WHEN METASTATIC PANCREATIC CANCER (mPC) PROGRESSES ON GEMCITABINE

HELP YOUR PATIENTS FIGHT ON

onivyde® (irinotecan liposome injection)

CONSIDER TWO CATEGORY 1 NATIONAL COMPREHENSIVE CANCER NETWORK® (NCCN®) RECOMMENDED TREATMENTS BACK-TO-BACK FOR METASTATIC PANCREATIC CANCER[1*†]

1L Certain gemcitabine-based therapies, such as gemcitabine + nab-paclitaxel[‡]

2L Liposomal irinotecan (ONIVYDE®) + 5-FU/LV, following gemcitabine-based therapy[§]

ONIVYDE® + 5-FU/LV IS THE #1 PRESCRIBED 2L REGIMEN FOR mPC PATIENTS WHO PROGRESS AFTER 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 recommendation 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 an ONIVYDE® treatment regimen.

5-FU=fluorouracil; LV=leucovorin; ECOG=Eastern Cooperative Oncology Group.

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

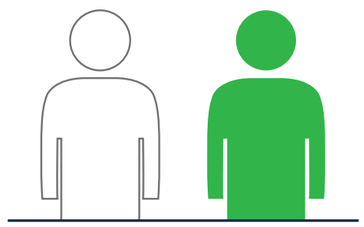
WARNING: SEVERE NEUTROPENIA and SEVERE DIARRHEA

- 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 throughout and accompanying full Prescribing Information, including Boxed WARNING.

Liposomal irinotecan (ONIVYDE®) IN COMBINATION WITH 5-FU/LV IS RECOMMENDED BY NCCN AS THE *ONLY* CATEGORY 1 SECOND-LINE TREATMENT OPTION[1]

IN POST-GEMCITABINE-BASED THERAPY FOR PATIENTS WITH METASTATIC PANCREATIC CANCER WITH GOOD PERFORMANCE STATUS AND DISEASE PROGRESSION[1*†]



Based on one author's analysis:

ABOUT 1 IN 2

mPC PATIENTS WHO COMPLETED 1L TREATMENT MAY BE ELIGIBLE FOR ACTIVE 2L TREATMENT[3]

HOW MANY OF YOUR mPC PATIENTS COULD BE APPROPRIATE FOR THE ONIVYDE® REGIMEN?

**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.

IMPORTANT SAFETY INFORMATION (CONTINUED)

