

IN CIS-ELIGIBLE MIBC

Consider the **FIRST** and **ONLY** FDA-approved IO-based perioperative regimen^{1,2*}:

The NIAGARA Regimen^{1†}





RADICAL CYSTECTOMY



Discover reasons to consider perioperative IMFINZI* + neoadjuvant gem-cis at IMFINZIhcp.com/mibc



The first and only NCCN Category 1, Preferred perioperative systemic treatment option for cis-eligible MIBC

Neoadjuvant durvalumab (IMFINZI®) + gemcitabine + cisplatin, followed by cystectomy, then adjuvant durvalumab (IMFINZI®) for cis-eligible MIBC³‡

NCCN=National Comprehensive Cancer Network® (NCCN®).

Study design: The NIAGARA study was a randomized, open-label, multicenter, Phase III study in patients who were candidates for RC and had not received prior systemic chemotherapy or immune-mediated therapy for the treatment of NMIBC or MIBC. It was designed to evaluate the efficacy and safety of neoadjuvant IMFINZI in combination with gemcitabine and cisplatin followed by adjuvant IMFINZI as a single agent following RC. 1063 patients were randomized 1:1 to receive neoadjuvant IMFINZI (1500 mg) + gemcitabine (1000 mg/m²) and cisplatin (70 mg/m²) (n=533) Q3W for 4 cycles prior to surgery, followed by IMFINZI (1500 mg) Q4W as a single-agent adjuvant treatment, or neoadjuvant gemcitabine (1000 mg/m²) and cisplatin (70 mg/m²) (n=530) Q3W for 4 cycles prior to surgery without adjuvant treatment. Patients with borderline renal function received split-dose cisplatin (35 mg/m² on Days 1 and 8 of each cycle). All treatments were given until disease progression that precludes definitive surgery, recurrence, unacceptable toxicity, or a maximum of 8 cycles after surgery. The dual primary endpoints were pCR and EFS. OS was a key secondary endpoint.^{1,4}

 * A perioperative regimen consists of both neoadjuvant and adjuvant treatment. 1

The NIAGARA Regimen is defined as neoadjuvant IMFINZI + gem-cis followed by adjuvant IMFINZI as a single agent after RC.¹

*See the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for detailed recommendations, including other preferred treatment options.3

Indication:

IMFINZI in combination with gemcitabine and cisplatin as neoadjuvant treatment, followed by single-agent IMFINZI as adjuvant treatment following radical cystectomy, is indicated for the treatment of adult patients with muscle-invasive bladder cancer (MIBC).

IMPORTANT SAFETY INFORMATION

There are no contraindications for IMFINZI® (durvalumab).

Severe and Fatal Immune-Mediated Adverse Reactions

Important immune-mediated adverse reactions listed under Warnings and Precautions may not include all possible severe and fatal immune-mediated reactions. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. Immune-mediated adverse reactions can occur at any time after starting treatment or after discontinuation. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions.

Please see additional Important Safety Information throughout and Full Prescribing Information including Medication Guide for IMFINZI.

Cis-eligible=cisplatin-eligible; EFS=event-free survival; gem-cis=gemcitabine-cisplatin; IO-immuno-oncology; MIBC=muscle-invasive bladder cancer, NMIBC=non-muscle-invasive bladder cancer; OS=overall survival; pCR=pathological complete response; Q3W=every 3 weeks; Q4W=every 4 weeks; RC=radical cystectomy.

PERIOPERATIVE IMFINZI* + neoadjuvant gem-cis: The **FIRST** and **ONLY** FDA-approved IO-based regimen to demonstrate superior EFS[†] and OS in a curative MIBC setting^{1,2}

Significantly prolonged EFS[†] with the NIAGARA Regimen^{1‡}

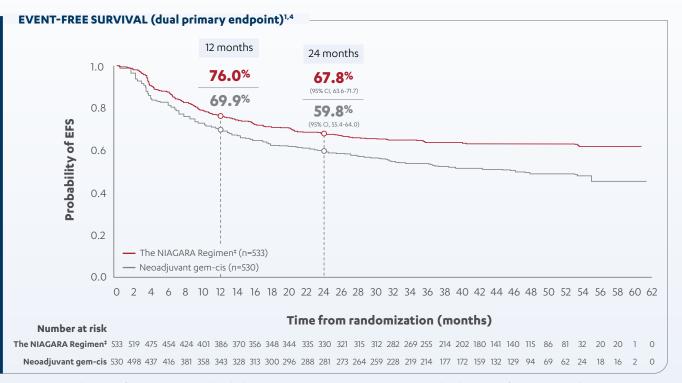
EVENT-FREE SURVIVAL (dual primary endpoint)4



