

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Trastuzumab-Deruxtecan (Enhertu[®])

Daiichi Sankyo Deutschland GmbH

Modul 4 B (Anhang 4-G)

*Behandlung von erwachsenen Patienten mit inoperablem oder
metastasiertem HER2-positivem Brustkrebs, die bereits
mindestens zwei gegen HER2 gerichtete Vorbehandlungen
erhalten haben*

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2. Datenschnitt DESTINY-Breast01 Studie vom 01. August 2019

Die Operationalisierung der einzelnen Endpunkte und Analysen ist dem Abschnitt 4.3.2.3.3 (Modul 4 A) zu entnehmen.

Gesamtüberleben (OS) – weitere Untersuchungen

Tabelle 1: Ergebnisse für den Endpunkt Gesamtüberleben (OS) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01	Trastuzumab Deruxtecan N=184 (ITT-Population)	
	n ^a /N (%)	Median (Monate) [95 %-KI]
Gesamtüberleben (OS)	25/184 (13,6)	NE [NE; NE]
	Kaplan-Meier-Schätzer [95 % KI]	
zu Monat 6	0,94 [0,89; 0,97]	
zu Monat 12	0,86 [0,80; 0,91]	
Zu Monat 24	NE [NE; NE]	
a: Ereignis bezieht sich auf Tod jeglicher Ursache.		
2. Datenschnitt: 01. August 2019		
Alle verwendeten Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

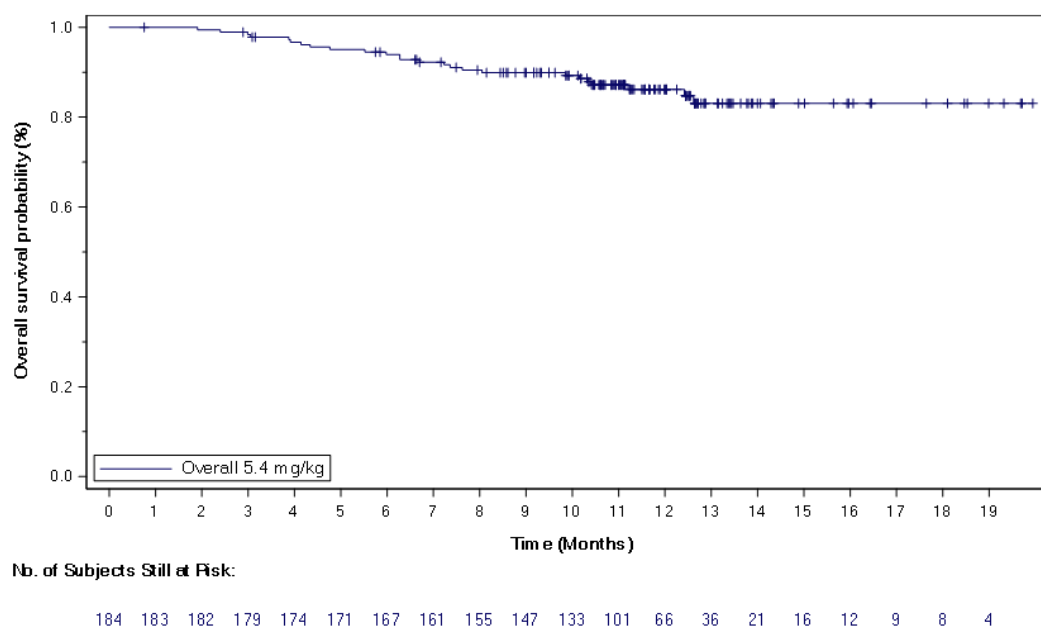


Abbildung 1: Kaplan-Meier-Plot für den Endpunkt OS aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel (ITT-Population, 2. Datenschnitt: 01. August 2019)

Progressionsfreies Überleben (PFS) – weitere Untersuchungen

Tabelle 2: Ergebnisse für den Endpunkt Progressionsfreies Überleben (PFS) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01	Trastuzumab Deruxtecan N=184 (ITT-Population)	
	n ^a /N (%)	Median (Monate) [95 %-KI]
Progressionsfreies Überleben (PFS)	58/184 (31,5)	16,4 [12,7; NE]
	Punktschätzer [95 % KI]	
zu Monat 6	0,81 [0,74; 0,86]	
zu Monat 12	0,65 [0,56; 0,72]	
Zu Monat 24	NE [NE; NE]	
a: Patienten mit Krankheitsprogression oder Tod jeglicher Ursache. 2. Datenschnitt: 01. August 2019 Alle verwendeten Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

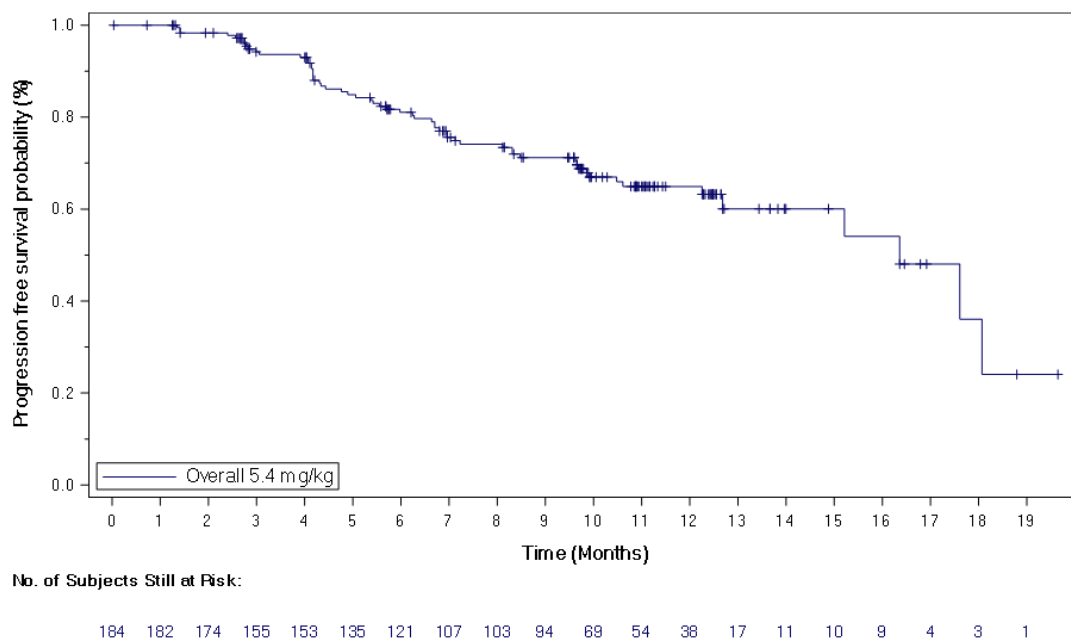


Abbildung 2: Kaplan-Meier-Plot für den Endpunkt PFS aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel (ITT-Population, 2. Datenschnitt: 01. August 2019).

Tumoransprechen – weitere Untersuchungen

Gesamtansprechrates (ORR) – weitere Untersuchungen

Tabelle 3: Bestes Gesamtansprechen aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01	Trastuzumab Deruxtecan N=184 (ITT-Population)	
	n/N (%)	95 %-KI
Gesamtansprechrates (ORR)	112 (60,9)	[53,4; 68,0]
	Beurteilung durch ICR, n (%)	
Vollständiges Ansprechen (CR)	11 (6,0)	
Partielles Ansprechen (PR)	101 (54,9)	
Stabile Erkrankung (SD)	67 (36,4)	
Krankheitsprogression (PD)	3 (1,6)	
nicht auswertbar (NE)	2 (1,1)	
2. Datenschnitt: 01. August 2019		
Alle verwendeten Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

Beste prozentuale Änderung des Tumordurchmessers (BPC) – weitere Untersuchungen

Tabelle 4: Ergebnisse für den Endpunkt Beste prozentuale Änderung des Tumordurchmessers (BPC) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01	Trastuzumab Deruxtecan N=184 (ITT-Population)	
	Mean (SD)	Median (Min; Max) [95 % KI]
Beste prozentuale Änderung des Tumordurchmessers (BPC) (n=168), Bewertung durch ICR	-53,1 % (30,12)	-55,5 % (-100,0; 22,0) [-62,0; -47,0]
2. Datenschnitt: 01. August 2019 Alle verwendeten Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

Rate der Krankheitskontrolle (DCR) – weitere Untersuchungen

Tabelle 5: Ergebnisse für den Endpunkt Rate der Krankheitskontrolle (DCR) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01	Trastuzumab Deruxtecan N=184 (ITT-Population)	
	n ^a /N	% [95 %-KI]
Rate der Krankheitskontrolle (DCR) Beurteilung durch ICR	179/184	97,3 [93,8; 99,1]
2. Datenschnitt: 01. August 2019 a: Patienten mit einem besten Gesamtansprechen der Kategorie CR, PR oder SD. Alle verwendeten Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

Zeit bis zum Ansprechen (TTR) – weitere Untersuchungen

Tabelle 6: Ergebnisse für den Endpunkt Zeit bis zum Ansprechen (TTR) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01	Trastuzumab Deruxtecan N=184 (ITT-Population)	
	n ^a /N (%)	Median (Monate) [95 %-KI]
Zeit bis zum Ansprechen (TTR) Beurteilung durch ICR	112/184 (60,9)	1,6 [1,4; 2,6]
2. Datenschnitt: 01. August 2019 a: Patienten mit einem besten Gesamtansprechen der Kategorie CR oder PR. Alle verwendeten Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

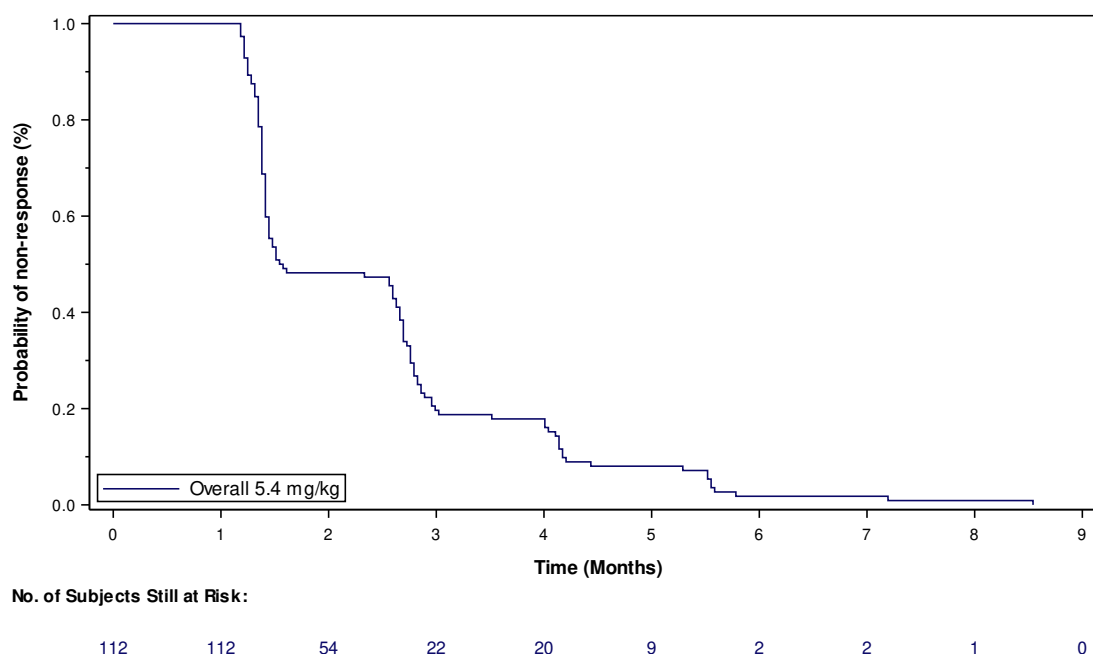


Abbildung 3: Kaplan-Meier-Plot für den Endpunkt TTR aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel (ITT-Population, 2. Datenschnitt: 01. August 2019).

Dauer des Ansprechens (DoR) – weitere Untersuchungen

Tabelle 7: Ergebnisse für den Endpunkt Dauer des Ansprechens (DoR) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01	Trastuzumab Deruxtecan N=184 (ITT-Population)	
	n ^a /N (%)	Median (Monate) [95 %-KI]
Dauer des Ansprechens (DoR) Beurteilung durch ICR	112/184 (60,9)	14,8 [13,8; 16,9]
	Kaplan-Meier-Schätzer % [95 % KI]	
zu Monat 6	0,81 [0,72; 0,88]	
zu Monat 12	0,70 [0,58; 0,79]	
Zu Monat 24	NE [NE; NE]	
2. Datenschnitt: 01. August 2019		
a: Patienten mit einem besten Gesamtansprechen der Kategorie CR oder PR.		
Alle verwendeten Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

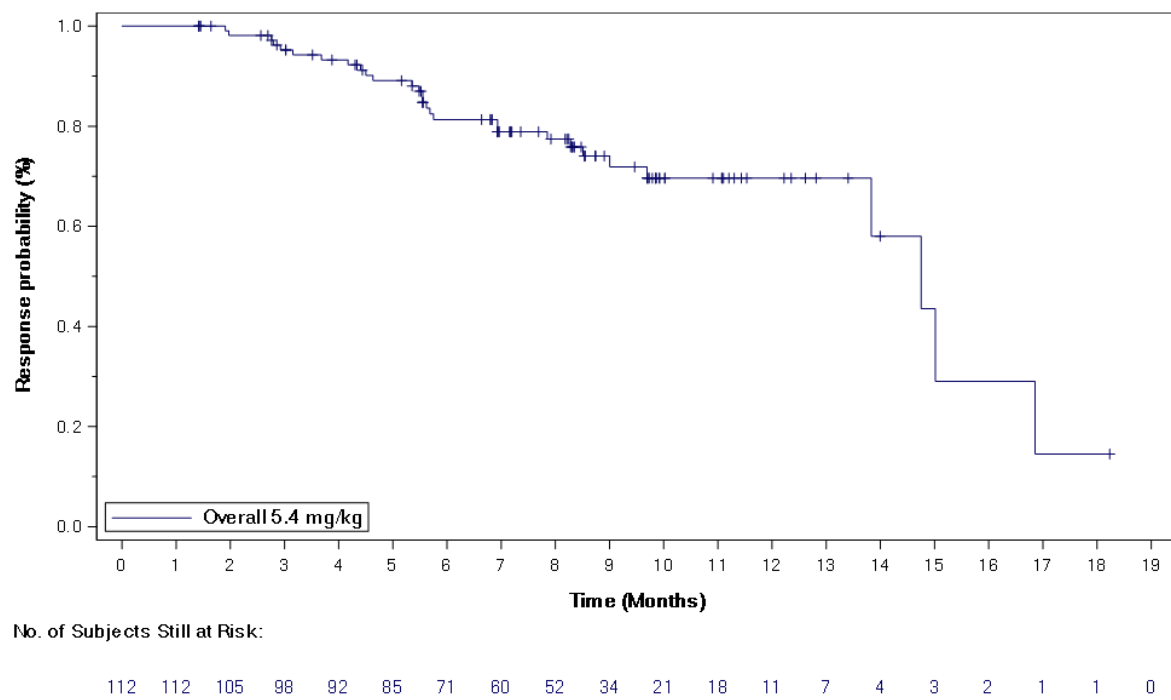


Abbildung 4: Kaplan-Meier-Plot für den Endpunkt DoR aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel (ITT-Population, 2. Datenschnitt: 01. August 2019)

Sicherheit – weitere Untersuchungen

Gesamtrate UE

Tabelle 8: Ergebnisse für die Endpunkte der UE Gesamtraten aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY- Breast01	Trastuzumab Deruxtecan N=184 (Safety Population), n (%) [95 %-KI]									
	Zyklus 1 N = 184	Zyklus 2 N = 181	Zyklus 3 N = 174	Zyklus 4 N = 169	Zyklus 5 N = 155	Zyklus 6 N = 152	Zyklus 7 N = 145	Zyklus ≥ 8 bis 18 N = 138	Zyklus ≥ 18 N = 35	Insgesamt N = 184
Gesamtrate UE	173 (94,0) [89,6; 97,0]	133 (72,3) [65,2; 78,6]	115 (62,5) [55,1; 69,5]	108 (58,7) [51,2; 65,9]	93 (50,5) [43,1; 58,0]	83 (45,1) [37,8; 52,6]	88 (47,8) [40,4; 55,3]	124 (67,4) [60,1; 74,1]	19 (10,3) [6,3; 15,7]	183 (99,5) [97,0; 100,0]
Gesamtrate SUE	8 (4,3) [1,9; 8,4]	9 (4,9) [2,3; 9,1]	6 (3,3) [1,2; 7,0]	7 (3,8) [1,5; 7,7]	5 (2,7) [0,9; 6,2]	2 (1,1) [0,1; 3,9]	4 (2,2) [0,6; 5,5]	16 (8,7) [5,1; 13,7]	0 (0,0) [0,0; 2,0]	42 (22,8) [17,0; 29,6]
Gesamtrate UE mit CTCAE- Grad <3	171 (92,9) [88,2; 96,2]	130 (70,7) [63,5; 77,1]	114 (62,0) [54,5; 69,0]	102 (55,4) [47,9; 62,7]	91 (49,5) [42,0; 56,9]	79 (42,9) [35,7; 50,4]	85 (46,2) [38,8; 53,7]	120 (65,2) [57,9; 72,1]	18 (9,8) [5,9; 15,0]	183 (99,5) [97,0; 100,0]
Gesamtrate UE mit CTCAE- Grad ≥ 3	38 (20,7) [15,0; 27,2]	27 (14,7) [9,9; 20,6]	14 (7,6) [4,2; 12,4]	18 (9,8) [5,9; 15,0]	10 (5,4) [2,6; 9,8]	8 (4,3) [1,9; 8,4]	14 (7,6) [4,2; 12,4]	41 (22,3) [16,5; 29,0]	4 (2,2) [0,6; 5,5]	105 (57,1) [49,6; 64,3]
Gesamtrate UE, die zum Therapieabbruch führten	3 (1,6) [0,3; 4,7]	2 (1,1) [0,1; 3,9]	1 (0,5) [0,0; 3,0]	1 (0,5) [0,0; 3,0]	0 (0,0) [0,0; 2,0]	3 (1,6) [0,3; 4,7]	3 (1,6) [0,3; 4,7]	13 (7,1) [3,8; 11,8]	2 (1,1) [0,1; 3,9]	28 (15,2) [10,4; 21,2]
Gesamtrate UE, die zum Tod führten	0 (0,0) [0,0; 2,0]	0 (0,0) [0,0; 2,0]	2 (1,1) [0,1; 3,9]	1 (0,5) [0,0; 3,0]	2 (1,1) [0,1; 3,9]	0 (0,0) [0,0; 2,0]	1 (0,5) [0,0; 3,0]	2 (1,1) [0,1; 3,9]	0 (0,0) [0,0; 2,0]	8 (4,3) [1,9; 8,4]
2. Datenschnitt: 01. August 2019										
Alle verwendeten Abkürzungen werden im Abkürzungsverzeichnis erläutert.										

UE nach SOC und PT, die bei mindestens 10 Patienten und mindestens 1 % der Patienten aufgetreten sind

Tabelle 9: Ergebnisse für den Endpunkt UE nach SOC und PT (≥ 10 Patienten und ≥ 1 % der Patienten) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01 SOC PT	Trastuzumab Deruxtecan	
	n/N	% [95 %-KI]
Erkrankungen des Gastrointestinaltrakts	171/184	92,9 [88,2; 96,2]
<i>Übelkeit</i>	143/184	77,7 [71,0; 83,5]
<i>Erbrechen</i>	84/184	45,7 [38,3; 53,1]
<i>Obstipation</i>	66/184	35,9 [28,9; 43,3]
<i>Diarrhö</i>	54/184	29,3 [22,9; 36,5]
<i>Dyspepsie</i>	26/184	14,1 [9,4; 20,0]
<i>Stomatitis</i>	25/184	13,6 [9,0; 19,4]
<i>Abdominalschmerz</i>	22/184	12,0 [7,6; 17,5]
<i>Gastroösophageale Refluxerkrankung</i>	17/184	9,2 [5,5; 14,4]
<i>Schmerzen Oberbauch</i>	12/184	6,5 [3,4; 11,1]
<i>Hämorrhoiden</i>	11/184	6,0 [3,0; 10,4]
Allgemeine Erkrankungen und Beschwerden am Verabreichungsort	135/184	73,4 [66,4; 79,6]
<i>Ermüdung</i>	91/184	49,5 [42,0; 56,9]
<i>Asthenie</i>	26/184	14,1 [9,4; 20,0]
<i>Ödem peripher</i>	14/184	7,6 [4,2; 12,4]
<i>Fieber</i>	14/184	7,6 [4,2; 12,4]
<i>Schleimhautentzündung</i>	13/184	7,1 [3,8; 11,8]
Erkrankungen der Haut und des Unterhautgewebes	111/184	60,3 [52,9; 67,4]
<i>Alopezie</i>	89/184	48,4 [41,0; 55,8]
<i>Ausschlag</i>	16/184	8,7 [5,1; 13,7]
<i>Trockene Haut</i>	10/184	5,4 [2,6; 9,8]
Untersuchungen	98/184	53,3 [45,8; 60,6]
<i>Neutrophilenzahl erniedrigt</i>	40/184	21,7 [16,0; 28,4]
<i>Leukozytenzahl erniedrigt</i>	34/184	18,5 [13,1; 24,9]
<i>Thrombozytenzahl vermindert</i>	28/184	15,2 [10,4; 21,2]

Studie DESTINY-Breast01 SOC PT	Trastuzumab Deruxtecan	
	n/N	% [95 %-KI]
<i>Aspartataminotransferase erhöht</i>	26/184	14,1 [9,4; 20,0]
<i>Alaninaminotransferase erhöht</i>	18/184	9,8 [5,9; 15,0]
<i>Lymphozytenzahl erniedrigt</i>	17/184	9,2 [5,5; 14,4]
<i>Gewicht erniedrigt</i>	14/184	7,6 [4,2; 12,4]
<i>Bilirubin im Blut erhöht</i>	13/184	7,1 [3,8; 11,8]
Erkrankungen der Atemwege, des Brustraums und Mediastinums	96/184	52,2 [44,7; 59,6]
<i>Husten</i>	35/184	19,0 [13,6; 25,4]
<i>Dyspnoe</i>	27/184	14,7 [9,9; 20,6]
<i>Epistaxis</i>	24/184	13,0 [8,5; 18,8]
<i>Pneumonitis</i>	13/184	7,1 [3,8; 11,8]
<i>Interstitielle Lungenerkrankung</i>	10/184	5,4 [2,6; 9,8]
Infektionen und parasitäre Erkrankungen	88/184	47,8 [40,4; 55,3]
<i>Infektion der oberen Atemwege</i>	20/184	10,9 [6,8; 16,3]
<i>Harnwegsinfektion</i>	18/184	9,8 [5,9; 15,0]
<i>Nasopharyngitis</i>	16/184	8,7 [5,1; 13,7]
Erkrankungen des Nervensystems	86/184	46,7 [39,4; 54,2]
<i>Kopfschmerzen</i>	36/184	19,6 [14,1; 26,0]
<i>Schwindelgefühl</i>	17/184	9,2 [5,5; 14,4]
<i>Dysgeusie</i>	16/184	8,7 [5,1; 13,7]
<i>Periphere sensorische Neuropathie</i>	15/184	8,2 [4,6; 13,1]
<i>Periphere Neuropathie</i>	11/184	6,0 [3,0; 10,4]
Stoffwechsel- und Ernährungsstörungen	81/184	44,0 [36,7; 51,5]
<i>Appetit vermindert</i>	57/184	31,0 [24,4; 38,2]
<i>Hypokaliämie</i>	21/184	11,4 [7,2; 16,9]
Erkrankungen des Blutes und des Lymphsystems	78/184	42,4 [35,2; 49,9]
<i>Anämie</i>	54/184	29,3 [22,9; 36,5]

Studie DESTINY-Breast01 SOC PT	Trastuzumab Deruxtecan	
	n/N	% [95 %-KI]
<i>Neutropenie</i>	25/184	13,6 [9,0; 19,4]
<i>Thrombozytopenie</i>	12/184	6,5 [3,4; 11,1]
<i>Lymphopenie</i>	10/184	5,4 [2,6; 9,8]
Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen	57/184	31,0 [24,4; 38,2]
<i>Rückenschmerzen</i>	17/184	9,2 [5,5; 14,4]
<i>Arthralgie</i>	13/184	7,1 [3,8; 11,8]
<i>Myalgie</i>	12/184	6,5 [3,4; 11,1]
<i>Muskelspasmen</i>	11/184	6,0 [3,0; 10,4]
Augenerkrankungen	54/184	29,3 [22,9; 36,5]
<i>Trockenes Auge</i>	21/184	11,4 [7,2; 16,9]
Psychiatrische Erkrankungen	25/184	13,6 [9,0; 19,4]
<i>Angst</i>	12/184	6,5 [3,4; 11,1]
<i>Schlaflosigkeit</i>	11/184	6,0 [3,0; 10,4]
Gefäßerkrankungen	23/184	12,5 [8,1; 18,2]
Herzkrankungen	17/184	9,2 [5,5; 14,4]
Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen	16/184	8,7 [5,1; 13,7]
Erkrankungen des Ohrs und des Labyrinths	13/184	7,1 [3,8; 11,8]
Erkrankungen der Nieren und Harnwege	13/184	7,1 [3,8; 11,8]
Erkrankungen der Geschlechtsorgane und der Brustdrüse	12/184	6,5 [3,4; 11,1]
2. Datenschnitt: 01. August 2019 Alle verwendeten Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

SUE nach SOC und PT, die bei mindestens 5 % der Patienten aufgetreten sind

Tabelle 10: Ergebnisse für den Endpunkt SUE nach SOC und PT (≥ 5 % der Patienten) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01 SOC PT	Trastuzumab-Deruxtecan	
	n/N	% [95 %-KI]
Infektionen und parasitäre Erkrankungen	16/184	8,7 [5,1; 13,7]
Erkrankungen der Atemwege, des Brustraums und Mediastinums	12/184	6,5 [3,4; 11,1]
Erkrankungen des Gastrointestinaltrakts	12/184	6,5 [3,4; 11,1]
2. Datenschnitt: 01. August 2019 Alle Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

UE mit CTCAE-Grad ≥ 3 nach SOC und PT, die bei mindestens 5 % der Patienten aufgetreten sind

Tabelle 11: Ergebnisse für den Endpunkt UE mit CTCAE-Grad ≥ 3 nach SOC und PT (≥ 5 % der Patienten) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01 SOC PT	Trastuzumab Deruxtecan	
	n/N	% [95 %-KI]
Untersuchungen	40/184	21,7 [16,0; 28,4]
<i>Neutrophilenzahl erniedrigt</i>	22/184	12,0 [7,6; 17,5]
<i>Leukozytenzahl erniedrigt</i>	10/184	5,4 [2,6; 9,8]
Erkrankungen des Blutes und des Lymphsystems	33/184	17,9 [12,7; 24,3]
<i>Anämie</i>	16/184	8,7 [5,1; 13,7]
<i>Neutropenie</i>	16/184	8,7 [5,1; 13,7]
Erkrankungen des Gastrointestinaltrakts	29/184	15,8 [10,8; 21,8]
<i>Übelkeit</i>	14/184	7,6 [4,2; 12,4]
Stoffwechsel- und Ernährungsstörungen	16/184	8,7 [5,1; 13,7]
Allgemeine Erkrankungen und Beschwerden am Verabreichungsort	14/184	7,6 [4,2; 12,4]
Infektionen und parasitäre Erkrankungen	14/184	7,6 [4,2; 12,4]
<i>Ermüdung</i>	11/184	6,0 [3,0; 10,4]
Erkrankungen der Atemwege, des Brustraums und Mediastinums	12/184	6,5 [3,4; 11,1]

Studie DESTINY-Breast01 SOC PT	Trastuzumab Deruxtecan	
	n/N	% [95 %-KI]
2. Datenschnitt: 01. August 2019 Alle verwendeten Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

UE nach SOC und PT, die zum Therapieabbruch führten

Tabelle 12: Ergebnisse für den Endpunkt UE, die zum Therapieabbruch führten nach SOC und PT aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01 SOC PT	Trastuzumab Deruxtecan	
	n/N	% [95 %-KI]
Erkrankungen der Atemwege, des Brustraums und Mediastinums	19/184	10,3 [6,3; 15,7]
<i>Pneumonitis</i>	11/184	6,0 [3,0; 10,4]
<i>Interstitielle Lungenerkrankung</i>	5/184	2,7 [0,9; 6,2]
<i>Alveolitis</i>	1/184	0,5 [0,0; 3,0]
<i>Dyspnoe</i>	1/184	0,5 [0,0; 3,0]
<i>Hypoxie</i>	1/184	0,5 [0,0; 3,0]
<i>Organisierende Pneumonie</i>	1/184	0,5 [0,0; 3,0]
Infektionen und parasitäre Erkrankungen	2/184	1,1 [0,1; 3,9]
Untersuchungen	2/184	1,1 [0,1; 3,9]
<i>Akute Hepatitis B</i>	1/184	0,5 [0,0; 3,0]
<i>Pneumonie</i>	1/184	0,5 [0,0; 3,0]
<i>Gamma-Glutamyltransferase erhöht</i>	1/184	0,5 [0,0; 3,0]
<i>Thrombozytenzahl vermindert</i>	1/184	0,5 [0,0; 3,0]
Erkrankungen des Blutes und des Lymphsystems	1/184	0,5 [0,0; 3,0]
<i>Thrombozytopenie</i>	1/184	0,5 [0,0; 3,0]
Herzerkrankungen	1/184	0,5 [0,0; 3,0]

Studie DESTINY-Breast01 SOC <i>PT</i>	Trastuzumab Deruxtecan	
	n/N	% [95 %-KI]
<i>Stauungsinsuffizienz</i>	1/184	0,5 [0,0; 3,0]
Erkrankungen des Gastrointestinaltrakts	1/184	0,5 [0,0; 3,0]
<i>Diarrhö</i>	1/184	0,5 [0,0; 3,0]
Allgemeine Erkrankungen und Beschwerden am Verabreichungsort	1/184	0,5 [0,0; 3,0]
<i>Leistung vermindert</i>	1/184	0,5 [0,0; 3,0]
Erkrankungen des Nervensystems	1/184	0,5 [0,0; 3,0]
<i>Periphere Neuropathie</i>	1/184	0,5 [0,0; 3,0]
2. Datenschnitt: 01. August 2019		
Alle verwendeten Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

UE von besonderem Interesse

Tabelle 13: Ergebnisse für den Endpunkt UE von besonderem Interesse aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel (DESTINY-Breast01)

Studie DESTINY-Breast01	Trastuzumab Deruxtecan N=184 (Safety Population), n (%) [95 %-KI]
Interstitielle Lungenerkrankung (ILD), Bewertung durch Prüfarzt	
ILD, unabhängig vom Schweregrad	24 (13,0) [8,5; 18,8]
ILD, SUE	5 (2,7) [0,9; 6,2]
ILD, CTCAE-Grad < 3	21 (11,4) [7,2; 16,9]
ILD, CTCAE-Grad ≥ 3	3 (1,6) [0,3; 4,7]
Interstitielle Lungenerkrankung (ILD), Bewertung durch AC	
ILD, unabhängig vom Schweregrad	27 (14,7) [9,9; 20,6]
ILD, SUE	9 (4,9) [2,3; 9,1]
ILD, CTCAE-Grad < 3	21 (11,4) [7,2; 16,9]
ILD, CTCAE-Grad ≥ 3	7 (3,8) [1,5; 7,7]
Verringerung der linksventrikulären Auswurfraction (LVEF)	
Verringerung der LVEF, unabhängig vom Schweregrad	5 (2,7) [0,9; 6,2]
Verringerung der LVEF, SUE	1 (0,5) [0,0; 3,0]
Verringerung der LVEF, CTCAE-Grad < 3	4 (2,2) [0,6; 5,5]
Verringerung der LVEF, CTCAE-Grad ≥ 3	1 (0,5) [0,0; 3,0]

Studie DESTINY-Breast01	Trastuzumab Deruxtecan N=184 (Safety Population), n (%) [95 %-KI]
Verlängerung des QT-Intervalls	
Verlängerung des QT-Intervalls, unabhängig vom Schweregrad	9 (4,9) [2,3; 9,1]
Verlängerung des QT-Intervalls, SUE	0 (0,0) [0,0; 2,0]
Verlängerung des QT-Intervalls, CTCAE-Grad < 3	7 (3,8) [1,5; 7,7]
Verlängerung des QT-Intervalls, CTCAE-Grad ≥ 3	2 (1,1) [0,1; 3,9]
Infusionsbedingte Reaktion (IRR)	
IRR, unabhängig vom Schweregrad	16 (8,7) [5,1; 13,7]
IRR, SUE	1 (0,5) [0,0; 3,0]
IRR, CTCAE-Grad < 3	16 (8,7) [5,1; 13,7]
IRR, CTCAE-Grad ≥ 3	0 (0,0) [0,0; 2,0]
2. Datenschnitt: 01. August 2019 Alle verwendeten Abkürzungen werden im Abkürzungsverzeichnis erläutert.	

Subgruppenanalysen

Follow-up und Exposition

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
A-Age classification 1	< 65 years		
Total number of subjects in subgroup category		140	129
Number (%) of subjects on treatment at data cut		58 (41.4)	50 (38.8)
Duration of Follow-up (months)			
n		140	129
Mean		10.7	10.6
Std. Dev.		3.35	3.42
Median		11.0	10.9
Minimum		1.9	1.9
Maximum		19.9	19.9
Treatment Duration			
<=3 months		23 (16.4)	23 (17.8)
>3 to <=6 months		24 (17.1)	23 (17.8)
>6 to <=9 months		17 (12.1)	16 (12.4)
>9 to <=12 months		41 (29.3)	36 (27.9)
>12 to <=24 months		35 (25.0)	31 (24.0)
>24 months		0	0
Dose Intensity (mg/kg/3 weeks)			
n		140	129
Mean		5.04	5.06
Std. Dev.		0.521	0.481
Median		5.30	5.30
Minimum		3.1	3.4
Maximum		5.6	5.6
Total Number of Cycles Initiated			
<=6 cycles		31 (22.1)	30 (23.3)
>6 to <=12 cycles		34 (24.3)	33 (25.6)
>12 to <=18 cycles		53 (37.9)	47 (36.4)
>18 to <=24 cycles		19 (13.6)	16 (12.4)
>24 to <=30 cycles		3 (2.1)	3 (2.3)
>30 cycles		0	0

Source Data: adam.adsl, adam.adex.

Table T2EX_ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
A-Age classification 1	>= 65 years		
	Total number of subjects in subgroup category Number (%) of subjects on treatment at data cut	44 21 (47.7)	40 19 (47.5)
	Duration of Follow-up (months)		
	n	44	40
	Mean	11.8	11.5
	Std. Dev.	3.62	3.55
	Median	11.6	11.6
	Minimum	0.7	0.7
	Maximum	19.7	19.7
	Treatment Duration		
	<=3 months	5 (11.4)	5 (12.5)
	>3 to <=6 months	4 (9.1)	4 (10.0)
	>6 to <=9 months	9 (20.5)	8 (20.0)
	>9 to <=12 months	11 (25.0)	10 (25.0)
	>12 to <=24 months	15 (34.1)	13 (32.5)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	44	40
	Mean	4.93	4.96
	Std. Dev.	0.752	0.713
	Median	5.25	5.25
	Minimum	2.5	2.5
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	8 (18.2)	8 (20.0)
	>6 to <=12 cycles	9 (20.5)	8 (20.0)
	>12 to <=18 cycles	19 (43.2)	17 (42.5)
	>18 to <=24 cycles	7 (15.9)	6 (15.0)
	>24 to <=30 cycles	1 (2.3)	1 (2.5)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX_ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

			Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
B-Region	Asia	Total number of subjects in subgroup category	63	57
		Number (%) of subjects on treatment at data cut	26 (41.3)	22 (38.6)
		Duration of Follow-up (months)		
		n	63	57
		Mean	12.1	12.0
		Std. Dev.	3.14	3.12
		Median	11.7	11.7
		Minimum	3.9	3.9
		Maximum	19.9	19.9
		Treatment Duration		
		<=3 months	8 (12.7)	8 (14.0)
		>3 to <=6 months	11 (17.5)	11 (19.3)
		>6 to <=9 months	9 (14.3)	8 (14.0)
		>9 to <=12 months	14 (22.2)	12 (21.1)
		>12 to <=24 months	21 (33.3)	18 (31.6)
		>24 months	0	0
		Dose Intensity (mg/kg/3 weeks)		
		n	63	57
		Mean	4.97	4.99
		Std. Dev.	0.628	0.594
		Median	5.20	5.20
		Minimum	2.5	2.5
		Maximum	5.6	5.6
		Total Number of Cycles Initiated		
		<=6 cycles	10 (15.9)	10 (17.5)
		>6 to <=12 cycles	19 (30.2)	18 (31.6)
		>12 to <=18 cycles	21 (33.3)	18 (31.6)
>18 to <=24 cycles	11 (17.5)	9 (15.8)		
>24 to <=30 cycles	2 (3.2)	2 (3.5)		
>30 cycles	0	0		

Source Data: adam.adsl, adam.adex.

Table T2EX_ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
B-Region	North America		
	Total number of subjects in subgroup category	53	49
	Number (%) of subjects on treatment at data cut	26 (49.1)	24 (49.0)
	Duration of Follow-up (months)		
	n	53	49
	Mean	10.9	10.7
	Std. Dev.	3.42	3.42
	Median	11.0	11.0
	Minimum	3.1	3.1
	Maximum	19.3	19.3
	Treatment Duration		
	<=3 months	9 (17.0)	9 (18.4)
	>3 to <=6 months	6 (11.3)	5 (10.2)
	>6 to <=9 months	6 (11.3)	6 (12.2)
	>9 to <=12 months	15 (28.3)	13 (26.5)
	>12 to <=24 months	17 (32.1)	16 (32.7)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	53	49
	Mean	4.97	4.97
	Std. Dev.	0.649	0.621
	Median	5.30	5.30
	Minimum	3.1	3.1
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	13 (24.5)	12 (24.5)
	>6 to <=12 cycles	7 (13.2)	7 (14.3)
	>12 to <=18 cycles	24 (45.3)	22 (44.9)
	>18 to <=24 cycles	7 (13.2)	6 (12.2)
	>24 to <=30 cycles	2 (3.8)	2 (4.1)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX_ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
B-Region	EU		
	Total number of subjects in subgroup category	68	63
	Number (%) of subjects on treatment at data cut	27 (39.7)	23 (36.5)
	Duration of Follow-up (months)		
	n	68	63
	Mean	9.9	9.7
	Std. Dev.	3.41	3.49
	Median	10.7	10.6
	Minimum	0.7	0.7
	Maximum	16.0	16.0
	Treatment Duration		
	<=3 months	11 (16.2)	11 (17.5)
	>3 to <=6 months	11 (16.2)	11 (17.5)
	>6 to <=9 months	11 (16.2)	10 (15.9)
	>9 to <=12 months	23 (33.8)	21 (33.3)
	>12 to <=24 months	12 (17.6)	10 (15.9)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	68	63
	Mean	5.10	5.13
	Std. Dev.	0.479	0.415
	Median	5.30	5.30
	Minimum	3.1	3.6
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	16 (23.5)	16 (25.4)
	>6 to <=12 cycles	17 (25.0)	16 (25.4)
	>12 to <=18 cycles	27 (39.7)	24 (38.1)
	>18 to <=24 cycles	8 (11.8)	7 (11.1)
	>24 to <=30 cycles	0	0
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

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Table T2EX_ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
C-ECOG performance status	Status 0		
Total number of subjects in subgroup category		102	92
Number (%) of subjects on treatment at data cut		50 (49.0)	45 (48.9)
Duration of Follow-up (months)			
n		102	92
Mean		11.4	11.2
Std. Dev.		3.43	3.42
Median		11.5	11.5
Minimum		0.7	0.7
Maximum		19.7	19.7
Treatment Duration			
<=3 months		8 (7.8)	8 (8.7)
>3 to <=6 months		15 (14.7)	14 (15.2)
>6 to <=9 months		15 (14.7)	13 (14.1)
>9 to <=12 months		31 (30.4)	28 (30.4)
>12 to <=24 months		33 (32.4)	29 (31.5)
>24 months		0	0
Dose Intensity (mg/kg/3 weeks)			
n		102	92
Mean		5.05	5.07
Std. Dev.		0.537	0.476
Median		5.30	5.30
Minimum		2.9	3.3
Maximum		5.6	5.6
Total Number of Cycles Initiated			
<=6 cycles		14 (13.7)	13 (14.1)
>6 to <=12 cycles		23 (22.5)	21 (22.8)
>12 to <=18 cycles		44 (43.1)	40 (43.5)
>18 to <=24 cycles		19 (18.6)	16 (17.4)
>24 to <=30 cycles		2 (2.0)	2 (2.2)
>30 cycles		0	0

Source Data: adam.adsl, adam.adex.

Table T2EX_ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
C-ECOG performance status	Status 1	81	76
	Total number of subjects in subgroup category Number (%) of subjects on treatment at data cut	29 (35.8)	24 (31.6)
Duration of Follow-up (months)			
n		81	76
Mean		10.5	10.4
Std. Dev.		3.30	3.38
Median		11.0	11.0
Minimum		3.0	3.0
Maximum		19.9	19.9
Treatment Duration			
<=3 months		19 (23.5)	19 (25.0)
>3 to <=6 months		13 (16.0)	13 (17.1)
>6 to <=9 months		11 (13.6)	11 (14.5)
>9 to <=12 months		21 (25.9)	18 (23.7)
>12 to <=24 months		17 (21.0)	15 (19.7)
>24 months		0	0
Dose Intensity (mg/kg/3 weeks)			
n		81	76
Mean		4.97	4.99
Std. Dev.		0.641	0.620
Median		5.30	5.30
Minimum		2.5	2.5
Maximum		5.6	5.6
Total Number of Cycles Initiated			
<=6 cycles		24 (29.6)	24 (31.6)
>6 to <=12 cycles		20 (24.7)	20 (26.3)
>12 to <=18 cycles		28 (34.6)	24 (31.6)
>18 to <=24 cycles		7 (8.6)	6 (7.9)
>24 to <=30 cycles		2 (2.5)	2 (2.6)
>30 cycles		0	0

Source Data: adam.adsl, adam.adex.

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Table T2EX_ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
D-Baseline sum of diameters of target lesions	< 5 cm		
	Total number of subjects in subgroup category	74	74
	Number (%) of subjects on treatment at data cut	35 (47.3)	35 (47.3)
	Duration of Follow-up (months)		
	n	74	74
	Mean	10.9	10.9
	Std. Dev.	3.65	3.65
	Median	11.1	11.1
	Minimum	0.7	0.7
	Maximum	19.9	19.9
	Treatment Duration		
	<=3 months	13 (17.6)	13 (17.6)
	>3 to <=6 months	10 (13.5)	10 (13.5)
	>6 to <=9 months	6 (8.1)	6 (8.1)
	>9 to <=12 months	23 (31.1)	23 (31.1)
	>12 to <=24 months	22 (29.7)	22 (29.7)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	74	74
	Mean	5.03	5.03
	Std. Dev.	0.523	0.523
	Median	5.30	5.30
	Minimum	3.3	3.3
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	15 (20.3)	15 (20.3)
	>6 to <=12 cycles	13 (17.6)	13 (17.6)
	>12 to <=18 cycles	31 (41.9)	31 (41.9)
	>18 to <=24 cycles	13 (17.6)	13 (17.6)
	>24 to <=30 cycles	2 (2.7)	2 (2.7)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

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Table T2EX_ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
D-Baseline sum of diameters of target lesions	>= 5 cm		
	Total number of subjects in subgroup category	95	95
	Number (%) of subjects on treatment at data cut	34 (35.8)	34 (35.8)
	Duration of Follow-up (months)		
	n	95	95
	Mean	10.7	10.7
	Std. Dev.	3.33	3.33
	Median	11.0	11.0
	Minimum	1.9	1.9
	Maximum	19.7	19.7
	Treatment Duration		
	<=3 months	15 (15.8)	15 (15.8)
	>3 to <=6 months	17 (17.9)	17 (17.9)
	>6 to <=9 months	18 (18.9)	18 (18.9)
	>9 to <=12 months	23 (24.2)	23 (24.2)
	>12 to <=24 months	22 (23.2)	22 (23.2)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	95	95
	Mean	5.05	5.05
	Std. Dev.	0.563	0.563
	Median	5.30	5.30
	Minimum	2.5	2.5
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	23 (24.2)	23 (24.2)
	>6 to <=12 cycles	28 (29.5)	28 (29.5)
	>12 to <=18 cycles	33 (34.7)	33 (34.7)
	>18 to <=24 cycles	9 (9.5)	9 (9.5)
	>24 to <=30 cycles	2 (2.1)	2 (2.1)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
E-HER2 Status	IHC3+	Total number of subjects in subgroup category Number (%) of subjects on treatment at data cut	154 70 (45.5)
		142 61 (43.0)	
Duration of Follow-up (months)			
n		154	142
Mean		11.2	11.0
Std. Dev.		3.46	3.47
Median		11.2	11.1
Minimum		1.9	1.9
Maximum		19.9	19.9
Treatment Duration			
<=3 months		24 (15.6)	24 (16.9)
>3 to <=6 months		22 (14.3)	22 (15.5)
>6 to <=9 months		20 (13.0)	18 (12.7)
>9 to <=12 months		41 (26.6)	37 (26.1)
>12 to <=24 months		47 (30.5)	41 (28.9)
>24 months		0	0
Dose Intensity (mg/kg/3 weeks)			
n		154	142
Mean		4.98	5.01
Std. Dev.		0.609	0.564
Median		5.30	5.30
Minimum		2.5	2.5
Maximum		5.6	5.6
Total Number of Cycles Initiated			
<=6 cycles		33 (21.4)	33 (23.2)
>6 to <=12 cycles		33 (21.4)	31 (21.8)
>12 to <=18 cycles		59 (38.3)	53 (37.3)
>18 to <=24 cycles		25 (16.2)	21 (14.8)
>24 to <=30 cycles		4 (2.6)	4 (2.8)
>30 cycles		0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
E-HER2 Status	ISH+ EXCEPT IHCR3+	28 8 (28.6)	25 7 (28.0)
	Total number of subjects in subgroup category Number (%) of subjects on treatment at data cut		
Duration of Follow-up (months)			
n		28	25
Mean		9.9	9.8
Std. Dev.		3.15	3.32
Median		10.7	10.4
Minimum		0.7	0.7
Maximum		16.0	16.0
Treatment Duration			
<=3 months		4 (14.3)	4 (16.0)
>3 to <=6 months		5 (17.9)	4 (16.0)
>6 to <=9 months		6 (21.4)	6 (24.0)
>9 to <=12 months		10 (35.7)	8 (32.0)
>12 to <=24 months		3 (10.7)	3 (12.0)
>24 months		0	0
Dose Intensity (mg/kg/3 weeks)			
n		28	25
Mean		5.19	5.16
Std. Dev.		0.410	0.426
Median		5.30	5.30
Minimum		3.8	3.8
Maximum		5.6	5.6
Total Number of Cycles Initiated			
<=6 cycles		6 (21.4)	5 (20.0)
>6 to <=12 cycles		9 (32.1)	9 (36.0)
>12 to <=18 cycles		12 (42.9)	10 (40.0)
>18 to <=24 cycles		1 (3.6)	1 (4.0)
>24 to <=30 cycles		0	0
>30 cycles		0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
F-Estrogen receptors	Positive		
	Total number of subjects in subgroup category	93	84
	Number (%) of subjects on treatment at data cut	35 (37.6)	31 (36.9)
	Duration of Follow-up (months)		
	n	93	84
	Mean	10.8	10.6
	Std. Dev.	2.99	2.95
	Median	11.0	11.0
	Minimum	1.9	1.9
	Maximum	18.5	18.1
	Treatment Duration		
	<=3 months	13 (14.0)	13 (15.5)
	>3 to <=6 months	13 (14.0)	12 (14.3)
	>6 to <=9 months	16 (17.2)	14 (16.7)
	>9 to <=12 months	29 (31.2)	26 (31.0)
	>12 to <=24 months	22 (23.7)	19 (22.6)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	93	84
	Mean	4.99	5.00
	Std. Dev.	0.615	0.594
	Median	5.30	5.30
	Minimum	2.5	2.5
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	18 (19.4)	17 (20.2)
	>6 to <=12 cycles	24 (25.8)	22 (26.2)
	>12 to <=18 cycles	42 (45.2)	38 (45.2)
	>18 to <=24 cycles	8 (8.6)	6 (7.1)
	>24 to <=30 cycles	1 (1.1)	1 (1.2)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
F-Estrogen receptors	Negative		
	Total number of subjects in subgroup category	88	82
	Number (%) of subjects on treatment at data cut	44 (50.0)	38 (46.3)
	Duration of Follow-up (months)		
	n	88	82
	Mean	11.2	11.1
	Std. Dev.	3.81	3.87
	Median	11.2	11.2
	Minimum	0.7	0.7
	Maximum	19.9	19.9
	Treatment Duration		
	<=3 months	13 (14.8)	13 (15.9)
	>3 to <=6 months	15 (17.0)	15 (18.3)
	>6 to <=9 months	10 (11.4)	10 (12.2)
	>9 to <=12 months	22 (25.0)	19 (23.2)
	>12 to <=24 months	28 (31.8)	25 (30.5)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	88	82
	Mean	5.03	5.06
	Std. Dev.	0.555	0.493
	Median	5.30	5.30
	Minimum	3.1	3.1
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	19 (21.6)	19 (23.2)
	>6 to <=12 cycles	19 (21.6)	19 (23.2)
	>12 to <=18 cycles	29 (33.0)	25 (30.5)
	>18 to <=24 cycles	18 (20.5)	16 (19.5)
	>24 to <=30 cycles	3 (3.4)	3 (3.7)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
G-Progesterone receptors	Positive		
	Total number of subjects in subgroup category	51	46
	Number (%) of subjects on treatment at data cut	22 (43.1)	18 (39.1)
	Duration of Follow-up (months)		
	n	51	46
	Mean	11.0	10.8
	Std. Dev.	2.79	2.78
	Median	11.1	11.0
	Minimum	3.9	3.9
	Maximum	17.8	17.8
	Treatment Duration		
	<=3 months	4 (7.8)	4 (8.7)
	>3 to <=6 months	7 (13.7)	6 (13.0)
	>6 to <=9 months	10 (19.6)	10 (21.7)
	>9 to <=12 months	17 (33.3)	16 (34.8)
	>12 to <=24 months	13 (25.5)	10 (21.7)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	51	46
	Mean	4.92	4.99
	Std. Dev.	0.715	0.618
	Median	5.30	5.30
	Minimum	2.5	2.5
	Maximum	5.5	5.5
	Total Number of Cycles Initiated		
	<=6 cycles	6 (11.8)	5 (10.9)
	>6 to <=12 cycles	14 (27.5)	14 (30.4)
	>12 to <=18 cycles	24 (47.1)	21 (45.7)
	>18 to <=24 cycles	7 (13.7)	6 (13.0)
	>24 to <=30 cycles	0	0
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
G-Progesterone receptors	Negative		
	Total number of subjects in subgroup category Number (%) of subjects on treatment at data cut	125 54 (43.2)	115 48 (41.7)
	Duration of Follow-up (months)		
	n	125	115
	Mean	11.0	10.9
	Std. Dev.	3.70	3.74
	Median	11.1	11.1
	Minimum	0.7	0.7
	Maximum	19.9	19.9
	Treatment Duration		
	<=3 months	21 (16.8)	21 (18.3)
	>3 to <=6 months	20 (16.0)	20 (17.4)
	>6 to <=9 months	16 (12.8)	14 (12.2)
	>9 to <=12 months	32 (25.6)	27 (23.5)
	>12 to <=24 months	36 (28.8)	33 (28.7)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	125	115
	Mean	5.04	5.03
	Std. Dev.	0.531	0.524
	Median	5.30	5.20
	Minimum	3.1	3.1
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	30 (24.0)	30 (26.1)
	>6 to <=12 cycles	28 (22.4)	26 (22.6)
	>12 to <=18 cycles	44 (35.2)	39 (33.9)
	>18 to <=24 cycles	19 (15.2)	16 (13.9)
	>24 to <=30 cycles	4 (3.2)	4 (3.5)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
H-Hormone receptors	Positive		
	Total number of subjects in subgroup category	97	87
	Number (%) of subjects on treatment at data cut	37 (38.1)	32 (36.8)
	Duration of Follow-up (months)		
	n	97	87
	Mean	10.9	10.7
	Std. Dev.	3.02	3.00
	Median	11.1	11.0
	Minimum	1.9	1.9
	Maximum	18.5	18.1
	Treatment Duration		
	<=3 months	13 (13.4)	13 (14.9)
	>3 to <=6 months	14 (14.4)	13 (14.9)
	>6 to <=9 months	16 (16.5)	14 (16.1)
	>9 to <=12 months	30 (30.9)	27 (31.0)
	>12 to <=24 months	24 (24.7)	20 (23.0)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	97	87
	Mean	4.97	4.99
	Std. Dev.	0.637	0.590
	Median	5.30	5.30
	Minimum	2.5	2.5
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	18 (18.6)	17 (19.5)
	>6 to <=12 cycles	25 (25.8)	23 (26.4)
	>12 to <=18 cycles	44 (45.4)	39 (44.8)
	>18 to <=24 cycles	9 (9.3)	7 (8.0)
	>24 to <=30 cycles	1 (1.0)	1 (1.1)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
H-Hormone receptors	Negative		
	Total number of subjects in subgroup category Number (%) of subjects on treatment at data cut	83 41 (49.4)	78 36 (46.2)
	Duration of Follow-up (months)		
	n	83	78
	Mean	11.1	11.0
	Std. Dev.	3.84	3.89
	Median	11.2	11.3
	Minimum	0.7	0.7
	Maximum	19.9	19.9
	Treatment Duration		
	<=3 months	13 (15.7)	13 (16.7)
	>3 to <=6 months	14 (16.9)	14 (17.9)
	>6 to <=9 months	10 (12.0)	10 (12.8)
	>9 to <=12 months	20 (24.1)	17 (21.8)
	>12 to <=24 months	26 (31.3)	24 (30.8)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	83	78
	Mean	5.05	5.06
	Std. Dev.	0.521	0.495
	Median	5.30	5.30
	Minimum	3.1	3.1
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	19 (22.9)	19 (24.4)
	>6 to <=12 cycles	18 (21.7)	18 (23.1)
	>12 to <=18 cycles	26 (31.3)	23 (29.5)
	>18 to <=24 cycles	17 (20.5)	15 (19.2)
	>24 to <=30 cycles	3 (3.6)	3 (3.8)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
I-Renal impairment	Normal		
	Total number of subjects in subgroup category	90	84
	Number (%) of subjects on treatment at data cut	43 (47.8)	39 (46.4)
	Duration of Follow-up (months)		
	n	90	84
	Mean	10.6	10.5
	Std. Dev.	3.43	3.46
	Median	10.9	10.8
	Minimum	1.9	1.9
	Maximum	19.9	19.9
	Treatment Duration		
	<=3 months	13 (14.4)	13 (15.5)
	>3 to <=6 months	12 (13.3)	12 (14.3)
	>6 to <=9 months	11 (12.2)	10 (11.9)
	>9 to <=12 months	30 (33.3)	26 (31.0)
	>12 to <=24 months	24 (26.7)	23 (27.4)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	90	84
	Mean	5.07	5.08
	Std. Dev.	0.504	0.481
	Median	5.30	5.30
	Minimum	3.1	3.1
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	18 (20.0)	18 (21.4)
	>6 to <=12 cycles	18 (20.0)	17 (20.2)
	>12 to <=18 cycles	38 (42.2)	34 (40.5)
	>18 to <=24 cycles	14 (15.6)	13 (15.5)
	>24 to <=30 cycles	2 (2.2)	2 (2.4)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
I-Renal impairment	Mild		
	Total number of subjects in subgroup category	69	61
	Number (%) of subjects on treatment at data cut	30 (43.5)	24 (39.3)
	Duration of Follow-up (months)		
	n	69	61
	Mean	11.2	11.1
	Std. Dev.	3.06	3.15
	Median	11.6	11.6
	Minimum	3.1	3.1
	Maximum	19.3	19.3
	Treatment Duration		
	<=3 months	10 (14.5)	10 (16.4)
	>3 to <=6 months	9 (13.0)	8 (13.1)
	>6 to <=9 months	11 (15.9)	10 (16.4)
	>9 to <=12 months	17 (24.6)	15 (24.6)
	>12 to <=24 months	22 (31.9)	18 (29.5)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	69	61
	Mean	4.95	4.99
	Std. Dev.	0.706	0.645
	Median	5.30	5.30
	Minimum	2.5	2.5
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	13 (18.8)	12 (19.7)
	>6 to <=12 cycles	17 (24.6)	16 (26.2)
	>12 to <=18 cycles	29 (42.0)	25 (41.0)
	>18 to <=24 cycles	8 (11.6)	6 (9.8)
	>24 to <=30 cycles	2 (2.9)	2 (3.3)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
I-Renal impairment	Moderate		
	Total number of subjects in subgroup category	25	24
	Number (%) of subjects on treatment at data cut	6 (24.0)	6 (25.0)
	Duration of Follow-up (months)		
	n	25	24
	Mean	11.4	11.1
	Std. Dev.	4.39	4.22
	Median	11.2	11.2
	Minimum	0.7	0.7
	Maximum	19.7	19.7
	Treatment Duration		
	<=3 months	5 (20.0)	5 (20.8)
	>3 to <=6 months	7 (28.0)	7 (29.2)
	>6 to <=9 months	4 (16.0)	4 (16.7)
	>9 to <=12 months	5 (20.0)	5 (20.8)
	>12 to <=24 months	4 (16.0)	3 (12.5)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	25	24
	Mean	5.02	5.01
	Std. Dev.	0.471	0.481
	Median	5.10	5.15
	Minimum	4.0	4.0
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	8 (32.0)	8 (33.3)
	>6 to <=12 cycles	8 (32.0)	8 (33.3)
	>12 to <=18 cycles	5 (20.0)	5 (20.8)
	>18 to <=24 cycles	4 (16.0)	3 (12.5)
	>24 to <=30 cycles	0	0
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
J-Hepatic impairment	Normal		
	Total number of subjects in subgroup category	105	94
	Number (%) of subjects on treatment at data cut	47 (44.8)	41 (43.6)
	Duration of Follow-up (months)		
	n	105	94
	Mean	11.4	11.3
	Std. Dev.	3.68	3.77
	Median	11.5	11.6
	Minimum	2.4	2.4
	Maximum	19.9	19.9
	Treatment Duration		
	<=3 months	14 (13.3)	14 (14.9)
	>3 to <=6 months	11 (10.5)	10 (10.6)
	>6 to <=9 months	16 (15.2)	14 (14.9)
	>9 to <=12 months	31 (29.5)	27 (28.7)
	>12 to <=24 months	33 (31.4)	29 (30.9)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	105	94
	Mean	4.96	4.99
	Std. Dev.	0.607	0.561
	Median	5.20	5.20
	Minimum	2.9	3.1
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	18 (17.1)	17 (18.1)
	>6 to <=12 cycles	24 (22.9)	22 (23.4)
	>12 to <=18 cycles	44 (41.9)	38 (40.4)
	>18 to <=24 cycles	15 (14.3)	13 (13.8)
	>24 to <=30 cycles	4 (3.8)	4 (4.3)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
J-Hepatic impairment	Mild		
	Total number of subjects in subgroup category	76	72
	Number (%) of subjects on treatment at data cut	32 (42.1)	28 (38.9)
	Duration of Follow-up (months)		
	n	76	72
	Mean	10.4	10.3
	Std. Dev.	2.95	2.90
	Median	11.0	10.9
	Minimum	0.7	0.7
	Maximum	17.8	17.8
	Treatment Duration		
	<=3 months	13 (17.1)	13 (18.1)
	>3 to <=6 months	15 (19.7)	15 (20.8)
	>6 to <=9 months	10 (13.2)	10 (13.9)
	>9 to <=12 months	21 (27.6)	19 (26.4)
	>12 to <=24 months	17 (22.4)	15 (20.8)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	76	72
	Mean	5.11	5.12
	Std. Dev.	0.538	0.507
	Median	5.30	5.30
	Minimum	2.5	2.5
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	20 (26.3)	20 (27.8)
	>6 to <=12 cycles	17 (22.4)	17 (23.6)
	>12 to <=18 cycles	28 (36.8)	26 (36.1)
	>18 to <=24 cycles	11 (14.5)	9 (12.5)
	>24 to <=30 cycles	0	0
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Daiichi Sankyo, Inc.
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Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
K-Brain metastases	Yes		
	Total number of subjects in subgroup category Number (%) of subjects on treatment at data cut	24 11 (45.8)	22 9 (40.9)
	Duration of Follow-up (months)		
	n	24	22
	Mean	10.3	10.2
	Std. Dev.	4.31	4.48
	Median	11.0	11.0
	Minimum	0.7	0.7
	Maximum	19.6	19.6
	Treatment Duration		
	<=3 months	4 (16.7)	4 (18.2)
	>3 to <=6 months	2 (8.3)	2 (9.1)
	>6 to <=9 months	4 (16.7)	4 (18.2)
	>9 to <=12 months	6 (25.0)	5 (22.7)
	>12 to <=24 months	8 (33.3)	7 (31.8)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	24	22
	Mean	5.17	5.17
	Std. Dev.	0.393	0.406
	Median	5.30	5.30
	Minimum	3.9	3.9
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	6 (25.0)	6 (27.3)
	>6 to <=12 cycles	4 (16.7)	4 (18.2)
	>12 to <=18 cycles	10 (41.7)	9 (40.9)
	>18 to <=24 cycles	4 (16.7)	3 (13.6)
	>24 to <=30 cycles	0	0
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

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Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
K-Brain metastases	No		
	Total number of subjects in subgroup category	160	147
	Number (%) of subjects on treatment at data cut	68 (42.5)	60 (40.8)
	Duration of Follow-up (months)		
	n	160	147
	Mean	11.0	10.9
	Std. Dev.	3.29	3.29
	Median	11.1	11.1
	Minimum	2.4	2.4
	Maximum	19.9	19.9
	Treatment Duration		
	<=3 months	24 (15.0)	24 (16.3)
	>3 to <=6 months	26 (16.3)	25 (17.0)
	>6 to <=9 months	22 (13.8)	20 (13.6)
	>9 to <=12 months	46 (28.8)	41 (27.9)
	>12 to <=24 months	42 (26.3)	37 (25.2)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	160	147
	Mean	4.99	5.02
	Std. Dev.	0.605	0.561
	Median	5.30	5.30
	Minimum	2.5	2.5
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	33 (20.6)	32 (21.8)
	>6 to <=12 cycles	39 (24.4)	37 (25.2)
	>12 to <=18 cycles	62 (38.8)	55 (37.4)
	>18 to <=24 cycles	22 (13.8)	19 (12.9)
	>24 to <=30 cycles	4 (2.5)	4 (2.7)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
L-Bone metastases	Yes		
	Total number of subjects in subgroup category	53	48
	Number (%) of subjects on treatment at data cut	18 (34.0)	16 (33.3)
	Duration of Follow-up (months)		
	n	53	48
	Mean	10.8	10.6
	Std. Dev.	3.83	3.86
	Median	11.2	11.2
	Minimum	0.7	0.7
	Maximum	19.9	19.9
	Treatment Duration		
	<=3 months	9 (17.0)	9 (18.8)
	>3 to <=6 months	9 (17.0)	9 (18.8)
	>6 to <=9 months	7 (13.2)	6 (12.5)
	>9 to <=12 months	16 (30.2)	13 (27.1)
	>12 to <=24 months	12 (22.6)	11 (22.9)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	53	48
	Mean	4.97	4.96
	Std. Dev.	0.634	0.657
	Median	5.30	5.30
	Minimum	2.5	2.5
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	12 (22.6)	12 (25.0)
	>6 to <=12 cycles	14 (26.4)	13 (27.1)
	>12 to <=18 cycles	19 (35.8)	16 (33.3)
	>18 to <=24 cycles	6 (11.3)	5 (10.4)
	>24 to <=30 cycles	2 (3.8)	2 (4.2)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

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Program Name: T2EX ASB0.sas
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Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
L-Bone metastases	No		
	Total number of subjects in subgroup category	131	121
	Number (%) of subjects on treatment at data cut	61 (46.6)	53 (43.8)
	Duration of Follow-up (months)		
	n	131	121
	Mean	11.0	10.9
	Std. Dev.	3.28	3.31
	Median	11.1	11.0
	Minimum	1.9	1.9
	Maximum	19.7	19.7
	Treatment Duration		
	<=3 months	19 (14.5)	19 (15.7)
	>3 to <=6 months	19 (14.5)	18 (14.9)
	>6 to <=9 months	19 (14.5)	18 (14.9)
	>9 to <=12 months	36 (27.5)	33 (27.3)
	>12 to <=24 months	38 (29.0)	33 (27.3)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	131	121
	Mean	5.04	5.07
	Std. Dev.	0.564	0.493
	Median	5.30	5.30
	Minimum	2.9	3.1
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	27 (20.6)	26 (21.5)
	>6 to <=12 cycles	29 (22.1)	28 (23.1)
	>12 to <=18 cycles	53 (40.5)	48 (39.7)
	>18 to <=24 cycles	20 (15.3)	17 (14.0)
	>24 to <=30 cycles	2 (1.5)	2 (1.7)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
M-History of visceral disease	Yes		
Total number of subjects in subgroup category		169	154
Number (%) of subjects on treatment at data cut		73 (43.2)	63 (40.9)
Duration of Follow-up (months)			
n		169	154
Mean		10.9	10.7
Std. Dev.		3.42	3.44
Median		11.1	11.0
Minimum		0.7	0.7
Maximum		19.7	19.7
Treatment Duration			
<=3 months		26 (15.4)	26 (16.9)
>3 to <=6 months		25 (14.8)	24 (15.6)
>6 to <=9 months		26 (15.4)	24 (15.6)
>9 to <=12 months		46 (27.2)	40 (26.0)
>12 to <=24 months		46 (27.2)	40 (26.0)
>24 months		0	0
Dose Intensity (mg/kg/3 weeks)			
n		169	154
Mean		5.02	5.04
Std. Dev.		0.595	0.553
Median		5.30	5.30
Minimum		2.5	2.5
Maximum		5.6	5.6
Total Number of Cycles Initiated			
<=6 cycles		37 (21.9)	36 (23.4)
>6 to <=12 cycles		40 (23.7)	38 (24.7)
>12 to <=18 cycles		65 (38.5)	57 (37.0)
>18 to <=24 cycles		24 (14.2)	20 (13.0)
>24 to <=30 cycles		3 (1.8)	3 (1.9)
>30 cycles		0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
M-History of visceral disease	No		
	Total number of subjects in subgroup category Number (%) of subjects on treatment at data cut	15 6 (40.0)	15 6 (40.0)
	Duration of Follow-up (months)		
	n	15	15
	Mean	11.5	11.5
	Std. Dev.	3.71	3.71
	Median	11.7	11.7
	Minimum	3.9	3.9
	Maximum	19.9	19.9
	Treatment Duration		
	<=3 months	2 (13.3)	2 (13.3)
	>3 to <=6 months	3 (20.0)	3 (20.0)
	>6 to <=9 months	0	0
	>9 to <=12 months	6 (40.0)	6 (40.0)
	>12 to <=24 months	4 (26.7)	4 (26.7)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	15	15
	Mean	5.03	5.03
	Std. Dev.	0.464	0.464
	Median	5.10	5.10
	Minimum	3.8	3.8
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	2 (13.3)	2 (13.3)
	>6 to <=12 cycles	3 (20.0)	3 (20.0)
	>12 to <=18 cycles	7 (46.7)	7 (46.7)
	>18 to <=24 cycles	2 (13.3)	2 (13.3)
	>24 to <=30 cycles	1 (6.7)	1 (6.7)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
N-T-DM1 last therapy	Yes	Total number of subjects in subgroup category	
		Number (%) of subjects on treatment at data cut	
		56	51
		31 (55.4)	26 (51.0)
		Duration of Follow-up (months)	
		n	56
		Mean	11.0
		Std. Dev.	3.75
		Median	11.1
		Minimum	0.7
		Maximum	19.9
		Treatment Duration	
		<=3 months	7 (12.5)
		>3 to <=6 months	9 (16.1)
		>6 to <=9 months	5 (8.9)
		>9 to <=12 months	17 (30.4)
		>12 to <=24 months	18 (32.1)
		>24 months	0
		Dose Intensity (mg/kg/3 weeks)	
		n	56
		Mean	5.06
		Std. Dev.	0.487
		Median	5.25
		Minimum	3.3
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	8 (14.3)
		>6 to <=12 cycles	12 (21.4)
		>12 to <=18 cycles	22 (39.3)
		>18 to <=24 cycles	11 (19.6)
		>24 to <=30 cycles	3 (5.4)
		>30 cycles	0

Source Data: adam.adsl, adam.adex.

