Transcript Details
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Evolving Treatment Approaches in EGFRm NSCLC

Announcer:
This medical industry feature, titled “Evolving Treatment Approaches in EGFRm NSCLC” is sponsored by Daiichi Sankyo Inc. and AstraZeneca.

Here’s your host, Dr. Jennifer Caudle.

Dr. Caudle:
This is ReachMD, and I’m your host, Dr. Jennifer Caudle. Joining me today to discuss DATROWAY’s approval for use in adults with locally advanced or metastatic EGFR-mutated non-small cell lung cancer, or NSCLC, is Dr. Hossein Borghaei. He’s the Chief of Thoracic Medical Oncology and Professor in the Department of Hematology and Oncology at Fox Chase Cancer Center in Philadelphia, Pennsylvania. Dr. Borghaei, welcome to the program.

Dr. Borghaei:
Thank you, I’m happy to be here.

Dr. Caudle:
Of course, before we dive in, let’s review some information for DATROWAY, also known by its generic name datopotamab deruxtecan, often abbreviated to Dato-DXd or Dato.

Announcer:
Important Safety Information
INDICATION

DATROWAY® is a Trop-2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with locally advanced or metastatic epidermal growth factor receptor (EGFR)-mutated non-small cell lung cancer (NSCLC) who have received prior EGFR-directed therapy and platinum-based chemotherapy.

This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial.

Dr. Caudle:
Now, to start off with some background, Dr. Borghaei, what are the current first-line treatment options for patients with locally advanced or metastatic EGFR-mutated NSCLC, and what challenges arise when patients progress beyond these options?

Dr. Borghaei:
Treatments for patients with EGFR-mutated locally advanced or metastatic Non-Small Cell Lung Cancer is an evolving field, and there are different first-line approaches—such as EGFR-directed therapies alone or in combination with platinum-based chemotherapy.[1-3] But each may come with different known toxicities—things like fatigue, GI side effects, and hematologic issues, just to name a few.[4-9]

Additionally, most patients eventually experience disease progression, usually within about two years, possibly due to developing resistance mechanisms. And it may be associated with about 50 to 65 percent survival at three years following initial treatment for advanced disease.[10-18]

So this is where we see a real unmet need.[18-20] And that is why emerging therapies like antibody-drug conjugates, or ADCs, could be

promising.[21,22] They're designed to utilize the specificity of antibodies to deliver potent antitumor payloads to cancer cells while aiming to reduce the systemic exposure and toxicity on healthy cells.[21,23]

Dr. Caudle:
Thank you for that context, Dr. Borghaei. And can you tell us a little about Dato?

Dr. Borghaei:
I'd be happy to. Dato is the first and only Trop-2-directed ADC approved for adults with locally advanced or metastatic EGFR-mutated NSCLC after EGFR-targeted therapy and platinum-based chemo.[24,25] This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial.

Dato is designed to induce selective tumor cell death and reduce systemic exposure to the antitumor payload.[24,25]

And to do this, it consists of three main components:

- There is a Trop-2-directed monoclonal antibody, which leverages a cell surface protein called Trop-2 to provide selective delivery of the cytotoxic agent,[24,25]
- Theres a tumor selective cleavable linker attaches the payload to the antibody, which is stable in plasma;[24-27] and
- Then there's a potent topoisomerase I inhibitor payload, also known as DXd.[24-26]

Although Dato is designed to be delivered to tumor cells, it may still affect other neighboring cells in the tumor microenvironment, also known as the bystander antitumor effect.[24-27] But let's dive into TROP-2 aspect of Dato.

Trop-2 has been associated with disease progression and may play a multifactorial role in tumor evolution.[28-31] On top of that, one retrospective study showed that over 90 percent of NSCLC tumors overexpressed the Trop-2 protein, so this makes Trop-2 a potential approach for developing targeted cancer therapies.[32]

Dr. Caudle:
So, Dato received accelerated approval based on a pooled analysis of patients with locally advanced or metastatic EGFR-mutated NSCLC from two studies.[25,33] Can you tell us more about the pooled analysis?

