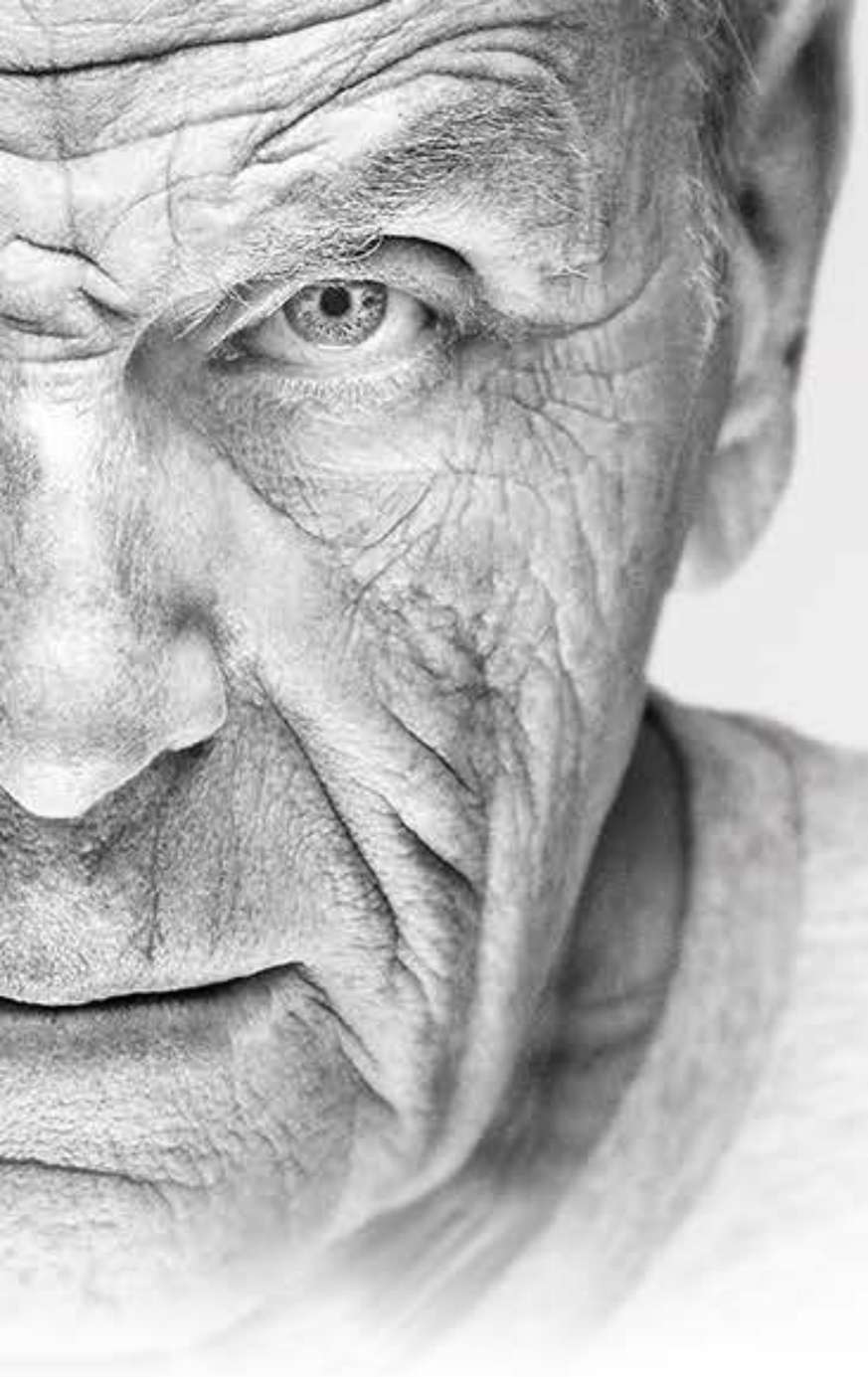

IN POST-GEMCITABINE METASTATIC PANCREATIC CANCER

THE EVIDENCE TO

FIGHT ON

The first and only FDA-approved treatment, in combination with 5-FU/LV, for metastatic pancreatic cancer after gemcitabine-based therapy, proven to extend overall survival[1]

onivyde® (irinotecan liposome injection)

- FDA-APPROVED FOR METASTATIC PANCREATIC CANCER AFTER GEMCITABINE[1]
- THE ONLY CATEGORY 1 NCCN CHEMOTHERAPY RECOMMENDATION IN POST-GEMCITABINE METASTATIC PANCREATIC CANCER[2]*
- PROVEN TO EXTEND OVERALL SURVIVAL[1]
- RECOMMENDED DOSING[1]
- SIDE EFFECTS AND DOSE MANAGEMENT

Liposomal irinotecan + 5-FU/LV is the only Category 1 National Comprehensive Cancer Network® (NCCN®) chemotherapy recommendation for patients with post-gemcitabine metastatic pancreatic cancer with good performance status and disease progression. Good performance status is defined as ECOG 0-1 with patent biliary stent and adequate nutritional intake.[2] 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.