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Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
N-T-DM1 last therapy	No		
	Total number of subjects in subgroup category Number (%) of subjects on treatment at data cut	128 48 (37.5)	118 43 (36.4)
	Duration of Follow-up (months)		
	n	128	118
	Mean	10.9	10.8
	Std. Dev.	3.31	3.33
	Median	11.1	11.1
	Minimum	1.9	1.9
	Maximum	19.7	19.7
	Treatment Duration		
	<=3 months	21 (16.4)	21 (17.8)
	>3 to <=6 months	19 (14.8)	18 (15.3)
	>6 to <=9 months	21 (16.4)	19 (16.1)
	>9 to <=12 months	35 (27.3)	31 (26.3)
	>12 to <=24 months	32 (25.0)	29 (24.6)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	128	118
	Mean	5.00	5.02
	Std. Dev.	0.623	0.585
	Median	5.30	5.30
	Minimum	2.5	2.5
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	31 (24.2)	30 (25.4)
	>6 to <=12 cycles	31 (24.2)	29 (24.6)
	>12 to <=18 cycles	50 (39.1)	44 (37.3)
	>18 to <=24 cycles	15 (11.7)	14 (11.9)
	>24 to <=30 cycles	1 (0.8)	1 (0.8)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

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Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
0-Prior treatment lines	< 3 lines	Total number of subjects in subgroup category Number (%) of subjects on treatment at data cut	17 13 (76.5)
		15 11 (73.3)	
Duration of Follow-up (months)			
n		17	15
Mean		11.7	11.6
Std. Dev.		3.48	3.70
Median		11.3	11.3
Minimum		4.1	4.1
Maximum		19.9	19.9
Treatment Duration			
<=3 months		0	0
>3 to <=6 months		2 (11.8)	2 (13.3)
>6 to <=9 months		1 (5.9)	1 (6.7)
>9 to <=12 months		7 (41.2)	6 (40.0)
>12 to <=24 months		7 (41.2)	6 (40.0)
>24 months		0	0
Dose Intensity (mg/kg/3 weeks)			
n		17	15
Mean		4.91	4.85
Std. Dev.		0.576	0.589
Median		5.10	4.90
Minimum		3.3	3.3
Maximum		5.5	5.5
Total Number of Cycles Initiated			
<=6 cycles		1 (5.9)	1 (6.7)
>6 to <=12 cycles		1 (5.9)	1 (6.7)
>12 to <=18 cycles		10 (58.8)	9 (60.0)
>18 to <=24 cycles		4 (23.5)	3 (20.0)
>24 to <=30 cycles		1 (5.9)	1 (6.7)
>30 cycles		0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
0-Prior treatment lines	>= 3 lines		
Total number of subjects in subgroup category		167	154
Number (%) of subjects on treatment at data cut		66 (39.5)	58 (37.7)
Duration of Follow-up (months)			
n		167	154
Mean		10.9	10.7
Std. Dev.		3.44	3.44
Median		11.1	11.0
Minimum		0.7	0.7
Maximum		19.7	19.7
Treatment Duration			
<=3 months		28 (16.8)	28 (18.2)
>3 to <=6 months		26 (15.6)	25 (16.2)
>6 to <=9 months		25 (15.0)	23 (14.9)
>9 to <=12 months		45 (26.9)	40 (26.0)
>12 to <=24 months		43 (25.7)	38 (24.7)
>24 months		0	0
Dose Intensity (mg/kg/3 weeks)			
n		167	154
Mean		5.03	5.06
Std. Dev.		0.585	0.538
Median		5.30	5.30
Minimum		2.5	2.5
Maximum		5.6	5.6
Total Number of Cycles Initiated			
<=6 cycles		38 (22.8)	37 (24.0)
>6 to <=12 cycles		42 (25.1)	40 (26.0)
>12 to <=18 cycles		62 (37.1)	55 (35.7)
>18 to <=24 cycles		22 (13.2)	19 (12.3)
>24 to <=30 cycles		3 (1.8)	3 (1.9)
>30 cycles		0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
P-Best Response to T-DM1 therapy	CR/PR/SD		
	Total number of subjects in subgroup category Number (%) of subjects on treatment at data cut	79 36 (45.6)	70 30 (42.9)
	Duration of Follow-up (months)		
	n	79	70
	Mean	11.5	11.3
	Std. Dev.	2.81	2.77
	Median	11.1	11.1
	Minimum	3.9	3.9
	Maximum	19.9	19.9
	Treatment Duration		
	<=3 months	9 (11.4)	9 (12.9)
	>3 to <=6 months	9 (11.4)	9 (12.9)
	>6 to <=9 months	13 (16.5)	11 (15.7)
	>9 to <=12 months	22 (27.8)	20 (28.6)
	>12 to <=24 months	26 (32.9)	21 (30.0)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	79	70
	Mean	4.91	4.94
	Std. Dev.	0.683	0.639
	Median	5.20	5.20
	Minimum	2.5	2.5
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	11 (13.9)	11 (15.7)
	>6 to <=12 cycles	20 (25.3)	18 (25.7)
	>12 to <=18 cycles	33 (41.8)	29 (41.4)
	>18 to <=24 cycles	13 (16.5)	10 (14.3)
	>24 to <=30 cycles	2 (2.5)	2 (2.9)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
P-Best Response to T-DM1 therapy	PD		
	Total number of subjects in subgroup category Number (%) of subjects on treatment at data cut	66 26 (39.4)	64 25 (39.1)
	Duration of Follow-up (months)		
	n	66	64
	Mean	10.9	10.8
	Std. Dev.	3.87	3.93
	Median	11.1	11.1
	Minimum	2.4	2.4
	Maximum	19.7	19.7
	Treatment Duration		
	<=3 months	10 (15.2)	10 (15.6)
	>3 to <=6 months	11 (16.7)	11 (17.2)
	>6 to <=9 months	9 (13.6)	9 (14.1)
	>9 to <=12 months	21 (31.8)	19 (29.7)
	>12 to <=24 months	15 (22.7)	15 (23.4)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	66	64
	Mean	5.09	5.10
	Std. Dev.	0.458	0.456
	Median	5.30	5.30
	Minimum	3.5	3.5
	Maximum	5.5	5.5
	Total Number of Cycles Initiated		
	<=6 cycles	15 (22.7)	15 (23.4)
	>6 to <=12 cycles	15 (22.7)	15 (23.4)
	>12 to <=18 cycles	28 (42.4)	26 (40.6)
	>18 to <=24 cycles	6 (9.1)	6 (9.4)
	>24 to <=30 cycles	2 (3.0)	2 (3.1)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg	
Q-Prior pertuzumab	Yes	Total number of subjects in subgroup category	121	111
		Number (%) of subjects on treatment at data cut	56 (46.3)	50 (45.0)
		Duration of Follow-up (months)		
		n	121	111
		Mean	11.3	11.1
		Std. Dev.	3.50	3.49
		Median	11.1	11.1
		Minimum	2.4	2.4
		Maximum	19.9	19.9
		Treatment Duration		
		<=3 months	14 (11.6)	14 (12.6)
		>3 to <=6 months	20 (16.5)	19 (17.1)
		>6 to <=9 months	16 (13.2)	14 (12.6)
		>9 to <=12 months	35 (28.9)	33 (29.7)
		>12 to <=24 months	36 (29.8)	31 (27.9)
		>24 months	0	0
		Dose Intensity (mg/kg/3 weeks)		
		n	121	111
		Mean	5.00	5.02
		Std. Dev.	0.602	0.568
		Median	5.30	5.30
		Minimum	2.5	2.5
		Maximum	5.6	5.6
		Total Number of Cycles Initiated		
		<=6 cycles	25 (20.7)	24 (21.6)
		>6 to <=12 cycles	26 (21.5)	24 (21.6)
		>12 to <=18 cycles	48 (39.7)	45 (40.5)
		>18 to <=24 cycles	18 (14.9)	14 (12.6)
		>24 to <=30 cycles	4 (3.3)	4 (3.6)
		>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
Q-Prior pertuzumab	No		
	Total number of subjects in subgroup category Number (%) of subjects on treatment at data cut	63 23 (36.5)	58 19 (32.8)
	Duration of Follow-up (months)		
	n	63	58
	Mean	10.3	10.2
	Std. Dev.	3.24	3.36
	Median	11.0	11.0
	Minimum	0.7	0.7
	Maximum	16.0	16.0
	Treatment Duration		
	<=3 months	14 (22.2)	14 (24.1)
	>3 to <=6 months	8 (12.7)	8 (13.8)
	>6 to <=9 months	10 (15.9)	10 (17.2)
	>9 to <=12 months	17 (27.0)	13 (22.4)
	>12 to <=24 months	14 (22.2)	13 (22.4)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	63	58
	Mean	5.05	5.08
	Std. Dev.	0.550	0.499
	Median	5.30	5.30
	Minimum	3.1	3.4
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	14 (22.2)	14 (24.1)
	>6 to <=12 cycles	17 (27.0)	17 (29.3)
	>12 to <=18 cycles	24 (38.1)	19 (32.8)
	>18 to <=24 cycles	8 (12.7)	8 (13.8)
	>24 to <=30 cycles	0	0
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
R-Pertuzumab before line 3	Yes	51 25 (49.0)	47 22 (46.8)
Duration of Follow-up (months)			
n		51	47
Mean		10.9	10.8
Std. Dev.		3.21	3.32
Median		11.1	11.1
Minimum		3.9	3.9
Maximum		19.9	19.9
Treatment Duration			
<=3 months		5 (9.8)	5 (10.6)
>3 to <=6 months		10 (19.6)	9 (19.1)
>6 to <=9 months		7 (13.7)	7 (14.9)
>9 to <=12 months		17 (33.3)	16 (34.0)
>12 to <=24 months		12 (23.5)	10 (21.3)
>24 months		0	0
Dose Intensity (mg/kg/3 weeks)			
n		51	47
Mean		5.08	5.05
Std. Dev.		0.464	0.474
Median		5.30	5.30
Minimum		3.3	3.3
Maximum		5.5	5.5
Total Number of Cycles Initiated			
<=6 cycles		11 (21.6)	10 (21.3)
>6 to <=12 cycles		11 (21.6)	11 (23.4)
>12 to <=18 cycles		22 (43.1)	21 (44.7)
>18 to <=24 cycles		5 (9.8)	3 (6.4)
>24 to <=30 cycles		2 (3.9)	2 (4.3)
>30 cycles		0	0

Source Data: adam.adsl, adam.adex.

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Table T2EX ASB0: Duration of follow-up and exposure
Analysis Set: Enrolled Analysis Set

		Overall - EAS 5.4 mg/kg	Overall - RES 5.4 mg/kg
R-Pertuzumab before line 3	No		
	Total number of subjects in subgroup category Number (%) of subjects on treatment at data cut	133 54 (40.6)	122 47 (38.5)
	Duration of Follow-up (months)		
	n	133	122
	Mean	11.0	10.8
	Std. Dev.	3.53	3.53
	Median	11.1	11.1
	Minimum	0.7	0.7
	Maximum	19.7	19.7
	Treatment Duration		
	<=3 months	23 (17.3)	23 (18.9)
	>3 to <=6 months	18 (13.5)	18 (14.8)
	>6 to <=9 months	19 (14.3)	17 (13.9)
	>9 to <=12 months	35 (26.3)	30 (24.6)
	>12 to <=24 months	38 (28.6)	34 (27.9)
	>24 months	0	0
	Dose Intensity (mg/kg/3 weeks)		
	n	133	122
	Mean	4.99	5.03
	Std. Dev.	0.624	0.571
	Median	5.30	5.30
	Minimum	2.5	2.5
	Maximum	5.6	5.6
	Total Number of Cycles Initiated		
	<=6 cycles	28 (21.1)	28 (23.0)
	>6 to <=12 cycles	32 (24.1)	30 (24.6)
	>12 to <=18 cycles	50 (37.6)	43 (35.2)
	>18 to <=24 cycles	21 (15.8)	19 (15.6)
	>24 to <=30 cycles	2 (1.5)	2 (1.6)
	>30 cycles	0	0

Source Data: adam.adsl, adam.adex.

Gesamtüberleben (OS) – weitere Untersuchungen

Table T2OS_EST0: Overall Survival
 Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
A-Age classification 1 < 65 years (N=140)	
Overall Survival, months	
Subjects with events (%)	19 (13.6)
Subjects censored (%)	121 (86.4)
25th Percentile	NE
95% CI	(12.4, NE)
Median	NE
95% CI	(NE, NE)
Overall Survival at specific timepoints	
at 6 Months (%)	93.5
95% CI [a]	(87.8, 96.5)
at 12 Months (%)	85.6
95% CI [a]	(77.8, 90.8)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
 log-log transformation of rates was applied
 Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
A-Age classification 1 < 65 years (N=140)	
Overall Survival, months	
Subjects with events (%)	19 (13.6)
Subjects censored (%)	121 (86.4)
25th Percentile	NE
95% CI	(12.4, NE)
Median	NE
95% CI	(NE, NE)
Overall Survival at specific timepoints	
at 6 Months (%)	93.5
95% CI [a]	(87.8, 96.5)
at 12 Months (%)	85.6
95% CI [a]	(77.8, 90.8)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
 Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
A-Age classification 1 >= 65 years (N=44)	
Overall Survival, months	
Subjects with events (%)	6 (13.6)
Subjects censored (%)	38 (86.4)
25th Percentile	NE
95% CI	(10.4, NE)
Median	NE
95% CI	(NE, NE)
Overall Survival at specific timepoints	
at 6 Months (%)	95.3
95% CI [a]	(82.7, 98.8)
at 12 Months (%)	88.0
95% CI [a]	(73.5, 94.8)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
 log-log transformation of rates was applied
 Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
A-Age classification 1 >= 65 years (N=44)	
Overall Survival, months	
Subjects with events (%)	6 (13.6)
Subjects censored (%)	38 (86.4)
25th Percentile	NE
95% CI	(10.4, NE)
Median	NE
95% CI	(NE, NE)
Overall Survival at specific timepoints	
at 6 Months (%)	95.3
95% CI [a]	(82.7, 98.8)
at 12 Months (%)	88.0
95% CI [a]	(73.5, 94.8)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
B-Region	Asia (N=63)	
	Overall Survival, months	
	Subjects with events (%)	6 (9.5)
	Subjects censored (%)	57 (90.5)
	25th Percentile	NE
	95% CI	(12.4, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	98.4
	95% CI [a]	(89.3, 99.8)
	at 12 Months (%)	90.7
	95% CI [a]	(78.7, 96.1)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
B-Region	North America (N=53)	Overall Survival, months
		Subjects with events (%)
		Subjects censored (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Overall Survival at specific timepoints
		at 6 Months (%)
		95% CI [a]
		at 12 Months (%)
		95% CI [a]
		at 24 Months (%)
		95% CI [a]

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
B-Region	EU (N=68)	
	Overall Survival, months	
	Subjects with events (%)	13 (19.1)
	Subjects censored (%)	55 (80.9)
	25th Percentile	12.6
	95% CI	(6.7, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	90.8
	95% CI [a]	(80.7, 95.8)
	at 12 Months (%)	81.0
	95% CI [a]	(69.0, 88.8)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
C-ECOG performance status	Status 0 (N=102)	
	Overall Survival, months	
	Subjects with events (%)	11 (10.8)
	Subjects censored (%)	91 (89.2)
	25th Percentile	NE
	95% CI	(12.6, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	97.0
	95% CI [a]	(91.0, 99.0)
	at 12 Months (%)	90.3
	95% CI [a]	(82.1, 94.9)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
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Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
C-ECOG performance status	Status 1 (N=81)	
	Overall Survival, months	
	Subjects with events (%)	13 (16.0)
	Subjects censored (%)	68 (84.0)
	25th Percentile	NE
	95% CI	(10.2, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	91.2
	95% CI [a]	(82.4, 95.7)
	at 12 Months (%)	81.8
	95% CI [a]	(70.1, 89.2)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions	< 5 cm (N=74)	Overall Survival, months
		Subjects with events (%)
		Subjects censored (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Overall Survival at specific timepoints
		at 6 Months (%)
		95% CI [a]
		at 12 Months (%)
		95% CI [a]
		at 24 Months (%)
		95% CI [a]

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions	>= 5 cm (N=95)	Overall Survival, months
		Subjects with events (%)
		Subjects censored (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Overall Survival at specific timepoints
		at 6 Months (%)
		95% CI [a]
		at 12 Months (%)
		95% CI [a]
		at 24 Months (%)
		95% CI [a]

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
E-HER2 Status	IHC3+ (N=154)	
	Overall Survival, months	
	Subjects with events (%)	20 (13.0)
	Subjects censored (%)	134 (87.0)
	25th Percentile	NE
	95% CI	(NE, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	94.7
	95% CI [a]	(89.8, 97.3)
	at 12 Months (%)	87.1
	95% CI [a]	(80.2, 91.8)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	
	Overall Survival, months	
	Subjects with events (%)	4 (14.3)
	Subjects censored (%)	24 (85.7)
	25th Percentile	NE
	95% CI	(5.5, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	92.6
	95% CI [a]	(73.5, 98.1)
	at 12 Months (%)	83.5
	95% CI [a]	(61.3, 93.6)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
F-Estrogen receptors	Positive (N=93)	Overall Survival, months
		Subjects with events (%)
		Subjects censored (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Overall Survival at specific timepoints
		at 6 Months (%)
		95% CI [a]
		at 12 Months (%)
		95% CI [a]
		at 24 Months (%)
		95% CI [a]

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
F-Estrogen receptors	Negative (N=88)	Overall Survival, months
		Subjects with events (%)
		Subjects censored (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Overall Survival at specific timepoints
		at 6 Months (%)
		95% CI [a]
		at 12 Months (%)
		95% CI [a]
		at 24 Months (%)
		95% CI [a]

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Positive (N=51)	
	Overall Survival, months	
	Subjects with events (%)	6 (11.8)
	Subjects censored (%)	45 (88.2)
	25th Percentile	NE
	95% CI	(12.4, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	94.1
	95% CI [a]	(82.7, 98.1)
	at 12 Months (%)	89.4
	95% CI [a]	(76.1, 95.5)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Negative (N=125)	
	Overall Survival, months	
	Subjects with events (%)	18 (14.4)
	Subjects censored (%)	107 (85.6)
	25th Percentile	NE
	95% CI	(12.6, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	94.3
	95% CI [a]	(88.3, 97.2)
	at 12 Months (%)	84.8
	95% CI [a]	(76.5, 90.3)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
H-Hormone receptors	Positive (N=97)	
	Overall Survival, months	
	Subjects with events (%)	13 (13.4)
	Subjects censored (%)	84 (86.6)
	25th Percentile	NE
	95% CI	(12.4, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	93.8
	95% CI [a]	(86.6, 97.1)
	at 12 Months (%)	86.9
	95% CI [a]	(77.1, 92.7)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
H-Hormone receptors	Negative (N=83)	
	Overall Survival, months	
	Subjects with events (%)	11 (13.3)
	Subjects censored (%)	72 (86.7)
	25th Percentile	NE
	95% CI	(NE, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	95.0
	95% CI [a]	(87.3, 98.1)
	at 12 Months (%)	85.6
	95% CI [a]	(75.4, 91.8)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
I-Renal impairment	Normal (N=90)	Overall Survival, months
		Subjects with events (%)
		Subjects censored (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Overall Survival at specific timepoints
		at 6 Months (%)
		95% CI [a]
		at 12 Months (%)
		95% CI [a]
		at 24 Months (%)
		95% CI [a]

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
I-Renal impairment	Mild (N=69)	
	Overall Survival, months	
	Subjects with events (%)	7 (10.1)
	Subjects censored (%)	62 (89.9)
	25th Percentile	NE
	95% CI	(12.4, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	97.1
	95% CI [a]	(88.8, 99.3)
	at 12 Months (%)	92.0
	95% CI [a]	(81.8, 96.6)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
I-Renal impairment	Moderate (N=25)	Overall Survival, months
		Subjects with events (%)
		Subjects censored (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Overall Survival at specific timepoints
		at 6 Months (%)
		95% CI [a]
		at 12 Months (%)
		95% CI [a]
		at 24 Months (%)
		95% CI [a]

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
J-Hepatic impairment	Normal (N=105)	
	Overall Survival, months	
	Subjects with events (%)	12 (11.4)
	Subjects censored (%)	93 (88.6)
	25th Percentile	NE
	95% CI	(NE, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	94.2
	95% CI [a]	(87.5, 97.3)
	at 12 Months (%)	88.3
	95% CI [a]	(79.6, 93.4)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
J-Hepatic impairment	Mild (N=76)	
	Overall Survival, months	
	Subjects with events (%)	12 (15.8)
	Subjects censored (%)	64 (84.2)
	25th Percentile	NE
	95% CI	(10.4, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	94.7
	95% CI [a]	(86.4, 98.0)
	at 12 Months (%)	84.2
	95% CI [a]	(73.2, 91.0)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
K-Brain metastases	Yes (N=24)	
	Overall Survival, months	
	Subjects with events (%)	2 (8.3)
	Subjects censored (%)	22 (91.7)
	25th Percentile	NE
	95% CI	(1.9, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	91.1
	95% CI [a]	(68.8, 97.7)
	at 12 Months (%)	91.1
	95% CI [a]	(68.8, 97.7)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
K-Brain metastases	No (N=160)	Overall Survival, months	
		Subjects with events (%)	23 (14.4)
		Subjects censored (%)	137 (85.6)
		25th Percentile	NE
		95% CI	(12.6, NE)
		Median	NE
		95% CI	(NE, NE)
		Overall Survival at specific timepoints	
		at 6 Months (%)	94.3
		95% CI [a]	(89.4, 97.0)
		at 12 Months (%)	85.5
		95% CI [a]	(78.5, 90.4)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
L-Bone metastases	Yes (N=53)	Overall Survival, months	
		Subjects with events (%)	10 (18.9)
		Subjects censored (%)	43 (81.1)
		25th Percentile	NE
		95% CI	(7.4, NE)
		Median	NE
		95% CI	(NE, NE)
		Overall Survival at specific timepoints	
		at 6 Months (%)	90.2
		95% CI [a]	(78.1, 95.8)
		at 12 Months (%)	80.8
		95% CI [a]	(65.9, 89.6)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup	No (N=131)	Overall - EAS (5.4 mg/kg)
L-Bone metastases		
		Overall Survival, months
		Subjects with events (%)
		Subjects censored (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Overall Survival at specific timepoints
		at 6 Months (%)
		95% CI [a]
		at 12 Months (%)
		95% CI [a]
		at 24 Months (%)
		95% CI [a]

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
M-History of visceral disease Yes (N=169)	
Overall Survival, months	
Subjects with events (%)	24 (14.2)
Subjects censored (%)	145 (85.8)
25th Percentile	NE
95% CI	(12.6, NE)
Median	NE
95% CI	(NE, NE)
Overall Survival at specific timepoints	
at 6 Months (%)	94.0
95% CI [a]	(89.1, 96.7)
at 12 Months (%)	85.5
95% CI [a]	(78.7, 90.3)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
M-History of visceral disease	
No (N=15)	
Overall Survival, months	
Subjects with events (%)	1 (6.7)
Subjects censored (%)	14 (93.3)
25th Percentile	NE
95% CI	(3.9, NE)
Median	NE
95% CI	(NE, NE)
Overall Survival at specific timepoints	
at 6 Months (%)	93.3
95% CI [a]	(61.3, 99.0)
at 12 Months (%)	93.3
95% CI [a]	(61.3, 99.0)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
N-T-DM1 last therapy	Yes (N=56)	
	Overall Survival, months	
	Subjects with events (%)	4 (7.1)
	Subjects censored (%)	52 (92.9)
	25th Percentile	NE
	95% CI	(NE, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	96.2
	95% CI [a]	(85.7, 99.0)
	at 12 Months (%)	92.1
	95% CI [a]	(80.3, 97.0)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
N-T-DM1 last therapy	No (N=128)	
	Overall Survival, months	
	Subjects with events (%)	21 (16.4)
	Subjects censored (%)	107 (83.6)
	25th Percentile	NE
	95% CI	(12.4, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	92.9
	95% CI [a]	(86.9, 96.3)
	at 12 Months (%)	83.8
	95% CI [a]	(75.5, 89.4)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
0-Prior treatment lines < 3 lines (N=17)	
Overall Survival, months	
Subjects with events (%)	1 (5.9)
Subjects censored (%)	16 (94.1)
25th Percentile	NE
95% CI	(4.1, NE)
Median	NE
95% CI	(NE, NE)
Overall Survival at specific timepoints	
at 6 Months (%)	94.1
95% CI [a]	(65.0, 99.1)
at 12 Months (%)	94.1
95% CI [a]	(65.0, 99.1)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
0-Prior treatment lines >= 3 lines (N=167)	
Overall Survival, months	
Subjects with events (%)	24 (14.4)
Subjects censored (%)	143 (85.6)
25th Percentile	NE
95% CI	(12.6, NE)
Median	NE
95% CI	(NE, NE)
Overall Survival at specific timepoints	
at 6 Months (%)	93.9
95% CI [a]	(88.9, 96.7)
at 12 Months (%)	85.3
95% CI [a]	(78.4, 90.2)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup	CR/PR/SD (N=79)	Overall Survival, months	Overall - EAS (5.4 mg/kg)
P-Best Response to T-DM1 therapy			
		Subjects with events (%)	6 (7.6)
		Subjects censored (%)	73 (92.4)
		25th Percentile	NE
		95% CI	(NE, NE)
		Median	NE
		95% CI	(NE, NE)
		Overall Survival at specific timepoints	
		at 6 Months (%)	97.5
		95% CI [a]	(90.3, 99.4)
		at 12 Months (%)	90.9
		95% CI [a]	(80.3, 95.9)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup	PD (N=66)	Overall Survival, months	Overall - EAS (5.4 mg/kg)
P-Best Response to T-DM1 therapy			
		Subjects with events (%)	10 (15.2)
		Subjects censored (%)	56 (84.8)
		25th Percentile	NE
		95% CI	(10.2, NE)
		Median	NE
		95% CI	(NE, NE)
		Overall Survival at specific timepoints	
		at 6 Months (%)	90.7
		95% CI [a]	(80.4, 95.7)
		at 12 Months (%)	85.5
		95% CI [a]	(73.9, 92.2)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
Q-Prior pertuzumab	Yes (N=121)	Overall Survival, months	
		Subjects with events (%)	15 (12.4)
		Subjects censored (%)	106 (87.6)
		25th Percentile	NE
		95% CI	(12.6, NE)
		Median	NE
		95% CI	(NE, NE)
		Overall Survival at specific timepoints	
		at 6 Months (%)	95.8
		95% CI [a]	(90.2, 98.2)
		at 12 Months (%)	87.6
		95% CI [a]	(79.4, 92.7)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
Q-Prior pertuzumab	No (N=63)	
	Overall Survival, months	
	Subjects with events (%)	10 (15.9)
	Subjects censored (%)	53 (84.1)
	25th Percentile	NE
	95% CI	(7.4, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	90.3
	95% CI [a]	(79.7, 95.5)
	at 12 Months (%)	83.3
	95% CI [a]	(71.1, 90.7)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
R-Pertuzumab before line 3	Yes (N=51)	
	Overall Survival, months	
	Subjects with events (%)	10 (19.6)
	Subjects censored (%)	41 (80.4)
	25th Percentile	12.6
	95% CI	(7.6, NE)
	Median	NE
	95% CI	(NE, NE)
	Overall Survival at specific timepoints	
	at 6 Months (%)	92.2
	95% CI [a]	(80.4, 97.0)
	at 12 Months (%)	81.8
	95% CI [a]	(67.8, 90.1)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2OS_EST0: Overall Survival
Enrolled Analysis Set

Subgroup	No (N=133)	Overall Survival, months	Overall - EAS (5.4 mg/kg)
R-Pertuzumab before line 3			
		Subjects with events (%)	15 (11.3)
		Subjects censored (%)	118 (88.7)
		25th Percentile	NE
		95% CI	(NE, NE)
		Median	NE
		95% CI	(NE, NE)
		Overall Survival at specific timepoints	
		at 6 Months (%)	94.6
		95% CI [a]	(89.0, 97.4)
		at 12 Months (%)	87.9
		95% CI [a]	(80.1, 92.7)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Progressionsfreies Überleben (PFS) – weitere Untersuchungen

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
A-Age classification 1	< 65 years (N=140)	Progression Free Survival, months	
		Subjects with events (%)	46 (32.9)
		Subjects censored (%)	94 (67.1)
		25th Percentile	6.8
		95% CI	(5.4, 9.7)
		Median	17.6
		95% CI	(12.3, 18.1)
		Progression Free Survival at specific timepoints	
		at 6 Months (%)	78.7
		95% CI [a]	(70.2, 85.0)
		at 12 Months (%)	62.0
		95% CI [a]	(51.9, 70.6)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
A-Age classification 1	>= 65 years (N=44)	Progression Free Survival, months	
		Subjects with events (%)	12 (27.3)
		Subjects censored (%)	32 (72.7)
		25th Percentile	9.9
		95% CI	(4.3, 16.4)
		Median	16.4
		95% CI	(12.7, NE)
		Progression Free Survival at specific timepoints	
		at 6 Months (%)	87.9
		95% CI [a]	(73.4, 94.8)
		at 12 Months (%)	73.7
		95% CI [a]	(56.2, 85.0)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
B-Region	Asia (N=63)	
	Progression Free Survival, months	
	Subjects with events (%)	20 (31.7)
	Subjects censored (%)	43 (68.3)
	25th Percentile	6.7
	95% CI	(4.4, 16.4)
	Median	18.1
	95% CI	(16.4, NE)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	80.7
	95% CI [a]	(67.9, 88.8)
	at 12 Months (%)	65.3
	95% CI [a]	(50.3, 76.7)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
B-Region	North America (N=53)	
	Progression Free Survival, months	
	Subjects with events (%)	13 (24.5)
	Subjects censored (%)	40 (75.5)
	25th Percentile	9.9
	95% CI	(4.3, 17.6)
	Median	17.6
	95% CI	(12.7, NE)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	84.3
	95% CI [a]	(69.8, 92.2)
	at 12 Months (%)	73.4
	95% CI [a]	(56.8, 84.5)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
B-Region	EU (N=68)	
	Progression Free Survival, months	
	Subjects with events (%)	25 (36.8)
	Subjects censored (%)	43 (63.2)
	25th Percentile	6.8
	95% CI	(4.2, 8.3)
	Median	15.2
	95% CI	(9.6, 15.2)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	78.7
	95% CI [a]	(66.2, 87.1)
	at 12 Months (%)	58.7
	95% CI [a]	(44.0, 70.7)
	at 24 Months (%)	0.0
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
C-ECOG performance status	Status 0 (N=102)	Progression Free Survival, months	
		Subjects with events (%)	32 (31.4)
		Subjects censored (%)	70 (68.6)
		25th Percentile	9.7
		95% CI	(6.6, 12.7)
		Median	17.6
		95% CI	(12.7, 18.1)
		Progression Free Survival at specific timepoints	
		at 6 Months (%)	86.5
		95% CI [a]	(77.8, 91.9)
		at 12 Months (%)	68.0
		95% CI [a]	(56.5, 77.0)
		at 24 Months (%)	0.0
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
C-ECOG performance status	Status 1 (N=81)	Progression Free Survival, months	
		Subjects with events (%)	25 (30.9)
		Subjects censored (%)	56 (69.1)
		25th Percentile	6.0
		95% CI	(4.1, 8.5)
		Median	16.4
		95% CI	(10.6, NE)
		Progression Free Survival at specific timepoints	
		at 6 Months (%)	74.1
		95% CI [a]	(61.6, 83.1)
		at 12 Months (%)	61.2
		95% CI [a]	(47.6, 72.3)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions < 5 cm (N=74)	
Progression Free Survival, months	
Subjects with events (%)	16 (21.6)
Subjects censored (%)	58 (78.4)
25th Percentile	10.5
95% CI	(5.6, NE)
Median	NE
95% CI	(15.2, NE)
Progression Free Survival at specific timepoints	
at 6 Months (%)	84.2
95% CI [a]	(72.6, 91.2)
at 12 Months (%)	73.6
95% CI [a]	(59.5, 83.4)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

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Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions >= 5 cm (N=95)	
Progression Free Survival, months	
Subjects with events (%)	40 (42.1)
Subjects censored (%)	55 (57.9)
25th Percentile	6.7
95% CI	(4.3, 8.3)
Median	12.7
95% CI	(8.5, 17.6)
Progression Free Survival at specific timepoints	
at 6 Months (%)	75.3
95% CI [a]	(64.7, 83.2)
at 12 Months (%)	54.5
95% CI [a]	(42.3, 65.2)
at 24 Months (%)	0.0
95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
E-HER2 Status	IHC3+ (N=154)	
	Progression Free Survival, months	
	Subjects with events (%)	44 (28.6)
	Subjects censored (%)	110 (71.4)
	25th Percentile	8.1
	95% CI	(6.2, 12.7)
	Median	17.6
	95% CI	(16.4, NE)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	82.7
	95% CI [a]	(75.3, 88.1)
	at 12 Months (%)	68.4
	95% CI [a]	(59.2, 75.9)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
E-HER2 Status	
ISH+ EXCEPT IHC3+ (N=28)	
Progression Free Survival, months	
Subjects with events (%)	12 (42.9)
Subjects censored (%)	16 (57.1)
25th Percentile	5.1
95% CI	(2.7, 9.7)
Median	12.3
95% CI	(6.6, 15.2)
Progression Free Survival at specific timepoints	
at 6 Months (%)	74.2
95% CI [a]	(51.3, 87.5)
at 12 Months (%)	52.3
95% CI [a]	(28.9, 71.3)
at 24 Months (%)	0.0
95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
F-Estrogen receptors	Positive (N=93)	
	Progression Free Survival, months	
	Subjects with events (%)	32 (34.4)
	Subjects censored (%)	61 (65.6)
	25th Percentile	7.0
	95% CI	(4.8, 9.9)
	Median	15.2
	95% CI	(10.6, NE)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	79.6
	95% CI [a]	(69.3, 86.8)
	at 12 Months (%)	60.9
	95% CI [a]	(48.2, 71.3)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
F-Estrogen receptors	Negative (N=88)	Progression Free Survival, months
		Subjects with events (%)
		Subjects censored (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Progression Free Survival at specific timepoints
		at 6 Months (%)
		95% CI [a]
		at 12 Months (%)
		95% CI [a]
		at 24 Months (%)
		95% CI [a]

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Positive (N=51)	
	Progression Free Survival, months	
	Subjects with events (%)	17 (33.3)
	Subjects censored (%)	34 (66.7)
	25th Percentile	8.3
	95% CI	(4.1, 15.2)
	Median	15.2
	95% CI	(12.3, NE)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	83.0
	95% CI [a]	(68.9, 91.1)
	at 12 Months (%)	66.9
	95% CI [a]	(50.0, 79.2)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Negative (N=125)	Progression Free Survival, months	
		Subjects with events (%)	37 (29.6)
		Subjects censored (%)	88 (70.4)
		25th Percentile	7.0
		95% CI	(5.4, 10.6)
		Median	17.6
		95% CI	(12.7, NE)
		Progression Free Survival at specific timepoints	
		at 6 Months (%)	79.9
		95% CI [a]	(71.1, 86.3)
		at 12 Months (%)	66.3
		95% CI [a]	(55.9, 74.8)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
H-Hormone receptors	Positive (N=97)	
	Progression Free Survival, months	
	Subjects with events (%)	33 (34.0)
	Subjects censored (%)	64 (66.0)
	25th Percentile	7.0
	95% CI	(4.4, 9.9)
	Median	15.2
	95% CI	(10.6, NE)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	79.4
	95% CI [a]	(69.3, 86.5)
	at 12 Months (%)	61.8
	95% CI [a]	(49.6, 71.9)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
H-Hormone receptors	Negative (N=83)	
	Progression Free Survival, months	
	Subjects with events (%)	23 (27.7)
	Subjects censored (%)	60 (72.3)
	25th Percentile	8.5
	95% CI	(5.4, 17.6)
	Median	17.6
	95% CI	(12.7, NE)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	83.5
	95% CI [a]	(72.7, 90.3)
	at 12 Months (%)	70.4
	95% CI [a]	(57.8, 79.9)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
I-Renal impairment	Normal (N=90)	
	Progression Free Survival, months	
	Subjects with events (%)	36 (40.0)
	Subjects censored (%)	54 (60.0)
	25th Percentile	6.6
	95% CI	(4.3, 9.7)
	Median	15.2
	95% CI	(9.9, NE)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	77.4
	95% CI [a]	(66.8, 84.9)
	at 12 Months (%)	57.6
	95% CI [a]	(45.5, 68.0)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
I-Renal impairment	Mild (N=69)	
	Progression Free Survival, months	
	Subjects with events (%)	15 (21.7)
	Subjects censored (%)	54 (78.3)
	25th Percentile	12.7
	95% CI	(6.2, NE)
	Median	NE
	95% CI	(12.7, NE)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	86.7
	95% CI [a]	(75.2, 93.1)
	at 12 Months (%)	76.7
	95% CI [a]	(63.1, 85.9)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
I-Renal impairment	Moderate (N=25)	
	Progression Free Survival, months	
	Subjects with events (%)	7 (28.0)
	Subjects censored (%)	18 (72.0)
	25th Percentile	8.5
	95% CI	(2.4, 18.1)
	Median	18.1
	95% CI	(8.5, 18.1)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	78.5
	95% CI [a]	(52.0, 91.4)
	at 12 Months (%)	55.8
	95% CI [a]	(22.3, 79.7)
	at 24 Months (%)	0.0
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
J-Hepatic impairment	Normal (N=105)	
	Progression Free Survival, months	
	Subjects with events (%)	30 (28.6)
	Subjects censored (%)	75 (71.4)
	25th Percentile	9.6
	95% CI	(6.2, 15.2)
	Median	17.6
	95% CI	(15.2, NE)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	85.2
	95% CI [a]	(76.3, 91.0)
	at 12 Months (%)	69.6
	95% CI [a]	(58.3, 78.4)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
J-Hepatic impairment	Mild (N=76)	
	Progression Free Survival, months	
	Subjects with events (%)	26 (34.2)
	Subjects censored (%)	50 (65.8)
	25th Percentile	6.7
	95% CI	(4.3, 9.7)
	Median	12.7
	95% CI	(9.7, NE)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	77.1
	95% CI [a]	(64.8, 85.5)
	at 12 Months (%)	59.9
	95% CI [a]	(46.0, 71.4)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
K-Brain metastases	Yes (N=24)	
	Progression Free Survival, months	
	Subjects with events (%)	9 (37.5)
	Subjects censored (%)	15 (62.5)
	25th Percentile	6.7
	95% CI	(1.4, 18.1)
	Median	18.1
	95% CI	(6.7, 18.1)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	77.6
	95% CI [a]	(54.3, 90.0)
	at 12 Months (%)	61.8
	95% CI [a]	(37.5, 79.0)
	at 24 Months (%)	0.0
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
K-Brain metastases	No (N=160)	Progression Free Survival, months	
		Subjects with events (%)	49 (30.6)
		Subjects censored (%)	111 (69.4)
		25th Percentile	7.2
		95% CI	(5.7, 10.5)
		Median	16.4
		95% CI	(12.7, NE)
		Progression Free Survival at specific timepoints	
		at 6 Months (%)	81.5
		95% CI [a]	(74.0, 87.0)
		at 12 Months (%)	65.4
		95% CI [a]	(56.2, 73.2)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
L-Bone metastases	Yes (N=53)	
	Progression Free Survival, months	
	Subjects with events (%)	19 (35.8)
	Subjects censored (%)	34 (64.2)
	25th Percentile	7.2
	95% CI	(4.3, 10.6)
	Median	16.4
	95% CI	(9.9, NE)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	78.3
	95% CI [a]	(63.4, 87.7)
	at 12 Months (%)	60.5
	95% CI [a]	(44.0, 73.5)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
L-Bone metastases	No (N=131)	Progression Free Survival, months	
		Subjects with events (%)	39 (29.8)
		Subjects censored (%)	92 (70.2)
		25th Percentile	7.1
		95% CI	(5.4, 12.7)
		Median	17.6
		95% CI	(12.7, NE)
		Progression Free Survival at specific timepoints	
		at 6 Months (%)	82.1
		95% CI [a]	(73.9, 88.0)
		at 12 Months (%)	67.0
		95% CI [a]	(56.8, 75.3)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
M-History of visceral disease	Yes (N=169)	Progression Free Survival, months
		Subjects with events (%)
		Subjects censored (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Progression Free Survival at specific timepoints
		at 6 Months (%)
		95% CI [a]
		at 12 Months (%)
		95% CI [a]
		at 24 Months (%)
		95% CI [a]

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
M-History of visceral disease	No (N=15)	
	Progression Free Survival, months	
	Subjects with events (%)	2 (13.3)
	Subjects censored (%)	13 (86.7)
	25th Percentile	12.3
	95% CI	(9.7, NE)
	Median	NE
	95% CI	(9.7, NE)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	100.0
	95% CI [a]	(NE, NE)
	at 12 Months (%)	87.5
	95% CI [a]	(38.7, 98.1)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
N-T-DM1 last therapy	Yes (N=56)	Progression Free Survival, months	
		Subjects with events (%)	12 (21.4)
		Subjects censored (%)	44 (78.6)
		25th Percentile	17.6
		95% CI	(5.4, NE)
		Median	17.6
		95% CI	(17.6, NE)
		Progression Free Survival at specific timepoints	
		at 6 Months (%)	84.3
		95% CI [a]	(71.0, 91.8)
		at 12 Months (%)	76.2
		95% CI [a]	(60.7, 86.3)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
N-T-DM1 last therapy	No (N=128)	Progression Free Survival, months	
		Subjects with events (%)	46 (35.9)
		Subjects censored (%)	82 (64.1)
		25th Percentile	6.7
		95% CI	(4.8, 8.5)
		Median	15.2
		95% CI	(10.6, 18.1)
		Progression Free Survival at specific timepoints	
		at 6 Months (%)	79.7
		95% CI [a]	(71.0, 86.0)
		at 12 Months (%)	60.1
		95% CI [a]	(49.6, 69.1)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
0-Prior treatment lines	< 3 lines (N=17)	Progression Free Survival, months	
		Subjects with events (%)	2 (11.8)
		Subjects censored (%)	15 (88.2)
		25th Percentile	NE
		95% CI	(4.1, NE)
		Median	NE
		95% CI	(NE, NE)
		Progression Free Survival at specific timepoints	
		at 6 Months (%)	88.2
		95% CI [a]	(60.6, 96.9)
		at 12 Months (%)	88.2
		95% CI [a]	(60.6, 96.9)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
0-Prior treatment lines	>= 3 lines (N=167)	Progression Free Survival, months	
		Subjects with events (%)	56 (33.5)
		Subjects censored (%)	111 (66.5)
		25th Percentile	7.0
		95% CI	(5.6, 9.7)
		Median	15.2
		95% CI	(12.7, 18.1)
		Progression Free Survival at specific timepoints	
		at 6 Months (%)	80.2
		95% CI [a]	(72.8, 85.8)
		at 12 Months (%)	61.9
		95% CI [a]	(52.7, 69.8)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	
	Progression Free Survival, months	
	Subjects with events (%)	23 (29.1)
	Subjects censored (%)	56 (70.9)
	25th Percentile	8.3
	95% CI	(6.7, 15.2)
	Median	16.4
	95% CI	(15.2, NE)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	87.4
	95% CI [a]	(77.1, 93.2)
	at 12 Months (%)	66.0
	95% CI [a]	(52.2, 76.6)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
P-Best Response to T-DM1 therapy	PD (N=66)	
	Progression Free Survival, months	
	Subjects with events (%)	25 (37.9)
	Subjects censored (%)	41 (62.1)
	25th Percentile	6.6
	95% CI	(4.3, 9.7)
	Median	17.6
	95% CI	(9.9, NE)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	75.1
	95% CI [a]	(62.2, 84.2)
	at 12 Months (%)	61.6
	95% CI [a]	(47.5, 73.0)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
Q-Prior pertuzumab	Yes (N=121)	
	Progression Free Survival, months	
	Subjects with events (%)	37 (30.6)
	Subjects censored (%)	84 (69.4)
	25th Percentile	8.3
	95% CI	(5.4, 12.3)
	Median	17.6
	95% CI	(12.7, NE)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	81.4
	95% CI [a]	(72.6, 87.6)
	at 12 Months (%)	67.4
	95% CI [a]	(56.8, 75.9)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
Q-Prior pertuzumab	No (N=63)	
	Progression Free Survival, months	
	Subjects with events (%)	21 (33.3)
	Subjects censored (%)	42 (66.7)
	25th Percentile	7.0
	95% CI	(4.3, 9.7)
	Median	15.2
	95% CI	(9.7, 15.2)
	Progression Free Survival at specific timepoints	
	at 6 Months (%)	80.2
	95% CI [a]	(67.1, 88.6)
	at 12 Months (%)	60.1
	95% CI [a]	(44.7, 72.4)
	at 24 Months (%)	0.0
	95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
R-Pertuzumab before line 3	Yes (N=51)	Progression Free Survival, months	
		Subjects with events (%)	14 (27.5)
		Subjects censored (%)	37 (72.5)
		25th Percentile	8.5
		95% CI	(4.2, 17.6)
		Median	17.6
		95% CI	(12.3, NE)
		Progression Free Survival at specific timepoints	
		at 6 Months (%)	80.2
		95% CI [a]	(65.3, 89.1)
		at 12 Months (%)	72.6
		95% CI [a]	(56.7, 83.5)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2PFS_EST0: Progression Free Survival
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
R-Pertuzumab before line 3	No (N=133)	Progression Free Survival, months	
		Subjects with events (%)	44 (33.1)
		Subjects censored (%)	89 (66.9)
		25th Percentile	7.0
		95% CI	(5.7, 9.9)
		Median	15.2
		95% CI	(12.7, NE)
		Progression Free Survival at specific timepoints	
		at 6 Months (%)	81.4
		95% CI [a]	(73.0, 87.3)
		at 12 Months (%)	62.0
		95% CI [a]	(51.6, 70.7)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Tumoransprechen – weitere Untersuchungen

Beste prozentuale Veränderung des Tumordurchmessers (BPC)

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 01Aug2019

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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
A-Age classification 1	< 65 years (N=140)	Baseline	
		n	129
		Mean	66.4
		Std. Dev.	43.23
		Median	57.0
		95% CI	(46.0,66.0)
		Min, Max	12,245
		Best % Change from Baseline	
		n	129
		Mean	-53.4
		Std. Dev.	30.80
		Median	-56.0
		95% CI	(-65.0,-47.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
A-Age classification 1	>= 65 years (N=44)	Baseline	
		n	40
		Mean	70.5
		Std. Dev.	48.67
		Median	54.0
		95% CI	(42.0,72.0)
		Min, Max	16,209
		Best % Change from Baseline	
		n	39
		Mean	-52.2
		Std. Dev.	28.11
		Median	-51.0
		95% CI	(-63.0,-39.0)
		Min, Max	-100,0

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
B-Region	Asia (N=63)	Baseline	
		n	57
		Mean	68.5
		Std. Dev.	42.85
		Median	59.0
		95% CI	(45.0,68.0)
		Min, Max	12,187
		Best % Change from Baseline	
		n	57
		Mean	-51.4
		Std. Dev.	33.00
		Median	-54.0
		95% CI	(-65.0,-39.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
B-Region	EU (N=68)	Baseline	
		n	63
		Mean	69.8
		Std. Dev.	46.98
		Median	57.0
		95% CI	(45.0, 68.0)
		Min, Max	15, 245
		Best % Change from Baseline	
		n	62
		Mean	-54.7
		Std. Dev.	29.62
		Median	-56.5
		95% CI	(-66.0, -44.0)
		Min, Max	-100, 0

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
B-Region	North America (N=53)	Baseline	
		n	49
		Mean	63.0
		Std. Dev.	43.56
		Median	54.0
		95% CI	(39.0,70.0)
		Min, Max	14,209
		Best % Change from Baseline	
		n	49
		Mean	-53.1
		Std. Dev.	27.63
		Median	-55.0
		95% CI	(-70.0,-42.0)
		Min, Max	-100,-3

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
C-ECOG performance status	Status 0 (N=102)	Baseline	
		n	92
		Mean	57.9
		Std. Dev.	37.73
		Median	49.0
		95% CI	(42.0,60.0)
		Min, Max	14,187
		Best % Change from Baseline	
		n	91
		Mean	-55.2
		Std. Dev.	28.83
		Median	-59.0
		95% CI	(-67.0,-49.0)
		Min, Max	-100,2

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
C-ECOG performance status	Status 1 (N=81)	Baseline	
		n	76
		Mean	79.1
		Std. Dev.	49.46
		Median	65.0
		95% CI	(54.0,82.0)
		Min, Max	12,245
		Best % Change from Baseline	
		n	76
		Mean	-50.6
		Std. Dev.	31.79
		Median	-49.5
		95% CI	(-63.0,-39.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions	< 5 cm (N=74)	Baseline	
		n	74
		Mean	31.5
		Std. Dev.	11.03
		Median	34.0
		95% CI	(26.0,39.0)
		Min, Max	12,49
		Best % Change from Baseline	
		n	73
		Mean	-54.9
		Std. Dev.	32.94
		Median	-56.0
		95% CI	(-68.0,-42.0)
		Min, Max	-100,2

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions	>= 5 cm (N=95)	Baseline	
		n	95
		Mean	95.3
		Std. Dev.	40.47
		Median	81.0
		95% CI	(71.0,95.0)
		Min, Max	50,245
		Best % Change from Baseline	
		n	95
		Mean	-51.7
		Std. Dev.	27.86
		Median	-52.0
		95% CI	(-63.0,-45.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
E-HER2 Status	IHC3+ (N=154)	Baseline	
		n	142
		Mean	69.0
		Std. Dev.	47.05
		Median	54.0
		95% CI	(45.0, 65.0)
		Min, Max	12, 245
		Best % Change from Baseline	
		n	142
		Mean	-54.7
		Std. Dev.	30.47
		Median	-57.5
		95% CI	(-64.0, -49.0)
		Min, Max	-100, 22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Baseline	
		n	25
		Mean	59.6
		Std. Dev.	26.39
		Median	66.0
		95% CI	(45.0,72.0)
		Min, Max	14,99
		Best % Change from Baseline	
		n	24
		Mean	-44.7
		Std. Dev.	28.20
		Median	-43.0
		95% CI	(-65.0,-20.0)
		Min, Max	-100,2

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

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Program Name: T2BPC_ESC0.sas
Run Date: 28AUG20:17:46

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
F-Estrogen receptors	Negative (N=88)	Baseline	
		n	82
		Mean	70.0
		Std. Dev.	50.11
		Median	59.5
		95% CI	(43.0,66.0)
		Min, Max	15,245
		Best % Change from Baseline	
		n	81
		Mean	-56.7
		Std. Dev.	27.30
		Median	-59.0
		95% CI	(-67.0,-50.0)
		Min, Max	-100,0

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
F-Estrogen receptors	Positive (N=93)	Baseline	
		n	84
		Mean	64.4
		Std. Dev.	38.75
		Median	54.0
		95% CI	(46.0,67.0)
		Min, Max	12,162
	Best % Change from Baseline		
		n	84
		Mean	-50.9
		Std. Dev.	32.06
		Median	-52.0
		95% CI	(-65.0,-42.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 01Aug2019

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Program Name: T2BPC_ESC0.sas
Run Date: 28AUG20:17:46

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Negative (N=125)	Baseline	
		n	115
		Mean	70.5
		Std. Dev.	47.53
		Median	57.0
		95% CI	(45.0,66.0)
		Min, Max	15,245
	Best % Change from Baseline		
		n	114
		Mean	-54.9
		Std. Dev.	30.71
		Median	-59.0
		95% CI	(-66.0,-49.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 01Aug2019

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Program Name: T2BPC_ESC0.sas
Run Date: 28AUG20:17:46

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Positive (N=51)	Baseline	
		n	46
		Mean	60.9
		Std. Dev.	37.69
		Median	54.0
		95% CI	(43.0,71.0)
		Min, Max	12,152
	Best % Change from Baseline		
		n	46
		Mean	-53.1
		Std. Dev.	28.47
		Median	-54.5
		95% CI	(-67.0,-43.0)
		Min, Max	-100,2

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 01Aug2019

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Program Name: T2BPC_ESC0.sas
Run Date: 28AUG20:17:46

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
H-Hormone receptors	Negative (N=83)	Baseline	
		n	78
		Mean	71.8
		Std. Dev.	50.56
		Median	62.5
		95% CI	(43.0,68.0)
		Min, Max	16,245
	Best % Change from Baseline	n	77
		Mean	-56.5
		Std. Dev.	27.21
		Median	-59.0
		95% CI	(-67.0,-49.0)
		Min, Max	-100,0

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 01Aug2019

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Program Name: T2BPC_ESC0.sas
Run Date: 28AUG20:17:46

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
H-Hormone receptors	Positive (N=97)	Baseline	
		n	87
		Mean	63.1
		Std. Dev.	38.79
		Median	54.0
		95% CI	(45.0,66.0)
		Min, Max	12,162
		Best % Change from Baseline	
		n	87
		Mean	-51.3
		Std. Dev.	32.16
		Median	-53.0
		95% CI	(-65.0,-42.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 01Aug2019

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Program Name: T2BPC_ESC0.sas
Run Date: 28AUG20:17:46

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
I-Renal impairment	Mild (N=69)	Baseline	
		n	61
		Mean	66.1
		Std. Dev.	39.22
		Median	65.0
		95% CI	(52.0,70.0)
		Min, Max	12,196
		Best % Change from Baseline	
		n	61
		Mean	-56.1
		Std. Dev.	31.71
		Median	-59.0
		95% CI	(-72.0,-45.0)
		Min, Max	-100,6

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
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Program Name: T2BPC_ESC0.sas
Run Date: 28AUG20:17:46

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
I-Renal impairment	Moderate (N=25)	Baseline	
		n	24
		Mean	70.4
		Std. Dev.	52.53
		Median	48.5
		95% CI	(37.0,116.0)
		Min, Max	17,209
		Best % Change from Baseline	
		n	23
		Mean	-40.1
		Std. Dev.	28.54
		Median	-35.0
		95% CI	(-61.0,-21.0)
		Min, Max	-91,9

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 01Aug2019

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Program Name: T2BPC_ESC0.sas
Run Date: 28AUG20:17:46

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
I-Renal impairment	Normal (N=90)	Baseline	
		n	84
		Mean	67.4
		Std. Dev.	46.05
		Median	53.5
		95% CI	(43.0, 64.0)
		Min, Max	14, 245
		Best % Change from Baseline	
		n	84
		Mean	-54.5
		Std. Dev.	28.76
		Median	-57.0
		95% CI	(-65.0, -47.0)
		Min, Max	-100, 22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 01Aug2019

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Program Name: T2BPC_ESC0.sas
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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
J-Hepatic impairment	Mild (N=76)	Baseline	
		n	72
		Mean	73.2
		Std. Dev.	51.61
		Median	63.0
		95% CI	(46.0, 68.0)
		Min, Max	12, 245
		Best % Change from Baseline	
		n	71
		Mean	-48.5
		Std. Dev.	30.83
		Median	-52.0
		95% CI	(-61.0, -37.0)
		Min, Max	-100, 22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 01Aug2019

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Program Name: T2BPC_ESC0.sas
Run Date: 28AUG20:17:46

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
J-Hepatic impairment	Normal (N=105)	Baseline	
		n	94
		Mean	62.4
		Std. Dev.	37.71
		Median	52.5
		95% CI	(43.0,66.0)
		Min, Max	14,159
		Best % Change from Baseline	
		n	94
		Mean	-56.9
		Std. Dev.	28.91
		Median	-58.5
		95% CI	(-66.0,-48.0)
		Min, Max	-100,9

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
K-Brain metastases	No (N=160)	Baseline	
		n	147
		Mean	66.4
		Std. Dev.	44.82
		Median	54.0
		95% CI	(46.0,64.0)
		Min, Max	14,245
		Best % Change from Baseline	
		n	147
		Mean	-53.7
		Std. Dev.	30.46
		Median	-57.0
		95% CI	(-63.0,-49.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 01Aug2019

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Program Name: T2BPC_ESC0.sas
Run Date: 28AUG20:17:46

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
K-Brain metastases	Yes (N=24)	Baseline	
		n	22
		Mean	74.0
		Std. Dev.	42.39
		Median	63.5
		95% CI	(43.0,99.0)
		Min, Max	12,151
		Best % Change from Baseline	
		n	21
		Mean	-49.2
		Std. Dev.	27.95
		Median	-44.0
		95% CI	(-72.0,-30.0)
		Min, Max	-100,-5

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 01Aug2019

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Program Name: T2BPC_ESC0.sas
Run Date: 28AUG20:17:46

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
L-Bone metastases	No (N=131)	Baseline	
		n	121
		Mean	64.2
		Std. Dev.	42.96
		Median	54.0
		95% CI	(45.0,65.0)
		Min, Max	12,245
		Best % Change from Baseline	
		n	121
		Mean	-54.5
		Std. Dev.	29.28
		Median	-56.0
		95% CI	(-65.0,-48.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 01Aug2019

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Program Name: T2BPC_ESC0.sas
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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
L-Bone metastases	Yes (N=53)	Baseline	
		n	48
		Mean	75.3
		Std. Dev.	47.61
		Median	61.0
		95% CI	(45.0,72.0)
		Min, Max	14,209
		Best % Change from Baseline	
		n	47
		Mean	-49.5
		Std. Dev.	32.22
		Median	-53.0
		95% CI	(-67.0,-36.0)
		Min, Max	-100,9

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 01Aug2019

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Program Name: T2BPC_ESC0.sas
Run Date: 28AUG20:17:46

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
M-History of visceral disease	No (N=15)	Baseline	
		n	15
		Mean	37.5
		Std. Dev.	25.51
		Median	30.0
		95% CI	(17.0,46.0)
		Min, Max	14,95
		Best % Change from Baseline	
		n	15
		Mean	-55.8
		Std. Dev.	29.16
		Median	-61.0
		95% CI	(-72.0,-29.0)
		Min, Max	-100,0

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 01Aug2019

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Program Name: T2BPC_ESC0.sas
Run Date: 28AUG20:17:46

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
M-History of visceral disease	Yes (N=169)	Baseline	
		n	154
		Mean	70.3
		Std. Dev.	44.89
		Median	61.0
		95% CI	(52.0,66.0)
		Min, Max	12,245
		Best % Change from Baseline	
		n	153
		Mean	-52.9
		Std. Dev.	30.29
		Median	-54.0
		95% CI	(-62.0,-46.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 01Aug2019

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Program Name: T2BPC_ESC0.sas
Run Date: 28AUG20:17:46

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
N-T-DM1 last therapy	No (N=128)	Baseline	
		n	118
		Mean	75.0
		Std. Dev.	47.94
		Median	64.5
		95% CI	(54.0,71.0)
		Min, Max	14,245
		Best % Change from Baseline	
		n	118
		Mean	-51.4
		Std. Dev.	29.66
		Median	-55.5
		95% CI	(-62.0,-44.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
N-T-DM1 last therapy	Yes (N=56)	Baseline	
		n	51
		Mean	49.7
		Std. Dev.	28.43
		Median	43.0
		95% CI	(40.0,50.0)
		Min, Max	12,148
		Best % Change from Baseline	
		n	50
		Mean	-57.1
		Std. Dev.	31.12
		Median	-55.0
		95% CI	(-67.0,-45.0)
		Min, Max	-100,6

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
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Program Name: T2BPC_ESC0.sas
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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
O-Prior treatment lines	< 3 lines (N=17)	Baseline	
		n	15
		Mean	40.6
		Std. Dev.	19.73
		Median	42.0
		95% CI	(23.0,50.0)
		Min, Max	16,81
		Best % Change from Baseline	
		n	15
		Mean	-60.5
		Std. Dev.	25.85
		Median	-62.0
		95% CI	(-78.0,-46.0)
		Min, Max	-100,0

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
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Program Name: T2BPC_ESC0.sas
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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
0-Prior treatment lines	>= 3 lines (N=167)	Baseline	
		n	154
		Mean	70.0
		Std. Dev.	45.36
		Median	62.5
		95% CI	(52.0,66.0)
		Min, Max	12,245
		Best % Change from Baseline	
		n	153
		Mean	-52.4
		Std. Dev.	30.48
		Median	-54.0
		95% CI	(-61.0,-45.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
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Data Cut Date: 01Aug2019

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Program Name: T2BPC_ESC0.sas
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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Baseline	
		n	70
		Mean	62.0
		Std. Dev.	41.44
		Median	47.5
		95% CI	(43.0,66.0)
		Min, Max	12,196
	Best % Change from Baseline		
		n	70
		Mean	-52.5
		Std. Dev.	32.10
		Median	-57.0
		95% CI	(-67.0,-43.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
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Program Name: T2BPC_ESC0.sas
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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
P-Best Response to T-DM1 therapy	PD (N=66)	Baseline	
		n	64
		Mean	71.8
		Std. Dev.	45.64
		Median	63.5
		95% CI	(47.0,79.0)
		Min, Max	15,209
		Best % Change from Baseline	
		n	64
		Mean	-55.2
		Std. Dev.	27.66
		Median	-56.5
		95% CI	(-68.0,-46.0)
		Min, Max	-100,-3

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
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Program Name: T2BPC_ESC0.sas
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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
Q-Prior pertuzumab	No (N=63)	Baseline	
		n	58
		Mean	64.5
		Std. Dev.	43.95
		Median	53.0
		95% CI	(43.0,66.0)
		Min, Max	12,196
		Best % Change from Baseline	
		n	57
		Mean	-50.2
		Std. Dev.	32.09
		Median	-48.0
		95% CI	(-61.0,-37.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Daiichi Sankyo, Inc.
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Program Name: T2BPC_ESC0.sas
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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
Q-Prior pertuzumab	Yes (N=121)	Baseline	
		n	111
		Mean	68.9
		Std. Dev.	44.85
		Median	59.0
		95% CI	(47.0, 68.0)
		Min, Max	14, 245
		Best % Change from Baseline	
		n	111
		Mean	-54.6
		Std. Dev.	29.10
		Median	-57.0
		95% CI	(-65.0, -49.0)
		Min, Max	-100, 9

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

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Program Name: T2BPC_ESC0.sas
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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

Subgroup	No (N=133)	Baseline	Overall - EAS (5.4 mg/kg)
R-Pertuzumab before line 3		n	122
		Mean	66.6
		Std. Dev.	43.33
		Median	54.5
		95% CI	(46.0,65.0)
		Min, Max	12,196
		Best % Change from Baseline	
		n	121
		Mean	-51.2
		Std. Dev.	31.20
		Median	-48.0
		95% CI	(-59.0,-42.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

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Program Name: T2BPC_ESC0.sas
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Table T2BPC_ESC0: Summary of best percentage change in sum of diameters
Enrolled Analysis Set

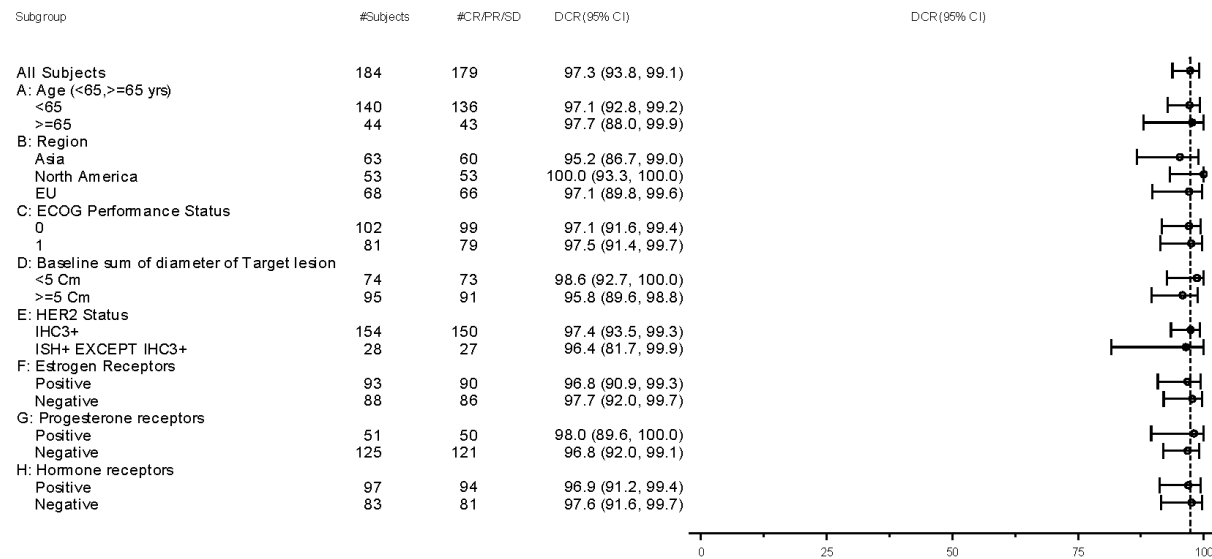
Subgroup			Overall - EAS (5.4 mg/kg)
R-Pertuzumab before line 3	Yes (N=51)	Baseline	
		n	47
		Mean	69.4
		Std. Dev.	47.69
		Median	59.0
		95% CI	(43.0,79.0)
		Min, Max	15,245
		Best % Change from Baseline	
		n	47
		Mean	-58.0
		Std. Dev.	26.85
		Median	-62.0
		95% CI	(-70.0,-56.0)
		Min, Max	-100,2

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date

Source Data: adam.adtr

Rate der Krankheitskontrolle (DCR)

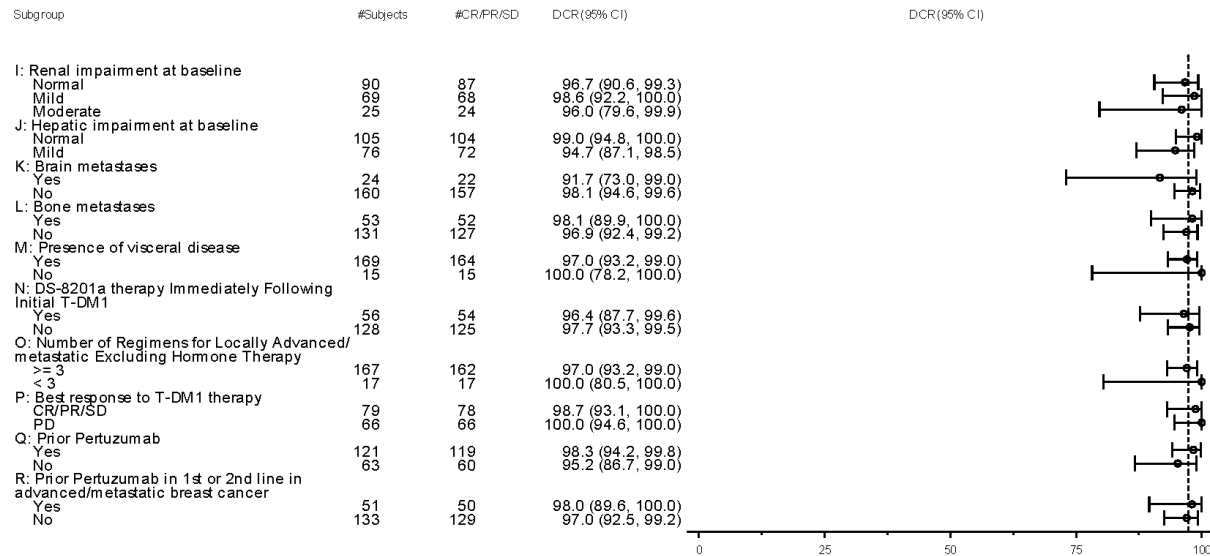
Figure F2DCR_ESP0: Forest plot of Disease Control Rate by Subgroups
Enrolled Analysis Set



Notes: CR=Complete Response, PR=Partial Response, SD=Stable Disease, DCR = disease control rate rate (% of subjects with best overall response of CR, PR and SD with confirmation by independent central review, based on RECIST criteria, Version 1.1).
The 2-sided 95% confidence intervals are based on the exact (Clopper-Pearson) binomial distribution.

Source Data: adam.adrs

Figure F2DCR_ESP0: Forest plot of Disease Control Rate by Subgroups
Enrolled Analysis Set



Notes: CR=Complete Response, PR=Partial Response, SD=Stable Disease, DCR = disease control rate rate (% of subjects with best overall response of CR, PR and SD with confirmation by independent central review, based on RECIST criteria, Version 1.1).
The 2-sided 95% confidence intervals are based on the exact (Clopper-Pearson) binomial distribution.

