Transcript Details
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Latest TROP2 ADC Approval for HR+ HER2- Metastatic Breast Cancer

ReachMD Announcer:
Welcome to ReachMD. This medical industry feature, titled "Latest TROP2 ADC Approval for HR+ HER2- Metastatic Breast Cancer," is sponsored by AstraZeneca and Daiichi-Sankyo. And now, here's your Host, Dr. Charles Turck.

Dr. Turck:
This is ReachMD, and I'm Dr. Charles Turck. Joining me today to discuss datopotamab deruxtecan-dlnk, or Dato-DXd, and its role in treating HR-positive HER2-negative metastatic breast cancer are Dr. Komal Jhaveri and Nurse Vanessa Soto-Romano. Dr. Jhaveri is a breast medical oncologist and early drug development specialist at Memorial Sloan Kettering Cancer Center in New York.

Dr. Jhaveri:
Thanks for having me.

Dr. Turck:
Also with us is Nurse Vanessa Soto-Romano. She's a Clinical Trials Nurse at Memorial Sloan Kettering Cancer Center in New York, New York. Nurse Soto-Romano, thank you for joining us today.

Nurse Soto-Romano:
Thank you, it's great to be here.

Dr. Turck:
So Dato-DXd is an antibody-drug conjugate, or ADC, that was approved for use in patients with HR-positive, HER2-negative metastatic breast cancer in January of 2025. Now, before we begin, let's take a moment to review the indication and usage for Dato-DXd.

ReachMD Announcer:
Indication
DATROWAY® is a Trop-2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with unresectable or metastatic, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received prior endocrine-based therapy and chemotherapy for unresectable or metastatic disease.

To see full Prescribing Information, please click on the link on the ReachMD landing page, and please stay tuned for Important Safety Information later in this video.

Dr. Turck:
With that information in mind, let's begin our discussion with you, Dr. Jhaveri. Why is the approval of Dato-DXd such an important advancement in the treatment of HR-positive, HER2-negative metastatic breast cancer?

Dr. Jhaveri:
So the treatment journey for patients with metastatic HR-positive HER2-negative breast cancer typically starts with endocrine therapy, paired with targeted treatments like CDK4/6 inhibitors. And this approach has been the mainstay of care for some time.[1]

But once the disease becomes resistant to both endocrine therapy and CDK4/6 inhibitors—or if patients aren't candidates—the next step usually depends on the presence of specific mutations. For those without identifiable somatic or germline mutations, treatment

options become much more limited.[1] And, unfortunately, chemo comes with a heavy burden of adverse reactions that can significantly impact quality of life.[2]

Recently, we've seen exciting progress with ADCs for HER2-low and HER2-negative breast cancers. These therapies are helping reshape the treatment landscape for patients who have already undergone endocrine and chemotherapy.[1-3]

But there's still an unmet need for metastatic HR-positive, HER2-negative patients with breast cancer.[1]

So this approval is a really promising step forward, as it gives us another valuable option in our treatment arsenal, especially for patients who have already received other therapies.

Dr. Turck:
And what makes Dato-DXd's design unique?

Dr. Jhaveri:
Well, developing targeted therapies is a universal challenge in oncology, but Dato-DXd is composed of a humanized anti-TROP2 IgG1 monoclonal antibody which is conjugated to a highly potent topoisomerase I inhibitor using a plasma-stable, cleavable tetrapeptide-based linker designed for selective delivery to TROP2-expressing cells. After binding to TROP2, including on tumor cells, Dato-DXd is internalized, and the linker is cleaved by lysosomal enzymes, releasing the DXd payload. Once released, DXd induces DNA damage, leading to apoptotic cell death. And because DXd can cross cell membranes, it may also produce a bystander effect and may impact both TROP2-positive cells and neighboring cells within the tumor microenvironment.[2,4-6]

Dr. Turck:
And turning to you now, Nurse Soto-Romano, what does the dosing regimen for Dato-DXd look like?

Nurse Soto-Romano:
Well, Dato-DXd is the only Trop2-directed ADC that offers dosing once every 3 weeks.[6]

The recommended dosage of Dato-DXd is six milligrams per kilogram, up to a maximum of 540 milligrams for patients 90 kilograms and over. It's administered as an intravenous, or IV, infusion once every three weeks, or every 21 days, until disease progression or unacceptable toxicity.[6]

Dr. Turck:
Now, with all this in mind, I'd like to discuss the TROPION-Breast01 trial and the efficacy and safety data for Dato-DXd, Dr. Jhaveri. Could you tell us more about the TROPION-Breast01 trial?

