


Video Transcript Part 1: Overview of Trodelvy	Slide #	Reference Material
<p>Linda:</p> <p>Welcome and thank you for joining us today for this case-based discussion on management of select adverse events for TRODELVY. I am pleased to introduce Dr. Yuan Yuan who will be presenting and leading today's discussion. Dr. Yuan is a breast medical oncologist and physician scientist who specializes in triple negative breast cancer and breast cancer immunotherapy. Dr. Yuan completed her medical degree in China and a fellowship in hematology and medical oncology at NYU. Additionally, she holds a PhD in biochemistry and molecular biology from the University of California Riverside. Thank you, Dr. Yuan, for being with us here today. Dr. Yuan, please take it away.</p>	1	
<p>Dr. Yuan:</p> <p>Thank you, Linda, and thank you to the sponsor for the opportunity to share some of the information for you. And this is a promotional program that is provided by Gilead and the content has been developed in accordance to FDA guidelines. So, I will try to abide by this information.</p>	2	<p>Disclosures</p> <ul style="list-style-type: none"> • This is a promotional program sponsored by and provided on behalf of Gilead Sciences, Inc. The speaker has been compensated for this presentation. • Content in this program has been developed in accordance with FDA guidelines and is consistent with TRODELVY Prescribing Information. <p><small>Please see Important Safety Information, including BOXED WARNING, on slides 4 and 12-16 and full Prescribing Information accompanying this presentation.</small></p>

<p>Dr. Yuan:</p> <p>So today we would like to take some time to understand TRODELVY key efficacy, safety and patient reported outcome data in patients with pretreated hormone receptor positive, HER2-metastatic breast cancer.</p>	<p>3</p>	<p>Objectives</p> <ul style="list-style-type: none"> Understand TRODELVY key efficacy, safety, and patient-reported outcomes data in patients with pretreated HR+/HER2- mBC^a <p><small>^aThe term "pretreated HR+/HER2-" is defined as after endocrine therapy and at least two additional systemic therapies in the metastatic setting. HER2, human epidermal growth factor receptor 2; HR, hormone receptor; mBC, metastatic breast cancer.</small></p> <p><small>Please see Important Safety Information, including BOXED WARNING, on slides 4 and 12. -16 and full Prescribing Information accompanying this presentation.</small></p>
<p>Dr. Yuan:</p> <p>So, as you know, TRODELVY indications have been extended to two areas. Initially, we had the FDA approval of TRODELVY in triple-negative breast cancer, which is for patients whose unresectable locally advanced or metastatic triple negative breast cancer who had received two or more prior systemic therapies, at least one of them from the metastatic setting. We now have the very exciting indication which is using TRODELVY in unresectable locally advanced or metastatic hormone receptor positive and HER2 negative breast cancer, in patients who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting. Indications, TRODELVY sacituzumab govitecan is a Trop-2-directed antibody and topoisomerase inhibitor conjugate indicated for treatment for the treatment of adult patients with, unresectable locally advanced or metastatic triple-negative breast cancer who have received two or more prior systemic therapies, at least one of them for metastatic disease. Unresectable locally advanced or metastatic hormone receptor-positive, HER2-negative, defined by immunohistochemistry or IHC zero or IHC one plus or IHC two plus, or ISH negative breast cancer who have received endocrine-</p>	<p>4</p>	<p>TRODELVY® Indications and Important Safety Information (1 of 6, continued on slide 12)</p> <p>INDICATIONS</p> <p>TRODELVY (sacituzumab govitecan-hzyl) is a Trop-2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with:</p> <ul style="list-style-type: none"> Unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received 2 or more prior systemic therapies, at least one of them for metastatic disease Unresectable locally advanced 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 endocrine-based therapy and at least 2 additional systemic therapies in the metastatic setting <p>IMPORTANT SAFETY INFORMATION</p> <p>BOXED WARNING: NEUTROPENIA AND DIARRHEA</p> <ul style="list-style-type: none"> Severe or life-threatening neutropenia may occur. Withhold TRODELVY for absolute neutrophil count below 1500/mm³ or neutropenic fever. Monitor blood cell counts periodically during treatment. Consider G-CSF for secondary prophylaxis. Initiate anti-infective treatment in patients with febrile neutropenia without delay. Severe diarrhea may occur. Monitor patients with diarrhea and give fluid and electrolytes as needed. At the onset of diarrhea, evaluate for infectious causes and, if negative, promptly initiate loperamide. If severe diarrhea occurs, withhold TRODELVY until resolved to ≤Grade 1 and reduce subsequent doses. <p>CONTRAINDICATIONS</p> <ul style="list-style-type: none"> Severe hypersensitivity reaction to TRODELVY <p><small>© CSP, granulocyte colony-stimulating factor; IHC, immunohistochemistry; ISH, in situ hybridization. TRODELVY (package insert). Foster City, CA: Ellie Sciences, Inc.; February 2023.</small></p> <p><small>Please see Important Safety Information, including BOXED WARNING, on slides 4 and 12-16 and full Prescribing Information accompanying this presentation.</small></p>

based therapy and at least two additional systemic therapies in the metastatic setting. TRODELVY has a Box Warning for neutropenia and diarrhea. Severe or life-threatening neutropenia may occur. Withhold TRODELVY for absolute neutrophil count below fifteen hundred or neutropenic fever. Monitor blood cell counts periodically during treatment. Consider G-CSF for secondary prophylaxis. Initiate anti-infective treatment in patients with febrile neutropenia without delay. Severe diarrhea may occur. Monitor patients with diarrhea and give fluid and electrolytes as needed. At the onset of diarrhea, evaluate for infectious causes and, if negative, promptly initiate loperamide. If severe diarrhea occurs, withhold TRODELVY until resolved to grade one or lower and reduce subsequent doses. TRODELVY is contraindicated in those with severe hypersensitivity to TRODELVY.

