Recent approaches in treating pancreatic adenocarcinoma, an aggressive disease with limited survival, include the use of liposomal irinotecan as an option when first-line therapy has failed. Liposomal irinotecan has been approved in combination with 5-fluorouracil and leucovorin for patients with metastatic pancreatic cancer. Liposomal irinotecan is a newer therapy requiring oncology nurses to obtain knowledge and skills for proper administration, monitoring of hypersensitivity reactions during infusion, managing side effects, and providing patient education. Nursing considerations when administering this drug include infusion time, premedication, risk for hypersensitivity reactions and adverse events, and side effects.

**AT A GLANCE**
- Never treatment for metastatic pancreatic adenocarcinoma involves the use of liposomal irinotecan as second-line therapy.
- Liposomal irinotecan can improve drug delivery and reduce toxicity in metastatic pancreatic adenocarcinoma.
- Oncology nursing considerations for liposomal irinotecan involve chemotherapy administration, adverse events, and side effects.

### Liposomal Irinotecan

Pancreatic ductal adenocarcinoma (PDAC) is an uncommon but highly aggressive and often fatal disease. Pancreatic cancer is the fourth-leading cause of cancer-related deaths in men and the fifth-leading cause of cancer-related deaths in women (Grapsa, Syrigos, & Saif, 2016). Patients with PDAC have frequently presented at the metastatic stage of disease at the initial time of diagnosis (Lamb & Scott, 2017). The one-year survival rate for patients with metastatic pancreatic cancer is 12%, whereas the five-year survival rate is 1% (Lamb & Scott, 2017). The high mortality rate associated with pancreatic cancer has often been related to late diagnosis, the aggressive nature of PDAC, disease resistance to treatment, and the presentation of PDAC at the metastatic stage of disease (Grapsa et al., 2016). Patients with metastatic PDAC often fail first-line treatment approaches with gemcitabine-based regimens (Ansari et al., 2016). Liposomal irinotecan (Onivyde®) was approved in 2015 as a second-line treatment for metastatic PDAC in combination with 5-fluorouracil (5-FU) and leucovorin, following failure of a regimen containing gemcitabine (Ansari et al., 2016; Merrimack, 2015).

### Liposomal Irinotecan Versus Irinotecan

Liposomal irinotecan and irinotecan are not interchangeable drugs because of their specific mechanisms of action. Irinotecan, a cytotoxic alkaloid derivative of synthetic camptothecin, targets the topoisomerase I enzyme involved in DNA replication, transcription, and repair (Grapsa et al., 2016). The active metabolite of this drug, known as SN-38, can cause significant neutropenia, cholinergic responses occurring within 24 hours (e.g., diaphoresis, flushing, abdominal cramping, early-onset diarrhea), and late-onset side effects occurring after 24 hours (e.g., diarrhea, anorexia, immunosuppression) (Ipsen Biopharmaceuticals, 2017). Nanoliposomal formulation of irinotecan improves pharmacokinetics delivery by increasing drug encapsulation and loading efficiency to prolong circulation with sustained release time for enhanced antitumor activity (from exposure to SN-38) while reducing gastrointestinal toxicity in the bloodstream compared to irinotecan (Kang et al., 2015; Zhang, 2016). Liposomal irinotecan remains in the bloodstream for 11.7 hours, whereas irinotecan remains in the bloodstream for 6.07 hours (Lamb & Scott, 2017). Advantages of choosing liposomal irinotecan over irinotecan include the ability to break up extensive growth of dense fibrous tissue, known as a desmoplastic response, found around tumors (Garrido-Laguna & Hidalgo, 2015) in people with metastatic PDAC.