REDUCTION IN RISK OF AN EVENT (progression, recurrence, death, or not undergoing RC)[†] with the NIAGARA Regimen[‡] vs neoadjuvant gem-cis (HR=0.68 [95% CI, 0.56-0.82]; P<0.0001)

Median EFS was not reached with the NIAGARA Regimen[‡] (95% CI, NR-NR) vs 46.1 months with neoadjuvant gem-cis (95% CI, 32.2-NR)

Median duration of follow-up: 42.3 months (range: 0.03-61.3).



- Approximately 68% of patients treated with the NIAGARA Regimen[‡] were estimated to be event free at 2 years⁴
- EFS rates at 12 and 24 months were not powered to determine statistical significance⁴
- EFS maturity is 39%⁴

pCR RESULTS: PRIMARY ANALYSIS AND EXPLORATORY REANALYSIS⁴

- At the primary analysis (data cutoff: January 2022), 33.8% (n=180/533; 95% CI, 29.8-38.0) of patients treated with the NIAGARA Regimen[‡] and 25.8% (n=137/530; 95% CI, 22.2-29.8) of patients treated with neoadjuvant gem-cis achieved a pCR
- pCR rates reported during the primary analysis did not reach statistical significance
- At the reanalysis (data cutoff: April 2024), 37.3% (n=199/533; 95% CI, 33.2-41.6) of patients treated with the NIAGARA Regimen[‡] and 27.5% (n=146/530; 95% CI, 23.8-31.6) of patients treated with neoadjuvant gem-cis achieved a pCR
- The reanalysis included an additional 59 patients§
- This analysis was exploratory and not powered to determine statistical significance

*A perioperative regimen consists of both neoadjuvant and adjuvant treatment.

†Event-free survival was defined as the time from randomization to first recurrence of disease post-RC, time to first documented progression in patients who were precluded from RC, time of expected surgery in patients who refused RC or failure to undergo RC due to residual disease, or death due to any cause, whichever occurs first.

[‡]The NIAGARA Regimen is defined as neoadjuvant IMFINZI + gem-cis followed by adjuvant IMFINZI as a single agent after RC.¹

The descriptive reanalysis of pCR included the results of 59 evaluable samples that were omitted from the primary analysis because the date of central assessment (which occurred after January 14, 2022), rather than the date of surgery (which occurred before January 14, 2022), was used as the data cutoff date.

CI=confidence interval; HR=hazard ratio; NR=not reached.

Significantly extended OS with the NIAGARA Regimen^{1‡}

OVERALL SURVIVAL (secondary endpoint)4



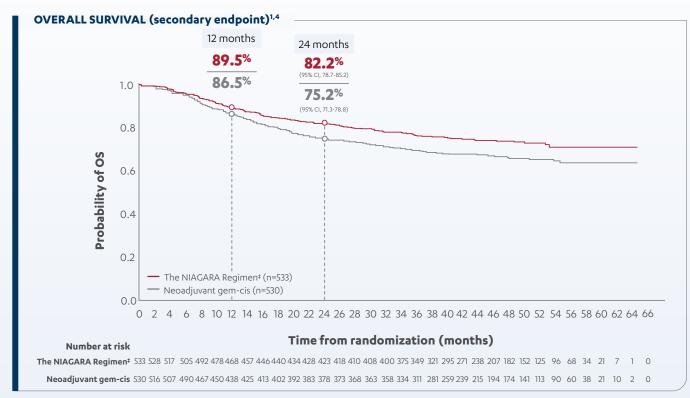
$\textbf{REDUCTION IN RISK OF DEATH} \ \ with the \ NIAGARA \ Regimen \ ^{\ddagger} \ vs \ neoadjuvant \ gem-cis$

(HR=0.75 [95% CI, 0.59-0.93]; P=0.01)

Median OS was not reached with the NIAGARA Regimen[‡] (95% CI, NR-NR) nor with neoadjuvant gem-cis (95% CI, NR-NR)

Median duration of follow-up: 46.3 months (range: 0.03-64.7).

The key secondary endpoint was OS as assessed with an alpha-allocation approach, following EFS in the statistical hierarchy.



