HELP PATIENTS GO ON AFTER PROGRESSION ON GEMCITABINE IN mPDAC[1]

onivyde® (irinotecan liposome injection)

A Category 1 National Comprehensive Cancer Network® (NCCN®) recommended option in mPDAC[1*†]

NCCN RECOMMENDED

Gemcitabine-based therapy, such as gemcitabine + nab-paclitaxel[‡]

Liposomal irinotecan (ONIVYDE) + 5-FU/LV, following gemcitabine-based therapy[§]

ONIVYDE® + 5-FU/LV is the FIRST AND ONLY FDA-approved regimen for mPDAC post-gemcitabine[2]

*NCCN Category 1 Recommendation: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

†For patients with good performance status defined as ECOG 0-1 with good biliary drainage and adequate nutritional intake.

‡FOLFIRINOX is also a Category 1 first-line recommended option for patients with metastatic pancreatic cancer. Please refer to the NCCN Guidelines for Pancreatic Adenocarcinoma for detailed recommendations.

§Based on metastatic pancreatic cancer patients who have had at least 3 cycles of a gemcitabine-based regimen and did not have pancreatic cancer-related activity for 60 days prior to beginning a liposomal irinotecan (ONIVYDE) treatment regimen.

NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

ECOG=Eastern Cooperative Oncology Group; mPDAC=metastatic pancreatic ductal adenocarcinoma.

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

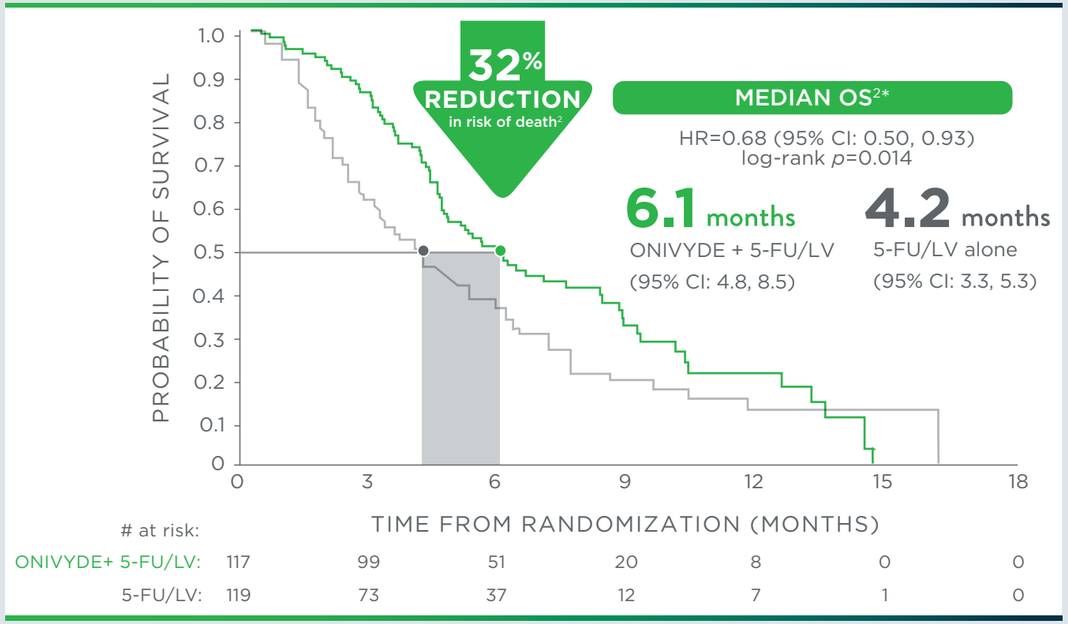
- **Fatal neutropenic sepsis occurred in 0.8% of patients receiving ONIVYDE. Severe or life-threatening neutropenic fever or sepsis occurred in 3% and severe or life-threatening neutropenia occurred in 20% of patients receiving ONIVYDE in combination with 5-FU and LV. Withhold ONIVYDE for absolute neutrophil 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**

Please see additional Important Safety Information on pages 4-5 and accompanying full Prescribing Information, including Boxed WARNING, for ONIVYDE.

THE EVIDENCE TO GO ON

onivyde® (irinotecan liposome injection)

ONIVYDE + 5-FU/LV increased median OS by approximately 2 months vs 5-FU/LV alone (primary endpoint)[2]



CONSIDER ONIVYDE + 5-FU/LV to extend overall survival after progression of mPDAC on gemcitabine-based therapy[2]

*ONIVYDE monotherapy had no effect on OS.[3]

CI=confidence interval; HR=hazard ratio; ORR=objective response rate; OS=overall survival; PFS=progression-free survival.