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

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.

References: 1. ONIVYDE® [package insert]. Basking Ridge, NJ. Ipsen Biopharmaceuticals, Inc.; 2017. 2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pancreatic Adenocarcinoma V.3.2017. © National Comprehensive Cancer Network, Inc. 2017. All rights reserved. Accessed November 2, 2017. To view the most recent and complete version of the guideline, go online to NCCN.org. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc.

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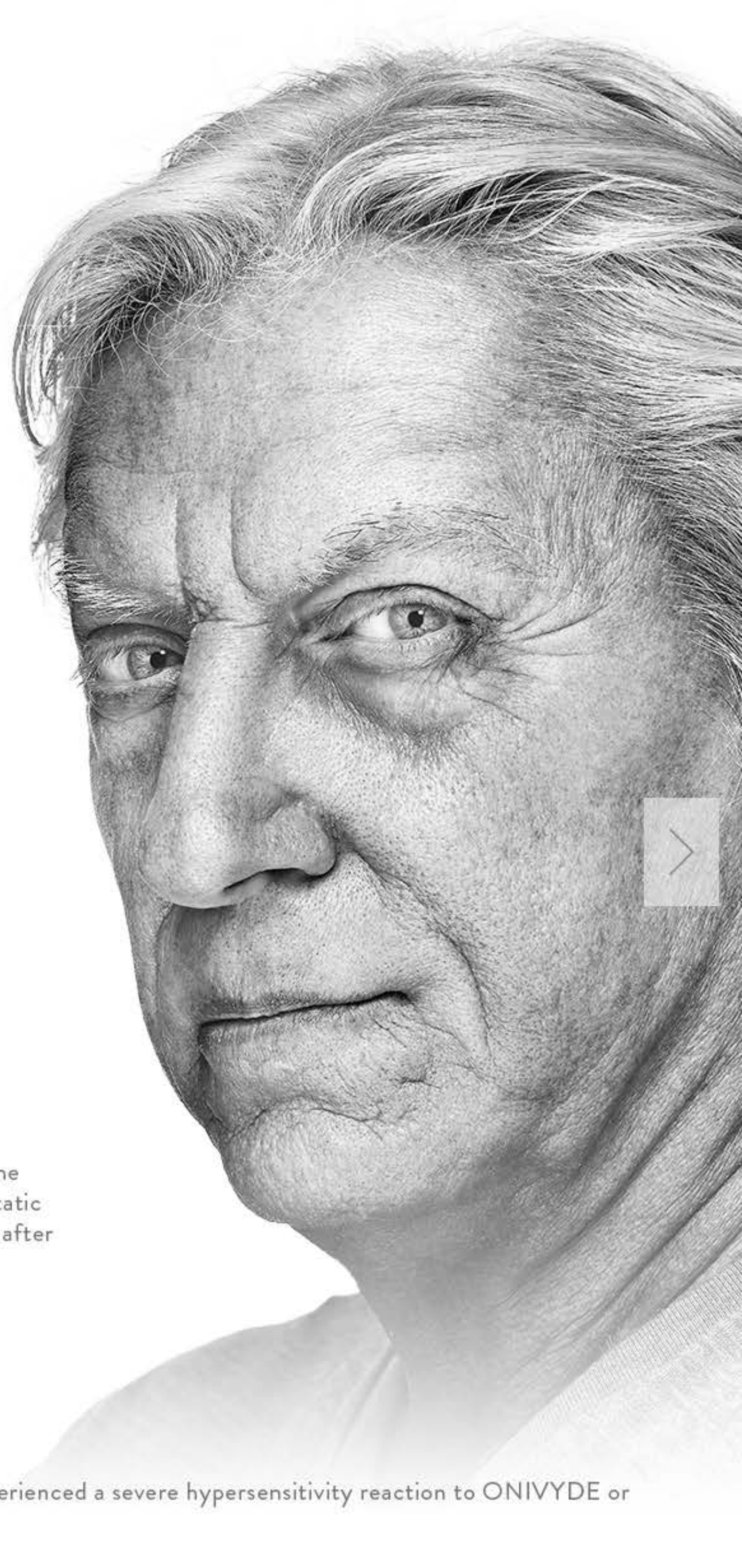
THE EVIDENCE TO HELP PATIENTS FIGHT ON