>82% estimated OS rate at 2 years with the NIAGARA Regimen^{4‡}

- Fewer deaths were reported with the NIAGARA Regimen[‡] (25.5%; n=136/533) vs neoadjuvant gem-cis (31.9%; n=169/530)^{1,4}
- OS rates at 12 and 24 months were not powered to determine statistical significance⁴
- OS maturity is 27%⁴

IMPORTANT SAFETY INFORMATION (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate. Withhold or permanently discontinue IMFINZI depending on severity. See USPI Dosing and Administration for specific details.

Please see additional Important Safety Information throughout and Full Prescribing Information including Medication Guide for IMFINZI.



IMPORTANT SAFETY INFORMATION (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

In general, if IMFINZI requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy.

Immune-Mediated Pneumonitis

IMFINZI can cause immune-mediated pneumonitis. The incidence of pneumonitis is higher in patients who have received prior thoracic radiation. In patients who did not receive recent prior radiation, the incidence of immune-mediated pneumonitis was 2.4% (34/1414), including fatal (<0.1%), and Grade 3-4 (0.4%) adverse reactions. The frequency and severity of immune-mediated pneumonitis in patients who did not receive definitive chemoradiation prior to IMFINZI were similar in patients who received IMFINZI as a single agent or with ES-SCLC or BTC when given in combination with chemotherapy.

Immune-Mediated Colitis

IMFINZI can cause immune-mediated colitis that is frequently associated with diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated colitis occurred in 2% (37/1889) of patients receiving IMFINZI, including Grade 4 (<0.1%) and Grade 3 (0.4%) adverse reactions.

Immune-Mediated Hepatitis

IMFINZI can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 2.8% (52/1889) of patients receiving IMFINZI, including fatal (0.2%), Grade 4 (0.3%) and Grade 3 (1.4%) adverse reactions.

Immune-Mediated Endocrinopathies

- Adrenal Insufficiency: IMFINZI can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Immune-mediated adrenal insufficiency occurred in 0.5% (9/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
- *Hypophysitis*: IMFINZI can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field cuts. Hypophysitis can cause hypopituitarism. Initiate symptomatic treatment including hormone replacement as clinically indicated. Grade 3 hypophysitis/ hypopituitarism occurred in <0.1% (1/1889) of patients who received IMFINZI.
- Thyroid Disorders (Thyroiditis, Hyperthyroidism, and Hypothyroidism): IMFINZI can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement therapy for hypothyroidism or institute medical management of hyperthyroidism as clinically indicated.
- **Thyroiditis**: Immune-mediated thyroiditis occurred in 0.5% (9/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
- Hyperthyroidism: Immune-mediated hyperthyroidism occurred in 2.1% (39/1889) of patients receiving IMFINZI.
- **Hypothyroidism**: Immune-mediated hypothyroidism occurred in 8.3% (156/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
- Type 1 Diabetes Mellitus, which can present with diabetic ketoacidosis: Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Grade 3 immune-mediated Type 1 diabetes mellitus occurred in <0.1% (1/1889) of patients receiving IMFINZI.

Immune-Mediated Nephritis with Renal Dysfunction

IMFINZI can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.5% (10/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.

Immune-Mediated Dermatology Reactions

IMFINZI can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson Syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN), has occurred with PD-1/L-1 and CTLA-4 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Immune-mediated rash or dermatitis occurred in 1.8% (34/1889) of patients receiving IMFINZI, including Grade 3 (0.4%) adverse reactions.

Other Immune-Mediated Adverse Reactions

The following clinically significant, immune-mediated adverse reactions occurred at an incidence of less than 1% each in patients who received IMFINZI or were reported with the use of other immune-checkpoint inhibitors.

- Cardiac/vascular: Myocarditis, pericarditis, vasculitis.
- **Nervous system**: Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy.
- **Ocular**: Uveitis, iritis, and other ocular inflammatory toxicities can occur. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada-like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss.
- Gastrointestinal: Pancreatitis including increases in serum amylase and lipase levels, gastritis, duodenitis.
- **Musculoskeletal and connective tissue disorders**: Myositis/polymyositis, rhabdomyolysis and associated sequelae including renal failure, arthritis, polymyalgia rheumatic.
- **Endocrine**: Hypoparathyroidism.
- Other (hematologic/immune): Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenia, solid organ transplant rejection, other transplant (including corneal graft) rejection.

