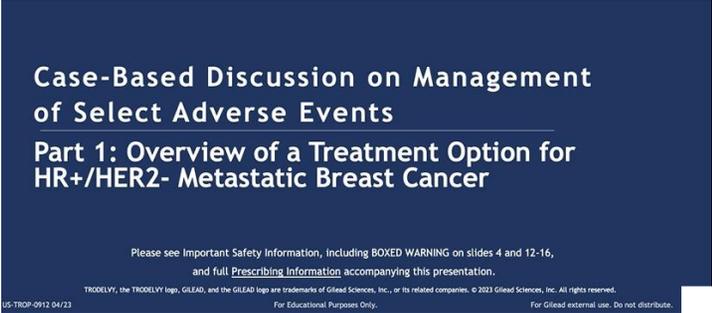


Video Transcript Part 1: Overview of Trodelvy	Slide #	Reference Material
<p><b>Linda:</b></p> <p>Welcome and thank you for joining us today for this case-based discussion on management of select adverse events for TRODELVY. I am pleased to introduce Dr. Yuan Yuan who will be presenting and leading today's 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>	<p>1</p>	 <p><b>Case-Based Discussion on Management of Select Adverse Events</b></p> <p><b>Part 1: Overview of a Treatment Option for HR+/HER2- Metastatic Breast Cancer</b></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><small>TRODELVY, the TRODELVY logo, GILEAD, and the GILEAD logo are trademarks of Gilead Sciences, Inc. or its related companies. © 2023 Gilead Sciences, Inc. All rights reserved.</small></p> <p><small>US-TROP-0912 04/23 For Educational Purposes Only. For Gilead external use. Do not distribute.</small></p>
<p><b>Dr. Yuan:</b></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 ComX and the content has been developed in accordance to FDA guidelines. So, I will try to abide by this information.</p>	<p>2</p>	<p><b>Disclosures</b></p> <ul style="list-style-type: none"> <li>• This is a promotional program sponsored by and provided on behalf of Gilead Sciences, Inc. The speaker has been compensated for this presentation.</li> <li>• Content in this program has been developed in accordance with FDA guidelines and is consistent with TRODELVY Prescribing Information.</li> </ul> <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><b>Dr. Yuan:</b> 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><b>Objectives</b></p> <ul style="list-style-type: none"> <li>Understand TRODELVY key efficacy, safety, and patient-reported outcomes data in patients with pretreated HR+ /HER2- mBC<sup>a</sup></li> </ul> <p><small><sup>a</sup>The term "pretreated HR+ /HER2-" is defined as after endocrine-based therapy and at least two additional systemic therapies in the metastatic setting. HR2, 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><b>Dr. Yuan:</b> 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><b>TRODELVY® Indications and Important Safety Information (1 of 6, continued on slide 12)</b></p> <p><b>INDICATIONS</b> 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"> <li>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</li> <li>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</li> </ul> <p><b>IMPORTANT SAFETY INFORMATION</b></p> <p><b>BOXED WARNING: NEUTROPENIA AND DIARRHEA</b></p> <ul style="list-style-type: none"> <li>Severe or life-threatening neutropenia may occur. Withhold TRODELVY for absolute neutrophil count below 1500/mm<sup>3</sup> 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.</li> <li>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.</li> </ul> <p><b>CONTRAINDICATIONS</b></p> <ul style="list-style-type: none"> <li>Severe hypersensitivity reaction to TRODELVY</li> </ul> <p><small>© 2023, sacituzumab govitecan-hzyl conjugate, Trodelvy, IHC, immunohistochemistry, ISH, in situ hybridization, TRODELVY (package insert), Foster City, CA: Silex 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>



