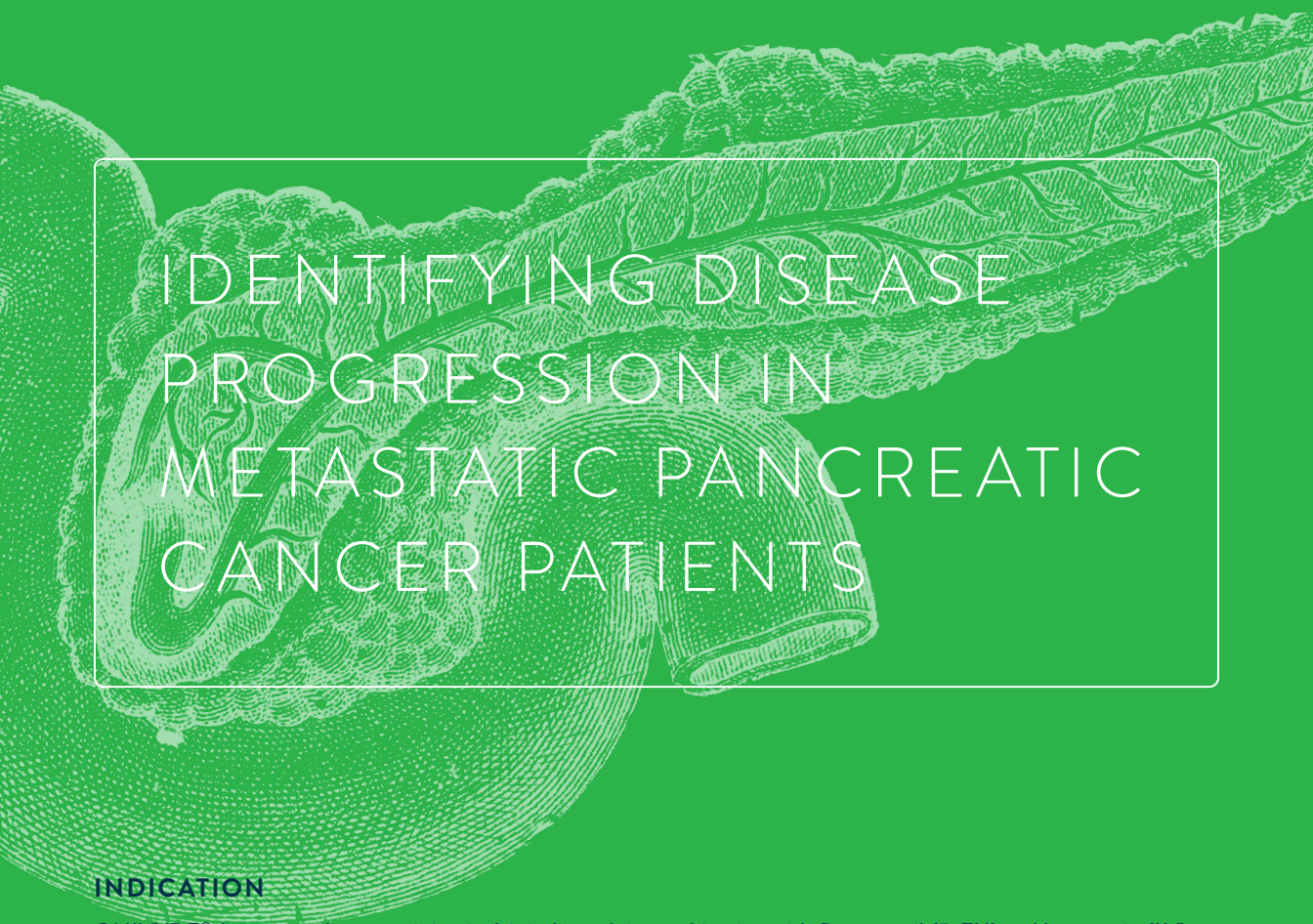


IDENTIFYING DISEASE PROGRESSION IN METASTATIC PANCREATIC CANCER PATIENTS

INDICATION

ONIVYDE® (irinotecan liposome injection) is indicated, in combination with fluorouracil (5-FU) and leucovorin (LV), for the treatment of patients with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy.

Limitation of Use: ONIVYDE is not indicated as a single agent for the treatment of patients with metastatic adenocarcinoma of the pancreas.

IMPORTANT SAFETY INFORMATION

WARNING: SEVERE NEUTROPENIA and SEVERE DIARRHEA

- **Fatal neutropenic sepsis occurred in 0.8% of patients receiving ONIVYDE. Severe or life-threatening neutropenic fever or sepsis occurred in 3% and severe or life-threatening neutropenia occurred in 20% of patients receiving ONIVYDE in combination with 5-FU and LV. Withhold ONIVYDE for absolute neutrophil count below 1500/mm^3 or neutropenic fever. Monitor blood cell counts periodically during treatment**
- **Severe diarrhea occurred in 13% of patients receiving ONIVYDE in combination with 5-FU/LV. Do not administer ONIVYDE to patients with bowel obstruction. Withhold ONIVYDE for diarrhea of Grade 2–4 severity. Administer loperamide for late diarrhea of any severity. Administer atropine, if not contraindicated, for early diarrhea of any severity**

CONTRAINDICATION

- ONIVYDE is contraindicated in patients who have experienced a severe hypersensitivity reaction or anaphylaxis to ONIVYDE or irinotecan HCl

5-FU=fluorouracil; LV=leucovorin.