Infusion-Related Reactions

IMFINZI can cause severe or life-threatening infusion-related reactions. Monitor for signs and symptoms of infusion-related reactions. Interrupt, slow the rate of, or permanently discontinue IMFINZI based on the severity. See USPI Dosing and Administration for specific details. For Grade 1 or 2 infusion-related reactions, consider using pre-medications with subsequent doses. Infusion-related reactions occurred in 2.2% (42/1889) of patients receiving IMFINZI, including Grade 3 (0.3%) adverse reactions.

Complications of Allogeneic HSCT after IMFINZI

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/L-1 blocking antibody. Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/L-1 blockade and allogeneic HSCT. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/L-1 blocking antibody prior to or after an allogeneic HSCT.

Embryo-Fetal Toxicity

Based on its mechanism of action and data from animal studies, IMFINZI can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. In females of reproductive potential, verify pregnancy status prior to initiating IMFINZI and advise them to use effective contraception during treatment with IMFINZI and for 3 months after the last dose of IMFINZI.

actation

There is no information regarding the presence of IMFINZI in human milk; however, because of the potential for serious adverse reactions in breastfed infants from IMFINZI, advise women not to breastfeed during treatment and for 3 months after the last dose.

Adverse Reactions

- The most common adverse reactions, including laboratory abnormalities, in the overall study (occurring in ≥20% of
 patients) were decreased hemoglobin, decreased neutrophils, increased blood creatinine, decreased sodium, nausea,
 increased ALT, decreased calcium, decreased platelets, fatigue, increased potassium, decreased lymphocytes, increased
 AST, constipation, decreased magnesium, decreased appetite, increased alkaline phosphate, rash, pyrexia, diarrhea,
 vomiting and abdominal pain.
- In patients with MIBC in the neoadjuvant phase of the NIAGARA study receiving IMFINZI in combination with gemcitabine and cisplatin (n=530), permanent discontinuation of IMFINZI due to an adverse reaction occurred in 9% of patients. Serious adverse reactions occurred in 24% of patients; the most frequent (≥1%) serious adverse reactions were pulmonary embolism (1.9%), febrile neutropenia (1.5%), acute kidney injury (1.3%), thrombocytopenia (1.3%), urinary tract infection (1.3%), and pneumonia (1.3%). Fatal adverse reactions occurred in 1.1% of patients including sepsis, myocardial infarction, and pulmonary embolism (0.2% each). One fatal adverse reaction of pneumonia was reported in 1 (0.2%) patient in the post-surgery phase before adjuvant treatment started. Of the 530 patients in the IMFINZI treatment arm and 526 patients in the chemotherapy treatment arm who received neoadjuvant treatment, 1 (0.2%) patient in each treatment arm did not receive surgery due to adverse reactions.

Please see additional Important Safety Information throughout and Full Prescribing Information including Medication Guide for <u>IMFINZI</u>.



IMPORTANT SAFETY INFORMATION (continued)

Adverse Reactions (continued)

The adverse reaction that led to cancellation of surgery in the IMFINZI treatment arm was interstitial lung disease.

• In patients with MIBC in the adjuvant phase of the NIAGARA study receiving IMFINZI as a single agent (n=383), permanent discontinuation of adjuvant IMFINZI due to an adverse reaction occurred in 5% of patients. Serious adverse reactions occurred in 26% of patients. The most frequent serious adverse reactions (occurring in ≥1% of patients) were urinary tract infection (7%), acute kidney injury (3.7%), hydronephrosis (2.1%), pyelonephritis (2.1%), urosepsis (1.8%) and sepsis (1.6%). Fatal adverse reactions occurred in 1.8% of patients, including COVID-19, severe acute respiratory syndrome, cardiopulmonary failure, gastrointestinal hemorrhage, and chronic hepatic failure (0.3% each).

The safety and effectiveness of IMFINZI has not been established in pediatric patients.

You may report side effects related to AstraZeneca products [2].

REFERENCES:

1. IMFINZI® (durvalumab) [Prescribing Information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2025. **2.** US Food and Drug Administration. Oncology (cancer)/hematologic malignancies approval notifications. Updated March 28, 2025. Accessed March 28, 2025. https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancerhematologic-malignancies-approval-notifications **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer V.1.2025. ©National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed March 25, 2025. 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. **4.** Powles T, Catto JWF, Galsky MD, et al. Perioperative durvalumab with neoadjuvant chemotherapy in operable bladder cancer. *N Engl J Med*. 2024;391(19):1773-1786.