Dr. Borghaei:
The pooled subgroup analysis evaluated the efficacy of Dato in 114 patients with locally advanced or metastatic EGFR-mutated NSCLC who were enrolled in the TROPION-Lung05 and TROPION-Lung01 trials.[25]

TROPION-Lung05 was a global, multicenter, single-arm, open-label study focused on patients with previously treated NSCLC that had an actionable genomic alteration. TROPION-Lung01, on the other hand, was a randomized, active-controlled, open-label trial—also global and multicenter—that included patients with previously treated NSCLC, with or without an actionable genomic alteration.[18,25,34]

For both trials, eligible patients with EGFR-mutated NSCLC had to have already been treated with EGFR-targeted therapy as well as a platinum-based chemotherapy.[18,25,34]

Now, there were also key exclusion criteria: patients were not eligible if they had a history of interstitial lung disease, or ILD, or pneumonitis that required steroids, had ongoing ILD or pneumonitis, or had clinically significant corneal disease at the time of screening. Patients with untreated and symptomatic brain metastases were also excluded.[18,25,34,35]

In both trials, patients received Dato at a dose of six milligrams per kilogram via intravenous infusion every three weeks, and continued treatment until either unacceptable toxicity or disease progression.[18,25,34]

In the pooled analysis, the major efficacy outcome was overall response rate, as assessed by blinded independent central review per RECIST version 1.1. Duration of response was also evaluated as an additional efficacy outcome.[25]

The median age in the pooled analysis was 63, and 63 percent of the patients were women. Most patients—68 percent—had an ECOG performance status of one at baseline, while the remaining 32 percent had a status of zero. When it comes to race and ethnicity, 70 percent were Asian, 22 percent were white, and 2 percent identified as Hispanic or Latino. Looking at metastases, 20 percent had liver metastases and 33 percent had brain metastases at baseline. More than half—roughly 53 percent—of the patients had a history of brain metastases.[25,36,37]

In terms of EGFR mutations, 53 percent of patients had exon 19 deletions, 34 percent had exon 21 L858R mutations, 28 percent had the T790M resistance mutation, 3 percent had exon 20 insertions, and 14 percent had other EGFR mutations.[25]

Most patients received at least three prior regimens in the locally advanced or metastatic setting. All patients had previously received EGFR-directed therapy, including 84 percent treated with osimertinib specifically. Nearly all—99 percent—had also received platinum-based chemotherapy, and about 28 percent had been treated with an anti–PD-1 or PD-L1 therapy.[25]

So, the overall response rate, which was the major efficacy outcome, is defined as the proportion of patients with a complete or partial response. Dato had an overall response rate of 45 percent with a 95 percent confidence interval between 35 and 54. 4.4 percent had a complete response, and 40 percent had a partial response.[25]

The median duration of response was 6.5 months, with 47 percent of patients continuing to respond for at least six months and 18 percent continuing their response for at least 12 months.[25]

So, overall, Dato has been evaluated in a population with prior EGFR-targeted therapy and chemotherapy, where treatment options are limited.[18,25]

Dr. Caudle:
Thank you for that. And now, let's turn to safety. What were some of the most common adverse reactions for patients taking Dato?

Dr. Borghaei:
So Before moving onto the general safety data for Dato in EGFR-mutated NSCLC, let's take a moment to review some warnings and precautions associated with Dato use.

There are four warnings and precautions outlined in the DATROWAY prescribing information. In the pooled safety population of 484 patients with NSCLC from TROPION-Lung01, TROPION-Lung05, and TROPION-PanTumor01, interstitial lung disease, also known as ILD, or pneumonitis occurred in seven percent of patients, with around one percent experiencing Grade three or four events. Eight cases, or 1.7 percent, were unfortunately fatal. The median time to onset was 1.4 months, with a range from as early as six days to as late as nine months. Dato was withheld in 2.3 percent of patients due to ILD, and 4.1 percent discontinued treatment permanently. 79 percent of those affected required corticosteroid treatment, and the condition resolved in 45 percent of cases.[25]

Ocular adverse reactions are also something to watch closely for. These can include dry eye, keratitis, blepharitis, meibomian gland dysfunction, increased lacrimation, conjunctivitis, and blurred vision. In a larger pooled safety population, which included 927 patients with NSCLC and other solid tumors from TROPION-Lung01, TROPION-Lung05, TROPION-PanTumor01, and another clinical trial, 36 percent of patients experienced an ocular adverse reaction. While most events were mild to moderate, 2.2 percent were Grade three which included keratitis, dry eye, and blurred vision and one patient experienced Grade four conjunctival hemorrhage. The most common ocular adverse reactions were dry eye, keratitis, and increased lacrimation. Median time to onset was 2.3 months, ranging from one day to almost two years. These reactions led to dose interruptions in 3.6 percent, dose reductions in 2.5 percent, and permanent discontinuation in one percent of patients. Among those affected, 39 percent had complete resolution, and 10 percent had partial improvement.[25]