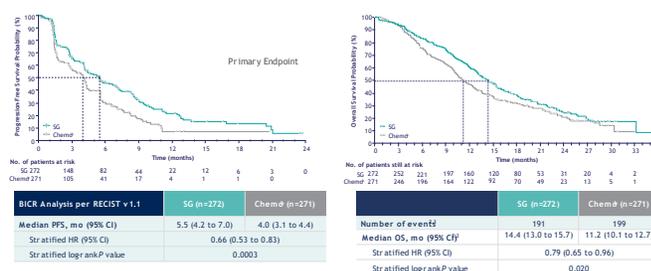


**Dr. Yuan:**

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**



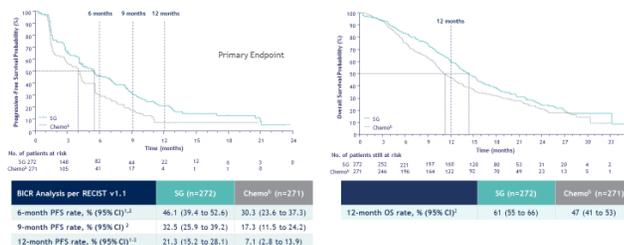
Median follow-up was 10.3 months for PFS and 12.5 months for OS.  
 \*Intention-to-treat population. †Single-agent chemotherapy.  
 BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; SG, sacituzumab govitecan.  
 1. Higazi H, et al. Clin Oncol. 2022;40(21):3188-97. 2. Higazi H, et al. Presented at European Society for Medical Oncology Congress, September 2022, Paris, France. Presentation 16827P (package insert).  
 3. Higazi H, et al. Clinical Oncology, Inc. February 2023.  
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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<sup>1-3,a</sup>**



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.