Source Data: adam.adrs

Zeit bis zum Ansprechen (TTR)

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
A-Age classification 1	< 65 years (N=140)	Time to Response, months	
		Subjects with events	85
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.5
A-Age classification 1	>= 65 years (N=44)	95% CI	(1.4, 2.6)
		Time to Response, months	
		Subjects with events	27
		25th Percentile	1.3
		95% CI	(1.2, 1.4)
		Median	2.6
		95% CI	(1.3, 2.8)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
B-Region	Asia (N=63)	Time to Response, months	
		Subjects with events	37
		25th Percentile	1.4
		95% CI	(1.2, 1.4)
		Median	2.6
		95% CI	(1.4, 2.8)
B-Region	North America (N=53)	Time to Response, months	
		Subjects with events	33
		25th Percentile	1.4
		95% CI	(1.2, 1.4)
		Median	1.5
		95% CI	(1.4, 2.7)
B-Region	EU (N=68)	Time to Response, months	
		Subjects with events	42
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.9
		95% CI	(1.4, 2.7)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
C-ECOG performance status	Status 0 (N=102)	Time to Response, months	
		Subjects with events	67
		25th Percentile	1.4
		95% CI	(1.3, 1.5)
		Median	2.6
		95% CI	(1.5, 2.8)
C-ECOG performance status	Status 1 (N=81)	Time to Response, months	
		Subjects with events	45
		25th Percentile	1.3
		95% CI	(1.2, 1.4)
		Median	1.4
		95% CI	(1.4, 1.6)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions	< 5 cm (N=74)	Time to Response, months	
		Subjects with events	47
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.4
		95% CI	(1.4, 2.6)
D-Baseline sum of diameters of target lesions	>= 5 cm (N=95)	Time to Response, months	
		Subjects with events	64
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	2.6
		95% CI	(1.4, 2.7)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
E-HER2 Status	IHC3+ (N=154)	Time to Response, months	
		Subjects with events	97
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.6
		95% CI	(1.4, 2.7)
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Time to Response, months	
		Subjects with events	13
		25th Percentile	1.4
		95% CI	(1.2, 1.4)
		Median	1.4
		95% CI	(1.3, 2.7)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
F-Estrogen receptors	Positive (N=93)	Time to Response, months	
		Subjects with events	54
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.5
F-Estrogen receptors	Negative (N=88)	95% CI	(1.4, 2.6)
		Time to Response, months	
		Subjects with events	58
		25th Percentile	1.4
		95% CI	(1.2, 1.4)
		Median	2.6
		95% CI	(1.4, 2.7)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Positive (N=51)	Time to Response, months	
		Subjects with events	31
		25th Percentile	1.3
		95% CI	(1.3, 1.4)
		Median	1.4
G-Progesterone receptors	Negative (N=125)	95% CI	(1.4, 2.6)
		Time to Response, months	
		Subjects with events	79
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	2.6
		95% CI	(1.4, 2.7)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
H-Hormone receptors	Positive (N=97)	Time to Response, months Subjects with events	56
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.5
		95% CI	(1.4, 2.6)
H-Hormone receptors	Negative (N=83)	Time to Response, months Subjects with events	55
		25th Percentile	1.4
		95% CI	(1.2, 1.4)
		Median	2.6
		95% CI	(1.4, 2.7)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
I-Renal impairment	Normal (N=90)	Time to Response, months	
		Subjects with events	59
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.6
I-Renal impairment	Mild (N=69)	95% CI	(1.4, 2.6)
		Time to Response, months	
		Subjects with events	44
		25th Percentile	1.3
		95% CI	(1.2, 1.4)
I-Renal impairment	Moderate (N=25)	Median	2.1
		95% CI	(1.4, 2.8)
		Time to Response, months	
		Subjects with events	9
		25th Percentile	1.4
		95% CI	(1.2, 1.5)
		Median	1.5
		95% CI	(1.2, 2.8)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
J-Hepatic impairment	Normal (N=105)	Time to Response, months	
		Subjects with events	68
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.5
J-Hepatic impairment	Mild (N=76)	95% CI	(1.4, 2.7)
		Time to Response, months	
		Subjects with events	43
		25th Percentile	1.3
		95% CI	(1.2, 1.4)
		Median	2.6
		95% CI	(1.4, 2.7)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
K-Brain metastases	Yes (N=24)	Time to Response, months	
		Subjects with events	14
		25th Percentile	1.3
		95% CI	(1.2, 2.8)
		Median	2.8
K-Brain metastases	No (N=160)	95% CI	(1.3, 4.1)
		Time to Response, months	
		Subjects with events	98
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.5
		95% CI	(1.4, 2.6)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
L-Bone metastases	Yes (N=53)	Time to Response, months	
		Subjects with events	29
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	2.6
L-Bone metastases	No (N=131)	95% CI	(1.4, 2.8)
		Time to Response, months	
		Subjects with events	83
		25th Percentile	1.3
		95% CI	(1.3, 1.4)
		Median	1.5
		95% CI	(1.4, 2.7)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
M-History of visceral disease	Yes (N=169)	Time to Response, months	
		Subjects with events	102
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.6
M-History of visceral disease	No (N=15)	95% CI	(1.4, 2.7)
		Time to Response, months	
		Subjects with events	10
		25th Percentile	1.4
		95% CI	(1.2, 2.6)
		Median	2.1
		95% CI	(1.2, 2.7)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
N-T-DM1 last therapy	Yes (N=56)	Time to Response, months	
		Subjects with events	36
		25th Percentile	1.4
		95% CI	(1.2, 1.4)
		Median	2.6
N-T-DM1 last therapy	No (N=128)	95% CI	(1.4, 2.7)
		Time to Response, months	
		Subjects with events	76
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.5
		95% CI	(1.4, 2.6)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
0-Prior treatment lines	< 3 lines (N=17)	Time to Response, months	
		Subjects with events	13
		25th Percentile	1.2
		95% CI	(1.2, 1.4)
		Median	1.4
0-Prior treatment lines	>= 3 lines (N=167)	95% CI	(1.2, 2.6)
		Time to Response, months	
		Subjects with events	99
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	2.3
		95% CI	(1.4, 2.7)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Time to Response, months	
		Subjects with events	47
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.5
P-Best Response to T-DM1 therapy	PD (N=66)	95% CI	(1.4, 2.7)
		Time to Response, months	
		Subjects with events	44
		25th Percentile	1.3
		95% CI	(1.2, 1.4)
		Median	1.4
		95% CI	(1.4, 2.7)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
Q-Prior pertuzumab	Yes (N=121)	Time to Response, months	
		Subjects with events	78
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	2.0
Q-Prior pertuzumab	No (N=63)	95% CI	(1.4, 2.7)
		Time to Response, months	
		Subjects with events	34
		25th Percentile	1.4
		95% CI	(1.2, 1.4)
		Median	1.5
		95% CI	(1.4, 2.7)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2TTR_EST0: Time to Response
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
R-Pertuzumab before line 3	Yes (N=51)	Time to Response, months	
		Subjects with events	38
		25th Percentile	1.3
		95% CI	(1.2, 1.4)
		Median	1.4
R-Pertuzumab before line 3	No (N=133)	95% CI	(1.4, 2.6)
		Time to Response, months	
		Subjects with events	74
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	2.6
		95% CI	(1.5, 2.7)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Dauer des Ansprechens (DoR)

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
A-Age classification 1 < 65 years (N=140)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	85
Subjects with events (%)	22 (25.9)
Subjects censored (%)	63 (74.1)
Ongoing without PD (%)	39 (45.9)
Other (%)	24 (28.2)
25th Percentile	8.3
95% CI	(5.6, 14.8)
Median	14.8
95% CI	(13.8, NE)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	81.9
95% CI [a]	(70.8, 89.1)
at 12 Months (%)	67.8
95% CI [a]	(52.8, 78.9)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
A-Age classification 1 >= 65 years (N=44)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	27
Subjects with events (%)	7 (25.9)
Subjects censored (%)	20 (74.1)
Ongoing without PD (%)	14 (51.9)
Other (%)	6 (22.2)
25th Percentile	8.5
95% CI	(4.2, 15.0)
Median	15.0
95% CI	(8.5, 15.0)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	79.9
95% CI [a]	(58.1, 91.1)
at 12 Months (%)	73.7
95% CI [a]	(49.7, 87.5)
at 24 Months (%)	0.0
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
B-Region	Asia (N=63)	Duration of Response (CR or PR), months
		Subjects with CR/PR
		Subjects with events (%)
		Subjects censored (%)
		Ongoing without PD (%)
		Other (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Duration of Response (CR or PR) at specific timepoints
		at 6 Months (%)
		95% CI [a]
		at 12 Months (%)
		95% CI [a]
		at 24 Months (%)
		95% CI [a]

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
B-Region	
North America (N=53)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	33
Subjects with events (%)	8 (24.2)
Subjects censored (%)	25 (75.8)
Ongoing without PD (%)	17 (51.5)
Other (%)	8 (24.2)
25th Percentile	8.5
95% CI	(2.9, 14.8)
Median	14.8
95% CI	(8.5, 14.8)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	83.0
95% CI [a]	(63.9, 92.6)
at 12 Months (%)	72.6
95% CI [a]	(49.8, 86.3)
at 24 Months (%)	0.0
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
B-Region	EU (N=68)	
	Duration of Response (CR or PR), months	
	Subjects with CR/PR	42
	Subjects with events (%)	12 (28.6)
	Subjects censored (%)	30 (71.4)
	Ongoing without PD (%)	20 (47.6)
	Other (%)	10 (23.8)
	25th Percentile	9.0
	95% CI	(4.5, 13.8)
	Median	13.8
	95% CI	(9.0, 13.8)
	Duration of Response (CR or PR) at specific timepoints	
	at 6 Months (%)	78.4
	95% CI [a]	(61.3, 88.6)
	at 12 Months (%)	59.4
	95% CI [a]	(33.9, 77.9)
	at 24 Months (%)	0.0
	95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
 Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)	
C-ECOG performance status	Status 0 (N=102)	Duration of Response (CR or PR), months
		Subjects with CR/PR
		Subjects with events (%)
		Subjects censored (%)
		Ongoing without PD (%)
		Other (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Duration of Response (CR or PR) at specific timepoints
		at 6 Months (%)
		95% CI [a]
		at 12 Months (%)
		95% CI [a]
		at 24 Months (%)
		95% CI [a]

Figure is considering only patients with response
 Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
 log-log transformation of rates was applied
 Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)	
C-ECOG performance status	Status 1 (N=81)	Duration of Response (CR or PR), months
		Subjects with CR/PR
		Subjects with events (%)
		Subjects censored (%)
		Ongoing without PD (%)
		Other (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Duration of Response (CR or PR) at specific timepoints
		at 6 Months (%)
		95% CI [a]
		at 12 Months (%)
		95% CI [a]
		at 24 Months (%)
		95% CI [a]

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions	
< 5 cm (N=74)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	47
Subjects with events (%)	7 (14.9)
Subjects censored (%)	40 (85.1)
Ongoing without PD (%)	25 (53.2)
Other (%)	15 (31.9)
25th Percentile	13.8
95% CI	(8.3, NE)
Median	13.8
95% CI	(13.8, NE)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	90.1
95% CI [a]	(75.5, 96.2)
at 12 Months (%)	81.1
95% CI [a]	(61.0, 91.5)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions	
>= 5 cm (N=95)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	64
Subjects with events (%)	22 (34.4)
Subjects censored (%)	42 (65.6)
Ongoing without PD (%)	27 (42.2)
Other (%)	15 (23.4)
25th Percentile	5.7
95% CI	(4.5, 9.7)
Median	14.8
95% CI	(8.5, 16.9)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	74.9
95% CI [a]	(61.3, 84.4)
at 12 Months (%)	60.8
95% CI [a]	(44.3, 73.8)
at 24 Months (%)	0.0
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
E-HER2 Status	IHC3+ (N=154)		
Duration of Response (CR or PR), months			
Subjects with CR/PR		97	
Subjects with events (%)		21 (21.6)	
Subjects censored (%)		76 (78.4)	
Ongoing without PD (%)		49 (50.5)	
Other (%)		27 (27.8)	
25th Percentile		9.0	
95% CI		(5.7, 15.0)	
Median		15.0	
95% CI		(14.8, NE)	
Duration of Response (CR or PR) at specific timepoints			
at 6 Months (%)		84.3	
95% CI [a]		(74.5, 90.6)	
at 12 Months (%)		75.0	
95% CI [a]		(62.4, 83.9)	
at 24 Months (%)		NE	
95% CI [a]		(NE, NE)	

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
E-HER2 Status	
ISH+ EXCEPT IHCR3+ (N=28)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	13
Subjects with events (%)	6 (46.2)
Subjects censored (%)	7 (53.8)
Ongoing without PD (%)	4 (30.8)
Other (%)	3 (23.1)
25th Percentile	3.7
95% CI	(2.8, 13.8)
Median	9.7
95% CI	(2.9, 13.8)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	74.1
95% CI [a]	(39.1, 90.9)
at 12 Months (%)	47.6
95% CI [a]	(13.8, 75.7)
at 24 Months (%)	0.0
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
 Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
F-Estrogen receptors	
Positive (N=93)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	54
Subjects with events (%)	15 (27.8)
Subjects censored (%)	39 (72.2)
Ongoing without PD (%)	22 (40.7)
Other (%)	17 (31.5)
25th Percentile	7.9
95% CI	(5.4, 13.8)
Median	13.8
95% CI	(9.7, 15.0)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	79.9
95% CI [a]	(64.8, 89.1)
at 12 Months (%)	65.4
95% CI [a]	(46.4, 79.0)
at 24 Months (%)	0.0
95% CI [a]	(NE, NE)

Figure is considering only patients with response
 Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
 log-log transformation of rates was applied
 Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
 Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
F-Estrogen receptors	
Negative (N=88)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	58
Subjects with events (%)	14 (24.1)
Subjects censored (%)	44 (75.9)
Ongoing without PD (%)	31 (53.4)
Other (%)	13 (22.4)
25th Percentile	8.5
95% CI	(5.6, 16.9)
Median	14.8
95% CI	(14.8, NE)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	82.5
95% CI [a]	(69.1, 90.5)
at 12 Months (%)	73.6
95% CI [a]	(57.2, 84.5)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Figure is considering only patients with response
 Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
 log-log transformation of rates was applied
 Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Positive (N=51)	Duration of Response (CR or PR), months	Overall - EAS (5.4 mg/kg)
G-Progesterone receptors		Subjects with CR/PR	31
		Subjects with events (%)	11 (35.5)
		Subjects censored (%)	20 (64.5)
		Ongoing without PD (%)	12 (38.7)
		Other (%)	8 (25.8)
		25th Percentile	5.6
		95% CI	(4.4, 13.8)
		Median	13.8
		95% CI	(5.7, 15.0)
		Duration of Response (CR or PR) at specific timepoints	
		at 6 Months (%)	70.2
		95% CI [a]	(48.9, 83.9)
		at 12 Months (%)	64.8
		95% CI [a]	(42.5, 80.2)
		at 24 Months (%)	0.0
		95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Negative (N=125)	
	Duration of Response (CR or PR), months	
	Subjects with CR/PR	79
	Subjects with events (%)	17 (21.5)
	Subjects censored (%)	62 (78.5)
	Ongoing without PD (%)	40 (50.6)
	Other (%)	22 (27.8)
	25th Percentile	9.0
	95% CI	(5.7, 16.9)
	Median	14.8
	95% CI	(14.8, NE)
	Duration of Response (CR or PR) at specific timepoints	
	at 6 Months (%)	85.3
	95% CI [a]	(74.3, 91.8)
	at 12 Months (%)	72.3
	95% CI [a]	(56.8, 83.1)
	at 24 Months (%)	NE
	95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
H-Hormone receptors	
Positive (N=97)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	56
Subjects with events (%)	15 (26.8)
Subjects censored (%)	41 (73.2)
Ongoing without PD (%)	23 (41.1)
Other (%)	18 (32.1)
25th Percentile	9.0
95% CI	(5.4, 15.0)
Median	13.8
95% CI	(9.7, 15.0)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	80.8
95% CI [a]	(66.2, 89.5)
at 12 Months (%)	67.4
95% CI [a]	(49.2, 80.2)
at 24 Months (%)	0.0
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
H-Hormone receptors	
Negative (N=83)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	55
Subjects with events (%)	14 (25.5)
Subjects censored (%)	41 (74.5)
Ongoing without PD (%)	29 (52.7)
Other (%)	12 (21.8)
25th Percentile	8.5
95% CI	(5.6, 16.9)
Median	14.8
95% CI	(14.8, NE)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	81.5
95% CI [a]	(67.3, 89.9)
at 12 Months (%)	71.8
95% CI [a]	(54.7, 83.4)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
I-Renal impairment	Normal (N=90)	Duration of Response (CR or PR), months
		Subjects with CR/PR
		Subjects with events (%)
		Subjects censored (%)
		Ongoing without PD (%)
		Other (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Duration of Response (CR or PR) at specific timepoints
		at 6 Months (%)
		95% CI [a]
		at 12 Months (%)
		95% CI [a]
		at 24 Months (%)
		95% CI [a]

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
I-Renal impairment	Mild (N=69)	
	Duration of Response (CR or PR), months	
	Subjects with CR/PR	44
	Subjects with events (%)	7 (15.9)
	Subjects censored (%)	37 (84.1)
	Ongoing without PD (%)	21 (47.7)
	Other (%)	16 (36.4)
	25th Percentile	15.0
	95% CI	(5.6, 15.0)
	Median	15.0
	95% CI	(NE, NE)
	Duration of Response (CR or PR) at specific timepoints	
	at 6 Months (%)	89.1
	95% CI [a]	(73.3, 95.8)
	at 12 Months (%)	81.2
	95% CI [a]	(61.9, 91.3)
	at 24 Months (%)	0.0
	95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
I-Renal impairment Moderate (N=25)	Duration of Response (CR or PR), months	
	Subjects with CR/PR	9
	Subjects with events (%)	3 (33.3)
	Subjects censored (%)	6 (66.7)
	Ongoing without PD (%)	3 (33.3)
	Other (%)	3 (33.3)
	25th Percentile	7.9
	95% CI	(5.6, 16.9)
	Median	16.9
	95% CI	(5.6, 16.9)
	Duration of Response (CR or PR) at specific timepoints	
	at 6 Months (%)	83.3
	95% CI [a]	(27.3, 97.5)
	at 12 Months (%)	66.7
	95% CI [a]	(19.5, 90.4)
	at 24 Months (%)	0.0
	95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
J-Hepatic impairment Normal (N=105)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	68
Subjects with events (%)	16 (23.5)
Subjects censored (%)	52 (76.5)
Ongoing without PD (%)	33 (48.5)
Other (%)	19 (27.9)
25th Percentile	9.7
95% CI	(6.9, 14.8)
Median	14.8
95% CI	(13.8, NE)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	86.7
95% CI [a]	(75.1, 93.2)
at 12 Months (%)	73.2
95% CI [a]	(56.9, 84.1)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
J-Hepatic impairment Mild (N=76)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	43
Subjects with events (%)	13 (30.2)
Subjects censored (%)	30 (69.8)
Ongoing without PD (%)	20 (46.5)
Other (%)	10 (23.3)
25th Percentile	5.6
95% CI	(4.2, 15.0)
Median	15.0
95% CI	(8.3, 15.0)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	71.7
95% CI [a]	(53.7, 83.7)
at 12 Months (%)	63.5
95% CI [a]	(44.0, 77.7)
at 24 Months (%)	0.0
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
K-Brain metastases Yes (N=24)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	14
Subjects with events (%)	4 (28.6)
Subjects censored (%)	10 (71.4)
Ongoing without PD (%)	7 (50.0)
Other (%)	3 (21.4)
25th Percentile	16.9
95% CI	(2.0, 16.9)
Median	16.9
95% CI	(5.7, 16.9)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	76.0
95% CI [a]	(42.2, 91.6)
at 12 Months (%)	76.0
95% CI [a]	(42.2, 91.6)
at 24 Months (%)	0.0
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	No (N=160)	Overall - EAS (5.4 mg/kg)
K-Brain metastases		
Duration of Response (CR or PR), months		
Subjects with CR/PR		98
Subjects with events (%)		25 (25.5)
Subjects censored (%)		73 (74.5)
Ongoing without PD (%)		46 (46.9)
Other (%)		27 (27.6)
25th Percentile		8.5
95% CI		(5.6, 14.8)
Median		14.8
95% CI		(13.8, NE)
Duration of Response (CR or PR) at specific timepoints		
at 6 Months (%)		82.1
95% CI [a]		(72.1, 88.9)
at 12 Months (%)		68.8
95% CI [a]		(55.5, 78.8)
at 24 Months (%)		NE
95% CI [a]		(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
L-Bone metastases	
Yes (N=53)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	29
Subjects with events (%)	9 (31.0)
Subjects censored (%)	20 (69.0)
Ongoing without PD (%)	13 (44.8)
Other (%)	7 (24.1)
25th Percentile	7.9
95% CI	(4.4, 15.0)
Median	15.0
95% CI	(7.9, NE)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	80.2
95% CI [a]	(58.6, 91.2)
at 12 Months (%)	63.9
95% CI [a]	(39.5, 80.6)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	No (N=131)	Overall - EAS (5.4 mg/kg)
L-Bone metastases		
Duration of Response (CR or PR), months		
Subjects with CR/PR		83
Subjects with events (%)		20 (24.1)
Subjects censored (%)		63 (75.9)
Ongoing without PD (%)		40 (48.2)
Other (%)		23 (27.7)
25th Percentile		9.0
95% CI		(5.6, 14.8)
Median		13.8
95% CI		(13.8, 16.9)
Duration of Response (CR or PR) at specific timepoints		
at 6 Months (%)		81.7
95% CI [a]		(70.5, 89.0)
at 12 Months (%)		71.9
95% CI [a]		(57.6, 82.2)
at 24 Months (%)		0.0
95% CI [a]		(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
M-History of visceral disease Yes (N=169)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	102
Subjects with events (%)	27 (26.5)
Subjects censored (%)	75 (73.5)
Ongoing without PD (%)	49 (48.0)
Other (%)	26 (25.5)
25th Percentile	8.5
95% CI	(5.6, 14.8)
Median	14.8
95% CI	(13.8, 16.9)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	79.7
95% CI [a]	(69.7, 86.7)
at 12 Months (%)	71.1
95% CI [a]	(59.1, 80.2)
at 24 Months (%)	0.0
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
M-History of visceral disease No (N=15)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	10
Subjects with events (%)	2 (20.0)
Subjects censored (%)	8 (80.0)
Ongoing without PD (%)	4 (40.0)
Other (%)	4 (40.0)
25th Percentile	9.7
95% CI	(8.3, NE)
Median	NE
95% CI	(8.3, NE)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	100.0
95% CI [a]	(NE, NE)
at 12 Months (%)	60.0
95% CI [a]	(12.6, 88.2)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
N-T-DM1 last therapy	Yes (N=56)	Duration of Response (CR or PR), months	
		Subjects with CR/PR	36
		Subjects with events (%)	7 (19.4)
		Subjects censored (%)	29 (80.6)
		Ongoing without PD (%)	20 (55.6)
		Other (%)	9 (25.0)
		25th Percentile	14.8
		95% CI	(3.7, NE)
		Median	14.8
		95% CI	(14.8, NE)
		Duration of Response (CR or PR) at specific timepoints	
		at 6 Months (%)	84.1
		95% CI [a]	(65.8, 93.1)
		at 12 Months (%)	80.4
		95% CI [a]	(61.3, 90.8)
		at 24 Months (%)	NE
		95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
N-T-DM1 last therapy No (N=128)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	76
Subjects with events (%)	22 (28.9)
Subjects censored (%)	54 (71.1)
Ongoing without PD (%)	33 (43.4)
Other (%)	21 (27.6)
25th Percentile	8.3
95% CI	(5.6, 13.8)
Median	13.8
95% CI	(9.7, 16.9)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	80.1
95% CI [a]	(68.1, 88.0)
at 12 Months (%)	64.0
95% CI [a]	(47.8, 76.3)
at 24 Months (%)	0.0
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
0-Prior treatment lines < 3 lines (N=17)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	13
Subjects with events (%)	2 (15.4)
Subjects censored (%)	11 (84.6)
Ongoing without PD (%)	10 (76.9)
Other (%)	1 (7.7)
25th Percentile	NE
95% CI	(2.8, NE)
Median	NE
95% CI	(NE, NE)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	84.6
95% CI [a]	(51.2, 95.9)
at 12 Months (%)	84.6
95% CI [a]	(51.2, 95.9)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
0-Prior treatment lines >= 3 lines (N=167)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	99
Subjects with events (%)	27 (27.3)
Subjects censored (%)	72 (72.7)
Ongoing without PD (%)	43 (43.4)
Other (%)	29 (29.3)
25th Percentile	8.3
95% CI	(5.6, 13.8)
Median	14.8
95% CI	(13.8, 16.9)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	80.8
95% CI [a]	(70.5, 87.8)
at 12 Months (%)	67.0
95% CI [a]	(53.6, 77.4)
at 24 Months (%)	0.0
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
P-Best Response to T-DM1 therapy	
CR/PR/SD (N=79)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	47
Subjects with events (%)	12 (25.5)
Subjects censored (%)	35 (74.5)
Ongoing without PD (%)	23 (48.9)
Other (%)	12 (25.5)
25th Percentile	9.0
95% CI	(5.6, 15.0)
Median	15.0
95% CI	(13.8, NE)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	84.5
95% CI [a]	(68.6, 92.7)
at 12 Months (%)	70.6
95% CI [a]	(51.1, 83.5)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
P-Best Response to T-DM1 therapy	PD (N=66)
Duration of Response (CR or PR), months	
Subjects with CR/PR	44
Subjects with events (%)	14 (31.8)
Subjects censored (%)	30 (68.2)
Ongoing without PD (%)	18 (40.9)
Other (%)	12 (27.3)
25th Percentile	8.3
95% CI	(3.7, 14.8)
Median	14.8
95% CI	(9.7, 16.9)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	75.3
95% CI [a]	(58.8, 85.9)
at 12 Months (%)	64.4
95% CI [a]	(43.2, 79.4)
at 24 Months (%)	0.0
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
Q-Prior pertuzumab Yes (N=121)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	78
Subjects with events (%)	18 (23.1)
Subjects censored (%)	60 (76.9)
Ongoing without PD (%)	38 (48.7)
Other (%)	22 (28.2)
25th Percentile	9.7
95% CI	(5.7, 15.0)
Median	15.0
95% CI	(14.8, NE)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	85.0
95% CI [a]	(73.8, 91.7)
at 12 Months (%)	72.3
95% CI [a]	(56.9, 82.9)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	No (N=63)	Duration of Response (CR or PR), months	Overall - EAS (5.4 mg/kg)
Q-Prior pertuzumab		Subjects with CR/PR	34
		Subjects with events (%)	11 (32.4)
		Subjects censored (%)	23 (67.6)
		Ongoing without PD (%)	15 (44.1)
		Other (%)	8 (23.5)
		25th Percentile	5.7
		95% CI	(4.2, 13.8)
		Median	13.8
		95% CI	(9.0, 13.8)
		Duration of Response (CR or PR) at specific timepoints	
		at 6 Months (%)	73.5
		95% CI [a]	(53.8, 85.8)
		at 12 Months (%)	64.6
		95% CI [a]	(43.4, 79.5)
		at 24 Months (%)	0.0
		95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
R-Pertuzumab before line 3	
Yes (N=51)	
Duration of Response (CR or PR), months	
Subjects with CR/PR	38
Subjects with events (%)	10 (26.3)
Subjects censored (%)	28 (73.7)
Ongoing without PD (%)	20 (52.6)
Other (%)	8 (21.1)
25th Percentile	9.7
95% CI	(2.9, NE)
Median	14.8
95% CI	(9.7, NE)
Duration of Response (CR or PR) at specific timepoints	
at 6 Months (%)	80.5
95% CI [a]	(63.3, 90.2)
at 12 Months (%)	68.6
95% CI [a]	(43.9, 84.1)
at 24 Months (%)	NE
95% CI [a]	(NE, NE)

Figure is considering only patients with response
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied
Source Data: adam.adtte.

Table T2DOR_EST0: Duration of Response (CR or PR)
 Enrolled Analysis Set

Subgroup	No (N=133)	Overall - EAS (5.4 mg/kg)
R-Pertuzumab before line 3		
Duration of Response (CR or PR), months		
Subjects with CR/PR		74
Subjects with events (%)		19 (25.7)
Subjects censored (%)		55 (74.3)
Ongoing without PD (%)		33 (44.6)
Other (%)		22 (29.7)
25th Percentile		8.5
95% CI		(5.6, 15.0)
Median		15.0
95% CI		(13.8, 16.9)
Duration of Response (CR or PR) at specific timepoints		
at 6 Months (%)		81.9
95% CI [a]		(69.7, 89.6)
at 12 Months (%)		69.8
95% CI [a]		(54.7, 80.7)
at 24 Months (%)		0.0
95% CI [a]		(NE, NE)

Figure is considering only patients with response
 Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
 log-log transformation of rates was applied
 Source Data: adam.adtte.

Sicherheit – weitere Untersuchungen

Gesamtrate UE

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	183 (99.5)	(97.0, 100.0)
		Cycle 1	184	173 (94.0)	(89.6, 97.0)
		Cycle 2	181	133 (72.3)	(65.2, 78.6)
		Cycle 3	174	115 (62.5)	(55.1, 69.5)
		Cycle 4	169	108 (58.7)	(51.2, 65.9)
		Cycle 5	155	93 (50.5)	(43.1, 58.0)
		Cycle 6	152	83 (45.1)	(37.8, 52.6)
		Cycle 7	145	88 (47.8)	(40.4, 55.3)
		Cycle >= 8 and < 18	138	124 (67.4)	(60.1, 74.1)
		Cycle >= 18	35	19 (10.3)	(6.3, 15.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	139 (99.3) (96.1, 100.0)
		Cycle 1	140	133 (95.0) (90.0, 98.0)
		Cycle 2	138	100 (71.4) (63.2, 78.7)
		Cycle 3	132	87 (62.1) (53.6, 70.2)
		Cycle 4	128	84 (60.0) (51.4, 68.2)
		Cycle 5	116	70 (50.0) (41.4, 58.6)
		Cycle 6	113	61 (43.6) (35.2, 52.2)
		Cycle 7	109	62 (44.3) (35.9, 52.9)
		Cycle >= 8 and < 18	103	91 (65.0) (56.5, 72.9)
		Cycle >= 18	24	12 (8.6) (4.5, 14.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	44 (100.0) (92.0, 100.0)
		Cycle 1	44	40 (90.9) (78.3, 97.5)
		Cycle 2	43	33 (75.0) (59.7, 86.8)
		Cycle 3	42	28 (63.6) (47.8, 77.6)
		Cycle 4	41	24 (54.5) (38.8, 69.6)
		Cycle 5	39	23 (52.3) (36.7, 67.5)
		Cycle 6	39	22 (50.0) (34.6, 65.4)
		Cycle 7	36	26 (59.1) (43.2, 73.7)
		Cycle >= 8 and < 18	35	33 (75.0) (59.7, 86.8)
		Cycle >= 18	11	7 (15.9) (6.6, 30.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	63 (100.0) (94.3, 100.0)
		Cycle 1	63	58 (92.1) (82.4, 97.4)
		Cycle 2	61	41 (65.1) (52.0, 76.7)
		Cycle 3	58	38 (60.3) (47.2, 72.4)
		Cycle 4	58	30 (47.6) (34.9, 60.6)
		Cycle 5	55	31 (49.2) (36.4, 62.1)
		Cycle 6	55	28 (44.4) (31.9, 57.5)
		Cycle 7	53	32 (50.8) (37.9, 63.6)
		Cycle >= 8 and < 18	49	44 (69.8) (57.0, 80.8)
		Cycle >= 18	15	8 (12.7) (5.6, 23.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	53 (100.0) (93.3, 100.0)
		Cycle 1	53	52 (98.1) (89.9, 100.0)
		Cycle 2	53	43 (81.1) (68.0, 90.6)
		Cycle 3	52	38 (71.7) (57.7, 83.2)
		Cycle 4	49	38 (71.7) (57.7, 83.2)
		Cycle 5	44	29 (54.7) (40.4, 68.4)
		Cycle 6	42	20 (37.7) (24.8, 52.1)
		Cycle 7	40	19 (35.8) (23.1, 50.2)
		Cycle >= 8 and < 18	39	34 (64.2) (49.8, 76.9)
		Cycle >= 18	11	6 (11.3) (4.3, 23.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	67 (98.5) (92.1, 100.0)
		Cycle 1	68	63 (92.6) (83.7, 97.6)
		Cycle 2	67	49 (72.1) (59.9, 82.3)
		Cycle 3	64	39 (57.4) (44.8, 69.3)
		Cycle 4	62	40 (58.8) (46.2, 70.6)
		Cycle 5	56	33 (48.5) (36.2, 61.0)
		Cycle 6	55	35 (51.5) (39.0, 63.8)
		Cycle 7	52	37 (54.4) (41.9, 66.5)
		Cycle >= 8 and < 18	50	46 (67.6) (55.2, 78.5)
		Cycle >= 18	9	5 (7.4) (2.4, 16.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	101 (99.0)	(94.7, 100.0)
		Cycle 1	102	94 (92.2)	(85.1, 96.6)
		Cycle 2	101	80 (78.4)	(69.2, 86.0)
		Cycle 3	100	73 (71.6)	(61.8, 80.1)
		Cycle 4	98	65 (63.7)	(53.6, 73.0)
		Cycle 5	94	60 (58.8)	(48.6, 68.5)
		Cycle 6	93	48 (47.1)	(37.1, 57.2)
		Cycle 7	88	56 (54.9)	(44.7, 64.8)
		Cycle >= 8 and < 18	86	78 (76.5)	(67.0, 84.3)
		Cycle >= 18	23	14 (13.7)	(7.7, 22.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	81 (100.0)	(95.5, 100.0)
		Cycle 1	81	78 (96.3)	(89.6, 99.2)
		Cycle 2	79	52 (64.2)	(52.8, 74.6)
		Cycle 3	73	41 (50.6)	(39.3, 61.9)
		Cycle 4	71	43 (53.1)	(41.7, 64.3)
		Cycle 5	61	33 (40.7)	(29.9, 52.2)
		Cycle 6	59	35 (43.2)	(32.2, 54.7)
		Cycle 7	57	32 (39.5)	(28.8, 51.0)
		Cycle >= 8 and < 18	52	46 (56.8)	(45.3, 67.8)
		Cycle >= 18	12	5 (6.2)	(2.0, 13.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
D-Baseline sum of diameters of target lesions < 5 cm (N=74)	Any TEAE	74	74 (100.0)	(95.1, 100.0)
	Cycle 1	74	70 (94.6)	(86.7, 98.5)
	Cycle 2	73	57 (77.0)	(65.8, 86.0)
	Cycle 3	71	49 (66.2)	(54.3, 76.8)
	Cycle 4	66	44 (59.5)	(47.4, 70.7)
	Cycle 5	61	36 (48.6)	(36.9, 60.6)
	Cycle 6	60	31 (41.9)	(30.5, 53.9)
	Cycle 7	59	34 (45.9)	(34.3, 57.9)
	Cycle >= 8 and < 18	54	49 (66.2)	(54.3, 76.8)
	Cycle >= 18	18	8 (10.8)	(4.8, 20.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

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			Overall 5.4 mg/kg SAF (N=184)		
Subgroup		Time Period	N patients in cycle	n (%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=95)	Any TEAE	95	94 (98.9)	(94.3, 100.0)
		Cycle 1	95	88 (92.6)	(85.4, 97.0)
		Cycle 2	93	64 (67.4)	(57.0, 76.6)
		Cycle 3	88	56 (58.9)	(48.4, 68.9)
		Cycle 4	88	56 (58.9)	(48.4, 68.9)
		Cycle 5	79	47 (49.5)	(39.1, 59.9)
		Cycle 6	77	42 (44.2)	(34.0, 54.8)
		Cycle 7	72	46 (48.4)	(38.0, 58.9)
		Cycle >= 8 and < 18	70	63 (66.3)	(55.9, 75.7)
		Cycle >= 18	13	9 (9.5)	(4.4, 17.2)

Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	153 (99.4)	(96.4, 100.0)
		Cycle 1	154	144 (93.5)	(88.4, 96.8)
		Cycle 2	152	116 (75.3)	(67.7, 81.9)
		Cycle 3	146	96 (62.3)	(54.2, 70.0)
		Cycle 4	141	90 (58.4)	(50.2, 66.3)
		Cycle 5	129	78 (50.6)	(42.5, 58.8)
		Cycle 6	127	69 (44.8)	(36.8, 53.0)
		Cycle 7	121	75 (48.7)	(40.6, 56.9)
		Cycle >= 8 and < 18	114	106 (68.8)	(60.9, 76.0)
		Cycle >= 18	33	19 (12.3)	(7.6, 18.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHCR3+ (N=28)	Any TEAE	28	28 (100.0) (87.7, 100.0)
		Cycle 1	28	28 (100.0) (87.7, 100.0)
		Cycle 2	27	16 (57.1) (37.2, 75.5)
		Cycle 3	26	17 (60.7) (40.6, 78.5)
		Cycle 4	26	16 (57.1) (37.2, 75.5)
		Cycle 5	24	14 (50.0) (30.6, 69.4)
		Cycle 6	23	12 (42.9) (24.5, 62.8)
		Cycle 7	22	12 (42.9) (24.5, 62.8)
		Cycle >= 8 and < 18	22	16 (57.1) (37.2, 75.5)
		Cycle >= 18	2	0 (0.0) (0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	92 (98.9)	(94.2, 100.0)
		Cycle 1	93	88 (94.6)	(87.9, 98.2)
		Cycle 2	92	67 (72.0)	(61.8, 80.9)
		Cycle 3	87	55 (59.1)	(48.5, 69.2)
		Cycle 4	84	57 (61.3)	(50.6, 71.2)
		Cycle 5	80	51 (54.8)	(44.2, 65.2)
		Cycle 6	78	43 (46.2)	(35.8, 56.9)
		Cycle 7	75	48 (51.6)	(41.0, 62.1)
		Cycle >= 8 and < 18	73	64 (68.8)	(58.4, 78.0)
		Cycle >= 18	12	3 (3.2)	(0.7, 9.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	88 (100.0)	(95.9, 100.0)
		Cycle 1	88	82 (93.2)	(85.7, 97.5)
		Cycle 2	86	65 (73.9)	(63.4, 82.7)
		Cycle 3	85	59 (67.0)	(56.2, 76.7)
		Cycle 4	84	51 (58.0)	(47.0, 68.4)
		Cycle 5	74	42 (47.7)	(37.0, 58.6)
		Cycle 6	73	40 (45.5)	(34.8, 56.4)
		Cycle 7	69	39 (44.3)	(33.7, 55.3)
		Cycle >= 8 and < 18	64	59 (67.0)	(56.2, 76.7)
		Cycle >= 18	23	16 (18.2)	(10.8, 27.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	50 (98.0)	(89.6, 100.0)
		Cycle 1	51	48 (94.1)	(83.8, 98.8)
		Cycle 2	50	34 (66.7)	(52.1, 79.2)
		Cycle 3	49	34 (66.7)	(52.1, 79.2)
		Cycle 4	49	28 (54.9)	(40.3, 68.9)
		Cycle 5	47	27 (52.9)	(38.5, 67.1)
		Cycle 6	46	22 (43.1)	(29.3, 57.8)
		Cycle 7	45	27 (52.9)	(38.5, 67.1)
		Cycle >= 8 and < 18	44	40 (78.4)	(64.7, 88.7)
		Cycle >= 18	8	2 (3.9)	(0.5, 13.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	125 (100.0) (97.1, 100.0)
		Cycle 1	125	117 (93.6) (87.8, 97.2)
		Cycle 2	123	94 (75.2) (66.7, 82.5)
		Cycle 3	118	78 (62.4) (53.3, 70.9)
		Cycle 4	114	77 (61.6) (52.5, 70.2)
		Cycle 5	103	64 (51.2) (42.1, 60.2)
		Cycle 6	101	59 (47.2) (38.2, 56.3)
		Cycle 7	95	58 (46.4) (37.4, 55.5)
		Cycle >= 8 and < 18	90	81 (64.8) (55.8, 73.1)
		Cycle >= 18	27	17 (13.6) (8.1, 20.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	96 (99.0)	(94.4, 100.0)
		Cycle 1	97	92 (94.8)	(88.4, 98.3)
		Cycle 2	96	71 (73.2)	(63.2, 81.7)
		Cycle 3	91	58 (59.8)	(49.3, 69.6)
		Cycle 4	88	58 (59.8)	(49.3, 69.6)
		Cycle 5	84	53 (54.6)	(44.2, 64.8)
		Cycle 6	82	44 (45.4)	(35.2, 55.8)
		Cycle 7	79	49 (50.5)	(40.2, 60.8)
		Cycle >= 8 and < 18	76	67 (69.1)	(58.9, 78.1)
		Cycle >= 18	13	4 (4.1)	(1.1, 10.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	83 (100.0)	(95.7, 100.0)
		Cycle 1	83	77 (92.8)	(84.9, 97.3)
		Cycle 2	81	60 (72.3)	(61.4, 81.6)
		Cycle 3	80	56 (67.5)	(56.3, 77.4)
		Cycle 4	79	50 (60.2)	(48.9, 70.8)
		Cycle 5	69	40 (48.2)	(37.1, 59.4)
		Cycle 6	68	39 (47.0)	(35.9, 58.3)
		Cycle 7	64	38 (45.8)	(34.8, 57.1)
		Cycle >= 8 and < 18	60	55 (66.3)	(55.1, 76.3)
		Cycle >= 18	22	15 (18.1)	(10.5, 28.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Normal (N=90)			
	Any TEAE	90	89 (98.9)	(94.0, 100.0)
	Cycle 1	90	85 (94.4)	(87.5, 98.2)
	Cycle 2	89	59 (65.6)	(54.8, 75.3)
	Cycle 3	85	53 (58.9)	(48.0, 69.2)
	Cycle 4	85	56 (62.2)	(51.4, 72.2)
	Cycle 5	76	46 (51.1)	(40.3, 61.8)
	Cycle 6	73	39 (43.3)	(32.9, 54.2)
	Cycle 7	72	43 (47.8)	(37.1, 58.6)
	Cycle >= 8 and < 18	69	59 (65.6)	(54.8, 75.3)
	Cycle >= 18	17	9 (10.0)	(4.7, 18.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	69 (100.0)	(94.8, 100.0)
		Cycle 1	69	65 (94.2)	(85.8, 98.4)
		Cycle 2	68	55 (79.7)	(68.3, 88.4)
		Cycle 3	66	47 (68.1)	(55.8, 78.8)
		Cycle 4	63	40 (58.0)	(45.5, 69.8)
		Cycle 5	59	35 (50.7)	(38.4, 63.0)
		Cycle 6	59	32 (46.4)	(34.3, 58.8)
		Cycle 7	56	34 (49.3)	(37.0, 61.6)
		Cycle >= 8 and < 18	54	51 (73.9)	(61.9, 83.7)
		Cycle >= 18	14	7 (10.1)	(4.2, 19.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	25 (100.0)	(86.3, 100.0)
		Cycle 1	25	23 (92.0)	(74.0, 99.0)
		Cycle 2	24	19 (76.0)	(54.9, 90.6)
		Cycle 3	23	15 (60.0)	(38.7, 78.9)
		Cycle 4	21	12 (48.0)	(27.8, 68.7)
		Cycle 5	20	12 (48.0)	(27.8, 68.7)
		Cycle 6	20	12 (48.0)	(27.8, 68.7)
		Cycle 7	17	11 (44.0)	(24.4, 65.1)
		Cycle >= 8 and < 18	15	14 (56.0)	(34.9, 75.6)
		Cycle >= 18	4	3 (12.0)	(2.5, 31.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	104 (99.0)	(94.8, 100.0)
		Cycle 1	105	100 (95.2)	(89.2, 98.4)
		Cycle 2	104	76 (72.4)	(62.8, 80.7)
		Cycle 3	102	69 (65.7)	(55.8, 74.7)
		Cycle 4	98	67 (63.8)	(53.9, 73.0)
		Cycle 5	90	49 (46.7)	(36.9, 56.7)
		Cycle 6	89	52 (49.5)	(39.6, 59.5)
		Cycle 7	87	53 (50.5)	(40.5, 60.4)
		Cycle >= 8 and < 18	84	77 (73.3)	(63.8, 81.5)
		Cycle >= 18	22	14 (13.3)	(7.5, 21.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	76 (100.0)	(95.3, 100.0)
		Cycle 1	76	70 (92.1)	(83.6, 97.0)
		Cycle 2	74	54 (71.1)	(59.5, 80.9)
		Cycle 3	69	44 (57.9)	(46.0, 69.1)
		Cycle 4	68	39 (51.3)	(39.6, 63.0)
		Cycle 5	63	43 (56.6)	(44.7, 67.9)
		Cycle 6	61	31 (40.8)	(29.6, 52.7)
		Cycle 7	56	34 (44.7)	(33.3, 56.6)
		Cycle >= 8 and < 18	54	47 (61.8)	(50.0, 72.8)
		Cycle >= 18	13	5 (6.6)	(2.2, 14.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	24 (100.0)	(85.8, 100.0)
		Cycle 1	24	22 (91.7)	(73.0, 99.0)
		Cycle 2	23	15 (62.5)	(40.6, 81.2)
		Cycle 3	22	13 (54.2)	(32.8, 74.4)
		Cycle 4	22	14 (58.3)	(36.6, 77.9)
		Cycle 5	19	9 (37.5)	(18.8, 59.4)
		Cycle 6	18	11 (45.8)	(25.6, 67.2)
		Cycle 7	18	15 (62.5)	(40.6, 81.2)
		Cycle >= 8 and < 18	18	18 (75.0)	(53.3, 90.2)
		Cycle >= 18	6	3 (12.5)	(2.7, 32.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	159 (99.4)	(96.6, 100.0)
		Cycle 1	160	151 (94.4)	(89.6, 97.4)
		Cycle 2	158	118 (73.8)	(66.2, 80.4)
		Cycle 3	152	102 (63.8)	(55.8, 71.2)
		Cycle 4	147	94 (58.8)	(50.7, 66.5)
		Cycle 5	136	84 (52.5)	(44.5, 60.4)
		Cycle 6	134	72 (45.0)	(37.1, 53.1)
		Cycle 7	127	73 (45.6)	(37.7, 53.7)
		Cycle >= 8 and < 18	120	106 (66.3)	(58.4, 73.5)
		Cycle >= 18	29	16 (10.0)	(5.8, 15.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	53 (100.0)	(93.3, 100.0)
		Cycle 1	53	51 (96.2)	(87.0, 99.5)
		Cycle 2	52	42 (79.2)	(65.9, 89.2)
		Cycle 3	49	29 (54.7)	(40.4, 68.4)
		Cycle 4	48	34 (64.2)	(49.8, 76.9)
		Cycle 5	43	26 (49.1)	(35.1, 63.2)
		Cycle 6	42	28 (52.8)	(38.6, 66.7)
		Cycle 7	41	30 (56.6)	(42.3, 70.2)
		Cycle >= 8 and < 18	39	37 (69.8)	(55.7, 81.7)
		Cycle >= 18	8	4 (7.5)	(2.1, 18.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	130 (99.2)	(95.8, 100.0)
		Cycle 1	131	122 (93.1)	(87.4, 96.8)
		Cycle 2	129	91 (69.5)	(60.8, 77.2)
		Cycle 3	125	86 (65.6)	(56.9, 73.7)
		Cycle 4	121	74 (56.5)	(47.6, 65.1)
		Cycle 5	112	67 (51.1)	(42.3, 60.0)
		Cycle 6	110	55 (42.0)	(33.4, 50.9)
		Cycle 7	104	58 (44.3)	(35.6, 53.2)
		Cycle >= 8 and < 18	99	87 (66.4)	(57.6, 74.4)
		Cycle >= 18	27	15 (11.5)	(6.6, 18.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	168 (99.4) (96.7, 100.0)
		Cycle 1	169	159 (94.1) (89.4, 97.1)
		Cycle 2	166	122 (72.2) (64.8, 78.8)
		Cycle 3	159	103 (60.9) (53.2, 68.3)
		Cycle 4	154	99 (58.6) (50.8, 66.1)
		Cycle 5	142	85 (50.3) (42.5, 58.1)
		Cycle 6	139	76 (45.0) (37.3, 52.8)
		Cycle 7	132	81 (47.9) (40.2, 55.7)
		Cycle >= 8 and < 18	125	112 (66.3) (58.6, 73.4)
		Cycle >= 18	31	17 (10.1) (6.0, 15.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	15 (100.0)	(78.2, 100.0)
		Cycle 1	15	14 (93.3)	(68.1, 99.8)
		Cycle 2	15	11 (73.3)	(44.9, 92.2)
		Cycle 3	15	12 (80.0)	(51.9, 95.7)
		Cycle 4	15	9 (60.0)	(32.3, 83.7)
		Cycle 5	13	8 (53.3)	(26.6, 78.7)
		Cycle 6	13	7 (46.7)	(21.3, 73.4)
		Cycle 7	13	7 (46.7)	(21.3, 73.4)
		Cycle >= 8 and < 18	13	12 (80.0)	(51.9, 95.7)
		Cycle >= 18	4	2 (13.3)	(1.7, 40.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	56 (100.0)	(93.6, 100.0)
		Cycle 1	56	54 (96.4)	(87.7, 99.6)
		Cycle 2	55	42 (75.0)	(61.6, 85.6)
		Cycle 3	54	36 (64.3)	(50.4, 76.6)
		Cycle 4	53	34 (60.7)	(46.8, 73.5)
		Cycle 5	49	29 (51.8)	(38.0, 65.3)
		Cycle 6	48	23 (41.1)	(28.1, 55.0)
		Cycle 7	48	27 (48.2)	(34.7, 62.0)
		Cycle >= 8 and < 18	45	39 (69.6)	(55.9, 81.2)
		Cycle >= 18	16	9 (16.1)	(7.6, 28.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	127 (99.2)	(95.7, 100.0)
		Cycle 1	128	119 (93.0)	(87.1, 96.7)
		Cycle 2	126	91 (71.1)	(62.4, 78.8)
		Cycle 3	120	79 (61.7)	(52.7, 70.2)
		Cycle 4	116	74 (57.8)	(48.8, 66.5)
		Cycle 5	106	64 (50.0)	(41.0, 59.0)
		Cycle 6	104	60 (46.9)	(38.0, 55.9)
		Cycle 7	97	61 (47.7)	(38.8, 56.7)
		Cycle >= 8 and < 18	93	85 (66.4)	(57.5, 74.5)
		Cycle >= 18	19	10 (7.8)	(3.8, 13.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
0-Prior treatment lines	< 3 lines (N=17)	Any TEAE	17	17 (100.0) (80.5, 100.0)
		Cycle 1	17	16 (94.1) (71.3, 99.9)
		Cycle 2	17	14 (82.4) (56.6, 96.2)
		Cycle 3	17	11 (64.7) (38.3, 85.8)
		Cycle 4	17	14 (82.4) (56.6, 96.2)
		Cycle 5	17	9 (52.9) (27.8, 77.0)
		Cycle 6	16	8 (47.1) (23.0, 72.2)
		Cycle 7	16	9 (52.9) (27.8, 77.0)
		Cycle >= 8 and < 18	16	14 (82.4) (56.6, 96.2)
		Cycle >= 18	6	2 (11.8) (1.5, 36.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
0-Prior treatment lines	>= 3 lines (N=167)	Any TEAE	167	166 (99.4) (96.7, 100.0)
		Cycle 1	167	157 (94.0) (89.3, 97.1)
		Cycle 2	164	119 (71.3) (63.8, 78.0)
		Cycle 3	157	104 (62.3) (54.5, 69.6)
		Cycle 4	152	94 (56.3) (48.4, 63.9)
		Cycle 5	138	84 (50.3) (42.5, 58.1)
		Cycle 6	136	75 (44.9) (37.2, 52.8)
		Cycle 7	129	79 (47.3) (39.5, 55.2)
		Cycle >= 8 and < 18	122	110 (65.9) (58.1, 73.0)
		Cycle >= 18	29	17 (10.2) (6.0, 15.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	78 (98.7) (93.1, 100.0)
		Cycle 1	79	74 (93.7) (85.8, 97.9)
		Cycle 2	78	57 (72.2) (60.9, 81.7)
		Cycle 3	75	49 (62.0) (50.4, 72.7)
		Cycle 4	73	43 (54.4) (42.8, 65.7)
		Cycle 5	70	44 (55.7) (44.1, 66.9)
		Cycle 6	69	37 (46.8) (35.5, 58.4)
		Cycle 7	68	42 (53.2) (41.6, 64.5)
		Cycle >= 8 and < 18	65	59 (74.7) (63.6, 83.8)
		Cycle >= 18	17	10 (12.7) (6.2, 22.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	66 (100.0) (94.6, 100.0)
		Cycle 1	66	62 (93.9) (85.2, 98.3)
		Cycle 2	66	46 (69.7) (57.1, 80.4)
		Cycle 3	64	39 (59.1) (46.3, 71.0)
		Cycle 4	61	39 (59.1) (46.3, 71.0)
		Cycle 5	55	26 (39.4) (27.6, 52.2)
		Cycle 6	53	27 (40.9) (29.0, 53.7)
		Cycle 7	51	31 (47.0) (34.6, 59.7)
		Cycle >= 8 and < 18	51	46 (69.7) (57.1, 80.4)
		Cycle >= 18	10	7 (10.6) (4.4, 20.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	121 (100.0) (97.0, 100.0)
		Cycle 1	121	113 (93.4) (87.4, 97.1)
		Cycle 2	120	87 (71.9) (63.0, 79.7)
		Cycle 3	119	78 (64.5) (55.2, 73.0)
		Cycle 4	115	78 (64.5) (55.2, 73.0)
		Cycle 5	106	68 (56.2) (46.9, 65.2)
		Cycle 6	103	55 (45.5) (36.4, 54.8)
		Cycle 7	96	56 (46.3) (37.2, 55.6)
		Cycle >= 8 and < 18	93	81 (66.9) (57.8, 75.2)
		Cycle >= 18	25	13 (10.7) (5.8, 17.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	62 (98.4)	(91.5, 100.0)
		Cycle 1	63	60 (95.2)	(86.7, 99.0)
		Cycle 2	61	46 (73.0)	(60.3, 83.4)
		Cycle 3	55	37 (58.7)	(45.6, 71.0)
		Cycle 4	54	30 (47.6)	(34.9, 60.6)
		Cycle 5	49	25 (39.7)	(27.6, 52.8)
		Cycle 6	49	28 (44.4)	(31.9, 57.5)
		Cycle 7	49	32 (50.8)	(37.9, 63.6)
		Cycle >= 8 and < 18	45	43 (68.3)	(55.3, 79.4)
		Cycle >= 18	10	6 (9.5)	(3.6, 19.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	51 (100.0)	(93.0, 100.0)
		Cycle 1	51	47 (92.2)	(81.1, 97.8)
		Cycle 2	50	37 (72.5)	(58.3, 84.1)
		Cycle 3	50	28 (54.9)	(40.3, 68.9)
		Cycle 4	49	34 (66.7)	(52.1, 79.2)
		Cycle 5	46	29 (56.9)	(42.2, 70.7)
		Cycle 6	44	22 (43.1)	(29.3, 57.8)
		Cycle 7	40	26 (51.0)	(36.6, 65.2)
		Cycle >= 8 and < 18	40	34 (66.7)	(52.1, 79.2)
		Cycle >= 18	10	3 (5.9)	(1.2, 16.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	132 (99.2)	(95.9, 100.0)
		Cycle 1	133	126 (94.7)	(89.5, 97.9)
		Cycle 2	131	96 (72.2)	(63.7, 79.6)
		Cycle 3	124	87 (65.4)	(56.7, 73.4)
		Cycle 4	120	74 (55.6)	(46.8, 64.2)
		Cycle 5	109	64 (48.1)	(39.4, 56.9)
		Cycle 6	108	61 (45.9)	(37.2, 54.7)
		Cycle 7	105	62 (46.6)	(37.9, 55.5)
		Cycle >= 8 and < 18	98	90 (67.7)	(59.0, 75.5)
		Cycle >= 18	25	16 (12.0)	(7.0, 18.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

SUE

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	42 (22.8)	(17.0, 29.6)
		Cycle 1	184	8 (4.3)	(1.9, 8.4)
		Cycle 2	181	9 (4.9)	(2.3, 9.1)
		Cycle 3	174	6 (3.3)	(1.2, 7.0)
		Cycle 4	169	7 (3.8)	(1.5, 7.7)
		Cycle 5	155	5 (2.7)	(0.9, 6.2)
		Cycle 6	152	2 (1.1)	(0.1, 3.9)
		Cycle 7	145	4 (2.2)	(0.6, 5.5)
		Cycle >= 8 and < 18	138	16 (8.7)	(5.1, 13.7)
		Cycle >= 18	35	0 (0.0)	(0.0, 2.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	32 (22.9) (16.2, 30.7)
		Cycle 1	140	8 (5.7) (2.5, 10.9)
		Cycle 2	138	5 (3.6) (1.2, 8.1)
		Cycle 3	132	5 (3.6) (1.2, 8.1)
		Cycle 4	128	6 (4.3) (1.6, 9.1)
		Cycle 5	116	5 (3.6) (1.2, 8.1)
		Cycle 6	113	2 (1.4) (0.2, 5.1)
		Cycle 7	109	4 (2.9) (0.8, 7.2)
		Cycle >= 8 and < 18	103	10 (7.1) (3.5, 12.7)
		Cycle >= 18	24	0 (0.0) (0.0, 2.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	10 (22.7) (11.5, 37.8)
		Cycle 1	44	0 (0.0) (0.0, 8.0)
		Cycle 2	43	4 (9.1) (2.5, 21.7)
		Cycle 3	42	1 (2.3) (0.1, 12.0)
		Cycle 4	41	1 (2.3) (0.1, 12.0)
		Cycle 5	39	0 (0.0) (0.0, 8.0)
		Cycle 6	39	0 (0.0) (0.0, 8.0)
		Cycle 7	36	0 (0.0) (0.0, 8.0)
		Cycle >= 8 and < 18	35	6 (13.6) (5.2, 27.4)
		Cycle >= 18	11	0 (0.0) (0.0, 8.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	9 (14.3) (6.7, 25.4)
		Cycle 1	63	1 (1.6) (0.0, 8.5)
		Cycle 2	61	2 (3.2) (0.4, 11.0)
		Cycle 3	58	1 (1.6) (0.0, 8.5)
		Cycle 4	58	1 (1.6) (0.0, 8.5)
		Cycle 5	55	0 (0.0) (0.0, 5.7)
		Cycle 6	55	2 (3.2) (0.4, 11.0)
		Cycle 7	53	0 (0.0) (0.0, 5.7)
		Cycle >= 8 and < 18	49	2 (3.2) (0.4, 11.0)
		Cycle >= 18	15	0 (0.0) (0.0, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	10 (18.9) (9.4, 32.0)
		Cycle 1	53	2 (3.8) (0.5, 13.0)
		Cycle 2	53	2 (3.8) (0.5, 13.0)
		Cycle 3	52	1 (1.9) (0.0, 10.1)
		Cycle 4	49	1 (1.9) (0.0, 10.1)
		Cycle 5	44	3 (5.7) (1.2, 15.7)
		Cycle 6	42	0 (0.0) (0.0, 6.7)
		Cycle 7	40	1 (1.9) (0.0, 10.1)
		Cycle >= 8 and < 18	39	3 (5.7) (1.2, 15.7)
		Cycle >= 18	11	0 (0.0) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	23 (33.8) (22.8, 46.3)
		Cycle 1	68	5 (7.4) (2.4, 16.3)
		Cycle 2	67	5 (7.4) (2.4, 16.3)
		Cycle 3	64	4 (5.9) (1.6, 14.4)
		Cycle 4	62	5 (7.4) (2.4, 16.3)
		Cycle 5	56	2 (2.9) (0.4, 10.2)
		Cycle 6	55	0 (0.0) (0.0, 5.3)
		Cycle 7	52	3 (4.4) (0.9, 12.4)
		Cycle >= 8 and < 18	50	11 (16.2) (8.4, 27.1)
		Cycle >= 18	9	0 (0.0) (0.0, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	19 (18.6) (11.6, 27.6)
		Cycle 1	102	4 (3.9) (1.1, 9.7)
		Cycle 2	101	4 (3.9) (1.1, 9.7)
		Cycle 3	100	3 (2.9) (0.6, 8.4)
		Cycle 4	98	0 (0.0) (0.0, 3.6)
		Cycle 5	94	2 (2.0) (0.2, 6.9)
		Cycle 6	93	1 (1.0) (0.0, 5.3)
		Cycle 7	88	2 (2.0) (0.2, 6.9)
		Cycle >= 8 and < 18	86	8 (7.8) (3.4, 14.9)
		Cycle >= 18	23	0 (0.0) (0.0, 3.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	22 (27.2)	(17.9, 38.2)
		Cycle 1	81	4 (4.9)	(1.4, 12.2)
		Cycle 2	79	5 (6.2)	(2.0, 13.8)
		Cycle 3	73	2 (2.5)	(0.3, 8.6)
		Cycle 4	71	7 (8.6)	(3.5, 17.0)
		Cycle 5	61	3 (3.7)	(0.8, 10.4)
		Cycle 6	59	1 (1.2)	(0.0, 6.7)
		Cycle 7	57	2 (2.5)	(0.3, 8.6)
		Cycle >= 8 and < 18	52	8 (9.9)	(4.4, 18.5)
		Cycle >= 18	12	0 (0.0)	(0.0, 4.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions < 5 cm (N=74)	Any TEAE	74	14 (18.9)	(10.7, 29.7)
	Cycle 1	74	1 (1.4)	(0.0, 7.3)
	Cycle 2	73	3 (4.1)	(0.8, 11.4)
	Cycle 3	71	2 (2.7)	(0.3, 9.4)
	Cycle 4	66	1 (1.4)	(0.0, 7.3)
	Cycle 5	61	2 (2.7)	(0.3, 9.4)
	Cycle 6	60	0 (0.0)	(0.0, 4.9)
	Cycle 7	59	2 (2.7)	(0.3, 9.4)
	Cycle >= 8 and < 18	54	7 (9.5)	(3.9, 18.5)
	Cycle >= 18	18	0 (0.0)	(0.0, 4.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

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			Overall 5.4 mg/kg SAF (N=184)		
Subgroup		Time Period	N patients in cycle	n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=95)	Any TEAE	95	24 (25.3)	(16.9, 35.2)
		Cycle 1	95	6 (6.3)	(2.4, 13.2)
		Cycle 2	93	6 (6.3)	(2.4, 13.2)
		Cycle 3	88	3 (3.2)	(0.7, 9.0)
		Cycle 4	88	5 (5.3)	(1.7, 11.9)
		Cycle 5	79	3 (3.2)	(0.7, 9.0)
		Cycle 6	77	2 (2.1)	(0.3, 7.4)
		Cycle 7	72	1 (1.1)	(0.0, 5.7)
		Cycle >= 8 and < 18	70	5 (5.3)	(1.7, 11.9)
		Cycle >= 18	13	0 (0.0)	(0.0, 3.8)

Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	35 (22.7) (16.4, 30.2)
		Cycle 1	154	7 (4.5) (1.8, 9.1)
		Cycle 2	152	8 (5.2) (2.3, 10.0)
		Cycle 3	146	5 (3.2) (1.1, 7.4)
		Cycle 4	141	7 (4.5) (1.8, 9.1)
		Cycle 5	129	4 (2.6) (0.7, 6.5)
		Cycle 6	127	2 (1.3) (0.2, 4.6)
		Cycle 7	121	4 (2.6) (0.7, 6.5)
		Cycle >= 8 and < 18	114	11 (7.1) (3.6, 12.4)
		Cycle >= 18	33	0 (0.0) (0.0, 2.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Any TEAE	28	6 (21.4) (8.3, 41.0)
		Cycle 1	28	1 (3.6) (0.1, 18.3)
		Cycle 2	27	1 (3.6) (0.1, 18.3)
		Cycle 3	26	1 (3.6) (0.1, 18.3)
		Cycle 4	26	0 (0.0) (0.0, 12.3)
		Cycle 5	24	1 (3.6) (0.1, 18.3)
		Cycle 6	23	0 (0.0) (0.0, 12.3)
		Cycle 7	22	0 (0.0) (0.0, 12.3)
		Cycle >= 8 and < 18	22	4 (14.3) (4.0, 32.7)
		Cycle >= 18	2	0 (0.0) (0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	25 (26.9)	(18.2, 37.1)
		Cycle 1	93	7 (7.5)	(3.1, 14.9)
		Cycle 2	92	8 (8.6)	(3.8, 16.2)
		Cycle 3	87	4 (4.3)	(1.2, 10.6)
		Cycle 4	84	4 (4.3)	(1.2, 10.6)
		Cycle 5	80	3 (3.2)	(0.7, 9.1)
		Cycle 6	78	0 (0.0)	(0.0, 3.9)
		Cycle 7	75	1 (1.1)	(0.0, 5.8)
		Cycle >= 8 and < 18	73	10 (10.8)	(5.3, 18.9)
		Cycle >= 18	12	0 (0.0)	(0.0, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	16 (18.2) (10.8, 27.8)
		Cycle 1	88	1 (1.1) (0.0, 6.2)
		Cycle 2	86	1 (1.1) (0.0, 6.2)
		Cycle 3	85	1 (1.1) (0.0, 6.2)
		Cycle 4	84	3 (3.4) (0.7, 9.6)
		Cycle 5	74	2 (2.3) (0.3, 8.0)
		Cycle 6	73	2 (2.3) (0.3, 8.0)
		Cycle 7	69	3 (3.4) (0.7, 9.6)
		Cycle >= 8 and < 18	64	6 (6.8) (2.5, 14.3)
		Cycle >= 18	23	0 (0.0) (0.0, 4.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	12 (23.5)	(12.8, 37.5)
		Cycle 1	51	3 (5.9)	(1.2, 16.2)
		Cycle 2	50	3 (5.9)	(1.2, 16.2)
		Cycle 3	49	3 (5.9)	(1.2, 16.2)
		Cycle 4	49	3 (5.9)	(1.2, 16.2)
		Cycle 5	47	1 (2.0)	(0.0, 10.4)
		Cycle 6	46	0 (0.0)	(0.0, 7.0)
		Cycle 7	45	2 (3.9)	(0.5, 13.5)
		Cycle >= 8 and < 18	44	5 (9.8)	(3.3, 21.4)
		Cycle >= 18	8	0 (0.0)	(0.0, 7.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	28 (22.4) (15.4, 30.7)
		Cycle 1	125	4 (3.2) (0.9, 8.0)
		Cycle 2	123	6 (4.8) (1.8, 10.2)
		Cycle 3	118	2 (1.6) (0.2, 5.7)
		Cycle 4	114	4 (3.2) (0.9, 8.0)
		Cycle 5	103	4 (3.2) (0.9, 8.0)
		Cycle 6	101	2 (1.6) (0.2, 5.7)
		Cycle 7	95	2 (1.6) (0.2, 5.7)
		Cycle >= 8 and < 18	90	11 (8.8) (4.5, 15.2)
		Cycle >= 18	27	0 (0.0) (0.0, 2.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	26 (26.8)	(18.3, 36.8)
		Cycle 1	97	7 (7.2)	(3.0, 14.3)
		Cycle 2	96	8 (8.2)	(3.6, 15.6)
		Cycle 3	91	4 (4.1)	(1.1, 10.2)
		Cycle 4	88	4 (4.1)	(1.1, 10.2)
		Cycle 5	84	3 (3.1)	(0.6, 8.8)
		Cycle 6	82	0 (0.0)	(0.0, 3.7)
		Cycle 7	79	2 (2.1)	(0.3, 7.3)
		Cycle >= 8 and < 18	76	10 (10.3)	(5.1, 18.1)
		Cycle >= 18	13	0 (0.0)	(0.0, 3.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	15 (18.1) (10.5, 28.0)
		Cycle 1	83	1 (1.2) (0.0, 6.5)
		Cycle 2	81	1 (1.2) (0.0, 6.5)
		Cycle 3	80	1 (1.2) (0.0, 6.5)
		Cycle 4	79	3 (3.6) (0.8, 10.2)
		Cycle 5	69	2 (2.4) (0.3, 8.4)
		Cycle 6	68	2 (2.4) (0.3, 8.4)
		Cycle 7	64	2 (2.4) (0.3, 8.4)
		Cycle >= 8 and < 18	60	6 (7.2) (2.7, 15.1)
		Cycle >= 18	22	0 (0.0) (0.0, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Normal (N=90)	Any TEAE	90	24 (26.7) (17.9, 37.0)
		Cycle 1	90	3 (3.3) (0.7, 9.4)
		Cycle 2	89	3 (3.3) (0.7, 9.4)
		Cycle 3	85	1 (1.1) (0.0, 6.0)
		Cycle 4	85	5 (5.6) (1.8, 12.5)
		Cycle 5	76	5 (5.6) (1.8, 12.5)
		Cycle 6	73	0 (0.0) (0.0, 4.0)
		Cycle 7	72	3 (3.3) (0.7, 9.4)
		Cycle >= 8 and < 18	69	10 (11.1) (5.5, 19.5)
		Cycle >= 18	17	0 (0.0) (0.0, 4.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	13 (18.8) (10.4, 30.1)
		Cycle 1	69	4 (5.8) (1.6, 14.2)
		Cycle 2	68	5 (7.2) (2.4, 16.1)
		Cycle 3	66	4 (5.8) (1.6, 14.2)
		Cycle 4	63	2 (2.9) (0.4, 10.1)
		Cycle 5	59	0 (0.0) (0.0, 5.2)
		Cycle 6	59	1 (1.4) (0.0, 7.8)
		Cycle 7	56	1 (1.4) (0.0, 7.8)
		Cycle >= 8 and < 18	54	5 (7.2) (2.4, 16.1)
		Cycle >= 18	14	0 (0.0) (0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	5 (20.0) (6.8, 40.7)
		Cycle 1	25	1 (4.0) (0.1, 20.4)
		Cycle 2	24	1 (4.0) (0.1, 20.4)
		Cycle 3	23	1 (4.0) (0.1, 20.4)
		Cycle 4	21	0 (0.0) (0.0, 13.7)
		Cycle 5	20	0 (0.0) (0.0, 13.7)
		Cycle 6	20	1 (4.0) (0.1, 20.4)
		Cycle 7	17	0 (0.0) (0.0, 13.7)
		Cycle >= 8 and < 18	15	1 (4.0) (0.1, 20.4)
		Cycle >= 18	4	0 (0.0) (0.0, 13.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	26 (24.8) (16.9, 34.1)
		Cycle 1	105	3 (2.9) (0.6, 8.1)
		Cycle 2	104	4 (3.8) (1.0, 9.5)
		Cycle 3	102	4 (3.8) (1.0, 9.5)
		Cycle 4	98	3 (2.9) (0.6, 8.1)
		Cycle 5	90	2 (1.9) (0.2, 6.7)
		Cycle 6	89	2 (1.9) (0.2, 6.7)
		Cycle 7	87	4 (3.8) (1.0, 9.5)
		Cycle >= 8 and < 18	84	13 (12.4) (6.8, 20.2)
		Cycle >= 18	22	0 (0.0) (0.0, 3.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	15 (19.7) (11.5, 30.5)
		Cycle 1	76	5 (6.6) (2.2, 14.7)
		Cycle 2	74	5 (6.6) (2.2, 14.7)
		Cycle 3	69	2 (2.6) (0.3, 9.2)
		Cycle 4	68	3 (3.9) (0.8, 11.1)
		Cycle 5	63	3 (3.9) (0.8, 11.1)
		Cycle 6	61	0 (0.0) (0.0, 4.7)
		Cycle 7	56	0 (0.0) (0.0, 4.7)
		Cycle >= 8 and < 18	54	3 (3.9) (0.8, 11.1)
		Cycle >= 18	13	0 (0.0) (0.0, 4.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	3 (12.5) (2.7, 32.4)
		Cycle 1	24	0 (0.0) (0.0, 14.2)
		Cycle 2	23	1 (4.2) (0.1, 21.1)
		Cycle 3	22	0 (0.0) (0.0, 14.2)
		Cycle 4	22	0 (0.0) (0.0, 14.2)
		Cycle 5	19	1 (4.2) (0.1, 21.1)
		Cycle 6	18	1 (4.2) (0.1, 21.1)
		Cycle 7	18	0 (0.0) (0.0, 14.2)
		Cycle >= 8 and < 18	18	0 (0.0) (0.0, 14.2)
		Cycle >= 18	6	0 (0.0) (0.0, 14.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	39 (24.4)	(17.9, 31.8)
		Cycle 1	160	8 (5.0)	(2.2, 9.6)
		Cycle 2	158	8 (5.0)	(2.2, 9.6)
		Cycle 3	152	6 (3.8)	(1.4, 8.0)
		Cycle 4	147	7 (4.4)	(1.8, 8.8)
		Cycle 5	136	4 (2.5)	(0.7, 6.3)
		Cycle 6	134	1 (0.6)	(0.0, 3.4)
		Cycle 7	127	4 (2.5)	(0.7, 6.3)
		Cycle >= 8 and < 18	120	16 (10.0)	(5.8, 15.7)
		Cycle >= 18	29	0 (0.0)	(0.0, 2.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	20 (37.7)	(24.8, 52.1)
		Cycle 1	53	5 (9.4)	(3.1, 20.7)
		Cycle 2	52	5 (9.4)	(3.1, 20.7)
		Cycle 3	49	2 (3.8)	(0.5, 13.0)
		Cycle 4	48	4 (7.5)	(2.1, 18.2)
		Cycle 5	43	2 (3.8)	(0.5, 13.0)
		Cycle 6	42	0 (0.0)	(0.0, 6.7)
		Cycle 7	41	1 (1.9)	(0.0, 10.1)
		Cycle >= 8 and < 18	39	10 (18.9)	(9.4, 32.0)
		Cycle >= 18	8	0 (0.0)	(0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	22 (16.8)	(10.8, 24.3)
		Cycle 1	131	3 (2.3)	(0.5, 6.5)
		Cycle 2	129	4 (3.1)	(0.8, 7.6)
		Cycle 3	125	4 (3.1)	(0.8, 7.6)
		Cycle 4	121	3 (2.3)	(0.5, 6.5)
		Cycle 5	112	3 (2.3)	(0.5, 6.5)
		Cycle 6	110	2 (1.5)	(0.2, 5.4)
		Cycle 7	104	3 (2.3)	(0.5, 6.5)
		Cycle >= 8 and < 18	99	6 (4.6)	(1.7, 9.7)
		Cycle >= 18	27	0 (0.0)	(0.0, 2.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
M-History of visceral disease Yes (N=169)	Any TEAE	169	39 (23.1)	(17.0, 30.2)
	Cycle 1	169	8 (4.7)	(2.1, 9.1)
	Cycle 2	166	9 (5.3)	(2.5, 9.9)
	Cycle 3	159	6 (3.6)	(1.3, 7.6)
	Cycle 4	154	7 (4.1)	(1.7, 8.3)
	Cycle 5	142	5 (3.0)	(1.0, 6.8)
	Cycle 6	139	2 (1.2)	(0.1, 4.2)
	Cycle 7	132	4 (2.4)	(0.6, 5.9)
	Cycle >= 8 and < 18	125	13 (7.7)	(4.2, 12.8)
	Cycle >= 18	31	0 (0.0)	(0.0, 2.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	3 (20.0)	(4.3, 48.1)
		Cycle 1	15	0 (0.0)	(0.0, 21.8)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	3 (20.0)	(4.3, 48.1)
		Cycle >= 18	4	0 (0.0)	(0.0, 21.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	7 (12.5)	(5.2, 24.1)
		Cycle 1	56	1 (1.8)	(0.0, 9.6)
		Cycle 2	55	1 (1.8)	(0.0, 9.6)
		Cycle 3	54	1 (1.8)	(0.0, 9.6)
		Cycle 4	53	1 (1.8)	(0.0, 9.6)
		Cycle 5	49	1 (1.8)	(0.0, 9.6)
		Cycle 6	48	0 (0.0)	(0.0, 6.4)
		Cycle 7	48	0 (0.0)	(0.0, 6.4)
		Cycle >= 8 and < 18	45	2 (3.6)	(0.4, 12.3)
		Cycle >= 18	16	0 (0.0)	(0.0, 6.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	35 (27.3)	(19.8, 35.9)
		Cycle 1	128	7 (5.5)	(2.2, 10.9)
		Cycle 2	126	8 (6.3)	(2.7, 11.9)
		Cycle 3	120	5 (3.9)	(1.3, 8.9)
		Cycle 4	116	6 (4.7)	(1.7, 9.9)
		Cycle 5	106	4 (3.1)	(0.9, 7.8)
		Cycle 6	104	2 (1.6)	(0.2, 5.5)
		Cycle 7	97	4 (3.1)	(0.9, 7.8)
		Cycle >= 8 and < 18	93	14 (10.9)	(6.1, 17.7)
		Cycle >= 18	19	0 (0.0)	(0.0, 2.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
0-Prior treatment lines	< 3 lines (N=17)	Any TEAE	17	1 (5.9) (0.1, 28.7)
		Cycle 1	17	0 (0.0) (0.0, 19.5)
		Cycle 2	17	0 (0.0) (0.0, 19.5)
		Cycle 3	17	0 (0.0) (0.0, 19.5)
		Cycle 4	17	0 (0.0) (0.0, 19.5)
		Cycle 5	17	1 (5.9) (0.1, 28.7)
		Cycle 6	16	0 (0.0) (0.0, 19.5)
		Cycle 7	16	0 (0.0) (0.0, 19.5)
		Cycle >= 8 and < 18	16	0 (0.0) (0.0, 19.5)
		Cycle >= 18	6	0 (0.0) (0.0, 19.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
0-Prior treatment lines	>= 3 lines (N=167)	Any TEAE	167	41 (24.6) (18.2, 31.8)
		Cycle 1	167	8 (4.8) (2.1, 9.2)
		Cycle 2	164	9 (5.4) (2.5, 10.0)
		Cycle 3	157	6 (3.6) (1.3, 7.7)
		Cycle 4	152	7 (4.2) (1.7, 8.4)
		Cycle 5	138	4 (2.4) (0.7, 6.0)
		Cycle 6	136	2 (1.2) (0.1, 4.3)
		Cycle 7	129	4 (2.4) (0.7, 6.0)
		Cycle >= 8 and < 18	122	16 (9.6) (5.6, 15.1)
		Cycle >= 18	29	0 (0.0) (0.0, 2.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	14 (17.7) (10.0, 27.9)
		Cycle 1	79	3 (3.8) (0.8, 10.7)
		Cycle 2	78	3 (3.8) (0.8, 10.7)
		Cycle 3	75	1 (1.3) (0.0, 6.9)
		Cycle 4	73	2 (2.5) (0.3, 8.8)
		Cycle 5	70	1 (1.3) (0.0, 6.9)
		Cycle 6	69	0 (0.0) (0.0, 4.6)
		Cycle 7	68	0 (0.0) (0.0, 4.6)
		Cycle >= 8 and < 18	65	6 (7.6) (2.8, 15.8)
		Cycle >= 18	17	0 (0.0) (0.0, 4.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	18 (27.3) (17.0, 39.6)
		Cycle 1	66	3 (4.5) (0.9, 12.7)
		Cycle 2	66	4 (6.1) (1.7, 14.8)
		Cycle 3	64	3 (4.5) (0.9, 12.7)
		Cycle 4	61	3 (4.5) (0.9, 12.7)
		Cycle 5	55	2 (3.0) (0.4, 10.5)
		Cycle 6	53	2 (3.0) (0.4, 10.5)
		Cycle 7	51	2 (3.0) (0.4, 10.5)
		Cycle >= 8 and < 18	51	7 (10.6) (4.4, 20.6)
		Cycle >= 18	10	0 (0.0) (0.0, 5.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	18 (14.9)	(9.1, 22.5)
		Cycle 1	121	4 (3.3)	(0.9, 8.2)
		Cycle 2	120	2 (1.7)	(0.2, 5.8)
		Cycle 3	119	3 (2.5)	(0.5, 7.1)
		Cycle 4	115	3 (2.5)	(0.5, 7.1)
		Cycle 5	106	4 (3.3)	(0.9, 8.2)
		Cycle 6	103	1 (0.8)	(0.0, 4.5)
		Cycle 7	96	1 (0.8)	(0.0, 4.5)
		Cycle >= 8 and < 18	93	5 (4.1)	(1.4, 9.4)
		Cycle >= 18	25	0 (0.0)	(0.0, 3.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	24 (38.1)	(26.1, 51.2)
		Cycle 1	63	4 (6.3)	(1.8, 15.5)
		Cycle 2	61	7 (11.1)	(4.6, 21.6)
		Cycle 3	55	3 (4.8)	(1.0, 13.3)
		Cycle 4	54	4 (6.3)	(1.8, 15.5)
		Cycle 5	49	1 (1.6)	(0.0, 8.5)
		Cycle 6	49	1 (1.6)	(0.0, 8.5)
		Cycle 7	49	3 (4.8)	(1.0, 13.3)
		Cycle >= 8 and < 18	45	11 (17.5)	(9.1, 29.1)
		Cycle >= 18	10	0 (0.0)	(0.0, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	6 (11.8) (4.4, 23.9)
		Cycle 1	51	2 (3.9) (0.5, 13.5)
		Cycle 2	50	0 (0.0) (0.0, 7.0)
		Cycle 3	50	0 (0.0) (0.0, 7.0)
		Cycle 4	49	3 (5.9) (1.2, 16.2)
		Cycle 5	46	3 (5.9) (1.2, 16.2)
		Cycle 6	44	0 (0.0) (0.0, 7.0)
		Cycle 7	40	0 (0.0) (0.0, 7.0)
		Cycle >= 8 and < 18	40	1 (2.0) (0.0, 10.4)
		Cycle >= 18	10	0 (0.0) (0.0, 7.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