In the larger pooled safety population of 927 patients, stomatitis, which includes mouth sores and oral mucositis occurred in 63 percent of patients. Most cases were grade one or two, with eight percent of patients experiencing Grade three reactions, and one patient experiencing Grade four. The median time to onset was around two weeks, ranging from one day to 18.6 months. Six percent of patients had a dose interruption, 11 percent had a dose reduction, and 0.5 percent of patients permanently discontinued treatment.[25]

The final warning and precaution to note is the potential for embryo-fetal harm.[25]

Now, the safety of Dato was evaluated in a pooled analysis of 125 patients with EGFRm Non-Small Cell Lung Cancer who received Dato six milligrams per kilogram as an IV infusion once every three weeks until disease progression or unacceptable toxicity.[25] The majority of common adverse reactions such as stomatitis, nausea, alopecia, and fatigue were either grade one or two.[25]

Common lab abnormalities included decreased hemoglobin, decreased lymphocytes, increased calcium, increased AST, decreased white blood cell count, increased LDH, and increased ALT.[25]

Grade three or higher adverse reactions and serious adverse reactions occurred in 24 percent and 26 percent of patients, respectively.[25,38]

Continuing review of the safety profile of Dato in this patient population, now let's take a closer look at adverse reactions of special

interest.

We'll start with stomatitis. Most cases were grade one or two, no patients had to stop treatment because of it.[38] Grade one stomatitis is either asymptomatic or mild, while grade two involves moderate pain or ulcers that don't interfere with oral intake but a modified diet may be indicated.[39]

Keratitis and dry eye followed a similar pattern, with the majority of cases being grade one or two.[38] Grade one keratitis or dry eye are generally asymptomatic or diagnosed by clinical or diagnostic observations and grade two keratitis or dry eye are symptomatic and may include moderate decrease in visual acuity. Keratitis led to discontinuation in one patient while dry eye did not lead to any discontinuation of study treatment.[38,39]

Lastly, adjudicated drug-related ILD was mainly grade one or two and led to permanent discontinuation in three patients. Grade one ILD is defined as asymptomatic while grade two is symptomatic.[38,39]

Dr. Caudle:
Thank you for that. So, Dr. Borghaei, you mentioned earlier that some adverse reactions may be managed with dose adjustments. Can you explain how Dato dosing is typically modified when patients experience adverse reactions?

Dr. Borghaei:
Yes absolutely. So Dato is administered at a dose of six milligram per kilogram by IV infusion once every three weeks. The recommended maximum dose is 540 milligrams for patients weighing 90 kilograms or more.[25]

The first dose reduction brings the dose down to four milligrams per kilogram, with a maximum of 360 milligrams for patients 90 kilograms and above. And the second dose reduction takes it down to three milligrams per kilogram, with a maximum of 270 milligrams for patients 90 kilograms and over.[25]

But if a patient requires a further dose reduction after the second dose reduction, the USPI states that treatment should be permanently discontinued in patients who are unable to tolerate three milligrams per kilogram IV once every three weeks.[25]

And it's important to note that the dose of Dato should not be re-escalated after a dose reduction has been made. Additionally, refer to the USPI for detailed guidance on dose modifications and management of adverse reactions with DATROWAY, including recommendations for dose delays, reductions, and discontinuations.[25]

Dr. Caudle:
And when it comes to managing or helping prevent these adverse reactions, what prophylactic and supportive care strategies should providers consider?

Dr. Borghaei:
Great question. When it comes to stomatitis, proactive management is key. Patients are advised to use a 0.1 milligram per milliliter dexamethasone oral solution—or a similar steroid-based mouthwash—four times a day and then as needed.[25,27] Patients should suck on ice chips or hold ice water in their mouths during the infusion. Some discussion points you may have with patients include swishing for one to two minutes before spitting out, as well as brushing with a soft toothbrush and continue flossing, if it's already part of their routine.[25,27]

For ocular adverse reactions, preservative-free lubricant drops should be used at least four times a day, and more often as needed. Refer patients to an eye care professional for an initial comprehensive ophthalmic exam at the start of treatment, followed by yearly check-ins during treatment, another at the end of treatment, and as clinically indicated. This eye care professional can be either an optometrist or ophthalmologist. During treatment, it's best for patients to avoid contact lenses unless directed by an eye care professional.[25]