Please see Important Safety Information for ONIVYDE® throughout, including Boxed WARNING on Severe Neutropenia and Severe Diarrhea, and accompanying full Prescribing Information as well as complete reference list.

onivyde®
(irinotecan liposome injection)

METASTATIC PANCREATIC CANCER—A UNIQUE CANCER FOR PROGRESSION

Since metastatic pancreatic cancer can progress rapidly, it's important to *closely monitor patients* for signs and symptoms of progression, which may present *before scan results*.[1,2]

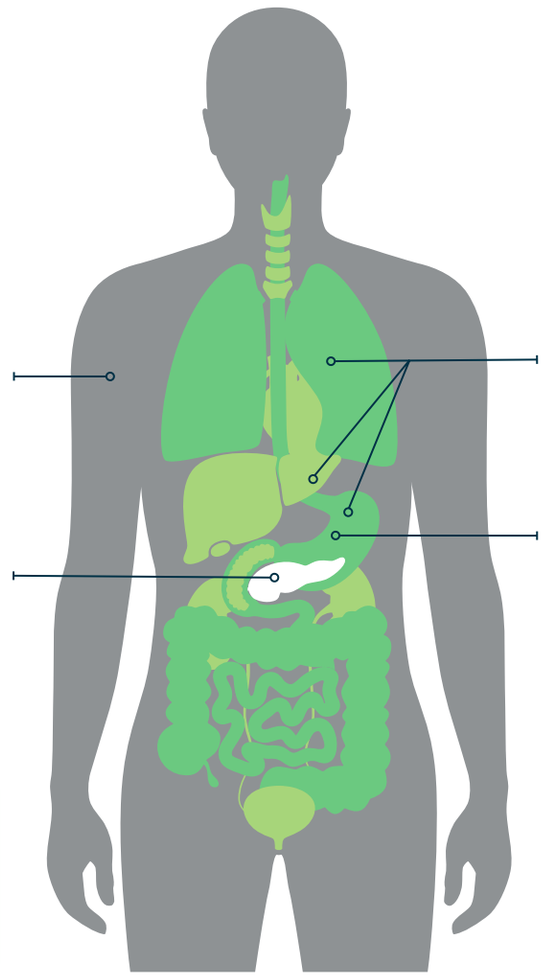
"*Patients with advanced disease may have abrupt changes in clinical status. Therefore, if treatment is begun, it should proceed with close follow-up.*"[2]

—NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pancreatic Adenocarcinoma

Increased general pain, weight loss, and **reduced activity** can indicate progression[3-7]

Increased back pain, increased lethargy, and **new-onset diabetes** are linked to pancreatic tumor activity[7,10]

Jaundice or **loss of appetite** can occur when a pancreatic tumor crowds the bile duct or stomach, respectively[7,12]



Side effects of chemotherapy and indicators of progression can present similarly: pain, lethargy, anorexia, weight loss, depression, and other symptoms can come from the tumor, the chemotherapy, or both[2,3,8,9]

Symptoms of metastasis can vary by site; most common for pancreatic tumors are the liver, lungs, and peritoneum[11]

Abdominal pain after meals may result from pancreatic enzyme insufficiency[7,13]

Keep in mind: *Caregivers may be able to provide valuable symptom information that patients may either forget or be unwilling to mention.*

Keep in mind: *Some symptoms may indicate a need for supportive care, such as pancreatic enzyme replacement, treatment for opioid-induced constipation, anticoagulants, and antidepressants.*[2]

TO IDENTIFY PROGRESSION IN METASTATIC PANCREATIC CANCER, **CONSIDER THE 3Cs**

CLINICAL SIGNS AND SYMPTOMS

- Potentially the earliest evidence for mPC progression[2]
- Monitor patients for pain, weight changes, and activity level
- Closely assess *at every visit*[14]

CA 19-9 BIOMARKER TESTS

- Indicate tumor activity; a *high, nondecreasing* CA 19-9 level, as well as an *increasing* level, may be a sign of progression[15-17]
- Ideally check *every month*

CT/PET SCANS

- Imaging at 2-3 months is recommended by ASCO[14,18]
- Worsening clinical signs/symptoms and/or CA 19-9 levels may be "red flags" to prompt an earlier scan; however, a stable scan result along with clinical signs/symptoms plus high/rising CA 19-9 may *still indicate clinical progression*[2,16]

Monitoring patients frequently and closely may help you detect progression earlier. A patient can then be switched to another therapy if eligible, and before their medical status deteriorates so far that another therapy is no longer feasible.