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Table T2AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	36 (27.1)	(19.7, 35.5)
		Cycle 1	133	6 (4.5)	(1.7, 9.6)
		Cycle 2	131	9 (6.8)	(3.1, 12.5)
		Cycle 3	124	6 (4.5)	(1.7, 9.6)
		Cycle 4	120	4 (3.0)	(0.8, 7.5)
		Cycle 5	109	2 (1.5)	(0.2, 5.3)
		Cycle 6	108	2 (1.5)	(0.2, 5.3)
		Cycle 7	105	4 (3.0)	(0.8, 7.5)
		Cycle >= 8 and < 18	98	15 (11.3)	(6.5, 17.9)
		Cycle >= 18	25	0 (0.0)	(0.0, 2.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

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Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	183 (99.5)	(97.0, 100.0)
		Cycle 1	184	171 (92.9)	(88.2, 96.2)
		Cycle 2	181	130 (70.7)	(63.5, 77.1)
		Cycle 3	174	114 (62.0)	(54.5, 69.0)
		Cycle 4	169	102 (55.4)	(47.9, 62.7)
		Cycle 5	155	91 (49.5)	(42.0, 56.9)
		Cycle 6	152	79 (42.9)	(35.7, 50.4)
		Cycle 7	145	85 (46.2)	(38.8, 53.7)
		Cycle >= 8 and < 18	138	120 (65.2)	(57.9, 72.1)
		Cycle >= 18	35	18 (9.8)	(5.9, 15.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	139 (99.3) (96.1, 100.0)
		Cycle 1	140	131 (93.6) (88.1, 97.0)
		Cycle 2	138	98 (70.0) (61.7, 77.4)
		Cycle 3	132	86 (61.4) (52.8, 69.5)
		Cycle 4	128	80 (57.1) (48.5, 65.5)
		Cycle 5	116	68 (48.6) (40.0, 57.2)
		Cycle 6	113	60 (42.9) (34.5, 51.5)
		Cycle 7	109	60 (42.9) (34.5, 51.5)
		Cycle >= 8 and < 18	103	88 (62.9) (54.3, 70.9)
		Cycle >= 18	24	11 (7.9) (4.0, 13.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	44 (100.0) (92.0, 100.0)
		Cycle 1	44	40 (90.9) (78.3, 97.5)
		Cycle 2	43	32 (72.7) (57.2, 85.0)
		Cycle 3	42	28 (63.6) (47.8, 77.6)
		Cycle 4	41	22 (50.0) (34.6, 65.4)
		Cycle 5	39	23 (52.3) (36.7, 67.5)
		Cycle 6	39	19 (43.2) (28.3, 59.0)
		Cycle 7	36	25 (56.8) (41.0, 71.7)
		Cycle >= 8 and < 18	35	32 (72.7) (57.2, 85.0)
		Cycle >= 18	11	7 (15.9) (6.6, 30.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	63 (100.0) (94.3, 100.0)
		Cycle 1	63	56 (88.9) (78.4, 95.4)
		Cycle 2	61	38 (60.3) (47.2, 72.4)
		Cycle 3	58	38 (60.3) (47.2, 72.4)
		Cycle 4	58	28 (44.4) (31.9, 57.5)
		Cycle 5	55	29 (46.0) (33.4, 59.1)
		Cycle 6	55	25 (39.7) (27.6, 52.8)
		Cycle 7	53	29 (46.0) (33.4, 59.1)
		Cycle >= 8 and < 18	49	42 (66.7) (53.7, 78.0)
		Cycle >= 18	15	8 (12.7) (5.6, 23.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	53 (100.0) (93.3, 100.0)
		Cycle 1	53	52 (98.1) (89.9, 100.0)
		Cycle 2	53	43 (81.1) (68.0, 90.6)
		Cycle 3	52	38 (71.7) (57.7, 83.2)
		Cycle 4	49	37 (69.8) (55.7, 81.7)
		Cycle 5	44	29 (54.7) (40.4, 68.4)
		Cycle 6	42	19 (35.8) (23.1, 50.2)
		Cycle 7	40	19 (35.8) (23.1, 50.2)
		Cycle >= 8 and < 18	39	34 (64.2) (49.8, 76.9)
		Cycle >= 18	11	6 (11.3) (4.3, 23.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	67 (98.5) (92.1, 100.0)
		Cycle 1	68	63 (92.6) (83.7, 97.6)
		Cycle 2	67	49 (72.1) (59.9, 82.3)
		Cycle 3	64	38 (55.9) (43.3, 67.9)
		Cycle 4	62	37 (54.4) (41.9, 66.5)
		Cycle 5	56	33 (48.5) (36.2, 61.0)
		Cycle 6	55	35 (51.5) (39.0, 63.8)
		Cycle 7	52	37 (54.4) (41.9, 66.5)
		Cycle >= 8 and < 18	50	44 (64.7) (52.2, 75.9)
		Cycle >= 18	9	4 (5.9) (1.6, 14.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	101 (99.0)	(94.7, 100.0)
		Cycle 1	102	94 (92.2)	(85.1, 96.6)
		Cycle 2	101	78 (76.5)	(67.0, 84.3)
		Cycle 3	100	73 (71.6)	(61.8, 80.1)
		Cycle 4	98	62 (60.8)	(50.6, 70.3)
		Cycle 5	94	58 (56.9)	(46.7, 66.6)
		Cycle 6	93	45 (44.1)	(34.3, 54.3)
		Cycle 7	88	55 (53.9)	(43.8, 63.8)
		Cycle >= 8 and < 18	86	76 (74.5)	(64.9, 82.6)
		Cycle >= 18	23	13 (12.7)	(7.0, 20.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	81 (100.0)	(95.5, 100.0)
		Cycle 1	81	76 (93.8)	(86.2, 98.0)
		Cycle 2	79	51 (63.0)	(51.5, 73.4)
		Cycle 3	73	41 (50.6)	(39.3, 61.9)
		Cycle 4	71	40 (49.4)	(38.1, 60.7)
		Cycle 5	61	33 (40.7)	(29.9, 52.2)
		Cycle 6	59	34 (42.0)	(31.1, 53.5)
		Cycle 7	57	30 (37.0)	(26.6, 48.5)
		Cycle >= 8 and < 18	52	44 (54.3)	(42.9, 65.4)
		Cycle >= 18	12	5 (6.2)	(2.0, 13.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
D-Baseline sum of diameters of target lesions < 5 cm (N=74)	Any TEAE	74	74 (100.0)	(95.1, 100.0)
	Cycle 1	74	69 (93.2)	(84.9, 97.8)
	Cycle 2	73	56 (75.7)	(64.3, 84.9)
	Cycle 3	71	48 (64.9)	(52.9, 75.6)
	Cycle 4	66	42 (56.8)	(44.7, 68.2)
	Cycle 5	61	36 (48.6)	(36.9, 60.6)
	Cycle 6	60	31 (41.9)	(30.5, 53.9)
	Cycle 7	59	33 (44.6)	(33.0, 56.6)
	Cycle >= 8 and < 18	54	46 (62.2)	(50.1, 73.2)
	Cycle >= 18	18	8 (10.8)	(4.8, 20.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

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			Overall 5.4 mg/kg SAF (N=184)		
Subgroup		Time Period	N patients in cycle	n (%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=95)	Any TEAE	95	94 (98.9)	(94.3, 100.0)
		Cycle 1	95	87 (91.6)	(84.1, 96.3)
		Cycle 2	93	62 (65.3)	(54.8, 74.7)
		Cycle 3	88	56 (58.9)	(48.4, 68.9)
		Cycle 4	88	52 (54.7)	(44.2, 65.0)
		Cycle 5	79	45 (47.4)	(37.0, 57.9)
		Cycle 6	77	39 (41.1)	(31.1, 51.6)
		Cycle 7	72	44 (46.3)	(36.0, 56.8)
		Cycle >= 8 and < 18	70	62 (65.3)	(54.8, 74.7)
		Cycle >= 18	13	8 (8.4)	(3.7, 15.9)

Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	153 (99.4)	(96.4, 100.0)
		Cycle 1	154	143 (92.9)	(87.6, 96.4)
		Cycle 2	152	113 (73.4)	(65.7, 80.2)
		Cycle 3	146	95 (61.7)	(53.5, 69.4)
		Cycle 4	141	85 (55.2)	(47.0, 63.2)
		Cycle 5	129	76 (49.4)	(41.2, 57.5)
		Cycle 6	127	65 (42.2)	(34.3, 50.4)
		Cycle 7	121	72 (46.8)	(38.7, 55.0)
		Cycle >= 8 and < 18	114	103 (66.9)	(58.9, 74.2)
		Cycle >= 18	33	18 (11.7)	(7.1, 17.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHCR3+ (N=28)	Any TEAE	28	28 (100.0) (87.7, 100.0)
		Cycle 1	28	27 (96.4) (81.7, 99.9)
		Cycle 2	27	16 (57.1) (37.2, 75.5)
		Cycle 3	26	17 (60.7) (40.6, 78.5)
		Cycle 4	26	15 (53.6) (33.9, 72.5)
		Cycle 5	24	14 (50.0) (30.6, 69.4)
		Cycle 6	23	12 (42.9) (24.5, 62.8)
		Cycle 7	22	12 (42.9) (24.5, 62.8)
		Cycle >= 8 and < 18	22	16 (57.1) (37.2, 75.5)
		Cycle >= 18	2	0 (0.0) (0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	92 (98.9)	(94.2, 100.0)
		Cycle 1	93	87 (93.5)	(86.5, 97.6)
		Cycle 2	92	65 (69.9)	(59.5, 79.0)
		Cycle 3	87	55 (59.1)	(48.5, 69.2)
		Cycle 4	84	55 (59.1)	(48.5, 69.2)
		Cycle 5	80	50 (53.8)	(43.1, 64.2)
		Cycle 6	78	41 (44.1)	(33.8, 54.8)
		Cycle 7	75	47 (50.5)	(40.0, 61.1)
		Cycle >= 8 and < 18	73	62 (66.7)	(56.1, 76.1)
		Cycle >= 18	12	3 (3.2)	(0.7, 9.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	88 (100.0)	(95.9, 100.0)
		Cycle 1	88	81 (92.0)	(84.3, 96.7)
		Cycle 2	86	64 (72.7)	(62.2, 81.7)
		Cycle 3	85	59 (67.0)	(56.2, 76.7)
		Cycle 4	84	47 (53.4)	(42.5, 64.1)
		Cycle 5	74	41 (46.6)	(35.9, 57.5)
		Cycle 6	73	38 (43.2)	(32.7, 54.2)
		Cycle 7	69	37 (42.0)	(31.6, 53.0)
		Cycle >= 8 and < 18	64	57 (64.8)	(53.9, 74.7)
		Cycle >= 18	23	15 (17.0)	(9.9, 26.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	50 (98.0) (89.6, 100.0)
		Cycle 1	51	48 (94.1) (83.8, 98.8)
		Cycle 2	50	34 (66.7) (52.1, 79.2)
		Cycle 3	49	34 (66.7) (52.1, 79.2)
		Cycle 4	49	27 (52.9) (38.5, 67.1)
		Cycle 5	47	27 (52.9) (38.5, 67.1)
		Cycle 6	46	21 (41.2) (27.6, 55.8)
		Cycle 7	45	26 (51.0) (36.6, 65.2)
		Cycle >= 8 and < 18	44	38 (74.5) (60.4, 85.7)
		Cycle >= 18	8	2 (3.9) (0.5, 13.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	125 (100.0) (97.1, 100.0)
		Cycle 1	125	115 (92.0) (85.8, 96.1)
		Cycle 2	123	91 (72.8) (64.1, 80.4)
		Cycle 3	118	78 (62.4) (53.3, 70.9)
		Cycle 4	114	72 (57.6) (48.4, 66.4)
		Cycle 5	103	62 (49.6) (40.5, 58.7)
		Cycle 6	101	56 (44.8) (35.9, 54.0)
		Cycle 7	95	56 (44.8) (35.9, 54.0)
		Cycle >= 8 and < 18	90	79 (63.2) (54.1, 71.6)
		Cycle >= 18	27	16 (12.8) (7.5, 20.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	96 (99.0)	(94.4, 100.0)
		Cycle 1	97	91 (93.8)	(87.0, 97.7)
		Cycle 2	96	69 (71.1)	(61.0, 79.9)
		Cycle 3	91	58 (59.8)	(49.3, 69.6)
		Cycle 4	88	56 (57.7)	(47.3, 67.7)
		Cycle 5	84	52 (53.6)	(43.2, 63.8)
		Cycle 6	82	42 (43.3)	(33.3, 53.7)
		Cycle 7	79	48 (49.5)	(39.2, 59.8)
		Cycle >= 8 and < 18	76	65 (67.0)	(56.7, 76.2)
		Cycle >= 18	13	4 (4.1)	(1.1, 10.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	83 (100.0)	(95.7, 100.0)
		Cycle 1	83	76 (91.6)	(83.4, 96.5)
		Cycle 2	81	59 (71.1)	(60.1, 80.5)
		Cycle 3	80	56 (67.5)	(56.3, 77.4)
		Cycle 4	79	46 (55.4)	(44.1, 66.3)
		Cycle 5	69	39 (47.0)	(35.9, 58.3)
		Cycle 6	68	37 (44.6)	(33.7, 55.9)
		Cycle 7	64	36 (43.4)	(32.5, 54.7)
		Cycle >= 8 and < 18	60	53 (63.9)	(52.6, 74.1)
		Cycle >= 18	22	14 (16.9)	(9.5, 26.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Normal (N=90)	Any TEAE	90	89 (98.9) (94.0, 100.0)
		Cycle 1	90	85 (94.4) (87.5, 98.2)
		Cycle 2	89	59 (65.6) (54.8, 75.3)
		Cycle 3	85	53 (58.9) (48.0, 69.2)
		Cycle 4	85	53 (58.9) (48.0, 69.2)
		Cycle 5	76	45 (50.0) (39.3, 60.7)
		Cycle 6	73	38 (42.2) (31.9, 53.1)
		Cycle 7	72	42 (46.7) (36.1, 57.5)
		Cycle >= 8 and < 18	69	56 (62.2) (51.4, 72.2)
		Cycle >= 18	17	8 (8.9) (3.9, 16.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	69 (100.0)	(94.8, 100.0)
		Cycle 1	69	63 (91.3)	(82.0, 96.7)
		Cycle 2	68	54 (78.3)	(66.7, 87.3)
		Cycle 3	66	47 (68.1)	(55.8, 78.8)
		Cycle 4	63	37 (53.6)	(41.2, 65.7)
		Cycle 5	59	35 (50.7)	(38.4, 63.0)
		Cycle 6	59	30 (43.5)	(31.6, 56.0)
		Cycle 7	56	32 (46.4)	(34.3, 58.8)
		Cycle >= 8 and < 18	54	50 (72.5)	(60.4, 82.5)
		Cycle >= 18	14	7 (10.1)	(4.2, 19.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	25 (100.0)	(86.3, 100.0)
		Cycle 1	25	23 (92.0)	(74.0, 99.0)
		Cycle 2	24	17 (68.0)	(46.5, 85.1)
		Cycle 3	23	14 (56.0)	(34.9, 75.6)
		Cycle 4	21	12 (48.0)	(27.8, 68.7)
		Cycle 5	20	11 (44.0)	(24.4, 65.1)
		Cycle 6	20	11 (44.0)	(24.4, 65.1)
		Cycle 7	17	11 (44.0)	(24.4, 65.1)
		Cycle >= 8 and < 18	15	14 (56.0)	(34.9, 75.6)
		Cycle >= 18	4	3 (12.0)	(2.5, 31.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	104 (99.0)	(94.8, 100.0)
		Cycle 1	105	98 (93.3)	(86.7, 97.3)
		Cycle 2	104	74 (70.5)	(60.8, 79.0)
		Cycle 3	102	68 (64.8)	(54.8, 73.8)
		Cycle 4	98	64 (61.0)	(50.9, 70.3)
		Cycle 5	90	49 (46.7)	(36.9, 56.7)
		Cycle 6	89	48 (45.7)	(36.0, 55.7)
		Cycle 7	87	52 (49.5)	(39.6, 59.5)
		Cycle >= 8 and < 18	84	75 (71.4)	(61.8, 79.8)
		Cycle >= 18	22	13 (12.4)	(6.8, 20.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	76 (100.0)	(95.3, 100.0)
		Cycle 1	76	70 (92.1)	(83.6, 97.0)
		Cycle 2	74	53 (69.7)	(58.1, 79.8)
		Cycle 3	69	44 (57.9)	(46.0, 69.1)
		Cycle 4	68	37 (48.7)	(37.0, 60.4)
		Cycle 5	63	41 (53.9)	(42.1, 65.5)
		Cycle 6	61	31 (40.8)	(29.6, 52.7)
		Cycle 7	56	32 (42.1)	(30.9, 54.0)
		Cycle >= 8 and < 18	54	45 (59.2)	(47.3, 70.4)
		Cycle >= 18	13	5 (6.6)	(2.2, 14.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	24 (100.0)	(85.8, 100.0)
		Cycle 1	24	22 (91.7)	(73.0, 99.0)
		Cycle 2	23	15 (62.5)	(40.6, 81.2)
		Cycle 3	22	13 (54.2)	(32.8, 74.4)
		Cycle 4	22	14 (58.3)	(36.6, 77.9)
		Cycle 5	19	9 (37.5)	(18.8, 59.4)
		Cycle 6	18	11 (45.8)	(25.6, 67.2)
		Cycle 7	18	15 (62.5)	(40.6, 81.2)
		Cycle >= 8 and < 18	18	18 (75.0)	(53.3, 90.2)
		Cycle >= 18	6	3 (12.5)	(2.7, 32.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	159 (99.4)	(96.6, 100.0)
		Cycle 1	160	149 (93.1)	(88.0, 96.5)
		Cycle 2	158	115 (71.9)	(64.2, 78.7)
		Cycle 3	152	101 (63.1)	(55.1, 70.6)
		Cycle 4	147	88 (55.0)	(46.9, 62.9)
		Cycle 5	136	82 (51.3)	(43.2, 59.2)
		Cycle 6	134	68 (42.5)	(34.7, 50.6)
		Cycle 7	127	70 (43.8)	(35.9, 51.8)
		Cycle >= 8 and < 18	120	102 (63.8)	(55.8, 71.2)
		Cycle >= 18	29	15 (9.4)	(5.3, 15.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	53 (100.0)	(93.3, 100.0)
		Cycle 1	53	50 (94.3)	(84.3, 98.8)
		Cycle 2	52	40 (75.5)	(61.7, 86.2)
		Cycle 3	49	29 (54.7)	(40.4, 68.4)
		Cycle 4	48	32 (60.4)	(46.0, 73.5)
		Cycle 5	43	25 (47.2)	(33.3, 61.4)
		Cycle 6	42	27 (50.9)	(36.8, 64.9)
		Cycle 7	41	30 (56.6)	(42.3, 70.2)
		Cycle >= 8 and < 18	39	36 (67.9)	(53.7, 80.1)
		Cycle >= 18	8	4 (7.5)	(2.1, 18.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	130 (99.2)	(95.8, 100.0)
		Cycle 1	131	121 (92.4)	(86.4, 96.3)
		Cycle 2	129	90 (68.7)	(60.0, 76.5)
		Cycle 3	125	85 (64.9)	(56.1, 73.0)
		Cycle 4	121	70 (53.4)	(44.5, 62.2)
		Cycle 5	112	66 (50.4)	(41.5, 59.2)
		Cycle 6	110	52 (39.7)	(31.3, 48.6)
		Cycle 7	104	55 (42.0)	(33.4, 50.9)
		Cycle >= 8 and < 18	99	84 (64.1)	(55.3, 72.3)
		Cycle >= 18	27	14 (10.7)	(6.0, 17.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	168 (99.4) (96.7, 100.0)
		Cycle 1	169	157 (92.9) (87.9, 96.3)
		Cycle 2	166	119 (70.4) (62.9, 77.2)
		Cycle 3	159	102 (60.4) (52.6, 67.8)
		Cycle 4	154	93 (55.0) (47.2, 62.7)
		Cycle 5	142	83 (49.1) (41.4, 56.9)
		Cycle 6	139	72 (42.6) (35.0, 50.4)
		Cycle 7	132	79 (46.7) (39.0, 54.6)
		Cycle >= 8 and < 18	125	109 (64.5) (56.8, 71.7)
		Cycle >= 18	31	16 (9.5) (5.5, 14.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	15 (100.0)	(78.2, 100.0)
		Cycle 1	15	14 (93.3)	(68.1, 99.8)
		Cycle 2	15	11 (73.3)	(44.9, 92.2)
		Cycle 3	15	12 (80.0)	(51.9, 95.7)
		Cycle 4	15	9 (60.0)	(32.3, 83.7)
		Cycle 5	13	8 (53.3)	(26.6, 78.7)
		Cycle 6	13	7 (46.7)	(21.3, 73.4)
		Cycle 7	13	6 (40.0)	(16.3, 67.7)
		Cycle >= 8 and < 18	13	11 (73.3)	(44.9, 92.2)
		Cycle >= 18	4	2 (13.3)	(1.7, 40.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	56 (100.0)	(93.6, 100.0)
		Cycle 1	56	53 (94.6)	(85.1, 98.9)
		Cycle 2	55	41 (73.2)	(59.7, 84.2)
		Cycle 3	54	36 (64.3)	(50.4, 76.6)
		Cycle 4	53	31 (55.4)	(41.5, 68.7)
		Cycle 5	49	29 (51.8)	(38.0, 65.3)
		Cycle 6	48	23 (41.1)	(28.1, 55.0)
		Cycle 7	48	26 (46.4)	(33.0, 60.3)
		Cycle >= 8 and < 18	45	38 (67.9)	(54.0, 79.7)
		Cycle >= 18	16	9 (16.1)	(7.6, 28.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	127 (99.2)	(95.7, 100.0)
		Cycle 1	128	118 (92.2)	(86.1, 96.2)
		Cycle 2	126	89 (69.5)	(60.8, 77.4)
		Cycle 3	120	78 (60.9)	(51.9, 69.4)
		Cycle 4	116	71 (55.5)	(46.4, 64.3)
		Cycle 5	106	62 (48.4)	(39.5, 57.4)
		Cycle 6	104	56 (43.8)	(35.0, 52.8)
		Cycle 7	97	59 (46.1)	(37.2, 55.1)
		Cycle >= 8 and < 18	93	82 (64.1)	(55.1, 72.3)
		Cycle >= 18	19	9 (7.0)	(3.3, 12.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
0-Prior treatment lines	< 3 lines (N=17)	Any TEAE	17	17 (100.0) (80.5, 100.0)
		Cycle 1	17	16 (94.1) (71.3, 99.9)
		Cycle 2	17	13 (76.5) (50.1, 93.2)
		Cycle 3	17	11 (64.7) (38.3, 85.8)
		Cycle 4	17	12 (70.6) (44.0, 89.7)
		Cycle 5	17	9 (52.9) (27.8, 77.0)
		Cycle 6	16	8 (47.1) (23.0, 72.2)
		Cycle 7	16	8 (47.1) (23.0, 72.2)
		Cycle >= 8 and < 18	16	13 (76.5) (50.1, 93.2)
		Cycle >= 18	6	2 (11.8) (1.5, 36.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
0-Prior treatment lines	>= 3 lines (N=167)	Any TEAE	167	166 (99.4) (96.7, 100.0)
		Cycle 1	167	155 (92.8) (87.8, 96.2)
		Cycle 2	164	117 (70.1) (62.5, 76.9)
		Cycle 3	157	103 (61.7) (53.8, 69.1)
		Cycle 4	152	90 (53.9) (46.0, 61.6)
		Cycle 5	138	82 (49.1) (41.3, 56.9)
		Cycle 6	136	71 (42.5) (34.9, 50.4)
		Cycle 7	129	77 (46.1) (38.4, 54.0)
		Cycle >= 8 and < 18	122	107 (64.1) (56.3, 71.3)
		Cycle >= 18	29	16 (9.6) (5.6, 15.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	78 (98.7) (93.1, 100.0)
		Cycle 1	79	72 (91.1) (82.6, 96.4)
		Cycle 2	78	54 (68.4) (56.9, 78.4)
		Cycle 3	75	49 (62.0) (50.4, 72.7)
		Cycle 4	73	40 (50.6) (39.1, 62.1)
		Cycle 5	70	42 (53.2) (41.6, 64.5)
		Cycle 6	69	35 (44.3) (33.1, 55.9)
		Cycle 7	68	41 (51.9) (40.4, 63.3)
		Cycle >= 8 and < 18	65	58 (73.4) (62.3, 82.7)
		Cycle >= 18	17	10 (12.7) (6.2, 22.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	66 (100.0) (94.6, 100.0)
		Cycle 1	66	62 (93.9) (85.2, 98.3)
		Cycle 2	66	46 (69.7) (57.1, 80.4)
		Cycle 3	64	38 (57.6) (44.8, 69.7)
		Cycle 4	61	38 (57.6) (44.8, 69.7)
		Cycle 5	55	26 (39.4) (27.6, 52.2)
		Cycle 6	53	25 (37.9) (26.2, 50.7)
		Cycle 7	51	29 (43.9) (31.7, 56.7)
		Cycle >= 8 and < 18	51	43 (65.2) (52.4, 76.5)
		Cycle >= 18	10	7 (10.6) (4.4, 20.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	121 (100.0) (97.0, 100.0)
		Cycle 1	121	112 (92.6) (86.3, 96.5)
		Cycle 2	120	85 (70.2) (61.3, 78.2)
		Cycle 3	119	77 (63.6) (54.4, 72.2)
		Cycle 4	115	74 (61.2) (51.9, 69.9)
		Cycle 5	106	68 (56.2) (46.9, 65.2)
		Cycle 6	103	51 (42.1) (33.2, 51.5)
		Cycle 7	96	55 (45.5) (36.4, 54.8)
		Cycle >= 8 and < 18	93	80 (66.1) (57.0, 74.5)
		Cycle >= 18	25	13 (10.7) (5.8, 17.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	62 (98.4)	(91.5, 100.0)
		Cycle 1	63	59 (93.7)	(84.5, 98.2)
		Cycle 2	61	45 (71.4)	(58.7, 82.1)
		Cycle 3	55	37 (58.7)	(45.6, 71.0)
		Cycle 4	54	28 (44.4)	(31.9, 57.5)
		Cycle 5	49	23 (36.5)	(24.7, 49.6)
		Cycle 6	49	28 (44.4)	(31.9, 57.5)
		Cycle 7	49	30 (47.6)	(34.9, 60.6)
		Cycle >= 8 and < 18	45	40 (63.5)	(50.4, 75.3)
		Cycle >= 18	10	5 (7.9)	(2.6, 17.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	51 (100.0)	(93.0, 100.0)
		Cycle 1	51	46 (90.2)	(78.6, 96.7)
		Cycle 2	50	36 (70.6)	(56.2, 82.5)
		Cycle 3	50	28 (54.9)	(40.3, 68.9)
		Cycle 4	49	32 (62.7)	(48.1, 75.9)
		Cycle 5	46	29 (56.9)	(42.2, 70.7)
		Cycle 6	44	22 (43.1)	(29.3, 57.8)
		Cycle 7	40	25 (49.0)	(34.8, 63.4)
		Cycle >= 8 and < 18	40	33 (64.7)	(50.1, 77.6)
		Cycle >= 18	10	3 (5.9)	(1.2, 16.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	132 (99.2)	(95.9, 100.0)
		Cycle 1	133	125 (94.0)	(88.5, 97.4)
		Cycle 2	131	94 (70.7)	(62.2, 78.2)
		Cycle 3	124	86 (64.7)	(55.9, 72.7)
		Cycle 4	120	70 (52.6)	(43.8, 61.3)
		Cycle 5	109	62 (46.6)	(37.9, 55.5)
		Cycle 6	108	57 (42.9)	(34.3, 51.7)
		Cycle 7	105	60 (45.1)	(36.5, 54.0)
		Cycle >= 8 and < 18	98	87 (65.4)	(56.7, 73.4)
		Cycle >= 18	25	15 (11.3)	(6.5, 17.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

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Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	105 (57.1)	(49.6, 64.3)
		Cycle 1	184	38 (20.7)	(15.0, 27.2)
		Cycle 2	181	27 (14.7)	(9.9, 20.6)
		Cycle 3	174	14 (7.6)	(4.2, 12.4)
		Cycle 4	169	18 (9.8)	(5.9, 15.0)
		Cycle 5	155	10 (5.4)	(2.6, 9.8)
		Cycle 6	152	8 (4.3)	(1.9, 8.4)
		Cycle 7	145	14 (7.6)	(4.2, 12.4)
		Cycle >= 8 and < 18	138	41 (22.3)	(16.5, 29.0)
		Cycle >= 18	35	4 (2.2)	(0.6, 5.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	77 (55.0) (46.4, 63.4)
		Cycle 1	140	30 (21.4) (14.9, 29.2)
		Cycle 2	138	16 (11.4) (6.7, 17.9)
		Cycle 3	132	10 (7.1) (3.5, 12.7)
		Cycle 4	128	12 (8.6) (4.5, 14.5)
		Cycle 5	116	8 (5.7) (2.5, 10.9)
		Cycle 6	113	3 (2.1) (0.4, 6.1)
		Cycle 7	109	12 (8.6) (4.5, 14.5)
		Cycle >= 8 and < 18	103	26 (18.6) (12.5, 26.0)
		Cycle >= 18	24	4 (2.9) (0.8, 7.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	28 (63.6) (47.8, 77.6)
		Cycle 1	44	8 (18.2) (8.2, 32.7)
		Cycle 2	43	11 (25.0) (13.2, 40.3)
		Cycle 3	42	4 (9.1) (2.5, 21.7)
		Cycle 4	41	6 (13.6) (5.2, 27.4)
		Cycle 5	39	2 (4.5) (0.6, 15.5)
		Cycle 6	39	5 (11.4) (3.8, 24.6)
		Cycle 7	36	2 (4.5) (0.6, 15.5)
		Cycle >= 8 and < 18	35	15 (34.1) (20.5, 49.9)
		Cycle >= 18	11	0 (0.0) (0.0, 8.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	34 (54.0) (40.9, 66.6)
		Cycle 1	63	13 (20.6) (11.5, 32.7)
		Cycle 2	61	7 (11.1) (4.6, 21.6)
		Cycle 3	58	4 (6.3) (1.8, 15.5)
		Cycle 4	58	2 (3.2) (0.4, 11.0)
		Cycle 5	55	3 (4.8) (1.0, 13.3)
		Cycle 6	55	6 (9.5) (3.6, 19.6)
		Cycle 7	53	6 (9.5) (3.6, 19.6)
		Cycle >= 8 and < 18	49	17 (27.0) (16.6, 39.7)
		Cycle >= 18	15	1 (1.6) (0.0, 8.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	31 (58.5) (44.1, 71.9)
		Cycle 1	53	12 (22.6) (12.3, 36.2)
		Cycle 2	53	10 (18.9) (9.4, 32.0)
		Cycle 3	52	7 (13.2) (5.5, 25.3)
		Cycle 4	49	9 (17.0) (8.1, 29.8)
		Cycle 5	44	5 (9.4) (3.1, 20.7)
		Cycle 6	42	1 (1.9) (0.0, 10.1)
		Cycle 7	40	3 (5.7) (1.2, 15.7)
		Cycle >= 8 and < 18	39	8 (15.1) (6.7, 27.6)
		Cycle >= 18	11	2 (3.8) (0.5, 13.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	40 (58.8) (46.2, 70.6)
		Cycle 1	68	13 (19.1) (10.6, 30.5)
		Cycle 2	67	10 (14.7) (7.3, 25.4)
		Cycle 3	64	3 (4.4) (0.9, 12.4)
		Cycle 4	62	7 (10.3) (4.2, 20.1)
		Cycle 5	56	2 (2.9) (0.4, 10.2)
		Cycle 6	55	1 (1.5) (0.0, 7.9)
		Cycle 7	52	5 (7.4) (2.4, 16.3)
		Cycle >= 8 and < 18	50	16 (23.5) (14.1, 35.4)
		Cycle >= 18	9	1 (1.5) (0.0, 7.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	56 (54.9)	(44.7, 64.8)
		Cycle 1	102	20 (19.6)	(12.4, 28.6)
		Cycle 2	101	17 (16.7)	(10.0, 25.3)
		Cycle 3	100	10 (9.8)	(4.8, 17.3)
		Cycle 4	98	5 (4.9)	(1.6, 11.1)
		Cycle 5	94	5 (4.9)	(1.6, 11.1)
		Cycle 6	93	5 (4.9)	(1.6, 11.1)
		Cycle 7	88	6 (5.9)	(2.2, 12.4)
		Cycle >= 8 and < 18	86	20 (19.6)	(12.4, 28.6)
		Cycle >= 18	23	4 (3.9)	(1.1, 9.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	48 (59.3)	(47.8, 70.1)
		Cycle 1	81	18 (22.2)	(13.7, 32.8)
		Cycle 2	79	10 (12.3)	(6.1, 21.5)
		Cycle 3	73	3 (3.7)	(0.8, 10.4)
		Cycle 4	71	13 (16.0)	(8.8, 25.9)
		Cycle 5	61	5 (6.2)	(2.0, 13.8)
		Cycle 6	59	3 (3.7)	(0.8, 10.4)
		Cycle 7	57	8 (9.9)	(4.4, 18.5)
		Cycle >= 8 and < 18	52	21 (25.9)	(16.8, 36.9)
		Cycle >= 18	12	0 (0.0)	(0.0, 4.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions < 5 cm (N=74)	Any TEAE	74	38 (51.4)	(39.4, 63.1)
	Cycle 1	74	8 (10.8)	(4.8, 20.2)
	Cycle 2	73	12 (16.2)	(8.7, 26.6)
	Cycle 3	71	6 (8.1)	(3.0, 16.8)
	Cycle 4	66	6 (8.1)	(3.0, 16.8)
	Cycle 5	61	3 (4.1)	(0.8, 11.4)
	Cycle 6	60	1 (1.4)	(0.0, 7.3)
	Cycle 7	59	7 (9.5)	(3.9, 18.5)
	Cycle >= 8 and < 18	54	17 (23.0)	(14.0, 34.2)
	Cycle >= 18	18	0 (0.0)	(0.0, 4.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

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			Overall 5.4 mg/kg SAF (N=184)		
Subgroup		Time Period	N patients in cycle	n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=95)	Any TEAE	95	58 (61.1)	(50.5, 70.9)
		Cycle 1	95	26 (27.4)	(18.7, 37.5)
		Cycle 2	93	11 (11.6)	(5.9, 19.8)
		Cycle 3	88	7 (7.4)	(3.0, 14.6)
		Cycle 4	88	12 (12.6)	(6.7, 21.0)
		Cycle 5	79	6 (6.3)	(2.4, 13.2)
		Cycle 6	77	6 (6.3)	(2.4, 13.2)
		Cycle 7	72	5 (5.3)	(1.7, 11.9)
		Cycle >= 8 and < 18	70	20 (21.1)	(13.4, 30.6)
		Cycle >= 18	13	3 (3.2)	(0.7, 9.0)

Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	91 (59.1)	(50.9, 66.9)
		Cycle 1	154	33 (21.4)	(15.2, 28.8)
		Cycle 2	152	23 (14.9)	(9.7, 21.6)
		Cycle 3	146	12 (7.8)	(4.1, 13.2)
		Cycle 4	141	15 (9.7)	(5.6, 15.6)
		Cycle 5	129	9 (5.8)	(2.7, 10.8)
		Cycle 6	127	8 (5.2)	(2.3, 10.0)
		Cycle 7	121	13 (8.4)	(4.6, 14.0)
		Cycle >= 8 and < 18	114	36 (23.4)	(16.9, 30.9)
		Cycle >= 18	33	4 (2.6)	(0.7, 6.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHCR3+ (N=28)			
	Any TEAE	28	13 (46.4)	(27.5, 66.1)
	Cycle 1	28	5 (17.9)	(6.1, 36.9)
	Cycle 2	27	4 (14.3)	(4.0, 32.7)
	Cycle 3	26	2 (7.1)	(0.9, 23.5)
	Cycle 4	26	3 (10.7)	(2.3, 28.2)
	Cycle 5	24	1 (3.6)	(0.1, 18.3)
	Cycle 6	23	0 (0.0)	(0.0, 12.3)
	Cycle 7	22	1 (3.6)	(0.1, 18.3)
	Cycle >= 8 and < 18	22	4 (14.3)	(4.0, 32.7)
	Cycle >= 18	2	0 (0.0)	(0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	54 (58.1)	(47.4, 68.2)
		Cycle 1	93	24 (25.8)	(17.3, 35.9)
		Cycle 2	92	18 (19.4)	(11.9, 28.9)
		Cycle 3	87	7 (7.5)	(3.1, 14.9)
		Cycle 4	84	8 (8.6)	(3.8, 16.2)
		Cycle 5	80	6 (6.5)	(2.4, 13.5)
		Cycle 6	78	3 (3.2)	(0.7, 9.1)
		Cycle 7	75	7 (7.5)	(3.1, 14.9)
		Cycle >= 8 and < 18	73	21 (22.6)	(14.6, 32.4)
		Cycle >= 18	12	0 (0.0)	(0.0, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	50 (56.8) (45.8, 67.3)
		Cycle 1	88	14 (15.9) (9.0, 25.2)
		Cycle 2	86	9 (10.2) (4.8, 18.5)
		Cycle 3	85	6 (6.8) (2.5, 14.3)
		Cycle 4	84	10 (11.4) (5.6, 19.9)
		Cycle 5	74	4 (4.5) (1.3, 11.2)
		Cycle 6	73	5 (5.7) (1.9, 12.8)
		Cycle 7	69	7 (8.0) (3.3, 15.7)
		Cycle >= 8 and < 18	64	20 (22.7) (14.5, 32.9)
		Cycle >= 18	23	4 (4.5) (1.3, 11.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	26 (51.0)	(36.6, 65.2)
		Cycle 1	51	12 (23.5)	(12.8, 37.5)
		Cycle 2	50	7 (13.7)	(5.7, 26.3)
		Cycle 3	49	3 (5.9)	(1.2, 16.2)
		Cycle 4	49	2 (3.9)	(0.5, 13.5)
		Cycle 5	47	3 (5.9)	(1.2, 16.2)
		Cycle 6	46	1 (2.0)	(0.0, 10.4)
		Cycle 7	45	6 (11.8)	(4.4, 23.9)
		Cycle >= 8 and < 18	44	12 (23.5)	(12.8, 37.5)
		Cycle >= 18	8	0 (0.0)	(0.0, 7.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	75 (60.0) (50.9, 68.7)
		Cycle 1	125	24 (19.2) (12.7, 27.2)
		Cycle 2	123	19 (15.2) (9.4, 22.7)
		Cycle 3	118	10 (8.0) (3.9, 14.2)
		Cycle 4	114	16 (12.8) (7.5, 20.0)
		Cycle 5	103	7 (5.6) (2.3, 11.2)
		Cycle 6	101	7 (5.6) (2.3, 11.2)
		Cycle 7	95	8 (6.4) (2.8, 12.2)
		Cycle >= 8 and < 18	90	29 (23.2) (16.1, 31.6)
		Cycle >= 18	27	4 (3.2) (0.9, 8.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	56 (57.7)	(47.3, 67.7)
		Cycle 1	97	25 (25.8)	(17.4, 35.7)
		Cycle 2	96	20 (20.6)	(13.1, 30.0)
		Cycle 3	91	7 (7.2)	(3.0, 14.3)
		Cycle 4	88	8 (8.2)	(3.6, 15.6)
		Cycle 5	84	7 (7.2)	(3.0, 14.3)
		Cycle 6	82	3 (3.1)	(0.6, 8.8)
		Cycle 7	79	8 (8.2)	(3.6, 15.6)
		Cycle >= 8 and < 18	76	21 (21.6)	(13.9, 31.2)
		Cycle >= 18	13	0 (0.0)	(0.0, 3.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	47 (56.6) (45.3, 67.5)
		Cycle 1	83	12 (14.5) (7.7, 23.9)
		Cycle 2	81	7 (8.4) (3.5, 16.6)
		Cycle 3	80	6 (7.2) (2.7, 15.1)
		Cycle 4	79	10 (12.0) (5.9, 21.0)
		Cycle 5	69	3 (3.6) (0.8, 10.2)
		Cycle 6	68	5 (6.0) (2.0, 13.5)
		Cycle 7	64	6 (7.2) (2.7, 15.1)
		Cycle >= 8 and < 18	60	20 (24.1) (15.4, 34.7)
		Cycle >= 18	22	4 (4.8) (1.3, 11.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Normal (N=90)	Any TEAE	90	49 (54.4) (43.6, 65.0)
		Cycle 1	90	18 (20.0) (12.3, 29.8)
		Cycle 2	89	8 (8.9) (3.9, 16.8)
		Cycle 3	85	4 (4.4) (1.2, 11.0)
		Cycle 4	85	10 (11.1) (5.5, 19.5)
		Cycle 5	76	7 (7.8) (3.2, 15.4)
		Cycle 6	73	1 (1.1) (0.0, 6.0)
		Cycle 7	72	8 (8.9) (3.9, 16.8)
		Cycle >= 8 and < 18	69	16 (17.8) (10.5, 27.3)
		Cycle >= 18	17	3 (3.3) (0.7, 9.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	42 (60.9) (48.4, 72.4)
		Cycle 1	69	16 (23.2) (13.9, 34.9)
		Cycle 2	68	12 (17.4) (9.3, 28.4)
		Cycle 3	66	7 (10.1) (4.2, 19.8)
		Cycle 4	63	7 (10.1) (4.2, 19.8)
		Cycle 5	59	2 (2.9) (0.4, 10.1)
		Cycle 6	59	5 (7.2) (2.4, 16.1)
		Cycle 7	56	6 (8.7) (3.3, 18.0)
		Cycle >= 8 and < 18	54	20 (29.0) (18.7, 41.2)
		Cycle >= 18	14	0 (0.0) (0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	14 (56.0) (34.9, 75.6)
		Cycle 1	25	4 (16.0) (4.5, 36.1)
		Cycle 2	24	7 (28.0) (12.1, 49.4)
		Cycle 3	23	3 (12.0) (2.5, 31.2)
		Cycle 4	21	1 (4.0) (0.1, 20.4)
		Cycle 5	20	1 (4.0) (0.1, 20.4)
		Cycle 6	20	2 (8.0) (1.0, 26.0)
		Cycle 7	17	0 (0.0) (0.0, 13.7)
		Cycle >= 8 and < 18	15	5 (20.0) (6.8, 40.7)
		Cycle >= 18	4	1 (4.0) (0.1, 20.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	68 (64.8) (54.8, 73.8)
		Cycle 1	105	22 (21.0) (13.6, 30.0)
		Cycle 2	104	19 (18.1) (11.3, 26.8)
		Cycle 3	102	11 (10.5) (5.3, 18.0)
		Cycle 4	98	8 (7.6) (3.3, 14.5)
		Cycle 5	90	5 (4.8) (1.6, 10.8)
		Cycle 6	89	7 (6.7) (2.7, 13.3)
		Cycle 7	87	9 (8.6) (4.0, 15.6)
		Cycle >= 8 and < 18	84	27 (25.7) (17.7, 35.2)
		Cycle >= 18	22	3 (2.9) (0.6, 8.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	34 (44.7) (33.3, 56.6)
		Cycle 1	76	15 (19.7) (11.5, 30.5)
		Cycle 2	74	8 (10.5) (4.7, 19.7)
		Cycle 3	69	3 (3.9) (0.8, 11.1)
		Cycle 4	68	8 (10.5) (4.7, 19.7)
		Cycle 5	63	5 (6.6) (2.2, 14.7)
		Cycle 6	61	1 (1.3) (0.0, 7.1)
		Cycle 7	56	4 (5.3) (1.5, 12.9)
		Cycle >= 8 and < 18	54	14 (18.4) (10.5, 29.0)
		Cycle >= 18	13	1 (1.3) (0.0, 7.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	13 (54.2)	(32.8, 74.4)
		Cycle 1	24	5 (20.8)	(7.1, 42.2)
		Cycle 2	23	2 (8.3)	(1.0, 27.0)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	1 (4.2)	(0.1, 21.1)
		Cycle 6	18	1 (4.2)	(0.1, 21.1)
		Cycle 7	18	2 (8.3)	(1.0, 27.0)
		Cycle >= 8 and < 18	18	9 (37.5)	(18.8, 59.4)
		Cycle >= 18	6	1 (4.2)	(0.1, 21.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	92 (57.5)	(49.4, 65.3)
		Cycle 1	160	33 (20.6)	(14.6, 27.7)
		Cycle 2	158	25 (15.6)	(10.4, 22.2)
		Cycle 3	152	14 (8.8)	(4.9, 14.2)
		Cycle 4	147	18 (11.3)	(6.8, 17.2)
		Cycle 5	136	9 (5.6)	(2.6, 10.4)
		Cycle 6	134	7 (4.4)	(1.8, 8.8)
		Cycle 7	127	12 (7.5)	(3.9, 12.7)
		Cycle >= 8 and < 18	120	32 (20.0)	(14.1, 27.0)
		Cycle >= 18	29	3 (1.9)	(0.4, 5.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	36 (67.9) (53.7, 80.1)
		Cycle 1	53	14 (26.4) (15.3, 40.3)
		Cycle 2	52	12 (22.6) (12.3, 36.2)
		Cycle 3	49	3 (5.7) (1.2, 15.7)
		Cycle 4	48	6 (11.3) (4.3, 23.0)
		Cycle 5	43	3 (5.7) (1.2, 15.7)
		Cycle 6	42	2 (3.8) (0.5, 13.0)
		Cycle 7	41	4 (7.5) (2.1, 18.2)
		Cycle >= 8 and < 18	39	14 (26.4) (15.3, 40.3)
		Cycle >= 18	8	0 (0.0) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	69 (52.7)	(43.8, 61.5)
		Cycle 1	131	24 (18.3)	(12.1, 26.0)
		Cycle 2	129	15 (11.5)	(6.6, 18.2)
		Cycle 3	125	11 (8.4)	(4.3, 14.5)
		Cycle 4	121	12 (9.2)	(4.8, 15.5)
		Cycle 5	112	7 (5.3)	(2.2, 10.7)
		Cycle 6	110	6 (4.6)	(1.7, 9.7)
		Cycle 7	104	10 (7.6)	(3.7, 13.6)
		Cycle >= 8 and < 18	99	27 (20.6)	(14.0, 28.6)
		Cycle >= 18	27	4 (3.1)	(0.8, 7.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	97 (57.4) (49.6, 65.0)
		Cycle 1	169	36 (21.3) (15.4, 28.3)
		Cycle 2	166	26 (15.4) (10.3, 21.7)
		Cycle 3	159	13 (7.7) (4.2, 12.8)
		Cycle 4	154	17 (10.1) (6.0, 15.6)
		Cycle 5	142	10 (5.9) (2.9, 10.6)
		Cycle 6	139	8 (4.7) (2.1, 9.1)
		Cycle 7	132	12 (7.1) (3.7, 12.1)
		Cycle >= 8 and < 18	125	36 (21.3) (15.4, 28.3)
		Cycle >= 18	31	4 (2.4) (0.6, 5.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	8 (53.3) (26.6, 78.7)
		Cycle 1	15	2 (13.3) (1.7, 40.5)
		Cycle 2	15	1 (6.7) (0.2, 31.9)
		Cycle 3	15	1 (6.7) (0.2, 31.9)
		Cycle 4	15	1 (6.7) (0.2, 31.9)
		Cycle 5	13	0 (0.0) (0.0, 21.8)
		Cycle 6	13	0 (0.0) (0.0, 21.8)
		Cycle 7	13	2 (13.3) (1.7, 40.5)
		Cycle >= 8 and < 18	13	5 (33.3) (11.8, 61.6)
		Cycle >= 18	4	0 (0.0) (0.0, 21.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	24 (42.9)	(29.7, 56.8)
		Cycle 1	56	7 (12.5)	(5.2, 24.1)
		Cycle 2	55	3 (5.4)	(1.1, 14.9)
		Cycle 3	54	3 (5.4)	(1.1, 14.9)
		Cycle 4	53	4 (7.1)	(2.0, 17.3)
		Cycle 5	49	1 (1.8)	(0.0, 9.6)
		Cycle 6	48	1 (1.8)	(0.0, 9.6)
		Cycle 7	48	4 (7.1)	(2.0, 17.3)
		Cycle >= 8 and < 18	45	9 (16.1)	(7.6, 28.3)
		Cycle >= 18	16	2 (3.6)	(0.4, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	81 (63.3)	(54.3, 71.6)
		Cycle 1	128	31 (24.2)	(17.1, 32.6)
		Cycle 2	126	24 (18.8)	(12.4, 26.6)
		Cycle 3	120	11 (8.6)	(4.4, 14.9)
		Cycle 4	116	14 (10.9)	(6.1, 17.7)
		Cycle 5	106	9 (7.0)	(3.3, 12.9)
		Cycle 6	104	7 (5.5)	(2.2, 10.9)
		Cycle 7	97	10 (7.8)	(3.8, 13.9)
		Cycle >= 8 and < 18	93	32 (25.0)	(17.8, 33.4)
		Cycle >= 18	19	2 (1.6)	(0.2, 5.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
0-Prior treatment lines	< 3 lines (N=17)	Any TEAE	17	9 (52.9) (27.8, 77.0)
		Cycle 1	17	3 (17.6) (3.8, 43.4)
		Cycle 2	17	1 (5.9) (0.1, 28.7)
		Cycle 3	17	1 (5.9) (0.1, 28.7)
		Cycle 4	17	3 (17.6) (3.8, 43.4)
		Cycle 5	17	1 (5.9) (0.1, 28.7)
		Cycle 6	16	1 (5.9) (0.1, 28.7)
		Cycle 7	16	2 (11.8) (1.5, 36.4)
		Cycle >= 8 and < 18	16	4 (23.5) (6.8, 49.9)
		Cycle >= 18	6	0 (0.0) (0.0, 19.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
0-Prior treatment lines	>= 3 lines (N=167)	Any TEAE	167	96 (57.5) (49.6, 65.1)
		Cycle 1	167	35 (21.0) (15.1, 27.9)
		Cycle 2	164	26 (15.6) (10.4, 22.0)
		Cycle 3	157	13 (7.8) (4.2, 12.9)
		Cycle 4	152	15 (9.0) (5.1, 14.4)
		Cycle 5	138	9 (5.4) (2.5, 10.0)
		Cycle 6	136	7 (4.2) (1.7, 8.4)
		Cycle 7	129	12 (7.2) (3.8, 12.2)
		Cycle >= 8 and < 18	122	37 (22.2) (16.1, 29.2)
		Cycle >= 18	29	4 (2.4) (0.7, 6.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	45 (57.0) (45.3, 68.1)
		Cycle 1	79	17 (21.5) (13.1, 32.2)
		Cycle 2	78	14 (17.7) (10.0, 27.9)
		Cycle 3	75	6 (7.6) (2.8, 15.8)
		Cycle 4	73	8 (10.1) (4.5, 19.0)
		Cycle 5	70	4 (5.1) (1.4, 12.5)
		Cycle 6	69	4 (5.1) (1.4, 12.5)
		Cycle 7	68	6 (7.6) (2.8, 15.8)
		Cycle >= 8 and < 18	65	18 (22.8) (14.1, 33.6)
		Cycle >= 18	17	0 (0.0) (0.0, 4.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	41 (62.1) (49.3, 73.8)
		Cycle 1	66	16 (24.2) (14.5, 36.4)
		Cycle 2	66	8 (12.1) (5.4, 22.5)
		Cycle 3	64	6 (9.1) (3.4, 18.7)
		Cycle 4	61	5 (7.6) (2.5, 16.8)
		Cycle 5	55	3 (4.5) (0.9, 12.7)
		Cycle 6	53	4 (6.1) (1.7, 14.8)
		Cycle 7	51	5 (7.6) (2.5, 16.8)
		Cycle >= 8 and < 18	51	18 (27.3) (17.0, 39.6)
		Cycle >= 18	10	2 (3.0) (0.4, 10.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	66 (54.5)	(45.2, 63.6)
		Cycle 1	121	25 (20.7)	(13.8, 29.0)
		Cycle 2	120	16 (13.2)	(7.8, 20.6)
		Cycle 3	119	9 (7.4)	(3.5, 13.7)
		Cycle 4	115	13 (10.7)	(5.8, 17.7)
		Cycle 5	106	7 (5.8)	(2.4, 11.6)
		Cycle 6	103	5 (4.1)	(1.4, 9.4)
		Cycle 7	96	6 (5.0)	(1.8, 10.5)
		Cycle >= 8 and < 18	93	23 (19.0)	(12.4, 27.1)
		Cycle >= 18	25	3 (2.5)	(0.5, 7.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	39 (61.9)	(48.8, 73.9)
		Cycle 1	63	13 (20.6)	(11.5, 32.7)
		Cycle 2	61	11 (17.5)	(9.1, 29.1)
		Cycle 3	55	5 (7.9)	(2.6, 17.6)
		Cycle 4	54	5 (7.9)	(2.6, 17.6)
		Cycle 5	49	3 (4.8)	(1.0, 13.3)
		Cycle 6	49	3 (4.8)	(1.0, 13.3)
		Cycle 7	49	8 (12.7)	(5.6, 23.5)
		Cycle >= 8 and < 18	45	18 (28.6)	(17.9, 41.3)
		Cycle >= 18	10	1 (1.6)	(0.0, 8.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	28 (54.9) (40.3, 68.9)
		Cycle 1	51	12 (23.5) (12.8, 37.5)
		Cycle 2	50	3 (5.9) (1.2, 16.2)
		Cycle 3	50	1 (2.0) (0.0, 10.4)
		Cycle 4	49	8 (15.7) (7.0, 28.6)
		Cycle 5	46	3 (5.9) (1.2, 16.2)
		Cycle 6	44	1 (2.0) (0.0, 10.4)
		Cycle 7	40	3 (5.9) (1.2, 16.2)
		Cycle >= 8 and < 18	40	12 (23.5) (12.8, 37.5)
		Cycle >= 18	10	1 (2.0) (0.0, 10.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	77 (57.9) (49.0, 66.4)
		Cycle 1	133	26 (19.5) (13.2, 27.3)
		Cycle 2	131	24 (18.0) (11.9, 25.6)
		Cycle 3	124	13 (9.8) (5.3, 16.1)
		Cycle 4	120	10 (7.5) (3.7, 13.4)
		Cycle 5	109	7 (5.3) (2.1, 10.5)
		Cycle 6	108	7 (5.3) (2.1, 10.5)
		Cycle 7	105	11 (8.3) (4.2, 14.3)
		Cycle >= 8 and < 18	98	29 (21.8) (15.1, 29.8)
		Cycle >= 18	25	3 (2.3) (0.5, 6.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

UE, die zum Therapieabbruch führten

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	28 (15.2)	(10.4, 21.2)
		Cycle 1	184	3 (1.6)	(0.3, 4.7)
		Cycle 2	181	2 (1.1)	(0.1, 3.9)
		Cycle 3	174	1 (0.5)	(0.0, 3.0)
		Cycle 4	169	1 (0.5)	(0.0, 3.0)
		Cycle 5	155	0 (0.0)	(0.0, 2.0)
		Cycle 6	152	3 (1.6)	(0.3, 4.7)
		Cycle 7	145	3 (1.6)	(0.3, 4.7)
		Cycle >= 8 and < 18	138	13 (7.1)	(3.8, 11.8)
		Cycle >= 18	35	2 (1.1)	(0.1, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	22 (15.7) (10.1, 22.8)
		Cycle 1	140	3 (2.1) (0.4, 6.1)
		Cycle 2	138	2 (1.4) (0.2, 5.1)
		Cycle 3	132	1 (0.7) (0.0, 3.9)
		Cycle 4	128	1 (0.7) (0.0, 3.9)
		Cycle 5	116	0 (0.0) (0.0, 2.6)
		Cycle 6	113	2 (1.4) (0.2, 5.1)
		Cycle 7	109	3 (2.1) (0.4, 6.1)
		Cycle >= 8 and < 18	103	9 (6.4) (3.0, 11.9)
		Cycle >= 18	24	1 (0.7) (0.0, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	6 (13.6) (5.2, 27.4)
		Cycle 1	44	0 (0.0) (0.0, 8.0)
		Cycle 2	43	0 (0.0) (0.0, 8.0)
		Cycle 3	42	0 (0.0) (0.0, 8.0)
		Cycle 4	41	0 (0.0) (0.0, 8.0)
		Cycle 5	39	0 (0.0) (0.0, 8.0)
		Cycle 6	39	1 (2.3) (0.1, 12.0)
		Cycle 7	36	0 (0.0) (0.0, 8.0)
		Cycle >= 8 and < 18	35	4 (9.1) (2.5, 21.7)
		Cycle >= 18	11	1 (2.3) (0.1, 12.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	14 (22.2) (12.7, 34.5)
		Cycle 1	63	2 (3.2) (0.4, 11.0)
		Cycle 2	61	1 (1.6) (0.0, 8.5)
		Cycle 3	58	0 (0.0) (0.0, 5.7)
		Cycle 4	58	0 (0.0) (0.0, 5.7)
		Cycle 5	55	0 (0.0) (0.0, 5.7)
		Cycle 6	55	1 (1.6) (0.0, 8.5)
		Cycle 7	53	2 (3.2) (0.4, 11.0)
		Cycle >= 8 and < 18	49	6 (9.5) (3.6, 19.6)
		Cycle >= 18	15	2 (3.2) (0.4, 11.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	5 (9.4) (3.1, 20.7)
		Cycle 1	53	0 (0.0) (0.0, 6.7)
		Cycle 2	53	0 (0.0) (0.0, 6.7)
		Cycle 3	52	0 (0.0) (0.0, 6.7)
		Cycle 4	49	1 (1.9) (0.0, 10.1)
		Cycle 5	44	0 (0.0) (0.0, 6.7)
		Cycle 6	42	2 (3.8) (0.5, 13.0)
		Cycle 7	40	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	2 (3.8) (0.5, 13.0)
		Cycle >= 18	11	0 (0.0) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	9 (13.2) (6.2, 23.6)
		Cycle 1	68	1 (1.5) (0.0, 7.9)
		Cycle 2	67	1 (1.5) (0.0, 7.9)
		Cycle 3	64	1 (1.5) (0.0, 7.9)
		Cycle 4	62	0 (0.0) (0.0, 5.3)
		Cycle 5	56	0 (0.0) (0.0, 5.3)
		Cycle 6	55	0 (0.0) (0.0, 5.3)
		Cycle 7	52	1 (1.5) (0.0, 7.9)
		Cycle >= 8 and < 18	50	5 (7.4) (2.4, 16.3)
		Cycle >= 18	9	0 (0.0) (0.0, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	18 (17.6) (10.8, 26.4)
		Cycle 1	102	2 (2.0) (0.2, 6.9)
		Cycle 2	101	0 (0.0) (0.0, 3.6)
		Cycle 3	100	1 (1.0) (0.0, 5.3)
		Cycle 4	98	0 (0.0) (0.0, 3.6)
		Cycle 5	94	0 (0.0) (0.0, 3.6)
		Cycle 6	93	3 (2.9) (0.6, 8.4)
		Cycle 7	88	1 (1.0) (0.0, 5.3)
		Cycle >= 8 and < 18	86	9 (8.8) (4.1, 16.1)
		Cycle >= 18	23	2 (2.0) (0.2, 6.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	10 (12.3) (6.1, 21.5)
		Cycle 1	81	1 (1.2) (0.0, 6.7)
		Cycle 2	79	2 (2.5) (0.3, 8.6)
		Cycle 3	73	0 (0.0) (0.0, 4.5)
		Cycle 4	71	1 (1.2) (0.0, 6.7)
		Cycle 5	61	0 (0.0) (0.0, 4.5)
		Cycle 6	59	0 (0.0) (0.0, 4.5)
		Cycle 7	57	2 (2.5) (0.3, 8.6)
		Cycle >= 8 and < 18	52	4 (4.9) (1.4, 12.2)
		Cycle >= 18	12	0 (0.0) (0.0, 4.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions < 5 cm (N=74)	Any TEAE	74	15 (20.3)	(11.8, 31.2)
	Cycle 1	74	0 (0.0)	(0.0, 4.9)
	Cycle 2	73	1 (1.4)	(0.0, 7.3)
	Cycle 3	71	1 (1.4)	(0.0, 7.3)
	Cycle 4	66	1 (1.4)	(0.0, 7.3)
	Cycle 5	61	0 (0.0)	(0.0, 4.9)
	Cycle 6	60	0 (0.0)	(0.0, 4.9)
	Cycle 7	59	3 (4.1)	(0.8, 11.4)
	Cycle >= 8 and < 18	54	8 (10.8)	(4.8, 20.2)
	Cycle >= 18	18	1 (1.4)	(0.0, 7.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

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			Overall 5.4 mg/kg SAF (N=184)	
Subgroup	Time Period	N patients in cycle	n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=95)	Any TEAE	95	9 (9.5) (4.4, 17.2)
		Cycle 1	95	3 (3.2) (0.7, 9.0)
		Cycle 2	93	1 (1.1) (0.0, 5.7)
		Cycle 3	88	0 (0.0) (0.0, 3.8)
		Cycle 4	88	0 (0.0) (0.0, 3.8)
		Cycle 5	79	0 (0.0) (0.0, 3.8)
		Cycle 6	77	2 (2.1) (0.3, 7.4)
		Cycle 7	72	0 (0.0) (0.0, 3.8)
		Cycle >= 8 and < 18	70	3 (3.2) (0.7, 9.0)
		Cycle >= 18	13	0 (0.0) (0.0, 3.8)

Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	24 (15.6)	(10.2, 22.3)
		Cycle 1	154	3 (1.9)	(0.4, 5.6)
		Cycle 2	152	2 (1.3)	(0.2, 4.6)
		Cycle 3	146	1 (0.6)	(0.0, 3.6)
		Cycle 4	141	1 (0.6)	(0.0, 3.6)
		Cycle 5	129	0 (0.0)	(0.0, 2.4)
		Cycle 6	127	2 (1.3)	(0.2, 4.6)
		Cycle 7	121	3 (1.9)	(0.4, 5.6)
		Cycle >= 8 and < 18	114	10 (6.5)	(3.2, 11.6)
		Cycle >= 18	33	2 (1.3)	(0.2, 4.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Any TEAE	28	3 (10.7) (2.3, 28.2)
		Cycle 1	28	0 (0.0) (0.0, 12.3)
		Cycle 2	27	0 (0.0) (0.0, 12.3)
		Cycle 3	26	0 (0.0) (0.0, 12.3)
		Cycle 4	26	0 (0.0) (0.0, 12.3)
		Cycle 5	24	0 (0.0) (0.0, 12.3)
		Cycle 6	23	1 (3.6) (0.1, 18.3)
		Cycle 7	22	0 (0.0) (0.0, 12.3)
		Cycle >= 8 and < 18	22	2 (7.1) (0.9, 23.5)
		Cycle >= 18	2	0 (0.0) (0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	14 (15.1)	(8.5, 24.0)
		Cycle 1	93	1 (1.1)	(0.0, 5.8)
		Cycle 2	92	1 (1.1)	(0.0, 5.8)
		Cycle 3	87	0 (0.0)	(0.0, 3.9)
		Cycle 4	84	1 (1.1)	(0.0, 5.8)
		Cycle 5	80	0 (0.0)	(0.0, 3.9)
		Cycle 6	78	2 (2.2)	(0.3, 7.6)
		Cycle 7	75	0 (0.0)	(0.0, 3.9)
		Cycle >= 8 and < 18	73	8 (8.6)	(3.8, 16.2)
		Cycle >= 18	12	1 (1.1)	(0.0, 5.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	14 (15.9) (9.0, 25.2)
		Cycle 1	88	2 (2.3) (0.3, 8.0)
		Cycle 2	86	1 (1.1) (0.0, 6.2)
		Cycle 3	85	1 (1.1) (0.0, 6.2)
		Cycle 4	84	0 (0.0) (0.0, 4.1)
		Cycle 5	74	0 (0.0) (0.0, 4.1)
		Cycle 6	73	1 (1.1) (0.0, 6.2)
		Cycle 7	69	3 (3.4) (0.7, 9.6)
		Cycle >= 8 and < 18	64	5 (5.7) (1.9, 12.8)
		Cycle >= 18	23	1 (1.1) (0.0, 6.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	7 (13.7)	(5.7, 26.3)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	1 (2.0)	(0.0, 10.4)
		Cycle 3	49	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	47	0 (0.0)	(0.0, 7.0)
		Cycle 6	46	1 (2.0)	(0.0, 10.4)
		Cycle 7	45	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	44	4 (7.8)	(2.2, 18.9)
		Cycle >= 18	8	1 (2.0)	(0.0, 10.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	21 (16.8) (10.7, 24.5)
		Cycle 1	125	3 (2.4) (0.5, 6.9)
		Cycle 2	123	1 (0.8) (0.0, 4.4)
		Cycle 3	118	1 (0.8) (0.0, 4.4)
		Cycle 4	114	1 (0.8) (0.0, 4.4)
		Cycle 5	103	0 (0.0) (0.0, 2.9)
		Cycle 6	101	2 (1.6) (0.2, 5.7)
		Cycle 7	95	3 (2.4) (0.5, 6.9)
		Cycle >= 8 and < 18	90	9 (7.2) (3.3, 13.2)
		Cycle >= 18	27	1 (0.8) (0.0, 4.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	15 (15.5)	(8.9, 24.2)
		Cycle 1	97	1 (1.0)	(0.0, 5.6)
		Cycle 2	96	1 (1.0)	(0.0, 5.6)
		Cycle 3	91	0 (0.0)	(0.0, 3.7)
		Cycle 4	88	1 (1.0)	(0.0, 5.6)
		Cycle 5	84	0 (0.0)	(0.0, 3.7)
		Cycle 6	82	2 (2.1)	(0.3, 7.3)
		Cycle 7	79	0 (0.0)	(0.0, 3.7)
		Cycle >= 8 and < 18	76	8 (8.2)	(3.6, 15.6)
		Cycle >= 18	13	2 (2.1)	(0.3, 7.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	13 (15.7)	(8.6, 25.3)
		Cycle 1	83	2 (2.4)	(0.3, 8.4)
		Cycle 2	81	1 (1.2)	(0.0, 6.5)
		Cycle 3	80	1 (1.2)	(0.0, 6.5)
		Cycle 4	79	0 (0.0)	(0.0, 4.3)
		Cycle 5	69	0 (0.0)	(0.0, 4.3)
		Cycle 6	68	1 (1.2)	(0.0, 6.5)
		Cycle 7	64	3 (3.6)	(0.8, 10.2)
		Cycle >= 8 and < 18	60	5 (6.0)	(2.0, 13.5)
		Cycle >= 18	22	0 (0.0)	(0.0, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Normal (N=90)	Any TEAE	90	12 (13.3)	(7.1, 22.1)
		Cycle 1	90	2 (2.2)	(0.3, 7.8)
		Cycle 2	89	1 (1.1)	(0.0, 6.0)
		Cycle 3	85	0 (0.0)	(0.0, 4.0)
		Cycle 4	85	0 (0.0)	(0.0, 4.0)
		Cycle 5	76	0 (0.0)	(0.0, 4.0)
		Cycle 6	73	0 (0.0)	(0.0, 4.0)
		Cycle 7	72	1 (1.1)	(0.0, 6.0)
		Cycle >= 8 and < 18	69	7 (7.8)	(3.2, 15.4)
		Cycle >= 18	17	1 (1.1)	(0.0, 6.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	11 (15.9) (8.2, 26.7)
		Cycle 1	69	1 (1.4) (0.0, 7.8)
		Cycle 2	68	1 (1.4) (0.0, 7.8)
		Cycle 3	66	0 (0.0) (0.0, 5.2)
		Cycle 4	63	1 (1.4) (0.0, 7.8)
		Cycle 5	59	0 (0.0) (0.0, 5.2)
		Cycle 6	59	2 (2.9) (0.4, 10.1)
		Cycle 7	56	1 (1.4) (0.0, 7.8)
		Cycle >= 8 and < 18	54	5 (7.2) (2.4, 16.1)
		Cycle >= 18	14	0 (0.0) (0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	5 (20.0) (6.8, 40.7)
		Cycle 1	25	0 (0.0) (0.0, 13.7)
		Cycle 2	24	0 (0.0) (0.0, 13.7)
		Cycle 3	23	1 (4.0) (0.1, 20.4)
		Cycle 4	21	0 (0.0) (0.0, 13.7)
		Cycle 5	20	0 (0.0) (0.0, 13.7)
		Cycle 6	20	1 (4.0) (0.1, 20.4)
		Cycle 7	17	1 (4.0) (0.1, 20.4)
		Cycle >= 8 and < 18	15	1 (4.0) (0.1, 20.4)
		Cycle >= 18	4	1 (4.0) (0.1, 20.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	17 (16.2)	(9.7, 24.7)
		Cycle 1	105	2 (1.9)	(0.2, 6.7)
		Cycle 2	104	0 (0.0)	(0.0, 3.5)
		Cycle 3	102	1 (1.0)	(0.0, 5.2)
		Cycle 4	98	0 (0.0)	(0.0, 3.5)
		Cycle 5	90	0 (0.0)	(0.0, 3.5)
		Cycle 6	89	1 (1.0)	(0.0, 5.2)
		Cycle 7	87	1 (1.0)	(0.0, 5.2)
		Cycle >= 8 and < 18	84	11 (10.5)	(5.3, 18.0)
		Cycle >= 18	22	1 (1.0)	(0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	10 (13.2) (6.5, 22.9)
		Cycle 1	76	1 (1.3) (0.0, 7.1)
		Cycle 2	74	2 (2.6) (0.3, 9.2)
		Cycle 3	69	0 (0.0) (0.0, 4.7)
		Cycle 4	68	1 (1.3) (0.0, 7.1)
		Cycle 5	63	0 (0.0) (0.0, 4.7)
		Cycle 6	61	2 (2.6) (0.3, 9.2)
		Cycle 7	56	1 (1.3) (0.0, 7.1)
		Cycle >= 8 and < 18	54	2 (2.6) (0.3, 9.2)
		Cycle >= 18	13	1 (1.3) (0.0, 7.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	2 (8.3)	(1.0, 27.0)
		Cycle 1	24	0 (0.0)	(0.0, 14.2)
		Cycle 2	23	0 (0.0)	(0.0, 14.2)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	0 (0.0)	(0.0, 14.2)
		Cycle 6	18	0 (0.0)	(0.0, 14.2)
		Cycle 7	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 8 and < 18	18	2 (8.3)	(1.0, 27.0)
		Cycle >= 18	6	0 (0.0)	(0.0, 14.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	26 (16.3)	(10.9, 22.9)
		Cycle 1	160	3 (1.9)	(0.4, 5.4)
		Cycle 2	158	2 (1.3)	(0.2, 4.4)
		Cycle 3	152	1 (0.6)	(0.0, 3.4)
		Cycle 4	147	1 (0.6)	(0.0, 3.4)
		Cycle 5	136	0 (0.0)	(0.0, 2.3)
		Cycle 6	134	3 (1.9)	(0.4, 5.4)
		Cycle 7	127	3 (1.9)	(0.4, 5.4)
		Cycle >= 8 and < 18	120	11 (6.9)	(3.5, 12.0)
		Cycle >= 18	29	2 (1.3)	(0.2, 4.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	11 (20.8) (10.8, 34.1)
		Cycle 1	53	0 (0.0) (0.0, 6.7)
		Cycle 2	52	0 (0.0) (0.0, 6.7)
		Cycle 3	49	1 (1.9) (0.0, 10.1)
		Cycle 4	48	0 (0.0) (0.0, 6.7)
		Cycle 5	43	0 (0.0) (0.0, 6.7)
		Cycle 6	42	1 (1.9) (0.0, 10.1)
		Cycle 7	41	1 (1.9) (0.0, 10.1)
		Cycle >= 8 and < 18	39	7 (13.2) (5.5, 25.3)
		Cycle >= 18	8	1 (1.9) (0.0, 10.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	17 (13.0)	(7.7, 20.0)
		Cycle 1	131	3 (2.3)	(0.5, 6.5)
		Cycle 2	129	2 (1.5)	(0.2, 5.4)
		Cycle 3	125	0 (0.0)	(0.0, 2.8)
		Cycle 4	121	1 (0.8)	(0.0, 4.2)
		Cycle 5	112	0 (0.0)	(0.0, 2.8)
		Cycle 6	110	2 (1.5)	(0.2, 5.4)
		Cycle 7	104	2 (1.5)	(0.2, 5.4)
		Cycle >= 8 and < 18	99	6 (4.6)	(1.7, 9.7)
		Cycle >= 18	27	1 (0.8)	(0.0, 4.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	25 (14.8) (9.8, 21.1)
		Cycle 1	169	3 (1.8) (0.4, 5.1)
		Cycle 2	166	2 (1.2) (0.1, 4.2)
		Cycle 3	159	1 (0.6) (0.0, 3.3)
		Cycle 4	154	1 (0.6) (0.0, 3.3)
		Cycle 5	142	0 (0.0) (0.0, 2.2)
		Cycle 6	139	3 (1.8) (0.4, 5.1)
		Cycle 7	132	3 (1.8) (0.4, 5.1)
		Cycle >= 8 and < 18	125	10 (5.9) (2.9, 10.6)
		Cycle >= 18	31	2 (1.2) (0.1, 4.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	3 (20.0)	(4.3, 48.1)
		Cycle 1	15	0 (0.0)	(0.0, 21.8)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	3 (20.0)	(4.3, 48.1)
		Cycle >= 18	4	0 (0.0)	(0.0, 21.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	7 (12.5)	(5.2, 24.1)
		Cycle 1	56	0 (0.0)	(0.0, 6.4)
		Cycle 2	55	1 (1.8)	(0.0, 9.6)
		Cycle 3	54	0 (0.0)	(0.0, 6.4)
		Cycle 4	53	0 (0.0)	(0.0, 6.4)
		Cycle 5	49	0 (0.0)	(0.0, 6.4)
		Cycle 6	48	0 (0.0)	(0.0, 6.4)
		Cycle 7	48	1 (1.8)	(0.0, 9.6)
		Cycle >= 8 and < 18	45	4 (7.1)	(2.0, 17.3)
		Cycle >= 18	16	1 (1.8)	(0.0, 9.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	21 (16.4)	(10.5, 24.0)
		Cycle 1	128	3 (2.3)	(0.5, 6.7)
		Cycle 2	126	1 (0.8)	(0.0, 4.3)
		Cycle 3	120	1 (0.8)	(0.0, 4.3)
		Cycle 4	116	1 (0.8)	(0.0, 4.3)
		Cycle 5	106	0 (0.0)	(0.0, 2.8)
		Cycle 6	104	3 (2.3)	(0.5, 6.7)
		Cycle 7	97	2 (1.6)	(0.2, 5.5)
		Cycle >= 8 and < 18	93	9 (7.0)	(3.3, 12.9)
		Cycle >= 18	19	1 (0.8)	(0.0, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
0-Prior treatment lines	< 3 lines (N=17)	Any TEAE	17	1 (5.9) (0.1, 28.7)
		Cycle 1	17	0 (0.0) (0.0, 19.5)
		Cycle 2	17	0 (0.0) (0.0, 19.5)
		Cycle 3	17	0 (0.0) (0.0, 19.5)
		Cycle 4	17	0 (0.0) (0.0, 19.5)
		Cycle 5	17	0 (0.0) (0.0, 19.5)
		Cycle 6	16	0 (0.0) (0.0, 19.5)
		Cycle 7	16	0 (0.0) (0.0, 19.5)
		Cycle >= 8 and < 18	16	0 (0.0) (0.0, 19.5)
		Cycle >= 18	6	1 (5.9) (0.1, 28.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
0-Prior treatment lines	>= 3 lines (N=167)	Any TEAE	167	27 (16.2) (10.9, 22.6)
		Cycle 1	167	3 (1.8) (0.4, 5.2)
		Cycle 2	164	2 (1.2) (0.1, 4.3)
		Cycle 3	157	1 (0.6) (0.0, 3.3)
		Cycle 4	152	1 (0.6) (0.0, 3.3)
		Cycle 5	138	0 (0.0) (0.0, 2.2)
		Cycle 6	136	3 (1.8) (0.4, 5.2)
		Cycle 7	129	3 (1.8) (0.4, 5.2)
		Cycle >= 8 and < 18	122	13 (7.8) (4.2, 12.9)
		Cycle >= 18	29	1 (0.6) (0.0, 3.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	12 (15.2) (8.1, 25.0)
		Cycle 1	79	1 (1.3) (0.0, 6.9)
		Cycle 2	78	2 (2.5) (0.3, 8.8)
		Cycle 3	75	1 (1.3) (0.0, 6.9)
		Cycle 4	73	1 (1.3) (0.0, 6.9)
		Cycle 5	70	0 (0.0) (0.0, 4.6)
		Cycle 6	69	1 (1.3) (0.0, 6.9)
		Cycle 7	68	1 (1.3) (0.0, 6.9)
		Cycle >= 8 and < 18	65	3 (3.8) (0.8, 10.7)
		Cycle >= 18	17	2 (2.5) (0.3, 8.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	10 (15.2) (7.5, 26.1)
		Cycle 1	66	1 (1.5) (0.0, 8.2)
		Cycle 2	66	0 (0.0) (0.0, 5.4)
		Cycle 3	64	0 (0.0) (0.0, 5.4)
		Cycle 4	61	0 (0.0) (0.0, 5.4)
		Cycle 5	55	0 (0.0) (0.0, 5.4)
		Cycle 6	53	0 (0.0) (0.0, 5.4)
		Cycle 7	51	0 (0.0) (0.0, 5.4)
		Cycle >= 8 and < 18	51	9 (13.6) (6.4, 24.3)
		Cycle >= 18	10	0 (0.0) (0.0, 5.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	16 (13.2)	(7.8, 20.6)
		Cycle 1	121	1 (0.8)	(0.0, 4.5)
		Cycle 2	120	0 (0.0)	(0.0, 3.0)
		Cycle 3	119	1 (0.8)	(0.0, 4.5)
		Cycle 4	115	1 (0.8)	(0.0, 4.5)
		Cycle 5	106	0 (0.0)	(0.0, 3.0)
		Cycle 6	103	3 (2.5)	(0.5, 7.1)
		Cycle 7	96	1 (0.8)	(0.0, 4.5)
		Cycle >= 8 and < 18	93	7 (5.8)	(2.4, 11.6)
		Cycle >= 18	25	2 (1.7)	(0.2, 5.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	12 (19.0)	(10.2, 30.9)
		Cycle 1	63	2 (3.2)	(0.4, 11.0)
		Cycle 2	61	2 (3.2)	(0.4, 11.0)
		Cycle 3	55	0 (0.0)	(0.0, 5.7)
		Cycle 4	54	0 (0.0)	(0.0, 5.7)
		Cycle 5	49	0 (0.0)	(0.0, 5.7)
		Cycle 6	49	0 (0.0)	(0.0, 5.7)
		Cycle 7	49	2 (3.2)	(0.4, 11.0)
		Cycle >= 8 and < 18	45	6 (9.5)	(3.6, 19.6)
		Cycle >= 18	10	0 (0.0)	(0.0, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	6 (11.8) (4.4, 23.9)
		Cycle 1	51	0 (0.0) (0.0, 7.0)
		Cycle 2	50	0 (0.0) (0.0, 7.0)
		Cycle 3	50	0 (0.0) (0.0, 7.0)
		Cycle 4	49	1 (2.0) (0.0, 10.4)
		Cycle 5	46	0 (0.0) (0.0, 7.0)
		Cycle 6	44	1 (2.0) (0.0, 10.4)
		Cycle 7	40	0 (0.0) (0.0, 7.0)
		Cycle >= 8 and < 18	40	3 (5.9) (1.2, 16.2)
		Cycle >= 18	10	1 (2.0) (0.0, 10.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	22 (16.5) (10.7, 24.0)
		Cycle 1	133	3 (2.3) (0.5, 6.5)
		Cycle 2	131	2 (1.5) (0.2, 5.3)
		Cycle 3	124	1 (0.8) (0.0, 4.1)
		Cycle 4	120	0 (0.0) (0.0, 2.7)
		Cycle 5	109	0 (0.0) (0.0, 2.7)
		Cycle 6	108	2 (1.5) (0.2, 5.3)
		Cycle 7	105	3 (2.3) (0.5, 6.5)
		Cycle >= 8 and < 18	98	10 (7.5) (3.7, 13.4)
		Cycle >= 18	25	1 (0.8) (0.0, 4.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