The best strategy for dealing with nausea is to stay ahead of the symptoms. This means giving antiemetic medications before each infusion, and again after as needed. 5-HT3 serotonin receptor antagonists are common go-to options, though other appropriate alternatives are fine, too.[25] Additionally, Datopotamab deruxtecan-dlnk, also known as Dato, is classified as a high emetic risk agent in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Antiemesis. Administer prophylactic antiemetic medications per local institutional guidelines for prevention of anticancer agent-induced nausea and vomiting.[40]

And to help prevent infusion-related reactions, premedication is key. About 30 to 60 minutes before each dose of Dato, patients should receive an antihistamine, such as diphenhydramine, along with an antipyretic such as acetaminophen.[25]

In my experience, some supportive or prophylactic medications may be part of a Dato order set or treatment plan. Please refer to your institution-specific EMR to determine if these should be ordered individually.

So ultimately, empowering providers to anticipate, monitor, and proactively manage potential adverse reactions with Dato, which in turn supports continuity of care, with the goal of achieving response.

Dr. Caudle:
I'd like to thank my guest, Dr. Hossein Borghaei, for speaking with us on DATROWAY's approval to treat adults with locally advanced or metastatic *EGFR*-mutated NSCLC.

Dr. Borghaei, it was great speaking with you today.

Dr. Borghaei:
Thank you for having me.

Dr. Caudle:
Of course. And for ReachMD, I'm your host Dr. Jennifer Caudle

Please stay tuned to hear some Important Safety Information.

Announcer:
IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS
Interstitial Lung Disease/Pneumonitis
DATROWAY can cause severe, life-threatening, or fatal interstitial lung disease (ILD) or pneumonitis.

Locally Advanced or Metastatic NSCLC
In the pooled safety population of 484 patients with NSCLC from TROPION-Lung01, TROPION-Lung05, and TROPION-PanTumor01, ILD/pneumonitis occurred in 7% of patients treated with DATROWAY, including 0.6% of patients with Grade 3 and 0.4% with Grade 4. There were 8 (1.7%) fatal cases. The median time to onset for ILD was 1.4 months (range: 0.2 months to 9 months). Eleven patients (2.3%) had DATROWAY withheld and 20 patients (4.1%) permanently discontinued DATROWAY due to ILD/pneumonitis. Systemic corticosteroids were required in 79% (26/33) of patients with ILD/pneumonitis. ILD/pneumonitis resolved in 45% of patients.

Patients were excluded from clinical studies for a history of ILD/pneumonitis requiring treatment with steroids or for ongoing ILD/pneumonitis.

Monitor patients for new or worsening respiratory symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, fever) during treatment with DATROWAY. For asymptomatic (Grade 1) ILD/pneumonitis, consider corticosteroid treatment (e.g., ≥0.5 mg/kg/day prednisolone or equivalent). For symptomatic ILD/pneumonitis (Grade 2 or greater), promptly initiate systemic corticosteroid treatment (e.g., ≥1 mg/kg/day prednisolone or equivalent) and continue for at least 14 days followed by gradual taper for at least 4 weeks.

Withhold DATROWAY in patients with suspected ILD/pneumonitis and permanently discontinue DATROWAY if ≥Grade 2 ILD/pneumonitis is confirmed.

Ocular Adverse Reactions
DATROWAY can cause ocular adverse reactions including dry eye, keratitis, blepharitis, meibomian gland dysfunction, increased lacrimation, conjunctivitis, and blurred vision.

Locally Advanced or Metastatic NSCLC and Other Solid Tumors
In patients with locally advanced or metastatic NSCLC and other solid tumors, ocular adverse reactions occurred in 36% of patients treated with DATROWAY. Twenty patients (2.2%) experienced Grade 3 ocular adverse reactions, which included keratitis, dry eye, and blurred vision, and one patient experienced a Grade 4 ocular adverse reaction of conjunctival hemorrhage. The most common (≥5%) ocular adverse reactions were dry eye (17%), keratitis (14%), and increased lacrimation (7%). The median time to onset for ocular adverse reactions was 2.3 months (range: 0.03 months to 23.2 months). Of the patients who experienced ocular adverse reactions, 39% had complete resolution, and 10% had partial improvement (defined as a decrease in severity by one or more grades from the worst grade at last follow up). Ocular adverse reactions led to dosage interruption in 3.6% of patients, dosage reductions in 2.5% of patients, and permanent discontinuation of DATROWAY in 1% of patients.

