therapies overcame the lack of selectivity associated with conventional antineoplastic therapy by targeting specific protein pathways. Although these pathways can be present in normal tissue, they are overexpressed or mutated in cancerous tissue. Cancer immunotherapy represents precision medicine, which helps the immune system fight cancer and offers a type of targeted or personalized therapy. In comparison, traditional cytotoxic chemotherapy attacks both malignant and nonmalignant cells, causing disruption of the cell cycle and other cell functions. Targeted therapy may not be more or less effective than traditional antineoplastic therapies, but it offers a unique approach to the treatment of cancer and other diseases and has toxicities different from those of traditional antineoplastic therapy. Because targeted therapies are more predictable and have fewer side effects than chemotherapy, patients tolerate them better. Chemotherapy, biotherapy, and targeted therapy may be administered concurrently, offering improved survival for many patients with cancer.

Targeted therapies can be divided into two broad categories: monoclonal antibodies (MoAbs) and small molecules. Many targeted therapies are named after the mechanism of action or the specific aimed kill target (Table 1).
### Table 1: Examples of Targeted Therapy and Immunotherapy Classifications and Approved Indications

<table>
<thead>
<tr>
<th>Target(s)</th>
<th>Agent(s)</th>
<th>Indication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MoAbs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EGFR</td>
<td>Cetuximab</td>
<td>• mCRC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• SCCHN</td>
</tr>
<tr>
<td>EGFR</td>
<td>Panitumumab</td>
<td>• mCRC</td>
</tr>
<tr>
<td>VEGF</td>
<td>Bevacizumab</td>
<td>• mCRC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• NSCLC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Glioblastoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• RCC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cervical</td>
</tr>
<tr>
<td>HER2</td>
<td>Trastuzumab</td>
<td>• Breast</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Gastric</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• GE junction</td>
</tr>
<tr>
<td>CD20 on B cells</td>
<td>Rituximab</td>
<td>• Non-Hodgkin lymphoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• CLL</td>
</tr>
<tr>
<td>CD52</td>
<td>Alemtuzumab</td>
<td>• CLL</td>
</tr>
<tr>
<td>Tyrosine kinase inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCR-ABL</td>
<td>Bosutinib</td>
<td>• CML</td>
</tr>
<tr>
<td>Dasatinib</td>
<td></td>
<td>• CML</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ALL Ph+</td>
</tr>
<tr>
<td>Imatinib</td>
<td></td>
<td>• ALL Ph+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MDS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• CML</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• GIST</td>
</tr>
<tr>
<td>Nilotinib</td>
<td></td>
<td>• CML</td>
</tr>
<tr>
<td>EGFR pathway</td>
<td>Lapatinib</td>
<td>Breast</td>
</tr>
<tr>
<td>HER2 (EGFR2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All EGFR</td>
<td>Afatinib</td>
<td>NSCLC</td>
</tr>
<tr>
<td>EGFR1</td>
<td>Erlotinib</td>
<td>• Metastatic NSCLC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Metastatic pancreatic</td>
</tr>
<tr>
<td>VEGF</td>
<td>Axitinib</td>
<td>RCC</td>
</tr>
<tr>
<td>MEK</td>
<td>Trametinib</td>
<td>Melanoma</td>
</tr>
<tr>
<td>mTOR inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mTOR pathway</td>
<td>Temsirolimus</td>
<td>• RCC</td>
</tr>
<tr>
<td></td>
<td>Everolimus</td>
<td>• RCC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• SEGA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Advanced breast</td>
</tr>
<tr>
<td>BRAF inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mutated BRAF</td>
<td>Dabrafenib</td>
<td>• Melanoma: unresectable or metastatic</td>
</tr>
<tr>
<td></td>
<td>Vemurafenib</td>
<td>• Melanoma</td>
</tr>
<tr>
<td>Multikinase inhibitors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blocks receptor tyrosine</td>
<td>Ceritinib</td>
<td>Metastatic NSCLC</td>
</tr>
<tr>
<td>kinases ALK, IGF-1R, InsR,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>and ROS1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Targeted Therapies and Immunotherapy: General Principles (Oncology) – CE