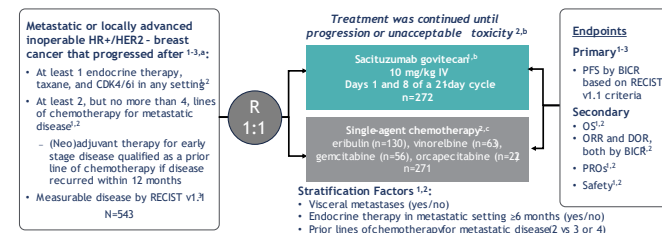
Dr. Yuan:

So, let's take a deep dive into the landmark TROPiCS-02 trial, which is a phase three randomized study specifically focused on patients with hormone receptor positive HER2 negative locally advanced inoperable or metastatic breast cancer. In this trial, patients were randomized one-on-one to sacituzumab govitecan, or TRODELVY, at the dose of 10 mg/kg on days one and eight, every 21 days, versus single-agent choice, or physician's choice, which include eribulin, vinorelbine, gemcitabine or capecitabine. These are the patients going back to the bar on the screen. Who are these patients? These are the patients who are hormone receptor positive disease, metastatic largely, and at least one endocrine therapy in the metastatic setting. And taxanes in the (Neo)adjuvant or metastatic setting and at least two but not more than four lines of chemo for the metastatic disease. So, you notice that this is an important feature of this population. They're rather

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TROPiCS-02: A Phase 3 Study of SG in HR+/HER2-locally Advanced Inoperable or Metastatic Breast Cancer^{1,2}

Sacituzumab govitecan was studied in this randomized, open-label, active-controlled trial vs single-agent chemotherapy (NCT03901339)



1. Disease history based on the ASCO-CAP criteria administered. SG was permitted beyond RECIST-defined disease progression if the patient was clinically stable and considered by the sponsor to be deriving clinical benefit. 2. Single-agent chemotherapy (eribulin, taxane, or CDK4/6i) was permitted if the patient was clinically stable and considered by the sponsor to be deriving clinical benefit. 3. ASCO-CAP: American Society of Clinical Oncology; College of American Pathologists; BICR: blinded independent central review; CDK4/6i: cyclin-dependent kinase 4/6 inhibitor; DOR: duration of response; HER2: human epidermal growth factor receptor 2; HR: hormone receptor; IV: intravenously; ORR: objective response rate; OS: overall survival; PFS: progression-free survival; PRO: patient-reported outcome; RECIST: Response Evaluation Criteria in Solid Tumors; RECIST v1.1: Response Evaluation Criteria in Solid Tumors version 1.1. 4. Safety. 5. Progression was defined as progression according to RECIST v1.1 criteria.

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heavily pretreated. Now they must have measurable disease by RECIST v1.1. As far as the endpoints, the primary endpoint is progression-free survival, and the secondary endpoint including overall survival and importantly patient reported outcomes and safety information.

Dr. Yuan:

Here are the characteristics of TROPiCS-02. If you look at the two arms, they're well-balanced, looking at the median age, race, ECOG performance status, they're similar, important features. Again, I want to draw your attention to the visceral metastases. Look at these patients, 95% in both arms had visceral metastasis at baseline. Again, this depicted their very heavily pretreated population and we're talking about visceral metastases. About 84 to 87% of the patient had liver met. About 29 to 22% of the patient had a de novo stage four disease. Now important features also included prior treatment. If you look at some breakdowns on the right-hand side, including prior CDK4/6 inhibitor, there's further characteristics including the time on initial CDK. About 60% of the patients had a relatively short, less than 12 months of CDK4/6 inhibitor treatment. Over 12 months, patients are only around 40%. So, this kind of speaks for, again, those in our practice we mentioned, those so-called fast progressors. Because considering CDK4/6 inhibitor in this population, medium progression-free survival usually gets 24 months.

So, these again speak for the TROPiCS-02 population. Very important for the later slides. Now median lines of therapy, you can see that they're again heavily pretreated. Over 60% of the patients had three or more lines of chemotherapy. And the median lines of chemo ranging between 1-9 in the sacituzumab arm, and then somewhere around 2-7 in the single agent chemotherapy arm.