Dr. Jhaveri:
I'd be happy to. The TROPION-Breast01 was a global, open-label, randomized, multi-center phase III clinical trial that compared Dato-DXd with investigator's choice single-agent chemotherapy in patients with inoperable or metastatic HR-positive HER2-negative breast cancer who may have received one or two prior lines of systemic chemotherapy.[7-14]

The trial enrolled 732 patients with inoperable or metastatic HR-positive, HER2-negative breast cancer. All patients had an IHC score of IHC 0, IHC 1+ or IHC 2+ and ISH negative. 365 patients received Dato-DXd starting at the standard dose, while 367 patients received the investigator's choice of chemotherapy, or ICC. Treatment continued until disease progression, unacceptable tolerability, or other discontinuation criteria. These patients were previously treated with one or two lines of chemotherapy and had progressed on and were not candidates for endocrine therapy.[7-14]

The TROPION-Breast01 trial had dual primary endpoints of progression-free survival, or PFS, as assessed by blinded independent central review, or BICR, as well as overall survival, or OS. Now, it's important to note that with dual primary endpoints, a significant improvement in either PFS or OS was enough for the trial to be considered positive. Additional efficacy outcomes included confirmed objective response rate, or ORR, and duration of response, or DOR, by BICR.[7-14]

Dr. Turck:
And looking at the dual primary endpoints, Dr. Jhaveri, what were the efficacy results?

Dr. Jhaveri:
Overall, Dato-DXd showed a statistically significant and clinically meaningful improvement in median PFS, or mPFS, and met its dual primary PFS endpoint.[14]

The mPFS was 6.9 months with Dato-DXd compared to 4.9 months with ICC. The hazard ratio was 0.63 with a 95 percent confidence

interval of 0.52 and 0.76. This means there was a 37 percent reduction in the risk of disease progression or death compared to ICC. So the mPFS was both statistically significant, with a p-value less than 0.0001, and clinically meaningful as it shows that Dato-DXd offers real potential to slow breast cancer progression.[14]

Now, median OS, or mOS, did not reach statistical significance in the intention-to-treat, or ITT, population. The mOS was 18.6 months for Dato-DXd compared to 18.3 months for ICC. The hazard ratio was 1.01, with a 95 percent confidence interval of 0.83 and 1.22.[6,15]

Dr. Turck:
Turning to you now, Nurse Soto-Romano, what can you tell us about the secondary endpoints?

Nurse Soto-Romano:
Well, the ORR was notably higher with Dato-DXd at 36 percent compared to 23 percent with ICC, with a 95 percent confidence interval of 31 and 42 for Dato-DXd and 19 and 28 for ICC. A majority of the ORR were partial responses. 0.5 percent of the Dato-DXd arm achieved a complete response, compared to 0 percent in the ICC group.[6,14] The median DOR was also slightly longer at 6.7 months for Dato-DXd and 5.7 months with ICC.[6,14]

So this is an encouraging sign that Dato-DXd isn't just delaying progression – as reflected by improvements in PFS — but is also actively shrinking tumors in a meaningful number of patients, as shown in the ORR.[6,14]

Dr. Turck:
For those just tuning in, you're listening to ReachMD. I'm Dr. Charles Turck, and today I'm speaking with Dr. Komal Jhaveri and Nurse Vanessa Soto-Romano about Dato-DXd as a treatment for HR-positive HER2-negative metastatic breast cancer.

We've spent some time talking about the efficacy data in TROPION-Breast01, so now let's talk about the safety data. Nurse Soto-Romano, can you tell us about the safety profile for Dato-DXd?