<table>
<thead>
<tr>
<th>Blocks receptor tyrosine kinases ALK, HGFR, c-MET</th>
<th>Crizotinib</th>
<th>Metastatic NSCLC that is ALK positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>VEGFR1,2,3; PDGF-R, FGFR</td>
<td>Pazopanib</td>
<td>– RCC – Sarcoma</td>
</tr>
<tr>
<td>VEGFR2, PDGF, RAF</td>
<td>Sorafenib</td>
<td>– RCC – Hepatocellular</td>
</tr>
</tbody>
</table>

#### Proteasome inhibitors

<table>
<thead>
<tr>
<th>Inhibits 20S proteasome</th>
<th>Carfilzomib</th>
<th>– Multiple myeloma – Mantle cell lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibits 26S proteasome</td>
<td>Bortezomib</td>
<td>– Multiple myeloma – Mantle cell lymphoma – Non-Hodgkin lymphoma</td>
</tr>
</tbody>
</table>

#### Immunomodulators

| Thalidomide | Lenalidomide | Pomalidomide | – Myeloma – Myeloma, MDS – Myeloma |

#### Immunotherapy

<table>
<thead>
<tr>
<th>PD1</th>
<th>Pembrolizumab</th>
<th>Melanoma</th>
</tr>
</thead>
</table>

| CTLA-4 | Ipilimumab | Melanoma |

---

**MoAbs** are large molecules that act similarly to immune system antibodies and are typically categorized as a type of immunotherapy. These drugs are given intravenously because they are proteins and would be destroyed by the gut. MoAbs are made by injecting animals (usually mice) with the target proteins, causing the animals to develop antibodies to that protein. These antibodies are then “humanized” by replacing most of the antibody with human antibody to make the resultant antibody less foreign to humans, thereby minimizing hypersensitivity reactions.

**Small molecules** are so named in reference to the drug’s ability to pass through cell membranes to interact with targets within a cell. Given orally, many of these agents act on multiple pathways in the cell. As a result, cell-signaling pathways that regulate basic cellular functions are blocked. Most of these agents are metabolized by the cytochrome P450 (CYP450) enzymes. Examples include tyrosine kinase inhibitors, proteasome inhibitors, and immunomodulators.
Targeted Therapies and Immunotherapy: General Principles (Oncology) – CE

inhibitors, hedgehog pathway antagonists, angiogenesis inhibitors, and mammalian target of rapamycin (mTOR) inhibitors.

MoAbs, such as cetuximab and trastuzumab, target epidermal growth factor receptors (EGFRs), including human epidermal growth factor receptor 1 (hEGFR1) and human epidermal growth factor receptor 2 (hEGFR2), as well as EGFRs found in the extracellular receptor kinase pathway. Rituximab specifically targets CD20-positive cells. Oftentimes, antibodies act directly on a receptor and are generally more specific than other targeted agents.

The intracellular signaling kinase pathway includes Src (proto-oncogene tyrosine-protein kinase), phosphatidylinositol 3-kinase (PI3k) or araA-sensitive gene (Ak+) or mTOR protein, and the mitogen-activated protein kinase pathway. These pathways are responsible for the communication between extracellular and intracellular signals. Two proteins, the breakpoint cluster region-tyrosine kinase protein, which is associated with chronic myeloid leukemia, and the mTOR protein, which is associated with renal cell, breast, ovarian, colon, and other cancers, are located intracellularly. Kinase inhibitors such as dasatinib, sorafenib, erlotinib, and gefitinib target tyrosine kinase found in the intracellular space as well. The third pathway, angiogenesis, involves the formation of new blood vessels (neovascularization) from existing vasculature and becomes abnormal in malignancy. Angiogenesis is stimulated by many factors, including hypoxia and growth factors such as vascular endothelial growth factor (VEGF). Overproduction of VEGF triggers abnormal angiogenesis. An example is the MoAb bevacizumab, which targets VEGF overexpression.

Novel agents designed to overcome resistance to targeted therapies and immunotherapies have been developed. Antibody drug conjugates (ADCs) are agents that consist of a cytotoxic agent and an antibody that targets an antigen expressed on malignant cells. Trastuzumab emtansine is an example of an ADC approved for the treatment of metastatic breast cancer that has demonstrated resistance to trastuzumab. Chimeric antigen receptor (CAR)-T cells are an example of adoptive cell transfer effective in many B-cell malignancies. Vaccine therapy, another type of immunotherapy, is aimed at preventing cancer.