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Demographics and Baseline Characteristics for TROPiCS^{1,2}

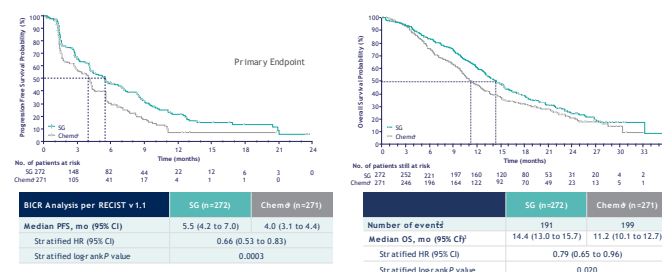
	SG (n=272)	Single-Agent Chemotherapy (n=274)		SG (n=272)	Single-Agent Chemotherapy (n=274)
Female, n (%)	270 (99)	268 (99)	Prior chemotherapy in (neo)adjuvant setting, n (%)	172 (64)	184 (68)
Median age, y, n (range)	55 (28-86)	55 (27-87)	Prior endocrine therapy use in the metastatic setting, n (%)	235 (86)	234 (86)
<65 y, n (%)	199 (73)	204 (75)	Prior CDK4/6 inhibitor use, n (%)		
Race or ethnic group, n (%)	73 (27)	67 (25)	Asian	161 (59)	166 (61)
White	184 (68)	178 (66)	>12 months	16 (19)	102 (38)
Black	8 (3)	13 (5)	Unknown	3 (2)	3 (1)
Hispanic	11 (4)	5 (2)	Median prior chemotherapy regimens in the metastatic setting, n (range)	3 (0-8)	3 (1-5)
Other ^a /not report ^b	69 (25)	75 (28)	1	1 (1)	0
ECOG PS, n (%)			2	8 (3)	2 (1)
0	116 (43)	126 (46)	3	104 (38)	118 (43)
1	156 (57)	145 (54)	≥3	159 (58)	151 (56)
Visceral metastases at baseline, n (%)	259 (95)	258 (95)	Median prior chemotherapy regimens, n (range)	4 (1-9)	4 (2-7)
Liver metastases ^c , n (%)	229 (84)	237 (87)	Median prior anticancer regimens ^d , n (range)	7 (1-7)	7 (3-16)
De novo metastatic breast cancer, n (%)	78 (29)	60 (22)			
Median time from initial metastatic diagnosis to randomization, mo (range)	48.5 (1.2-240.8)	46.6 (3.0-248.8)			

*Includes American Indian or Alaska Native, Pacific Hawaiian Islander, Pacific Islander; *Not reported indicates local regulators did not allow collection of race or ethnicity information; †Assessed baseline target; ‡Outright target; §Indicates per RECIST v1.1 by a local investigator; ||Reported number of prior therapies was inaccurate at screening for some patients; ¶Patients received prior chemotherapy; **Market setting outside the preprotocol range for inclusion criteria and were included in the intent-to-treat population; ††Anti-CDK4/6 requires for any treatment regimen that was used to treat breast cancer in any setting and includes endocrine therapy and venetoclax.

Dr. Yuan:

So, this is a big primary endpoint progression-free survival and the secondary endpoint overall survival. We can see that in this, again, heavily pretreated population, the central review versus criteria showing that sacituzumab govitecan has a significant improved progression-free survival of 5.5 months, in comparison with the chemotherapy arm's 4.0 months. This actually reached the primary endpoint, and fit into the initial statistical design, has a ratio of 0.66 and log rank P-value less than 0.0003 and look at the progression-free survival. Despite a modest improvement of progression-free survival, you can see a significant improvement of three months comparing sacituzumab govitecan versus chemotherapy with a hazard ratio of 0.79. And so, I think this is very important data that we're hoping to understand better the mechanism of action.

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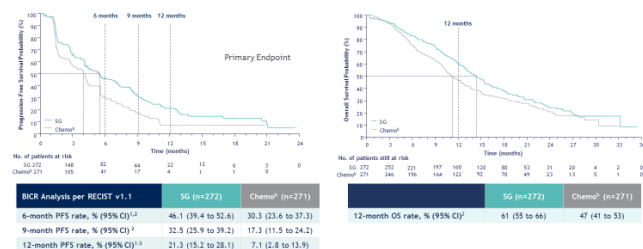
SG Demonstrated a Statistically Significant Improvement in PFS and OS

Median follow-up was 10.2 months for PFS and 12.5 months for OS.
 *Intention-to-treat population. †Single-agent chemotherapy.
 BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; SG, sacituzumab govitecan.
 1. Rajaghi, et al. J Clin Oncol. 2022;40(25):3380-3390. 2. Rajaghi, et al. Presented at European Society for Medical Oncology Congress, September 2022, Paris, France. Presentation 1620T0002P (package insert).
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Dr. Yuan:

So, an important, I would say, landmark time point really helps us to grasp what is the improvement. So, if you look at the left side of the table here at six months of time, the sacituzumab govitecan treated a patient, 46% of them have remained progression-free and the chemotherapy is 30%. But if you move on to 12 months, you can see that the differences further widen. The chemotherapy arm only has 7% of patients still on treatment not progressing. But for sacituzumab govitecan that is increased to 21%. I think that's really important data to share with patients and clinics, how to we explain the efficacy. And again, you look at the 12 months overall survival rate, in SG treated patients, overall survival, 61%, in chemotherapy, 47%. This analysis was prespecified but was not powered for statistical significance and should be considered descriptive only. Therefore,