Nurse Soto-Romano:
Of course. So, in the TROPION-Breast01 trial, the safety of Dato-DXd was evaluated in over 700 patients—360 received Dato-DXd and 351 were treated with ICC.[6]

For all grade adverse reactions and lab abnormalities, stomatitis and nausea were the most frequently reported in the Dato-DXd group, while leukocytopenia and neutropenia were the most common in the ICC group.[6]

Now, when we look at the more serious adverse reactions — which are Grade three or four — what really stands out is the difference in neutropenia rates: 35 percent of patients receiving ICC experienced grade three and four neutropenia compared to 1.6 percent with Dato-DXd.[6] In fact, grade three or higher treatment-related adverse events were reported in approximately 21 percent of patients with Dato-DXd—which is less than half the rate seen with ICC, which came in at nearly 45 percent.[14] 3.1 percent of patients had to permanently discontinue Dato-DXd due to adverse reactions, and dose interruptions occurred in 22 percent while dose reductions occurred in 23 percent.[6]

Dr. Turck:
So let's discuss how we can address adverse events of special interest. Dr. Jhaveri, could you speak to the incidence of stomatitis and share the recommended management strategies for patients?

Dr. Jhaveri:
So, as Nurse Soto-Romano mentioned, stomatitis was one of the most common adverse reactions with patients who received Dato-DXd. More specifically, in the pooled safety analysis with patients with breast cancer and lung cancer from TROPION-Breast01, TROPION-Lung05, TROPION-Lung01, and TROPION-PanTumor01, stomatitis occurred in 63 percent of patients treated with Dato-DXd, including eight percent of patients with Grade three events and one patient with a Grade four reaction. The median time to onset was 0.5 months, with a range of 0.03 months to 18.6 months.[6]

Six percent of patients required dose interruptions, 11 percent had dose reductions, and 0.5 percent permanently discontinued treatment.[6]

To help prevent and manage stomatitis, the US Prescribing Information recommends using a steroid-containing mouthwash—such as a 0.1 milligram per milliliter dexamethasone oral solution—four times a day and as needed. Patients are also advised to hold ice chips or ice water in their mouth during the infusion of Dato-DXd. Providers should monitor for signs and symptoms of stomatitis. In patients who received Dato-DXd in TROPION-Breast01, 39 percent used a mouthwash containing corticosteroid for management or prophylaxis of

stomatitis or oral mucositis at any time during the treatment.[6]

Overall, Dato-DXd showed a consistent safety profile in TROPION-Breast01 in line with what was seen in earlier studies, which is important to consider when balancing treatment efficacy with tolerability.[6,14]

Dr. Turck:
So now that we've covered stomatitis, let's focus on managing ocular adverse reactions, such as keratitis. Nurse Soto-Romano, what was the incidence of ocular adverse reactions, and what strategies do you recommend for managing them in patients?

Nurse Soto-Romano:
Ocular adverse reactions were reported in patients receiving Dato-DXd.

The pooled safety analysis showed 36 percent of patients treated with Dato-DXd experienced an ocular adverse reaction. But a majority of those reactions – about 34 percent – were Grade one or two. 2.2 percent were Grade three or higher, which included keratitis, dry eye, and blurred vision, and one patient experienced a grade four ocular adverse reaction or conjunctival hemorrhage.[6]

The time to onset ranged from 0.03 months to 23.2 months with a median time to onset of 2.3 months. So it's important to continue checking in with patients throughout their treatment.[6]

But what's encouraging is, up until the last follow-up, 39 percent of patients who experienced ocular adverse reactions had complete resolution while ten percent showed partial improvement. And partial improvement is defined as decreased severity by one or more grades from the worst grade at last follow-up. Patients with clinically significant corneal disease were excluded from clinical studies. Ocular adverse reactions led to dosage interruption in 3.6 percent of patients and dosage reductions in 2.5 percent of patients and permanent discontinuation in one percent of patients.[6]

As far as management, the US Prescribing Information recommends patients use preservative-free lubricant eye drops at least four times daily and as needed to reduce the risk and manage symptoms of ocular adverse reactions. Providers should also advise patients to avoid using contact lenses unless directed by an optometrist or ophthalmologist. On top of that, providers should refer patients to an eye care professional for ophthalmic exams including visual acuity testing, slit lamp examination with fluorescein staining, intraocular pressure, and fundoscopy—at treatment initiation, annually while on therapy, at the end of treatment, and as clinically indicated.[6]

But throughout the course of treatment, providers should closely monitor for signs of ocular issues, especially because the time to onset is so broad.[6]

This safety profile is consistent with prior findings, and, again, while ocular adverse reactions are common, majority of ocular adverse reactions were grades one or two.[6]

Dr. Turck:
And were there any other adverse events of special interest?