Patients with clinically significant corneal disease were excluded from clinical studies.

Advise patients to use preservative-free lubricant eye drops several times daily for prophylaxis. Advise patients to avoid use of contact lenses unless directed by an eye care professional.

Refer patients to an eye care professional for an ophthalmic exam including visual acuity testing, slit lamp examination (with fluorescein staining), intraocular pressure, and fundoscopy at treatment initiation, annually while on treatment, at end of treatment, and as clinically indicated.

Promptly refer patients to an eye care professional for any new or worsening ocular adverse reactions. Monitor patients for ocular adverse reactions during treatment with DATROWAY, and if diagnosis is confirmed, withhold, reduce the dose, or permanently discontinue DATROWAY based on severity.

Stomatitis
DATROWAY can cause stomatitis, including mouth ulcers and oral mucositis.

Locally Advanced or Metastatic NSCLC and Other Solid Tumors
In patients with locally advanced or metastatic NSCLC and other solid tumors, stomatitis occurred in 63% of patients treated with DATROWAY, including 8% of patients with Grade 3 events and one patient with a Grade 4 reaction. The median time to first onset of stomatitis was 0.5 months (range: 0.03 months to 18.6 months). Stomatitis led to dosage interruption in 6% of patients, dosage reductions in 11% of patients, and permanent discontinuation of DATROWAY in 0.5% of patients.

Advise patients to use a steroid-containing mouthwash for prophylaxis and treatment of stomatitis. Instruct the patient to hold ice chips or ice water in the mouth throughout the infusion of DATROWAY.

Monitor patients for signs and symptoms of stomatitis. If stomatitis occurs, increase the frequency of mouthwash and administer other topical treatments as clinically indicated. Based on the severity of the adverse reaction, withhold, reduce the dose, or permanently discontinue DATROWAY.

Embryo-Fetal Toxicity
Based on its mechanism of action, DATROWAY can cause embryo-fetal harm when administered to a pregnant woman because the topoisomerase inhibitor component of DATROWAY, DXd, is genotoxic and affects actively dividing cells.

Advise patients of the potential risk to a fetus. Advise female patients of reproductive potential to use effective contraception during treatment with DATROWAY and for 7 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with DATROWAY and for 4 months after the last dose.

ADVERSE REACTIONS
Locally Advanced or Metastatic NSCLC and Other Solid Tumors
The pooled safety population described in WARNINGS AND PRECAUTIONS reflects exposure to DATROWAY as a single agent at 6 mg/kg administered as an intravenous infusion once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity in 927 patients in TROPION-Lung05, TROPION-Lung01, TROPION-PanTumor01, and other clinical trials. Among these patients who received DATROWAY, 45% were exposed for 6 months or longer and 19% were exposed for greater than one year. In this pooled safety population, the most common (≥ 20%) adverse reactions were stomatitis (63%), nausea (52%), fatigue (45%), alopecia (38%), constipation (28%), decreased appetite (23%), rash (23%), vomiting (22%), and musculoskeletal pain (20%). In this pooled safety population, the most common (≥2%) Grade 3 or 4 laboratory abnormalities were decreased lymphocytes (9%) and decreased hemoglobin (3.5%).

Locally Advanced or Metastatic EGFR-Mutated Non-Small Cell Lung Cancer
TROPION-Lung05, TROPION-Lung01, TROPION-PanTumor01
The safety of DATROWAY was evaluated in 125 patients with EGFR-mutated NSCLC who received DATROWAY 6 mg/kg administered as an intravenous infusion once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity in TROPION-Lung05 and TROPION-Lung01 as well as TROPION-PanTumor01. Among these patients, the median duration of treatment was 6.1 months (range 0.7 months to 41.7 months).

The median age was 63 years (range: 36 to 81), 56% of patients were <65 years, 62% of patients were female; 66% were Asian, 26% were White, 0.8% were Black, 6% were other races; and 2.4% were of Hispanic ethnicity.

Serious adverse reactions occurred in 26% of patients who received DATROWAY. Serious adverse reactions in >1% of patients who received DATROWAY were COVID-19 (4%), stomatitis (2.4%), and pneumonia (1.6%). Fatal adverse reactions occurred in 1.6% of patients who received DATROWAY, due to death not otherwise specified.

Permanent discontinuation of DATROWAY due to an adverse reaction occurred in 8% of patients. Adverse reactions which resulted in permanent discontinuation of DATROWAY in >1% of patients included ILD/pneumonitis (2.4%) and abnormal hepatic function (1.6%).