FDA-APPROVED BASED ON EVIDENCE

Proven in combination with 5-FU/LV[1], in the largest phase 3 trial in patients with metastatic pancreatic cancer with disease progression after gemcitabine-based therapy[2,3]

SELECTED IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

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

WARNINGS AND PRECAUTIONS

Severe Neutropenia

ONIVYDE can cause severe or life-threatening neutropenia and fatal neutropenic sepsis. In a clinical study, the incidence of fatal neutropenic sepsis was 0.8% among patients receiving ONIVYDE, occurring in 1/117 patients in the ONIVYDE + 5-FU/LV arm and 1/147 patients receiving ONIVYDE as a single agent. Severe or life-threatening neutropenia occurred in 20% of patients receiving ONIVYDE + 5-FU/LV vs 2% of patients receiving 5-FU/LV. Grade 3/4 neutropenic fever/neutropenic sepsis occurred in 3% of patients receiving ONIVYDE + 5-FU/LV, and did not occur in patients receiving 5-FU/LV. 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.

5-FU=fluorouracil; LV=leucovorin.

References: 1. ONIVYDE® [package insert]. Basking Ridge, NJ. Ipsen Biopharmaceuticals, Inc.; 2017. **2.** Data on file #1. Basking Ridge, NJ. Ipsen Biopharmaceuticals, Inc.; 2015. **3.** Wang-Gillam A, Li C-P, Bodoky G, et al. *Lancet*. 2016;387:545-557.

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onivyde® (irinotecan liposome injection)

THE CONFIDENCE TO FIGHT ON

THE ONLY CATEGORY 1 NCCN CHEMOTHERAPY RECOMMENDATION

In patients with post-gemcitabine metastatic pancreatic cancer with good performance status and disease progression[1*]

TUMOR TYPE
Metastatic pancreatic cancer
LINE OF THERAPY
Second-line, with previous gemcitabine-based therapy
NCCN RECOMMENDATION
5-FU/LV + liposomal irinotecan for patients with metastatic pancreatic cancer who have a good performance status*
NCCN CATEGORY
1

SELECTED IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Severe Diarrhea

ONIVYDE can cause severe and life-threatening diarrhea. Do not administer ONIVYDE to patients with bowel obstruction. Severe and life-threatening late-onset (onset >24 hours after chemotherapy) and early-onset diarrhea (onset ≤24 hours after chemotherapy, sometimes with other symptoms of cholinergic reaction) were observed. An individual patient may experience both early- and late-onset diarrhea.

In a clinical study, Grade 3/4 diarrhea occurred in 13% of patients receiving ONIVYDE + 5-FU/LV vs 4% receiving 5-FU/LV. Grade 3/4 late-onset diarrhea occurred in 9% of patients receiving ONIVYDE + 5-FU/LV vs 4% in patients receiving 5-FU/LV; the incidences of early-onset diarrhea were 3% and no Grade 3/4 incidences, respectively. Of patients receiving ONIVYDE + 5-FU/LV, 34% received loperamide for late-onset diarrhea and 26% received atropine for early-onset diarrhea.

5-FU=fluorouracil; LV=leucovorin.

**Defined as ECOG 0-1 with patent biliary stent and adequate nutritional intake.*

Therapies are categorized on the following rating system based on National Comprehensive Cancer Network® (NCCN®) categories of evidence and consensus. 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate; 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate; 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate. All recommendations are category 2A unless otherwise noted.[1]

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.

Reference: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pancreatic Adenocarcinoma V.3.2017. © National Comprehensive Cancer Network, Inc. 2017. All rights reserved. Accessed November 2, 2017. To view the most recent and complete version of the guideline, go online to NCCN.org. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc.