Median follow-up was 11.2 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. Higazi H, et al. Clin Oncol. 2022;40(21):3188-97. 2. Higazi H, et al. Presented at European Society for Medical Oncology Congress, September 9-13, 2022, Paris, France. Presentation 16827P (package insert).  
 3. Higazi H, et al. Clinical Oncology, Inc. February 2023.  
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<p>the results require cautious interpretation and could represent chance findings.</p>																										
<p><b>Dr. Yuan:</b></p> <p>Time to deterioration of global health status/QoL, fatigue and pain were prespecified secondary endpoints. SG statistically and significantly extended time to deterioration of global health status or QoL and fatigue. Limitation EORTC QLQ-C30 is not all-inclusive and does not include adequate assessment of additional expected treatment-related symptoms or overall side effects both from the patient's perspective. The results should be interpreted with caution due to the open-label design of the study and because time to deterioration may be confounded by events not related to disease or treatment. Need to cut from 10:20 to 10:49</p>	<p>9</p>	<p><b>EORTC QLQ-C30 Time to Deterioration Endpoints</b></p> <ul style="list-style-type: none"> <li>• Prespecified secondary endpoints in the statistical hierarchy included TTD in the global health status/QoL, pain, and fatigue domains of the EORTC QLQ-C30.<sup>1</sup></li> <li>• HRQL available patients included those in the TTT population who completed the EORTC QLQ-C30 at baseline and at least 1 post-baseline visit (SG: n/N=236/272; single-agent chemotherapy: n/N=210/271), with HRQL assessed at baseline, Day 1 of each treatment cycle from Cycle 2, end-of-treatment visit, and at the long-term follow-up visit.<sup>1</sup></li> <li>• Baseline demographics, clinical characteristics, and mean HRQL scores were comparable between treatment arms.<sup>1</sup></li> <li>• TTD was defined as the time from randomization to the first date a patient achieved <math>\geq 10</math>-point deterioration from baseline or died due to any cause, whichever occurred first.<sup>2,3</sup></li> </ul> <table border="1"> <thead> <tr> <th>TTD</th> <th>Patients SG/Single-Agent Chemotherapy, n/n</th> <th>SG Median TTD, mo (95% CI)</th> <th>Single-Agent Chemotherapy Median TTD, mo (95% CI)</th> <th>Stratified HR (95% CI)</th> <th>Stratified Log-Rank P Value</th> </tr> </thead> <tbody> <tr> <td>Global health status/QoL</td> <td>234/207</td> <td>4.3 (3.1 to 5.7)</td> <td>3.0 (2.2 to 3.9)</td> <td>0.75 (0.61 to 0.92)</td> <td>0.006<sup>a</sup></td> </tr> <tr> <td>Fatigue</td> <td>234/205</td> <td>2.2 (1.6 to 2.8)</td> <td>1.4 (1.1 to 1.9)</td> <td>0.73 (0.60 to 0.89)</td> <td>0.002<sup>a</sup></td> </tr> <tr> <td>Pain</td> <td>229/202</td> <td>3.8 (2.8 to 5.0)</td> <td>3.5 (2.8 to 5.0)</td> <td>0.92 (0.75 to 1.13)</td> <td>0.415, not statistically significant</td> </tr> </tbody> </table> <p><b>SG significantly extended TTD of global health status and fatigue vs single-agent chemotherapy</b></p> <p>Limitation: EORTC QLQ-C30 is not all-inclusive and does not include adequate assessment of additional expected treatment-related symptoms or overall side effect both from the patient perspective. The results should be interpreted with caution due to the open-label design of the study and because TTD may be confounded by events not related to disease or treatment.</p> <p><small>Footnote: a) not statistically significant. Interpretation as the time of analysis were based on the baseline assessment data. Patients without baseline or post-baseline patient-reported outcome assessments were excluded at the randomization date. b) not statistically significant. c) EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire. d) HRQL, health-related quality of life; ITT, intent-to-treat; QoL, quality of life; SG, sacituzumab; TTD, time to deterioration.