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Numerically Higher PFS and OS Rates at Landmark Timepoints^{1,3,a}

Limitation: This analysis was prespecified but was not powered for statistical significance and should be considered descriptive only. Therefore, the results require cautious interpretation and could represent chance findings.
 *Intention-to-treat population. †Single-agent chemotherapy.
 BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; SG, sacituzumab govitecan.
 1. Rajaghi, et al. J Clin Oncol. 2022;40(25):3380-3390. 2. Rajaghi, et al. Presented at European Society for Medical Oncology Congress, September 9-13, 2022, Paris, France. Presentation 1620T0002P (package insert).
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Dr. Yuan:

The most common which is defined by 25% or more adverse events, including lab abnormalities with SG were decreased leukocyte, decreased neutrophil, decreased hemoglobin, decreased lymphocyte, diarrhea, fatigue, nausea, alopecia, increased glucose, constipation, and decreased albumin.

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Adverse Reactions and Lab Abnormalities Reported in Patients in the TROPiCS-02 Study

Adverse Reactions Reported In ≥10% of Patients With HR+/HER2BC in TROPiCS-02				
Adverse reaction	SG (n=248)		Single-Agent Chemotherapy ^a (n=249)	
	All grades, %	Grade 3 to 4, %	All grades, %	Grade 3 to 4, %
Gastrointestinal disorders				
Diarrhea	62	10	23	1
Nausea	39	1	25	3
Constipation	34	1	25	0
Vomiting	23	1	16	2
Abdominal pain	20	0	14	0
Dyspepsia ^b	11	0	6	0
General disorders and administration site conditions				
Fatigue	60	8	51	4
Metabolites and nutrition disorders				
Decreased appetite	21	2	21	0
Hypokalemia	10	2	4	0
Musculoskeletal and connective tissue disorders				
Arthralgia	15	0	12	0
Nervous system disorders				
Headache	16	1	15	1
Respiratory, thoracic, and mediastinal disorders				
Dyspnea ^c	20	0	17	0
Cough	12	0	7	0
Skin and subcutaneous tissue disorders				
Alopecia	48	0	19	0
Pruritus	12	0	2	0

^a The most common lab abnormalities occurring in ≥25% of patients treated with SG were decreased leukocyte count (88% for SG vs 73% for single-agent chemotherapy), decreased neutrophil count (83% for SG vs 67% for single-agent chemotherapy), decreased hemoglobin (73% for SG vs 59% for single-agent chemotherapy), decreased lymphocyte count (65% for SG vs 47% for single-agent chemotherapy), increased glucose (37% for SG vs 31% for single-agent chemotherapy), and decreased albumin (32% for SG vs 27% for single-agent chemotherapy).

^b Graded per NCI CTCAE v5.0. Dyspepsia was defined as one of the following single symptoms: heartburn, acid reflux, or gastroesophageal reflux disease resulting in pain, indigestion, or bloating.

^c CTCAE Common Terminology Criteria for Adverse Events (CTCAE). HR, human epidermal growth factor receptor 2; HER2, human epidermal growth factor receptor 2; BC, breast cancer; SG, single-agent chemotherapy; TROPiCS-02, TROPiCS-02 Study.

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Dr. Yuan:

Okay, now let's take a deeper dive into these individual toxicities we mentioned earlier. Neutropenia, severe, life-threatening, or fatal neutropenia can occur and may require dose modification. Neutropenia occurred in 64% of patients treated with TRODELVY. Grade three to four neutropenia occurred in 49% of the patients. Febrile neutropenia occurred in 6%. Neutropenic colitis occurred in 1.4%. Withhold TRODELVY for absolute neutrophil count below 1500 on day 1 of any cycle or neutrophil counts below 1000 on day 8 of any cycle. Withhold TRODELVY for neutropenic fever. Administer G-CSF as clinically indicated or indicated in Table 1 of USPI. Diarrhea occurred in 64% of all patients treated with TRODELVY. Grade 3 to 4 diarrhea occurred in 11% of patients. One patient had intestinal perforation following diarrhea. Diarrhea that led to dehydration and subsequent acute kidney injury occurred in 0.7% of all patients. Withhold TRODELVY for grade 3 to 4 diarrhea and resume when resolved to grade 1 or lower. At onset, evaluate for infectious causes and if negative, promptly initiate loperamide, which is dosed at 4 mg initially followed by 2

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TRODELVY Important Safety Information (2 of 6, continued from slide 4)

WARNINGS AND PRECAUTIONS

Neutropenia

- Severe, life-threatening, or fatal neutropenia can occur and may require dose modification. Neutropenia occurred in 64% of patients treated with TRODELVY. Grade 3 to 4 neutropenia occurred in 49% of patients. Febrile neutropenia occurred in 6%. Neutropenic colitis occurred in 1.4%. Withhold TRODELVY for absolute neutrophil count below 1500/ μm^3 on Day 1 of any cycle or neutrophil count below 1000/ μm^3 on Day 8 of any cycle. Withhold TRODELVY for neutropenic fever. Administer G-CSF as clinically indicated or indicated in Table 1 of USPI.

