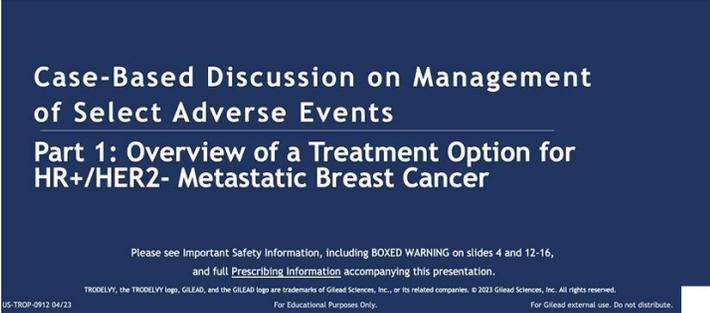


Video Transcript Part 1: Overview of Trodelvy	Slide #	Reference Material
<p>Linda:</p> <p>Welcome and thank you for joining us today for this case-based discussion on management of select adverse events for TRODELVY. I am pleased to introduce Dr. Yuan Yuan who will be presenting and leading today's discussion. 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>	<p>1</p>	 <p>Case-Based Discussion on Management of Select Adverse Events</p> <p>Part 1: Overview of a Treatment Option for HR+/HER2- Metastatic Breast Cancer</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>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 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>Disclosure</p> <ul style="list-style-type: none"> 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>

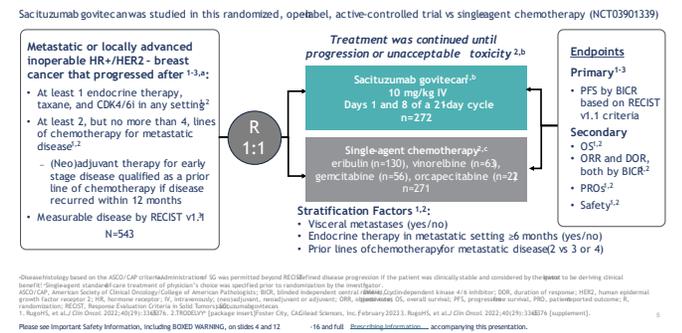
<p>Dr. Yuan: So today we would like to take some time to understand TRODELVY key efficacy, safety and patient reported outcome data in patients with pretreated hormone receptor positive, HER2-metastatic breast cancer.</p>	<p>3</p>	<p>Objectives</p> <ul style="list-style-type: none"> Understand TRODELVY 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-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>Dr. Yuan: 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 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>© 2023, sacituzumab govitecan-hzyl conjugate. Sacituzumab govitecan-hzyl is a registered trademark of AstraZeneca. 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>

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

5

TROPiCS-02: A Phase 3 Study of SG in HR+/HER2-locally Advanced Inoperable or Metastatic Breast Cancer²



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.

6

Demographics and Baseline Characteristics for TROPiCS-02^{1,2}

	SG (n=272)	Single-Agent Chemotherapy (n=271)		SG (n=272)	Single-Agent Chemotherapy (n=271)
Female, n (%)	270 (99)	268 (99)	Prior chemotherapy in (neo)adjuvant setting, n (%)	173 (64)	184 (68)
Median age, y (range)	57 (29-86)	55 (27-78)	Prior endocrine therapy use in the metastatic setting ≥6 mo, n (%)	235 (86)	234 (86)
<65 y, n (%)	199 (73)	204 (75)	Prior CDK4/6 inhibitor use, n (%)		
≥65 y, n (%)	73 (27)	67 (25)	<12 months	161 (59)	166 (61)
Race or ethnic group, n (%)			>12 months	106 (39)	102 (38)
White	184 (68)	178 (66)	Unknown	5 (2)	3 (1)
Black	8 (3)	13 (5)	Median prior chemotherapy regimens in the metastatic setting, n (range)	3 (0-8)	3 (1-5)
Asian	11 (4)	5 (2)	0	1 (<1)	0
Other ^a /not reported ^b	69 (25)	75 (28)	1	8 (3)	2 (1)
ECOG PS, n (%)			2	104 (38)	118 (43)
0	116 (43)	126 (46)	≥3	159 (58)	151 (56)
1	156 (57)	145 (54)	Median prior chemotherapy regimens, n (range)	4 (1-9)	4 (2-7)
Visceral metastases at baseline, n (%)	259 (95)	258 (95)	Median prior anticancer regimens, n (range)	7 (3-17)	7 (3-16)
Liver metastases, n (%)	229 (84)	237 (87)			
De novo metastatic breast cancer, n (%)	78 (29)	60 (22)			
Median time from initial metastatic diagnosis to randomization, mo (range)	48.5 (1.2-243.8)	46.6 (3.0-248.8)			