</small></p> <p><small>1. Bagheri, et al. Presented at: European Society for Medical Oncology Congress, September 2022, Paris, France. Presentation 1532. Immunomedica Inc. Published December 21, 2018. Abstract # 2022. <a href="https://eprints.oxfordscholarship.com/handle/10139/52532/2/1/oxfordscholarship-com-2022-09-21-0902.pdf">https://eprints.oxfordscholarship.com/handle/10139/52532/2/1/oxfordscholarship-com-2022-09-21-0902.pdf</a></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>	TTD	Patients SG/Single-Agent Chemotherapy, n/n	SG Median TTD, mo (95% CI)	Single-Agent Chemotherapy Median TTD, mo (95% CI)	Stratified HR (95% CI)	Stratified Log-Rank P Value	Global health status/QoL	234/207	4.3 (3.1 to 5.7)	3.0 (2.2 to 3.9)	0.75 (0.61 to 0.92)	0.006 <sup>a</sup>	Fatigue	234/205	2.2 (1.6 to 2.8)	1.4 (1.1 to 1.9)	0.73 (0.60 to 0.89)	0.002 <sup>a</sup>	Pain	229/202	3.8 (2.8 to 5.0)	3.5 (2.8 to 5.0)	0.92 (0.75 to 1.13)	0.415, not statistically significant
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<p><b>Dr. Yuan:</b></p> <p>So important adverse events which are reported in the TROPiCS-02 study. So there are some, you can find information in the package insert, but in total, severe adverse events occurred in 28% of the patients. Which includes severe diarrhea happened in 5%, febrile neutropenia, 4%, neutropenia 3%. Also including other, 2% each of abdominal pain, colitis, neutropenic colitis, et cetera. Fatal activity of adverse reaction occurred in 2% of the patient who received sacituzumab, including arrhythmia, nervous disorder and pulmonary embolism. Permanent discontinuation rate is relatively low, in 6% of the patients. And again was similar to the other causes we discussed earlier. The causes of the discontinuation were highlighted here in the third and fourth bullet points. And notice that in TROPiCS-02 there was no ILD (interstitial lung disease). That's an important distinction with the other FDA-approved drug antibody conjugates. And note that in this study, 54% of the patient received supportive G-CSF.</p>	<p>10</p>	<p><b>Adverse Reactions Reported in Patients in the TROPiCS Study</b></p> <ul style="list-style-type: none"> <li>• Serious adverse reactions occurred in 28% of patients.<sup>1</sup></li> <li>• Serious adverse reactions in &gt;1% of patients receiving SG included diarrhea (5%), febrile neutropenia (4%), neutropenia (3%), abdominal pain, colitis, neutropenic colitis, pneumonia, and vomiting (each 2%).<sup>1</sup></li> <li>• Fatal adverse reactions occurred in 2% of patients who received SG, including arrhythmia, COVID-19, nervous system disorder, pulmonary embolism, and septic shock (each 0.4%).<sup>1</sup></li> <li>• SG was permanently discontinued for adverse reactions in 6% of patients. The most frequent (<math>\geq 0.5\%</math>) adverse reactions leading to permanent discontinuation in patients who received SG were asthenia, general physical health deterioration, and neutropenia (each 0.7%).<sup>1</sup></li> <li>• Adverse reactions leading to treatment interruptions of SG occurred in 66% of patients. The most frequent (<math>\geq 5\%</math>) adverse reaction leading to treatment interruption was neutropenia (50%).<sup>1</sup></li> <li>• Adverse reactions leading to a dose reduction of SG occurred in 33% of patients. The most frequent (<math>\geq 5\%</math>) adverse reactions leading to dose reduction were neutropenia (16%) and diarrhea (8%).<sup>1</sup></li> <li>• G-CSF was used in 54% of patients who received SG.<sup>1</sup></li> <li>• In TROPiCS-02, there were no events of ILD with SG.<sup>2</sup></li> </ul> <p><small>G-CSF, granulocyte colony-stimulating factor; ILD, interstitial lung disease; SG, sacituzumab.</small></p> <p><small>1. TROPiCS-02 package insert. Foster City, CA: Genentech, Inc.; February 2023. Bagheri, et al. Sacituzumab: a novel human epidermal growth factor receptor 2 inhibitor for the treatment of metastatic breast cancer. J Clin Oncol. 2022;40(24):3483-91.</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>																								