For your patients who progress on gemcitabine-based therapy, consider ONIVYDE® + 5-FU/LV, proven to extend overall survival (median OS: 6.1 months vs 4.2 months for 5-FU/LV alone).[19*]

**NAPOLI-1 was a global, phase 3, randomized, open-label, multicenter trial in patients (N=417) with metastatic adenocarcinoma of the pancreas whose disease had progressed following gemcitabine-based therapy. Patients were initially randomized to receive ONIVYDE® (100 mg/m² every 3 weeks) or 5-FU/LV. After 63 patients were enrolled, a third arm, ONIVYDE® (70 mg/m² every 2 weeks) + 5-FU/LV, was added. Treatment was continued until disease progression or unacceptable toxicity. The primary endpoint, median OS, was assessed with 2 pair-wise comparisons: ONIVYDE® (n=151) vs 5-FU/LV (n=149) and ONIVYDE® + 5-FU/LV (n=117) vs 5-FU/LV (n=119, post-protocol amendment). There was no improvement in OS for ONIVYDE® vs 5-FU/LV (HR=1.00, p=0.97 [2-sided log-rank]). Additional efficacy endpoints were PFS and ORR.*[19,20]

PFS=progression-free survival; ORR=overall response rate; OS=overall survival.

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS

- **Severe Neutropenia: See Boxed WARNING.** In patients receiving ONIVYDE/5-FU/LV, the incidence of Grade 3/4 neutropenia was higher among Asian (18/33 [55%]) vs White patients (13/73 [18%]). Neutropenic fever/neutropenic sepsis was reported in 6% of Asian vs 1% of White patients
- **Severe Diarrhea: See Boxed WARNING.** Severe and life-threatening late-onset (onset >24 hours after chemotherapy [9%]) and early-onset diarrhea (onset ≤24 hours after chemotherapy [3%], sometimes with other symptoms of cholinergic reaction) were observed

Please see Important Safety Information for ONIVYDE® throughout, including Boxed WARNING on Severe Neutropenia and Severe Diarrhea, and accompanying full Prescribing Information as well as complete reference list.

onivyde® (irinotecan liposome injection)

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (CONTINUED)

- **Interstitial Lung Disease (ILD):** Irinotecan HCl can cause severe and fatal ILD. Withhold ONIVYDE in patients with new or progressive dyspnea, cough, and fever, pending diagnostic evaluation. Discontinue ONIVYDE in patients with a confirmed diagnosis of ILD
- **Severe Hypersensitivity Reactions:** Irinotecan including ONIVYDE can cause severe hypersensitivity reactions, including anaphylactic reactions. Permanently discontinue ONIVYDE in patients who experience a severe hypersensitivity reaction
- **Embryo-Fetal Toxicity:** ONIVYDE can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during and for 7 months after the last dose of ONIVYDE treatment

ADVERSE REACTIONS

- The most common adverse reactions (≥20%) were diarrhea (59%), fatigue/asthenia (56%), vomiting (52%), nausea (51%), decreased appetite (44%), stomatitis (32%), and pyrexia (23%)
- The most common Grade 3/4 adverse reactions (≥10%) were diarrhea (13%), fatigue/asthenia (21%), and vomiting (11%)
- Adverse reactions led to permanent discontinuation of ONIVYDE in 11% of patients receiving ONIVYDE/5-FU/LV; The most frequent adverse reactions resulting in discontinuation of ONIVYDE were diarrhea, vomiting, and sepsis
- Dose reductions of ONIVYDE for adverse reactions occurred in 33% of patients receiving ONIVYDE/5-FU/LV; the most frequent adverse reactions requiring dose reductions were neutropenia, diarrhea, nausea, and anemia
- ONIVYDE was withheld or delayed for adverse reactions in 62% of patients receiving ONIVYDE/5-FU/LV; the most frequent adverse reactions requiring interruption or delays were neutropenia, diarrhea, fatigue, vomiting, and thrombocytopenia
- The most common laboratory abnormalities (≥20%) were anemia (97%), lymphopenia (81%), neutropenia (52%), increased ALT (51%), hypoalbuminemia (43%), thrombocytopenia (41%), hypomagnesemia (35%), hypokalemia (32%), hypocalcemia (32%), hypophosphatemia (29%), and hyponatremia (27%)
- The following adverse reactions have been identified during post approval use of ONIVYDE. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

  Immune system disorders: Hypersensitivity (including Anaphylactic reaction and Angioedema)

DRUG INTERACTIONS

- Avoid the use of strong CYP3A4 inducers, if possible, and substitute non-enzyme inducing therapies ≥2 weeks prior to initiation of ONIVYDE
- Avoid the use of strong CYP3A4 or UGT1A1 inhibitors, if possible, and discontinue strong CYP3A4 inhibitors ≥1 week prior to starting therapy

USE IN SPECIFIC POPULATIONS

- **Pregnancy and Reproductive Potential:** See WARNINGS & PRECAUTIONS. Advise males with female partners of reproductive potential to use condoms during and for 4 months after the last dose of ONIVYDE treatment
- **Lactation:** Advise nursing women not to breastfeed during and for 1 month after the last dose of ONIVYDE treatment

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FOR MORE INFORMATION VISIT ONIVYDE.COM

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Innovation for patient care

March 2023 ONV-US-002725 v2.0

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