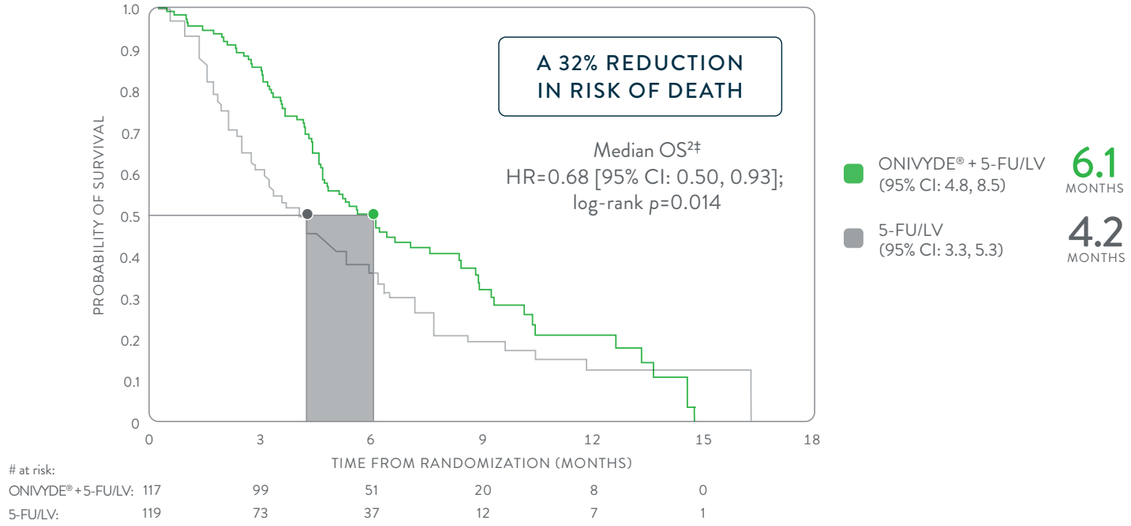
CONTRAINDICATION

- ONIVYDE is contraindicated in patients who have experienced a severe hypersensitivity reaction 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
- **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
- **Severe Hypersensitivity Reactions:** Irinotecan HCl 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 1 month after ONIVYDE treatment

DON'T MISS YOUR OPPORTUNITY: OFFER THE POSSIBILITY OF MORE SURVIVAL TIME WITH ONIVYDE® + 5-FU/LV[4]



In the NAPOLI-1 trial, ONIVYDE® + 5-FU/LV increased overall survival by approximately 2 months compared with 5-FU/LV alone[5,6‡]

- In an exploratory analysis, 1-year probability of survival was 24% with ONIVYDE® + 5-FU/LV and 17% with 5-FU/LV[7] alone
  Limitations: This should not be interpreted as a treatment difference between arms at 1 year due to potential bias and no formal statistical protection for false positive findings. The NAPOLI-1 final analysis included an exploratory, post-hoc analysis of a long-term (≥1 year) survivor subgroup, which was not prespecified and was not powered for statistical significance, so its results should be interpreted with caution.

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]).[4,6]

‡ONIVYDE® monotherapy had no effect on OS.
5-FU=fluorouracil; LV=leucovorin; HR=hazard ratio; CI=confidence interval; OS=overall survival.

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

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed WARNING.

onivyde® (irinotecan liposome injection)

UPON PROGRESSION ON GEMCITABINE-BASED THERAPY

CONSIDER liposomal irinotecan (ONIVYDE®) + 5-FU/LV – THE *ONLY* NCCN CATEGORY 1 CHEMOTHERAPY RECOMMENDATION FOR 2L METASTATIC PANCREATIC CANCER[1]*

onivyde® (irinotecan liposome injection)

- Prescribed to more than **18,000** US patients[8] by over **2,000** US HCPs since FDA approval[9]
- Covered on over **400** health plans for appropriate patients[10]†

**NCCN Category 1 Recommendation: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.*
†Prior authorization may be required. Refer to your patient's health plan.

IMPORTANT SAFETY INFORMATION (CONTINUED)

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%)

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 ONIVYDE treatment
- **Lactation:** Advise nursing women not to breastfeed during and for 1 month after ONIVYDE treatment

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed WARNING.

FOR MORE INFORMATION VISIT ONIVYDE.COM

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pancreatic Adenocarcinoma V.1.2020. © National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Accessed November 26, 2019. To view the most recent and complete version of the guideline, go online to NCCN.org. 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. **2.** Ipsen data on file: IQVIA medical claims post-gemcitabine usage analysis, June 2018 - May 2019. **3.** Abrams TA, Meyer G, Meyerhardt JA, Wolpin BM, Schrag D, Fuchs CS. Patterns of chemotherapy use in U.S.-based cohort of patients with metastatic pancreatic cancer. *Oncologist*. 2017;22:925-933. **4.** ONIVYDE® [package insert]. Basking Ridge, NJ. Ipsen Biopharmaceuticals, Inc.; 2017. **5.** Data on file #1. Basking Ridge, NJ. Ipsen Biopharmaceuticals, Inc.; 2015. **6.** Wang-Gillam A, Li C-P, Bodoky G, et al. *Lancet*. 2016;387:545-557. **7.** Data on file #3. Basking Ridge, NJ. Ipsen Biopharmaceuticals, Inc.; 2015. **8.** Ipsen data on file. **9.** Ipsen data on file: IQVIA APLD medical claims 2015-2019. **10.** Ipsen data on file: Zitter Policy & Access Tracking Tool, Q3 2019.

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