**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 <sup>a</sup> (n=247)	
	All grades, %	Grade 3 to 4, %	All grades, %	Grade 3 to 4, %
<b>Gastrointestinal disorders</b>				
Diarrhea	62	10	23	1
Nausea	39	1	35	3
Constipation	34	1	25	0
Vomiting	23	1	16	2
Abdominal pain	20	0	14	0
Dyspepsia <sup>b</sup>	11	0	6	0
<b>General disorders and administration site conditions</b>				
Fatigue	60	8	51	4
<b>Metabolism and nutrition disorders</b>				
Decreased appetite	21	2	21	0
Hypokalemia	10	2	4	0
<b>Musculoskeletal and connective tissue disorders</b>				
Arthralgia	15	0	12	0
<b>Nervous system disorders</b>				
Headache	16	1	15	1
<b>Respiratory, thoracic, and mediastinal disorders</b>				
Dyspnea <sup>c</sup>	20	0	17	0
Cough	12	0	7	0
<b>Skin and subcutaneous tissue disorders</b>				
Alopecia	48	0	19	0
Pruritus	12	0	2	0

<sup>a</sup> 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 (22% for SG vs 27% for single-agent chemotherapy).

<sup>b</sup> Graded per NCI CTCAE v5.0. Single-agent chemotherapy includes one of the following single agents: epirubicin (n=130), vinorelbine (n=43), gemtuzumab (n=56), or capecitabine (n=112).  
<sup>c</sup> CTCAE Common Terminology Criteria for Adverse Events; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; metastatic breast cancer; NCI, National Cancer Institute; US, United States.

TRODELVY (package insert); Foster City, CA: Gilead Sciences, Inc.; February 2023.  
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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/ $\mu$ mol/L on Day 1 of any cycle or neutrophil count below 1000/ $\mu$ mol/L 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 (eg, fluid and electrolyte substitution) may also be employed as clinically indicated. Patients who exhibit an excessive cholinergic response to treatment can receive appropriate premedication (eg, atropine) for subsequent treatments.