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Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	16 (8.7)	(5.1, 13.7)
		Cycle 1	184	6 (3.3)	(1.2, 7.0)
		Cycle 2	181	1 (0.5)	(0.0, 3.0)
		Cycle 3	174	1 (0.5)	(0.0, 3.0)
		Cycle 4	169	2 (1.1)	(0.1, 3.9)
		Cycle 5	155	0 (0.0)	(0.0, 2.0)
		Cycle 6	152	2 (1.1)	(0.1, 3.9)
		Cycle 7	145	2 (1.1)	(0.1, 3.9)
		Cycle >= 8 and < 18	138	4 (2.2)	(0.6, 5.5)
		Cycle >= 18	35	0 (0.0)	(0.0, 2.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	9 (6.4) (3.0, 11.9)
		Cycle 1	140	5 (3.6) (1.2, 8.1)
		Cycle 2	138	0 (0.0) (0.0, 2.6)
		Cycle 3	132	1 (0.7) (0.0, 3.9)
		Cycle 4	128	1 (0.7) (0.0, 3.9)
		Cycle 5	116	0 (0.0) (0.0, 2.6)
		Cycle 6	113	0 (0.0) (0.0, 2.6)
		Cycle 7	109	1 (0.7) (0.0, 3.9)
		Cycle >= 8 and < 18	103	2 (1.4) (0.2, 5.1)
		Cycle >= 18	24	0 (0.0) (0.0, 2.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	7 (15.9) (6.6, 30.1)
		Cycle 1	44	1 (2.3) (0.1, 12.0)
		Cycle 2	43	1 (2.3) (0.1, 12.0)
		Cycle 3	42	0 (0.0) (0.0, 8.0)
		Cycle 4	41	1 (2.3) (0.1, 12.0)
		Cycle 5	39	0 (0.0) (0.0, 8.0)
		Cycle 6	39	2 (4.5) (0.6, 15.5)
		Cycle 7	36	1 (2.3) (0.1, 12.0)
		Cycle >= 8 and < 18	35	2 (4.5) (0.6, 15.5)
		Cycle >= 18	11	0 (0.0) (0.0, 8.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	4 (6.3) (1.8, 15.5)
		Cycle 1	63	2 (3.2) (0.4, 11.0)
		Cycle 2	61	1 (1.6) (0.0, 8.5)
		Cycle 3	58	0 (0.0) (0.0, 5.7)
		Cycle 4	58	0 (0.0) (0.0, 5.7)
		Cycle 5	55	0 (0.0) (0.0, 5.7)
		Cycle 6	55	0 (0.0) (0.0, 5.7)
		Cycle 7	53	1 (1.6) (0.0, 8.5)
		Cycle >= 8 and < 18	49	0 (0.0) (0.0, 5.7)
		Cycle >= 18	15	0 (0.0) (0.0, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	7 (13.2) (5.5, 25.3)
		Cycle 1	53	2 (3.8) (0.5, 13.0)
		Cycle 2	53	0 (0.0) (0.0, 6.7)
		Cycle 3	52	1 (1.9) (0.0, 10.1)
		Cycle 4	49	1 (1.9) (0.0, 10.1)
		Cycle 5	44	0 (0.0) (0.0, 6.7)
		Cycle 6	42	1 (1.9) (0.0, 10.1)
		Cycle 7	40	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	3 (5.7) (1.2, 15.7)
		Cycle >= 18	11	0 (0.0) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	5 (7.4) (2.4, 16.3)
		Cycle 1	68	2 (2.9) (0.4, 10.2)
		Cycle 2	67	0 (0.0) (0.0, 5.3)
		Cycle 3	64	0 (0.0) (0.0, 5.3)
		Cycle 4	62	1 (1.5) (0.0, 7.9)
		Cycle 5	56	0 (0.0) (0.0, 5.3)
		Cycle 6	55	1 (1.5) (0.0, 7.9)
		Cycle 7	52	1 (1.5) (0.0, 7.9)
		Cycle >= 8 and < 18	50	1 (1.5) (0.0, 7.9)
		Cycle >= 18	9	0 (0.0) (0.0, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	7 (6.9)	(2.8, 13.6)
		Cycle 1	102	4 (3.9)	(1.1, 9.7)
		Cycle 2	101	0 (0.0)	(0.0, 3.6)
		Cycle 3	100	0 (0.0)	(0.0, 3.6)
		Cycle 4	98	0 (0.0)	(0.0, 3.6)
		Cycle 5	94	0 (0.0)	(0.0, 3.6)
		Cycle 6	93	0 (0.0)	(0.0, 3.6)
		Cycle 7	88	2 (2.0)	(0.2, 6.9)
		Cycle >= 8 and < 18	86	2 (2.0)	(0.2, 6.9)
		Cycle >= 18	23	0 (0.0)	(0.0, 3.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	8 (9.9) (4.4, 18.5)
		Cycle 1	81	1 (1.2) (0.0, 6.7)
		Cycle 2	79	1 (1.2) (0.0, 6.7)
		Cycle 3	73	1 (1.2) (0.0, 6.7)
		Cycle 4	71	2 (2.5) (0.3, 8.6)
		Cycle 5	61	0 (0.0) (0.0, 4.5)
		Cycle 6	59	2 (2.5) (0.3, 8.6)
		Cycle 7	57	0 (0.0) (0.0, 4.5)
		Cycle >= 8 and < 18	52	2 (2.5) (0.3, 8.6)
		Cycle >= 18	12	0 (0.0) (0.0, 4.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions < 5 cm (N=74)	Any TEAE	74	6 (8.1)	(3.0, 16.8)
	Cycle 1	74	4 (5.4)	(1.5, 13.3)
	Cycle 2	73	0 (0.0)	(0.0, 4.9)
	Cycle 3	71	1 (1.4)	(0.0, 7.3)
	Cycle 4	66	0 (0.0)	(0.0, 4.9)
	Cycle 5	61	0 (0.0)	(0.0, 4.9)
	Cycle 6	60	0 (0.0)	(0.0, 4.9)
	Cycle 7	59	0 (0.0)	(0.0, 4.9)
	Cycle >= 8 and < 18	54	2 (2.7)	(0.3, 9.4)
	Cycle >= 18	18	0 (0.0)	(0.0, 4.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

			Overall 5.4 mg/kg SAF (N=184)	
Subgroup	Time Period	N patients in cycle	n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=95)	Any TEAE	95	9 (9.5) (4.4, 17.2)
		Cycle 1	95	2 (2.1) (0.3, 7.4)
		Cycle 2	93	1 (1.1) (0.0, 5.7)
		Cycle 3	88	0 (0.0) (0.0, 3.8)
		Cycle 4	88	2 (2.1) (0.3, 7.4)
		Cycle 5	79	0 (0.0) (0.0, 3.8)
		Cycle 6	77	2 (2.1) (0.3, 7.4)
		Cycle 7	72	1 (1.1) (0.0, 5.7)
		Cycle >= 8 and < 18	70	2 (2.1) (0.3, 7.4)
		Cycle >= 18	13	0 (0.0) (0.0, 3.8)

Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	12 (7.8) (4.1, 13.2)
		Cycle 1	154	4 (2.6) (0.7, 6.5)
		Cycle 2	152	1 (0.6) (0.0, 3.6)
		Cycle 3	146	1 (0.6) (0.0, 3.6)
		Cycle 4	141	1 (0.6) (0.0, 3.6)
		Cycle 5	129	0 (0.0) (0.0, 2.4)
		Cycle 6	127	2 (1.3) (0.2, 4.6)
		Cycle 7	121	2 (1.3) (0.2, 4.6)
		Cycle >= 8 and < 18	114	2 (1.3) (0.2, 4.6)
		Cycle >= 18	33	0 (0.0) (0.0, 2.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Any TEAE	28	4 (14.3) (4.0, 32.7)
		Cycle 1	28	2 (7.1) (0.9, 23.5)
		Cycle 2	27	0 (0.0) (0.0, 12.3)
		Cycle 3	26	0 (0.0) (0.0, 12.3)
		Cycle 4	26	1 (3.6) (0.1, 18.3)
		Cycle 5	24	0 (0.0) (0.0, 12.3)
		Cycle 6	23	0 (0.0) (0.0, 12.3)
		Cycle 7	22	0 (0.0) (0.0, 12.3)
		Cycle >= 8 and < 18	22	2 (7.1) (0.9, 23.5)
		Cycle >= 18	2	0 (0.0) (0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
F-Estrogen receptors	Positive (N=93)			
	Any TEAE	93	8 (8.6)	(3.8, 16.2)
	Cycle 1	93	4 (4.3)	(1.2, 10.6)
	Cycle 2	92	0 (0.0)	(0.0, 3.9)
	Cycle 3	87	0 (0.0)	(0.0, 3.9)
	Cycle 4	84	0 (0.0)	(0.0, 3.9)
	Cycle 5	80	0 (0.0)	(0.0, 3.9)
	Cycle 6	78	1 (1.1)	(0.0, 5.8)
	Cycle 7	75	1 (1.1)	(0.0, 5.8)
	Cycle >= 8 and < 18	73	3 (3.2)	(0.7, 9.1)
	Cycle >= 18	12	0 (0.0)	(0.0, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	7 (8.0)	(3.3, 15.7)
		Cycle 1	88	1 (1.1)	(0.0, 6.2)
		Cycle 2	86	1 (1.1)	(0.0, 6.2)
		Cycle 3	85	1 (1.1)	(0.0, 6.2)
		Cycle 4	84	2 (2.3)	(0.3, 8.0)
		Cycle 5	74	0 (0.0)	(0.0, 4.1)
		Cycle 6	73	1 (1.1)	(0.0, 6.2)
		Cycle 7	69	1 (1.1)	(0.0, 6.2)
		Cycle >= 8 and < 18	64	1 (1.1)	(0.0, 6.2)
		Cycle >= 18	23	0 (0.0)	(0.0, 4.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	4 (7.8)	(2.2, 18.9)
		Cycle 1	51	2 (3.9)	(0.5, 13.5)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	49	1 (2.0)	(0.0, 10.4)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	47	0 (0.0)	(0.0, 7.0)
		Cycle 6	46	0 (0.0)	(0.0, 7.0)
		Cycle 7	45	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	44	2 (3.9)	(0.5, 13.5)
		Cycle >= 18	8	0 (0.0)	(0.0, 7.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	11 (8.8) (4.5, 15.2)
		Cycle 1	125	3 (2.4) (0.5, 6.9)
		Cycle 2	123	1 (0.8) (0.0, 4.4)
		Cycle 3	118	0 (0.0) (0.0, 2.9)
		Cycle 4	114	2 (1.6) (0.2, 5.7)
		Cycle 5	103	0 (0.0) (0.0, 2.9)
		Cycle 6	101	2 (1.6) (0.2, 5.7)
		Cycle 7	95	2 (1.6) (0.2, 5.7)
		Cycle >= 8 and < 18	90	2 (1.6) (0.2, 5.7)
		Cycle >= 18	27	0 (0.0) (0.0, 2.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	9 (9.3)	(4.3, 16.9)
		Cycle 1	97	4 (4.1)	(1.1, 10.2)
		Cycle 2	96	0 (0.0)	(0.0, 3.7)
		Cycle 3	91	1 (1.0)	(0.0, 5.6)
		Cycle 4	88	0 (0.0)	(0.0, 3.7)
		Cycle 5	84	0 (0.0)	(0.0, 3.7)
		Cycle 6	82	1 (1.0)	(0.0, 5.6)
		Cycle 7	79	1 (1.0)	(0.0, 5.6)
		Cycle >= 8 and < 18	76	3 (3.1)	(0.6, 8.8)
		Cycle >= 18	13	0 (0.0)	(0.0, 3.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
H-Hormone receptors	Negative (N=83)			
	Any TEAE	83	6 (7.2)	(2.7, 15.1)
	Cycle 1	83	1 (1.2)	(0.0, 6.5)
	Cycle 2	81	1 (1.2)	(0.0, 6.5)
	Cycle 3	80	0 (0.0)	(0.0, 4.3)
	Cycle 4	79	2 (2.4)	(0.3, 8.4)
	Cycle 5	69	0 (0.0)	(0.0, 4.3)
	Cycle 6	68	1 (1.2)	(0.0, 6.5)
	Cycle 7	64	1 (1.2)	(0.0, 6.5)
	Cycle >= 8 and < 18	60	1 (1.2)	(0.0, 6.5)
	Cycle >= 18	22	0 (0.0)	(0.0, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Normal (N=90)			
	Any TEAE	90	7 (7.8)	(3.2, 15.4)
	Cycle 1	90	2 (2.2)	(0.3, 7.8)
	Cycle 2	89	1 (1.1)	(0.0, 6.0)
	Cycle 3	85	1 (1.1)	(0.0, 6.0)
	Cycle 4	85	1 (1.1)	(0.0, 6.0)
	Cycle 5	76	0 (0.0)	(0.0, 4.0)
	Cycle 6	73	0 (0.0)	(0.0, 4.0)
	Cycle 7	72	1 (1.1)	(0.0, 6.0)
	Cycle >= 8 and < 18	69	2 (2.2)	(0.3, 7.8)
	Cycle >= 18	17	0 (0.0)	(0.0, 4.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	5 (7.2) (2.4, 16.1)
		Cycle 1	69	1 (1.4) (0.0, 7.8)
		Cycle 2	68	0 (0.0) (0.0, 5.2)
		Cycle 3	66	0 (0.0) (0.0, 5.2)
		Cycle 4	63	1 (1.4) (0.0, 7.8)
		Cycle 5	59	0 (0.0) (0.0, 5.2)
		Cycle 6	59	2 (2.9) (0.4, 10.1)
		Cycle 7	56	1 (1.4) (0.0, 7.8)
		Cycle >= 8 and < 18	54	1 (1.4) (0.0, 7.8)
		Cycle >= 18	14	0 (0.0) (0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	4 (16.0) (4.5, 36.1)
		Cycle 1	25	3 (12.0) (2.5, 31.2)
		Cycle 2	24	0 (0.0) (0.0, 13.7)
		Cycle 3	23	0 (0.0) (0.0, 13.7)
		Cycle 4	21	0 (0.0) (0.0, 13.7)
		Cycle 5	20	0 (0.0) (0.0, 13.7)
		Cycle 6	20	0 (0.0) (0.0, 13.7)
		Cycle 7	17	0 (0.0) (0.0, 13.7)
		Cycle >= 8 and < 18	15	1 (4.0) (0.1, 20.4)
		Cycle >= 18	4	0 (0.0) (0.0, 13.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	13 (12.4) (6.8, 20.2)
		Cycle 1	105	6 (5.7) (2.1, 12.0)
		Cycle 2	104	0 (0.0) (0.0, 3.5)
		Cycle 3	102	1 (1.0) (0.0, 5.2)
		Cycle 4	98	1 (1.0) (0.0, 5.2)
		Cycle 5	90	0 (0.0) (0.0, 3.5)
		Cycle 6	89	1 (1.0) (0.0, 5.2)
		Cycle 7	87	2 (1.9) (0.2, 6.7)
		Cycle >= 8 and < 18	84	3 (2.9) (0.6, 8.1)
		Cycle >= 18	22	0 (0.0) (0.0, 3.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	3 (3.9) (0.8, 11.1)
		Cycle 1	76	0 (0.0) (0.0, 4.7)
		Cycle 2	74	1 (1.3) (0.0, 7.1)
		Cycle 3	69	0 (0.0) (0.0, 4.7)
		Cycle 4	68	1 (1.3) (0.0, 7.1)
		Cycle 5	63	0 (0.0) (0.0, 4.7)
		Cycle 6	61	1 (1.3) (0.0, 7.1)
		Cycle 7	56	0 (0.0) (0.0, 4.7)
		Cycle >= 8 and < 18	54	1 (1.3) (0.0, 7.1)
		Cycle >= 18	13	0 (0.0) (0.0, 4.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	4 (16.7)	(4.7, 37.4)
		Cycle 1	24	1 (4.2)	(0.1, 21.1)
		Cycle 2	23	1 (4.2)	(0.1, 21.1)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	0 (0.0)	(0.0, 14.2)
		Cycle 6	18	0 (0.0)	(0.0, 14.2)
		Cycle 7	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 8 and < 18	18	2 (8.3)	(1.0, 27.0)
		Cycle >= 18	6	0 (0.0)	(0.0, 14.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	12 (7.5) (3.9, 12.7)
		Cycle 1	160	5 (3.1) (1.0, 7.1)
		Cycle 2	158	0 (0.0) (0.0, 2.3)
		Cycle 3	152	1 (0.6) (0.0, 3.4)
		Cycle 4	147	2 (1.3) (0.2, 4.4)
		Cycle 5	136	0 (0.0) (0.0, 2.3)
		Cycle 6	134	2 (1.3) (0.2, 4.4)
		Cycle 7	127	2 (1.3) (0.2, 4.4)
		Cycle >= 8 and < 18	120	2 (1.3) (0.2, 4.4)
		Cycle >= 18	29	0 (0.0) (0.0, 2.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	3 (5.7) (1.2, 15.7)
		Cycle 1	53	2 (3.8) (0.5, 13.0)
		Cycle 2	52	0 (0.0) (0.0, 6.7)
		Cycle 3	49	0 (0.0) (0.0, 6.7)
		Cycle 4	48	1 (1.9) (0.0, 10.1)
		Cycle 5	43	0 (0.0) (0.0, 6.7)
		Cycle 6	42	1 (1.9) (0.0, 10.1)
		Cycle 7	41	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	1 (1.9) (0.0, 10.1)
		Cycle >= 18	8	0 (0.0) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	13 (9.9)	(5.4, 16.4)
		Cycle 1	131	4 (3.1)	(0.8, 7.6)
		Cycle 2	129	1 (0.8)	(0.0, 4.2)
		Cycle 3	125	1 (0.8)	(0.0, 4.2)
		Cycle 4	121	1 (0.8)	(0.0, 4.2)
		Cycle 5	112	0 (0.0)	(0.0, 2.8)
		Cycle 6	110	1 (0.8)	(0.0, 4.2)
		Cycle 7	104	2 (1.5)	(0.2, 5.4)
		Cycle >= 8 and < 18	99	3 (2.3)	(0.5, 6.5)
		Cycle >= 18	27	0 (0.0)	(0.0, 2.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	14 (8.3) (4.6, 13.5)
		Cycle 1	169	4 (2.4) (0.6, 5.9)
		Cycle 2	166	1 (0.6) (0.0, 3.3)
		Cycle 3	159	1 (0.6) (0.0, 3.3)
		Cycle 4	154	2 (1.2) (0.1, 4.2)
		Cycle 5	142	0 (0.0) (0.0, 2.2)
		Cycle 6	139	2 (1.2) (0.1, 4.2)
		Cycle 7	132	2 (1.2) (0.1, 4.2)
		Cycle >= 8 and < 18	125	3 (1.8) (0.4, 5.1)
		Cycle >= 18	31	0 (0.0) (0.0, 2.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	2 (13.3)	(1.7, 40.5)
		Cycle 1	15	2 (13.3)	(1.7, 40.5)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	1 (6.7)	(0.2, 31.9)
		Cycle >= 18	4	0 (0.0)	(0.0, 21.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	3 (5.4) (1.1, 14.9)
		Cycle 1	56	1 (1.8) (0.0, 9.6)
		Cycle 2	55	0 (0.0) (0.0, 6.4)
		Cycle 3	54	0 (0.0) (0.0, 6.4)
		Cycle 4	53	0 (0.0) (0.0, 6.4)
		Cycle 5	49	0 (0.0) (0.0, 6.4)
		Cycle 6	48	0 (0.0) (0.0, 6.4)
		Cycle 7	48	0 (0.0) (0.0, 6.4)
		Cycle >= 8 and < 18	45	2 (3.6) (0.4, 12.3)
		Cycle >= 18	16	0 (0.0) (0.0, 6.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	13 (10.2) (5.5, 16.7)
		Cycle 1	128	5 (3.9) (1.3, 8.9)
		Cycle 2	126	1 (0.8) (0.0, 4.3)
		Cycle 3	120	1 (0.8) (0.0, 4.3)
		Cycle 4	116	2 (1.6) (0.2, 5.5)
		Cycle 5	106	0 (0.0) (0.0, 2.8)
		Cycle 6	104	2 (1.6) (0.2, 5.5)
		Cycle 7	97	2 (1.6) (0.2, 5.5)
		Cycle >= 8 and < 18	93	2 (1.6) (0.2, 5.5)
		Cycle >= 18	19	0 (0.0) (0.0, 2.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
0-Prior treatment lines	< 3 lines (N=17)	Any TEAE	17	1 (5.9) (0.1, 28.7)
		Cycle 1	17	0 (0.0) (0.0, 19.5)
		Cycle 2	17	0 (0.0) (0.0, 19.5)
		Cycle 3	17	0 (0.0) (0.0, 19.5)
		Cycle 4	17	0 (0.0) (0.0, 19.5)
		Cycle 5	17	0 (0.0) (0.0, 19.5)
		Cycle 6	16	0 (0.0) (0.0, 19.5)
		Cycle 7	16	0 (0.0) (0.0, 19.5)
		Cycle >= 8 and < 18	16	1 (5.9) (0.1, 28.7)
		Cycle >= 18	6	0 (0.0) (0.0, 19.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
0-Prior treatment lines	>= 3 lines (N=167)	Any TEAE	167	15 (9.0) (5.1, 14.4)
		Cycle 1	167	6 (3.6) (1.3, 7.7)
		Cycle 2	164	1 (0.6) (0.0, 3.3)
		Cycle 3	157	1 (0.6) (0.0, 3.3)
		Cycle 4	152	2 (1.2) (0.1, 4.3)
		Cycle 5	138	0 (0.0) (0.0, 2.2)
		Cycle 6	136	2 (1.2) (0.1, 4.3)
		Cycle 7	129	2 (1.2) (0.1, 4.3)
		Cycle >= 8 and < 18	122	3 (1.8) (0.4, 5.2)
		Cycle >= 18	29	0 (0.0) (0.0, 2.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	7 (8.9) (3.6, 17.4)
		Cycle 1	79	2 (2.5) (0.3, 8.8)
		Cycle 2	78	1 (1.3) (0.0, 6.9)
		Cycle 3	75	0 (0.0) (0.0, 4.6)
		Cycle 4	73	1 (1.3) (0.0, 6.9)
		Cycle 5	70	0 (0.0) (0.0, 4.6)
		Cycle 6	69	1 (1.3) (0.0, 6.9)
		Cycle 7	68	1 (1.3) (0.0, 6.9)
		Cycle >= 8 and < 18	65	3 (3.8) (0.8, 10.7)
		Cycle >= 18	17	0 (0.0) (0.0, 4.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	7 (10.6) (4.4, 20.6)
		Cycle 1	66	4 (6.1) (1.7, 14.8)
		Cycle 2	66	0 (0.0) (0.0, 5.4)
		Cycle 3	64	0 (0.0) (0.0, 5.4)
		Cycle 4	61	0 (0.0) (0.0, 5.4)
		Cycle 5	55	0 (0.0) (0.0, 5.4)
		Cycle 6	53	1 (1.5) (0.0, 8.2)
		Cycle 7	51	1 (1.5) (0.0, 8.2)
		Cycle >= 8 and < 18	51	1 (1.5) (0.0, 8.2)
		Cycle >= 18	10	0 (0.0) (0.0, 5.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	11 (9.1) (4.6, 15.7)
		Cycle 1	121	5 (4.1) (1.4, 9.4)
		Cycle 2	120	0 (0.0) (0.0, 3.0)
		Cycle 3	119	1 (0.8) (0.0, 4.5)
		Cycle 4	115	1 (0.8) (0.0, 4.5)
		Cycle 5	106	0 (0.0) (0.0, 3.0)
		Cycle 6	103	1 (0.8) (0.0, 4.5)
		Cycle 7	96	1 (0.8) (0.0, 4.5)
		Cycle >= 8 and < 18	93	3 (2.5) (0.5, 7.1)
		Cycle >= 18	25	0 (0.0) (0.0, 3.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	5 (7.9)	(2.6, 17.6)
		Cycle 1	63	1 (1.6)	(0.0, 8.5)
		Cycle 2	61	1 (1.6)	(0.0, 8.5)
		Cycle 3	55	0 (0.0)	(0.0, 5.7)
		Cycle 4	54	1 (1.6)	(0.0, 8.5)
		Cycle 5	49	0 (0.0)	(0.0, 5.7)
		Cycle 6	49	1 (1.6)	(0.0, 8.5)
		Cycle 7	49	1 (1.6)	(0.0, 8.5)
		Cycle >= 8 and < 18	45	1 (1.6)	(0.0, 8.5)
		Cycle >= 18	10	0 (0.0)	(0.0, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	3 (5.9) (1.2, 16.2)
		Cycle 1	51	0 (0.0) (0.0, 7.0)
		Cycle 2	50	0 (0.0) (0.0, 7.0)
		Cycle 3	50	0 (0.0) (0.0, 7.0)
		Cycle 4	49	1 (2.0) (0.0, 10.4)
		Cycle 5	46	0 (0.0) (0.0, 7.0)
		Cycle 6	44	0 (0.0) (0.0, 7.0)
		Cycle 7	40	0 (0.0) (0.0, 7.0)
		Cycle >= 8 and < 18	40	2 (3.9) (0.5, 13.5)
		Cycle >= 18	10	0 (0.0) (0.0, 7.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	13 (9.8) (5.3, 16.1)
		Cycle 1	133	6 (4.5) (1.7, 9.6)
		Cycle 2	131	1 (0.8) (0.0, 4.1)
		Cycle 3	124	1 (0.8) (0.0, 4.1)
		Cycle 4	120	1 (0.8) (0.0, 4.1)
		Cycle 5	109	0 (0.0) (0.0, 2.7)
		Cycle 6	108	2 (1.5) (0.2, 5.3)
		Cycle 7	105	2 (1.5) (0.2, 5.3)
		Cycle >= 8 and < 18	98	2 (1.5) (0.2, 5.3)
		Cycle >= 18	25	0 (0.0) (0.0, 2.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

UE von besonderem Interesse – Interstitielle Lungenerkrankung (ILD), unabhängig vom Schweregrad

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	24 (13.0)	(8.5, 18.8)
		Cycle 1	184	0 (0.0)	(0.0, 2.0)
		Cycle 2	181	1 (0.5)	(0.0, 3.0)
		Cycle 3	174	1 (0.5)	(0.0, 3.0)
		Cycle 4	169	1 (0.5)	(0.0, 3.0)
		Cycle 5	155	2 (1.1)	(0.1, 3.9)
		Cycle 6	152	5 (2.7)	(0.9, 6.2)
		Cycle 7	145	2 (1.1)	(0.1, 3.9)
		Cycle >= 8 and < 18	138	13 (7.1)	(3.8, 11.8)
		Cycle >= 18	35	2 (1.1)	(0.1, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	16 (11.4) (6.7, 17.9)
		Cycle 1	140	0 (0.0) (0.0, 2.6)
		Cycle 2	138	1 (0.7) (0.0, 3.9)
		Cycle 3	132	1 (0.7) (0.0, 3.9)
		Cycle 4	128	0 (0.0) (0.0, 2.6)
		Cycle 5	116	1 (0.7) (0.0, 3.9)
		Cycle 6	113	4 (2.9) (0.8, 7.2)
		Cycle 7	109	2 (1.4) (0.2, 5.1)
		Cycle >= 8 and < 18	103	8 (5.7) (2.5, 10.9)
		Cycle >= 18	24	1 (0.7) (0.0, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	8 (18.2) (8.2, 32.7)
		Cycle 1	44	0 (0.0) (0.0, 8.0)
		Cycle 2	43	0 (0.0) (0.0, 8.0)
		Cycle 3	42	0 (0.0) (0.0, 8.0)
		Cycle 4	41	1 (2.3) (0.1, 12.0)
		Cycle 5	39	1 (2.3) (0.1, 12.0)
		Cycle 6	39	1 (2.3) (0.1, 12.0)
		Cycle 7	36	0 (0.0) (0.0, 8.0)
		Cycle >= 8 and < 18	35	5 (11.4) (3.8, 24.6)
		Cycle >= 18	11	1 (2.3) (0.1, 12.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	13 (20.6) (11.5, 32.7)
		Cycle 1	63	0 (0.0) (0.0, 5.7)
		Cycle 2	61	0 (0.0) (0.0, 5.7)
		Cycle 3	58	0 (0.0) (0.0, 5.7)
		Cycle 4	58	1 (1.6) (0.0, 8.5)
		Cycle 5	55	1 (1.6) (0.0, 8.5)
		Cycle 6	55	3 (4.8) (1.0, 13.3)
		Cycle 7	53	1 (1.6) (0.0, 8.5)
		Cycle >= 8 and < 18	49	7 (11.1) (4.6, 21.6)
		Cycle >= 18	15	2 (3.2) (0.4, 11.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	3 (5.7) (1.2, 15.7)
		Cycle 1	53	0 (0.0) (0.0, 6.7)
		Cycle 2	53	0 (0.0) (0.0, 6.7)
		Cycle 3	52	0 (0.0) (0.0, 6.7)
		Cycle 4	49	0 (0.0) (0.0, 6.7)
		Cycle 5	44	0 (0.0) (0.0, 6.7)
		Cycle 6	42	2 (3.8) (0.5, 13.0)
		Cycle 7	40	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	1 (1.9) (0.0, 10.1)
		Cycle >= 18	11	0 (0.0) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	8 (11.8)	(5.2, 21.9)
		Cycle 1	68	0 (0.0)	(0.0, 5.3)
		Cycle 2	67	1 (1.5)	(0.0, 7.9)
		Cycle 3	64	1 (1.5)	(0.0, 7.9)
		Cycle 4	62	0 (0.0)	(0.0, 5.3)
		Cycle 5	56	1 (1.5)	(0.0, 7.9)
		Cycle 6	55	0 (0.0)	(0.0, 5.3)
		Cycle 7	52	1 (1.5)	(0.0, 7.9)
		Cycle >= 8 and < 18	50	5 (7.4)	(2.4, 16.3)
		Cycle >= 18	9	0 (0.0)	(0.0, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	18 (17.6) (10.8, 26.4)
		Cycle 1	102	0 (0.0) (0.0, 3.6)
		Cycle 2	101	1 (1.0) (0.0, 5.3)
		Cycle 3	100	1 (1.0) (0.0, 5.3)
		Cycle 4	98	1 (1.0) (0.0, 5.3)
		Cycle 5	94	2 (2.0) (0.2, 6.9)
		Cycle 6	93	4 (3.9) (1.1, 9.7)
		Cycle 7	88	1 (1.0) (0.0, 5.3)
		Cycle >= 8 and < 18	86	8 (7.8) (3.4, 14.9)
		Cycle >= 18	23	2 (2.0) (0.2, 6.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	6 (7.4)	(2.8, 15.4)
		Cycle 1	81	0 (0.0)	(0.0, 4.5)
		Cycle 2	79	0 (0.0)	(0.0, 4.5)
		Cycle 3	73	0 (0.0)	(0.0, 4.5)
		Cycle 4	71	0 (0.0)	(0.0, 4.5)
		Cycle 5	61	0 (0.0)	(0.0, 4.5)
		Cycle 6	59	1 (1.2)	(0.0, 6.7)
		Cycle 7	57	1 (1.2)	(0.0, 6.7)
		Cycle >= 8 and < 18	52	5 (6.2)	(2.0, 13.8)
		Cycle >= 18	12	0 (0.0)	(0.0, 4.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions < 5 cm (N=74)	Any TEAE	74	12 (16.2)	(8.7, 26.6)
	Cycle 1	74	0 (0.0)	(0.0, 4.9)
	Cycle 2	73	1 (1.4)	(0.0, 7.3)
	Cycle 3	71	1 (1.4)	(0.0, 7.3)
	Cycle 4	66	0 (0.0)	(0.0, 4.9)
	Cycle 5	61	1 (1.4)	(0.0, 7.3)
	Cycle 6	60	1 (1.4)	(0.0, 7.3)
	Cycle 7	59	2 (2.7)	(0.3, 9.4)
	Cycle >= 8 and < 18	54	7 (9.5)	(3.9, 18.5)
	Cycle >= 18	18	1 (1.4)	(0.0, 7.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

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			Overall 5.4 mg/kg SAF (N=184)	
Subgroup	Time Period	N patients in cycle	n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=95)	Any TEAE	95	7 (7.4) (3.0, 14.6)
		Cycle 1	95	0 (0.0) (0.0, 3.8)
		Cycle 2	93	0 (0.0) (0.0, 3.8)
		Cycle 3	88	0 (0.0) (0.0, 3.8)
		Cycle 4	88	1 (1.1) (0.0, 5.7)
		Cycle 5	79	0 (0.0) (0.0, 3.8)
		Cycle 6	77	3 (3.2) (0.7, 9.0)
		Cycle 7	72	0 (0.0) (0.0, 3.8)
		Cycle >= 8 and < 18	70	3 (3.2) (0.7, 9.0)
		Cycle >= 18	13	0 (0.0) (0.0, 3.8)

Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	22 (14.3)	(9.2, 20.8)
		Cycle 1	154	0 (0.0)	(0.0, 2.4)
		Cycle 2	152	1 (0.6)	(0.0, 3.6)
		Cycle 3	146	1 (0.6)	(0.0, 3.6)
		Cycle 4	141	1 (0.6)	(0.0, 3.6)
		Cycle 5	129	2 (1.3)	(0.2, 4.6)
		Cycle 6	127	4 (2.6)	(0.7, 6.5)
		Cycle 7	121	2 (1.3)	(0.2, 4.6)
		Cycle >= 8 and < 18	114	12 (7.8)	(4.1, 13.2)
		Cycle >= 18	33	2 (1.3)	(0.2, 4.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Any TEAE	28	2 (7.1) (0.9, 23.5)
		Cycle 1	28	0 (0.0) (0.0, 12.3)
		Cycle 2	27	0 (0.0) (0.0, 12.3)
		Cycle 3	26	0 (0.0) (0.0, 12.3)
		Cycle 4	26	0 (0.0) (0.0, 12.3)
		Cycle 5	24	0 (0.0) (0.0, 12.3)
		Cycle 6	23	1 (3.6) (0.1, 18.3)
		Cycle 7	22	0 (0.0) (0.0, 12.3)
		Cycle >= 8 and < 18	22	1 (3.6) (0.1, 18.3)
		Cycle >= 18	2	0 (0.0) (0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	12 (12.9)	(6.8, 21.5)
		Cycle 1	93	0 (0.0)	(0.0, 3.9)
		Cycle 2	92	0 (0.0)	(0.0, 3.9)
		Cycle 3	87	0 (0.0)	(0.0, 3.9)
		Cycle 4	84	0 (0.0)	(0.0, 3.9)
		Cycle 5	80	2 (2.2)	(0.3, 7.6)
		Cycle 6	78	2 (2.2)	(0.3, 7.6)
		Cycle 7	75	0 (0.0)	(0.0, 3.9)
		Cycle >= 8 and < 18	73	8 (8.6)	(3.8, 16.2)
		Cycle >= 18	12	1 (1.1)	(0.0, 5.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	12 (13.6) (7.2, 22.6)
		Cycle 1	88	0 (0.0) (0.0, 4.1)
		Cycle 2	86	1 (1.1) (0.0, 6.2)
		Cycle 3	85	1 (1.1) (0.0, 6.2)
		Cycle 4	84	1 (1.1) (0.0, 6.2)
		Cycle 5	74	0 (0.0) (0.0, 4.1)
		Cycle 6	73	3 (3.4) (0.7, 9.6)
		Cycle 7	69	2 (2.3) (0.3, 8.0)
		Cycle >= 8 and < 18	64	5 (5.7) (1.9, 12.8)
		Cycle >= 18	23	1 (1.1) (0.0, 6.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	7 (13.7)	(5.7, 26.3)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	49	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	47	2 (3.9)	(0.5, 13.5)
		Cycle 6	46	1 (2.0)	(0.0, 10.4)
		Cycle 7	45	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	44	4 (7.8)	(2.2, 18.9)
		Cycle >= 18	8	1 (2.0)	(0.0, 10.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	17 (13.6) (8.1, 20.9)
		Cycle 1	125	0 (0.0) (0.0, 2.9)
		Cycle 2	123	1 (0.8) (0.0, 4.4)
		Cycle 3	118	1 (0.8) (0.0, 4.4)
		Cycle 4	114	1 (0.8) (0.0, 4.4)
		Cycle 5	103	0 (0.0) (0.0, 2.9)
		Cycle 6	101	4 (3.2) (0.9, 8.0)
		Cycle 7	95	2 (1.6) (0.2, 5.7)
		Cycle >= 8 and < 18	90	9 (7.2) (3.3, 13.2)
		Cycle >= 18	27	1 (0.8) (0.0, 4.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	13 (13.4)	(7.3, 21.8)
		Cycle 1	97	0 (0.0)	(0.0, 3.7)
		Cycle 2	96	0 (0.0)	(0.0, 3.7)
		Cycle 3	91	0 (0.0)	(0.0, 3.7)
		Cycle 4	88	0 (0.0)	(0.0, 3.7)
		Cycle 5	84	2 (2.1)	(0.3, 7.3)
		Cycle 6	82	2 (2.1)	(0.3, 7.3)
		Cycle 7	79	0 (0.0)	(0.0, 3.7)
		Cycle >= 8 and < 18	76	8 (8.2)	(3.6, 15.6)
		Cycle >= 18	13	2 (2.1)	(0.3, 7.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	11 (13.3) (6.8, 22.5)
		Cycle 1	83	0 (0.0) (0.0, 4.3)
		Cycle 2	81	1 (1.2) (0.0, 6.5)
		Cycle 3	80	1 (1.2) (0.0, 6.5)
		Cycle 4	79	1 (1.2) (0.0, 6.5)
		Cycle 5	69	0 (0.0) (0.0, 4.3)
		Cycle 6	68	3 (3.6) (0.8, 10.2)
		Cycle 7	64	2 (2.4) (0.3, 8.4)
		Cycle >= 8 and < 18	60	5 (6.0) (2.0, 13.5)
		Cycle >= 18	22	0 (0.0) (0.0, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Normal (N=90)			
	Any TEAE	90	8 (8.9)	(3.9, 16.8)
	Cycle 1	90	0 (0.0)	(0.0, 4.0)
	Cycle 2	89	0 (0.0)	(0.0, 4.0)
	Cycle 3	85	0 (0.0)	(0.0, 4.0)
	Cycle 4	85	0 (0.0)	(0.0, 4.0)
	Cycle 5	76	1 (1.1)	(0.0, 6.0)
	Cycle 6	73	0 (0.0)	(0.0, 4.0)
	Cycle 7	72	1 (1.1)	(0.0, 6.0)
	Cycle >= 8 and < 18	69	5 (5.6)	(1.8, 12.5)
	Cycle >= 18	17	1 (1.1)	(0.0, 6.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	8 (11.6) (5.1, 21.6)
		Cycle 1	69	0 (0.0) (0.0, 5.2)
		Cycle 2	68	0 (0.0) (0.0, 5.2)
		Cycle 3	66	0 (0.0) (0.0, 5.2)
		Cycle 4	63	0 (0.0) (0.0, 5.2)
		Cycle 5	59	1 (1.4) (0.0, 7.8)
		Cycle 6	59	2 (2.9) (0.4, 10.1)
		Cycle 7	56	0 (0.0) (0.0, 5.2)
		Cycle >= 8 and < 18	54	6 (8.7) (3.3, 18.0)
		Cycle >= 18	14	0 (0.0) (0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	8 (32.0) (14.9, 53.5)
		Cycle 1	25	0 (0.0) (0.0, 13.7)
		Cycle 2	24	1 (4.0) (0.1, 20.4)
		Cycle 3	23	1 (4.0) (0.1, 20.4)
		Cycle 4	21	1 (4.0) (0.1, 20.4)
		Cycle 5	20	0 (0.0) (0.0, 13.7)
		Cycle 6	20	3 (12.0) (2.5, 31.2)
		Cycle 7	17	1 (4.0) (0.1, 20.4)
		Cycle >= 8 and < 18	15	2 (8.0) (1.0, 26.0)
		Cycle >= 18	4	1 (4.0) (0.1, 20.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	17 (16.2)	(9.7, 24.7)
		Cycle 1	105	0 (0.0)	(0.0, 3.5)
		Cycle 2	104	1 (1.0)	(0.0, 5.2)
		Cycle 3	102	1 (1.0)	(0.0, 5.2)
		Cycle 4	98	1 (1.0)	(0.0, 5.2)
		Cycle 5	90	2 (1.9)	(0.2, 6.7)
		Cycle 6	89	2 (1.9)	(0.2, 6.7)
		Cycle 7	87	1 (1.0)	(0.0, 5.2)
		Cycle >= 8 and < 18	84	10 (9.5)	(4.7, 16.8)
		Cycle >= 18	22	1 (1.0)	(0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	7 (9.2) (3.8, 18.1)
		Cycle 1	76	0 (0.0) (0.0, 4.7)
		Cycle 2	74	0 (0.0) (0.0, 4.7)
		Cycle 3	69	0 (0.0) (0.0, 4.7)
		Cycle 4	68	0 (0.0) (0.0, 4.7)
		Cycle 5	63	0 (0.0) (0.0, 4.7)
		Cycle 6	61	3 (3.9) (0.8, 11.1)
		Cycle 7	56	1 (1.3) (0.0, 7.1)
		Cycle >= 8 and < 18	54	3 (3.9) (0.8, 11.1)
		Cycle >= 18	13	1 (1.3) (0.0, 7.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	5 (20.8)	(7.1, 42.2)
		Cycle 1	24	0 (0.0)	(0.0, 14.2)
		Cycle 2	23	0 (0.0)	(0.0, 14.2)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	1 (4.2)	(0.1, 21.1)
		Cycle 6	18	1 (4.2)	(0.1, 21.1)
		Cycle 7	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 8 and < 18	18	3 (12.5)	(2.7, 32.4)
		Cycle >= 18	6	0 (0.0)	(0.0, 14.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	19 (11.9)	(7.3, 17.9)
		Cycle 1	160	0 (0.0)	(0.0, 2.3)
		Cycle 2	158	1 (0.6)	(0.0, 3.4)
		Cycle 3	152	1 (0.6)	(0.0, 3.4)
		Cycle 4	147	1 (0.6)	(0.0, 3.4)
		Cycle 5	136	1 (0.6)	(0.0, 3.4)
		Cycle 6	134	4 (2.5)	(0.7, 6.3)
		Cycle 7	127	2 (1.3)	(0.2, 4.4)
		Cycle >= 8 and < 18	120	10 (6.3)	(3.0, 11.2)
		Cycle >= 18	29	2 (1.3)	(0.2, 4.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	11 (20.8)	(10.8, 34.1)
		Cycle 1	53	0 (0.0)	(0.0, 6.7)
		Cycle 2	52	1 (1.9)	(0.0, 10.1)
		Cycle 3	49	1 (1.9)	(0.0, 10.1)
		Cycle 4	48	0 (0.0)	(0.0, 6.7)
		Cycle 5	43	1 (1.9)	(0.0, 10.1)
		Cycle 6	42	2 (3.8)	(0.5, 13.0)
		Cycle 7	41	1 (1.9)	(0.0, 10.1)
		Cycle >= 8 and < 18	39	6 (11.3)	(4.3, 23.0)
		Cycle >= 18	8	1 (1.9)	(0.0, 10.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	13 (9.9)	(5.4, 16.4)
		Cycle 1	131	0 (0.0)	(0.0, 2.8)
		Cycle 2	129	0 (0.0)	(0.0, 2.8)
		Cycle 3	125	0 (0.0)	(0.0, 2.8)
		Cycle 4	121	1 (0.8)	(0.0, 4.2)
		Cycle 5	112	1 (0.8)	(0.0, 4.2)
		Cycle 6	110	3 (2.3)	(0.5, 6.5)
		Cycle 7	104	1 (0.8)	(0.0, 4.2)
		Cycle >= 8 and < 18	99	7 (5.3)	(2.2, 10.7)
		Cycle >= 18	27	1 (0.8)	(0.0, 4.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	22 (13.0)	(8.3, 19.0)
		Cycle 1	169	0 (0.0)	(0.0, 2.2)
		Cycle 2	166	1 (0.6)	(0.0, 3.3)
		Cycle 3	159	1 (0.6)	(0.0, 3.3)
		Cycle 4	154	1 (0.6)	(0.0, 3.3)
		Cycle 5	142	2 (1.2)	(0.1, 4.2)
		Cycle 6	139	5 (3.0)	(1.0, 6.8)
		Cycle 7	132	2 (1.2)	(0.1, 4.2)
		Cycle >= 8 and < 18	125	11 (6.5)	(3.3, 11.3)
		Cycle >= 18	31	2 (1.2)	(0.1, 4.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	2 (13.3)	(1.7, 40.5)
		Cycle 1	15	0 (0.0)	(0.0, 21.8)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	2 (13.3)	(1.7, 40.5)
		Cycle >= 18	4	0 (0.0)	(0.0, 21.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	5 (8.9) (3.0, 19.6)
		Cycle 1	56	0 (0.0) (0.0, 6.4)
		Cycle 2	55	0 (0.0) (0.0, 6.4)
		Cycle 3	54	0 (0.0) (0.0, 6.4)
		Cycle 4	53	0 (0.0) (0.0, 6.4)
		Cycle 5	49	0 (0.0) (0.0, 6.4)
		Cycle 6	48	1 (1.8) (0.0, 9.6)
		Cycle 7	48	1 (1.8) (0.0, 9.6)
		Cycle >= 8 and < 18	45	3 (5.4) (1.1, 14.9)
		Cycle >= 18	16	1 (1.8) (0.0, 9.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	19 (14.8)	(9.2, 22.2)
		Cycle 1	128	0 (0.0)	(0.0, 2.8)
		Cycle 2	126	1 (0.8)	(0.0, 4.3)
		Cycle 3	120	1 (0.8)	(0.0, 4.3)
		Cycle 4	116	1 (0.8)	(0.0, 4.3)
		Cycle 5	106	2 (1.6)	(0.2, 5.5)
		Cycle 6	104	4 (3.1)	(0.9, 7.8)
		Cycle 7	97	1 (0.8)	(0.0, 4.3)
		Cycle >= 8 and < 18	93	10 (7.8)	(3.8, 13.9)
		Cycle >= 18	19	1 (0.8)	(0.0, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
0-Prior treatment lines	< 3 lines (N=17)	Any TEAE	17	1 (5.9) (0.1, 28.7)
		Cycle 1	17	0 (0.0) (0.0, 19.5)
		Cycle 2	17	0 (0.0) (0.0, 19.5)
		Cycle 3	17	0 (0.0) (0.0, 19.5)
		Cycle 4	17	0 (0.0) (0.0, 19.5)
		Cycle 5	17	0 (0.0) (0.0, 19.5)
		Cycle 6	16	0 (0.0) (0.0, 19.5)
		Cycle 7	16	0 (0.0) (0.0, 19.5)
		Cycle >= 8 and < 18	16	0 (0.0) (0.0, 19.5)
		Cycle >= 18	6	1 (5.9) (0.1, 28.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
0-Prior treatment lines	>= 3 lines (N=167)	Any TEAE	167	23 (13.8) (8.9, 19.9)
		Cycle 1	167	0 (0.0) (0.0, 2.2)
		Cycle 2	164	1 (0.6) (0.0, 3.3)
		Cycle 3	157	1 (0.6) (0.0, 3.3)
		Cycle 4	152	1 (0.6) (0.0, 3.3)
		Cycle 5	138	2 (1.2) (0.1, 4.3)
		Cycle 6	136	5 (3.0) (1.0, 6.8)
		Cycle 7	129	2 (1.2) (0.1, 4.3)
		Cycle >= 8 and < 18	122	13 (7.8) (4.2, 12.9)
		Cycle >= 18	29	1 (0.6) (0.0, 3.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	9 (11.4) (5.3, 20.5)
		Cycle 1	79	0 (0.0) (0.0, 4.6)
		Cycle 2	78	1 (1.3) (0.0, 6.9)
		Cycle 3	75	1 (1.3) (0.0, 6.9)
		Cycle 4	73	0 (0.0) (0.0, 4.6)
		Cycle 5	70	1 (1.3) (0.0, 6.9)
		Cycle 6	69	1 (1.3) (0.0, 6.9)
		Cycle 7	68	0 (0.0) (0.0, 4.6)
		Cycle >= 8 and < 18	65	5 (6.3) (2.1, 14.2)
		Cycle >= 18	17	2 (2.5) (0.3, 8.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	11 (16.7) (8.6, 27.9)
		Cycle 1	66	0 (0.0) (0.0, 5.4)
		Cycle 2	66	0 (0.0) (0.0, 5.4)
		Cycle 3	64	0 (0.0) (0.0, 5.4)
		Cycle 4	61	1 (1.5) (0.0, 8.2)
		Cycle 5	55	1 (1.5) (0.0, 8.2)
		Cycle 6	53	1 (1.5) (0.0, 8.2)
		Cycle 7	51	0 (0.0) (0.0, 5.4)
		Cycle >= 8 and < 18	51	8 (12.1) (5.4, 22.5)
		Cycle >= 18	10	0 (0.0) (0.0, 5.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	17 (14.0)	(8.4, 21.5)
		Cycle 1	121	0 (0.0)	(0.0, 3.0)
		Cycle 2	120	1 (0.8)	(0.0, 4.5)
		Cycle 3	119	1 (0.8)	(0.0, 4.5)
		Cycle 4	115	1 (0.8)	(0.0, 4.5)
		Cycle 5	106	2 (1.7)	(0.2, 5.8)
		Cycle 6	103	5 (4.1)	(1.4, 9.4)
		Cycle 7	96	1 (0.8)	(0.0, 4.5)
		Cycle >= 8 and < 18	93	7 (5.8)	(2.4, 11.6)
		Cycle >= 18	25	2 (1.7)	(0.2, 5.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	7 (11.1)	(4.6, 21.6)
		Cycle 1	63	0 (0.0)	(0.0, 5.7)
		Cycle 2	61	0 (0.0)	(0.0, 5.7)
		Cycle 3	55	0 (0.0)	(0.0, 5.7)
		Cycle 4	54	0 (0.0)	(0.0, 5.7)
		Cycle 5	49	0 (0.0)	(0.0, 5.7)
		Cycle 6	49	0 (0.0)	(0.0, 5.7)
		Cycle 7	49	1 (1.6)	(0.0, 8.5)
		Cycle >= 8 and < 18	45	6 (9.5)	(3.6, 19.6)
		Cycle >= 18	10	0 (0.0)	(0.0, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	6 (11.8)	(4.4, 23.9)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	50	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	46	1 (2.0)	(0.0, 10.4)
		Cycle 6	44	1 (2.0)	(0.0, 10.4)
		Cycle 7	40	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	40	3 (5.9)	(1.2, 16.2)
		Cycle >= 18	10	1 (2.0)	(0.0, 10.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	18 (13.5)	(8.2, 20.5)
		Cycle 1	0 (0.0)	(0.0, 2.7)
		Cycle 2	1 (0.8)	(0.0, 4.1)
		Cycle 3	1 (0.8)	(0.0, 4.1)
		Cycle 4	1 (0.8)	(0.0, 4.1)
		Cycle 5	1 (0.8)	(0.0, 4.1)
		Cycle 6	4 (3.0)	(0.8, 7.5)
		Cycle 7	2 (1.5)	(0.2, 5.3)
		Cycle >= 8 and < 18	10 (7.5)	(3.7, 13.4)
		Cycle >= 18	1 (0.8)	(0.0, 4.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

UE von besonderem Interesse – Interstitielle Lungenerkrankung (ILD) mit CTCAE-Grad < 3

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	21 (11.4)	(7.2, 16.9)
		Cycle 1	184	0 (0.0)	(0.0, 2.0)
		Cycle 2	181	1 (0.5)	(0.0, 3.0)
		Cycle 3	174	1 (0.5)	(0.0, 3.0)
		Cycle 4	169	1 (0.5)	(0.0, 3.0)
		Cycle 5	155	2 (1.1)	(0.1, 3.9)
		Cycle 6	152	5 (2.7)	(0.9, 6.2)
		Cycle 7	145	1 (0.5)	(0.0, 3.0)
		Cycle >= 8 and < 18	138	11 (6.0)	(3.0, 10.4)
		Cycle >= 18	35	2 (1.1)	(0.1, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	14 (10.0) (5.6, 16.2)
		Cycle 1	140	0 (0.0) (0.0, 2.6)
		Cycle 2	138	1 (0.7) (0.0, 3.9)
		Cycle 3	132	1 (0.7) (0.0, 3.9)
		Cycle 4	128	0 (0.0) (0.0, 2.6)
		Cycle 5	116	1 (0.7) (0.0, 3.9)
		Cycle 6	113	4 (2.9) (0.8, 7.2)
		Cycle 7	109	1 (0.7) (0.0, 3.9)
		Cycle >= 8 and < 18	103	7 (5.0) (2.0, 10.0)
		Cycle >= 18	24	1 (0.7) (0.0, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	7 (15.9) (6.6, 30.1)
		Cycle 1	44	0 (0.0) (0.0, 8.0)
		Cycle 2	43	0 (0.0) (0.0, 8.0)
		Cycle 3	42	0 (0.0) (0.0, 8.0)
		Cycle 4	41	1 (2.3) (0.1, 12.0)
		Cycle 5	39	1 (2.3) (0.1, 12.0)
		Cycle 6	39	1 (2.3) (0.1, 12.0)
		Cycle 7	36	0 (0.0) (0.0, 8.0)
		Cycle >= 8 and < 18	35	4 (9.1) (2.5, 21.7)
		Cycle >= 18	11	1 (2.3) (0.1, 12.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	13 (20.6) (11.5, 32.7)
		Cycle 1	63	0 (0.0) (0.0, 5.7)
		Cycle 2	61	0 (0.0) (0.0, 5.7)
		Cycle 3	58	0 (0.0) (0.0, 5.7)
		Cycle 4	58	1 (1.6) (0.0, 8.5)
		Cycle 5	55	1 (1.6) (0.0, 8.5)
		Cycle 6	55	3 (4.8) (1.0, 13.3)
		Cycle 7	53	1 (1.6) (0.0, 8.5)
		Cycle >= 8 and < 18	49	7 (11.1) (4.6, 21.6)
		Cycle >= 18	15	2 (3.2) (0.4, 11.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	3 (5.7) (1.2, 15.7)
		Cycle 1	53	0 (0.0) (0.0, 6.7)
		Cycle 2	53	0 (0.0) (0.0, 6.7)
		Cycle 3	52	0 (0.0) (0.0, 6.7)
		Cycle 4	49	0 (0.0) (0.0, 6.7)
		Cycle 5	44	0 (0.0) (0.0, 6.7)
		Cycle 6	42	2 (3.8) (0.5, 13.0)
		Cycle 7	40	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	1 (1.9) (0.0, 10.1)
		Cycle >= 18	11	0 (0.0) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	5 (7.4)	(2.4, 16.3)
		Cycle 1	68	0 (0.0)	(0.0, 5.3)
		Cycle 2	67	1 (1.5)	(0.0, 7.9)
		Cycle 3	64	1 (1.5)	(0.0, 7.9)
		Cycle 4	62	0 (0.0)	(0.0, 5.3)
		Cycle 5	56	1 (1.5)	(0.0, 7.9)
		Cycle 6	55	0 (0.0)	(0.0, 5.3)
		Cycle 7	52	0 (0.0)	(0.0, 5.3)
		Cycle >= 8 and < 18	50	3 (4.4)	(0.9, 12.4)
		Cycle >= 18	9	0 (0.0)	(0.0, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	16 (15.7) (9.2, 24.2)
		Cycle 1	102	0 (0.0) (0.0, 3.6)
		Cycle 2	101	1 (1.0) (0.0, 5.3)
		Cycle 3	100	1 (1.0) (0.0, 5.3)
		Cycle 4	98	1 (1.0) (0.0, 5.3)
		Cycle 5	94	2 (2.0) (0.2, 6.9)
		Cycle 6	93	4 (3.9) (1.1, 9.7)
		Cycle 7	88	0 (0.0) (0.0, 3.6)
		Cycle >= 8 and < 18	86	7 (6.9) (2.8, 13.6)
		Cycle >= 18	23	2 (2.0) (0.2, 6.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	5 (6.2) (2.0, 13.8)
		Cycle 1	81	0 (0.0) (0.0, 4.5)
		Cycle 2	79	0 (0.0) (0.0, 4.5)
		Cycle 3	73	0 (0.0) (0.0, 4.5)
		Cycle 4	71	0 (0.0) (0.0, 4.5)
		Cycle 5	61	0 (0.0) (0.0, 4.5)
		Cycle 6	59	1 (1.2) (0.0, 6.7)
		Cycle 7	57	1 (1.2) (0.0, 6.7)
		Cycle >= 8 and < 18	52	4 (4.9) (1.4, 12.2)
		Cycle >= 18	12	0 (0.0) (0.0, 4.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions < 5 cm (N=74)	Any TEAE	74	10 (13.5)	(6.7, 23.5)
	Cycle 1	74	0 (0.0)	(0.0, 4.9)
	Cycle 2	73	1 (1.4)	(0.0, 7.3)
	Cycle 3	71	1 (1.4)	(0.0, 7.3)
	Cycle 4	66	0 (0.0)	(0.0, 4.9)
	Cycle 5	61	1 (1.4)	(0.0, 7.3)
	Cycle 6	60	1 (1.4)	(0.0, 7.3)
	Cycle 7	59	1 (1.4)	(0.0, 7.3)
	Cycle >= 8 and < 18	54	6 (8.1)	(3.0, 16.8)
	Cycle >= 18	18	1 (1.4)	(0.0, 7.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

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			Overall 5.4 mg/kg SAF (N=184)		
Subgroup		Time Period	N patients in cycle	n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=95)	Any TEAE	95	7 (7.4)	(3.0, 14.6)
		Cycle 1	95	0 (0.0)	(0.0, 3.8)
		Cycle 2	93	0 (0.0)	(0.0, 3.8)
		Cycle 3	88	0 (0.0)	(0.0, 3.8)
		Cycle 4	88	1 (1.1)	(0.0, 5.7)
		Cycle 5	79	0 (0.0)	(0.0, 3.8)
		Cycle 6	77	3 (3.2)	(0.7, 9.0)
		Cycle 7	72	0 (0.0)	(0.0, 3.8)
		Cycle >= 8 and < 18	70	3 (3.2)	(0.7, 9.0)
		Cycle >= 18	13	0 (0.0)	(0.0, 3.8)

Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	19 (12.3) (7.6, 18.6)
		Cycle 1	154	0 (0.0) (0.0, 2.4)
		Cycle 2	152	1 (0.6) (0.0, 3.6)
		Cycle 3	146	1 (0.6) (0.0, 3.6)
		Cycle 4	141	1 (0.6) (0.0, 3.6)
		Cycle 5	129	2 (1.3) (0.2, 4.6)
		Cycle 6	127	4 (2.6) (0.7, 6.5)
		Cycle 7	121	1 (0.6) (0.0, 3.6)
		Cycle >= 8 and < 18	114	10 (6.5) (3.2, 11.6)
		Cycle >= 18	33	2 (1.3) (0.2, 4.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Any TEAE	28	2 (7.1) (0.9, 23.5)
		Cycle 1	28	0 (0.0) (0.0, 12.3)
		Cycle 2	27	0 (0.0) (0.0, 12.3)
		Cycle 3	26	0 (0.0) (0.0, 12.3)
		Cycle 4	26	0 (0.0) (0.0, 12.3)
		Cycle 5	24	0 (0.0) (0.0, 12.3)
		Cycle 6	23	1 (3.6) (0.1, 18.3)
		Cycle 7	22	0 (0.0) (0.0, 12.3)
		Cycle >= 8 and < 18	22	1 (3.6) (0.1, 18.3)
		Cycle >= 18	2	0 (0.0) (0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	10 (10.8)	(5.3, 18.9)
		Cycle 1	93	0 (0.0)	(0.0, 3.9)
		Cycle 2	92	0 (0.0)	(0.0, 3.9)
		Cycle 3	87	0 (0.0)	(0.0, 3.9)
		Cycle 4	84	0 (0.0)	(0.0, 3.9)
		Cycle 5	80	2 (2.2)	(0.3, 7.6)
		Cycle 6	78	2 (2.2)	(0.3, 7.6)
		Cycle 7	75	0 (0.0)	(0.0, 3.9)
		Cycle >= 8 and < 18	73	6 (6.5)	(2.4, 13.5)
		Cycle >= 18	12	1 (1.1)	(0.0, 5.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	11 (12.5) (6.4, 21.3)
		Cycle 1	88	0 (0.0) (0.0, 4.1)
		Cycle 2	86	1 (1.1) (0.0, 6.2)
		Cycle 3	85	1 (1.1) (0.0, 6.2)
		Cycle 4	84	1 (1.1) (0.0, 6.2)
		Cycle 5	74	0 (0.0) (0.0, 4.1)
		Cycle 6	73	3 (3.4) (0.7, 9.6)
		Cycle 7	69	1 (1.1) (0.0, 6.2)
		Cycle >= 8 and < 18	64	5 (5.7) (1.9, 12.8)
		Cycle >= 18	23	1 (1.1) (0.0, 6.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	7 (13.7)	(5.7, 26.3)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	49	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	47	2 (3.9)	(0.5, 13.5)
		Cycle 6	46	1 (2.0)	(0.0, 10.4)
		Cycle 7	45	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	44	4 (7.8)	(2.2, 18.9)
		Cycle >= 18	8	1 (2.0)	(0.0, 10.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	14 (11.2) (6.3, 18.1)
		Cycle 1	125	0 (0.0) (0.0, 2.9)
		Cycle 2	123	1 (0.8) (0.0, 4.4)
		Cycle 3	118	1 (0.8) (0.0, 4.4)
		Cycle 4	114	1 (0.8) (0.0, 4.4)
		Cycle 5	103	0 (0.0) (0.0, 2.9)
		Cycle 6	101	4 (3.2) (0.9, 8.0)
		Cycle 7	95	1 (0.8) (0.0, 4.4)
		Cycle >= 8 and < 18	90	7 (5.6) (2.3, 11.2)
		Cycle >= 18	27	1 (0.8) (0.0, 4.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	11 (11.3)	(5.8, 19.4)
		Cycle 1	97	0 (0.0)	(0.0, 3.7)
		Cycle 2	96	0 (0.0)	(0.0, 3.7)
		Cycle 3	91	0 (0.0)	(0.0, 3.7)
		Cycle 4	88	0 (0.0)	(0.0, 3.7)
		Cycle 5	84	2 (2.1)	(0.3, 7.3)
		Cycle 6	82	2 (2.1)	(0.3, 7.3)
		Cycle 7	79	0 (0.0)	(0.0, 3.7)
		Cycle >= 8 and < 18	76	6 (6.2)	(2.3, 13.0)
		Cycle >= 18	13	2 (2.1)	(0.3, 7.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	10 (12.0) (5.9, 21.0)
		Cycle 1	83	0 (0.0) (0.0, 4.3)
		Cycle 2	81	1 (1.2) (0.0, 6.5)
		Cycle 3	80	1 (1.2) (0.0, 6.5)
		Cycle 4	79	1 (1.2) (0.0, 6.5)
		Cycle 5	69	0 (0.0) (0.0, 4.3)
		Cycle 6	68	3 (3.6) (0.8, 10.2)
		Cycle 7	64	1 (1.2) (0.0, 6.5)
		Cycle >= 8 and < 18	60	5 (6.0) (2.0, 13.5)
		Cycle >= 18	22	0 (0.0) (0.0, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Normal (N=90)			
	Any TEAE	90	5 (5.6)	(1.8, 12.5)
	Cycle 1	90	0 (0.0)	(0.0, 4.0)
	Cycle 2	89	0 (0.0)	(0.0, 4.0)
	Cycle 3	85	0 (0.0)	(0.0, 4.0)
	Cycle 4	85	0 (0.0)	(0.0, 4.0)
	Cycle 5	76	1 (1.1)	(0.0, 6.0)
	Cycle 6	73	0 (0.0)	(0.0, 4.0)
	Cycle 7	72	0 (0.0)	(0.0, 4.0)
	Cycle >= 8 and < 18	69	3 (3.3)	(0.7, 9.4)
	Cycle >= 18	17	1 (1.1)	(0.0, 6.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	8 (11.6) (5.1, 21.6)
		Cycle 1	69	0 (0.0) (0.0, 5.2)
		Cycle 2	68	0 (0.0) (0.0, 5.2)
		Cycle 3	66	0 (0.0) (0.0, 5.2)
		Cycle 4	63	0 (0.0) (0.0, 5.2)
		Cycle 5	59	1 (1.4) (0.0, 7.8)
		Cycle 6	59	2 (2.9) (0.4, 10.1)
		Cycle 7	56	0 (0.0) (0.0, 5.2)
		Cycle >= 8 and < 18	54	6 (8.7) (3.3, 18.0)
		Cycle >= 18	14	0 (0.0) (0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	8 (32.0) (14.9, 53.5)
		Cycle 1	25	0 (0.0) (0.0, 13.7)
		Cycle 2	24	1 (4.0) (0.1, 20.4)
		Cycle 3	23	1 (4.0) (0.1, 20.4)
		Cycle 4	21	1 (4.0) (0.1, 20.4)
		Cycle 5	20	0 (0.0) (0.0, 13.7)
		Cycle 6	20	3 (12.0) (2.5, 31.2)
		Cycle 7	17	1 (4.0) (0.1, 20.4)
		Cycle >= 8 and < 18	15	2 (8.0) (1.0, 26.0)
		Cycle >= 18	4	1 (4.0) (0.1, 20.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	14 (13.3)	(7.5, 21.4)
		Cycle 1	105	0 (0.0)	(0.0, 3.5)
		Cycle 2	104	1 (1.0)	(0.0, 5.2)
		Cycle 3	102	1 (1.0)	(0.0, 5.2)
		Cycle 4	98	1 (1.0)	(0.0, 5.2)
		Cycle 5	90	2 (1.9)	(0.2, 6.7)
		Cycle 6	89	2 (1.9)	(0.2, 6.7)
		Cycle 7	87	0 (0.0)	(0.0, 3.5)
		Cycle >= 8 and < 18	84	8 (7.6)	(3.3, 14.5)
		Cycle >= 18	22	1 (1.0)	(0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	7 (9.2)	(3.8, 18.1)
		Cycle 1	76	0 (0.0)	(0.0, 4.7)
		Cycle 2	74	0 (0.0)	(0.0, 4.7)
		Cycle 3	69	0 (0.0)	(0.0, 4.7)
		Cycle 4	68	0 (0.0)	(0.0, 4.7)
		Cycle 5	63	0 (0.0)	(0.0, 4.7)
		Cycle 6	61	3 (3.9)	(0.8, 11.1)
		Cycle 7	56	1 (1.3)	(0.0, 7.1)
		Cycle >= 8 and < 18	54	3 (3.9)	(0.8, 11.1)
		Cycle >= 18	13	1 (1.3)	(0.0, 7.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	5 (20.8)	(7.1, 42.2)
		Cycle 1	24	0 (0.0)	(0.0, 14.2)
		Cycle 2	23	0 (0.0)	(0.0, 14.2)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	1 (4.2)	(0.1, 21.1)
		Cycle 6	18	1 (4.2)	(0.1, 21.1)
		Cycle 7	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 8 and < 18	18	3 (12.5)	(2.7, 32.4)
		Cycle >= 18	6	0 (0.0)	(0.0, 14.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	16 (10.0)	(5.8, 15.7)
		Cycle 1	160	0 (0.0)	(0.0, 2.3)
		Cycle 2	158	1 (0.6)	(0.0, 3.4)
		Cycle 3	152	1 (0.6)	(0.0, 3.4)
		Cycle 4	147	1 (0.6)	(0.0, 3.4)
		Cycle 5	136	1 (0.6)	(0.0, 3.4)
		Cycle 6	134	4 (2.5)	(0.7, 6.3)
		Cycle 7	127	1 (0.6)	(0.0, 3.4)
		Cycle >= 8 and < 18	120	8 (5.0)	(2.2, 9.6)
		Cycle >= 18	29	2 (1.3)	(0.2, 4.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	9 (17.0) (8.1, 29.8)
		Cycle 1	53	0 (0.0) (0.0, 6.7)
		Cycle 2	52	1 (1.9) (0.0, 10.1)
		Cycle 3	49	1 (1.9) (0.0, 10.1)
		Cycle 4	48	0 (0.0) (0.0, 6.7)
		Cycle 5	43	1 (1.9) (0.0, 10.1)
		Cycle 6	42	2 (3.8) (0.5, 13.0)
		Cycle 7	41	1 (1.9) (0.0, 10.1)
		Cycle >= 8 and < 18	39	4 (7.5) (2.1, 18.2)
		Cycle >= 18	8	1 (1.9) (0.0, 10.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	12 (9.2)	(4.8, 15.5)
		Cycle 1	131	0 (0.0)	(0.0, 2.8)
		Cycle 2	129	0 (0.0)	(0.0, 2.8)
		Cycle 3	125	0 (0.0)	(0.0, 2.8)
		Cycle 4	121	1 (0.8)	(0.0, 4.2)
		Cycle 5	112	1 (0.8)	(0.0, 4.2)
		Cycle 6	110	3 (2.3)	(0.5, 6.5)
		Cycle 7	104	0 (0.0)	(0.0, 2.8)
		Cycle >= 8 and < 18	99	7 (5.3)	(2.2, 10.7)
		Cycle >= 18	27	1 (0.8)	(0.0, 4.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	19 (11.2) (6.9, 17.0)
		Cycle 1	169	0 (0.0) (0.0, 2.2)
		Cycle 2	166	1 (0.6) (0.0, 3.3)
		Cycle 3	159	1 (0.6) (0.0, 3.3)
		Cycle 4	154	1 (0.6) (0.0, 3.3)
		Cycle 5	142	2 (1.2) (0.1, 4.2)
		Cycle 6	139	5 (3.0) (1.0, 6.8)
		Cycle 7	132	1 (0.6) (0.0, 3.3)
		Cycle >= 8 and < 18	125	9 (5.3) (2.5, 9.9)
		Cycle >= 18	31	2 (1.2) (0.1, 4.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	2 (13.3)	(1.7, 40.5)
		Cycle 1	15	0 (0.0)	(0.0, 21.8)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	2 (13.3)	(1.7, 40.5)
		Cycle >= 18	4	0 (0.0)	(0.0, 21.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	5 (8.9)	(3.0, 19.6)
		Cycle 1	56	0 (0.0)	(0.0, 6.4)
		Cycle 2	55	0 (0.0)	(0.0, 6.4)
		Cycle 3	54	0 (0.0)	(0.0, 6.4)
		Cycle 4	53	0 (0.0)	(0.0, 6.4)
		Cycle 5	49	0 (0.0)	(0.0, 6.4)
		Cycle 6	48	1 (1.8)	(0.0, 9.6)
		Cycle 7	48	1 (1.8)	(0.0, 9.6)
		Cycle >= 8 and < 18	45	3 (5.4)	(1.1, 14.9)
		Cycle >= 18	16	1 (1.8)	(0.0, 9.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	16 (12.5) (7.3, 19.5)
		Cycle 1	128	0 (0.0) (0.0, 2.8)
		Cycle 2	126	1 (0.8) (0.0, 4.3)
		Cycle 3	120	1 (0.8) (0.0, 4.3)
		Cycle 4	116	1 (0.8) (0.0, 4.3)
		Cycle 5	106	2 (1.6) (0.2, 5.5)
		Cycle 6	104	4 (3.1) (0.9, 7.8)
		Cycle 7	97	0 (0.0) (0.0, 2.8)
		Cycle >= 8 and < 18	93	8 (6.3) (2.7, 11.9)
		Cycle >= 18	19	1 (0.8) (0.0, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
0-Prior treatment lines	< 3 lines (N=17)	Any TEAE	17	1 (5.9) (0.1, 28.7)
		Cycle 1	17	0 (0.0) (0.0, 19.5)
		Cycle 2	17	0 (0.0) (0.0, 19.5)
		Cycle 3	17	0 (0.0) (0.0, 19.5)
		Cycle 4	17	0 (0.0) (0.0, 19.5)
		Cycle 5	17	0 (0.0) (0.0, 19.5)
		Cycle 6	16	0 (0.0) (0.0, 19.5)
		Cycle 7	16	0 (0.0) (0.0, 19.5)
		Cycle >= 8 and < 18	16	0 (0.0) (0.0, 19.5)
		Cycle >= 18	6	1 (5.9) (0.1, 28.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
0-Prior treatment lines	>= 3 lines (N=167)	Any TEAE	167	20 (12.0) (7.5, 17.9)
		Cycle 1	167	0 (0.0) (0.0, 2.2)
		Cycle 2	164	1 (0.6) (0.0, 3.3)
		Cycle 3	157	1 (0.6) (0.0, 3.3)
		Cycle 4	152	1 (0.6) (0.0, 3.3)
		Cycle 5	138	2 (1.2) (0.1, 4.3)
		Cycle 6	136	5 (3.0) (1.0, 6.8)
		Cycle 7	129	1 (0.6) (0.0, 3.3)
		Cycle >= 8 and < 18	122	11 (6.6) (3.3, 11.5)
		Cycle >= 18	29	1 (0.6) (0.0, 3.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	8 (10.1) (4.5, 19.0)
		Cycle 1	79	0 (0.0) (0.0, 4.6)
		Cycle 2	78	1 (1.3) (0.0, 6.9)
		Cycle 3	75	1 (1.3) (0.0, 6.9)
		Cycle 4	73	0 (0.0) (0.0, 4.6)
		Cycle 5	70	1 (1.3) (0.0, 6.9)
		Cycle 6	69	1 (1.3) (0.0, 6.9)
		Cycle 7	68	0 (0.0) (0.0, 4.6)
		Cycle >= 8 and < 18	65	4 (5.1) (1.4, 12.5)
		Cycle >= 18	17	2 (2.5) (0.3, 8.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	10 (15.2) (7.5, 26.1)
		Cycle 1	66	0 (0.0) (0.0, 5.4)
		Cycle 2	66	0 (0.0) (0.0, 5.4)
		Cycle 3	64	0 (0.0) (0.0, 5.4)
		Cycle 4	61	1 (1.5) (0.0, 8.2)
		Cycle 5	55	1 (1.5) (0.0, 8.2)
		Cycle 6	53	1 (1.5) (0.0, 8.2)
		Cycle 7	51	0 (0.0) (0.0, 5.4)
		Cycle >= 8 and < 18	51	7 (10.6) (4.4, 20.6)
		Cycle >= 18	10	0 (0.0) (0.0, 5.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	16 (13.2) (7.8, 20.6)
		Cycle 1	121	0 (0.0) (0.0, 3.0)
		Cycle 2	120	1 (0.8) (0.0, 4.5)
		Cycle 3	119	1 (0.8) (0.0, 4.5)
		Cycle 4	115	1 (0.8) (0.0, 4.5)
		Cycle 5	106	2 (1.7) (0.2, 5.8)
		Cycle 6	103	5 (4.1) (1.4, 9.4)
		Cycle 7	96	1 (0.8) (0.0, 4.5)
		Cycle >= 8 and < 18	93	6 (5.0) (1.8, 10.5)
		Cycle >= 18	25	2 (1.7) (0.2, 5.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	5 (7.9)	(2.6, 17.6)
		Cycle 1	63	0 (0.0)	(0.0, 5.7)
		Cycle 2	61	0 (0.0)	(0.0, 5.7)
		Cycle 3	55	0 (0.0)	(0.0, 5.7)
		Cycle 4	54	0 (0.0)	(0.0, 5.7)
		Cycle 5	49	0 (0.0)	(0.0, 5.7)
		Cycle 6	49	0 (0.0)	(0.0, 5.7)
		Cycle 7	49	0 (0.0)	(0.0, 5.7)
		Cycle >= 8 and < 18	45	5 (7.9)	(2.6, 17.6)
		Cycle >= 18	10	0 (0.0)	(0.0, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	6 (11.8) (4.4, 23.9)
		Cycle 1	51	0 (0.0) (0.0, 7.0)
		Cycle 2	50	0 (0.0) (0.0, 7.0)
		Cycle 3	50	0 (0.0) (0.0, 7.0)
		Cycle 4	49	0 (0.0) (0.0, 7.0)
		Cycle 5	46	1 (2.0) (0.0, 10.4)
		Cycle 6	44	1 (2.0) (0.0, 10.4)
		Cycle 7	40	0 (0.0) (0.0, 7.0)
		Cycle >= 8 and < 18	40	3 (5.9) (1.2, 16.2)
		Cycle >= 18	10	1 (2.0) (0.0, 10.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	15 (11.3) (6.5, 17.9)
		Cycle 1	133	0 (0.0) (0.0, 2.7)
		Cycle 2	131	1 (0.8) (0.0, 4.1)
		Cycle 3	124	1 (0.8) (0.0, 4.1)
		Cycle 4	120	1 (0.8) (0.0, 4.1)
		Cycle 5	109	1 (0.8) (0.0, 4.1)
		Cycle 6	108	4 (3.0) (0.8, 7.5)
		Cycle 7	105	1 (0.8) (0.0, 4.1)
		Cycle >= 8 and < 18	98	8 (6.0) (2.6, 11.5)
		Cycle >= 18	25	1 (0.8) (0.0, 4.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

UE von besonderem Interesse – Interstitielle Lungenerkrankung (ILD) unabhängig vom Schweregrad, Bewertung durch AC

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	27 (14.7)	(9.9, 20.6)
		Cycle 1	184	0 (0.0)	(0.0, 2.0)
		Cycle 2	181	2 (1.1)	(0.1, 3.9)
		Cycle 3	174	2 (1.1)	(0.1, 3.9)
		Cycle 4	169	2 (1.1)	(0.1, 3.9)
		Cycle 5	155	2 (1.1)	(0.1, 3.9)
		Cycle 6	152	4 (2.2)	(0.6, 5.5)
		Cycle 7	145	1 (0.5)	(0.0, 3.0)
		Cycle >= 8 and < 18	138	14 (7.6)	(4.2, 12.4)
		Cycle >= 18	35	2 (1.1)	(0.1, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	20 (14.3) (8.9, 21.2)
		Cycle 1	140	0 (0.0) (0.0, 2.6)
		Cycle 2	138	2 (1.4) (0.2, 5.1)
		Cycle 3	132	2 (1.4) (0.2, 5.1)
		Cycle 4	128	1 (0.7) (0.0, 3.9)
		Cycle 5	116	1 (0.7) (0.0, 3.9)
		Cycle 6	113	3 (2.1) (0.4, 6.1)
		Cycle 7	109	1 (0.7) (0.0, 3.9)
		Cycle >= 8 and < 18	103	10 (7.1) (3.5, 12.7)
		Cycle >= 18	24	1 (0.7) (0.0, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	7 (15.9) (6.6, 30.1)
		Cycle 1	44	0 (0.0) (0.0, 8.0)
		Cycle 2	43	0 (0.0) (0.0, 8.0)
		Cycle 3	42	0 (0.0) (0.0, 8.0)
		Cycle 4	41	1 (2.3) (0.1, 12.0)
		Cycle 5	39	1 (2.3) (0.1, 12.0)
		Cycle 6	39	1 (2.3) (0.1, 12.0)
		Cycle 7	36	0 (0.0) (0.0, 8.0)
		Cycle >= 8 and < 18	35	4 (9.1) (2.5, 21.7)
		Cycle >= 18	11	1 (2.3) (0.1, 12.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	11 (17.5) (9.1, 29.1)
		Cycle 1	63	0 (0.0) (0.0, 5.7)
		Cycle 2	61	0 (0.0) (0.0, 5.7)
		Cycle 3	58	0 (0.0) (0.0, 5.7)
		Cycle 4	58	1 (1.6) (0.0, 8.5)
		Cycle 5	55	1 (1.6) (0.0, 8.5)
		Cycle 6	55	2 (3.2) (0.4, 11.0)
		Cycle 7	53	0 (0.0) (0.0, 5.7)
		Cycle >= 8 and < 18	49	6 (9.5) (3.6, 19.6)
		Cycle >= 18	15	2 (3.2) (0.4, 11.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	3 (5.7) (1.2, 15.7)
		Cycle 1	53	0 (0.0) (0.0, 6.7)
		Cycle 2	53	0 (0.0) (0.0, 6.7)
		Cycle 3	52	0 (0.0) (0.0, 6.7)
		Cycle 4	49	0 (0.0) (0.0, 6.7)
		Cycle 5	44	0 (0.0) (0.0, 6.7)
		Cycle 6	42	2 (3.8) (0.5, 13.0)
		Cycle 7	40	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	1 (1.9) (0.0, 10.1)
		Cycle >= 18	11	0 (0.0) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	13 (19.1) (10.6, 30.5)
		Cycle 1	68	0 (0.0) (0.0, 5.3)
		Cycle 2	67	2 (2.9) (0.4, 10.2)
		Cycle 3	64	2 (2.9) (0.4, 10.2)
		Cycle 4	62	1 (1.5) (0.0, 7.9)
		Cycle 5	56	1 (1.5) (0.0, 7.9)
		Cycle 6	55	0 (0.0) (0.0, 5.3)
		Cycle 7	52	1 (1.5) (0.0, 7.9)
		Cycle >= 8 and < 18	50	7 (10.3) (4.2, 20.1)
		Cycle >= 18	9	0 (0.0) (0.0, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	18 (17.6) (10.8, 26.4)
		Cycle 1	102	0 (0.0) (0.0, 3.6)
		Cycle 2	101	1 (1.0) (0.0, 5.3)
		Cycle 3	100	1 (1.0) (0.0, 5.3)
		Cycle 4	98	1 (1.0) (0.0, 5.3)
		Cycle 5	94	2 (2.0) (0.2, 6.9)
		Cycle 6	93	4 (3.9) (1.1, 9.7)
		Cycle 7	88	1 (1.0) (0.0, 5.3)
		Cycle >= 8 and < 18	86	8 (7.8) (3.4, 14.9)
		Cycle >= 18	23	2 (2.0) (0.2, 6.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	8 (9.9)	(4.4, 18.5)
		Cycle 1	81	0 (0.0)	(0.0, 4.5)
		Cycle 2	79	1 (1.2)	(0.0, 6.7)
		Cycle 3	73	0 (0.0)	(0.0, 4.5)
		Cycle 4	71	1 (1.2)	(0.0, 6.7)
		Cycle 5	61	0 (0.0)	(0.0, 4.5)
		Cycle 6	59	0 (0.0)	(0.0, 4.5)
		Cycle 7	57	0 (0.0)	(0.0, 4.5)
		Cycle >= 8 and < 18	52	6 (7.4)	(2.8, 15.4)
		Cycle >= 18	12	0 (0.0)	(0.0, 4.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions < 5 cm (N=74)	Any TEAE	74	13 (17.6)	(9.7, 28.2)
	Cycle 1	74	0 (0.0)	(0.0, 4.9)
	Cycle 2	73	2 (2.7)	(0.3, 9.4)
	Cycle 3	71	2 (2.7)	(0.3, 9.4)
	Cycle 4	66	0 (0.0)	(0.0, 4.9)
	Cycle 5	61	1 (1.4)	(0.0, 7.3)
	Cycle 6	60	0 (0.0)	(0.0, 4.9)
	Cycle 7	59	1 (1.4)	(0.0, 7.3)
	Cycle >= 8 and < 18	54	7 (9.5)	(3.9, 18.5)
	Cycle >= 18	18	1 (1.4)	(0.0, 7.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

			Overall 5.4 mg/kg SAF (N=184)	
Subgroup	Time Period	N patients in cycle	n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=95)	Any TEAE	95	9 (9.5) (4.4, 17.2)
		Cycle 1	95	0 (0.0) (0.0, 3.8)
		Cycle 2	93	0 (0.0) (0.0, 3.8)
		Cycle 3	88	0 (0.0) (0.0, 3.8)
		Cycle 4	88	2 (2.1) (0.3, 7.4)
		Cycle 5	79	0 (0.0) (0.0, 3.8)
		Cycle 6	77	3 (3.2) (0.7, 9.0)
		Cycle 7	72	0 (0.0) (0.0, 3.8)
		Cycle >= 8 and < 18	70	4 (4.2) (1.2, 10.4)
		Cycle >= 18	13	0 (0.0) (0.0, 3.8)

Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	24 (15.6)	(10.2, 22.3)
		Cycle 1	154	0 (0.0)	(0.0, 2.4)
		Cycle 2	152	2 (1.3)	(0.2, 4.6)
		Cycle 3	146	2 (1.3)	(0.2, 4.6)
		Cycle 4	141	2 (1.3)	(0.2, 4.6)
		Cycle 5	129	2 (1.3)	(0.2, 4.6)
		Cycle 6	127	3 (1.9)	(0.4, 5.6)
		Cycle 7	121	1 (0.6)	(0.0, 3.6)
		Cycle >= 8 and < 18	114	12 (7.8)	(4.1, 13.2)
		Cycle >= 18	33	2 (1.3)	(0.2, 4.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Any TEAE	28	2 (7.1) (0.9, 23.5)
		Cycle 1	28	0 (0.0) (0.0, 12.3)
		Cycle 2	27	0 (0.0) (0.0, 12.3)
		Cycle 3	26	0 (0.0) (0.0, 12.3)
		Cycle 4	26	0 (0.0) (0.0, 12.3)
		Cycle 5	24	0 (0.0) (0.0, 12.3)
		Cycle 6	23	1 (3.6) (0.1, 18.3)
		Cycle 7	22	0 (0.0) (0.0, 12.3)
		Cycle >= 8 and < 18	22	1 (3.6) (0.1, 18.3)
		Cycle >= 18	2	0 (0.0) (0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	14 (15.1)	(8.5, 24.0)
		Cycle 1	93	0 (0.0)	(0.0, 3.9)
		Cycle 2	92	1 (1.1)	(0.0, 5.8)
		Cycle 3	87	0 (0.0)	(0.0, 3.9)
		Cycle 4	84	0 (0.0)	(0.0, 3.9)
		Cycle 5	80	2 (2.2)	(0.3, 7.6)
		Cycle 6	78	2 (2.2)	(0.3, 7.6)
		Cycle 7	75	0 (0.0)	(0.0, 3.9)
		Cycle >= 8 and < 18	73	9 (9.7)	(4.5, 17.6)
		Cycle >= 18	12	1 (1.1)	(0.0, 5.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	12 (13.6) (7.2, 22.6)
		Cycle 1	88	0 (0.0) (0.0, 4.1)
		Cycle 2	86	1 (1.1) (0.0, 6.2)
		Cycle 3	85	1 (1.1) (0.0, 6.2)
		Cycle 4	84	2 (2.3) (0.3, 8.0)
		Cycle 5	74	0 (0.0) (0.0, 4.1)
		Cycle 6	73	2 (2.3) (0.3, 8.0)
		Cycle 7	69	1 (1.1) (0.0, 6.2)
		Cycle >= 8 and < 18	64	5 (5.7) (1.9, 12.8)
		Cycle >= 18	23	1 (1.1) (0.0, 6.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	8 (15.7)	(7.0, 28.6)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	1 (2.0)	(0.0, 10.4)
		Cycle 3	49	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	47	2 (3.9)	(0.5, 13.5)
		Cycle 6	46	1 (2.0)	(0.0, 10.4)
		Cycle 7	45	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	44	4 (7.8)	(2.2, 18.9)
		Cycle >= 18	8	1 (2.0)	(0.0, 10.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	17 (13.6) (8.1, 20.9)
		Cycle 1	125	0 (0.0) (0.0, 2.9)
		Cycle 2	123	1 (0.8) (0.0, 4.4)
		Cycle 3	118	1 (0.8) (0.0, 4.4)
		Cycle 4	114	2 (1.6) (0.2, 5.7)
		Cycle 5	103	0 (0.0) (0.0, 2.9)
		Cycle 6	101	3 (2.4) (0.5, 6.9)
		Cycle 7	95	1 (0.8) (0.0, 4.4)
		Cycle >= 8 and < 18	90	9 (7.2) (3.3, 13.2)
		Cycle >= 18	27	1 (0.8) (0.0, 4.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	15 (15.5)	(8.9, 24.2)
		Cycle 1	97	0 (0.0)	(0.0, 3.7)
		Cycle 2	96	1 (1.0)	(0.0, 5.6)
		Cycle 3	91	0 (0.0)	(0.0, 3.7)
		Cycle 4	88	0 (0.0)	(0.0, 3.7)
		Cycle 5	84	2 (2.1)	(0.3, 7.3)
		Cycle 6	82	2 (2.1)	(0.3, 7.3)
		Cycle 7	79	0 (0.0)	(0.0, 3.7)
		Cycle >= 8 and < 18	76	9 (9.3)	(4.3, 16.9)
		Cycle >= 18	13	2 (2.1)	(0.3, 7.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	11 (13.3) (6.8, 22.5)
		Cycle 1	83	0 (0.0) (0.0, 4.3)
		Cycle 2	81	1 (1.2) (0.0, 6.5)
		Cycle 3	80	1 (1.2) (0.0, 6.5)
		Cycle 4	79	2 (2.4) (0.3, 8.4)
		Cycle 5	69	0 (0.0) (0.0, 4.3)
		Cycle 6	68	2 (2.4) (0.3, 8.4)
		Cycle 7	64	1 (1.2) (0.0, 6.5)
		Cycle >= 8 and < 18	60	5 (6.0) (2.0, 13.5)
		Cycle >= 18	22	0 (0.0) (0.0, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Normal (N=90)	Any TEAE	90	12 (13.3)	(7.1, 22.1)
		Cycle 1	90	0 (0.0)	(0.0, 4.0)
		Cycle 2	89	1 (1.1)	(0.0, 6.0)
		Cycle 3	85	0 (0.0)	(0.0, 4.0)
		Cycle 4	85	1 (1.1)	(0.0, 6.0)
		Cycle 5	76	1 (1.1)	(0.0, 6.0)
		Cycle 6	73	0 (0.0)	(0.0, 4.0)
		Cycle 7	72	1 (1.1)	(0.0, 6.0)
		Cycle >= 8 and < 18	69	7 (7.8)	(3.2, 15.4)
		Cycle >= 18	17	1 (1.1)	(0.0, 6.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	7 (10.1) (4.2, 19.8)
		Cycle 1	69	0 (0.0) (0.0, 5.2)
		Cycle 2	68	0 (0.0) (0.0, 5.2)
		Cycle 3	66	0 (0.0) (0.0, 5.2)
		Cycle 4	63	0 (0.0) (0.0, 5.2)
		Cycle 5	59	1 (1.4) (0.0, 7.8)
		Cycle 6	59	2 (2.9) (0.4, 10.1)
		Cycle 7	56	0 (0.0) (0.0, 5.2)
		Cycle >= 8 and < 18	54	5 (7.2) (2.4, 16.1)
		Cycle >= 18	14	0 (0.0) (0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	8 (32.0) (14.9, 53.5)
		Cycle 1	25	0 (0.0) (0.0, 13.7)
		Cycle 2	24	1 (4.0) (0.1, 20.4)
		Cycle 3	23	2 (8.0) (1.0, 26.0)
		Cycle 4	21	1 (4.0) (0.1, 20.4)
		Cycle 5	20	0 (0.0) (0.0, 13.7)
		Cycle 6	20	2 (8.0) (1.0, 26.0)
		Cycle 7	17	0 (0.0) (0.0, 13.7)
		Cycle >= 8 and < 18	15	2 (8.0) (1.0, 26.0)
		Cycle >= 18	4	1 (4.0) (0.1, 20.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	21 (20.0) (12.8, 28.9)
		Cycle 1	105	0 (0.0) (0.0, 3.5)
		Cycle 2	104	1 (1.0) (0.0, 5.2)
		Cycle 3	102	2 (1.9) (0.2, 6.7)
		Cycle 4	98	2 (1.9) (0.2, 6.7)
		Cycle 5	90	2 (1.9) (0.2, 6.7)
		Cycle 6	89	2 (1.9) (0.2, 6.7)
		Cycle 7	87	1 (1.0) (0.0, 5.2)
		Cycle >= 8 and < 18	84	12 (11.4) (6.0, 19.1)
		Cycle >= 18	22	1 (1.0) (0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	6 (7.9) (3.0, 16.4)
		Cycle 1	76	0 (0.0) (0.0, 4.7)
		Cycle 2	74	1 (1.3) (0.0, 7.1)
		Cycle 3	69	0 (0.0) (0.0, 4.7)
		Cycle 4	68	0 (0.0) (0.0, 4.7)
		Cycle 5	63	0 (0.0) (0.0, 4.7)
		Cycle 6	61	2 (2.6) (0.3, 9.2)
		Cycle 7	56	0 (0.0) (0.0, 4.7)
		Cycle >= 8 and < 18	54	2 (2.6) (0.3, 9.2)
		Cycle >= 18	13	1 (1.3) (0.0, 7.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	4 (16.7)	(4.7, 37.4)
		Cycle 1	24	0 (0.0)	(0.0, 14.2)
		Cycle 2	23	0 (0.0)	(0.0, 14.2)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	1 (4.2)	(0.1, 21.1)
		Cycle 6	18	1 (4.2)	(0.1, 21.1)
		Cycle 7	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 8 and < 18	18	2 (8.3)	(1.0, 27.0)
		Cycle >= 18	6	0 (0.0)	(0.0, 14.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	23 (14.4)	(9.3, 20.8)
		Cycle 1	160	0 (0.0)	(0.0, 2.3)
		Cycle 2	158	2 (1.3)	(0.2, 4.4)
		Cycle 3	152	2 (1.3)	(0.2, 4.4)
		Cycle 4	147	2 (1.3)	(0.2, 4.4)
		Cycle 5	136	1 (0.6)	(0.0, 3.4)
		Cycle 6	134	3 (1.9)	(0.4, 5.4)
		Cycle 7	127	1 (0.6)	(0.0, 3.4)
		Cycle >= 8 and < 18	120	12 (7.5)	(3.9, 12.7)
		Cycle >= 18	29	2 (1.3)	(0.2, 4.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	12 (22.6) (12.3, 36.2)
		Cycle 1	53	0 (0.0) (0.0, 6.7)
		Cycle 2	52	1 (1.9) (0.0, 10.1)
		Cycle 3	49	1 (1.9) (0.0, 10.1)
		Cycle 4	48	1 (1.9) (0.0, 10.1)
		Cycle 5	43	1 (1.9) (0.0, 10.1)
		Cycle 6	42	1 (1.9) (0.0, 10.1)
		Cycle 7	41	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	7 (13.2) (5.5, 25.3)
		Cycle >= 18	8	1 (1.9) (0.0, 10.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	15 (11.5)	(6.6, 18.2)
		Cycle 1	131	0 (0.0)	(0.0, 2.8)
		Cycle 2	129	1 (0.8)	(0.0, 4.2)
		Cycle 3	125	1 (0.8)	(0.0, 4.2)
		Cycle 4	121	1 (0.8)	(0.0, 4.2)
		Cycle 5	112	1 (0.8)	(0.0, 4.2)
		Cycle 6	110	3 (2.3)	(0.5, 6.5)
		Cycle 7	104	1 (0.8)	(0.0, 4.2)
		Cycle >= 8 and < 18	99	7 (5.3)	(2.2, 10.7)
		Cycle >= 18	27	1 (0.8)	(0.0, 4.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	25 (14.8) (9.8, 21.1)
		Cycle 1	169	0 (0.0) (0.0, 2.2)
		Cycle 2	166	2 (1.2) (0.1, 4.2)
		Cycle 3	159	2 (1.2) (0.1, 4.2)
		Cycle 4	154	2 (1.2) (0.1, 4.2)
		Cycle 5	142	2 (1.2) (0.1, 4.2)
		Cycle 6	139	4 (2.4) (0.6, 5.9)
		Cycle 7	132	1 (0.6) (0.0, 3.3)
		Cycle >= 8 and < 18	125	12 (7.1) (3.7, 12.1)
		Cycle >= 18	31	2 (1.2) (0.1, 4.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	2 (13.3)	(1.7, 40.5)
		Cycle 1	15	0 (0.0)	(0.0, 21.8)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	2 (13.3)	(1.7, 40.5)
		Cycle >= 18	4	0 (0.0)	(0.0, 21.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	5 (8.9)	(3.0, 19.6)
		Cycle 1	56	0 (0.0)	(0.0, 6.4)
		Cycle 2	55	1 (1.8)	(0.0, 9.6)
		Cycle 3	54	0 (0.0)	(0.0, 6.4)
		Cycle 4	53	0 (0.0)	(0.0, 6.4)
		Cycle 5	49	0 (0.0)	(0.0, 6.4)
		Cycle 6	48	0 (0.0)	(0.0, 6.4)
		Cycle 7	48	0 (0.0)	(0.0, 6.4)
		Cycle >= 8 and < 18	45	3 (5.4)	(1.1, 14.9)
		Cycle >= 18	16	1 (1.8)	(0.0, 9.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	22 (17.2)	(11.1, 24.9)
		Cycle 1	128	0 (0.0)	(0.0, 2.8)
		Cycle 2	126	1 (0.8)	(0.0, 4.3)
		Cycle 3	120	2 (1.6)	(0.2, 5.5)
		Cycle 4	116	2 (1.6)	(0.2, 5.5)
		Cycle 5	106	2 (1.6)	(0.2, 5.5)
		Cycle 6	104	4 (3.1)	(0.9, 7.8)
		Cycle 7	97	1 (0.8)	(0.0, 4.3)
		Cycle >= 8 and < 18	93	11 (8.6)	(4.4, 14.9)
		Cycle >= 18	19	1 (0.8)	(0.0, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
0-Prior treatment lines	< 3 lines (N=17)	Any TEAE	17	1 (5.9) (0.1, 28.7)
		Cycle 1	17	0 (0.0) (0.0, 19.5)
		Cycle 2	17	0 (0.0) (0.0, 19.5)
		Cycle 3	17	0 (0.0) (0.0, 19.5)
		Cycle 4	17	0 (0.0) (0.0, 19.5)
		Cycle 5	17	0 (0.0) (0.0, 19.5)
		Cycle 6	16	0 (0.0) (0.0, 19.5)
		Cycle 7	16	0 (0.0) (0.0, 19.5)
		Cycle >= 8 and < 18	16	0 (0.0) (0.0, 19.5)
		Cycle >= 18	6	1 (5.9) (0.1, 28.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
0-Prior treatment lines	>= 3 lines (N=167)	Any TEAE	167	26 (15.6) (10.4, 22.0)
		Cycle 1	167	0 (0.0) (0.0, 2.2)
		Cycle 2	164	2 (1.2) (0.1, 4.3)
		Cycle 3	157	2 (1.2) (0.1, 4.3)
		Cycle 4	152	2 (1.2) (0.1, 4.3)
		Cycle 5	138	2 (1.2) (0.1, 4.3)
		Cycle 6	136	4 (2.4) (0.7, 6.0)
		Cycle 7	129	1 (0.6) (0.0, 3.3)
		Cycle >= 8 and < 18	122	14 (8.4) (4.7, 13.7)
		Cycle >= 18	29	1 (0.6) (0.0, 3.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	10 (12.7) (6.2, 22.0)
		Cycle 1	79	0 (0.0) (0.0, 4.6)
		Cycle 2	78	2 (2.5) (0.3, 8.8)
		Cycle 3	75	1 (1.3) (0.0, 6.9)
		Cycle 4	73	0 (0.0) (0.0, 4.6)
		Cycle 5	70	1 (1.3) (0.0, 6.9)
		Cycle 6	69	1 (1.3) (0.0, 6.9)
		Cycle 7	68	0 (0.0) (0.0, 4.6)
		Cycle >= 8 and < 18	65	5 (6.3) (2.1, 14.2)
		Cycle >= 18	17	2 (2.5) (0.3, 8.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	13 (19.7) (10.9, 31.3)
		Cycle 1	66	0 (0.0) (0.0, 5.4)
		Cycle 2	66	0 (0.0) (0.0, 5.4)
		Cycle 3	64	1 (1.5) (0.0, 8.2)
		Cycle 4	61	1 (1.5) (0.0, 8.2)
		Cycle 5	55	1 (1.5) (0.0, 8.2)
		Cycle 6	53	1 (1.5) (0.0, 8.2)
		Cycle 7	51	0 (0.0) (0.0, 5.4)
		Cycle >= 8 and < 18	51	9 (13.6) (6.4, 24.3)
		Cycle >= 18	10	0 (0.0) (0.0, 5.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	16 (13.2)	(7.8, 20.6)
		Cycle 1	121	0 (0.0)	(0.0, 3.0)
		Cycle 2	120	1 (0.8)	(0.0, 4.5)
		Cycle 3	119	2 (1.7)	(0.2, 5.8)
		Cycle 4	115	1 (0.8)	(0.0, 4.5)
		Cycle 5	106	2 (1.7)	(0.2, 5.8)
		Cycle 6	103	4 (3.3)	(0.9, 8.2)
		Cycle 7	96	0 (0.0)	(0.0, 3.0)
		Cycle >= 8 and < 18	93	6 (5.0)	(1.8, 10.5)
		Cycle >= 18	25	2 (1.7)	(0.2, 5.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	11 (17.5)	(9.1, 29.1)
		Cycle 1	63	0 (0.0)	(0.0, 5.7)
		Cycle 2	61	1 (1.6)	(0.0, 8.5)
		Cycle 3	55	0 (0.0)	(0.0, 5.7)
		Cycle 4	54	1 (1.6)	(0.0, 8.5)
		Cycle 5	49	0 (0.0)	(0.0, 5.7)
		Cycle 6	49	0 (0.0)	(0.0, 5.7)
		Cycle 7	49	1 (1.6)	(0.0, 8.5)
		Cycle >= 8 and < 18	45	8 (12.7)	(5.6, 23.5)
		Cycle >= 18	10	0 (0.0)	(0.0, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	6 (11.8) (4.4, 23.9)
		Cycle 1	51	0 (0.0) (0.0, 7.0)
		Cycle 2	50	0 (0.0) (0.0, 7.0)
		Cycle 3	50	0 (0.0) (0.0, 7.0)
		Cycle 4	49	0 (0.0) (0.0, 7.0)
		Cycle 5	46	1 (2.0) (0.0, 10.4)
		Cycle 6	44	1 (2.0) (0.0, 10.4)
		Cycle 7	40	0 (0.0) (0.0, 7.0)
		Cycle >= 8 and < 18	40	3 (5.9) (1.2, 16.2)
		Cycle >= 18	10	1 (2.0) (0.0, 10.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	21 (15.8) (10.0, 23.1)
		Cycle 1	133	0 (0.0) (0.0, 2.7)
		Cycle 2	131	2 (1.5) (0.2, 5.3)
		Cycle 3	124	2 (1.5) (0.2, 5.3)
		Cycle 4	120	2 (1.5) (0.2, 5.3)
		Cycle 5	109	1 (0.8) (0.0, 4.1)
		Cycle 6	108	3 (2.3) (0.5, 6.5)
		Cycle 7	105	1 (0.8) (0.0, 4.1)
		Cycle >= 8 and < 18	98	11 (8.3) (4.2, 14.3)
		Cycle >= 18	25	1 (0.8) (0.0, 4.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

UE von besonderem Interesse – Interstitielle Lungenerkrankung (ILD) mit CTCAE-Grad < 3, Bewertung durch AC

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	21 (11.4)	(7.2, 16.9)
		Cycle 1	184	0 (0.0)	(0.0, 2.0)
		Cycle 2	181	2 (1.1)	(0.1, 3.9)
		Cycle 3	174	1 (0.5)	(0.0, 3.0)
		Cycle 4	169	1 (0.5)	(0.0, 3.0)
		Cycle 5	155	2 (1.1)	(0.1, 3.9)
		Cycle 6	152	4 (2.2)	(0.6, 5.5)
		Cycle 7	145	0 (0.0)	(0.0, 2.0)
		Cycle >= 8 and < 18	138	11 (6.0)	(3.0, 10.4)
		Cycle >= 18	35	2 (1.1)	(0.1, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	15 (10.7) (6.1, 17.1)
		Cycle 1	140	0 (0.0) (0.0, 2.6)
		Cycle 2	138	2 (1.4) (0.2, 5.1)
		Cycle 3	132	1 (0.7) (0.0, 3.9)
		Cycle 4	128	0 (0.0) (0.0, 2.6)
		Cycle 5	116	1 (0.7) (0.0, 3.9)
		Cycle 6	113	3 (2.1) (0.4, 6.1)
		Cycle 7	109	0 (0.0) (0.0, 2.6)
		Cycle >= 8 and < 18	103	8 (5.7) (2.5, 10.9)
		Cycle >= 18	24	1 (0.7) (0.0, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	6 (13.6) (5.2, 27.4)
		Cycle 1	44	0 (0.0) (0.0, 8.0)
		Cycle 2	43	0 (0.0) (0.0, 8.0)
		Cycle 3	42	0 (0.0) (0.0, 8.0)
		Cycle 4	41	1 (2.3) (0.1, 12.0)
		Cycle 5	39	1 (2.3) (0.1, 12.0)
		Cycle 6	39	1 (2.3) (0.1, 12.0)
		Cycle 7	36	0 (0.0) (0.0, 8.0)
		Cycle >= 8 and < 18	35	3 (6.8) (1.4, 18.7)
		Cycle >= 18	11	1 (2.3) (0.1, 12.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	11 (17.5) (9.1, 29.1)
		Cycle 1	63	0 (0.0) (0.0, 5.7)
		Cycle 2	61	0 (0.0) (0.0, 5.7)
		Cycle 3	58	0 (0.0) (0.0, 5.7)
		Cycle 4	58	1 (1.6) (0.0, 8.5)
		Cycle 5	55	1 (1.6) (0.0, 8.5)
		Cycle 6	55	2 (3.2) (0.4, 11.0)
		Cycle 7	53	0 (0.0) (0.0, 5.7)
		Cycle >= 8 and < 18	49	6 (9.5) (3.6, 19.6)
		Cycle >= 18	15	2 (3.2) (0.4, 11.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	3 (5.7) (1.2, 15.7)
		Cycle 1	53	0 (0.0) (0.0, 6.7)
		Cycle 2	53	0 (0.0) (0.0, 6.7)
		Cycle 3	52	0 (0.0) (0.0, 6.7)
		Cycle 4	49	0 (0.0) (0.0, 6.7)
		Cycle 5	44	0 (0.0) (0.0, 6.7)
		Cycle 6	42	2 (3.8) (0.5, 13.0)
		Cycle 7	40	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	1 (1.9) (0.0, 10.1)
		Cycle >= 18	11	0 (0.0) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	7 (10.3)	(4.2, 20.1)
		Cycle 1	68	0 (0.0)	(0.0, 5.3)
		Cycle 2	67	2 (2.9)	(0.4, 10.2)
		Cycle 3	64	1 (1.5)	(0.0, 7.9)
		Cycle 4	62	0 (0.0)	(0.0, 5.3)
		Cycle 5	56	1 (1.5)	(0.0, 7.9)
		Cycle 6	55	0 (0.0)	(0.0, 5.3)
		Cycle 7	52	0 (0.0)	(0.0, 5.3)
		Cycle >= 8 and < 18	50	4 (5.9)	(1.6, 14.4)
		Cycle >= 18	9	0 (0.0)	(0.0, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	16 (15.7)	(9.2, 24.2)
		Cycle 1	0 (0.0)	(0.0, 3.6)
		Cycle 2	1 (1.0)	(0.0, 5.3)
		Cycle 3	1 (1.0)	(0.0, 5.3)
		Cycle 4	1 (1.0)	(0.0, 5.3)
		Cycle 5	2 (2.0)	(0.2, 6.9)
		Cycle 6	4 (3.9)	(1.1, 9.7)
		Cycle 7	0 (0.0)	(0.0, 3.6)
		Cycle >= 8 and < 18	7 (6.9)	(2.8, 13.6)
		Cycle >= 18	2 (2.0)	(0.2, 6.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	5 (6.2)	(2.0, 13.8)
		Cycle 1	81	0 (0.0)	(0.0, 4.5)
		Cycle 2	79	1 (1.2)	(0.0, 6.7)
		Cycle 3	73	0 (0.0)	(0.0, 4.5)
		Cycle 4	71	0 (0.0)	(0.0, 4.5)
		Cycle 5	61	0 (0.0)	(0.0, 4.5)
		Cycle 6	59	0 (0.0)	(0.0, 4.5)
		Cycle 7	57	0 (0.0)	(0.0, 4.5)
		Cycle >= 8 and < 18	52	4 (4.9)	(1.4, 12.2)
		Cycle >= 18	12	0 (0.0)	(0.0, 4.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions < 5 cm (N=74)	Any TEAE	74	9 (12.2)	(5.7, 21.8)
	Cycle 1	74	0 (0.0)	(0.0, 4.9)
	Cycle 2	73	2 (2.7)	(0.3, 9.4)
	Cycle 3	71	1 (1.4)	(0.0, 7.3)
	Cycle 4	66	0 (0.0)	(0.0, 4.9)
	Cycle 5	61	1 (1.4)	(0.0, 7.3)
	Cycle 6	60	0 (0.0)	(0.0, 4.9)
	Cycle 7	59	0 (0.0)	(0.0, 4.9)
	Cycle >= 8 and < 18	54	5 (6.8)	(2.2, 15.1)
	Cycle >= 18	18	1 (1.4)	(0.0, 7.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

			Overall 5.4 mg/kg SAF (N=184)	
Subgroup	Time Period	N patients in cycle	n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=95)	Any TEAE	95	8 (8.4) (3.7, 15.9)
		Cycle 1	95	0 (0.0) (0.0, 3.8)
		Cycle 2	93	0 (0.0) (0.0, 3.8)
		Cycle 3	88	0 (0.0) (0.0, 3.8)
		Cycle 4	88	1 (1.1) (0.0, 5.7)
		Cycle 5	79	0 (0.0) (0.0, 3.8)
		Cycle 6	77	3 (3.2) (0.7, 9.0)
		Cycle 7	72	0 (0.0) (0.0, 3.8)
		Cycle >= 8 and < 18	70	4 (4.2) (1.2, 10.4)
		Cycle >= 18	13	0 (0.0) (0.0, 3.8)

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	19 (12.3)	(7.6, 18.6)
		Cycle 1	154	0 (0.0)	(0.0, 2.4)
		Cycle 2	152	2 (1.3)	(0.2, 4.6)
		Cycle 3	146	1 (0.6)	(0.0, 3.6)
		Cycle 4	141	1 (0.6)	(0.0, 3.6)
		Cycle 5	129	2 (1.3)	(0.2, 4.6)
		Cycle 6	127	3 (1.9)	(0.4, 5.6)
		Cycle 7	121	0 (0.0)	(0.0, 2.4)
		Cycle >= 8 and < 18	114	10 (6.5)	(3.2, 11.6)
		Cycle >= 18	33	2 (1.3)	(0.2, 4.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Any TEAE	28	2 (7.1) (0.9, 23.5)
		Cycle 1	28	0 (0.0) (0.0, 12.3)
		Cycle 2	27	0 (0.0) (0.0, 12.3)
		Cycle 3	26	0 (0.0) (0.0, 12.3)
		Cycle 4	26	0 (0.0) (0.0, 12.3)
		Cycle 5	24	0 (0.0) (0.0, 12.3)
		Cycle 6	23	1 (3.6) (0.1, 18.3)
		Cycle 7	22	0 (0.0) (0.0, 12.3)
		Cycle >= 8 and < 18	22	1 (3.6) (0.1, 18.3)
		Cycle >= 18	2	0 (0.0) (0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	11 (11.8)	(6.1, 20.2)
		Cycle 1	93	0 (0.0)	(0.0, 3.9)
		Cycle 2	92	1 (1.1)	(0.0, 5.8)
		Cycle 3	87	0 (0.0)	(0.0, 3.9)
		Cycle 4	84	0 (0.0)	(0.0, 3.9)
		Cycle 5	80	2 (2.2)	(0.3, 7.6)
		Cycle 6	78	2 (2.2)	(0.3, 7.6)
		Cycle 7	75	0 (0.0)	(0.0, 3.9)
		Cycle >= 8 and < 18	73	6 (6.5)	(2.4, 13.5)
		Cycle >= 18	12	1 (1.1)	(0.0, 5.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	10 (11.4)	(5.6, 19.9)
		Cycle 1	88	0 (0.0)	(0.0, 4.1)
		Cycle 2	86	1 (1.1)	(0.0, 6.2)
		Cycle 3	85	1 (1.1)	(0.0, 6.2)
		Cycle 4	84	1 (1.1)	(0.0, 6.2)
		Cycle 5	74	0 (0.0)	(0.0, 4.1)
		Cycle 6	73	2 (2.3)	(0.3, 8.0)
		Cycle 7	69	0 (0.0)	(0.0, 4.1)
		Cycle >= 8 and < 18	64	5 (5.7)	(1.9, 12.8)
		Cycle >= 18	23	1 (1.1)	(0.0, 6.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	7 (13.7)	(5.7, 26.3)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	1 (2.0)	(0.0, 10.4)
		Cycle 3	49	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	47	2 (3.9)	(0.5, 13.5)
		Cycle 6	46	1 (2.0)	(0.0, 10.4)
		Cycle 7	45	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	44	3 (5.9)	(1.2, 16.2)
		Cycle >= 18	8	1 (2.0)	(0.0, 10.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	13 (10.4)	(5.7, 17.1)
		Cycle 1	125	0 (0.0)	(0.0, 2.9)
		Cycle 2	123	1 (0.8)	(0.0, 4.4)
		Cycle 3	118	1 (0.8)	(0.0, 4.4)
		Cycle 4	114	1 (0.8)	(0.0, 4.4)
		Cycle 5	103	0 (0.0)	(0.0, 2.9)
		Cycle 6	101	3 (2.4)	(0.5, 6.9)
		Cycle 7	95	0 (0.0)	(0.0, 2.9)
		Cycle >= 8 and < 18	90	7 (5.6)	(2.3, 11.2)
		Cycle >= 18	27	1 (0.8)	(0.0, 4.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	12 (12.4)	(6.6, 20.6)
		Cycle 1	97	0 (0.0)	(0.0, 3.7)
		Cycle 2	96	1 (1.0)	(0.0, 5.6)
		Cycle 3	91	0 (0.0)	(0.0, 3.7)
		Cycle 4	88	0 (0.0)	(0.0, 3.7)
		Cycle 5	84	2 (2.1)	(0.3, 7.3)
		Cycle 6	82	2 (2.1)	(0.3, 7.3)
		Cycle 7	79	0 (0.0)	(0.0, 3.7)
		Cycle >= 8 and < 18	76	6 (6.2)	(2.3, 13.0)
		Cycle >= 18	13	2 (2.1)	(0.3, 7.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	9 (10.8) (5.1, 19.6)
		Cycle 1	83	0 (0.0) (0.0, 4.3)
		Cycle 2	81	1 (1.2) (0.0, 6.5)
		Cycle 3	80	1 (1.2) (0.0, 6.5)
		Cycle 4	79	1 (1.2) (0.0, 6.5)
		Cycle 5	69	0 (0.0) (0.0, 4.3)
		Cycle 6	68	2 (2.4) (0.3, 8.4)
		Cycle 7	64	0 (0.0) (0.0, 4.3)
		Cycle >= 8 and < 18	60	5 (6.0) (2.0, 13.5)
		Cycle >= 18	22	0 (0.0) (0.0, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Normal (N=90)			
	Any TEAE	90	7 (7.8)	(3.2, 15.4)
	Cycle 1	90	0 (0.0)	(0.0, 4.0)
	Cycle 2	89	1 (1.1)	(0.0, 6.0)
	Cycle 3	85	0 (0.0)	(0.0, 4.0)
	Cycle 4	85	0 (0.0)	(0.0, 4.0)
	Cycle 5	76	1 (1.1)	(0.0, 6.0)
	Cycle 6	73	0 (0.0)	(0.0, 4.0)
	Cycle 7	72	0 (0.0)	(0.0, 4.0)
	Cycle >= 8 and < 18	69	4 (4.4)	(1.2, 11.0)
	Cycle >= 18	17	1 (1.1)	(0.0, 6.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	7 (10.1) (4.2, 19.8)
		Cycle 1	69	0 (0.0) (0.0, 5.2)
		Cycle 2	68	0 (0.0) (0.0, 5.2)
		Cycle 3	66	0 (0.0) (0.0, 5.2)
		Cycle 4	63	0 (0.0) (0.0, 5.2)
		Cycle 5	59	1 (1.4) (0.0, 7.8)
		Cycle 6	59	2 (2.9) (0.4, 10.1)
		Cycle 7	56	0 (0.0) (0.0, 5.2)
		Cycle >= 8 and < 18	54	5 (7.2) (2.4, 16.1)
		Cycle >= 18	14	0 (0.0) (0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	7 (28.0) (12.1, 49.4)
		Cycle 1	25	0 (0.0) (0.0, 13.7)
		Cycle 2	24	1 (4.0) (0.1, 20.4)
		Cycle 3	23	1 (4.0) (0.1, 20.4)
		Cycle 4	21	1 (4.0) (0.1, 20.4)
		Cycle 5	20	0 (0.0) (0.0, 13.7)
		Cycle 6	20	2 (8.0) (1.0, 26.0)
		Cycle 7	17	0 (0.0) (0.0, 13.7)
		Cycle >= 8 and < 18	15	2 (8.0) (1.0, 26.0)
		Cycle >= 18	4	1 (4.0) (0.1, 20.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	15 (14.3)	(8.2, 22.5)
		Cycle 1	105	0 (0.0)	(0.0, 3.5)
		Cycle 2	104	1 (1.0)	(0.0, 5.2)
		Cycle 3	102	1 (1.0)	(0.0, 5.2)
		Cycle 4	98	1 (1.0)	(0.0, 5.2)
		Cycle 5	90	2 (1.9)	(0.2, 6.7)
		Cycle 6	89	2 (1.9)	(0.2, 6.7)
		Cycle 7	87	0 (0.0)	(0.0, 3.5)
		Cycle >= 8 and < 18	84	9 (8.6)	(4.0, 15.6)
		Cycle >= 18	22	1 (1.0)	(0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	6 (7.9) (3.0, 16.4)
		Cycle 1	76	0 (0.0) (0.0, 4.7)
		Cycle 2	74	1 (1.3) (0.0, 7.1)
		Cycle 3	69	0 (0.0) (0.0, 4.7)
		Cycle 4	68	0 (0.0) (0.0, 4.7)
		Cycle 5	63	0 (0.0) (0.0, 4.7)
		Cycle 6	61	2 (2.6) (0.3, 9.2)
		Cycle 7	56	0 (0.0) (0.0, 4.7)
		Cycle >= 8 and < 18	54	2 (2.6) (0.3, 9.2)
		Cycle >= 18	13	1 (1.3) (0.0, 7.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	4 (16.7) (4.7, 37.4)
		Cycle 1	24	0 (0.0) (0.0, 14.2)
		Cycle 2	23	0 (0.0) (0.0, 14.2)
		Cycle 3	22	0 (0.0) (0.0, 14.2)
		Cycle 4	22	0 (0.0) (0.0, 14.2)
		Cycle 5	19	1 (4.2) (0.1, 21.1)
		Cycle 6	18	1 (4.2) (0.1, 21.1)
		Cycle 7	18	0 (0.0) (0.0, 14.2)
		Cycle >= 8 and < 18	18	2 (8.3) (1.0, 27.0)
		Cycle >= 18	6	0 (0.0) (0.0, 14.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	17 (10.6)	(6.3, 16.5)
		Cycle 1	160	0 (0.0)	(0.0, 2.3)
		Cycle 2	158	2 (1.3)	(0.2, 4.4)
		Cycle 3	152	1 (0.6)	(0.0, 3.4)
		Cycle 4	147	1 (0.6)	(0.0, 3.4)
		Cycle 5	136	1 (0.6)	(0.0, 3.4)
		Cycle 6	134	3 (1.9)	(0.4, 5.4)
		Cycle 7	127	0 (0.0)	(0.0, 2.3)
		Cycle >= 8 and < 18	120	9 (5.6)	(2.6, 10.4)
		Cycle >= 18	29	2 (1.3)	(0.2, 4.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	8 (15.1)	(6.7, 27.6)
		Cycle 1	53	0 (0.0)	(0.0, 6.7)
		Cycle 2	52	1 (1.9)	(0.0, 10.1)
		Cycle 3	49	1 (1.9)	(0.0, 10.1)
		Cycle 4	48	0 (0.0)	(0.0, 6.7)
		Cycle 5	43	1 (1.9)	(0.0, 10.1)
		Cycle 6	42	1 (1.9)	(0.0, 10.1)
		Cycle 7	41	0 (0.0)	(0.0, 6.7)
		Cycle >= 8 and < 18	39	4 (7.5)	(2.1, 18.2)
		Cycle >= 18	8	1 (1.9)	(0.0, 10.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	13 (9.9)	(5.4, 16.4)
		Cycle 1	131	0 (0.0)	(0.0, 2.8)
		Cycle 2	129	1 (0.8)	(0.0, 4.2)
		Cycle 3	125	0 (0.0)	(0.0, 2.8)
		Cycle 4	121	1 (0.8)	(0.0, 4.2)
		Cycle 5	112	1 (0.8)	(0.0, 4.2)
		Cycle 6	110	3 (2.3)	(0.5, 6.5)
		Cycle 7	104	0 (0.0)	(0.0, 2.8)
		Cycle >= 8 and < 18	99	7 (5.3)	(2.2, 10.7)
		Cycle >= 18	27	1 (0.8)	(0.0, 4.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	19 (11.2)	(6.9, 17.0)
		Cycle 1	169	0 (0.0)	(0.0, 2.2)
		Cycle 2	166	2 (1.2)	(0.1, 4.2)
		Cycle 3	159	1 (0.6)	(0.0, 3.3)
		Cycle 4	154	1 (0.6)	(0.0, 3.3)
		Cycle 5	142	2 (1.2)	(0.1, 4.2)
		Cycle 6	139	4 (2.4)	(0.6, 5.9)
		Cycle 7	132	0 (0.0)	(0.0, 2.2)
		Cycle >= 8 and < 18	125	9 (5.3)	(2.5, 9.9)
		Cycle >= 18	31	2 (1.2)	(0.1, 4.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	2 (13.3)	(1.7, 40.5)
		Cycle 1	15	0 (0.0)	(0.0, 21.8)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	2 (13.3)	(1.7, 40.5)
		Cycle >= 18	4	0 (0.0)	(0.0, 21.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	5 (8.9) (3.0, 19.6)
		Cycle 1	56	0 (0.0) (0.0, 6.4)
		Cycle 2	55	1 (1.8) (0.0, 9.6)
		Cycle 3	54	0 (0.0) (0.0, 6.4)
		Cycle 4	53	0 (0.0) (0.0, 6.4)
		Cycle 5	49	0 (0.0) (0.0, 6.4)
		Cycle 6	48	0 (0.0) (0.0, 6.4)
		Cycle 7	48	0 (0.0) (0.0, 6.4)
		Cycle >= 8 and < 18	45	3 (5.4) (1.1, 14.9)
		Cycle >= 18	16	1 (1.8) (0.0, 9.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	16 (12.5)	(7.3, 19.5)
		Cycle 1	128	0 (0.0)	(0.0, 2.8)
		Cycle 2	126	1 (0.8)	(0.0, 4.3)
		Cycle 3	120	1 (0.8)	(0.0, 4.3)
		Cycle 4	116	1 (0.8)	(0.0, 4.3)
		Cycle 5	106	2 (1.6)	(0.2, 5.5)
		Cycle 6	104	4 (3.1)	(0.9, 7.8)
		Cycle 7	97	0 (0.0)	(0.0, 2.8)
		Cycle >= 8 and < 18	93	8 (6.3)	(2.7, 11.9)
		Cycle >= 18	19	1 (0.8)	(0.0, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
0-Prior treatment lines	< 3 lines (N=17)	Any TEAE	17	1 (5.9) (0.1, 28.7)
		Cycle 1	17	0 (0.0) (0.0, 19.5)
		Cycle 2	17	0 (0.0) (0.0, 19.5)
		Cycle 3	17	0 (0.0) (0.0, 19.5)
		Cycle 4	17	0 (0.0) (0.0, 19.5)
		Cycle 5	17	0 (0.0) (0.0, 19.5)
		Cycle 6	16	0 (0.0) (0.0, 19.5)
		Cycle 7	16	0 (0.0) (0.0, 19.5)
		Cycle >= 8 and < 18	16	0 (0.0) (0.0, 19.5)
		Cycle >= 18	6	1 (5.9) (0.1, 28.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
0-Prior treatment lines	>= 3 lines (N=167)	Any TEAE	167	20 (12.0) (7.5, 17.9)
		Cycle 1	167	0 (0.0) (0.0, 2.2)
		Cycle 2	164	2 (1.2) (0.1, 4.3)
		Cycle 3	157	1 (0.6) (0.0, 3.3)
		Cycle 4	152	1 (0.6) (0.0, 3.3)
		Cycle 5	138	2 (1.2) (0.1, 4.3)
		Cycle 6	136	4 (2.4) (0.7, 6.0)
		Cycle 7	129	0 (0.0) (0.0, 2.2)
		Cycle >= 8 and < 18	122	11 (6.6) (3.3, 11.5)
		Cycle >= 18	29	1 (0.6) (0.0, 3.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	9 (11.4) (5.3, 20.5)
		Cycle 1	79	0 (0.0) (0.0, 4.6)
		Cycle 2	78	2 (2.5) (0.3, 8.8)
		Cycle 3	75	1 (1.3) (0.0, 6.9)
		Cycle 4	73	0 (0.0) (0.0, 4.6)
		Cycle 5	70	1 (1.3) (0.0, 6.9)
		Cycle 6	69	1 (1.3) (0.0, 6.9)
		Cycle 7	68	0 (0.0) (0.0, 4.6)
		Cycle >= 8 and < 18	65	4 (5.1) (1.4, 12.5)
		Cycle >= 18	17	2 (2.5) (0.3, 8.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	10 (15.2) (7.5, 26.1)
		Cycle 1	66	0 (0.0) (0.0, 5.4)
		Cycle 2	66	0 (0.0) (0.0, 5.4)
		Cycle 3	64	0 (0.0) (0.0, 5.4)
		Cycle 4	61	1 (1.5) (0.0, 8.2)
		Cycle 5	55	1 (1.5) (0.0, 8.2)
		Cycle 6	53	1 (1.5) (0.0, 8.2)
		Cycle 7	51	0 (0.0) (0.0, 5.4)
		Cycle >= 8 and < 18	51	7 (10.6) (4.4, 20.6)
		Cycle >= 18	10	0 (0.0) (0.0, 5.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	14 (11.6)	(6.5, 18.7)
		Cycle 1	121	0 (0.0)	(0.0, 3.0)
		Cycle 2	120	1 (0.8)	(0.0, 4.5)
		Cycle 3	119	1 (0.8)	(0.0, 4.5)
		Cycle 4	115	1 (0.8)	(0.0, 4.5)
		Cycle 5	106	2 (1.7)	(0.2, 5.8)
		Cycle 6	103	4 (3.3)	(0.9, 8.2)
		Cycle 7	96	0 (0.0)	(0.0, 3.0)
		Cycle >= 8 and < 18	93	5 (4.1)	(1.4, 9.4)
		Cycle >= 18	25	2 (1.7)	(0.2, 5.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	7 (11.1)	(4.6, 21.6)
		Cycle 1	63	0 (0.0)	(0.0, 5.7)
		Cycle 2	61	1 (1.6)	(0.0, 8.5)
		Cycle 3	55	0 (0.0)	(0.0, 5.7)
		Cycle 4	54	0 (0.0)	(0.0, 5.7)
		Cycle 5	49	0 (0.0)	(0.0, 5.7)
		Cycle 6	49	0 (0.0)	(0.0, 5.7)
		Cycle 7	49	0 (0.0)	(0.0, 5.7)
		Cycle >= 8 and < 18	45	6 (9.5)	(3.6, 19.6)
		Cycle >= 18	10	0 (0.0)	(0.0, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	6 (11.8) (4.4, 23.9)
		Cycle 1	51	0 (0.0) (0.0, 7.0)
		Cycle 2	50	0 (0.0) (0.0, 7.0)
		Cycle 3	50	0 (0.0) (0.0, 7.0)
		Cycle 4	49	0 (0.0) (0.0, 7.0)
		Cycle 5	46	1 (2.0) (0.0, 10.4)
		Cycle 6	44	1 (2.0) (0.0, 10.4)
		Cycle 7	40	0 (0.0) (0.0, 7.0)
		Cycle >= 8 and < 18	40	3 (5.9) (1.2, 16.2)
		Cycle >= 18	10	1 (2.0) (0.0, 10.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event
Source Data: adam.adae

Table T2ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	15 (11.3)	(6.5, 17.9)
		Cycle 1	133	0 (0.0)	(0.0, 2.7)
		Cycle 2	131	2 (1.5)	(0.2, 5.3)
		Cycle 3	124	1 (0.8)	(0.0, 4.1)
		Cycle 4	120	1 (0.8)	(0.0, 4.1)
		Cycle 5	109	1 (0.8)	(0.0, 4.1)
		Cycle 6	108	3 (2.3)	(0.5, 6.5)
		Cycle 7	105	0 (0.0)	(0.0, 2.7)
		Cycle >= 8 and < 18	98	8 (6.0)	(2.6, 11.5)
		Cycle >= 18	25	1 (0.8)	(0.0, 4.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

3. Datenschnitt DESTINY-Breast01 vom 08. Juni 2020

Gesamtüberleben (OS)

Tabelle 14: Ergebnisse für den Endpunkt Gesamtüberleben (OS) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01	Trastuzumab-Deruxtecan N=184 (ITT-Population)	
	n ^a /N (%)	Median (Monate) [95 %-KI]
Gesamtüberleben (OS)	65 (35,3)	24,6 [23,1; NE]
	Kaplan-Meier-Schätzer [95 %-KI]	
zu Monat 6	93,9 [89,3; 96,6]	
zu Monat 12	85,4 [79,3; 89,8]	
Zu Monat 24	52,6 [41,3; 62,7]	
3. Datenschnitt: 08.06.2020		
a: Ereignis bezieht sich auf Tod jeglicher Ursache.		
Alle Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

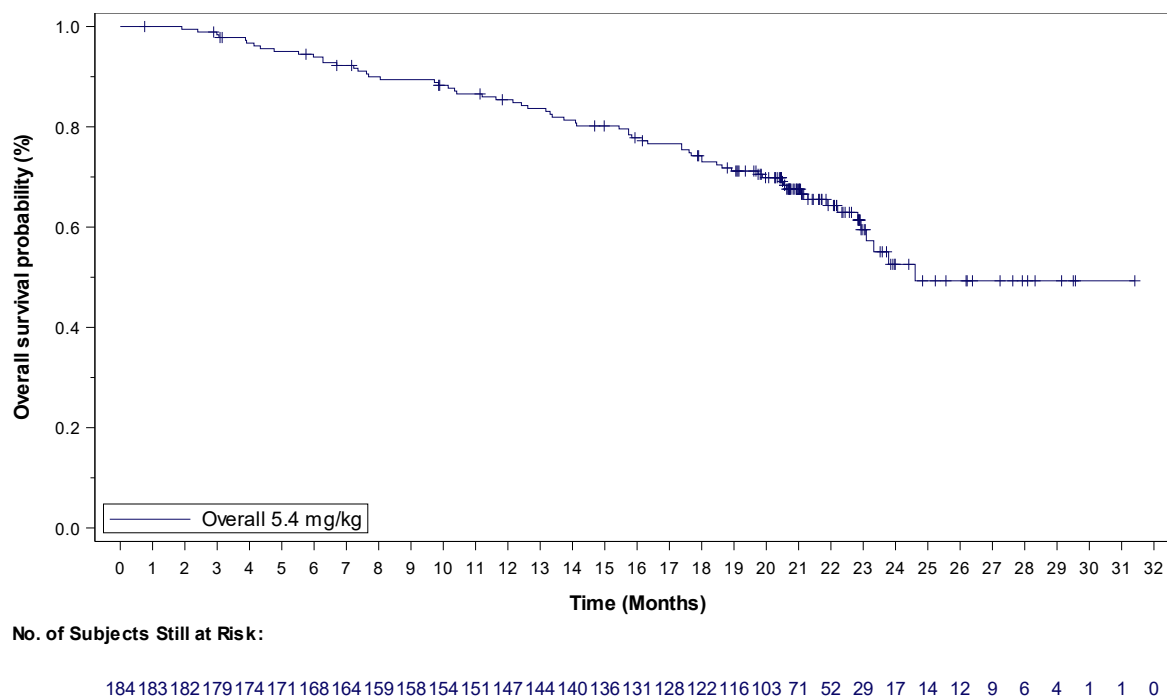


Abbildung 5: Kaplan-Meier-Kurve für den Endpunkt Gesamtüberleben (OS) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel (ITT-Population, 3. Datenschnitt: 08.06.2020)

Progressionsfreies Überleben (PFS)

Tabelle 15: Ergebnisse für den Endpunkt Progressionsfreies Überleben (PFS) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01	Trastuzumab-Deruxtecan (ITT-Population)	
	n ^a /N (%)	Median (Monate) [95 %-KI]
Progressionsfreies Überleben (PFS)	70/184 (38,0)	19,4 [14,1; NE]
	Kaplan-Meier-Schätzer (%) [95 %-KI]	
zu Monat 6	80,4 [73,4; 85,7]	
zu Monat 12	65,8 [57,5; 72,8]	
Zu Monat 24	42,3 [29,9; 54,1]	
3. Datenschnitt: 08.06.2020		
a: Patienten mit Krankheitsprogression oder Tod jeglicher Ursache.		
Alle Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

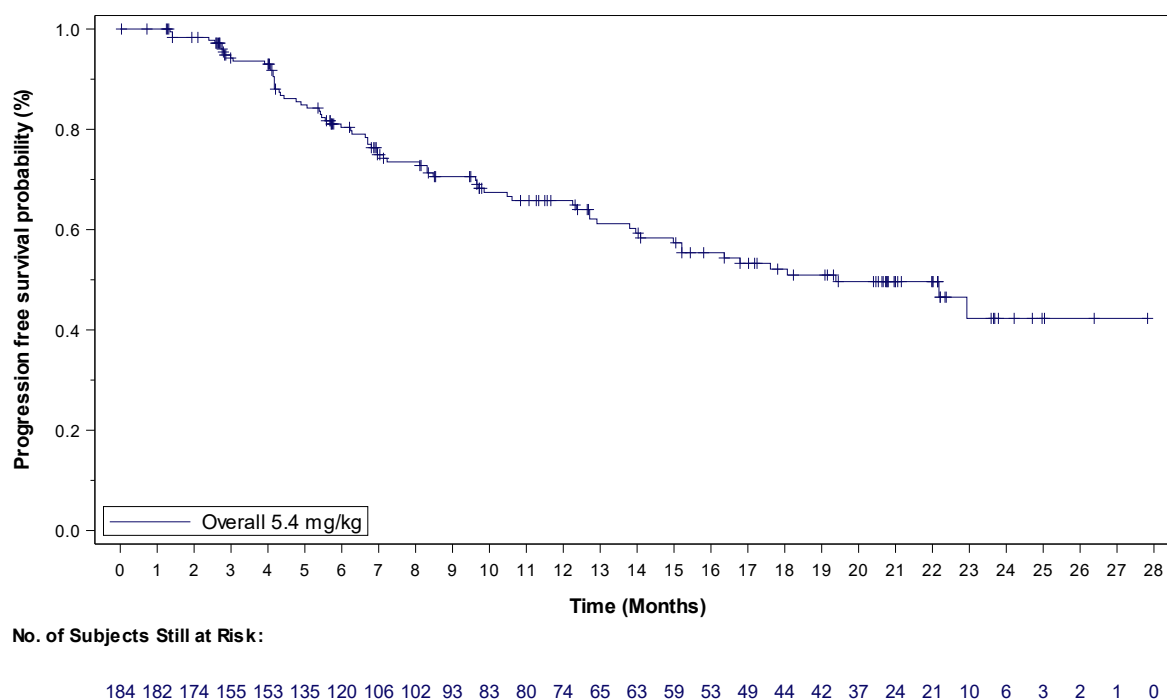


Abbildung 6: Kaplan-Meier-Kurve für den Endpunkt Progressionsfreies Überleben (PFS) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel (ITT-Population, 3. Datenschnitt: 08.06.2020)

Tumoransprechen

Gesamtansprechrage (ORR)

Tabelle 16: Ergebnisse für den Endpunkt Gesamtansprechrage (ORR) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01	Trastuzumab-Deruxtecán N=184 (ITT-Population)	
	n/N (%)	95 %-KI
Gesamtansprechrage (ORR)	113 (61,4)	[54,0; 68,5]
	Beurteilung durch ICR, n (%)	
Vollständiges Ansprechen (CR)	12 (6,5)	
Partielles Ansprechen (PR)	101 (54,9)	
Stabile Erkrankung (SD)	66 (35,9)	
Krankheitsprogression (PD)	3 (1,6)	
nicht auswertbar	2 (1,1)	
3. Datenschnitt: 08.06.2020		
Alle Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

Beste prozentuale Änderung des Tumordurchmessers (BPC)

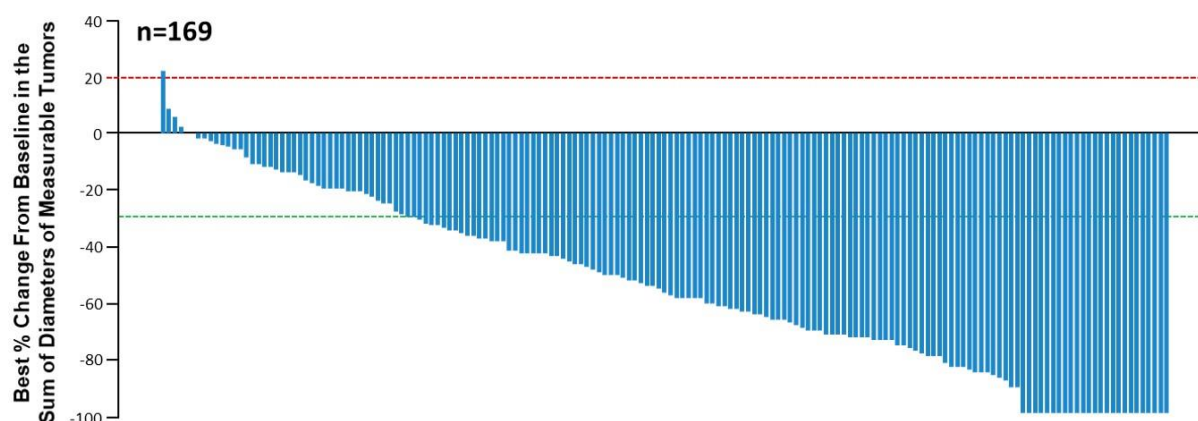


Abbildung 7: Waterfallplot für den Endpunkt Beste prozentuale Änderung des Tumordurchmessers (BPC) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel (ITT-Population, 3. Datenschnitt: 08.06.2020)