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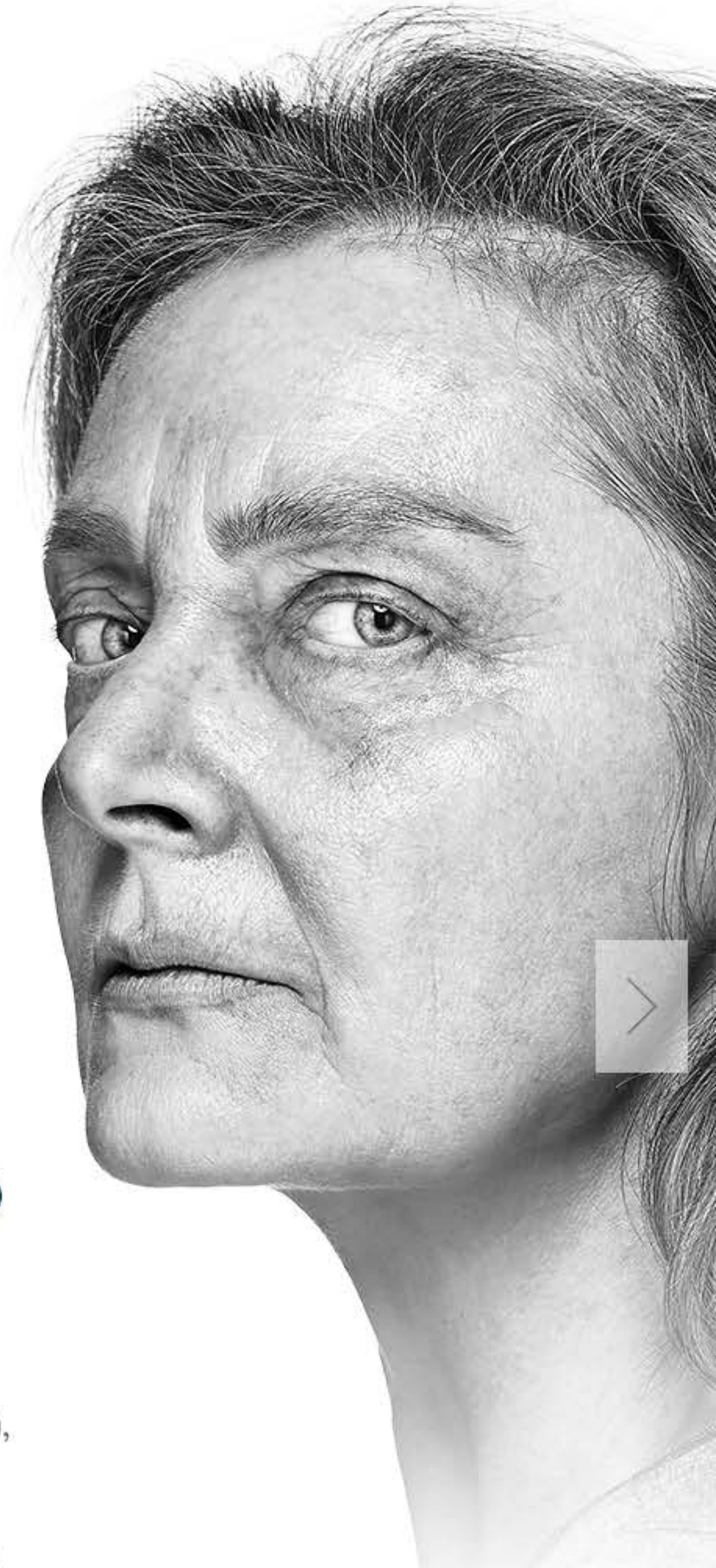
FIGHT ON WITH INCREASED OVERALL SURVIVAL (OS)[1]

IN THE NAPOLI-1 TRIAL*



ONIVYDE® + 5-FU/LV INCREASED OS BY APPROXIMATELY 2 MONTHS COMPARED WITH 5-FU/LV ALONE[1]

- Median OS: 6.1 months for ONIVYDE® + 5-FU/LV (95% CI: 4.8, 8.5) vs 4.2 months for 5-FU/LV alone (95% CI: 3.3, 5.3); Hazard ratio=0.68 (95% CI: 0.50, 0.93), log-rank p=0.014[1]
- Median progression-free survival: 3.1 months for ONIVYDE® + 5-FU/LV (95% CI: 2.7, 4.2) vs 1.5 months for 5-FU/LV alone (95% CI: 1.4, 1.8)[1]

SELECTED IMPORTANT SAFETY INFORMATION

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 HCl can cause severe hypersensitivity reactions, including anaphylactic reactions. Permanently discontinue ONIVYDE in patients who experience a severe hypersensitivity reaction.

5-FU=fluorouracil; LV=leucovorin.