IMPORTANT SAFETY INFORMATION (CONTINUED)

CONTRAINDICATION

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

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

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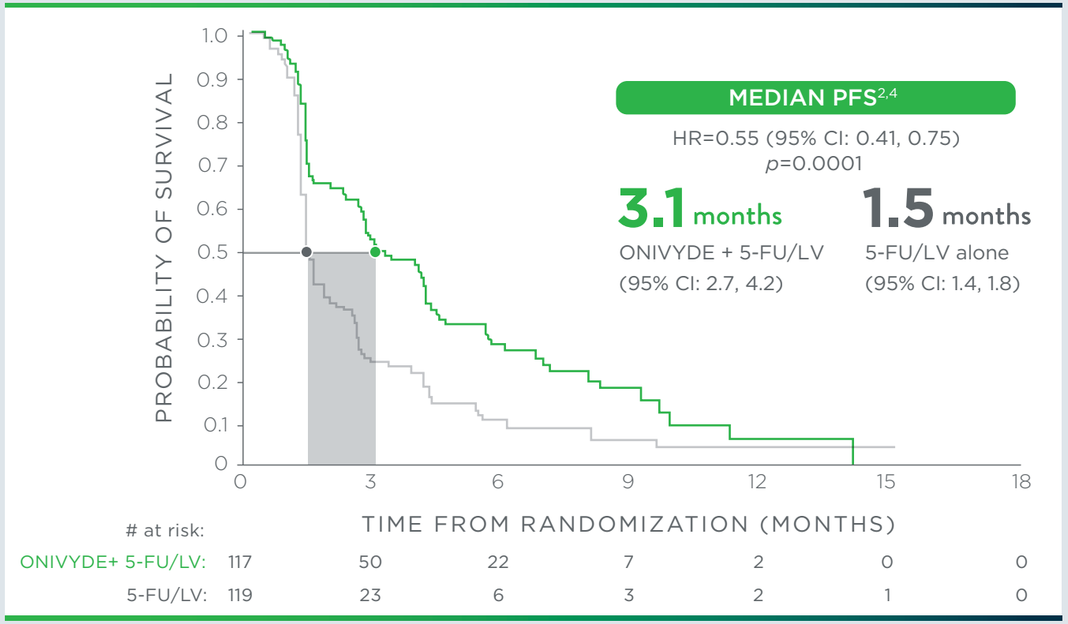
ONIVYDE + 5-FU/LV extended median PFS vs 5-FU/LV alone (secondary endpoint)[2,4]



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/m^2 every 3 weeks) or 5-FU/LV (fluorouracil 2000 mg/m^2 and leucovorin 200 mg/m^2 over 24 hours weekly for 4 weeks, followed by 2 weeks' rest). After 63 patients were enrolled, a third arm, ONIVYDE (70 mg/m^2 every 2 weeks) + 5-FU/LV (fluorouracil 2400 mg/m^2 and leucovorin 400 mg/m^2 every 2 weeks), 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 endpoints were PFS and ORR.[2,3]

WARNINGS AND PRECAUTIONS (CONTINUED)

- **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
- **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

INDICATION AND IMPORTANT SAFETY INFORMATION

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- **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

ADVERSE REACTIONS (CONTINUED)

- 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

To report SUSPECTED ADVERSE REACTIONS, contact Ipsen Biopharmaceuticals, Inc. at 1-855-463-5127 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see accompanying full Prescribing Information, including Boxed WARNING.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pancreatic Adenocarcinoma V.1.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed May 5, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. **2.** ONIVYDE® [package insert]. Basking Ridge, NJ. Ipsen Biopharmaceuticals, Inc.; 2023. **3.** Wang-Gillam A, Li C-P, Bodoky G, et al. Nanoliposomal irinotecan with fluorouracil and folinic acid in metastatic pancreatic cancer after previous gemcitabine-based therapy (NAPOLI-1): a global, randomised, open-label, phase 3 trial. *Lancet*. 2016;387(10018):545-557. **4.** Data on file #1. Basking Ridge, NJ. Ipsen Biopharmaceuticals, Inc.; 2015. **5.** Department of Health and Human Services. U.S. Food and Drug Administration. ONIVYDE (irinotecan liposome injection) Approval Letter. NDA 207793. October 22, 2015. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/207793Orig1s000Approv.pdf. Accessed March 28, 2022. **6.** Ipsen data on file: IQVIA medical claims post-gemcitabine usage analysis, June 2018 – October 2021. **7.** Ipsen data on file: ONIVYDE PBRER (periodic benefit risk evaluation report), April 23, 2019 – October 22, 2019. **8.** Ipsen data on file: Breakaway Partners dashboard.

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THE PROVEN EXPERIENCE TO GO ON

Consider ONIVYDE + 5-FU/LV for your appropriate patients with mPDAC after gemcitabine[2]

FDA APPROVED
IN 2015[5]

#1 PRESCRIBED AND FASTEST GROWING
2L REGIMEN FOR mPDAC POST-GEMCITABINE[6*]

- Prescribed to more than 30,000 patients by more than 2000 oncologists[7]
- Covered on more than 500 health plans for appropriate patients[8†]

Scan QR code to visit
www.ONIVYDE.com/hcp
and learn more about ONIVYDE

*Based on metastatic pancreatic cancer patients who have had at least 3 cycles of a gemcitabine-based regimen and did not have pancreatic cancer-related activity for 60 days prior to beginning an ONIVYDE treatment regimen. Based on data from Q4 2016 through Q3 2021.

†Prior authorization may be required. Refer to your patient's health plan.

2L=second line.

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IPSEN Innovation for patient care

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