THE NIAGARA REGIMEN

(neoadjuvant IMFINZI + gem-cis followed by adjuvant IMFINZI)



The **FIRST** and **ONLY** FDA-approved IO-based perioperative regimen[†] to significantly improve survival^{1,2}

32° REDUCTION IN THE RISK OF AN EVENT^{1,4}

(progression, recurrence, death, or not undergoing RC)‡ with the NIAGARA Regimen* vs neoadjuvant gem-cis (HR=0.68 [95% CI, 0.56-0.82]; P<0.0001). Median EFS was not reached with the NIAGARA Regimen* (95% CI, NR-NR) vs 46.1 months with neoadjuvant gem-cis (95% CI, 32.2-NR).

25° REDUCTION IN THE RISK OF DEATH 1,4

with the NIAGARA Regimen* vs neoadjuvant gem-cis (HR=0.75 [95% CI, 0.59-0.93]; P=0.01) Median OS was not reached with the NIAGARA Regimen* (95% CI, NR-NR) nor with neoadjuvant gem-cis (95% CI, NR-NR). >82% estimated OS rate at 2 years with the NIAGARA Regimen*. OS rates at 24 months were not powered to determine statistical significance.

LOW DISCONTINUATION RATES DUE TO ARs1

In the neoadjuvant phase, 9% of patients discontinued IMFINZI due to an AR. The most frequent ARs ($\geq 0.5\%$) leading to permanent discontinuation of IMFINZI were increased blood creatinine (0.9%), neutropenia, acute kidney injury, asthenia, and fatigue (0.6% each).

In the adjuvant phase, 5% of patients discontinued IMFINZI due to an AR. The most frequent ARs (≥0.5%) leading to permanent discontinuation of IMFINZI were nephritis (0.8%), fatigue, diarrhea, decreased appetite, and pneumonitis (0.5% each).

Indication:

IMFINZI in combination with gemcitabine and cisplatin as neoadjuvant treatment, followed by single-agent IMFINZI as adjuvant treatment following radical cystectomy, is indicated for the treatment of adult patients with muscle-invasive bladder cancer (MIBC).

Safety and tolerability in the NIAGARA study

- The most common ARs (≥20% of patients; all grades), including laboratory abnormalities, overall in the study were decreased hemoglobin, decreased neutrophils, increased blood creatinine, decreased sodium, nausea, increased ALT, decreased calcium, decreased platelets, fatique, increased potassium, decreased lymphocytes, increased AST, constipation, decreased magnesium, decreased appetite, increased alkaline phosphate, rash, pyrexia, diarrhea, vomiting, and abdominal pain¹
- In the neoadjuvant phase, serious ARs occurred in 24% of patients who received IMFINZI in combination with gem-cis (n=530); the most frequent serious ARs (≥1%) were pulmonary embolism (1.9%), febrile neutropenia (1.5%), acute kidney injury, thrombocytopenia, urinary tract infection, and pneumonia (1.3% each)¹
- In the neoadjuvant phase, fatal ARs occurred in 1.1% of patients, including sepsis, myocardial infarction, and pulmonary embolism (0.2%) each). One fatal AR of pneumonia (0.2%) was reported in the post-RC phase before adjuvant treatment started
- In the adjuvant phase, serious ARs occurred in 26% of patients who received IMFINZI (n=383); the most frequent serious ARs (≥1%) were urinary tract infection (7%), acute kidney injury (3.7%), hydronephrosis (2.1%), pyelonephritis (2.1%), urosepsis (1.8%), and sepsis (1.6%)¹
- In the adjuvant phase, fatal ARs occurred in 1.8% of patients, including COVID-19, severe acute

Explore the opportunity for increased survival with the NIAGARA Regimen* at IMFINZIhcp.com/mibc

respiratory syndrome, cardiopulmonary failure, gastrointestinal hemorrhage, and chronic hepatic failure (0.3% each)¹

Please see additional Important Safety Information throughout and Full Prescribing Information including Medication Guide for IMFINZI.



^{*}The NIAGARA Regimen is defined as neoadjuvant IMFINZI + gem-cis followed by adjuvant IMFINZI as a single agent after RC.

[†]A perioperative regimen consists of both neoadjuvant and adjuvant treatment. ¹

^{*}Event-free survival was defined as the time from randomization to first recurrence of disease post-RC, time to first documented progression in patients who were precluded from RC, time of expected surgery in patients who refused RC or failure to undergo RC due to residual disease, or death due to any cause, whichever occurs first.