Dose modifications, delays, or discontinuation of these therapies may be necessary when intolerable side effects develop, tumor progression occurs, or resistance develops. Dermatologic and gastrointestinal problems, specifically diarrhea, are common side effects of targeted therapy. Dermatologic side effects typically include rash (most common), xerosis, and nail and hair changes. Hypersensitivity reactions (e.g., anaphylaxis, infusion-related symptoms) are also common and potentially life threatening, and they are especially common when MoAbs are given. Antiangiogenic agents can cause gastrointestinal perforation and interfere with surgical and wound healing. Less common but severe side effects include cardiac (e.g., hypertension, congestive heart failure, decreased left ventricular ejection fraction), pulmonary (e.g., interstitial lung disease), metabolic (e.g., hypomagnesemia), and ocular toxicities (e.g., eyelid changes, corneal erosions). The severity of toxicities is rated using a validated toxicity grading tool (e.g., Common Terminology Criteria for Adverse Events). If other antineoplastic therapies are part of the treatment regimen, patients also may develop toxicities associated with the additional specific agent(s).
Targeted Therapies and Immunotherapy: General Principles (Oncology) – CE

Patient and caregiver education is critical to ensure that the completion of therapy occurs while maintaining quality of life. Education should include the rationale for the targeted therapies and immunotherapies, the therapy schedule, toxicities (early and late), and strategies for self-management of toxicities. Many targeted therapies are taken continuously for months to years until unwanted side effects, disease progression, or disease resistance occurs. Adherence and safe handling practices should be discussed regularly with the patient and caregiver to identify any difficulties or nonadherence to the dosing plan. If the patient expresses concern regarding accuracy of a medication, the medication should not be given. The concern should be explored, the practitioner notified, and the order verified.

EDUCATION

- Provide developmentally and culturally appropriate education based on the desire for knowledge, readiness to learn, and overall neurologic and psychosocial state.
- Explain the rationale for targeted therapy or immunotherapy, including indications (diagnosis).
- Discuss the treatment goals (e.g., cure, control, palliation) and how the responses to therapy are measured.
- Discuss the route, dose, and estimated time to completion of treatment. Provide the patient and caregiver with written materials on the route, rationale, dose, frequency, and toxicities related to targeted therapy; self-care measures to minimize and prevent side effects; safe handling techniques; and important contact information.
- Educate the patient and caregiver regarding the potential side effects and adverse reactions of the medication.
- Instruct the patient and caregiver to report adverse reactions promptly; some troublesome side effects can be managed effectively.
- Educate the patient and caregiver on the administration, storage, and handling of oral agents, including the importance of taking them as scheduled, swallowing oral drugs whole, and taking unused oral agents to the clinic or pharmacy for proper disposal.
- Instruct the patient and caregiver that drugs taken continuously will result in metabolites continually being excreted in body fluids; therefore, they must practice safe handling precautions.
- Instruct the patient and caregiver to notify the nurse immediately regarding any toxicities (e.g., pain, burning at the injection site, shortness of breath, chest heaviness, impending sense of doom) during administration of these agents.
- Instruct the patient and caregiver on the importance of keeping appointments for laboratory tests and clinical examinations. Ensure that the patient and caregiver have a reliable phone number to call in case they have questions.
- Teach the patient and caregiver how and when to take the patient’s temperature.
- Instruct the patient to avoid crowds and people with colds and coughs when his or her white blood cell count is low.
- Discuss fertility issues with patients of childbearing age before, during, and at completion of targeted therapy and immunotherapy.
- Instruct the patient and caregiver to alert the practitioner if the patient experiences symptoms indicating toxicity (Table 2).
<table>
<thead>
<tr>
<th><strong>Table 2</strong> Therapy Side Effects with Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Side effect(s) or reaction(s)</strong></td>
</tr>
<tr>
<td>Gastrointestinal</td>
</tr>
</tbody>
</table>
| Diarrhea | • Loose watery stools  
• Abdominal cramping  
• Electrolyte imbalances  
• Dehydration  
• Perianal irritation and breakdown | • Gefitinib  
• Ipilimumab  
• Dasatinib  
• Erlotinib  
• Gefitinib  
• Imatinib  
• Lapatinib  
• Sunitinib  
• Temsirolimus  
• Thalidomide |
| Mucositis | • Mild to moderate  
• Oral ulceration  
• Mouth pain  
• Dysgeusia | • Everolimus  
• Temsirolimus |
| Integumentary | | |
| Side effects more common with targeted therapies. Presence of these side effects may indicate successful treatment. |
| Rash | • Rash begins around the nose and cheeks and chest and back.  
• Hyperpigmentation occurs 1-2 weeks after therapy begins and typically resolves 2-3 weeks after therapy is complete; may be permanent.  
| • Cetuximab  
• Erlotinib  
• Everolimus  
• Lapatinib  
• Sorafenib  
• Sunitinib  
• Trastuzumab |
| Papulopustular rash | • Diffuse erythema over the face and body progressing to follicular papules and pustules; in many cases resembles acne  
• Can be itchy and tender lesions  
• Rarely overt necrosis and ulceration | • Cetuximab  
• Erlotinib  
• Everolimus  
• Gefitinib  
• Lapatinib  
• Sunitinib  
• Temsirolimus |
| Xerosis (dry skin) | • Usually occurs with a rash  
• Abnormal dryness of skin, mucous membranes, or conjunctiva | • Axitinib  
• Cetuximab  
• Erlotinib  
• Gefitinib  
• Sorafenib  
• Sunitinib  
• Temsirolimus |
| Stevens-Johnson syndrome | • Rare disorder  
• Skin and mucous membrane react severely to therapy  
• Begins with flu-like symptoms followed by painful red rash that spreads and blisters occur  
• Eventually skin sloughs | • Gefitinib  
• Ipilimumab |
## Targeted Therapies and Immunotherapy: General Principles (Oncology) – CE