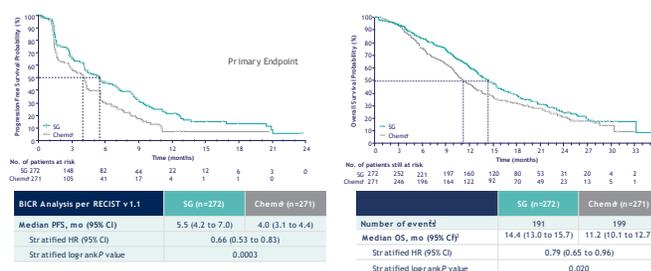
^aIncludes American Indian or Alaska Native, Native Hawaiian or Pacific Islander. ^bNot reported indicates local regulators did not allow collection of race or ethnicity information. ^cIncludes target biopsy (range) from metastases per RECIST v1.1. ^dBy local investigator report. ^eNumber of prior therapies was miscounted at screening for some patients. ^f8 patients received prior chemotherapy in the metastatic setting outside the approved range for inclusion criteria and were included in the relevant population. ^gAnticancer regimens refer to any treatment regimen that was used to treat breast cancer in any setting and includes endocrine therapy and metformin. ^hCDK4/6, cyclin-dependent kinase 4/6; ECOG PS, Eastern Cooperative Oncology Group performance status; (neo)adjuvant, neoadjuvant; RECIST, Response Evaluation Criteria in Solid Tumors; SG, sacituzumab. ¹ Rugier, et al. J Clin Oncol. 2022;40(29):3348-76. ² Rugier, et al. Presented at: European Society for Medical Oncology Congress, September 2022, Paris, France. Presentation LB47. Please see Important Safety Information, including BOXED WARNING, on slides 4 and 12. ³ -16 and Full [Prescribing Information](#), accompanying this presentation.

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.

7

SG Demonstrated a Statistically Significant Improvement in PFS and OS



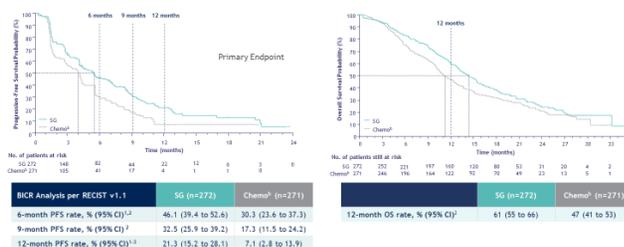
Median follow-up was 10.3 months for PFS and 12.5 months for OS.
 *Intention-to-treat population. ¹Single-agent chemotherapy.
 BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; SG, sacituzumab govitecan.
 1. Higazi H, et al. Clin Oncol. 2022;40(2):138-147. 2. Higazi H, et al. Presented at European Society for Medical Oncology Congress, September 2022, Paris, France. Presentation LB2702020P (package insert).
 3. Higazi H, et al. Clinical Oncology, Inc. February 2023.
 Please see important safety information, including BOXED WARNING, on slides 4 and 12. -16 and full Prescribing information accompanying this presentation.

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,

8

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.
 Median follow-up was 10.3 months for PFS and 12.5 months for OS.
 *Intention-to-treat population. ¹Single-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(2):138-147. 2. Higazi H, et al. Presented at European Society for Medical Oncology Congress, September 11-15, 2022, Paris, France. Presentation LB2702020P (package insert).
 3. Higazi H, et al. Clinical Oncology, Inc. February 2023.
 Please see important safety information, including BOXED WARNING, on slides 4 and 12-16 and full Prescribing information accompanying this presentation.