Diarrhea

- Diarrhea occurred in 64% of all patients treated with TRODELVY. Grade 3 to 4 diarrhea occurred in 11% of patients. One patient had intestinal perforation following diarrhea. Diarrhea that led to dehydration and subsequent acute kidney injury occurred in 0.7% of all patients. Withhold TRODELVY for Grade 3 to 4 diarrhea and resume when resolved to \leq Grade 1. At onset, evaluate for infectious causes and if negative, promptly initiate loperamide, 4 mg initially followed by 2 mg with every episode of diarrhea for a maximum of 16 mg daily. Discontinue loperamide 12 hours after diarrhea resolves. Additional supportive measures (e.g., fluid and electrolyte substitution) may also be employed as clinically indicated. Patients who exhibit an excessive cholinergic response to treatment can receive appropriate premedication (e.g., atropine) for subsequent treatments.

G-CSF, granulocyte colony-stimulating factor; TRODELVY (package insert); Foster City, CA: Gilead Sciences, Inc.; February 2023.

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-16 and full [Prescribing Information](#), accompanying this presentation.

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<p>mg with every episode of diarrhea for a maximum of 16 mg daily. Discontinue loperamide 12 hours after diarrhea resolves. Additional supportive measures, including fluids and electrolyte substitution, may also be employed as clinically indicated. Patients who exhibit an excessive cholinergic response to treatment can receive appropriate premedication for such as atropine for subsequent treatments.</p>		
<p>Dr. Yuan:</p> <p>Hypersensitivity and infusion-related reactions. Serious hypersensitivity reactions including life-threatening anaphylactic reactions have occurred with TRODELVY. Severe signs and symptoms included cardiac arrest, hypotension, wheezing, angioedema, swelling, pneumonitis, and skin reactions. Hypersensitivity reactions within 24 hours of dosing occurred in 35% of patients. Grade 3 to 4 hypersensitivity occurred in 2% of patients. The incidence of hypersensitivity reactions leading to permanent discontinuation of TRODELVY was 0.2%. The incidence of anaphylactic reactions was 0.2%. Pre-infusion medication is recommended. Have medications and emergency equipment to treat such reactions available for immediate use. Observe patients closely for hypersensitivity and infusion-related reactions during each infusion and for at least 30 minutes after completion of each infusion. Permanently discontinued through delving for Grade 4 infusion-related reactions.</p> <p>Nausea and vomiting. Nausea occurred in 64% of all patients treated with TRODELVY and grade 3 to 4 nausea occurred in 3% of these patients. Vomiting occurred in 35% of patients and grade 3 to 4 vomiting occurred in 2% of these patients. Premedicate with a 2 or 3-drug combination regimen such as dexamethasone, with either a 5-HT3 receptor antagonist or an NK1 receptor antagonist,</p>	<p>13</p>	<p>TRODELVY Important Safety Information (3 of 6)</p> <p>WARNINGS AND PRECAUTIONS (cont'd)</p> <div> <div> <p>Hypersensitivity and Infusion-Related Reactions</p> <ul style="list-style-type: none"> Serious hypersensitivity reactions including life-threatening anaphylactic reactions have occurred with TRODELVY. Severe signs and symptoms included cardiac arrest, hypotension, wheezing, angioedema, swelling, pneumonitis, and skin reactions. Hypersensitivity reactions within 24 hours of dosing occurred in 35% of patients. Grade 3 to 4 hypersensitivity occurred in 2% of patients. The incidence of hypersensitivity reactions leading to permanent discontinuation of TRODELVY was 0.2%. The incidence of anaphylactic reactions was 0.2%. Pre-infusion medication is recommended. Have medications and emergency equipment to treat such reactions available for immediate use. Observe patients closely for hypersensitivity and infusion-related reactions during each infusion and for at least 30 minutes after completion of each infusion. Permanently discontinue TRODELVY for Grade 4 infusion-related reactions. </div> <div> <p>Nausea and Vomiting</p> <ul style="list-style-type: none"> Nausea occurred in 64% of all patients treated with TRODELVY and Grade 3 to 4 nausea occurred in 3% of these patients. Vomiting occurred in 35% of patients and Grade 3 to 4 vomiting occurred in 2% of these patients. Premedicate with a 2 or 3 drug combination regimen, dexamethasone with either a 5-HT3 receptor antagonist or an NK1 receptor antagonist as well as other drugs as indicated for prevention of chemotherapy induced nausea and vomiting (CINV). Withhold TRODELVY doses for Grade 3 nausea or Grade 3 to 4 vomiting and resume with additional supportive measures when resolved to Grade 1. Additional antiemetics and other supportive measures may also be employed as clinically indicated. All patients should be given take-home medications with clear instructions for prevention and treatment of nausea and vomiting. </div> </div> <p><small>TRODELVY (package insert), Foster City, CA: Glaxo Sciences, Inc.; February 2023. Please see Important Safety Information, including BOXED WARNING, on slides 4 and 12.</small></p> <p><small>-16 and full Prescribing Information, accompanying this presentation.</small></p> <p><small>13</small></p>