Tabelle 17: Ergebnisse für den Endpunkt Beste prozentuale Änderung des Tumordurchmessers (BPC) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01	Trastuzumab-Deruxtecan N=184 (ITT-Population)	
	Mean (SD)	Median (Min; Max) [95 %-KI]
Beste prozentuale Änderung des Tumordurchmessers (BPC) (n=169)	-54,4 % (31,22)	-57,0 % (-100; 22) [-64,0; - 48,0]
3. Datenschnitt: 08.06.2020 Alle Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

Rate der Krankheitskontrolle (DCR)

Tabelle 18: Ergebnisse für den Endpunkt Rate der Krankheitskontrolle (DCR) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01	Trastuzumab-Deruxtecan (ITT-Population)	
	n ^a /N	% [95 %-KI]
Rate der Krankheitskontrolle (DCR)	179/184	97,3 [93,8; 99,1]
3. Datenschnitt: 08.06.2020 a: Patienten mit einem besten Gesamtansprechen der Kategorie CR, PR oder SD. Alle Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

Zeit bis zum Ansprechen (TTR)

Tabelle 19: Ergebnisse für den Endpunkt Zeit bis zum Ansprechen (TTR) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01	Trastuzumab-Deruxtecan (ITT-Population)	
	n ^a /N (%)	Median (Monate) [95 %-KI]
Zeit bis zum Ansprechen (TTR)	112 ^b /184 (60,9)	1,6 [1,4; 2,6]
3. Datenschnitt: 08.06.2020 a: Patienten mit einem besten Gesamtansprechen der Kategorie CR oder PR. b: Ein Patient hatte vor dem Zeitpunkt des 3. Datenschnitts ein bestes Gesamtansprechen der Kategorie PR, das erst nach dem Datenschnitt bestätigt wurde. Der Patient wurde in der Analyse nicht berücksichtigt. Alle Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

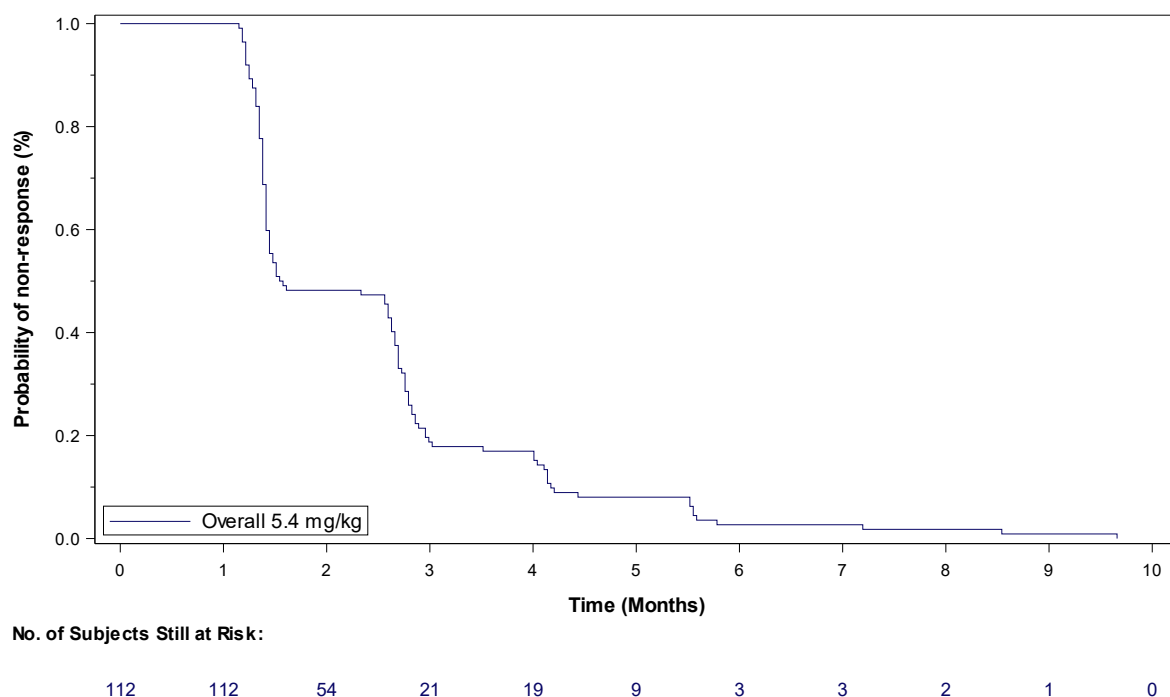


Abbildung 8: Kaplan-Meier-Kurve für den Endpunkt TTR aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel (3. Datenschnitt: 08.06.2020)

Dauer des Ansprechens (DoR)

Tabelle 20: Ergebnisse für den Endpunkt Dauer des Ansprechens (DoR) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01	Trastuzumab-Deruxtecan N=184 (ITT-Population)	
	n ^a (%)	Median (Monate) [95 %-KI]
Dauer des Ansprechens (DoR)	112 ^b (60,9)	20,8 [15,0; NE]
	Kaplan-Meier-Schätzer % [95 %-KI]	
zu Monat 6	81,5 [72,2; 88,0]	
zu Monat 12	65,7 [54,7; 74,6]	
Zu Monat 24	NE [NE; NE]	
3. Datenschnitt: 08.06.2020		
a: Patienten mit einem besten Gesamtansprechen der Kategorie CR oder PR.		
b: Ein Patient hatte vor dem Zeitpunkt des 3. Datenschnitts ein bestes Gesamtansprechen der Kategorie PR, das erst nach dem Datenschnitt bestätigt wurde. Der Patient wurde in der Analyse nicht berücksichtigt.		
Alle Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

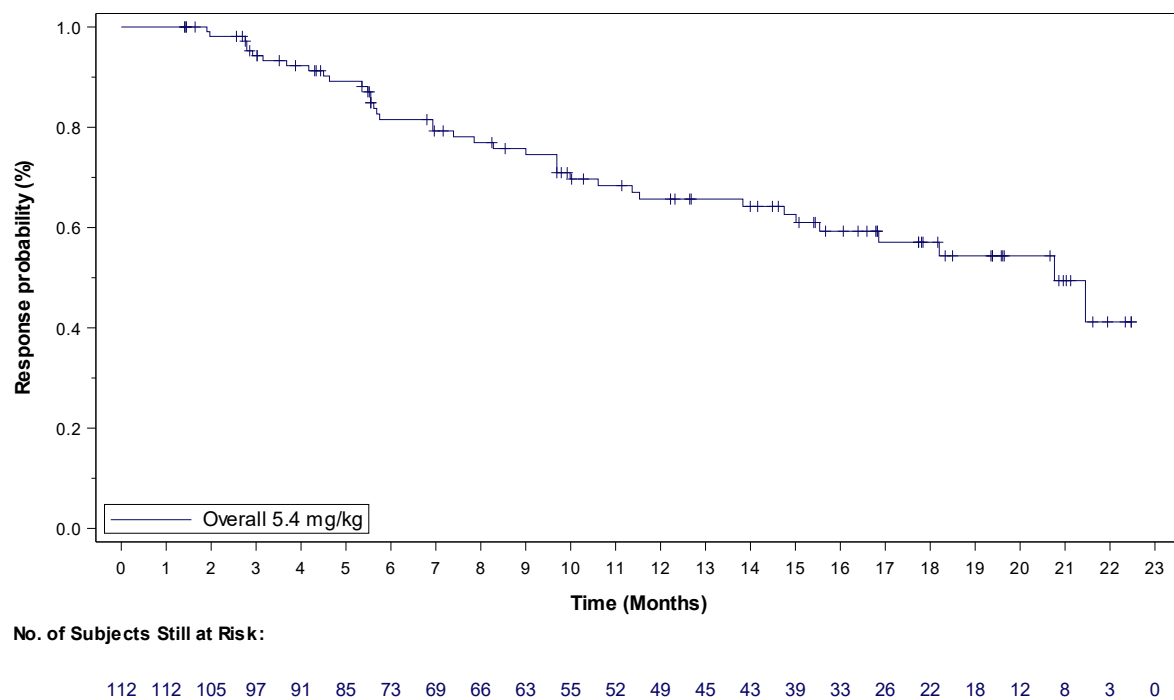


Abbildung 9: Kaplan-Meier-Kurve für den Endpunkt DoR aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel (3. Datenschnitt: 08.06.2020)

Sicherheit

Gesamtrate UE

Tabelle 21: Ergebnisse für die Endpunkte der UE Gesamtraten aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01	Trastuzumab-Deruxtecan N=184 (Safety-Population), n (%) [95 %-KI]									
	Zyklus 1	Zyklus 2	Zyklus 3	Zyklus 4	Zyklus 5	Zyklus 6	Zyklus 7	Zyklus ≥ 8 bis 18	Zyklus ≥ 18	insgesamt
Gesamtrate UE	173 (94,0) [89,6; 97,0]	133 (72,3) [65,2; 78,6]	115 (62,5) [55,1; 69,5]	108 (58,7) [51,2; 65,9]	93 (50,5) [43,1; 58,0]	83 (45,1) [37,8; 52,6]	88 (47,8) [40,4; 55,3]	124 (67,4) [60,1; 74,1]	69 (37,5) [30,5; 44,9]	183 (99,5) [97,0; 100,0]
Gesamtrate SUE	8 (4,3) [1,9; 8,4]	9 (4,9) [2,3; 9,1]	6 (3,3) [1,2; 7,0]	7 (3,8) [1,5; 7,7]	5 (2,7) [0,9; 6,2]	2 (1,1) [0,1; 3,9]	4 (2,2) [0,6; 5,5]	17 (9,2) [5,5; 14,4]	9 (4,9) [2,3; 9,1]	50 (27,2) [20,9; 34,2]
Gesamtrate UE mit CTCAE-Grad <3	171 (92,9) [88,2; 96,2]	130 (70,7) [63,5; 77,1]	114 (62,0) [54,5; 69,0]	102 (55,4) [47,9; 62,7]	91 (49,5) [42,0; 56,9]	79 (42,9) [35,7; 50,4]	85 (46,2) [38,8; 53,7]	121 (65,8) [58,4; 72,6]	69 (37,5) [30,5; 44,9]	183 (99,5) [97,0; 100,0]
Gesamtrate UE mit CTCAE-Grad ≥ 3	37 (20,1) [14,6; 26,6]	27 (14,7) [9,9; 20,6]	14 (7,6) [4,2; 12,4]	18 (9,8) [5,9; 15,0]	10 (5,4) [2,6; 9,8]	8 (4,3) [1,9; 8,4]	14 (7,6) [4,2; 12,4]	43 (23,4) [17,5; 30,2]	25 (13,6) [9,0; 19,4]	113 (61,4) [54,0; 68,5]
Gesamtrate UE, die zum Therapieabbruch führten	4 (2,2) [0,6; 5,5]	2 (1,1) [0,1; 3,9]	1 (0,5) [0,0; 3,0]	1 (0,5) [0,0; 3,0]	0 (0,0) [0,0; 2,0]	3 (1,6) [0,3; 4,7]	3 (1,6) [0,3; 4,7]	13 (7,1) [3,8; 11,8]	8 (4,3) [1,9; 8,4]	34 (18,5) [13,1; 24,9]
Gesamtrate UE, die zum Tod führten	0 (0,0) [0,0; 2,0]	0 (0,0) [0,0; 2,0]	2 (1,1) [0,1; 3,9]	1 (0,5) [0,0; 3,0]	2 (1,1) [0,1; 3,9]	0 (0,0) [0,0; 2,0]	1 (0,5) [0,0; 3,0]	2 (1,1) [0,1; 3,9]	1 (0,5) [0,0; 3,0]	9 (4,9) [2,3; 9,1]
3. Datenschnitt: 08.06.2020 Alle Abkürzungen werden im Abkürzungsverzeichnis erläutert.										

UE nach SOC und PT, die bei mindestens 10 Patienten und mindestens 1 % der Patienten in einem Studienarm aufgetreten sind

Tabelle 22: Ergebnisse für den Endpunkt UE (unabhängig vom Schweregrad) nach SOC und PT (≥ 10 Patienten und mindestens 1 % der Patienten) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01 SOC PT	Trastuzumab-Deruxtecan	
	n/N	% [95 %-KI]
Jegliche UE	183/184	99,5 [97,0; 100,0]
Erkrankungen des Gastrointestinaltrakts	173/184	94,0 [89,6; 97,0]
<i>Übelkeit</i>	143/184	77,7 [71,0; 83,5]
<i>Erbrechen</i>	87/184	47,3 [39,9; 54,8]
<i>Obstipation</i>	65/184	35,3 [28,4; 42,7]
<i>Diarrhö</i>	57/184	31,0 [24,4; 38,2]
<i>Dyspepsie</i>	29/184	15,8 [10,8; 21,8]
<i>Stomatitis</i>	28/184	15,2 [10,4; 21,2]
<i>Abdominalschmerz</i>	22/184	12,0 [7,6; 17,5]
<i>Gastrooesophageale Refluxerkrankung</i>	18/184	9,8 [5,9; 15,0]
<i>Schmerzen Oberbauch</i>	16/184	8,7 [5,1; 13,7]
<i>Haemorrhoiden</i>	11/184	6,0 [3,0; 10,4]
Allgemeine Erkrankungen und Beschwerden am Verabreichungsort	138/184	75,0 [68,1; 81,1]
<i>Ermüdung</i>	92/184	50,0 [42,6; 57,4]
<i>Asthenie</i>	26/184	14,1 [9,4; 20,0]
<i>Ödem peripher</i>	17/184	9,2 [5,5; 14,4]
<i>Schleimhautentzündung</i>	16/184	8,7 [5,1; 13,7]
<i>Fieber</i>	16/184	8,7 [5,1; 13,7]
<i>Grippeähnliche Erkrankung</i>	12/184	6,5 [3,4; 11,1]
Erkrankungen der Haut und des Unterhautgewebes	115/184	62,5 [55,1; 69,5]
<i>Alopezie</i>	89/184	48,4 [41,0; 55,8]
<i>Ausschlag</i>	18/184	9,8 [5,9; 15,0]
<i>Trockene Haut</i>	10/184	5,4 [2,6; 9,8]
<i>Nagelerkrankung</i>	10/184	5,4 [2,6; 9,8]
Untersuchungen	106/184	57,6 [50,1; 64,8]
<i>Neutrophilenzahl erniedrigt</i>	41/184	22,3 [16,5; 29,0]
<i>Leukozytenzahl erniedrigt</i>	35/184	19,0 [13,6; 25,4]

Studie DESTINY-Breast01 SOC PT	Trastuzumab-Deruxtecan	
	n/N	% [95 %-KI]
<i>Aspartataminotransferase erhöht</i>	31/184	16,8 [11,7; 23,1]
<i>Thrombozytenzahl vermindert</i>	29/184	15,8 [10,8; 21,8]
<i>Alaninaminotransferase erhöht</i>	19/184	10,3 [6,3; 15,7]
<i>Lymphozytenzahl erniedrigt</i>	19/184	10,3 [6,3; 15,7]
<i>Bilirubin im Blut erhöht</i>	15/184	8,2 [4,6; 13,1]
<i>Gewicht erniedrigt</i>	15/184	8,2 [4,6; 13,1]
<i>Alkalische Phosphatase im Blut erhöht</i>	11/184	6,0 [3,0; 10,4]
<i>Elektrokardiogramm QT verlängert</i>	11/184	6,0 [3,0; 10,4]
Erkrankungen der Atemwege, des Brustraums und Mediastinums	104/184	56,5 [49,0; 63,8]
<i>Husten</i>	41/184	22,3 [16,5; 29,0]
<i>Dyspnö</i>	30/184	16,3 [11,3; 22,5]
<i>Epistaxis</i>	25/184	13,6 [9,0; 19,4]
<i>Pneumonitis</i>	16/184	8,7 [5,1; 13,7]
<i>Interstitielle Lungenerkrankung</i>	11/184	6,0 [3,0; 10,4]
Infektionen und parasitäre Erkrankungen	98/184	53,3 [45,8; 60,6]
<i>Infektion der oberen Atemwege</i>	24/184	13,0 [8,5; 18,8]
<i>Nasopharyngitis</i>	20/184	10,9 [6,8; 16,3]
<i>Harnwegsinfektion</i>	19/184	10,3 [6,3; 15,7]
<i>Pneumonie</i>	10/184	5,4 [2,6; 9,8]
Erkrankungen des Nervensystems	89/184	48,4 [41,0; 55,8]
<i>Kopfschmerzen</i>	38/184	20,7 [15,0; 27,2]
<i>Schwindelgefühl</i>	18/184	9,8 [5,9; 15,0]
<i>Periphere sensorische Neuropathie</i>	15/184	8,2 [4,6; 13,1]
<i>Geschmacksstörung</i>	13/184	7,1 [3,8; 11,8]
<i>Periphere Neuropathie</i>	12/184	6,5 [3,4; 11,1]
Stoffwechsel- und Ernährungsstörungen	83/184	45,1 [37,8; 52,6]
<i>Appetit vermindert</i>	59/184	32,1 [25,4; 39,3]

Studie DESTINY-Breast01 SOC PT	Trastuzumab-Deruxtecan	
	n/N	% [95 %-KI]
<i>Hypokaliämie</i>	22/184	12,0 [7,6; 17,5]
Erkrankungen des Blutes und des Lymphsystems	78/184	42,4 [35,2; 49,9]
<i>Anämie</i>	55/184	29,9 [23,4; 37,1]
<i>Neutropenie</i>	27/184	14,7 [9,9; 20,6]
<i>Thrombozytopenie</i>	12/184	6,5 [3,4; 11,1]
<i>Lymphopenie</i>	11/184	6,0 [3,0; 10,4]
Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen	64/184	34,8 [27,9; 42,1]
<i>Arthralgie</i>	18/184	9,8 [5,9; 15,0]
<i>Rückenschmerzen</i>	18/184	9,8 [5,9; 15,0]
<i>Myalgie</i>	15/184	8,2 [4,6; 13,1]
<i>Muskelspasmen</i>	14/184	7,6 [4,2; 12,4]
Augenerkrankungen	61/184	33,2 [26,4; 40,5]
<i>Trockenes Auge</i>	21/184	11,4 [7,2; 16,9]
Psychiatrische Erkrankungen	27/184	14,7 [9,9; 20,6]
<i>Schlaflosigkeit</i>	13/184	7,1 [3,8; 11,8]
<i>Angst</i>	12/184	6,5 [3,4; 11,1]
Gefäßerkrankungen	26/184	14,1 [9,4; 20,0]
Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen	23/184	12,5 [8,1; 18,2]
Herzerkrankungen	18/184	9,8 [5,9; 15,0]
Erkrankungen des Ohrs und des Labyrinths	18/184	9,8 [5,9; 15,0]
Erkrankungen der Nieren und Harnwege	16/184	8,7 [5,1; 13,7]
Erkrankungen der Geschlechtsorgane und der Brustdrüse	11/184	6,0 [3,0; 10,4]
3. Datenschnitt: 08.06.2020 Alle Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

SUE nach SOC und PT, die bei mindestens 5 % der Patienten aufgetreten sind

Tabelle 23: Ergebnisse für den Endpunkt SUE nach SOC und PT (≥ 5 % der Patienten) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01 SOC PT	Trastuzumab-Deruxtecan	
	n/N	% [95 %-KI]
Infektionen und parasitäre Erkrankungen	18/184	9,8 [5,9; 15,0]
Erkrankungen der Atemwege, des Brustraums und Mediastinums	14/184	7,6 [4,2; 12,4]
Erkrankungen des Gastrointestinaltrakts	13/184	7,1 [3,8; 11,8]
3. Datenschnitt: 08.06.2020 Alle Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

UE mit CTCAE-Grad ≥ 3 nach SOC und PT, die bei mindestens 5 % der Patienten aufgetreten sind

Tabelle 24: Ergebnisse für den Endpunkt UE mit CTCAE-Grad ≥ 3 nach SOC und PT (≥ 5 % der Patienten) aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01 SOC PT	Trastuzumab-Deruxtecan	
	n/N	% [95 %-KI]
Untersuchungen	47/184	25,5 [19,4; 32,5]
<i>Neutrophilenzahl erniedrigt</i>	24/184	13,0 [8,5; 18,8]
<i>Leukozytenzahl erniedrigt</i>	12/184	6,5 [3,4; 11,1]
Erkrankungen des Blutes und des Lymphsystems	34/184	18,5 [13,1; 24,9]
<i>Neutropenie</i>	18/184	9,8 [5,9; 15,0]
<i>Anämie</i>	16/184	8,7 [5,1; 13,7]
Erkrankungen des Gastrointestinaltrakts	30/184	16,3 [11,3; 22,5]
<i>Übelkeit</i>	14/184	7,6 [4,2; 12,4]
Allgemeine Erkrankungen und Beschwerden am Verabreichungsort	16/184	8,7 [5,1; 13,7]
<i>Ermüdung</i>	13/184	7,1 [3,8; 11,8]
Infektionen und parasitäre Erkrankungen	16/184	8,7 [5,1; 13,7]
Stoffwechsel- und Ernährungsstörungen	16/184	8,7 [5,1; 13,7]
Erkrankungen der Atemwege, des Brustraums und Mediastinums	14/184	7,6 [4,2; 12,4]

Studie DESTINY-Breast01 SOC PT	Trastuzumab-Deruxtecan	
	n/N	% [95 %-KI]
3. Datenschnitt: 08.06.2020 Alle Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

UE nach SOC und PT, die zum Therapieabbruch führten

Tabelle 25: Ergebnisse für den Endpunkt UE, die zum Therapieabbruch führten nach SOC und PT aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01 SOC PT	Trastuzumab-Deruxtecan	
	n/N	% [95 %-KI]
Erkrankungen der Atemwege, des Brustraums und Mediastinums	23/184	12,5 [8,1; 18,2]
<i>Pneumonitis</i>	14/184	7,6 [4,2; 12,4]
<i>Interstitielle Lungenerkrankung</i>	6/184	3,3 [1,2; 7,0]
<i>Alveolitis</i>	1/184	0,5 [0,0; 3,0]
<i>Dyspnö</i>	1/184	0,5 [0,0; 3,0]
<i>Hypoxie</i>	1/184	0,5 [0,0; 3,0]
<i>Organisierende Pneumonie</i>	1/184	0,5 [0,0; 3,0]
Untersuchungen	3/184	1,6 [0,3; 4,7]
<i>Thrombozytenzahl vermindert</i>	2/184	1,1 [0,1; 3,9]
<i>Gamma-Glutamyltransferase erhöht</i>	1/184	0,5 [0,0; 3,0]
<i>Neutrophilenzahl erniedrigt</i>	1/184	0,5 [0,0; 3,0]
<i>Leukozytenzahl erniedrigt</i>	1/184	0,5 [0,0; 3,0]
Infektionen und parasitäre Erkrankungen	2/184	1,1 [0,1; 3,9]
<i>Akute Hepatitis B</i>	1/184	0,5 [0,0; 3,0]
<i>Pneumonie</i>	1/184	0,5 [0,0; 3,0]
Erkrankungen des Blutes und des Lymphsystems	1/184	0,5 [0,0; 3,0]
<i>Thrombozytopenie</i>	1/184	0,5 [0,0; 3,0]
Herzerkrankungen	1/184	0,5 [0,0; 3,0]
<i>Stauungsinsuffizienz</i>	1/184	0,5 [0,0; 3,0]
Erkrankungen des Gastrointestinaltrakts	1/184	0,5 [0,0; 3,0]
<i>Diarrhö</i>	1/184	0,5 [0,0; 3,0]
Allgemeine Erkrankungen und Beschwerden am Verabreichungsort	1/184	0,5 [0,0; 3,0]

Studie DESTINY-Breast01 SOC PT	Trastuzumab-Deruxtecan	
	n/N	% [95 %-KI]
<i>Leistung vermindert</i>	1/184	0,5 [0,0; 3,0]
Leber- und Gallenerkrankungen	1/184	0,5 [0,0; 3,0]
<i>Leberkrankheit mit Venenokklusion</i>	1/184	0,5 [0,0; 3,0]
Erkrankungen des Nervensystems	1/184	0,5 [0,0; 3,0]
<i>Periphere Neuropathie</i>	1/184	0,5 [0,0; 3,0]
3. Datenschnitt: 08.06.2020 Alle Abkürzungen werden im Abkürzungsverzeichnis erläutert.		

UE von besonderem Interesse

Tabelle 26: Ergebnisse für den Endpunkt UE von besonderem Interesse aus weiteren Untersuchungen mit dem zu bewertenden Arzneimittel

Studie DESTINY-Breast01	Trastuzumab-Deruxtecan N=184 (Safety-Population), n (%) [95 %-KI]
Interstitielle Lungenerkrankung (ILD), Bewertung durch Prüfarzt	
ILD, unabhängig vom Schweregrad	28 (15,2) [10,4; 21,2]
ILD, SUE	6 (3,3) [1,2; 7,0]
ILD, CTCAE-Grad < 3	23 (12,5) [8,1; 18,2]
ILD, CTCAE-Grad ≥ 3	5 (2,7) [0,9; 6,2]
Interstitielle Lungenerkrankung (ILD), Bewertung durch AC	
ILD, unabhängig vom Schweregrad	30 (16,3) [11,3; 22,5]
ILD, SUE	10 (5,4) [2,6; 9,8]
ILD, CTCAE-Grad < 3	23 (12,5) [8,1; 18,2]
ILD, CTCAE-Grad ≥ 3	8 (4,3) [1,9; 8,4]
Verringerung der linksventrikulären Auswurffraktion (LVEF)	
Verringerung der LVEF, unabhängig vom Schweregrad	6 (3,3) [1,2; 7,0]
Verringerung der LVEF, SUE	1 (0,5) [0,0; 3,0]
Verringerung der LVEF, CTCAE-Grad < 3	5 (2,7) [0,9; 6,2]
Verringerung der LVEF, CTCAE-Grad ≥ 3	1 (0,5) [0,0; 3,0]
Verlängerung des QT-Intervalls	
Verlängerung des QT-Intervalls, unabhängig vom Schweregrad	11 (6,0) [3,0; 10,4]
Verlängerung des QT-Intervalls, SUE	1 (0,5) [0,0; 3,0]
Verlängerung des QT-Intervalls, CTCAE-Grad < 3	8 (4,3) [1,9; 8,4]
Verlängerung des QT-Intervalls, CTCAE-Grad ≥ 3	3 (1,6) [0,3; 4,7]

Infusionsbedingte Reaktion (IRR)	
IRR, unabhängig vom Schweregrad	18 (9,8) [5,9; 15,0]
IRR, SUE	1 (0,5) [0,0; 3,0]
IRR, CTCAE-Grad < 3	18 (9,8) [5,9; 15,0]
IRR, CTCAE-Grad $\geq$ 3	0 (0,0) [0,0; 2,0]
3. Datenschnitt: 08.06.2020 Alle Abkürzungen werden im Abkürzungsverzeichnis erläutert.	

Subgruppenanalysen

Follow-up und Exposition

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
A-Age classification 1	< 65 years	Total number of subjects in subgroup category	140
		Number (%) of subjects on treatment at data cut	29 (20.7)
		Duration of Follow-up (months)	
		n	140
		Mean	17.8
		Std. Dev.	6.71
		Median	20.6
		Minimum	1.9
		Maximum	29.5
		Treatment Duration	
		<=3 months	23 (16.4)
		>3 to <=6 months	24 (17.1)
		>6 to <=9 months	17 (12.1)
		>9 to <=12 months	17 (12.1)
		>12 to <=24 months	51 (36.4)
		>24 months	8 (5.7)
		Dose Intensity (mg/kg/3 weeks)	
		n	140
		Mean	5.00
		Std. Dev.	0.552
		Median	5.20
		Minimum	3.1
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	31 (22.1)
		>6 to <=12 cycles	34 (24.3)
		>12 to <=18 cycles	20 (14.3)
		>18 to <=24 cycles	13 (9.3)
		>24 to <=30 cycles	18 (12.9)
		>30 cycles	24 (17.1)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
A-Age classification 1	>= 65 years	Total number of subjects in subgroup category	44
		Number (%) of subjects on treatment at data cut	8 (18.2)
		Duration of Follow-up (months)	
		n	44
		Mean	18.8
		Std. Dev.	6.69
		Median	20.4
		Minimum	0.7
		Maximum	31.4
		Treatment Duration	
		<=3 months	5 (11.4)
		>3 to <=6 months	4 (9.1)
		>6 to <=9 months	9 (20.5)
		>9 to <=12 months	5 (11.4)
		>12 to <=24 months	18 (40.9)
		>24 months	3 (6.8)
		Dose Intensity (mg/kg/3 weeks)	
		n	44
		Mean	4.89
		Std. Dev.	0.789
		Median	5.20
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	8 (18.2)
		>6 to <=12 cycles	9 (20.5)
		>12 to <=18 cycles	10 (22.7)
		>18 to <=24 cycles	5 (11.4)
		>24 to <=30 cycles	5 (11.4)
		>30 cycles	7 (15.9)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
B-Region	Asia	Total number of subjects in subgroup category	63
		Number (%) of subjects on treatment at data cut	18 (28.6)
		Duration of Follow-up (months)	
		n	63
		Mean	20.2
		Std. Dev.	5.56
		Median	21.0
		Minimum	3.9
		Maximum	31.4
		Treatment Duration	
		<=3 months	8 (12.7)
		>3 to <=6 months	11 (17.5)
		>6 to <=9 months	9 (14.3)
		>9 to <=12 months	4 (6.3)
		>12 to <=24 months	26 (41.3)
		>24 months	5 (7.9)
		Dose Intensity (mg/kg/3 weeks)	
		n	63
		Mean	4.94
		Std. Dev.	0.671
		Median	5.20
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	10 (15.9)
		>6 to <=12 cycles	19 (30.2)
		>12 to <=18 cycles	5 (7.9)
		>18 to <=24 cycles	7 (11.1)
		>24 to <=30 cycles	7 (11.1)
		>30 cycles	15 (23.8)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
B-Region	North America	Total number of subjects in subgroup category	53
		Number (%) of subjects on treatment at data cut	7 (13.2)
		Duration of Follow-up (months)	
		n	53
		Mean	17.8
		Std. Dev.	6.81
		Median	20.3
		Minimum	3.1
		Maximum	29.6
		Treatment Duration	
		<=3 months	9 (17.0)
		>3 to <=6 months	6 (11.3)
		>6 to <=9 months	6 (11.3)
		>9 to <=12 months	8 (15.1)
		>12 to <=24 months	20 (37.7)
		>24 months	4 (7.5)
		Dose Intensity (mg/kg/3 weeks)	
		n	53
		Mean	4.91
		Std. Dev.	0.694
		Median	5.20
		Minimum	2.8
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	13 (24.5)
		>6 to <=12 cycles	7 (13.2)
		>12 to <=18 cycles	13 (24.5)
		>18 to <=24 cycles	6 (11.3)
		>24 to <=30 cycles	7 (13.2)
		>30 cycles	7 (13.2)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
B-Region	EU	Total number of subjects in subgroup category	68
		Number (%) of subjects on treatment at data cut	12 (17.6)
		Duration of Follow-up (months)	
		n	68
		Mean	16.3
		Std. Dev.	7.12
		Median	20.0
		Minimum	0.7
		Maximum	25.8
		Treatment Duration	
		<=3 months	11 (16.2)
		>3 to <=6 months	11 (16.2)
		>6 to <=9 months	11 (16.2)
		>9 to <=12 months	10 (14.7)
		>12 to <=24 months	23 (33.8)
		>24 months	2 (2.9)
		Dose Intensity (mg/kg/3 weeks)	
		n	68
		Mean	5.06
		Std. Dev.	0.486
		Median	5.20
		Minimum	3.1
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	16 (23.5)
		>6 to <=12 cycles	17 (25.0)
		>12 to <=18 cycles	12 (17.6)
		>18 to <=24 cycles	5 (7.4)
		>24 to <=30 cycles	9 (13.2)
		>30 cycles	9 (13.2)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
C-ECOG performance status	Status 0	Total number of subjects in subgroup category	102
		Number (%) of subjects on treatment at data cut	22 (21.6)
		Duration of Follow-up (months)	
		n	102
		Mean	19.3
		Std. Dev.	6.31
		Median	20.8
		Minimum	0.7
		Maximum	31.4
		Treatment Duration	
		<=3 months	8 (7.8)
		>3 to <=6 months	15 (14.7)
		>6 to <=9 months	15 (14.7)
		>9 to <=12 months	14 (13.7)
		>12 to <=24 months	43 (42.2)
		>24 months	7 (6.9)
		Dose Intensity (mg/kg/3 weeks)	
		n	102
		Mean	5.00
		Std. Dev.	0.574
		Median	5.20
		Minimum	2.7
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	14 (13.7)
		>6 to <=12 cycles	23 (22.5)
		>12 to <=18 cycles	18 (17.6)
		>18 to <=24 cycles	12 (11.8)
		>24 to <=30 cycles	16 (15.7)
		>30 cycles	19 (18.6)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
C-ECOG performance status	Status 1	Total number of subjects in subgroup category	81
		Number (%) of subjects on treatment at data cut	15 (18.5)
		Duration of Follow-up (months)	
		n	81
		Mean	16.7
		Std. Dev.	6.77
		Median	19.7
		Minimum	3.0
		Maximum	29.6
		Treatment Duration	
		<=3 months	19 (23.5)
		>3 to <=6 months	13 (16.0)
		>6 to <=9 months	11 (13.6)
		>9 to <=12 months	8 (9.9)
		>12 to <=24 months	26 (32.1)
		>24 months	4 (4.9)
		Dose Intensity (mg/kg/3 weeks)	
		n	81
		Mean	4.94
		Std. Dev.	0.669
		Median	5.30
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	24 (29.6)
		>6 to <=12 cycles	20 (24.7)
		>12 to <=18 cycles	12 (14.8)
		>18 to <=24 cycles	6 (7.4)
		>24 to <=30 cycles	7 (8.6)
		>30 cycles	12 (14.8)

Source Data: adam.adsl, adam.adex.

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Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
D-Baseline sum of diameters of target lesions	< 5 cm	Total number of subjects in subgroup category	73
		Number (%) of subjects on treatment at data cut	19 (26.0)
		Duration of Follow-up (months)	
		n	73
		Mean	18.1
		Std. Dev.	6.93
		Median	20.7
		Minimum	0.7
		Maximum	29.6
		Treatment Duration	
		<=3 months	13 (17.8)
		>3 to <=6 months	10 (13.7)
		>6 to <=9 months	6 (8.2)
		>9 to <=12 months	10 (13.7)
		>12 to <=24 months	30 (41.1)
		>24 months	4 (5.5)
		Dose Intensity (mg/kg/3 weeks)	
		n	73
		Mean	4.96
		Std. Dev.	0.562
		Median	5.20
		Minimum	3.2
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	15 (20.5)
		>6 to <=12 cycles	13 (17.8)
		>12 to <=18 cycles	12 (16.4)
		>18 to <=24 cycles	7 (9.6)
		>24 to <=30 cycles	11 (15.1)
		>30 cycles	15 (20.5)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
D-Baseline sum of diameters of target lesions	>= 5 cm	Total number of subjects in subgroup category	97
		Number (%) of subjects on treatment at data cut	13 (13.4)
		Duration of Follow-up (months)	
		n	97
		Mean	17.6
		Std. Dev.	6.72
		Median	20.3
		Minimum	1.9
		Maximum	31.4
		Treatment Duration	
		<=3 months	15 (15.5)
		>3 to <=6 months	17 (17.5)
		>6 to <=9 months	18 (18.6)
		>9 to <=12 months	10 (10.3)
		>12 to <=24 months	32 (33.0)
		>24 months	5 (5.2)
		Dose Intensity (mg/kg/3 weeks)	
		n	97
		Mean	5.02
		Std. Dev.	0.587
		Median	5.20
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	23 (23.7)
		>6 to <=12 cycles	28 (28.9)
		>12 to <=18 cycles	15 (15.5)
		>18 to <=24 cycles	9 (9.3)
		>24 to <=30 cycles	10 (10.3)
		>30 cycles	12 (12.4)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
E-HER2 Status	IHC3+	Total number of subjects in subgroup category	154
		Number (%) of subjects on treatment at data cut	36 (23.4)
		Duration of Follow-up (months)	
		n	154
		Mean	18.5
		Std. Dev.	6.62
		Median	20.7
		Minimum	1.9
		Maximum	31.4
		Treatment Duration	
		<=3 months	24 (15.6)
		>3 to <=6 months	22 (14.3)
		>6 to <=9 months	20 (13.0)
		>9 to <=12 months	14 (9.1)
		>12 to <=24 months	64 (41.6)
		>24 months	10 (6.5)
		Dose Intensity (mg/kg/3 weeks)	
		n	154
		Mean	4.94
		Std. Dev.	0.640
		Median	5.20
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	33 (21.4)
		>6 to <=12 cycles	33 (21.4)
		>12 to <=18 cycles	21 (13.6)
		>18 to <=24 cycles	15 (9.7)
		>24 to <=30 cycles	23 (14.9)
		>30 cycles	29 (18.8)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
E-HER2 Status	ISH+ EXCEPT IHC3+	Total number of subjects in subgroup category	28
		Number (%) of subjects on treatment at data cut	1 (3.6)
		Duration of Follow-up (months)	
		n	28
		Mean	16.0
		Std. Dev.	6.72
		Median	18.9
		Minimum	0.7
		Maximum	25.8
		Treatment Duration	
		<=3 months	4 (14.3)
		>3 to <=6 months	5 (17.9)
		>6 to <=9 months	6 (21.4)
		>9 to <=12 months	8 (28.6)
		>12 to <=24 months	4 (14.3)
		>24 months	1 (3.6)
		Dose Intensity (mg/kg/3 weeks)	
		n	28
		Mean	5.18
		Std. Dev.	0.449
		Median	5.30
		Minimum	3.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	6 (21.4)
		>6 to <=12 cycles	9 (32.1)
		>12 to <=18 cycles	8 (28.6)
		>18 to <=24 cycles	3 (10.7)
		>24 to <=30 cycles	0
		>30 cycles	2 (7.1)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
F-Estrogen receptors	Positive	Total number of subjects in subgroup category	93
		Number (%) of subjects on treatment at data cut	14 (15.1)
		Duration of Follow-up (months)	
		n	93
		Mean	18.0
		Std. Dev.	6.16
		Median	20.3
		Minimum	1.9
		Maximum	28.3
		Treatment Duration	
		<=3 months	13 (14.0)
		>3 to <=6 months	13 (14.0)
		>6 to <=9 months	16 (17.2)
		>9 to <=12 months	13 (14.0)
		>12 to <=24 months	35 (37.6)
		>24 months	3 (3.2)
		Dose Intensity (mg/kg/3 weeks)	
		n	93
		Mean	4.95
		Std. Dev.	0.652
		Median	5.20
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	18 (19.4)
		>6 to <=12 cycles	24 (25.8)
		>12 to <=18 cycles	18 (19.4)
		>18 to <=24 cycles	14 (15.1)
		>24 to <=30 cycles	9 (9.7)
		>30 cycles	10 (10.8)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
F-Estrogen receptors	Negative	Total number of subjects in subgroup category	88
		Number (%) of subjects on treatment at data cut	23 (26.1)
		Duration of Follow-up (months)	
		n	88
		Mean	18.3
		Std. Dev.	7.12
		Median	20.7
		Minimum	0.7
		Maximum	31.4
		Treatment Duration	
		<=3 months	13 (14.8)
		>3 to <=6 months	15 (17.0)
		>6 to <=9 months	10 (11.4)
		>9 to <=12 months	8 (9.1)
		>12 to <=24 months	34 (38.6)
		>24 months	8 (9.1)
		Dose Intensity (mg/kg/3 weeks)	
		n	88
		Mean	4.99
		Std. Dev.	0.582
		Median	5.20
		Minimum	2.8
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	19 (21.6)
		>6 to <=12 cycles	19 (21.6)
		>12 to <=18 cycles	11 (12.5)
		>18 to <=24 cycles	4 (4.5)
		>24 to <=30 cycles	14 (15.9)
		>30 cycles	21 (23.9)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
G-Progesterone receptors	Positive	Total number of subjects in subgroup category	51
		Number (%) of subjects on treatment at data cut	8 (15.7)
		Duration of Follow-up (months)	
		n	51
		Mean	18.4
		Std. Dev.	5.60
		Median	20.3
		Minimum	3.9
		Maximum	27.2
		Treatment Duration	
		<=3 months	4 (7.8)
		>3 to <=6 months	7 (13.7)
		>6 to <=9 months	10 (19.6)
		>9 to <=12 months	6 (11.8)
		>12 to <=24 months	21 (41.2)
		>24 months	3 (5.9)
		Dose Intensity (mg/kg/3 weeks)	
		n	51
		Mean	4.87
		Std. Dev.	0.753
		Median	5.30
		Minimum	2.5
		Maximum	5.5
		Total Number of Cycles Initiated	
		<=6 cycles	6 (11.8)
		>6 to <=12 cycles	14 (27.5)
		>12 to <=18 cycles	11 (21.6)
		>18 to <=24 cycles	9 (17.6)
		>24 to <=30 cycles	5 (9.8)
		>30 cycles	6 (11.8)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
G-Progesterone receptors	Negative	Total number of subjects in subgroup category	125
		Number (%) of subjects on treatment at data cut	29 (23.2)
		Duration of Follow-up (months)	
		n	125
		Mean	18.1
		Std. Dev.	7.13
		Median	20.6
		Minimum	0.7
		Maximum	31.4
		Treatment Duration	
		<=3 months	21 (16.8)
		>3 to <=6 months	20 (16.0)
		>6 to <=9 months	16 (12.8)
		>9 to <=12 months	14 (11.2)
		>12 to <=24 months	46 (36.8)
		>24 months	8 (6.4)
		Dose Intensity (mg/kg/3 weeks)	
		n	125
		Mean	5.00
		Std. Dev.	0.563
		Median	5.20
		Minimum	2.8
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	30 (24.0)
		>6 to <=12 cycles	28 (22.4)
		>12 to <=18 cycles	17 (13.6)
		>18 to <=24 cycles	9 (7.2)
		>24 to <=30 cycles	16 (12.8)
		>30 cycles	25 (20.0)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
H-Hormone receptors	Positive	Total number of subjects in subgroup category	97
		Number (%) of subjects on treatment at data cut	15 (15.5)
		Duration of Follow-up (months)	
		n	97
		Mean	18.2
		Std. Dev.	6.15
		Median	20.4
		Minimum	1.9
		Maximum	28.3
		Treatment Duration	
		<=3 months	13 (13.4)
		>3 to <=6 months	14 (14.4)
		>6 to <=9 months	16 (16.5)
		>9 to <=12 months	13 (13.4)
		>12 to <=24 months	38 (39.2)
		>24 months	3 (3.1)
		Dose Intensity (mg/kg/3 weeks)	
		n	97
		Mean	4.92
		Std. Dev.	0.669
		Median	5.20
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	18 (18.6)
		>6 to <=12 cycles	25 (25.8)
		>12 to <=18 cycles	19 (19.6)
		>18 to <=24 cycles	15 (15.5)
		>24 to <=30 cycles	9 (9.3)
		>30 cycles	11 (11.3)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
H-Hormone receptors	Negative	Total number of subjects in subgroup category	83
		Number (%) of subjects on treatment at data cut	22 (26.5)
		Duration of Follow-up (months)	
		n	83
		Mean	18.2
		Std. Dev.	7.21
		Median	20.7
		Minimum	0.7
		Maximum	31.4
		Treatment Duration	
		<=3 months	13 (15.7)
		>3 to <=6 months	14 (16.9)
		>6 to <=9 months	10 (12.0)
		>9 to <=12 months	8 (9.6)
		>12 to <=24 months	30 (36.1)
		>24 months	8 (9.6)
		Dose Intensity (mg/kg/3 weeks)	
		n	83
		Mean	5.01
		Std. Dev.	0.555
		Median	5.20
		Minimum	2.8
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	19 (22.9)
		>6 to <=12 cycles	18 (21.7)
		>12 to <=18 cycles	10 (12.0)
		>18 to <=24 cycles	3 (3.6)
		>24 to <=30 cycles	13 (15.7)
		>30 cycles	20 (24.1)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
I-Renal impairment	Normal	Total number of subjects in subgroup category	90
		Number (%) of subjects on treatment at data cut	19 (21.1)
		Duration of Follow-up (months)	
		n	90
		Mean	17.7
		Std. Dev.	6.87
		Median	20.6
		Minimum	1.9
		Maximum	29.1
		Treatment Duration	
		<=3 months	13 (14.4)
		>3 to <=6 months	12 (13.3)
		>6 to <=9 months	11 (12.2)
		>9 to <=12 months	12 (13.3)
		>12 to <=24 months	37 (41.1)
		>24 months	5 (5.6)
		Dose Intensity (mg/kg/3 weeks)	
		n	90
		Mean	5.03
		Std. Dev.	0.545
		Median	5.20
		Minimum	2.8
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	18 (20.0)
		>6 to <=12 cycles	18 (20.0)
		>12 to <=18 cycles	14 (15.6)
		>18 to <=24 cycles	10 (11.1)
		>24 to <=30 cycles	15 (16.7)
		>30 cycles	15 (16.7)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
I-Renal impairment	Mild	Total number of subjects in subgroup category	69
		Number (%) of subjects on treatment at data cut	17 (24.6)
		Duration of Follow-up (months)	
		n	69
		Mean	18.5
		Std. Dev.	6.13
		Median	20.7
		Minimum	3.1
		Maximum	29.6
		Treatment Duration	
		<=3 months	10 (14.5)
		>3 to <=6 months	9 (13.0)
		>6 to <=9 months	11 (15.9)
		>9 to <=12 months	8 (11.6)
		>12 to <=24 months	26 (37.7)
		>24 months	5 (7.2)
		Dose Intensity (mg/kg/3 weeks)	
		n	69
		Mean	4.89
		Std. Dev.	0.734
		Median	5.20
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	13 (18.8)
		>6 to <=12 cycles	17 (24.6)
		>12 to <=18 cycles	13 (18.8)
		>18 to <=24 cycles	5 (7.2)
		>24 to <=30 cycles	7 (10.1)
		>30 cycles	14 (20.3)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
I-Renal impairment	Moderate	Total number of subjects in subgroup category	25
		Number (%) of subjects on treatment at data cut	1 (4.0)
		Duration of Follow-up (months)	
		n	25
		Mean	18.1
		Std. Dev.	7.75
		Median	19.9
		Minimum	0.7
		Maximum	31.4
		Treatment Duration	
		<=3 months	5 (20.0)
		>3 to <=6 months	7 (28.0)
		>6 to <=9 months	4 (16.0)
		>9 to <=12 months	2 (8.0)
		>12 to <=24 months	6 (24.0)
		>24 months	1 (4.0)
		Dose Intensity (mg/kg/3 weeks)	
		n	25
		Mean	5.02
		Std. Dev.	0.488
		Median	5.20
		Minimum	4.0
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	8 (32.0)
		>6 to <=12 cycles	8 (32.0)
		>12 to <=18 cycles	3 (12.0)
		>18 to <=24 cycles	3 (12.0)
		>24 to <=30 cycles	1 (4.0)
		>30 cycles	2 (8.0)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
J-Hepatic impairment	Normal	Total number of subjects in subgroup category	105
		Number (%) of subjects on treatment at data cut	23 (21.9)
		Duration of Follow-up (months)	
		n	105
		Mean	19.0
		Std. Dev.	6.78
		Median	20.7
		Minimum	2.4
		Maximum	31.4
		Treatment Duration	
		<=3 months	14 (13.3)
		>3 to <=6 months	11 (10.5)
		>6 to <=9 months	16 (15.2)
		>9 to <=12 months	17 (16.2)
		>12 to <=24 months	38 (36.2)
		>24 months	9 (8.6)
		Dose Intensity (mg/kg/3 weeks)	
		n	105
		Mean	4.92
		Std. Dev.	0.640
		Median	5.20
		Minimum	2.7
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	18 (17.1)
		>6 to <=12 cycles	24 (22.9)
		>12 to <=18 cycles	19 (18.1)
		>18 to <=24 cycles	10 (9.5)
		>24 to <=30 cycles	16 (15.2)
		>30 cycles	18 (17.1)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
J-Hepatic impairment	Mild	Total number of subjects in subgroup category	76
		Number (%) of subjects on treatment at data cut	14 (18.4)
		Duration of Follow-up (months)	
		n	76
		Mean	16.9
		Std. Dev.	6.34
		Median	19.7
		Minimum	0.7
		Maximum	27.2
		Treatment Duration	
		<=3 months	13 (17.1)
		>3 to <=6 months	15 (19.7)
		>6 to <=9 months	10 (13.2)
		>9 to <=12 months	5 (6.6)
		>12 to <=24 months	31 (40.8)
		>24 months	2 (2.6)
		Dose Intensity (mg/kg/3 weeks)	
		n	76
		Mean	5.07
		Std. Dev.	0.572
		Median	5.30
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	20 (26.3)
		>6 to <=12 cycles	17 (22.4)
		>12 to <=18 cycles	11 (14.5)
		>18 to <=24 cycles	8 (10.5)
		>24 to <=30 cycles	7 (9.2)
		>30 cycles	13 (17.1)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
K-Brain metastases	Yes	Total number of subjects in subgroup category	24
		Number (%) of subjects on treatment at data cut	6 (25.0)
		Duration of Follow-up (months)	
		n	24
		Mean	17.3
		Std. Dev.	8.33
		Median	20.4
		Minimum	0.7
		Maximum	29.5
		Treatment Duration	
		<=3 months	4 (16.7)
		>3 to <=6 months	2 (8.3)
		>6 to <=9 months	4 (16.7)
		>9 to <=12 months	3 (12.5)
		>12 to <=24 months	8 (33.3)
		>24 months	3 (12.5)
		Dose Intensity (mg/kg/3 weeks)	
		n	24
		Mean	5.15
		Std. Dev.	0.459
		Median	5.30
		Minimum	3.9
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	6 (25.0)
		>6 to <=12 cycles	4 (16.7)
		>12 to <=18 cycles	5 (20.8)
		>18 to <=24 cycles	1 (4.2)
		>24 to <=30 cycles	2 (8.3)
		>30 cycles	6 (25.0)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
K-Brain metastases	No	Total number of subjects in subgroup category	160
		Number (%) of subjects on treatment at data cut	31 (19.4)
		Duration of Follow-up (months)	
		n	160
		Mean	18.2
		Std. Dev.	6.45
		Median	20.5
		Minimum	2.4
		Maximum	31.4
		Treatment Duration	
		<=3 months	24 (15.0)
		>3 to <=6 months	26 (16.3)
		>6 to <=9 months	22 (13.8)
		>9 to <=12 months	19 (11.9)
		>12 to <=24 months	61 (38.1)
		>24 months	8 (5.0)
		Dose Intensity (mg/kg/3 weeks)	
		n	160
		Mean	4.95
		Std. Dev.	0.634
		Median	5.20
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	33 (20.6)
		>6 to <=12 cycles	39 (24.4)
		>12 to <=18 cycles	25 (15.6)
		>18 to <=24 cycles	17 (10.6)
		>24 to <=30 cycles	21 (13.1)
		>30 cycles	25 (15.6)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
L-Bone metastases	Yes	Total number of subjects in subgroup category	53
		Number (%) of subjects on treatment at data cut	7 (13.2)
		Duration of Follow-up (months)	
		n	53
		Mean	17.2
		Std. Dev.	7.31
		Median	20.1
		Minimum	0.7
		Maximum	28.3
		Treatment Duration	
		<=3 months	9 (17.0)
		>3 to <=6 months	9 (17.0)
		>6 to <=9 months	7 (13.2)
		>9 to <=12 months	7 (13.2)
		>12 to <=24 months	19 (35.8)
		>24 months	2 (3.8)
		Dose Intensity (mg/kg/3 weeks)	
		n	53
		Mean	4.94
		Std. Dev.	0.656
		Median	5.20
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	12 (22.6)
		>6 to <=12 cycles	14 (26.4)
		>12 to <=18 cycles	11 (20.8)
		>18 to <=24 cycles	5 (9.4)
		>24 to <=30 cycles	5 (9.4)
		>30 cycles	6 (11.3)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
L-Bone metastases	No	Total number of subjects in subgroup category	131
		Number (%) of subjects on treatment at data cut	30 (22.9)
		Duration of Follow-up (months)	
		n	131
		Mean	18.4
		Std. Dev.	6.44
		Median	20.6
		Minimum	1.9
		Maximum	31.4
		Treatment Duration	
		<=3 months	19 (14.5)
		>3 to <=6 months	19 (14.5)
		>6 to <=9 months	19 (14.5)
		>9 to <=12 months	15 (11.5)
		>12 to <=24 months	50 (38.2)
		>24 months	9 (6.9)
		Dose Intensity (mg/kg/3 weeks)	
		n	131
		Mean	4.99
		Std. Dev.	0.601
		Median	5.20
		Minimum	2.7
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	27 (20.6)
		>6 to <=12 cycles	29 (22.1)
		>12 to <=18 cycles	19 (14.5)
		>18 to <=24 cycles	13 (9.9)
		>24 to <=30 cycles	18 (13.7)
		>30 cycles	25 (19.1)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
M-History of visceral disease	Yes	Total number of subjects in subgroup category	169
		Number (%) of subjects on treatment at data cut	35 (20.7)
		Duration of Follow-up (months)	
		n	169
		Mean	18.0
		Std. Dev.	6.74
		Median	20.5
		Minimum	0.7
		Maximum	31.4
		Treatment Duration	
		<=3 months	26 (15.4)
		>3 to <=6 months	25 (14.8)
		>6 to <=9 months	26 (15.4)
		>9 to <=12 months	17 (10.1)
		>12 to <=24 months	64 (37.9)
		>24 months	11 (6.5)
		Dose Intensity (mg/kg/3 weeks)	
		n	169
		Mean	4.97
		Std. Dev.	0.624
		Median	5.20
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	37 (21.9)
		>6 to <=12 cycles	40 (23.7)
		>12 to <=18 cycles	25 (14.8)
		>18 to <=24 cycles	17 (10.1)
		>24 to <=30 cycles	22 (13.0)
		>30 cycles	28 (16.6)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
M-History of visceral disease	No	Total number of subjects in subgroup category	15
		Number (%) of subjects on treatment at data cut	2 (13.3)
		Duration of Follow-up (months)	
		n	15
		Mean	18.2
		Std. Dev.	6.51
		Median	20.4
		Minimum	3.9
		Maximum	24.6
		Treatment Duration	
		<=3 months	2 (13.3)
		>3 to <=6 months	3 (20.0)
		>6 to <=9 months	0
		>9 to <=12 months	5 (33.3)
		>12 to <=24 months	5 (33.3)
		>24 months	0
		Dose Intensity (mg/kg/3 weeks)	
		n	15
		Mean	5.00
		Std. Dev.	0.542
		Median	5.20
		Minimum	3.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	2 (13.3)
		>6 to <=12 cycles	3 (20.0)
		>12 to <=18 cycles	5 (33.3)
		>18 to <=24 cycles	1 (6.7)
		>24 to <=30 cycles	1 (6.7)
		>30 cycles	3 (20.0)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
N-T-DM1 last therapy	Yes	Total number of subjects in subgroup category	56
		Number (%) of subjects on treatment at data cut	18 (32.1)
		Duration of Follow-up (months)	
		n	56
		Mean	18.4
		Std. Dev.	6.90
		Median	20.7
		Minimum	0.7
		Maximum	29.1
		Treatment Duration	
		<=3 months	7 (12.5)
		>3 to <=6 months	9 (16.1)
		>6 to <=9 months	5 (8.9)
		>9 to <=12 months	3 (5.4)
		>12 to <=24 months	30 (53.6)
		>24 months	2 (3.6)
		Dose Intensity (mg/kg/3 weeks)	
		n	56
		Mean	4.99
		Std. Dev.	0.538
		Median	5.20
		Minimum	3.2
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	8 (14.3)
		>6 to <=12 cycles	12 (21.4)
		>12 to <=18 cycles	5 (8.9)
		>18 to <=24 cycles	4 (7.1)
		>24 to <=30 cycles	12 (21.4)
		>30 cycles	15 (26.8)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
N-T-DM1 last therapy	No	Total number of subjects in subgroup category	128
		Number (%) of subjects on treatment at data cut	19 (14.8)
		Duration of Follow-up (months)	
		n	128
		Mean	17.9
		Std. Dev.	6.64
		Median	20.4
		Minimum	1.9
		Maximum	31.4
		Treatment Duration	
		<=3 months	21 (16.4)
		>3 to <=6 months	19 (14.8)
		>6 to <=9 months	21 (16.4)
		>9 to <=12 months	19 (14.8)
		>12 to <=24 months	39 (30.5)
		>24 months	9 (7.0)
		Dose Intensity (mg/kg/3 weeks)	
		n	128
		Mean	4.97
		Std. Dev.	0.650
		Median	5.20
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	31 (24.2)
		>6 to <=12 cycles	31 (24.2)
		>12 to <=18 cycles	25 (19.5)
		>18 to <=24 cycles	14 (10.9)
		>24 to <=30 cycles	11 (8.6)
		>30 cycles	16 (12.5)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
0-Prior treatment lines	< 3 lines	Total number of subjects in subgroup category	17
		Number (%) of subjects on treatment at data cut	8 (47.1)
		Duration of Follow-up (months)	
		n	17
		Mean	19.9
		Std. Dev.	5.74
		Median	21.0
		Minimum	4.1
		Maximum	27.2
		Treatment Duration	
		<=3 months	0
		>3 to <=6 months	2 (11.8)
		>6 to <=9 months	1 (5.9)
		>9 to <=12 months	0
		>12 to <=24 months	14 (82.4)
		>24 months	0
		Dose Intensity (mg/kg/3 weeks)	
		n	17
		Mean	4.86
		Std. Dev.	0.632
		Median	5.10
		Minimum	3.2
		Maximum	5.5
		Total Number of Cycles Initiated	
		<=6 cycles	1 (5.9)
		>6 to <=12 cycles	1 (5.9)
		>12 to <=18 cycles	1 (5.9)
		>18 to <=24 cycles	4 (23.5)
		>24 to <=30 cycles	3 (17.6)
		>30 cycles	7 (41.2)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
0-Prior treatment lines	>= 3 lines	Total number of subjects in subgroup category	167
		Number (%) of subjects on treatment at data cut	29 (17.4)
		Duration of Follow-up (months)	
		n	167
		Mean	17.9
		Std. Dev.	6.78
		Median	20.4
		Minimum	0.7
		Maximum	31.4
		Treatment Duration	
		<=3 months	28 (16.8)
		>3 to <=6 months	26 (15.6)
		>6 to <=9 months	25 (15.0)
		>9 to <=12 months	22 (13.2)
		>12 to <=24 months	55 (32.9)
		>24 months	11 (6.6)
		Dose Intensity (mg/kg/3 weeks)	
		n	167
		Mean	4.99
		Std. Dev.	0.615
		Median	5.20
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	38 (22.8)
		>6 to <=12 cycles	42 (25.1)
		>12 to <=18 cycles	29 (17.4)
		>18 to <=24 cycles	14 (8.4)
		>24 to <=30 cycles	20 (12.0)
		>30 cycles	24 (14.4)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
P-Best Response to T-DM1 therapy	CR/PR/SD	Total number of subjects in subgroup category	79
		Number (%) of subjects on treatment at data cut	18 (22.8)
		Duration of Follow-up (months)	
		n	79
		Mean	19.4
		Std. Dev.	5.11
		Median	20.7
		Minimum	3.9
		Maximum	27.9
		Treatment Duration	
		<=3 months	9 (11.4)
		>3 to <=6 months	9 (11.4)
		>6 to <=9 months	13 (16.5)
		>9 to <=12 months	9 (11.4)
		>12 to <=24 months	36 (45.6)
		>24 months	3 (3.8)
		Dose Intensity (mg/kg/3 weeks)	
		n	79
		Mean	4.88
		Std. Dev.	0.724
		Median	5.20
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	11 (13.9)
		>6 to <=12 cycles	20 (25.3)
		>12 to <=18 cycles	11 (13.9)
		>18 to <=24 cycles	11 (13.9)
		>24 to <=30 cycles	12 (15.2)
		>30 cycles	14 (17.7)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
P-Best Response to T-DM1 therapy	PD	Total number of subjects in subgroup category	66
		Number (%) of subjects on treatment at data cut	11 (16.7)
		Duration of Follow-up (months)	
		n	66
		Mean	17.5
		Std. Dev.	7.70
		Median	20.3
		Minimum	2.4
		Maximum	31.4
		Treatment Duration	
		<=3 months	10 (15.2)
		>3 to <=6 months	11 (16.7)
		>6 to <=9 months	9 (13.6)
		>9 to <=12 months	11 (16.7)
		>12 to <=24 months	19 (28.8)
		>24 months	6 (9.1)
		Dose Intensity (mg/kg/3 weeks)	
		n	66
		Mean	5.04
		Std. Dev.	0.474
		Median	5.20
		Minimum	3.3
		Maximum	5.5
		Total Number of Cycles Initiated	
		<=6 cycles	15 (22.7)
		>6 to <=12 cycles	15 (22.7)
		>12 to <=18 cycles	14 (21.2)
		>18 to <=24 cycles	6 (9.1)
		>24 to <=30 cycles	7 (10.6)
		>30 cycles	9 (13.6)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
Q-Prior pertuzumab	Yes	Total number of subjects in subgroup category	121
		Number (%) of subjects on treatment at data cut	25 (20.7)
		Duration of Follow-up (months)	
		n	121
		Mean	18.5
		Std. Dev.	6.68
		Median	20.5
		Minimum	2.4
		Maximum	31.4
		Treatment Duration	
		<=3 months	14 (11.6)
		>3 to <=6 months	20 (16.5)
		>6 to <=9 months	16 (13.2)
		>9 to <=12 months	14 (11.6)
		>12 to <=24 months	50 (41.3)
		>24 months	7 (5.8)
		Dose Intensity (mg/kg/3 weeks)	
		n	121
		Mean	4.96
		Std. Dev.	0.629
		Median	5.20
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	25 (20.7)
		>6 to <=12 cycles	26 (21.5)
		>12 to <=18 cycles	19 (15.7)
		>18 to <=24 cycles	14 (11.6)
		>24 to <=30 cycles	17 (14.0)
		>30 cycles	20 (16.5)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
Q-Prior pertuzumab	No	Total number of subjects in subgroup category	63
		Number (%) of subjects on treatment at data cut	12 (19.0)
		Duration of Follow-up (months)	
		n	63
		Mean	17.3
		Std. Dev.	6.74
		Median	20.6
		Minimum	0.7
		Maximum	25.8
		Treatment Duration	
		<=3 months	14 (22.2)
		>3 to <=6 months	8 (12.7)
		>6 to <=9 months	10 (15.9)
		>9 to <=12 months	8 (12.7)
		>12 to <=24 months	19 (30.2)
		>24 months	4 (6.3)
		Dose Intensity (mg/kg/3 weeks)	
		n	63
		Mean	5.01
		Std. Dev.	0.595
		Median	5.30
		Minimum	3.1
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	14 (22.2)
		>6 to <=12 cycles	17 (27.0)
		>12 to <=18 cycles	11 (17.5)
		>18 to <=24 cycles	4 (6.3)
		>24 to <=30 cycles	6 (9.5)
		>30 cycles	11 (17.5)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
R-Pertuzumab before line 3	Yes	Total number of subjects in subgroup category	51
		Number (%) of subjects on treatment at data cut	11 (21.6)
		Duration of Follow-up (months)	
		n	51
		Mean	17.6
		Std. Dev.	6.58
		Median	20.4
		Minimum	3.9
		Maximum	29.1
		Treatment Duration	
		<=3 months	5 (9.8)
		>3 to <=6 months	10 (19.6)
		>6 to <=9 months	7 (13.7)
		>9 to <=12 months	5 (9.8)
		>12 to <=24 months	24 (47.1)
		>24 months	0
		Dose Intensity (mg/kg/3 weeks)	
		n	51
		Mean	5.02
		Std. Dev.	0.491
		Median	5.20
		Minimum	3.2
		Maximum	5.5
		Total Number of Cycles Initiated	
		<=6 cycles	11 (21.6)
		>6 to <=12 cycles	11 (21.6)
		>12 to <=18 cycles	7 (13.7)
		>18 to <=24 cycles	5 (9.8)
		>24 to <=30 cycles	9 (17.6)
		>30 cycles	8 (15.7)

Source Data: adam.adsl, adam.adex.

Table T3EX_ASB0: Duration of follow-up and exposure by subgroups
Analysis Set: Enrolled Analysis Set

		Overall - EAS	
		5.4 mg/kg	
R-Pertuzumab before line 3	No	Total number of subjects in subgroup category	133
		Number (%) of subjects on treatment at data cut	26 (19.5)
		Duration of Follow-up (months)	
		n	133
		Mean	18.2
		Std. Dev.	6.77
		Median	20.5
		Minimum	0.7
		Maximum	31.4
		Treatment Duration	
		<=3 months	23 (17.3)
		>3 to <=6 months	18 (13.5)
		>6 to <=9 months	19 (14.3)
		>9 to <=12 months	17 (12.8)
		>12 to <=24 months	45 (33.8)
		>24 months	11 (8.3)
		Dose Intensity (mg/kg/3 weeks)	
		n	133
		Mean	4.96
		Std. Dev.	0.659
		Median	5.20
		Minimum	2.5
		Maximum	5.6
		Total Number of Cycles Initiated	
		<=6 cycles	28 (21.1)
		>6 to <=12 cycles	32 (24.1)
		>12 to <=18 cycles	23 (17.3)
		>18 to <=24 cycles	13 (9.8)
		>24 to <=30 cycles	14 (10.5)
		>30 cycles	23 (17.3)

Source Data: adam.adsl, adam.adex.