### Nursing Considerations

Nursing considerations for liposomal irinotecan therapy involve premedication...
for nausea, drug-related adverse events, and both cholinergic and late-onset side effects. Liposomal irinotecan administration as a chemotherapy agent is dosed at 70 mg/m² infused for 90 minutes via a peripheral or central venous catheter every two weeks. Liposomal irinotecan is administered alone prior to the infusion of leucovorin and 5-FU. Liposomal irinotecan should be protected from light and dispensed in a light-sensitive bag during infusion. According to the liposomal irinotecan package insert, a corticosteroid and an antiemetic should be administered 30 minutes prior to initiation of this drug therapy (Ipsen Biopharmaceuticals, 2017). Patients with a history of severe hypersensitivity reaction to irinotecan are not candidates for and should not receive liposomal irinotecan. In addition, patients who experience a severe hypersensitivity reaction, such as anaphylaxis, during drug administration should have immediate drug discontinuation without any further rechallenge of drug administration (Ipsen Biopharmaceuticals, 2017). The signs and symptoms of a hypersensitivity reaction include skin rash, itching, hives, shortness of breath, chest tightness, dizziness, wheezing, and angioedema of the eyes, lips, and face. In the event of a hypersensitivity reaction, upon stopping the drug, management of the reaction may include administering oxygen, steroids, or antihistamines, and/or epinephrine when ordered as appropriate interventions per institutional guidelines. Similar to irinotecan, liposomal irinotecan can cause cholinergic effects, such as rhinitis (runny nose), increased saliva production, flushing, bradycardia, abdominal cramping, and diarrhea as early-onset (within 24 hours) side effects. In some cases, atropine may be used as a premedication to eliminate or reduce the cholinergic effects caused by this drug. People homozygous for allele UGT1A1*28 require dose reductions because they are prone to adverse reactions to this drug therapy (Ipsen Biopharmaceuticals, 2017).

The most common adverse events of liposomal irinotecan include diarrhea, fatigue, neutropenia, nausea, vomiting, decreased appetite, stomatitis, and fever. Some patients may develop lung problems (although rare) like interstitial lung disease, exhibited by symptoms of new onset cough, difficulty breathing, and fever. In patients who develop interstitial lung disease, this drug should be discontinued. Certain foods (i.e., grapefruit) and drugs can also increase the plasma concentrations of liposomal irinotecan and should

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**FIGURE 1.**
LIPOSMAL IRINOTECAN NURSING IMPLICATIONS AND PATIENT EDUCATION TOPICS

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**CHEMOTHERAPY ADMINISTRATION**

Nursing implications
- **Dose = 70 mg/m²; IV administration for 90 minutes every two weeks**
- Premedications include an antiemetic and corticosteroid.
- Administer alone prior to leucovorin and 5-fluorouracil.
- Protect from light during infusion in a light-sensitive bag.
- Monitor for hypersensitivity reaction.
- **Patient education**
  - Teach signs and symptoms of an infection and low blood counts, including fever, chills, dizziness, shortness of breath, excessive bruising, and/or mouth sores.
  - Immediately report a fever of greater than 100.4°F (38°C). Instruct on proper handwashing and avoiding crowds and people with acute illness.
  - Provide information on self-pacing and low-impact activity guidelines.
  - Review cholinergic treatment guidelines and use of loperamide hydrochloride for early-onset diarrhea.
  - **Patient education**
    - Provide information on self-pacing and low-impact activity guidelines.
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    - Review cholinergic treatment guidelines and use of loperamide hydrochloride for early-onset diarrhea.
    - **ADVERSE EVENTS AND SIDE EFFECTS**
      - Nursing implications
        - **Hematologic effects** include anemia, thrombocytopenia, and neutropenia.
        - Liposomal irinotecan can cause fatigue.
        - Cholinergic effects, such as flushing, diarrhea, and abdominal cramping, can occur within the first 24 hours.
        - Gastrointestinal effects may include diarrhea, nausea, and vomiting, and decreased appetite.
        - **Patient education**
          - Instruct on cholinergic effects during infusion, including runny nose, increased saliva, flushing, bradycardia, abdominal cramping, and diarrhea.
          - Teach signs and symptoms of an infection and low blood counts, including fever, chills, dizziness, shortness of breath, excessive bruising, and/or mouth sores.
          - Immediately report a fever of greater than 100.4°F (38°C). Instruct on proper handwashing and avoiding crowds and people with acute illness.
          - Provide information on self-pacing and low-impact activity guidelines.
          - Review cholinergic treatment guidelines and use of loperamide hydrochloride for early-onset diarrhea.
          - **Patient education**
            - Teach signs and symptoms of an infection and low blood counts, including fever, chills, dizziness, shortness of breath, excessive bruising, and/or mouth sores.
            - Immediately report a fever of greater than 100.4°F (38°C). Instruct on proper handwashing and avoiding crowds and people with acute illness.
            - Provide information on self-pacing and low-impact activity guidelines.
            - Review cholinergic treatment guidelines and use of loperamide hydrochloride for early-onset diarrhea.
          - **DRUGS AND FOODS TO AVOID**
            - Nursing implications
              - Drugs to avoid include CYP3A4 or UGT1A1 inhibitors, including voriconazole, clarithromycin, telithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, and saquinavir.
              - Avoid grapefruit.
          - Patient education
            - Instruct on the avoidance of foods (grapefruit) and drugs (CYP3A4 and UGT1A1 inhibitors) that interact with therapy.