<p>as well as other drugs as indicated for prevention of chemotherapy-induced nausea and vomiting. Withhold TRODELVY doses for grade 3 nausea or grade 3 to 4 vomiting and resume with additional supportive measures when resolved to grade 1 or lower. Additional antiemetics and other supportive measures may also be employed as clinically indicated. All patients should be given take-home medications with clear instructions for prevention and treatment of nausea and vomiting.</p>		
<p>Dr. Yuan: Cut from 17:52 to 17:56</p> <p>Increased risk of adverse reactions in patients with reduced UGT1A1 activity. Patients with homozygous for the UGT1A1*28 allele are at increased risk for neutropenia, febrile neutropenia, and anemia, and may be at increased risk for other adverse reactions with TRODELVY. The incidence of grade 3 to 4 neutropenia was 58% in patients homozygous for the UGT1A1*28 allele, 49% in patients heterozygous for the UGT1A1*28 allele, and 43% in patients homozygous for the wild-type allele. The incidence of grade 3 to 4 anemia was 21% in patients homozygous for the UGT1A1*28 allele, 10% in patients heterozygous for the UGT1A1*28 allele, and 9% in patients homozygous for the wild-type allele. Closely monitor patients with known reduced UGT 1A1 activity for adverse reactions. Withhold or permanently discontinue TRODELVY based on clinical assessment of the onset, duration, and severity of the observed adverse reactions in patients with evidence of acute early-onset or usually severe adverse reactions, which may indicate reduced UGT 1A1 function.</p> <p>Embryo-fetal toxicity. Based on its mechanism of action TRODELVY can cause teratogenicity and/or embryo-fetal lethality when administered to a pregnant woman. TRODELVY contains a genotoxic component SN-38 and targets rapidly dividing cells.</p>	<p>14</p>	<p>TRODELVY Important Safety Information (4 of 6)</p> <p>WARNINGS AND PRECAUTIONS (cont'd)</p> <div> <div> <p>Increased Risk of Adverse Reactions in Patients with Reduced UGT1A1 Activity</p> <ul style="list-style-type: none"> Patients homozygous for the uridine diphosphoglucuronosyl transferase 1A1 (UGT1A1)*28 allele are at increased risk for neutropenia, febrile neutropenia, and anemia and may be at increased risk for other adverse reactions with TRODELVY. The incidence of Grade 3 to 4 neutropenia was 58% in patients homozygous for the UGT1A1*28 allele, 49% in patients heterozygous for the UGT1A1*28 allele, and 43% in patients homozygous for the wildtype allele. The incidence of Grade 3 to 4 anemia was 21% in patients homozygous for the UGT1A1*28 allele, 10% in patients heterozygous for the UGT1A1*28 allele, and 9% in patients homozygous for the wildtype allele. Closely monitor patients with known reduced UGT1A1 activity for adverse reactions. Withhold or permanently discontinue TRODELVY based on clinical assessment of the onset, duration and severity of the observed adverse reactions in patients with evidence of acute early-onset or unusually severe adverse reactions, which may indicate reduced UGT1A1 function </div> <div> <p>Embryo-Fetal Toxicity</p> <ul style="list-style-type: none"> Based on its mechanism of action, TRODELVY can cause teratogenicity and/or embryofetal lethality when administered to a pregnant woman. TRODELVY contains a genotoxic component, SN38, and targets rapidly dividing cells. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TRODELVY and for 6 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TRODELVY and for 3 months after the last dose </div> </div> <p><small>TRODELVY (package insert), Foster City, CA: Glaxo Sciences, Inc.; February 2023. Please see Important Safety Information, including BOXED WARNING, on slides 4 and 12</small></p> <p><small>-16 and full Prescribing Information, accompanying this presentation.</small></p> <p><small>14</small></p>