Nurse Soto-Romano
Yes, Dato-DXd also caused interstitial lung disease, or ILD, and pneumonitis.

In a pooled safety population from the TROPION-Breast01 and TROPION-PanTumor01 trial, which included 443 patients with unresectable or metastatic breast cancer only, ILD or pneumonitis occurred in 3.6 percent of patients –2.7 percent were grades one or two so most were low grade. But ILD and pneumonitis can be severe or fatal, 0.7 percent of patients had grade three and one case was fatal. So, it's important that providers monitor patients for ILD and pneumonitis symptoms, and encourage patients to report symptoms of cough, dyspnea, fever, or any new or worsening respiratory symptoms.[6] In fact, 1.6 percent of patients discontinued Dato-DXd due to ILD or pneumonitis and 0.9 percent of patients had Dato-DXd withheld. Systemic corticosteroids were required for 60 percent of patients with ILD or pneumonitis, and was resolved in 40 percent of patients. Patients were excluded from clinical studies for a history of ILD or pneumonitis requiring treatment with steroids or for ongoing ILD or pneumonitis.[6]

The median time for ILD or pneumonitis to onset was 2.8 months, but it occurred as early as 1.1 months and as late as 10.8 months which, again, highlights the importance of consistent monitoring.[6]

According to Dato-DXd's prescribing information, patients with asymptomatic grade one ILD or pneumonitis should stop Dato-DXd until ILD is completely resolved and receive corticosteroid treatment, such as at least 0.5 milligrams per kilogram per day of prednisolone or an equivalent. But patients experiencing grade two or higher symptomatic ILD or pneumonitis should discontinue Dato-DXd and receive systemic corticosteroid treatment, for example at least one milligram per kilogram per day of prednisolone, for at least 14 days followed

by a gradual taper for at least four weeks.[6]

Dr. Turck:
Turning back to you, Dr. Jhaveri, are there management strategies for other common adverse events associated with Dato-DXd?

Dr. Jhaveri:
Certainly. So we've already talked about how to manage stomatitis and ocular adverse reactions, but it's also important to remember that providers can offer supportive care for nausea, vomiting, and infusion-related events. In fact, datopotamab deruxtecan-dlnk, or DATROWAY®, is categorized as a high emetic risk agent in the NCCN Clinical Practical Guidelines in Oncology for Antiemesis, and it's recommended to administer prophylactic antiemetic medications for prevention of treatment-induced nausea and vomiting.[16]

To help prevent or ease nausea and vomiting, patients can receive anti-nausea pre-medications before each infusion and additional doses afterward if needed. These typically include medications like 5-HT3 serotonin receptor antagonists or other suitable antiemetics based on the patient's needs.[6]

For infusion-related reactions, it's recommended to give antihistamines and antipyretics—such as diphenhydramine and acetaminophen—about 30 to 60 minutes before the infusion.[6]

Lastly, I think it's important to reiterate that recognizing symptoms early can reduce the severity of adverse reactions—especially those that could impact a patient's quality of life and even therapy adherence.

So by taking a proactive approach and encouraging patients to report symptoms as soon as they appear, providers can intervene early and help patients stay on track with their therapy.

Dr. Turck:
Well, with those important insights in mind, I want to thank my guests, Dr. Komal Jhaveri and Nurse Vanessa Soto-Romano for joining me to discuss the efficacy and safety of Dato-DXd in patients with HR-positive HER2-negative metastatic breast cancer. Dr. Jhaveri, Ms. Soto-Romano, it was great speaking with you both today.

Dr. Jhaveri:
Thanks for having me.

Nurse Soto-Romano:
It was great to be here.

Dr. Turck:
For ReachMD, I'm Dr. Charles Turck. Please stay tuned to hear important safety information.

ReachMD Announcer:
Warnings and Precautions
Interstitial Lung Disease/Pneumonitis

DATROWAY can cause severe, life-threatening, or fatal interstitial lung disease (ILD) or pneumonitis.

Unresectable or Metastatic Breast Cancer

In the pooled safety population of 443 patients with breast cancer from TROPION-Breast01 and TROPION-PanTumor01, ILD/pneumonitis occurred in 3.6% of patients treated with DATROWAY, including 0.7% of patients with Grade 3. There was one fatal case (0.2%). The median time to onset for ILD was 2.8 months (range: 1.1 months to 10.8 months). Four patients (0.9%) had DATROWAY withheld and 7 patients (1.6%) permanently discontinued DATROWAY due to ILD/pneumonitis. Systemic corticosteroids were required in 60% (9/15) of patients with ILD/pneumonitis. ILD/pneumonitis resolved in 40% 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.