Dosage interruptions of DATROWAY due to an adverse reaction occurred in 43% of patients. Adverse reactions which required dosage interruption in >1% of patients included COVID-19 (13%), stomatitis (7%), fatigue (6%), pneumonia (4%), anemia (2.4%), amylase increased (2.4%), keratitis (2.4%), ILD/pneumonitis (1.6%), decreased appetite (1.6%), dyspnea (1.6%), rash (1.6%), and infusion-related reaction (1.6%).

Dose reductions of DATROWAY due to an adverse reaction occurred in 26% of patients. Adverse reactions which required dose reduction in >1% of patients included stomatitis (14%), keratitis (1.6%), fatigue (1.6%), decreased weight (1.6%) and COVID-19 (1.6%).

The most common (≥20%) adverse reactions, including laboratory abnormalities, were stomatitis (71%), nausea (50%), alopecia (49%), fatigue (42%), decreased hemoglobin (34%), decreased lymphocytes (32%), constipation (31%), increased calcium (31%), increased AST (28%), decreased white blood cell count (27%), increased lactate dehydrogenase (23%), musculoskeletal pain (22%), decreased appetite (20%), increased ALT (20%), and rash (20%).

Clinically relevant adverse reactions occurring in <10% of patients who received DATROWAY included dry skin, blurred vision, abdominal pain, conjunctivitis, dry mouth, ILD/pneumonitis, skin hyperpigmentation, increased lacrimation, and visual impairment.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** Based on its mechanism of action, DATROWAY can cause embryo-fetal harm when administered to a pregnant woman because the topoisomerase inhibitor component of DATROWAY, DXd, is genotoxic and affects actively dividing cells. There are no available data on the use of DATROWAY in pregnant women to inform a drug-associated risk. Advise patients of the potential risks to a fetus.
- **Lactation:** There are no data regarding the presence of datopotamab deruxtecan-dlnk or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment with DATROWAY and for 1 month after the last dose.
- **Females and Males of Reproductive Potential:** Pregnancy Testing: Verify pregnancy status of females of reproductive potential prior to initiation of DATROWAY. Contraception: *Females:* Advise females of reproductive potential to use effective contraception during treatment with DATROWAY and for 7 months after the last dose. *Males:* Because of the potential for genotoxicity, advise male patients with female partners of reproductive potential to use effective contraception during treatment with DATROWAY and for 4 months after the last dose. Infertility: Based on findings in animal toxicity studies, DATROWAY may impair male and female reproductive function and fertility. The effects on reproductive organs in animals were irreversible.
- **Pediatric Use:** Safety and effectiveness of DATROWAY have not been established in pediatric patients.
- **Geriatric Use:** Of the 125 patients with EGFR-mutated NSCLC in TROPION-Lung05, TROPION-Lung01, TROPION-PanTumor01 treated with DATROWAY 6 mg/kg, 44% were ≥65 years of age and 10% were ≥75 years of age. No clinically meaningful differences in efficacy and safety were observed between patients ≥65 years of age versus younger patients.
- **Renal Impairment:** A higher incidence of ILD/pneumonitis has been observed in patients with mild and moderate renal impairment (creatinine clearance [CLcr] 30 to <90 mL/min). Monitor patients with renal impairment for increased adverse reactions, including respiratory reactions. No dosage adjustment is recommended in patients with mild to moderate renal impairment. The effect of severe renal impairment (CLcr <30 mL/min) on the pharmacokinetics of datopotamab deruxtecan-dlnk or DXd is unknown.
- **Hepatic Impairment:** No dosage adjustment is recommended in patients with mild hepatic impairment (total bilirubin ≤ULN and any AST >ULN or total bilirubin >1 to 1.5 times ULN and any AST). Limited data are available in patients with moderate hepatic impairment (total bilirubin >1.5 to 3 times ULN and any AST). Monitor patients with moderate hepatic impairment for increased adverse reactions. The recommended dosage of DATROWAY has not been established for patients with severe hepatic impairment (total bilirubin >3 times ULN and any AST).

To report SUSPECTED ADVERSE REACTIONS, contact Daiichi Sankyo, Inc. at 1-877-437-7763 or FDA at 1-800-FDA-1088 or fda.gov/medwatch.

Please see accompanying full Prescribing Information, including WARNINGS AND PRECAUTIONS, and Medication Guide.

Announcer:
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