<p>Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TRODELVY and 6 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TRODELVY and for 3 months after the last dose.</p>		
<p>Dr. Yuan:</p> <p>Adverse reactions.</p> <p>In the pooled safety population, the most common which is defined by 25% or more adverse reactions including lab abnormalities were decreased leukocyte count 84%, decreased neutrophil count 75%, decreased hemoglobin 69%, diarrhea 64%, nausea 64%, decreased lymphocyte count 63%, fatigue 51%, alopecia 45%, constipation 37%, increased glucose 37%, decreased albumin 35%, vomiting 35%, decreased appetite 30%, decreased creatinine clearance 28%, increased alkaline phosphatase 28%, decreased magnesium 27%, decreased potassium 26%, and decreased sodium 26%.</p> <p>In the ASCENT study, locally advanced or metastatic triple-negative breast cancer, the most common adverse reactions incidence 25% or more were fatigue, diarrhea, nausea, alopecia, constipation, vomiting, abdominal pain, and decreased appetite. The most frequent serious adverse reactions, which is defined by over 1% were neutropenia 7%, diarrhea 4%, and pneumonia 3%. Serious adverse reactions were reported in 27% of patients and 5% discontinued therapy due to adverse reactions. The most common grade three to four lab abnormalities, incidence 25% or more in the ASCENT study, were reduced neutrophils, leukocytes, and lymphocytes.</p>	15	<p>TRODELVY Important Safety Information (5 of 6)</p> <p>ADVERSE REACTIONS</p> <ul style="list-style-type: none"> In the pooled safety population, the most common (≥ 25%) adverse reactions including laboratory abnormalities were decreased leukocyte count (84%), decreased neutrophil count (75%), decreased hemoglobin (69%), diarrhea (64%), nausea (64%), decreased lymphocyte count (63%), fatigue (51%), alopecia (45%), constipation (37%), increased glucose (37%), decreased albumin (35%), vomiting (35%), decreased appetite (30%), decreased creatinine clearance (28%), increased alkaline phosphatase (28%), decreased magnesium (27%), decreased potassium (26%), and decreased sodium (26%). In the ASCENT study (locally advanced or metastatic triple-negative breast cancer) the most common adverse reactions (incidence ≥ 25%) were fatigue, diarrhea, nausea, alopecia, constipation, vomiting, abdominal pain, and decreased appetite. The most frequent serious adverse reactions (SAR) (>1%) were neutropenia (7%), diarrhea (4%), and pneumonia (3%). SAR were reported in 27% of patients, and 5% discontinued therapy due to adverse reactions. The most common Grade 3 to 4 lab abnormalities (incidence ≥ 25% in the ASCENT study) were reduced neutrophils, leukocytes, and lymphocytes. In the TROPICS-02 study (locally advanced or metastatic HER2-positive, HER2-negative breast cancer) the most common adverse reactions (incidence ≥ 25%) were diarrhea, fatigue, nausea, alopecia, and constipation. The most frequent serious adverse reactions (SAR) (>1%) were diarrhea (5%), febrile neutropenia (4%), neutropenia (3%), abdominal pain, colitis, neutropenic colitis, pneumonia, and vomiting (each 2%). SAR were reported in 28% of patients, and 6% discontinued therapy due to adverse reactions. The most common Grade 3 to 4 lab abnormalities (incidence ≥ 25%) in the TROPICS-02 study were reduced neutrophils and leukocytes. <p><small>TRODELVY (sacitaxin injection) Foster City, CA: Gilead Sciences, Inc.; February 2023. Please see Important Safety Information, including BOXED WARNING, on slides 4 and 12.</small></p> <p><small>-16 and full Prescribing Information accompanying this presentation.</small></p> <p><small>15</small></p>

<p>Remember to cut here repeated twice for tropics</p> <p>In the Tropics-02 study, for locally advanced or metastatic HR-positive, HER2-negative breast cancer, the most common adverse reactions which is defined by incidence of 25% or more were diarrhea, fatigue, nausea, alopecia, and constipation. The most frequent serious adverse reactions defined by over 1% were diarrhea 5%, febrile neutropenia 4%, neutropenia 3%, abdominal pain, colitis, neutropenic colitis, pneumonia, and vomiting each 2% Serious adverse reactions were reported in 28% of patients and 6% discontinued therapy due to adverse reactions. The most common grade 3 to 4 lab abnormalities, which is defined by incidence of 25% or more in the TROPiCS-02 study were reduced neutrophils and leukocytes.</p>		
<p>Dr. Yuan:</p> <p>Drug interactions, again, because of the UGT1A1 frequency, so precautions need to be taken when the patient is concurrently using UGT1A1 inhibitors or inducers. Please refer to the full prescribing information for details.</p>	<p>16</p>	<p>TRODELVY Important Safety Information (6 of 6)</p> <p>DRUG INTERACTIONS</p> <ul style="list-style-type: none"> • UGT1A1 Inhibitors:Concomitant administration of TRODELVY with inhibitors of UGT1A1 may increase the incidence of adverse reactions due to potential increase in systemic exposure to SN38. Avoid administering UGT1A1 inhibitors with TRODELVY. • UGT1A1 Inducers:Exposure to SN38 may be reduced in patients concomitantly receiving UGT1A1 enzyme inducers. Avoid administering UGT1A1 inducers with TRODELVY. <p>Please see accompanying full Prescribing Information, including BOXED WARNING.</p> <p><small>TRODELVY (sacitaxin mesylate), Foster City, CA: Genentech, Inc.; February 2023. Please see Important Safety Information, including BOXED WARNING, on pages 4 and 17. 16 of 68. Prescribing Information. Reproduction of this presentation.</small></p>

Dr. Yuan:

So, this is an important table that we'll probably using in the cases to practice, in the next part of the talk. So, we want you to pay attention to this. So, if the patient develops adverse reactions, such as grade four neutropenia over seven Days, if the first occurrence, we need the dose reduced by 25%, and administer G-CSF. If grade three to four neutropenia, then the same thing. Or at time of scheduled treatment grade three to four neutropenia delays the dose by two or three weeks for recovery to less than a grade one. All three criteria would lead to further dose reduction. So, then you have some guidance here. If a patient had a first or second occurrence, then you dose reduce accordingly. But if the patient, despite all the management, dose reduction, and a third recurrence happens, then that's going to drive us to permanently discontinue the treatment.