Unresectable or Metastatic Breast Cancer and Other Solid Tumors

In patients with unresectable or metastatic breast cancer 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.

Unresectable or Metastatic Breast Cancer and Other Solid Tumors

In patients with unresectable or metastatic breast cancer 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.

In patients who received DATROWAY in TROPION-Breast01, 39% used a mouthwash containing corticosteroid for management or prophylaxis of stomatitis/oral mucositis at any time during the treatment.

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

Unresectable or Metastatic Breast Cancer 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-Breast01 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%).

Unresectable or Metastatic, HR-Positive, HER2-Negative Breast Cancer

TROPION-Breast01

The safety of DATROWAY was evaluated in 360 patients with unresectable or metastatic HR-positive, HER2-negative (IHC 0, IHC1+ or IHC2+/ISH-) breast cancer who received at least one dose of DATROWAY 6 mg/kg in TROPION-Breast01. DATROWAY was administered by intravenous infusion once every three weeks. The median duration of treatment was 6.7 months (range: 0.7 months to 16.1 months) for patients who received DATROWAY.

Serious adverse reactions occurred in 15% of patients who received DATROWAY. Serious adverse reactions in >0.5% of patients who received DATROWAY were urinary tract infection (1.9%), COVID-19 infection (1.7%), ILD/pneumonitis (1.1%), acute kidney injury, pulmonary embolism, vomiting, diarrhea, hemiparesis, and anemia (0.6% each). Fatal adverse reactions occurred in 0.3% of patients who received DATROWAY and were due to ILD/pneumonitis.

Adverse Reactions cont.

Permanent discontinuation of DATROWAY due to an adverse reaction occurred in 3.1% of patients. Adverse reactions which resulted in permanent discontinuation of DATROWAY in >0.5% of patients included ILD/pneumonitis (1.7%) and fatigue (0.6%).

Dosage interruptions of DATROWAY due to an adverse reaction occurred in 22% of patients. Adverse reactions which required dosage interruption in >1% of patients included COVID-19 (3.3%), infusion-related reaction (1.4%), ILD/pneumonitis (1.9%), stomatitis (1.9%), fatigue (1.7%), keratitis (1.4%), acute kidney injury (1.1%), and pneumonia (1.1%).

Dose reductions of DATROWAY due to an adverse reaction occurred in 23% of patients. Adverse reactions which required dose reduction in >1% of patients included stomatitis (13%), fatigue (3.1%), nausea (2.5%), and weight decrease (1.9%).

The most common (≥20%) adverse reactions, including laboratory abnormalities, were stomatitis (59%), nausea (56%), fatigue (44%), decreased leukocytes (41%), decreased calcium (39%), alopecia (38%), decreased lymphocytes (36%), decreased hemoglobin (35%), constipation (34%), decreased neutrophils (30%), dry eye (27%), vomiting (24%), increased ALT (24%), keratitis (24%), increased AST (23%), and increased alkaline phosphatase (23%).

Clinically relevant adverse reactions occurring in <10% of patients who received DATROWAY included infusion-related reactions (including bronchospasm), ILD/pneumonitis, headache, pruritus, dry skin, dry mouth, conjunctivitis, blepharitis, meibomian gland dysfunction, blurred vision, increased lacrimation, photophobia, visual impairment, skin hyperpigmentation, and madarosis.

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.

Use in Specific Populations contd.

Geriatric Use: Of the 365 patients in TROPION-Breast01 treated with DATROWAY 6 mg/kg, 25% were ≥65 years of age and 5% were ≥75 years of age. Grade ≥3 and serious adverse reactions were more common in patients ≥65 years (42% and 25%, respectively) compared to patients <65 years (33% and 15%, respectively). In TROPION-Breast01, no other meaningful differences in safety or efficacy 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 see full Prescribing Information, please click on the link on the ReachMD landing page.

This medical industry feature was sponsored by AstraZeneca and Daiichi Sankyo. If you missed any part of this discussion, visit Industry Features on ReachMD.com, where you can Be Part of the Knowledge.

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