**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]).*[1,2]

References: 1. ONIVYDE® [package insert]. Basking Ridge, NJ. Ipsen Biopharmaceuticals, Inc.; 2017. 2. Wang-Gillam A, Li C-P, Bodoky G, et al. *Lancet*. 2016;387:545-557.

onivyde® (irinotecan liposome injection)

RECOMMENDED DOSING FOR METASTATIC PANCREATIC CANCER PATIENTS[1]

ADMINISTER ONIVYDE® PRIOR TO LEUCOVORIN AND 5-FU[1]

ONIVYDE®
70
mg/m² IV
OVER 90 MINUTES

↓

LEUCOVORIN
400
mg/m² IV
OVER 30 MINUTES

↓

2 WEEK CYCLE

FLUOROURACIL
2,400
mg/m² IV
OVER 46 HOURS

IN THE NAPOLI-1 TRIAL[1,2]

- Treatment continued until disease progression or unacceptable toxicity
- The median duration of therapy in the ONIVYDE® + 5-FU/LV arm was 9 weeks

The recommended starting dose of ONIVYDE® in patients known to be homozygous for the UGT1A1*28 allele is 50 mg/m² administered by IV infusion over 90 minutes. Increase the dose of ONIVYDE® to 70 mg/m², as tolerated, in subsequent cycles.[1]

There is no recommended dose of ONIVYDE® for patients with serum bilirubin above the upper limit of normal.[1]

IMPORTANT DOSING INFORMATION[1]

- Do not substitute ONIVYDE® for other drugs containing irinotecan hydrochloride
- Premedicate with a corticosteroid and an anti-emetic 30 minutes prior to ONIVYDE® infusion
- Monitor complete blood cell counts on Days 1 and 8 of every cycle and more frequently if clinically indicated
- Avoid the use of strong CYP3A4 inducers if possible; substitute non-enzyme–inducing therapies at least 2 weeks prior to initiation of ONIVYDE®
- Avoid the use of strong CYP3A4 or UGT1A1 inhibitors, if possible; discontinue strong CYP3A4 inhibitors at least 1 week prior to starting therapy

SELECTED IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Embryo-Fetal Toxicity

Based on animal data with irinotecan HCl and the mechanism of action of ONIVYDE, ONIVYDE can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during and for 1 month after ONIVYDE treatment.

5-FU=fluorouracil; LV=leucovorin.

References: 1. ONIVYDE® [package insert]. Basking Ridge, NJ. Ipsen Biopharmaceuticals, Inc.; 2017. 2. Data on file #1. Basking Ridge, NJ. Ipsen Biopharmaceuticals, Inc.; 2015.

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MANAGING CERTAIN SIDE EFFECTS IN YOUR PATIENTS

ADVERSE REACTIONS OCCURRING AT A HIGHER INCIDENCE IN THE ONIVYDE® + 5-FU/LV ARM THAN IN THE 5-FU/LV ARM (BETWEEN-ARM DIFFERENCE OF ≥5% [GRADES 1-4]* OR ≥2% [GRADES 3 AND 4])[1]

	ONIVYDE® + 5-FU/LV n=117		5-FU/LV n=134	
	GRADES 1-4 (%)	GRADES 3-4 (%)	GRADES 1-4 (%)	GRADES 3-4 (%)
GASTROINTESTINAL DISORDERS				
Diarrhea	59	13	26	4
Diarrhea, early†	30	3	15	0
Diarrhea, late‡	43	9	17	4
Vomiting	52	11	26	3
Nausea	51	8	34	4
Stomatitis§	32	4	12	1
INFECTIONS AND INFESTATIONS	38	17	15	10
Sepsis	4	3	2	1
Neutropenic fever/neutropenic sepsis‖	3	3	1	0
Gastroenteritis	3	3	0	0
Intravenous catheter-related infection	3	3	0	0
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS				
Fatigue/asthenia	56	21	43	10
Pyrexia	23	2	11	1
METABOLISM AND NUTRITION DISORDERS				
Decreased appetite	44	4	32	2
Weight loss	17	2	7	0
Dehydration	8	4	7	2
SKIN AND SUBCUTANEOUS TISSUE DISORDERS				
Alopecia	14	1	5	0

- Discontinuation rate due to adverse reactions was 11%[1]
- There were no overall differences in safety observed between younger (<65 years) and older patients (≥65 years)[1]
- The most common serious adverse reactions (≥2%) of ONIVYDE®, alone or in combination, were diarrhea, vomiting, neutropenic fever or neutropenic sepsis, nausea, pyrexia, sepsis, dehydration, septic shock, pneumonia, acute renal failure, and thrombocytopenia

National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0 used for grading.
†*Early diarrhea: onset ≤24 hours after ONIVYDE® administration.*
‡*Late diarrhea: onset >1 day after ONIVYDE® administration.*
§*Includes stomatitis, aphthous stomatitis, mouth ulceration, mucosal inflammation.*
‖*Includes febrile neutropenia.*