| Palmar-plantar erythrodysesthesia (hand-foot syndrome) | • Initially mild redness of the palms and soles progressing to intense burning pain and tenderness  
• Calluses  
• Palms and soles edematous  
• Ulceration may occur  
• May interfere with walking or grasping objects | • Axitinib  
• Everolimus  
• Lapatinib  
• Pazopanib  
• Sorafenib  
• Sunitinib |
| --- | --- | --- |
| Alterations in nails | • Pain  
• Fissures  
• Tenderness  
• Paronychial  
• Inflammation of the lateral nail folds, toes, and fingers (especially the great toe and thumbs)  
• Nail shedding | • Sunitinib  
• Sorafenib  
• Cetuximab  
• Everolimus |
| Alterations in hair color | • Pigmentation changes are temporary | • Sunitinib  
• Imatinib |
| Alopecia | • Hair thinning  
• Dry, brittle hair  
• Hair loss | • Axitinib  
• Cetuximab  
• Gefitinib  
• Panitumumab  
• Sorafenib |
| **Hypersensitivity** | | |
| Anaphylaxis | • Can be mild to severe or fatal  
• May develop during therapy or just hours after it begins  
• Symptoms may include fever, nausea, vomiting, flushing, rashes, urticaria, angioedema, bronchospasm, back pain, shortness of breath, alterations in heart rate and blood pressure, rigors | • More common with murine MoAbs (with suffix of -momab)  
• Least common with fully humanized MoAb (with suffix of -umab)  
• MoAbs |
| Ocular | • Ocular discomfort  
• Visual blurring  
• Conjunctivitis  
• Lacrimation | • Epidermal growth factor receptor inhibitors  
• Gefitinib  
• Cetuximab  
• Erlotinib |
| Cardiovascular | | |
| Thrombosis | • Clot formation  
• Cardiac ischemia | • Bevacizumab  
• Sorafenib  
• Sunitinib |
| QT prolongation | • Arrhythmia  
• Asymptomatic | • Crizotinib  
• Dabrafenib  
• Lapatinib  
• Sorafenib  
• Sunitinib  
• Nilotinib |
Hypertension  • Elevated blood pressure  • Pazopanib  • Axitinib  • Bevacizumab