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Dose Modifications to Manage Severe Neutropenia

Severe Neutropenia		
Adverse Reaction	Occurrence	Dose Modification
Grade 4 neutropenia ≥ 7 days, OR Grade 3 to 4 febrile neutropenia, OR At time of scheduled treatment, Grade 3 to 4 neutropenia, which delays dosing by 3 weeks for recovery to \leq Grade 1	First	25% dose reduction and administer G-CSF
	Second	50% dose reduction and administer G-CSF
At time of scheduled treatment, Grade 3 to 4 neutropenia, which delays dosing by 3 weeks for recovery to \leq Grade 1	Third	Discontinue treatment and administer G-CSF
	First	Discontinue treatment and administer G-CSF

- Withhold or discontinue SG to manage adverse reactions as described here
- Do not reescalate the SG dose after a dose reduction for adverse reactions has been made
- Slow or interrupt the infusion rate if the patient develops an infusional reaction
- Permanently discontinue SG for life-threatening infusion-related reactions

G-CSF, granulocyte colony-stimulating factor; SG, sacituzumabgoviteces
TRODELVY (package insert), Foster City, CA: Gilead Sciences, Inc.; February 2023.
Please see Important Safety Information, including BOXED WARNING, on slides 4 and 12

-16 and full [Prescribing Information](#), accompanying this presentation.

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Dr. Yuan:

Similarly, in the management table for GI toxicities, there's three or four different scenarios here. Any grade four diarrhea, of any duration, or grade three to four diarrhea that is not controlled with antidiarrheal agents, or other grade three to four diarrhea persisting over 48 hours, despite optimal medical management, will drive us to have dose reduction for the following treatment, including first time occurrence, 25% dose reduction, second time, which is going to lead to dose going down to five milligram per kg. And then there's no third tier, so the patient will have to discontinue the treatment permanently. Now, so again, this, there's detailed information you can find in the package insert regarding how to manage this therapy.

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Dose Modifications to Manage Severe Diarrhea

Diarrhea Severity	Occurrence	Dose Modification
Grade 4 diarrhea of any duration, OR Any Grade 3 to 4 diarrhea due to treatment that is not controlled with anti-diarrheal agents, OR Other Grade 3 to 4 diarrhea persisting >48 hours despite optimal medical management, OR At time of scheduled treatment, Grade 3 to 4 diarrhea, which delays dose by 2 or 3 weeks for recovery to Grade ≤ 1	First	25% dose reduction
	Second	50% dose reduction
In the event of Grade 3 to 4 diarrhea, which does not recover to Grade ≤ 1 within 3 weeks	Third	Discontinue treatment
	First	Discontinue treatment

Management of Diarrhea:

- Withhold SG for Grade 3 to 4 diarrhea at the time of scheduled treatment administration and resume when resolved to Grade ≤ 1
- At the onset of diarrhea, evaluate for infectious causes, and if negative, promptly initiate loperamide 4 mg initially followed by 2 mg, with every episode of diarrhea for a maximum of 16 mg daily
 - Discontinue loperamide 12 hours after diarrhea resolves
- Additional supportive measures (e.g., fluid and electrolyte substitution) may also be employed as clinically indicated
- Patients who exhibit an excessive cholinergic response to treatment with SG (e.g., abdominal cramping, diarrhea, salivation, etc.) can receive appropriate premedication (e.g., atropine) for subsequent treatments

SG, sacituzumabgoviteces
TRODELVY (package insert), Foster City, CA: Gilead Sciences, Inc.; February 2023.
Please see Important Safety Information, including BOXED WARNING, on slides 4 and 12

-16 and full [Prescribing Information](#), accompanying this presentation.

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Dr. Yuan:

For severe non-neutropenic toxicity. This is a sort of a lump sum table providing similar guidance, any grade four event or grade three to four event that is not controlled, or other grades three to four non-hematological events persisting over 48 hours. And then there's somewhat of a repetition comparing to the first two table, but literally we only have two chance of dose reduced, but no third dose reduction.

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Dose Modifications to Manage Severe Non-Neutropenic Toxicity

Severe Non-Neutropenic Toxicity		
Adverse Reaction	Occurrence	Dose Modification
Grade 4 nonhematologic toxicity of any duration, OR Any Grade 3 to 4 nausea, vomiting, or diarrhea due to treatment that is not controlled with antiemetics and antidiarrheal agents, OR Other Grade 3 to 4 nonhematologic toxicity persisting >48 hours despite optimal medical management, OR At time of scheduled treatment, Grade 3 to 4 nonneutropenic hematologic or non-hematologic toxicity, which delays dose by 2 or 3 weeks for recovery to ≤Grade 1	First	25% dose reduction
	Second	50% dose reduction
	Third	Discontinue treatment
In the event of Grade 3 to 4 nonneutropenic hematologic or nonhematologic toxicity, which does not recover to ≤Grade 1 within 3 weeks	First	Discontinue treatment

- Withhold or discontinue SG to manage adverse reactions as described here
- Do not reescalate the SG dose after a dose reduction for adverse reactions has been made
- Slow or interrupt the infusion rate if the patient develops an infusion-related reaction
- Permanently discontinue SG for life-threatening infusion-related reactions

SG, sacitricarbonylprolegrastin
TRODELVY (package insert). Foster City, CA: Eisai Research, Inc.; February 2023.
Please see Important Safety Information, including BOXED WARNING, on slides 4 and 12

-16 and full Prescribing Information accompanying this presentation.

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**Please click link below to continue to Part 2
Hypothetical Patient Case #1 and Questions**