SELECTED IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

The most common (≥20%) adverse reactions in which patients receiving ONIVYDE + 5-FU/LV experienced a ≥5% higher incidence of any Grade vs the 5-FU/LV arm, were diarrhea (any 59%, 26%; severe 13%, 4%) (early diarrhea [any 30%, 15%; severe 3%, 0%], late diarrhea [any 43%, 17%; severe 9%, 4%]), fatigue/asthenia (any 56%, 43%; severe 21%, 10%), vomiting (any 52%, 26%; severe 11%, 3%), nausea (any 51%, 34%; severe 8%, 4%), decreased appetite (any 44%, 32%; severe 4%, 2%), stomatitis (any 32%, 12%; severe 4%, 1%), pyrexia (any 23%, 11%; severe 2%, 1%).

Reference: 1. ONIVYDE® [package insert]. Basking Ridge, NJ. Ipsen Biopharmaceuticals, Inc.; 2017.

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onivyde® (irinotecan liposome injection)

MANAGING CERTAIN SIDE EFFECTS IN YOUR PATIENTS

MANAGEMENT OF SEVERE DIARRHEA[1]

- Severe or life-threatening diarrhea followed one of two patterns:
  - Late-onset diarrhea (onset more than 24 hours following chemotherapy); and
  - Early-onset diarrhea (onset within 24 hours of chemotherapy, sometimes occurring with other symptoms of cholinergic reaction)
  - An individual patient may experience both early- and late-onset diarrhea
- Withhold ONIVYDE® for diarrhea of Grade 2–4 severity
- Administer loperamide for late diarrhea of any severity; 34% of patients received loperamide for late-onset diarrhea
- Administer atropine for early diarrhea of any severity; 26% of patients received atropine for early-onset diarrhea
- Following recovery to Grade 1 diarrhea, resume ONIVYDE® at a reduced dose

MANAGEMENT OF SEVERE NEUTROPENIA[1]

- Monitor complete blood cell counts on Days 1 and 8 of every cycle and more frequently if clinically indicated
- Withhold ONIVYDE® for absolute neutrophil count below 1500/mm^3 or neutropenic fever
- Upon recovery to ANC ≥1500/mm^3, reduce ONIVYDE® dose for Grade 3–4 neutropenia or neutropenic fever
- Special considerations:
  - Grade 3 or 4 neutropenia was higher among Asian patients (18 of 33 [55%]) compared to White patients (13 of 73 [18%]). Neutropenic fever/neutropenic sepsis was reported in 6% of Asian patients compared to 1% of White patients

SELECTED IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

The most common (≥20%) adverse reactions in which patients receiving ONIVYDE + 5-FU/LV experienced a ≥5% higher incidence of any Grade vs the 5-FU/LV arm, were diarrhea (any 59%, 26%; severe 13%, 4%) (early diarrhea [any 30%, 15%; severe 3%, 0%], late diarrhea [any 43%, 17%; severe 9%, 4%]), fatigue/asthenia (any 56%, 43%; severe 21%, 10%), vomiting (any 52%, 26%; severe 11%, 3%), nausea (any 51%, 34%; severe 8%, 4%), decreased appetite (any 44%, 32%; severe 4%, 2%), stomatitis (any 32%, 12%; severe 4%, 1%), pyrexia (any 23%, 11%; severe 2%, 1%).

Reference: 1. ONIVYDE® [package insert]. Basking Ridge, NJ. Ipsen Biopharmaceuticals, Inc.; 2017.

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onivyde® (irinotecan liposome injection)