MoAb, monoclonal antibody


- Dermatologic toxicity: Rash, palmar-plantar erythrodysaesthesia (hand-foot syndrome), and alterations in nail and hair color (90% of patients receiving therapy have dermatologic reactions within the first few weeks of therapy)9,10
- Anaphylaxis: Impending sense of doom and rapid onset of hypotension
- Infusion-related reactions (immediate or delayed): Chills, fever, headache, pruritus, skin rash, and loss of strength
- Ocular toxicity: Changes in eyelids or tear ducts and abnormal eyelash growth
- Pulmonary interstitial lung disease: Breathing difficulties, change in breathing ability, unproductive cough, chest pain, increased fatigue, low-grade fever, and increased heart rate
- Cardiac toxicity: Fatigue, unproductive cough, shortness of breath, and fluid retention in feet and ankles
- Vascular toxicity: Bruising, bleeding from wounds, nose bleeds, vomiting blood, and abnormally heavy menstruation
- Electrolyte imbalance: Muscle cramps, abnormal heart rhythm, feelings of hyperexcitability, irritability, confusion, and seizures
- Persistent diarrhea not controlled with pharmacologic management
- Persistent nausea and vomiting not controlled with pharmacologic management
- Stomatitis associated with administration of mTOR inhibitors

- Educate the patient and caregiver on acute and long-term toxicities specific to targeted therapy or immunotherapy (Table 2).
- Instruct the patient on self-care measures to manage acute and long-term toxicities specific to the drug(s) he or she is receiving (Table 3).
- Encourage questions and answer them as they arise.

**Table 3** Patient Education: Preemptive Self-Care Measures for Targeted Therapy Dermatologic Toxicities

<table>
<thead>
<tr>
<th>Do</th>
<th>Do not</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintain adequate hydration</td>
<td>Use lotions and creams containing irritants such as alcohol, perfume, and dyes</td>
</tr>
<tr>
<td>Use water-based, non-alcohol-based skin care products</td>
<td>Use alcohol-based skin care products</td>
</tr>
<tr>
<td>Use heavy moisturizer and water-based facial cleansers</td>
<td>Expose skin to sun</td>
</tr>
<tr>
<td>Use camouflage makeup</td>
<td></td>
</tr>
<tr>
<td>Use sunscreen containing a sun protection factor &gt;30 containing zinc oxide or titanium dioxide</td>
<td></td>
</tr>
<tr>
<td>Use lukewarm water to bathe using mild soap</td>
<td></td>
</tr>
</tbody>
</table>
Targeted Therapies and Immunotherapy: General Principles (Oncology) – CE

- Follow up with skin assessments every clinic visit
- Use prophylactic antibiotics and other medications as prescribed
- Use topical corticosteroids as prescribed
- Use oral histamines as needed
- Use extremely hot or cold water
- Perform harsh skin cleansing


ASSESSMENT AND PREPARATION

Assessment
1. Perform hand hygiene and don PPE as indicated for needed isolation precautions.
2. Introduce yourself to the patient.
3. Verify the correct patient using two identifiers.
4. Assess the patient’s knowledge and understanding of targeted therapy and immunotherapy.

a. Knowledge and experience (including preconceived notions)

    Rationale: The patient’s knowledge and understanding will affect his or her motivation to participate actively in treatment.

b. Goals for therapy, such as being cured, living to a certain event, or regaining mobility

5. Determine what specific information (e.g., side effects, prognosis, timing of treatments) the patient wants to learn, and ensure that this information is addressed.

    Rationale: Information the patient wants to know may be missed if only a teaching template about the side effects, prognosis, or timing of treatments is followed.

6. Determine the baseline history and physical assessment information (Table 4) required for each therapy agent.

| **Table 4** Baseline History and Physical Examination Before and During Targeted Therapies, Immunotherapy, and Chemotherapy |
|------------------|------------------|
| **Type**         | **Assessments**  |
| Health history   | • Type of cancer |
|                  | • Disease and previous treatments |
|                  | • History of chemotherapy or biotherapy toxicity |
|                  | • Previous self-interventions to manage toxicity and their effectiveness |
|                  | • Nutritional history |
|                  | • Complementary and alternative therapy |
|                  | • Other comorbidities |
|                  | • Medications and supplements |
|                  | • Allergies |
### Targeted Therapies and Immunotherapy: General Principles (Oncology) – CE