<p>the results require cautious interpretation and could represent chance findings.</p>																										
<p>Dr. Yuan:</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>EORTC QLQ-C30 Time to Deterioration Endpoints</p> <ul style="list-style-type: none"> • Prespecified secondary endpoints in the statistical hierarchy included TTD in the global health status/QoL, pain, and fatigue domains of the EORTC QLQ-C30.¹ • 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.¹ • Baseline demographics, clinical characteristics, and mean HRQL scores were comparable between treatment arms.¹ • TTD was defined as the time from randomization to the first date a patient achieved ≥ 10-point deterioration from baseline or died due to any cause, whichever occurred first.^{2,3} <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^a</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^a</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>SG significantly extended TTD of global health status and fatigue vs single-agent chemotherapy</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. Accession # 2022. https://eprints.oxfordjournals.org/doi/full/10.1093/annonc/ndac002.html. The present. 2022;33:3030-3031.</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 ^a	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 ^a	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
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 ^a																					
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 ^a																					
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																					
<p>Dr. Yuan:</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>Adverse Reactions Reported in Patients in the TROPiCS Study</p> <ul style="list-style-type: none"> • Serious adverse reactions occurred in 28% of patients.¹ • Serious adverse reactions in >1% of patients receiving SG included diarrhea (5%), febrile neutropenia (4%), neutropenia (3%), abdominal pain, colitis, neutropenic colitis, pneumonia, and vomiting (each 2%).¹ • 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%).¹ • SG was permanently discontinued for adverse reactions in 6% of patients. The most frequent ($\geq 0.5\%$) adverse reactions leading to permanent discontinuation in patients who received SG were asthenia, general physical health deterioration, and neutropenia (each 0.7%).¹ • Adverse reactions leading to treatment interruptions of SG occurred in 66% of patients. The most frequent ($\geq 5\%$) adverse reaction leading to treatment interruption was neutropenia (50%).¹ • Adverse reactions leading to a dose reduction of SG occurred in 33% of patients. The most frequent ($\geq 5\%$) adverse reactions leading to dose reduction were neutropenia (16%) and diarrhea (8%).¹ • G-CSF was used in 54% of patients who received SG.¹ • In TROPiCS-02, there were no events of ILD with SG.² <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 antibody conjugate for the treatment of metastatic breast cancer. J Clin Oncol. 2022;40(21):3883-3891.</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.

11

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

Adverse Reactions Reported in ≥10% of Patients With HR+/HER2- in TROPiCS-02

Adverse reaction	SG (n=248)		Single-Agent Chemotherapy ^a (n=247)	
	All grades, %	Grade 3 to 4, %	All grades, %	Grade 3 to 4, %
Gastrointestinal disorders				
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 ^b	11	0	6	0
General disorders and administration site conditions				
Fatigue	60	8	51	4
Metabolism 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 (22% for SG vs 27% for single-agent chemotherapy).

b. 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=102).

c. CTCAE Common Terminology Criteria for Adverse Events; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; metastatic breast cancer; NCI, National Cancer Institute; @HumanaGenomics TRODELVY [package insert]; Foster City, CA: GlaxoSmithKline; Feb 2023.

Please see Important Safety Information, including BOXED WARNING, on slides 4 and 12. -16 and full Prescribing Information accompanying this presentation.

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

12

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/ μ mol/L on Day 1 of any cycle or neutrophil count below 1000/ μ 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: GlaxoSmithKline, Inc.; February 2023. Please see Important Safety Information, including BOXED WARNING, on slides 4 and 12. -16 and full Prescribing Information accompanying this presentation.

<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 style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <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 style="width: 45%;"> <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: GlaxoSmithKline, Inc.; February 2023. Please see Important Safety Information, including BOXED WARNING, on slides 4 and 12. -16 and full prescribing information, 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>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 style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <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 style="width: 45%;"> <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 (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 proceedings information, accompanying this presentation.</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 (sargamostim), 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.</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.

17

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/sgn-151
 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.

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.

18

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/sgn-151
 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.

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.

19

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