G-CSF, granulocyte colony-stimulating factor; 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. 12

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<p><b>Dr. Yuan:</b></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><b>TRODELVY Important Safety Information (3 of 6)</b></p> <p>WARNINGS AND PRECAUTIONS (cont'd)</p> <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p><b>Hypersensitivity and Infusion-Related Reactions</b></p> <ul style="list-style-type: none"> <li>• 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.</li> </ul> </div> <div style="width: 45%;"> <p><b>Nausea and Vomiting</b></p> <ul style="list-style-type: none"> <li>• 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.</li> </ul> </div> </div> <p><small>TRODELVY (package insert), Foster City, CA: GlaxoSmithKline, Inc.; February 2023. Please see Important Safety Information, including BOXED WARNING, on slides 4 and 12. -16 and full <a href="#"> prescribing information</a>, accompanying this presentation. 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><b>Dr. Yuan:</b> 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><b>TRODELVY Important Safety Information (4 of 6)</b></p> <p><b>WARNINGS AND PRECAUTIONS (cont'd)</b></p> <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p><b>Increased Risk of Adverse Reactions in Patients with Reduced UGT1A1 Activity</b></p> <ul style="list-style-type: none"> <li>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.</li> </ul> </div> <div style="width: 45%;"> <p><b>Embryo-Fetal Toxicity</b></p> <ul style="list-style-type: none"> <li>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.</li> </ul> </div> </div> <p><small>TRODELVY (pack-ages insert), Foster City, CA: Genentech, Inc.; February 2023. Please see Important Safety Information, including BOXED WARNING, on slides 4 and 12. -16 and full <a href="#">proceedings information</a>, accompanying this presentation.</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><b>Dr. Yuan:</b> 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>	<p>15</p>	<p><b>TRODELVY Important Safety Information (5 of 6)</b></p> <p><b>ADVERSE REACTIONS</b></p> <ul style="list-style-type: none"> <li>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%).</li> <li>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) (&gt;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.</li> <li>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) (&gt;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.</li> </ul> <p><small>TRODELVY (enfortumab vedin) Injection, 150 mg/15 mL, 300 mg/30 mL, 450 mg/45 mL, 600 mg/60 mL, 750 mg/75 mL, 900 mg/90 mL, 1050 mg/105 mL, 1200 mg/120 mL, 1350 mg/135 mL, 1500 mg/150 mL, 1650 mg/165 mL, 1800 mg/180 mL, 1950 mg/195 mL, 2100 mg/210 mL, 2250 mg/225 mL, 2400 mg/240 mL, 2550 mg/255 mL, 2700 mg/270 mL, 2850 mg/285 mL, 3000 mg/300 mL, 3150 mg/315 mL, 3300 mg/330 mL, 3450 mg/345 mL, 3600 mg/360 mL, 3750 mg/375 mL, 3900 mg/390 mL, 4050 mg/405 mL, 4200 mg/420 mL, 4350 mg/435 mL, 4500 mg/450 mL, 4650 mg/465 mL, 4800 mg/480 mL, 4950 mg/495 mL, 5100 mg/510 mL, 5250 mg/525 mL, 5400 mg/540 mL, 5550 mg/555 mL, 5700 mg/570 mL, 5850 mg/585 mL, 6000 mg/600 mL, 6150 mg/615 mL, 6300 mg/630 mL, 6450 mg/645 mL, 6600 mg/660 mL, 6750 mg/675 mL, 6900 mg/690 mL, 7050 mg/705 mL, 7200 mg/720 mL, 7350 mg/735 mL, 7500 mg/750 mL, 7650 mg/765 mL, 7800 mg/780 mL, 7950 mg/795 mL, 8100 mg/810 mL, 8250 mg/825 mL, 8400 mg/840 mL, 8550 mg/855 mL, 8700 mg/870 mL, 8850 mg/885 mL, 9000 mg/900 mL, 9150 mg/915 mL, 9300 mg/930 mL, 9450 mg/945 mL, 9600 mg/960 mL, 9750 mg/975 mL, 9900 mg/990 mL, 10050 mg/1005 mL, 10200 mg/1020 mL, 10350 mg/1035 mL, 10500 mg/1050 mL, 10650 mg/1065 mL, 10800 mg/1080 mL, 10950 mg/1095 mL, 11100 mg/1110 mL, 11250 mg/1125 mL, 11400 mg/1140 mL, 11550 mg/1155 mL, 11700 mg/1170 mL, 11850 mg/1185 mL, 12000 mg/1200 mL, 12150 mg/1215 mL, 12300 mg/1230 mL, 12450 mg/1245 mL, 12600 mg/1260 mL, 12750 mg/1275 mL, 12900 mg/1290 mL, 13050 mg/1305 mL, 13200 mg/1320 mL, 13350 mg/1335 mL, 13500 mg/1350 mL, 13650 mg/1365 mL, 13800 mg/1380 mL, 13950 mg/1395 mL, 14100 mg/1410 mL, 14250 mg/1425 mL, 14400 mg/1440 mL, 14550 mg/1455 mL, 14700 mg/1470 mL, 14850 mg/1485 mL, 15000 mg/1500 mL, 15150 mg/1515 mL, 15300 mg/1530 mL, 15450 mg/1545 mL, 15600 mg/1560 mL, 15750 mg/1575 mL, 15900 mg/1590 mL, 16050 mg/1605 mL, 16200 mg/1620 mL, 16350 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<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><b>Dr. Yuan:</b></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><b>TRODELVY Important Safety Information (6 of 6)</b></p> <p><b>DRUG INTERACTIONS</b></p> <ul style="list-style-type: none"> <li>• <b>UGT1A1 Inhibitors:</b>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.</li> <li>• <b>UGT1A1 Inducers:</b>Exposure to SN38 may be reduced in patients concomitantly receiving UGT1A1 enzyme inducers. Avoid administering UGT1A1 inducers with TRODELVY.</li> </ul> <p>Please see accompanying full <a href="#">Prescribing Information</a>, including <b>BOXED WARNING</b>.</p> <p><small>TRODELVY (sargamostim), Foster City, CA: Gilead Sciences, Inc.; February 2023. Please see Important Safety Information, including <b>BOXED WARNING</b>, on slides 4 and 12. -16 and full <a href="#">Prescribing Information</a>, accompanying 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 ≤Grade 1	First	25% dose reduction and administer G-CSF
	Second	50% dose reduction and administer G-CSF
	Third	Discontinue treatment and administer G-CSF
At time of scheduled treatment, Grade 3 to 4 neutropenia, which delays dosing by 3 weeks for recovery to ≤Grade 1	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 infusion-related reaction
- Permanently discontinue SG for life-threatening infusion-related reactions

G-CSF, granulocyte colony-stimulating factor; SG, saracatinib/sgnibines. 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. 11

**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
	Third	Discontinue treatment
In the event of Grade 3 to 4 diarrhea, which does not recover to Grade ≤1 within 3 weeks	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 (eg, fluid and electrolyte substitution) may also be employed as clinically indicated
- Patients who exhibit an excessive cholinergic response to treatment with SG (eg, abdominal cramping, diarrhea, salivation, etc.) can receive appropriate premedication (eg, atropine) for subsequent treatments

SG, saracatinib/sgnibines. 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. 11

**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 neutropenic hematologic or non-hematologic toxicity, which delays dose by 2 or 3 weeks for recovery to ≤Grade 1	First	25% dose reduction
In the event of Grade 3 to 4 neutropenic hematologic or nonhematologic toxicity, which does not recover to ≤Grade 1 within 3 weeks	Second	50% dose reduction
	Third	Discontinue treatment
	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, sacitricumab/gemtuzumab  
 TRODELVY (package insert), Foster City, CA: Genentech, Inc.; February 2023.  
 Please see important safety information, including BOXED WARNING, on slides 4 and 12. -16 and full Prescribing Information accompanying this presentation. 11

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