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reproductive history</td>
<td>• Pain</td>
</tr>
<tr>
<td></td>
<td>• Fatigue</td>
</tr>
<tr>
<td></td>
<td>• Sleep</td>
</tr>
<tr>
<td></td>
<td>• Distress</td>
</tr>
<tr>
<td></td>
<td>• Over-the-counter medications, including herbals and supplements</td>
</tr>
<tr>
<td>Laboratory analysis</td>
<td>• Complete blood count with differential</td>
</tr>
<tr>
<td></td>
<td>• Other laboratory tests, as indicated by clinical trials or as prescribed</td>
</tr>
<tr>
<td>Vital signs</td>
<td>• Blood pressure</td>
</tr>
<tr>
<td></td>
<td>• Heart rate</td>
</tr>
<tr>
<td></td>
<td>• Respiratory rate</td>
</tr>
<tr>
<td></td>
<td>• Temperature</td>
</tr>
<tr>
<td>Hematologic</td>
<td>• Color of skin and mucous membranes</td>
</tr>
<tr>
<td></td>
<td>• Presence of bruising or petechiae</td>
</tr>
<tr>
<td></td>
<td>• Signs of infection</td>
</tr>
<tr>
<td></td>
<td>• Intolerance to activity</td>
</tr>
<tr>
<td>Neurologic</td>
<td>• Preexisting motor or sensory deficits</td>
</tr>
<tr>
<td></td>
<td>• Cognitive and behavioral functioning</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>• Rhythm</td>
</tr>
<tr>
<td></td>
<td>• Depth of respirations</td>
</tr>
<tr>
<td></td>
<td>• Use of accessory muscles</td>
</tr>
<tr>
<td></td>
<td>• Cough</td>
</tr>
<tr>
<td></td>
<td>• Shortness of breath</td>
</tr>
<tr>
<td></td>
<td>• Dyspnea</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>• Heart sounds</td>
</tr>
<tr>
<td></td>
<td>• Rhythm</td>
</tr>
<tr>
<td></td>
<td>• Peripheral edema</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>• Integrity of lips, gums, teeth, mucosa, and tongue</td>
</tr>
<tr>
<td></td>
<td>• Oral cavity moisture</td>
</tr>
<tr>
<td></td>
<td>• Presence of bowel sounds</td>
</tr>
<tr>
<td></td>
<td>• Pattern of bowel movements</td>
</tr>
<tr>
<td></td>
<td>• Presence of hemorrhoids</td>
</tr>
<tr>
<td></td>
<td>• Pain</td>
</tr>
<tr>
<td></td>
<td>• Bleeding</td>
</tr>
<tr>
<td>Renal</td>
<td>• Pattern of urinary elimination</td>
</tr>
<tr>
<td></td>
<td>• Urine color</td>
</tr>
<tr>
<td></td>
<td>• Urine amount</td>
</tr>
<tr>
<td></td>
<td>• Urination frequency</td>
</tr>
</tbody>
</table>


a. Review package inserts, clinical trial protocols, and journal articles for specific information.

b. Review baseline tests (e.g., echocardiogram, pulmonary function testing).

c. Review genomic tests (i.e., presence of the K-ras oncogene [KRAS] in patients with colorectal cancer).
**Targeted Therapies and Immunotherapy: General Principles (Oncology) – CE**

**Rationale:** Patients with a mutation of the KRAS oncogene (40% of people with colorectal cancer) are resistant to cetuximab and panitumumab therapy. Different genomic tests are associated with resistance to different drugs, so genomic review is important for all patients.\(^7\)

d. Review the potential side effects of each agent and the patient’s history of adverse reactions.

e. Review the potential drug–drug and drug–food interactions.

7. Assess the patient for specific contraindications to receiving targeted therapy or immunotherapy and advise the practitioner accordingly.

8. Assess toxicities before each subsequent dose using a validated toxicity grading tool.

9. Assess the need for pretreatment interventions (e.g., to prevent hypersensitivity reactions and fluid retention; antiemetics).

**Preparation**

1. Ensure that informed consent is obtained and available for review per the organization’s practice.

2. Verify the patient’s actual admission weight in kilograms. Reweigh the patient if appropriate.\(^6\) Stated, estimated, or historical weight should not be used.\(^6\) Obtain the patient’s height.

3. Recalculate drug doses based on weight and height before each new cycle of antineoplastic therapy.

    **Rationale:** Doses of some antineoplastic agents are based on body surface area (BSA). Accurate measurement of the patient’s height and weight is needed to perform this calculation. Patients may understate or overstate their height and weight, so measurements must be performed.