MANAGING CERTAIN SIDE EFFECTS IN YOUR PATIENTS

Toxicity NCI CTCAE v4.0*	Directions	ONIVYDE® adjustment in patients receiving 70 mg/m²	Patients homozygous for UGT1A1*28 (who are currently receiving 50 mg/m²)
Grade 2 Diarrhea	Withhold ONIVYDE®. Administer loperamide for late diarrhea of any severity. Administer atropine, if not contraindicated, for early diarrhea of any severity	N/A	N/A
Grade 3 or 4 Diarrhea	Withhold ONIVYDE®. Initiate loperamide for late-onset diarrhea of any severity. Administer intravenous or subcutaneous atropine 0.25 to 1 mg (unless clinically contraindicated) for early-onset diarrhea of any severity. Upon recovery to ≤Grade 1, resume ONIVYDE® at a modified dose	FIRST OCCURRENCE: 50 mg/m²	FIRST OCCURRENCE: 43 mg/m²
		SECOND OCCURRENCE: 43 mg/m²	SECOND OCCURRENCE: 35 mg/m²
		THIRD OCCURRENCE: Discontinue ONIVYDE®	THIRD OCCURRENCE: Discontinue ONIVYDE®
Grade 3 or 4 Adverse Reactions	Withhold ONIVYDE®. Upon recovery to ≤Grade 1, resume ONIVYDE® at a modified dose	FIRST OCCURRENCE: 50 mg/m²	FIRST OCCURRENCE: 43 mg/m²
		SECOND OCCURRENCE: 43 mg/m²	SECOND OCCURRENCE: 35 mg/m²
		THIRD OCCURRENCE: Discontinue ONIVYDE®	THIRD OCCURRENCE: Discontinue ONIVYDE®
Interstitial Lung Disease	FIRST OCCURRENCE: Discontinue ONIVYDE®		
Anaphylactic Reaction	FIRST OCCURRENCE: Discontinue ONIVYDE®		

National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0 used for grading.

When ONIVYDE® was withheld or discontinued for adverse reactions, 5-FU was also withheld or discontinued.[1]

When the dose of ONIVYDE® was reduced for adverse reactions, the dose of 5-FU was reduced by 25%.[1]

- 62% of patients withheld or delayed
  - Adverse reactions leading to withholding or delaying ONIVYDE® + 5-FU/LV were neutropenia, diarrhea, fatigue, vomiting, and thrombocytopenia
- 33% of patients dose reduced
  - Adverse reactions leading to dose reductions of ONIVYDE® + 5-FU/LV were neutropenia, diarrhea, nausea, and anemia
- 11% of patients discontinued
  - Adverse reactions leading to permanent discontinuation of ONIVYDE® + 5-FU/LV included diarrhea, vomiting, and sepsis

SELECTED IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS (CONTINUED)

Of less common (<20%) adverse reactions, patients receiving ONIVYDE + 5-FU/LV who experienced Grade 3/4 adverse reactions at a ≥2% higher incidence of Grade 3/4 toxicity vs the 5-FU/LV arm, respectively, were sepsis (3%, 1%), neutropenic fever/neutropenic sepsis (3%, 0%), gastroenteritis (3%, 0%), intravenous catheter-related infection (3%, 0%), weight loss (2%, 0%), and dehydration (4%, 2%).

Reference: 1. ONIVYDE® [package insert]. Basking Ridge, NJ. Ipsen Biopharmaceuticals, Inc.; 2017.

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onivyde® (irinotecan liposome injection)

IMPORTANT SAFETY INFORMATION

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 to ONIVYDE or irinotecan HCl.

WARNINGS AND PRECAUTIONS

Severe Neutropenia

ONIVYDE can cause severe or life-threatening neutropenia and fatal neutropenic sepsis. In a clinical study, the incidence of fatal neutropenic sepsis was 0.8% among patients receiving ONIVYDE, occurring in 1/117 patients in the ONIVYDE + 5-FU/LV arm and 1/147 patients receiving ONIVYDE as a single agent. Severe or life-threatening neutropenia occurred in 20% of patients receiving ONIVYDE + 5-FU/LV vs 2% of patients receiving 5-FU/LV. Grade 3/4 neutropenic fever/neutropenic sepsis occurred in 3% of patients receiving ONIVYDE + 5-FU/LV, and did not occur in patients receiving 5-FU/LV. 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

ONIVYDE can cause severe and life-threatening diarrhea. Do not administer ONIVYDE to patients with bowel obstruction. Severe and life-threatening late-onset (onset >24 hours after chemotherapy) and early-onset diarrhea (onset ≤24 hours after chemotherapy, sometimes with other symptoms of cholinergic reaction) were observed. An individual patient may experience both early- and late-onset diarrhea.

In a clinical study, Grade 3/4 diarrhea occurred in 13% of patients receiving ONIVYDE + 5-FU/LV vs 4% receiving 5-FU/LV. Grade 3/4 late-onset diarrhea occurred in 9% of patients receiving ONIVYDE + 5-FU/LV vs 4% in patients receiving 5-FU/LV; the incidences of early-onset diarrhea were 3% and no Grade 3/4 incidences, respectively. Of patients receiving ONIVYDE + 5-FU/LV, 34% received loperamide for late-onset diarrhea and 26% received atropine for early-onset diarrhea.

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

Based on animal data with irinotecan HCl and the mechanism of action of ONIVYDE, ONIVYDE can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during and for 1 month after ONIVYDE treatment.