**Note.** Based on information from Ipsen Biopharmaceuticals, 2017.
be avoided within one week of receiving the drug. These drugs, known as CYP3A4 or UGT1A1 inhibitors, including voriconazole, clarithromycin, telithromycin, atazanavir, indinavir, nefavozano, nelfinavir, ritonavir, and saquinavir, should be avoided (Ipsen Biopharmaceuticals, 2017).

**Liposomal Irinotecan Patient Education**

Patient education on liposomal irinotecan therapy should consist of verbal and written instructions on drug administration, including the potential for adverse events like hypersensitivity reaction, and information on how to manage side effects. Patients should be instructed on the use of premedication with a corticosteroid and an antientemic to prevent nausea and vomiting. In particular, side effects of corticosteroids, such as facial puffiness, high blood pressure, headache, increased blood sugar, insomnia, mood swings, and bone thinning, should be reviewed. Patients premedicated with an antientemic to prevent or reduce nausea and vomiting related to this drug may be prescribed additional antientemics to be taken at home as needed. The 5-HT₃ receptor antagonists used as antientemics can cause headaches, constipation, or diarrhea.

Diarrhea, neutropenia, and infection are important considerations for patient and family education. Diarrhea can develop as early as 24 hours after the administration of liposomal irinotecan. Diarrhea may present in combination with abdominal cramping and symptoms of dehydration, such as dizziness or light-headedness. Diarrhea may be treated with antidiarrheal agents as needed. Nurses should emphasize proper daily fluid intake and dietary considerations (e.g., low fiber) and monitor for moderate or severe toxicity for urgent clinical evaluation needs. Dose reduction of the drug may be necessary if diarrhea becomes unmanageable. Neutropenia, defined as a low white blood cell count with an absolute neutrophil count of less than 1,500/ml, may result from use of this drug. Recommendations by the drug manufacturer indicate checking complete blood counts with differential every two weeks to monitor for immunosuppression (Ipsen Biopharmaceuticals, 2017), whereas clinicians may opt to check laboratory values in between cycles of drug therapy or only prior to infusion.

Patients are more prone to developing an infection when neutropenic, and they should be aware of signs and symptoms of an infection, such as fever, chills, or influenza. Patients should check their temperature daily and immediately communicate a fever higher than 100.4°F (38°C) to a clinician, anticipating further guidance depending on reported symptoms. Patients should also promptly report new onset cough and difficulty breathing with fever because these could be potential signs of interstitial lung disease. In addition, patients may experience a decreased appetite; it may be beneficial for patients to eat meals slowly and frequently and to avoid sweet, fatty, or fried foods (Ipsen Biopharmaceuticals, 2017). Patients should frequently communicate with their clinical team to ensure that all symptoms are being managed appropriately (see Figure 1).

**Conclusion**

Liposomal irinotecan is a newer therapy option for treating patients with metastatic PDAC. Liposomal irinotecan in combination with leucovorin and 5-FU can be used as second-line therapy for patients with metastatic pancreatic cancer after first-line therapy with a regimen containing gemcitabine. Liposomal irinotecan and irinotecan are both used in the treatment of metastatic pancreatic cancer but have different mechanisms of action. Oncology nurses and prescribers should be knowledgeable about adverse events, risk for hypersensitivity reactions, and the management of side effects related to liposomal irinotecan. Nurses should continually educate patients to ensure awareness of therapy side effects and knowledge on how to manage them, encouraging them to report adverse events to enhance effective communication and care between patients and the clinical team.

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"Liposomal irinotecan has been approved as a second-line treatment for metastatic pancreatic ductal adenocarcinoma."
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REFERENCES


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