4. Obtain the medication, check the practitioner’s order, verify the expiration date, and inspect the medication for particulates, discoloration, or other loss of integrity.

    **Do not use medication that is cloudy or precipitated unless such is indicated by its manufacturer as being safe.**

5. Review medication reference information pertinent to the medication’s action, purpose, onset of action and peak action, normal dose, and common side effects and implications.

6. Anticipate orders for baseline and ongoing diagnostic tests before administering therapy.

7. Notify the practitioner if the patient shows evidence of worsening toxicities.

8. Notify the practitioner of abnormal laboratory or diagnostic results and anticipate modifications to the therapy dose.

    **Rationale:** Clinical signs, symptoms, and results of laboratory and diagnostic tests help to determine whether targeted therapy can be given at full dose, dose reduction, dose delay, or withheld.

9. Stress to the patient and caregiver the importance of receiving the therapy dose on time, except when dose-limiting side effects are present.

10. Ensure that an antineoplastic therapy spill kit is available.
Targeted Therapies and Immunotherapy: General Principles (Oncology) – CE

11. Ensure that emergency equipment is readily available in the event of a hypersensitivity reaction or other emergency situation.

PROcedure

1. Perform hand hygiene and don gloves and appropriate PPE based on the patient’s signs and symptoms and indications for isolation precautions. Use the ONS interim guidelines for PPE recommendations during an emergent shortage of PPE (e.g., pandemic) (Table 5).13

<table>
<thead>
<tr>
<th>PPE</th>
<th>ONS recommendations*</th>
<th>Pandemic interim guidelines (in descending order)</th>
</tr>
</thead>
</table>
| Gown     | Disposable poly-coated gown | • Regular disposable gown (water resistant)  
       |                       | • Cloth gown (facility laundered) for infection control and nonhazardous drugs |
| Mask     | Mask with face and eye protection required only if splashing likely and for spill cleanup | • N95 mask for symptomatic or patients with COVID-19 and hazardous drug spills and cleanup  
       |                       | • PAPR |
| Eye protection | Mask with eye protection or goggles if splashing likely or spill cleanup | • Full facepiece air-purifying respirator or PAPR |
| Gloves   | Double chemotherapy-tested gloves | • Single chemotherapy-tested gloves  
       |                       | • Double standard examination gloves  
       |                       | • Single standard examination gloves |
| Shoe covers | Only in area for compounding hazardous drugs | • Work-only, washable shoes |

COVID, coronavirus; PAPR, powered air purifying respirator; PPE, personal protective equipment

*Highest-level recommended practice based on supplies of available PPE

2. When no PPE shortage exists, don double chemotherapy-tested gloves, impervious chemotherapy-resistant gown with long sleeves that closes in the back, respirator in case of aerosol exposure, and eye protection and face shield in case of splashing when handling hazardous drugs (targeted therapy or immunotherapy)14,15 or the bodily fluids of a patient who has received them within the past 48 hours.3,14 If only oral agents are given, don one pair of chemotherapy-tested gloves only, unless there is a risk of aerosolization and provided the capsule or tablet is intact.14,15

3. Two practitioners or personnel approved to prepare or administer antineoplastic therapies verify the patient using two identifiers, confirm with the patient the planned treatment, and verify the drug name, dose, volume, rate and route of administration, expiration dates and times, and appearance and integrity of the drugs.

4. Explain the procedure to the patient and ensure that he or she agrees to treatment.
Targeted Therapies and Immunotherapy: General Principles (Oncology) – CE

5. Ensure the six rights of medication safety: right medication, right dose, right time, right route, right patient, and right documentation. Use a bar code system or compare the medication administration record to the patient’s identification band.

6. Label all medications, medication containers, and other solutions. The only exceptions are medications that are still in their original container or medications that are administered immediately by the person who prepared them.

7. Obtain IV access if needed or access the vascular access device (VAD). Prepare an infusion pump with appropriate IV tubing to administer the agent.

8. Ensure the patency of the route used to deliver the agent(s) before each administration and during continuous administration. IV-line patency may be determined by blood return.

9. Administer pretreatment hydration IV fluids, antiemetics, antipyretics, steroids, or other recommended therapies per the practitioner’s orders.