ADVERSE REACTIONS

- The most common (≥20%) adverse reactions in which patients receiving ONIVYDE + 5-FU/LV experienced a ≥5% higher incidence of any Grade vs the 5-FU/LV arm, were diarrhea (any 59%, 26%; severe 13%, 4%) (early diarrhea [any 30%, 15%; severe 3%, 0%], late diarrhea [any 43%, 17%; severe 9%, 4%]), fatigue/asthenia (any 56%, 43%; severe 21%, 10%), vomiting (any 52%, 26%; severe 11%, 3%), nausea (any 51%, 34%; severe 8%, 4%), decreased appetite (any 44%, 32%; severe 4%, 2%), stomatitis (any 32%, 12%; severe 4%, 1%), pyrexia (any 23%, 11%; severe 2%, 1%).
- Of less common (<20%) adverse reactions, patients receiving ONIVYDE + 5-FU/LV who experienced Grade 3/4 adverse reactions at a ≥2% higher incidence of Grade 3/4 toxicity vs the 5-FU/LV arm, respectively, were sepsis (3%, 1%), neutropenic fever/neutropenic sepsis (3%, 0%), gastroenteritis (3%, 0%), intravenous catheter-related infection (3%, 0%), weight loss (2%, 0%), and dehydration (4%, 2%).

CLOSE ISI

onivyde® (irinotecan liposome injection)

IMPORTANT SAFETY INFORMATION (CONTINUED)

- The laboratory abnormalities in which patients receiving ONIVYDE + 5-FU/LV experienced a ≥5% higher incidence vs the 5-FU/LV arm, were anemia (any 97%, 86%; severe 6%, 5%), lymphopenia (any 81%, 75%; severe 27%, 17%), neutropenia (any 52%, 6%; severe 20%, 2%), thrombocytopenia (any 41%, 33%; severe 2%, 0%), increased alanine aminotransferase (any 51%, 37%; severe 6%, 1%), hypoalbuminemia (any 43%, 30%; severe 2%, 0%), hypomagnesemia (any 35%, 21%; severe 0%, 0%), hypokalemia (any 32%, 19%; severe 2%, 2%), hypocalcemia (any 32%, 20%; severe 1%, 0%), hypophosphatemia (any 29%, 18%; severe 4%, 1%), hyponatremia (any 27%, 12%; severe 5%, 3%), increased creatinine (any 18%, 13%; severe 0%, 0%).
- ONIVYDE can cause cholinergic reactions manifesting as rhinitis, increased salivation, flushing, bradycardia, miosis, lacrimation, diaphoresis, and intestinal hyperperistalsis with abdominal cramping and early-onset diarrhea. Grade 1/2 cholinergic symptoms other than early diarrhea occurred in 12 (4.5%) ONIVYDE-treated patients.
- Infusion reactions, consisting of rash, urticaria, periorbital edema, or pruritus, occurring on the day of ONIVYDE administration were reported in 3% of patients receiving ONIVYDE or ONIVYDE + 5-FU/LV.
- The most common serious adverse reactions (≥2%) of ONIVYDE were diarrhea, vomiting, neutropenic fever or neutropenic sepsis, nausea, pyrexia, sepsis, dehydration, septic shock, pneumonia, acute renal failure, and thrombocytopenia.

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

Advise pregnant women of the potential risk to a fetus. Advise males with female partners of reproductive potential to use effective contraception during and for 4 months after ONIVYDE treatment.

Lactation

Advise nursing women not to breastfeed during and for 1 month after ONIVYDE treatment.

Pediatric

Safety and effectiveness of ONIVYDE have not been established in pediatric patients.

DOSAGE AND ADMINISTRATION

The recommended dose of ONIVYDE is 70 mg/m^2 intravenous (IV) infusion over 90 minutes every 2 weeks, administered prior to LV and 5-FU. The recommended starting dose of ONIVYDE in patients known to be homozygous for the UGT1A1*28 allele is 50 mg/m^2 administered by IV infusion over 90 minutes. There is no recommended dose of ONIVYDE for patients with serum bilirubin above the upper limit of normal. Premedicate with a corticosteroid and an anti-emetic 30 minutes prior to ONIVYDE. Withhold ONIVYDE for Grade 3/4 adverse reactions. Resume ONIVYDE with reduced dose once adverse reaction recovered to ≤Grade 1. Discontinue ONIVYDE in patients who experience a severe hypersensitivity reaction and in patients with a confirmed diagnosis of ILD.

Do not substitute ONIVYDE for other drugs containing irinotecan HCl.

Please see Ipsen representative for Full Prescribing Information.

IPSEN Innovation for patient care

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