10. Begin administration of the ordered therapy per the organization’s practice.

11. Assess for acute toxicity (e.g., anaphylaxis, infusion-related reactions) specific to the agent(s) administered.

   **Rationale:** Acute toxicity occurs during administration.

   Monitor vital signs frequently before and during the infusions per the organization’s practice. If the patient develops anaphylaxis or an infusion-related reaction, stop the infusion immediately and notify the practitioner.

12. Flush the VAD with an appropriate solution and amount upon completion of IV administration.

13. Discard supplies, remove PPE, and perform hand hygiene.


**MONITORING AND CARE**

1. Before administering each dose of targeted therapy or immunotherapy agents, review up-to-date patient information to determine whether the prescribed therapy can continue to be given at full dose or whether a dose reduction, dose delay, or discontinuation of therapy is necessary. Review:

   a. Vital signs
   b. Patient history, including evidence of rash, diarrhea, constipation, nausea, vomiting, and weight loss
   c. Laboratory tests, including complete blood count (CBC) with differential
   d. Neurotoxicity assessment
   e. Dermatologic toxicity assessment
   f. Ocular assessment
   g. Pulmonary assessment
   h. Cardiac assessment
   i. Nutritional assessment

2. Monitor for improvement of the disease and improvement of signs and symptoms related to the disease.

3. Monitor the patient for adverse and allergic reactions to targeted therapies or immunotherapy. Recognize and immediately treat respiratory distress and circulatory
collapse, which are signs of a severe anaphylactic reaction. Follow the organization’s practice for emergency response.

4. Assess the VAD exit site for signs of infection, infiltration, and extravasation.

5. Verify the patient’s adherence to his or her oral self-administration schedule at home.

6. Assess, treat, and reassess pain.

EXPECTED OUTCOMES
- Complete, partial, or controlled response to treatment
- Early recognition of toxicities
- Minimal or no major dose-limiting toxicities
- Medication administered per the six rights of medication safety
- Entire planned targeted therapy dose received

UNEXPECTED OUTCOMES
- Cancer unresponsive to treatment
- Delayed or no recognition of side effects
- Major dose-limiting side effects, leading to discontinuation of therapy
- Medication not administered per the six rights of medication safety
- Nonadherence to oral therapy

DOCUMENTATION
- Drug interactions
- Follow-up schedule and results of follow-up calls
- History and physical assessment results
- Laboratory and diagnostic test results
- Modifications to teaching approaches for individualized learning needs
- Education and patient and caregiver’s response to education
- Patient’s adherence and motivation
- Patient’s and caregiver’s response to information and education
- Pretreatment medications and other interventions
- Side effects and methods for grading them
- Targeted therapy medications administered and order of administration
- Patient’s response to the medication, including any adverse reactions
- Patient’s weight in kilograms and height per the organization’s practice
- Psychosocial support provided
- Unexpected outcomes and related interventions

SPECIAL CONSIDERATIONS
- Older adults with comorbidities may have an altered drug metabolism; therefore, they may have a higher risk of toxicity.

REFERENCES
Targeted Therapies and Immunotherapy: General Principles (Oncology) – CE


Targeted Therapies and Immunotherapy: General Principles (Oncology) – CE


ADDITIONAL READINGS

Elsevier Skills Levels of Evidence
- Level I - Systematic review of all relevant randomized controlled trials
- Level II - At least one well-designed randomized controlled trial
- Level III - Well-designed controlled trials without randomization
- Level IV - Well-designed case-controlled or cohort studies
- Level V - Descriptive or qualitative studies
- Level VI - Single descriptive or qualitative study
- Level VII - Authority opinion or expert committee reports

Supplies
- Appropriate flushing solution
- Drug package inserts, clinical trial protocols, journal articles reviewing randomized controlled trials, or case studies
- Antineoplastic spill kit
- Emergency equipment and medications (e.g., oxygen, epinephrine)
- Hazardous medical disposal containers
- Infusion pump, if needed
- IV tubing
- Pretreatment agent(s)
- PPE
  - For isolation precautions: gloves and PPE, as indicated
  - For antineoplastic administration: double chemotherapy-tested gloves, eye protection, face shield, impervious chemotherapy-resistant gown with long sleeves that closes in the back, and respirator
- Supportive agent(s)
- Venipuncture kit (if initiating a peripheral IV line) or VAD access kit

Clinical Review: Heather T. Mackey, MSN, RN, ANP-BC, AOCN®
Published: April 2020