Gesamtüberleben (OS) – weitere Untersuchungen

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
A-Age classification 1 < 65 years (N=140)	
Overall survival by subgroup, months	
Subjects with events (%)	50 (35.7)
Subjects censored (%)	90 (64.3)
25th Percentile	17.6
95% CI	(13.2, 20.6)
Median	24.6
95% CI	(23.1, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	93.5
95% CI	(87.8, 96.5)
at 12 Months (%)	84.5
95% CI	(77.2, 89.6)
at 24 Months (%)	51.7
95% CI	(38.4, 63.5)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
A-Age classification 1 >= 65 years (N=44)	
Overall survival by subgroup, months	
Subjects with events (%)	15 (34.1)
Subjects censored (%)	29 (65.9)
25th Percentile	18.0
95% CI	(10.4, 22.9)
Median	NE
95% CI	(21.9, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	95.3
95% CI	(82.7, 98.8)
at 12 Months (%)	88.4
95% CI	(74.3, 95.0)
at 24 Months (%)	53.9
95% CI	(30.8, 72.3)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
 Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
B-Region	
Asia (N=63)	
Overall survival by subgroup, months	
Subjects with events (%)	22 (34.9)
Subjects censored (%)	41 (65.1)
25th Percentile	20.5
95% CI	(13.7, 23.3)
Median	24.6
95% CI	(23.1, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	98.4
95% CI	(89.3, 99.8)
at 12 Months (%)	90.3
95% CI	(79.8, 95.5)
at 24 Months (%)	54.7
95% CI	(36.0, 70.0)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
 log-log transformation of rates was applied.
 Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
B-Region	
North America (N=53)	
Overall survival by subgroup, months	
Subjects with events (%)	15 (28.3)
Subjects censored (%)	38 (71.7)
25th Percentile	18.0
95% CI	(10.4, NE)
Median	NE
95% CI	(22.8, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	92.3
95% CI	(80.9, 97.1)
at 12 Months (%)	86.4
95% CI	(73.5, 93.3)
at 24 Months (%)	59.2
95% CI	(36.5, 76.1)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
B-Region	EU (N=68)	Overall survival by subgroup, months
		Subjects with events (%) 28 (41.2)
		Subjects censored (%) 40 (58.8)
		25th Percentile 15.4
		95% CI (7.2, 18.5)
		Median 22.2
		95% CI (19.9, NE)
		Overall survival by subgroup at specific timepoints
		at 6 Months (%) 90.9
		95% CI (80.8, 95.8)
		at 12 Months (%) 79.9
		95% CI (67.8, 87.8)
		at 24 Months (%) 48.6
		95% CI (32.6, 62.8)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)	
C-ECOG performance status	Status 0 (N=102)	Overall survival by subgroup, months
		Subjects with events (%)
		Subjects censored (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Overall survival by subgroup at specific timepoints
		at 6 Months (%)
		95% CI
		at 12 Months (%)
		95% CI
		at 24 Months (%)
		95% CI

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)	
C-ECOG performance status	Status 1 (N=81)	Overall survival by subgroup, months
		Subjects with events (%)
		Subjects censored (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Overall survival by subgroup at specific timepoints
		at 6 Months (%)
		95% CI
		at 12 Months (%)
		95% CI
		at 24 Months (%)
		95% CI

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions	
< 5 cm (N=73)	
Overall survival by subgroup, months	
Subjects with events (%)	17 (23.3)
Subjects censored (%)	56 (76.7)
25th Percentile	22.9
95% CI	(16.2, NE)
Median	NE
95% CI	(24.6, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	92.9
95% CI	(83.8, 97.0)
at 12 Months (%)	91.4
95% CI	(81.9, 96.1)
at 24 Months (%)	70.8
95% CI	(52.5, 83.1)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
- Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions	
>= 5 cm (N=97)	
Overall survival by subgroup, months	
Subjects with events (%)	46 (47.4)
Subjects censored (%)	51 (52.6)
25th Percentile	14.1
95% CI	(10.2, 17.6)
Median	22.8
95% CI	(20.5, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	93.8
95% CI	(86.7, 97.2)
at 12 Months (%)	80.0
95% CI	(70.5, 86.8)
at 24 Months (%)	38.8
95% CI	(25.4, 52.1)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
E-HER2 Status	
IHC3+ (N=154)	
Overall survival by subgroup, months	
Subjects with events (%)	54 (35.1)
Subjects censored (%)	100 (64.9)
25th Percentile	18.0
95% CI	(13.4, 21.1)
Median	NE
95% CI	(23.1, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	94.7
95% CI	(89.8, 97.3)
at 12 Months (%)	86.0
95% CI	(79.3, 90.6)
at 24 Months (%)	54.3
95% CI	(42.3, 64.8)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	
	Overall survival by subgroup, months	
	Subjects with events (%)	10 (35.7)
	Subjects censored (%)	18 (64.3)
	25th Percentile	17.4
	95% CI	(5.5, 22.8)
	Median	22.8
	95% CI	(17.4, NE)
	Overall survival by subgroup at specific timepoints	
	at 6 Months (%)	92.6
	95% CI	(73.5, 98.1)
	at 12 Months (%)	84.7
	95% CI	(64.2, 94.0)
	at 24 Months (%)	41.0
	95% CI	(9.5, 71.3)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
F-Estrogen receptors Positive (N=93)	
Overall survival by subgroup, months	
Subjects with events (%)	31 (33.3)
Subjects censored (%)	62 (66.7)
25th Percentile	16.2
95% CI	(12.6, 21.9)
Median	NE
95% CI	(22.8, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	93.5
95% CI	(86.1, 97.0)
at 12 Months (%)	85.7
95% CI	(76.7, 91.5)
at 24 Months (%)	58.9
95% CI	(44.6, 70.6)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
F-Estrogen receptors Negative (N=88)	
Overall survival by subgroup, months	
Subjects with events (%)	32 (36.4)
Subjects censored (%)	56 (63.6)
25th Percentile	18.5
95% CI	(12.2, 22.2)
Median	24.6
95% CI	(22.9, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	95.3
95% CI	(88.0, 98.2)
at 12 Months (%)	85.7
95% CI	(76.2, 91.6)
at 24 Months (%)	50.6
95% CI	(34.7, 64.5)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Positive (N=51)	Overall survival by subgroup, months
		Subjects with events (%)
		Subjects censored (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Overall survival by subgroup at specific timepoints
		at 6 Months (%)
		95% CI
		at 12 Months (%)
		95% CI
		at 24 Months (%)
		95% CI

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Negative (N=125)	Overall survival by subgroup, months
		Subjects with events (%) 46 (36.8)
		Subjects censored (%) 79 (63.2)
		25th Percentile 17.7
		95% CI (13.3, 20.6)
		Median 24.6
		95% CI (22.9, NE)
		Overall survival by subgroup at specific timepoints
		at 6 Months (%) 94.3
		95% CI (88.3, 97.2)
		at 12 Months (%) 84.2
		95% CI (76.3, 89.6)
		at 24 Months (%) 51.2
		95% CI (38.0, 63.0)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
H-Hormone receptors Positive (N=97)	
Overall survival by subgroup, months	
Subjects with events (%)	33 (34.0)
Subjects censored (%)	64 (66.0)
25th Percentile	16.2
95% CI	(12.6, 21.9)
Median	NE
95% CI	(22.2, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	93.8
95% CI	(86.6, 97.1)
at 12 Months (%)	86.3
95% CI	(77.6, 91.8)
at 24 Months (%)	56.8
95% CI	(42.5, 68.8)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
H-Hormone receptors	
Negative (N=83)	
Overall survival by subgroup, months	
Subjects with events (%)	30 (36.1)
Subjects censored (%)	53 (63.9)
25th Percentile	18.5
95% CI	(10.2, 22.9)
Median	24.6
95% CI	(22.9, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	95.0
95% CI	(87.3, 98.1)
at 12 Months (%)	84.8
95% CI	(74.8, 91.1)
at 24 Months (%)	50.9
95% CI	(34.3, 65.3)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
I-Renal impairment	Normal (N=90)	Overall survival by subgroup, months
		Subjects with events (%)
		Subjects censored (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Overall survival by subgroup at specific timepoints
		at 6 Months (%)
		95% CI
		at 12 Months (%)
		95% CI
		at 24 Months (%)
		95% CI

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
I-Renal impairment	
Mild (N=69)	
Overall survival by subgroup, months	
Subjects with events (%)	24 (34.8)
Subjects censored (%)	45 (65.2)
25th Percentile	17.6
95% CI	(13.3, 22.2)
Median	23.8
95% CI	(22.2, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	97.1
95% CI	(88.8, 99.3)
at 12 Months (%)	89.5
95% CI	(79.2, 94.8)
at 24 Months (%)	47.2
95% CI	(26.3, 65.5)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
I-Renal impairment	Moderate (N=25)	Overall survival by subgroup, months
		Subjects with events (%)
		Subjects censored (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Overall survival by subgroup at specific timepoints
		at 6 Months (%)
		95% CI
		at 12 Months (%)
		95% CI
		at 24 Months (%)
		95% CI

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
J-Hepatic impairment Normal (N=105)	
Overall survival by subgroup, months	
Subjects with events (%)	29 (27.6)
Subjects censored (%)	76 (72.4)
25th Percentile	22.2
95% CI	(16.2, 23.8)
Median	NE
95% CI	(23.8, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	94.2
95% CI	(87.5, 97.3)
at 12 Months (%)	89.2
95% CI	(81.3, 93.9)
at 24 Months (%)	62.6
95% CI	(48.0, 74.1)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
J-Hepatic impairment Mild (N=76)	
Overall survival by subgroup, months	
Subjects with events (%)	34 (44.7)
Subjects censored (%)	42 (55.3)
25th Percentile	14.1
95% CI	(9.7, 18.9)
Median	21.9
95% CI	(19.7, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	94.7
95% CI	(86.4, 98.0)
at 12 Months (%)	81.0
95% CI	(70.0, 88.3)
at 24 Months (%)	35.5
95% CI	(14.7, 57.2)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
K-Brain metastases Yes (N=24)	
Overall survival by subgroup, months	
Subjects with events (%)	6 (25.0)
Subjects censored (%)	18 (75.0)
25th Percentile	21.3
95% CI	(1.9, NE)
Median	NE
95% CI	(21.3, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	91.1
95% CI	(68.8, 97.7)
at 12 Months (%)	91.1
95% CI	(68.8, 97.7)
at 24 Months (%)	67.5
95% CI	(39.7, 84.6)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	No (N=160)	Overall survival by subgroup, months	Overall - EAS (5.4 mg/kg)
K-Brain metastases			
		Subjects with events (%)	59 (36.9)
		Subjects censored (%)	101 (63.1)
		25th Percentile	17.4
		95% CI	(13.3, 20.5)
		Median	24.6
		95% CI	(22.9, NE)
		Overall survival by subgroup at specific timepoints	
		at 6 Months (%)	94.3
		95% CI	(89.4, 97.0)
		at 12 Months (%)	84.7
		95% CI	(78.0, 89.5)
		at 24 Months (%)	50.5
		95% CI	(38.2, 61.5)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
L-Bone metastases	
Yes (N=53)	
Overall survival by subgroup, months	
Subjects with events (%)	20 (37.7)
Subjects censored (%)	33 (62.3)
25th Percentile	14.1
95% CI	(7.4, 21.9)
Median	24.6
95% CI	(21.9, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	90.2
95% CI	(78.1, 95.8)
at 12 Months (%)	78.4
95% CI	(64.3, 87.4)
at 24 Months (%)	56.2
95% CI	(38.2, 70.8)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	No (N=131)	Overall survival by subgroup, months	Overall - EAS (5.4 mg/kg)
L-Bone metastases			
		Subjects with events (%)	45 (34.4)
		Subjects censored (%)	86 (65.6)
		25th Percentile	18.0
		95% CI	(14.1, 21.1)
		Median	NE
		95% CI	(22.9, NE)
		Overall survival by subgroup at specific timepoints	
		at 6 Months (%)	95.4
		95% CI	(90.0, 97.9)
		at 12 Months (%)	88.2
		95% CI	(81.2, 92.7)
		at 24 Months (%)	51.6
		95% CI	(37.9, 63.8)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
M-History of visceral disease Yes (N=169)	
Overall survival by subgroup, months	
Subjects with events (%)	59 (34.9)
Subjects censored (%)	110 (65.1)
25th Percentile	17.4
95% CI	(13.3, 20.5)
Median	NE
95% CI	(23.1, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	94.0
95% CI	(89.1, 96.7)
at 12 Months (%)	84.7
95% CI	(78.3, 89.4)
at 24 Months (%)	54.9
95% CI	(43.7, 64.8)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
 - Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
M-History of visceral disease	No (N=15)
Overall survival by subgroup, months	
Subjects with events (%)	6 (40.0)
Subjects censored (%)	9 (60.0)
25th Percentile	22.9
95% CI	(3.9, 23.3)
Median	23.3
95% CI	(19.7, 24.6)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	93.3
95% CI	(61.3, 99.0)
at 12 Months (%)	93.3
95% CI	(61.3, 99.0)
at 24 Months (%)	25.5
95% CI	(1.1, 66.0)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
 Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
N-T-DM1 last therapy Yes (N=56)	
Overall survival by subgroup, months	
Subjects with events (%)	12 (21.4)
Subjects censored (%)	44 (78.6)
25th Percentile	23.8
95% CI	(17.7, NE)
Median	NE
95% CI	(23.8, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	96.2
95% CI	(85.7, 99.0)
at 12 Months (%)	92.3
95% CI	(80.7, 97.0)
at 24 Months (%)	68.4
95% CI	(40.1, 85.4)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
- Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
N-T-DM1 last therapy	No (N=128)	Overall survival by subgroup, months	
		Subjects with events (%)	53 (41.4)
		Subjects censored (%)	75 (58.6)
		25th Percentile	15.7
		95% CI	(11.6, 18.6)
		Median	23.1
		95% CI	(21.9, NE)
		Overall survival by subgroup at specific timepoints	
		at 6 Months (%)	92.9
		95% CI	(86.9, 96.3)
		at 12 Months (%)	82.6
		95% CI	(74.8, 88.2)
		at 24 Months (%)	46.7
		95% CI	(34.5, 58.0)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
0-Prior treatment lines < 3 lines (N=17)	
Overall survival by subgroup, months	
Subjects with events (%)	2 (11.8)
Subjects censored (%)	15 (88.2)
25th Percentile	24.6
95% CI	(4.1, NE)
Median	24.6
95% CI	(24.6, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	94.1
95% CI	(65.0, 99.1)
at 12 Months (%)	94.1
95% CI	(65.0, 99.1)
at 24 Months (%)	94.1
95% CI	(65.0, 99.1)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
0-Prior treatment lines >= 3 lines (N=167)	
Overall survival by subgroup, months	
Subjects with events (%)	63 (37.7)
Subjects censored (%)	104 (62.3)
25th Percentile	16.3
95% CI	(13.3, 19.7)
Median	23.8
95% CI	(22.8, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	93.9
95% CI	(89.0, 96.7)
at 12 Months (%)	84.5
95% CI	(78.0, 89.3)
at 24 Months (%)	49.1
95% CI	(37.6, 59.6)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
P-Best Response to T-DM1 therapy	
CR/PR/SD (N=79)	
Overall survival by subgroup, months	
Subjects with events (%)	25 (31.6)
Subjects censored (%)	54 (68.4)
25th Percentile	20.5
95% CI	(15.7, 22.9)
Median	NE
95% CI	(22.2, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	97.5
95% CI	(90.3, 99.4)
at 12 Months (%)	92.3
95% CI	(83.7, 96.5)
at 24 Months (%)	58.7
95% CI	(41.6, 72.4)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
- Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
P-Best Response to T-DM1 therapy	PD (N=66)
Overall survival by subgroup, months	
Subjects with events (%)	22 (33.3)
Subjects censored (%)	44 (66.7)
25th Percentile	17.4
95% CI	(8.0, 23.3)
Median	NE
95% CI	(22.8, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	90.7
95% CI	(80.4, 95.7)
at 12 Months (%)	80.9
95% CI	(68.8, 88.7)
at 24 Months (%)	55.4
95% CI	(37.6, 70.1)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
Q-Prior pertuzumab Yes (N=121)	
Overall survival by subgroup, months	
Subjects with events (%)	39 (32.2)
Subjects censored (%)	82 (67.8)
25th Percentile	18.0
95% CI	(13.3, 22.9)
Median	NE
95% CI	(23.1, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	95.8
95% CI	(90.2, 98.2)
at 12 Months (%)	86.3
95% CI	(78.5, 91.3)
at 24 Months (%)	54.3
95% CI	(39.7, 66.9)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	No (N=63)	Overall survival by subgroup, months	Overall - EAS (5.4 mg/kg)
Q-Prior pertuzumab			
		Subjects with events (%)	26 (41.3)
		Subjects censored (%)	37 (58.7)
		25th Percentile	16.2
		95% CI	(7.4, 19.9)
		Median	NE
		95% CI	(19.9, NE)
		Overall survival by subgroup at specific timepoints	
		at 6 Months (%)	90.3
		95% CI	(79.7, 95.5)
		at 12 Months (%)	83.7
		95% CI	(71.9, 90.9)
		at 24 Months (%)	51.0
		95% CI	(35.5, 64.6)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
R-Pertuzumab before line 3	Yes (N=51)
Overall survival by subgroup, months	
Subjects with events (%)	18 (35.3)
Subjects censored (%)	33 (64.7)
25th Percentile	17.4
95% CI	(7.6, 23.8)
Median	23.8
95% CI	(23.3, NE)
Overall survival by subgroup at specific timepoints	
at 6 Months (%)	92.2
95% CI	(80.4, 97.0)
at 12 Months (%)	82.2
95% CI	(68.5, 90.3)
at 24 Months (%)	46.2
95% CI	(18.8, 70.0)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3OS_EST0: Overall survival by subgroup
Enrolled Analysis Set

Subgroup	No (N=133)	Overall survival by subgroup, months	Overall - EAS (5.4 mg/kg)
R-Pertuzumab before line 3			
		Subjects with events (%)	47 (35.3)
		Subjects censored (%)	86 (64.7)
		25th Percentile	18.0
		95% CI	(13.7, 20.6)
		Median	NE
		95% CI	(22.8, NE)
		Overall survival by subgroup at specific timepoints	
		at 6 Months (%)	94.6
		95% CI	(89.1, 97.4)
		at 12 Months (%)	86.7
		95% CI	(79.5, 91.5)
		at 24 Months (%)	53.9
		95% CI	(41.9, 64.5)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Progressionsfreies Überleben (PFS) – weitere Untersuchungen

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
A-Age classification 1	
< 65 years (N=140)	
Progression free survival by subgroup, months	
Subjects with events (%)	53 (37.9)
Subjects censored (%)	87 (62.1)
25th Percentile	6.8
95% CI	(5.4, 9.7)
Median	22.2
95% CI	(13.8, NE)
Progression free survival by subgroup at specific timepoints	
at 6 Months (%)	78.7
95% CI	(70.2, 85.0)
at 12 Months (%)	63.9
95% CI	(54.2, 72.1)
at 24 Months (%)	45.5
95% CI	(32.7, 57.5)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
A-Age classification 1	>= 65 years (N=44)	Progression free survival by subgroup, months	
		Subjects with events (%)	17 (38.6)
		Subjects censored (%)	27 (61.4)
		25th Percentile	
		95% CI	(4.3, 16.4)
		Median	19.4
		95% CI	(12.4, NE)
		Progression free survival by subgroup at specific timepoints	
		at 6 Months (%)	85.5
		95% CI	(70.5, 93.2)
		at 12 Months (%)	71.4
		95% CI	(54.1, 83.2)
		at 24 Months (%)	36.0
		95% CI	(13.2, 59.7)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
B-Region	Asia (N=63)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	24 (38.1)
	Subjects censored (%)	39 (61.9)
	25th Percentile	6.7
	95% CI	(4.4, 12.7)
	Median	22.2
	95% CI	(12.7, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	80.7
	95% CI	(67.9, 88.8)
	at 12 Months (%)	65.4
	95% CI	(50.4, 76.8)
	at 24 Months (%)	45.1
	95% CI	(27.1, 61.4)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
B-Region	North America (N=53)	Progression free survival by subgroup, months
		Subjects with events (%) 15 (28.3)
		Subjects censored (%) 38 (71.7)
		25th Percentile 12.4
		95% CI (4.3, 22.9)
		Median 22.9
		95% CI (13.8, NE)
		Progression free survival by subgroup at specific timepoints
		at 6 Months (%) 84.3
		95% CI (69.8, 92.2)
		at 12 Months (%) 76.7
		95% CI (60.9, 86.8)
		at 24 Months (%) 49.0
		95% CI (22.8, 70.9)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
B-Region	EU (N=68)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	31 (45.6)
	Subjects censored (%)	37 (54.4)
	25th Percentile	6.6
	95% CI	(4.2, 8.3)
	Median	15.0
	95% CI	(8.3, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	77.0
	95% CI	(64.3, 85.7)
	at 12 Months (%)	58.0
	95% CI	(43.9, 69.7)
	at 24 Months (%)	NE
	95% CI	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
C-ECOG performance status	Status 0 (N=102)	Progression free survival by subgroup, months	
		Subjects with events (%)	38 (37.3)
		Subjects censored (%)	64 (62.7)
		25th Percentile	9.6
		95% CI	(6.3, 12.9)
		Median	22.9
		95% CI	(14.0, NE)
		Progression free survival by subgroup at specific timepoints	
		at 6 Months (%)	85.4
		95% CI	(76.6, 91.1)
		at 12 Months (%)	69.2
		95% CI	(58.1, 77.8)
		at 24 Months (%)	45.0
		95% CI	(27.8, 60.8)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
C-ECOG performance status	Status 1 (N=81)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	31 (38.3)
	Subjects censored (%)	50 (61.7)
	25th Percentile	6.0
	95% CI	(4.1, 8.5)
	Median	16.4
	95% CI	(10.6, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	74.1
	95% CI	(61.6, 83.1)
	at 12 Months (%)	61.6
	95% CI	(48.2, 72.5)
	at 24 Months (%)	40.1
	95% CI	(24.0, 55.7)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions < 5 cm (N=73)	
Progression free survival by subgroup, months	
Subjects with events (%)	20 (27.4)
Subjects censored (%)	53 (72.6)
25th Percentile	9.7
95% CI	(5.5, 22.2)
Median	22.9
95% CI	(22.2, NE)
Progression free survival by subgroup at specific timepoints	
at 6 Months (%)	82.3
95% CI	(70.3, 89.8)
at 12 Months (%)	72.4
95% CI	(58.7, 82.2)
at 24 Months (%)	44.6
95% CI	(16.7, 69.4)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions >= 5 cm (N=97)	
Progression free survival by subgroup, months	
Subjects with events (%)	47 (48.5)
Subjects censored (%)	50 (51.5)
25th Percentile	6.7
95% CI	(4.3, 8.3)
Median	12.9
95% CI	(9.6, 17.6)
Progression free survival by subgroup at specific timepoints	
at 6 Months (%)	75.9
95% CI	(65.4, 83.6)
at 12 Months (%)	57.9
95% CI	(46.1, 68.0)
at 24 Months (%)	33.7
95% CI	(22.0, 45.7)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
E-HER2 Status	IHC3+ (N=154)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	55 (35.7)
	Subjects censored (%)	99 (64.3)
	25th Percentile	7.2
	95% CI	(5.7, 12.4)
	Median	22.9
	95% CI	(16.4, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	81.9
	95% CI	(74.4, 87.4)
	at 12 Months (%)	68.2
	95% CI	(59.3, 75.6)
	at 24 Months (%)	45.9
	95% CI	(32.2, 58.6)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
E-HER2 Status	
ISH+ EXCEPT IHC3+ (N=28)	
Progression free survival by subgroup, months	
Subjects with events (%)	13 (46.4)
Subjects censored (%)	15 (53.6)
25th Percentile	5.1
95% CI	(2.7, 9.7)
Median	12.3
95% CI	(6.6, 15.2)
Progression free survival by subgroup at specific timepoints	
at 6 Months (%)	74.2
95% CI	(51.3, 87.5)
at 12 Months (%)	52.3
95% CI	(28.9, 71.3)
at 24 Months (%)	NE
95% CI	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
F-Estrogen receptors	Positive (N=93)	
		Progression free survival by subgroup, months
		Subjects with events (%) 39 (41.9)
		Subjects censored (%) 54 (58.1)
		25th Percentile 7.0
		95% CI (4.8, 10.5)
		Median 14.1
		95% CI (12.3, NE)
		Progression free survival by subgroup at specific timepoints
		at 6 Months (%) 79.6
		95% CI (69.3, 86.8)
		at 12 Months (%) 63.7
		95% CI (51.6, 73.5)
		at 24 Months (%) 40.9
		95% CI (27.9, 53.4)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
F-Estrogen receptors	Negative (N=88)	Progression free survival by subgroup, months
		Subjects with events (%) 29 (33.0)
		Subjects censored (%) 59 (67.0)
		25th Percentile 8.1
		95% CI (5.4, 17.6)
		Median 22.9
		95% CI (18.1, NE)
		Progression free survival by subgroup at specific timepoints
		at 6 Months (%) 81.9
		95% CI (71.4, 88.9)
		at 12 Months (%) 70.0
		95% CI (58.0, 79.2)
		at 24 Months (%) 48.0
		95% CI (30.0, 64.0)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Positive (N=51)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	21 (41.2)
	Subjects censored (%)	30 (58.8)
	25th Percentile	8.3
	95% CI	(4.1, 12.9)
	Median	15.2
	95% CI	(12.7, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	83.0
	95% CI	(68.9, 91.1)
	at 12 Months (%)	70.4
	95% CI	(54.3, 81.8)
	at 24 Months (%)	43.4
	95% CI	(26.3, 59.5)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Negative (N=125)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	45 (36.0)
	Subjects censored (%)	80 (64.0)
	25th Percentile	6.8
	95% CI	(5.4, 10.6)
	Median	22.2
	95% CI	(14.0, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	79.0
	95% CI	(70.1, 85.5)
	at 12 Months (%)	66.1
	95% CI	(55.9, 74.4)
	at 24 Months (%)	44.0
	95% CI	(28.5, 58.5)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
H-Hormone receptors	Positive (N=97)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	40 (41.2)
	Subjects censored (%)	57 (58.8)
	25th Percentile	7.0
	95% CI	(4.4, 10.6)
	Median	15.0
	95% CI	(12.7, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	79.4
	95% CI	(69.3, 86.5)
	at 12 Months (%)	64.3
	95% CI	(52.6, 73.8)
	at 24 Months (%)	42.8
	95% CI	(30.0, 54.9)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
H-Hormone receptors	Negative (N=83)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	28 (33.7)
	Subjects censored (%)	55 (66.3)
	25th Percentile	8.1
	95% CI	(5.4, 17.6)
	Median	22.9
	95% CI	(17.6, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	82.1
	95% CI	(71.1, 89.2)
	at 12 Months (%)	69.2
	95% CI	(56.6, 78.8)
	at 24 Months (%)	47.1
	95% CI	(29.2, 63.1)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
I-Renal impairment	Normal (N=90)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	41 (45.6)
	Subjects censored (%)	49 (54.4)
	25th Percentile	6.3
	95% CI	(4.3, 8.3)
	Median	17.6
	95% CI	(9.9, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	76.1
	95% CI	(65.5, 83.9)
	at 12 Months (%)	59.1
	95% CI	(47.5, 69.0)
	at 24 Months (%)	41.3
	95% CI	(26.4, 55.6)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
I-Renal impairment	Mild (N=69)	Progression free survival by subgroup, months	
		Subjects with events (%)	20 (29.0)
		Subjects censored (%)	49 (71.0)
		25th Percentile	12.7
		95% CI	(6.2, 16.4)
		Median	NE
		95% CI	(14.1, NE)
		Progression free survival by subgroup at specific timepoints	
		at 6 Months (%)	86.7
		95% CI	(75.2, 93.1)
		at 12 Months (%)	76.8
		95% CI	(63.2, 85.9)
		at 24 Months (%)	56.3
		95% CI	(39.7, 70.0)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
I-Renal impairment	Moderate (N=25)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	9 (36.0)
	Subjects censored (%)	16 (64.0)
	25th Percentile	8.5
	95% CI	(2.4, 12.7)
	Median	12.7
	95% CI	(8.5, 22.9)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	78.5
	95% CI	(52.0, 91.4)
	at 12 Months (%)	58.1
	95% CI	(26.3, 80.2)
	at 24 Months (%)	0.0
	95% CI	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
J-Hepatic impairment	Normal (N=105)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	38 (36.2)
	Subjects censored (%)	67 (63.8)
	25th Percentile	8.3
	95% CI	(6.2, 13.8)
	Median	22.2
	95% CI	(15.0, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	84.1
	95% CI	(75.1, 90.1)
	at 12 Months (%)	69.2
	95% CI	(58.3, 77.9)
	at 24 Months (%)	44.0
	95% CI	(28.2, 58.8)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
J-Hepatic impairment	Mild (N=76)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	30 (39.5)
	Subjects censored (%)	46 (60.5)
	25th Percentile	6.7
	95% CI	(4.3, 9.7)
	Median	16.4
	95% CI	(9.7, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	77.1
	95% CI	(64.8, 85.5)
	at 12 Months (%)	62.5
	95% CI	(48.9, 73.4)
	at 24 Months (%)	45.1
	95% CI	(30.5, 58.7)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
K-Brain metastases	Yes (N=24)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	9 (37.5)
	Subjects censored (%)	15 (62.5)
	25th Percentile	6.7
	95% CI	(1.4, 18.1)
	Median	NE
	95% CI	(6.7, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	77.6
	95% CI	(54.3, 90.0)
	at 12 Months (%)	61.8
	95% CI	(37.5, 79.0)
	at 24 Months (%)	53.0
	95% CI	(27.1, 73.4)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
K-Brain metastases	No (N=160)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	61 (38.1)
	Subjects censored (%)	99 (61.9)
	25th Percentile	7.1
	95% CI	(5.6, 10.5)
	Median	19.4
	95% CI	(14.0, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	80.7
	95% CI	(73.1, 86.4)
	at 12 Months (%)	66.4
	95% CI	(57.5, 73.9)
	at 24 Months (%)	40.8
	95% CI	(27.2, 54.0)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
L-Bone metastases	Yes (N=53)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	23 (43.4)
	Subjects censored (%)	30 (56.6)
	25th Percentile	7.2
	95% CI	(4.3, 12.3)
	Median	15.0
	95% CI	(10.6, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	78.3
	95% CI	(63.4, 87.7)
	at 12 Months (%)	63.9
	95% CI	(47.8, 76.2)
	at 24 Months (%)	NE
	95% CI	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
L-Bone metastases	No (N=131)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	47 (35.9)
	Subjects censored (%)	84 (64.1)
	25th Percentile	7.0
	95% CI	(5.4, 10.5)
	Median	22.9
	95% CI	(15.2, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	81.3
	95% CI	(72.9, 87.3)
	at 12 Months (%)	66.8
	95% CI	(56.8, 74.9)
	at 24 Months (%)	46.6
	95% CI	(31.9, 60.0)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
M-History of visceral disease	Yes (N=169)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	65 (38.5)
	Subjects censored (%)	104 (61.5)
	25th Percentile	7.0
	95% CI	(5.4, 9.7)
	Median	18.1
	95% CI	(14.0, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	79.4
	95% CI	(71.9, 85.0)
	at 12 Months (%)	64.6
	95% CI	(55.9, 71.9)
	at 24 Months (%)	48.1
	95% CI	(38.4, 57.1)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
M-History of visceral disease	No (N=15)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	5 (33.3)
	Subjects censored (%)	10 (66.7)
	25th Percentile	12.3
	95% CI	(5.5, 22.9)
	Median	22.2
	95% CI	(9.7, 22.9)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	92.3
	95% CI	(56.6, 98.9)
	at 12 Months (%)	80.8
	95% CI	(41.0, 95.0)
	at 24 Months (%)	0.0
	95% CI	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
N-T-DM1 last therapy	Yes (N=56)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	16 (28.6)
	Subjects censored (%)	40 (71.4)
	25th Percentile	12.7
	95% CI	(5.4, 22.2)
	Median	NE
	95% CI	(17.6, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	82.3
	95% CI	(68.7, 90.4)
	at 12 Months (%)	77.3
	95% CI	(62.5, 86.8)
	at 24 Months (%)	56.2
	95% CI	(33.0, 74.1)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
N-T-DM1 last therapy	No (N=128)	Progression free survival by subgroup, months	
		Subjects with events (%)	54 (42.2)
		Subjects censored (%)	74 (57.8)
		25th Percentile	6.7
		95% CI	(4.8, 8.5)
		Median	15.2
		95% CI	(12.3, 22.9)
		Progression free survival by subgroup at specific timepoints	
		at 6 Months (%)	79.7
		95% CI	(71.0, 86.0)
		at 12 Months (%)	60.8
		95% CI	(50.6, 69.6)
		at 24 Months (%)	37.1
		95% CI	(24.2, 50.0)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
0-Prior treatment lines	< 3 lines (N=17)	Progression free survival by subgroup, months	
		Subjects with events (%)	5 (29.4)
		Subjects censored (%)	12 (70.6)
		25th Percentile	16.8
		95% CI	(4.1, NE)
		Median	22.2
		95% CI	(16.8, NE)
		Progression free survival by subgroup at specific timepoints	
		at 6 Months (%)	88.2
		95% CI	(60.6, 96.9)
		at 12 Months (%)	88.2
		95% CI	(60.6, 96.9)
		at 24 Months (%)	NE
		95% CI	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
0-Prior treatment lines	>= 3 lines (N=167)	Progression free survival by subgroup, months	
		Subjects with events (%)	65 (38.9)
		Subjects censored (%)	102 (61.1)
		25th Percentile	6.8
		95% CI	(5.5, 9.6)
		Median	17.6
		95% CI	(12.9, NE)
		Progression free survival by subgroup at specific timepoints	
		at 6 Months (%)	79.5
		95% CI	(72.0, 85.2)
		at 12 Months (%)	62.8
		95% CI	(53.9, 70.5)
		at 24 Months (%)	41.9
		95% CI	(30.0, 53.3)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	32 (40.5)
	Subjects censored (%)	47 (59.5)
	25th Percentile	8.1
	95% CI	(6.2, 12.4)
	Median	19.4
	95% CI	(12.4, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	85.9
	95% CI	(75.3, 92.2)
	at 12 Months (%)	65.4
	95% CI	(52.1, 75.8)
	at 24 Months (%)	25.6
	95% CI	(6.4, 50.9)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
P-Best Response to T-DM1 therapy	PD (N=66)	Progression free survival by subgroup, months	
		Subjects with events (%)	28 (42.4)
		Subjects censored (%)	38 (57.6)
		25th Percentile	6.6
		95% CI	(4.3, 9.7)
		Median	17.6
		95% CI	(9.9, NE)
		Progression free survival by subgroup at specific timepoints	
		at 6 Months (%)	75.1
		95% CI	(62.2, 84.2)
		at 12 Months (%)	61.9
		95% CI	(48.0, 73.2)
		at 24 Months (%)	43.9
		95% CI	(28.6, 58.3)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
Q-Prior pertuzumab	Yes (N=121)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	47 (38.8)
	Subjects censored (%)	74 (61.2)
	25th Percentile	8.1
	95% CI	(5.4, 12.4)
	Median	19.4
	95% CI	(13.8, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	80.4
	95% CI	(71.5, 86.8)
	at 12 Months (%)	68.5
	95% CI	(58.4, 76.7)
	at 24 Months (%)	38.9
	95% CI	(23.0, 54.6)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
Q-Prior pertuzumab	No (N=63)	
	Progression free survival by subgroup, months	
	Subjects with events (%)	23 (36.5)
	Subjects censored (%)	40 (63.5)
	25th Percentile	7.0
	95% CI	(4.3, 9.7)
	Median	15.2
	95% CI	(9.7, NE)
	Progression free survival by subgroup at specific timepoints	
	at 6 Months (%)	80.2
	95% CI	(67.1, 88.6)
	at 12 Months (%)	60.2
	95% CI	(44.9, 72.5)
	at 24 Months (%)	49.5
	95% CI	(32.9, 64.0)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
R-Pertuzumab before line 3	Yes (N=51)	Progression free survival by subgroup, months	
		Subjects with events (%)	18 (35.3)
		Subjects censored (%)	33 (64.7)
		25th Percentile	8.5
		95% CI	(4.2, 16.8)
		Median	22.2
		95% CI	(12.7, NE)
		Progression free survival by subgroup at specific timepoints	
		at 6 Months (%)	80.2
		95% CI	(65.3, 89.1)
		at 12 Months (%)	72.6
		95% CI	(56.7, 83.5)
		at 24 Months (%)	NE
		95% CI	(NE, NE)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3PFS_EST0: Progression free survival by subgroup
Enrolled Analysis Set

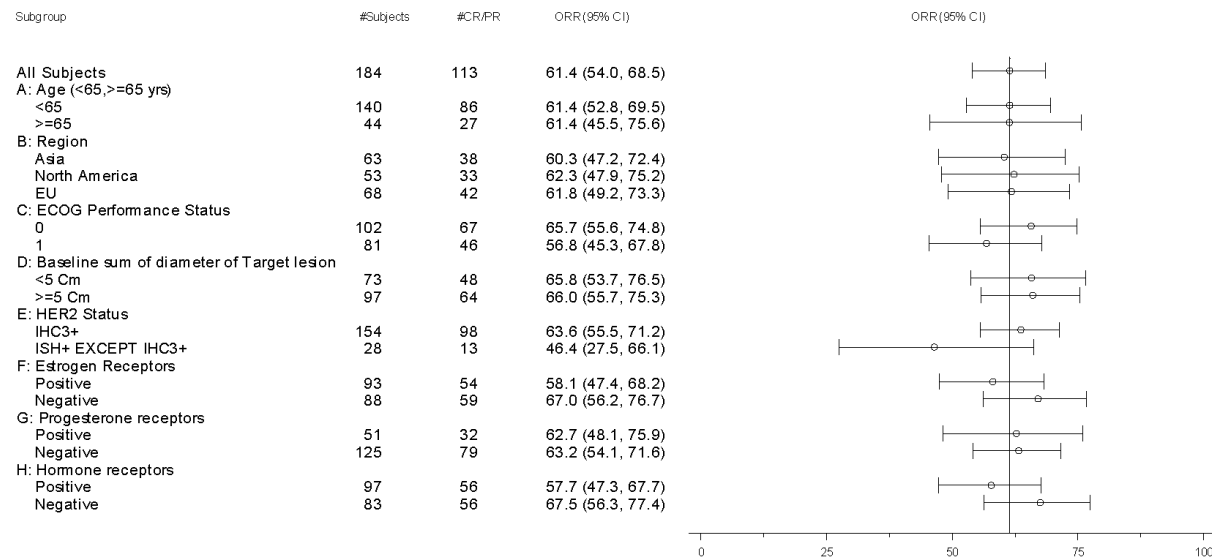
Subgroup			Overall - EAS (5.4 mg/kg)
R-Pertuzumab before line 3	No (N=133)	Progression free survival by subgroup, months	
		Subjects with events (%)	52 (39.1)
		Subjects censored (%)	81 (60.9)
		25th Percentile	7.0
		95% CI	(5.6, 9.7)
		Median	18.1
		95% CI	(12.9, NE)
		Progression free survival by subgroup at specific timepoints	
		at 6 Months (%)	80.5
		95% CI	(72.1, 86.6)
		at 12 Months (%)	62.9
		95% CI	(52.9, 71.5)
		at 24 Months (%)	42.8
		95% CI	(30.1, 55.0)

Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Tumoransprechen – weitere Untersuchungen

Gesamtansprechrates (ORR)

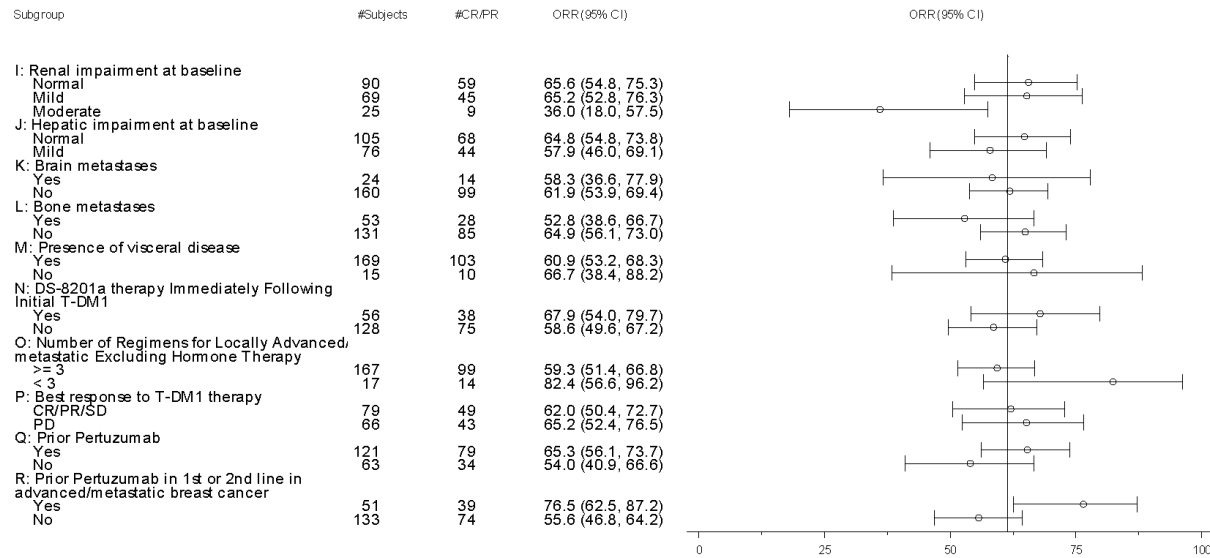
Figure F3ORR_ESP0: Forest plot of objective response rate by subgroup
Enrolled Analysis Set



Notes: CR=Complete Response, PR=Partial Response, SD=Stable Disease,
ORR = objective response rate (% of subjects with best overall response of CR and PR with confirmation by independent central review, based on RECIST criteria, Version 1.1).
The 2-sided 95% confidence intervals are based on the exact (Clopper-Pearson) binomial distribution.

Source Data: adam.adrs

Figure F3ORR_ESP0: Forest plot of objective response rate by subgroup
Enrolled Analysis Set



Notes: CR=Complete Response, PR=Partial Response, SD=Stable Disease,
ORR = objective response rate (% of subjects with best overall response of CR and PR with confirmation by independent central review, based on RECIST criteria, Version 1.1).
The 2-sided 95% confidence intervals are based on the exact (Clopper-Pearson) binomial distribution.

Source Data: adam.adrs

Beste prozentuale Veränderung des Tumordurchmessers (BPC)

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 08Jun2020

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
A-Age classification 1	< 65 years (N=140)	Baseline	
		n	130
		Mean	67.0
		Std. Dev.	43.00
		Median	59.5
		95% CI	(46.0,66.0)
		Min, Max	12,245
		Best % Change from Baseline	
		n	130
		Mean	-54.5
		Std. Dev.	31.57
		Median	-58.5
		95% CI	(-66.0,-49.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
A-Age classification 1	>= 65 years (N=44)	Baseline	
		n	40
		Mean	71.6
		Std. Dev.	48.62
		Median	56.0
		95% CI	(42.0,84.0)
		Min, Max	17,209
		Best % Change from Baseline	
		n	39
		Mean	-53.9
		Std. Dev.	30.44
		Median	-51.0
		95% CI	(-72.0,-39.0)
		Min, Max	-100,0

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
B-Region	Asia (N=63)	Baseline	
		n	58
		Mean	68.9
		Std. Dev.	42.71
		Median	59.5
		95% CI	(44.0, 68.0)
		Min, Max	12, 187
		Best % Change from Baseline	
		n	58
		Mean	-53.3
		Std. Dev.	33.39
		Median	-56.0
		95% CI	(-67.0, -43.0)
		Min, Max	-100, 22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
B-Region	EU (N=68)	Baseline	
		n	63
		Mean	70.8
		Std. Dev.	46.65
		Median	58.0
		95% CI	(45.0,69.0)
		Min, Max	15,245
		Best % Change from Baseline	
		n	62
		Mean	-55.7
		Std. Dev.	30.89
		Median	-58.5
		95% CI	(-69.0,-43.0)
		Min, Max	-100,0

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
B-Region	North America (N=53)	Baseline	
		n	49
		Mean	63.6
		Std. Dev.	43.53
		Median	55.0
		95% CI	(39.0,70.0)
		Min, Max	14,209
		Best % Change from Baseline	
		n	49
		Mean	-54.0
		Std. Dev.	29.53
		Median	-55.0
		95% CI	(-72.0,-39.0)
		Min, Max	-100,-2

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
C-ECOG performance status	Status 0 (N=102)	Baseline	
		n	92
		Mean	59.1
		Std. Dev.	37.54
		Median	52.0
		95% CI	(42.0,63.0)
		Min, Max	14,187
		Best % Change from Baseline	
		n	91
		Mean	-56.9
		Std. Dev.	30.39
		Median	-59.0
		95% CI	(-68.0,-51.0)
		Min, Max	-100,2

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
C-ECOG performance status	Status 1 (N=81)	Baseline	
		n	77
		Mean	79.0
		Std. Dev.	49.47
		Median	65.0
		95% CI	(54.0,82.0)
		Min, Max	12,245
		Best % Change from Baseline	
		n	77
		Mean	-51.5
		Std. Dev.	32.32
		Median	-51.0
		95% CI	(-65.0,-39.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions	
< 5 cm (N=73)	
Baseline	
n	73
Mean	31.6
Std. Dev.	10.75
Median	34.0
95% CI	(28.0,39.0)
Min, Max	12,49
Best % Change from Baseline	
n	72
Mean	-58.0
Std. Dev.	33.80
Median	-58.0
95% CI	(-77.0,-43.0)
Min, Max	-100,2

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions	>= 5 cm (N=97)	Baseline	
		n	97
		Mean	95.5
		Std. Dev.	39.95
		Median	83.0
		95% CI	(71.0,95.0)
		Min, Max	50,245
		Best % Change from Baseline	
		n	97
		Mean	-51.7
		Std. Dev.	29.05
		Median	-53.0
		95% CI	(-64.0,-44.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
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Program Name: T3BPC_ESC0.sas
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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
E-HER2 Status	IHC3+ (N=154)	Baseline	
		n	143
		Mean	69.8
		Std. Dev.	46.80
		Median	58.0
		95% CI	(46.0, 65.0)
		Min, Max	12, 245
		Best % Change from Baseline	
		n	143
		Mean	-56.1
		Std. Dev.	31.66
		Median	-59.0
		95% CI	(-67.0, -51.0)
		Min, Max	-100, 22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 08Jun2020

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Program Name: T3BPC_ESC0.sas
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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Baseline	
		n	25
		Mean	59.6
		Std. Dev.	26.39
		Median	66.0
		95% CI	(45.0,72.0)
		Min, Max	14,99
		Best % Change from Baseline	
		n	24
		Mean	-45.0
		Std. Dev.	28.45
		Median	-43.0
		95% CI	(-65.0,-20.0)
		Min, Max	-100,2

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
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Program Name: T3BPC_ESC0.sas
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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
F-Estrogen receptors	Negative (N=88)	Baseline	
		n	82
		Mean	70.5
		Std. Dev.	49.91
		Median	60.0
		95% CI	(43.0,66.0)
		Min, Max	15,245
		Best % Change from Baseline	
		n	81
		Mean	-59.1
		Std. Dev.	28.35
		Median	-61.0
		95% CI	(-68.0,-51.0)
		Min, Max	-100,0

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Program Name: T3BPC_ESC0.sas
Run Date: 11MAR21:15:37

Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
F-Estrogen receptors	Positive (N=93)	Baseline	
		n	85
		Mean	65.4
		Std. Dev.	38.69
		Median	55.0
		95% CI	(46.0,69.0)
		Min, Max	12,162
		Best % Change from Baseline	
		n	85
		Mean	-51.1
		Std. Dev.	32.98
		Median	-52.0
		95% CI	(-65.0,-39.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Negative (N=125)	Baseline	
		n	115
		Mean	71.2
		Std. Dev.	47.44
		Median	60.0
		95% CI	(46.0,66.0)
		Min, Max	15,245
	Best % Change from Baseline		
		n	114
		Mean	-55.9
		Std. Dev.	31.86
		Median	-60.0
		95% CI	(-68.0,-47.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Positive (N=51)	Baseline	
		n	47
		Mean	61.7
		Std. Dev.	37.35
		Median	54.0
		95% CI	(43.0,71.0)
		Min, Max	12,152
	Best % Change from Baseline		
		n	47
		Mean	-54.7
		Std. Dev.	29.54
		Median	-56.0
		95% CI	(-71.0,-43.0)
		Min, Max	-100,2

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
H-Hormone receptors	Negative (N=83)	Baseline	
		n	78
		Mean	72.3
		Std. Dev.	50.33
		Median	62.5
		95% CI	(43.0, 68.0)
		Min, Max	17, 245
	Best % Change from Baseline	n	77
		Mean	-58.9
		Std. Dev.	28.33
		Median	-61.0
		95% CI	(-69.0, -50.0)
		Min, Max	-100, 0

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
H-Hormone receptors	Positive (N=97)	Baseline	
		n	88
		Mean	64.0
		Std. Dev.	38.76
		Median	54.0
		95% CI	(45.0,67.0)
		Min, Max	12,162
	Best % Change from Baseline	n	88
		Mean	-51.5
		Std. Dev.	33.04
		Median	-52.5
		95% CI	(-65.0,-42.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
I-Renal impairment	Mild (N=69)	Baseline	
		n	62
		Mean	65.4
		Std. Dev.	39.01
		Median	63.0
		95% CI	(50.0,69.0)
		Min, Max	12,196
		Best % Change from Baseline	
		n	62
		Mean	-56.8
		Std. Dev.	32.54
		Median	-59.0
		95% CI	(-73.0,-44.0)
		Min, Max	-100,6

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
I-Renal impairment	Moderate (N=25)	Baseline	
		n	24
		Mean	72.5
		Std. Dev.	52.70
		Median	50.5
		95% CI	(37.0,116.0)
		Min, Max	17,209
		Best % Change from Baseline	
		n	23
		Mean	-40.9
		Std. Dev.	29.95
		Median	-35.0
		95% CI	(-61.0,-21.0)
		Min, Max	-100,9

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
I-Renal impairment	Normal (N=90)	Baseline	
		n	84
		Mean	68.7
		Std. Dev.	45.75
		Median	54.5
		95% CI	(44.0, 67.0)
		Min, Max	14, 245
		Best % Change from Baseline	
		n	84
		Mean	-56.3
		Std. Dev.	29.98
		Median	-59.0
		95% CI	(-68.0, -51.0)
		Min, Max	-100, 22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
J-Hepatic impairment	Mild (N=76)	Baseline	
		n	72
		Mean	74.7
		Std. Dev.	51.31
		Median	63.0
		95% CI	(53.0, 68.0)
		Min, Max	12, 245
		Best % Change from Baseline	
		n	71
		Mean	-50.0
		Std. Dev.	31.59
		Median	-54.0
		95% CI	(-65.0, -37.0)
		Min, Max	-100, 22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
J-Hepatic impairment	Normal (N=105)	Baseline	
		n	95
		Mean	62.6
		Std. Dev.	37.55
		Median	52.0
		95% CI	(42.0,66.0)
		Min, Max	14,159
		Best % Change from Baseline	
		n	95
		Mean	-57.9
		Std. Dev.	30.43
		Median	-58.0
		95% CI	(-71.0,-48.0)
		Min, Max	-100,9

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
K-Brain metastases	No (N=160)	Baseline	
		n	148
		Mean	66.9
		Std. Dev.	44.68
		Median	56.0
		95% CI	(46.0, 65.0)
		Min, Max	14, 245
		Best % Change from Baseline	
		n	148
		Mean	-54.9
		Std. Dev.	31.66
		Median	-59.0
		95% CI	(-65.0, -49.0)
		Min, Max	-100, 22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
K-Brain metastases	Yes (N=24)	Baseline	
		n	22
		Mean	76.0
		Std. Dev.	41.61
		Median	65.5
		95% CI	(44.0,99.0)
		Min, Max	12,151
		Best % Change from Baseline	
		n	21
		Mean	-50.7
		Std. Dev.	28.42
		Median	-45.0
		95% CI	(-72.0,-36.0)
		Min, Max	-100,-5

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
L-Bone metastases	No (N=131)	Baseline	
		n	122
		Mean	65.2
		Std. Dev.	42.77
		Median	55.5
		95% CI	(46.0, 66.0)
		Min, Max	12, 245
		Best % Change from Baseline	
		n	122
		Mean	-56.7
		Std. Dev.	30.34
		Median	-58.5
		95% CI	(-67.0, -49.0)
		Min, Max	-100, 22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
L-Bone metastases	Yes (N=53)	Baseline	
		n	48
		Mean	75.2
		Std. Dev.	47.64
		Median	61.0
		95% CI	(45.0,72.0)
		Min, Max	14,209
		Best % Change from Baseline	
		n	47
		Mean	-48.4
		Std. Dev.	32.99
		Median	-53.0
		95% CI	(-66.0,-32.0)
		Min, Max	-100,9

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
M-History of visceral disease	No (N=15)	Baseline	
		n	15
		Mean	37.4
		Std. Dev.	25.49
		Median	30.0
		95% CI	(17.0,46.0)
		Min, Max	14,95
		Best % Change from Baseline	
		n	15
		Mean	-59.3
		Std. Dev.	32.69
		Median	-61.0
		95% CI	(-100.0,-29.0)
		Min, Max	-100,0

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
M-History of visceral disease	Yes (N=169)	Baseline	
		n	155
		Mean	71.0
		Std. Dev.	44.64
		Median	63.0
		95% CI	(53.0, 66.0)
		Min, Max	12, 245
		Best % Change from Baseline	
		n	154
		Mean	-53.9
		Std. Dev.	31.15
		Median	-55.0
		95% CI	(-64.0, -47.0)
		Min, Max	-100, 22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
N-T-DM1 last therapy	No (N=128)	Baseline	
		n	118
		Mean	75.8
		Std. Dev.	47.63
		Median	65.0
		95% CI	(57.0,72.0)
		Min, Max	14,245
		Best % Change from Baseline	
		n	118
		Mean	-52.1
		Std. Dev.	31.01
		Median	-55.0
		95% CI	(-64.0,-43.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
N-T-DM1 last therapy	Yes (N=56)	Baseline	
		n	52
		Mean	50.5
		Std. Dev.	29.00
		Median	43.0
		95% CI	(37.0,52.0)
		Min, Max	12,148
		Best % Change from Baseline	
		n	51
		Mean	-59.6
		Std. Dev.	31.39
		Median	-59.0
		95% CI	(-72.0,-47.0)
		Min, Max	-100,6

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
0-Prior treatment lines	< 3 lines (N=17)	Baseline	
		n	16
		Mean	43.4
		Std. Dev.	23.94
		Median	40.5
		95% CI	(27.0,60.0)
		Min, Max	17,101
		Best % Change from Baseline	
		n	16
		Mean	-62.3
		Std. Dev.	27.97
		Median	-65.0
		95% CI	(-80.0,-42.0)
		Min, Max	-100,0

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
0-Prior treatment lines	>= 3 lines (N=167)	Baseline	
		n	154
		Mean	70.6
		Std. Dev.	45.16
		Median	63.0
		95% CI	(53.0,66.0)
		Min, Max	12,245
		Best % Change from Baseline	
		n	153
		Mean	-53.5
		Std. Dev.	31.51
		Median	-55.0
		95% CI	(-63.0,-45.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Baseline	
		n	71
		Mean	62.3
		Std. Dev.	41.43
		Median	46.0
		95% CI	(42.0,66.0)
		Min, Max	12,196
		Best % Change from Baseline	
		n	71
		Mean	-54.8
		Std. Dev.	32.95
		Median	-59.0
		95% CI	(-67.0,-43.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
P-Best Response to T-DM1 therapy	PD (N=66)	Baseline	
		n	64
		Mean	73.5
		Std. Dev.	45.06
		Median	64.5
		95% CI	(53.0,83.0)
		Min, Max	15,209
		Best % Change from Baseline	
		n	64
		Mean	-55.1
		Std. Dev.	29.21
		Median	-56.5
		95% CI	(-66.0,-43.0)
		Min, Max	-100,-2

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup	No (N=63)	Baseline	Overall - EAS (5.4 mg/kg)
Q-Prior pertuzumab		n	58
		Mean	65.3
		Std. Dev.	43.89
		Median	54.0
		95% CI	(44.0, 66.0)
		Min, Max	12, 196
		Best % Change from Baseline	
		n	57
		Mean	-50.9
		Std. Dev.	32.77
		Median	-52.0
		95% CI	(-61.0, -37.0)
		Min, Max	-100, 22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
Q-Prior pertuzumab	Yes (N=121)	Baseline	
		n	112
		Mean	69.5
		Std. Dev.	44.61
		Median	59.5
		95% CI	(47.0, 68.0)
		Min, Max	14, 245
		Best % Change from Baseline	
		n	112
		Mean	-56.1
		Std. Dev.	30.41
		Median	-60.0
		95% CI	(-67.0, -50.0)
		Min, Max	-100, 9

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
R-Pertuzumab before line 3	No (N=133)	Baseline	
		n	122
		Mean	67.4
		Std. Dev.	43.13
		Median	57.5
		95% CI	(47.0,66.0)
		Min, Max	12,196
		Best % Change from Baseline	
		n	121
		Mean	-52.3
		Std. Dev.	32.34
		Median	-50.0
		95% CI	(-59.0,-42.0)
		Min, Max	-100,22

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

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Table T3BPC_ESC0: Summary of best percentage change in sum of diameters by subgroups
Enrolled Analysis Set

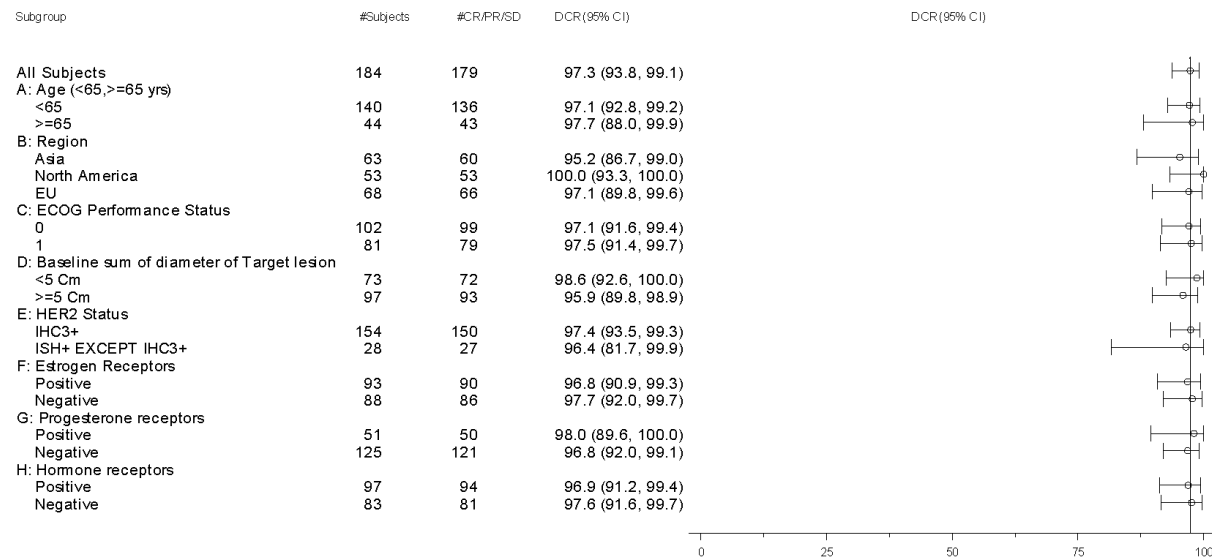
Subgroup		Overall - EAS (5.4 mg/kg)	
R-Pertuzumab before line 3	Yes (N=51)	Baseline	
		n	48
		Mean	69.8
		Std. Dev.	47.51
		Median	59.5
		95% CI	(42.0,80.0)
		Min, Max	15,245
		Best % Change from Baseline	
		n	48
		Mean	-59.5
		Std. Dev.	27.87
		Median	-64.5
		95% CI	(-72.0,-56.0)
		Min, Max	-100,2

Notes: Baseline is defined as the last non-missing value taken before randomization/registration date.

Source Data: adam.adtr

Rate der Krankheitskontrolle (DCR)

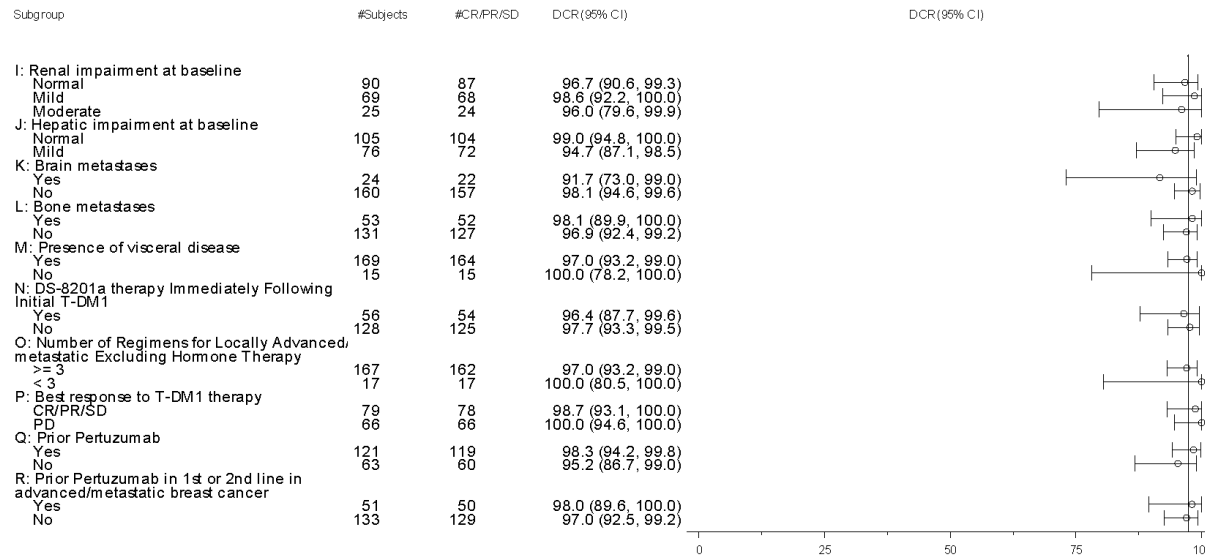
Figure F3DCR_ESP0: Forest plot of disease control rate by subgroup
Enrolled Analysis Set



Notes: CR=Complete Response, PR=Partial Response, SD=Stable Disease, DCR = disease control rate rate (% of subjects with best overall response of CR, PR and SD with confirmation by independent central review, based on RECIST criteria, Version 1.1).
The 2-sided 95% confidence intervals are based on the exact (Clopper-Pearson) binomial distribution.

Source Data: adam.adrs

Figure F3DCR_ESP0: Forest plot of disease control rate by subgroup
Enrolled Analysis Set



Notes: CR=Complete Response, PR=Partial Response, SD=Stable Disease, DCR = disease control rate rate (% of subjects with best overall response of CR, PR and SD with confirmation by independent central review, based on RECIST criteria, Version 1.1).
The 2-sided 95% confidence intervals are based on the exact (Clopper-Pearson) binomial distribution.

Source Data: adam.adrs

Zeit bis zum Ansprechen (TTR)

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
A-Age classification 1	< 65 years (N=140)	Time to response by subgroup, months	
		Subjects with events	85
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.5
A-Age classification 1	>= 65 years (N=44)	95% CI	(1.4, 2.6)
		Time to response by subgroup, months	
		Subjects with events	27
		25th Percentile	1.3
		95% CI	(1.2, 1.4)
		Median	2.7
		95% CI	(1.3, 2.9)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
B-Region	Asia (N=63)	Time to response by subgroup, months	
		Subjects with events	38
		25th Percentile	1.3
		95% CI	(1.2, 1.4)
		Median	1.5
		95% CI	(1.4, 2.7)
B-Region	North America (N=53)	Time to response by subgroup, months	
		Subjects with events	32
		25th Percentile	1.4
		95% CI	(1.2, 1.4)
		Median	1.5
		95% CI	(1.4, 2.7)
B-Region	EU (N=68)	Time to response by subgroup, months	
		Subjects with events	42
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	2.5
		95% CI	(1.4, 2.7)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
C-ECOG performance status	Status 0 (N=102)	Time to response by subgroup, months	
		Subjects with events	66
		25th Percentile	1.4
		95% CI	(1.3, 1.5)
		Median	2.6
C-ECOG performance status	Status 1 (N=81)	95% CI	(1.5, 2.7)
		Time to response by subgroup, months	
		Subjects with events	46
		25th Percentile	1.3
		95% CI	(1.2, 1.4)
C-ECOG performance status	Status 1 (N=81)	Median	1.4
		95% CI	(1.4, 2.6)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
D-Baseline sum of diameters of target lesions	< 5 cm (N=73)	Time to response by subgroup, months	
		Subjects with events	47
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.4
D-Baseline sum of diameters of target lesions	>= 5 cm (N=97)	95% CI	(1.4, 2.6)
		Time to response by subgroup, months	
		Subjects with events	64
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	2.6
		95% CI	(1.4, 2.7)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
E-HER2 Status	IHC3+ (N=154)	Time to response by subgroup, months	
		Subjects with events	97
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.6
		95% CI	(1.4, 2.7)
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Time to response by subgroup, months	
		Subjects with events	13
		25th Percentile	1.4
		95% CI	(1.2, 1.4)
		Median	1.4
		95% CI	(1.3, 2.7)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
F-Estrogen receptors	Positive (N=93)	Time to response by subgroup, months	
		Subjects with events	54
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.5
		95% CI	(1.4, 2.6)
F-Estrogen receptors	Negative (N=88)	Time to response by subgroup, months	
		Subjects with events	58
		25th Percentile	1.4
		95% CI	(1.2, 1.4)
		Median	2.6
		95% CI	(1.4, 2.7)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Positive (N=51)	Time to response by subgroup, months	
		Subjects with events	32
		25th Percentile	1.3
		95% CI	(1.3, 1.4)
		Median	1.4
		95% CI	(1.4, 2.6)
G-Progesterone receptors	Negative (N=125)	Time to response by subgroup, months	
		Subjects with events	78
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	2.6
		95% CI	(1.4, 2.7)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
H-Hormone receptors	Positive (N=97)	Time to response by subgroup, months	
		Subjects with events	56
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.5
		95% CI	(1.4, 2.6)
H-Hormone receptors	Negative (N=83)	Time to response by subgroup, months	
		Subjects with events	55
		25th Percentile	1.4
		95% CI	(1.2, 1.4)
		Median	2.6
		95% CI	(1.4, 2.7)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
I-Renal impairment	Normal (N=90)	Time to response by subgroup, months	
		Subjects with events	59
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.6
		95% CI	(1.4, 2.6)
I-Renal impairment	Mild (N=69)	Time to response by subgroup, months	
		Subjects with events	44
		25th Percentile	1.3
		95% CI	(1.2, 1.4)
		Median	1.5
		95% CI	(1.4, 2.7)
I-Renal impairment	Moderate (N=25)	Time to response by subgroup, months	
		Subjects with events	9
		25th Percentile	1.4
		95% CI	(1.2, 1.5)
		Median	1.5
		95% CI	(1.2, 2.8)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
J-Hepatic impairment	Normal (N=105)	Time to response by subgroup, months	
		Subjects with events	68
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.5
		95% CI	(1.4, 2.7)
J-Hepatic impairment	Mild (N=76)	Time to response by subgroup, months	
		Subjects with events	43
		25th Percentile	1.3
		95% CI	(1.2, 1.4)
		Median	2.6
		95% CI	(1.4, 2.7)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
K-Brain metastases	Yes (N=24)	Time to response by subgroup, months	
		Subjects with events	14
		25th Percentile	1.3
		95% CI	(1.1, 2.6)
		Median	2.7
K-Brain metastases	No (N=160)	95% CI	(1.3, 4.1)
		Time to response by subgroup, months	
		Subjects with events	98
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.5
		95% CI	(1.4, 2.6)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
L-Bone metastases	Yes (N=53)	Time to response by subgroup, months	
		Subjects with events	28
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	2.6
L-Bone metastases	No (N=131)	95% CI	(1.4, 2.8)
		Time to response by subgroup, months	
		Subjects with events	84
		25th Percentile	1.3
		95% CI	(1.3, 1.4)
		Median	1.5
		95% CI	(1.4, 2.6)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
M-History of visceral disease	Yes (N=169)	Time to response by subgroup, months	
		Subjects with events	102
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.6
		95% CI	(1.4, 2.6)
M-History of visceral disease	No (N=15)	Time to response by subgroup, months	
		Subjects with events	10
		25th Percentile	1.4
		95% CI	(1.2, 2.6)
		Median	2.1
		95% CI	(1.2, 2.7)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
N-T-DM1 last therapy	Yes (N=56)	Time to response by subgroup, months	
		Subjects with events	37
		25th Percentile	1.4
		95% CI	(1.2, 1.4)
		Median	2.6
N-T-DM1 last therapy	No (N=128)	95% CI	(1.4, 2.7)
		Time to response by subgroup, months	
		Subjects with events	75
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.5
		95% CI	(1.4, 2.6)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
0-Prior treatment lines	< 3 lines (N=17)	Time to response by subgroup, months	
		Subjects with events	14
		25th Percentile	1.2
		95% CI	(1.2, 1.3)
		Median	1.4
		95% CI	(1.2, 2.7)
0-Prior treatment lines	>= 3 lines (N=167)	Time to response by subgroup, months	
		Subjects with events	98
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	2.0
		95% CI	(1.4, 2.7)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Time to response by subgroup, months	
		Subjects with events	48
		25th Percentile	1.4
		95% CI	(1.2, 1.4)
		Median	1.5
P-Best Response to T-DM1 therapy	PD (N=66)	95% CI	(1.4, 2.7)
		Time to response by subgroup, months	
		Subjects with events	43
		25th Percentile	1.3
		95% CI	(1.2, 1.4)
		Median	1.4
		95% CI	(1.4, 2.7)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup			Overall - EAS (5.4 mg/kg)
Q-Prior pertuzumab	Yes (N=121)	Time to response by subgroup, months	
		Subjects with events	78
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.6
Q-Prior pertuzumab	No (N=63)	95% CI	(1.4, 2.7)
		Time to response by subgroup, months	
		Subjects with events	34
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	1.5
		95% CI	(1.4, 2.7)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3TTR_EST0: Time to response by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
R-Pertuzumab before line 3	Yes (N=51)	Time to response by subgroup, months	
		Subjects with events	39
		25th Percentile	1.3
		95% CI	(1.2, 1.4)
		Median	1.4
R-Pertuzumab before line 3	No (N=133)	95% CI	(1.3, 2.6)
		Time to response by subgroup, months	
		Subjects with events	73
		25th Percentile	1.4
		95% CI	(1.3, 1.4)
		Median	2.6
		95% CI	(1.4, 2.7)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Dauer des Ansprechens (DoR)

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
A-Age classification 1 < 65 years (N=140)	
Duration of response by subgroup, months	
Subjects with CR/PR	85
Subjects with events (%)	27 (31.8)
Subjects censored (%)	58 (68.2)
Ongoing without PD (%)	23 (27.1)
Other (%)	35 (41.2)
25th Percentile	9.0
95% CI	(5.6, 13.8)
Median	NE
95% CI	(14.8, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	83.5
95% CI	(72.6, 90.3)
at 12 Months (%)	65.7
95% CI	(52.9, 75.9)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
A-Age classification 1 >= 65 years (N=44)	
Duration of response by subgroup, months	
Subjects with CR/PR	27
Subjects with events (%)	12 (44.4)
Subjects censored (%)	15 (55.6)
Ongoing without PD (%)	4 (14.8)
Other (%)	11 (40.7)
25th Percentile	9.7
95% CI	(2.8, 15.5)
Median	15.5
95% CI	(9.7, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	76.0
95% CI	(54.0, 88.4)
at 12 Months (%)	64.7
95% CI	(40.7, 81.1)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
B-Region	Asia (N=63)	Duration of response by subgroup, months
		Subjects with CR/PR
		Subjects with events (%)
		Subjects censored (%)
		Ongoing without PD (%)
		Other (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Duration of response by subgroup at specific timepoints
		at 6 Months (%)
		95% CI
		at 12 Months (%)
		95% CI
		at 24 Months (%)
		95% CI

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
B-Region	North America (N=53)	Duration of response by subgroup, months
		Subjects with CR/PR
		Subjects with events (%)
		Subjects censored (%)
		Ongoing without PD (%)
		Other (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Duration of response by subgroup at specific timepoints
		at 6 Months (%)
		95% CI
		at 12 Months (%)
		95% CI
		at 24 Months (%)
		95% CI

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
B-Region	EU (N=68)	
	Duration of response by subgroup, months	
	Subjects with CR/PR	42
	Subjects with events (%)	16 (38.1)
	Subjects censored (%)	26 (61.9)
	Ongoing without PD (%)	11 (26.2)
	Other (%)	15 (35.7)
	25th Percentile	6.9
	95% CI	(3.7, 10.6)
	Median	18.2
	95% CI	(9.7, NE)
	Duration of response by subgroup at specific timepoints	
	at 6 Months (%)	75.8
	95% CI	(58.5, 86.6)
	at 12 Months (%)	60.0
	95% CI	(41.7, 74.2)
	at 24 Months (%)	NE
	95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)	
C-ECOG performance status	Status 0 (N=102)	Duration of response by subgroup, months
		Subjects with CR/PR
		Subjects with events (%)
		Subjects censored (%)
		Ongoing without PD (%)
		Other (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Duration of response by subgroup at specific timepoints
		at 6 Months (%)
		95% CI
		at 12 Months (%)
		95% CI
		at 24 Months (%)
		95% CI

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
C-ECOG performance status	Status 1 (N=81)	
	Duration of response by subgroup, months	
	Subjects with CR/PR	46
	Subjects with events (%)	16 (34.8)
	Subjects censored (%)	30 (65.2)
	Ongoing without PD (%)	12 (26.1)
	Other (%)	18 (39.1)
	25th Percentile	7.9
	95% CI	(4.6, 15.0)
	Median	20.8
	95% CI	(11.5, NE)
	Duration of response by subgroup at specific timepoints	
	at 6 Months (%)	79.8
	95% CI	(63.6, 89.4)
	at 12 Months (%)	64.3
	95% CI	(46.2, 77.8)
	at 24 Months (%)	NE
	95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions	
< 5 cm (N=73)	
Duration of response by subgroup, months	
Subjects with CR/PR	47
Subjects with events (%)	11 (23.4)
Subjects censored (%)	36 (76.6)
Ongoing without PD (%)	14 (29.8)
Other (%)	22 (46.8)
25th Percentile	15.5
95% CI	(5.7, 21.5)
Median	21.5
95% CI	(20.8, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	87.8
95% CI	(73.0, 94.8)
at 12 Months (%)	81.8
95% CI	(65.2, 91.0)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
D-Baseline sum of diameters of target lesions	
>= 5 cm (N=97)	
Duration of response by subgroup, months	
Subjects with CR/PR	64
Subjects with events (%)	28 (43.8)
Subjects censored (%)	36 (56.3)
Ongoing without PD (%)	12 (18.8)
Other (%)	24 (37.5)
25th Percentile	6.9
95% CI	(5.4, 9.7)
Median	15.0
95% CI	(9.7, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	76.9
95% CI	(63.6, 85.9)
at 12 Months (%)	53.8
95% CI	(39.0, 66.4)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
 Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
E-HER2 Status	IHC3+ (N=154)	Duration of response by subgroup, months	
		Subjects with CR/PR	97
		Subjects with events (%)	30 (30.9)
		Subjects censored (%)	67 (69.1)
		Ongoing without PD (%)	26 (26.8)
		Other (%)	41 (42.3)
		25th Percentile	10.6
		95% CI	(5.7, 16.9)
		Median	21.5
		95% CI	(16.9, NE)
		Duration of response by subgroup at specific timepoints	
		at 6 Months (%)	83.4
		95% CI	(73.5, 89.8)
		at 12 Months (%)	70.7
		95% CI	(59.0, 79.6)
		at 24 Months (%)	NE
		95% CI	(NE, NE)

Table is considering only patients with response.
 Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
 log-log transformation of rates was applied.
 Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
E-HER2 Status	
ISH+ EXCEPT IHC3+ (N=28)	
Duration of response by subgroup, months	
Subjects with CR/PR	13
Subjects with events (%)	7 (53.8)
Subjects censored (%)	6 (46.2)
Ongoing without PD (%)	1 (7.7)
Other (%)	5 (38.5)
25th Percentile	3.7
95% CI	(2.8, 10.0)
Median	10.0
95% CI	(2.9, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	74.1
95% CI	(39.1, 90.9)
at 12 Months (%)	42.3
95% CI	(13.5, 69.1)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
F-Estrogen receptors Positive (N=93)	
Duration of response by subgroup, months	
Subjects with CR/PR	54
Subjects with events (%)	20 (37.0)
Subjects censored (%)	34 (63.0)
Ongoing without PD (%)	10 (18.5)
Other (%)	24 (44.4)
25th Percentile	9.0
95% CI	(5.5, 10.6)
Median	15.0
95% CI	(10.0, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	82.5
95% CI	(67.9, 90.9)
at 12 Months (%)	55.7
95% CI	(38.8, 69.6)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
F-Estrogen receptors Negative (N=88)	
Duration of response by subgroup, months	
Subjects with CR/PR	58
Subjects with events (%)	19 (32.8)
Subjects censored (%)	39 (67.2)
Ongoing without PD (%)	17 (29.3)
Other (%)	22 (37.9)
25th Percentile	9.7
95% CI	(4.5, 18.2)
Median	21.5
95% CI	(16.9, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	80.7
95% CI	(67.0, 89.2)
at 12 Months (%)	74.2
95% CI	(59.6, 84.2)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Positive (N=51)	
	Duration of response by subgroup, months	
	Subjects with CR/PR	32
	Subjects with events (%)	13 (40.6)
	Subjects censored (%)	19 (59.4)
	Ongoing without PD (%)	6 (18.8)
	Other (%)	13 (40.6)
	25th Percentile	5.7
	95% CI	(4.6, 10.6)
	Median	15.0
	95% CI	(7.4, NE)
	Duration of response by subgroup at specific timepoints	
	at 6 Months (%)	74.8
	95% CI	(54.1, 87.2)
	at 12 Months (%)	58.8
	95% CI	(37.8, 74.8)
	at 24 Months (%)	NE
	95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
G-Progesterone receptors	Negative (N=125)	
	Duration of response by subgroup, months	
	Subjects with CR/PR	78
	Subjects with events (%)	25 (32.1)
	Subjects censored (%)	53 (67.9)
	Ongoing without PD (%)	21 (26.9)
	Other (%)	32 (41.0)
	25th Percentile	9.7
	95% CI	(5.6, 16.9)
	Median	21.5
	95% CI	(16.9, NE)
	Duration of response by subgroup at specific timepoints	
	at 6 Months (%)	83.8
	95% CI	(72.6, 90.7)
	at 12 Months (%)	69.3
	95% CI	(55.8, 79.3)
	at 24 Months (%)	NE
	95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
H-Hormone receptors	
Positive (N=97)	
Duration of response by subgroup, months	
Subjects with CR/PR	56
Subjects with events (%)	20 (35.7)
Subjects censored (%)	36 (64.3)
Ongoing without PD (%)	11 (19.6)
Other (%)	25 (44.6)
25th Percentile	9.0
95% CI	(5.5, 11.4)
Median	NE
95% CI	(10.0, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	83.2
95% CI	(69.2, 91.3)
at 12 Months (%)	57.9
95% CI	(41.4, 71.3)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
H-Hormone receptors	
Negative (N=83)	
Duration of response by subgroup, months	
Subjects with CR/PR	55
Subjects with events (%)	19 (34.5)
Subjects censored (%)	36 (65.5)
Ongoing without PD (%)	16 (29.1)
Other (%)	20 (36.4)
25th Percentile	8.3
95% CI	(4.5, 18.2)
Median	21.5
95% CI	(16.9, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	79.5
95% CI	(65.2, 88.5)
at 12 Months (%)	72.5
95% CI	(57.2, 83.1)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
I-Renal impairment	Normal (N=90)	Duration of response by subgroup, months
		Subjects with CR/PR
		Subjects with events (%)
		Subjects censored (%)
		Ongoing without PD (%)
		Other (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Duration of response by subgroup at specific timepoints
		at 6 Months (%)
		95% CI
		at 12 Months (%)
		95% CI
		at 24 Months (%)
		95% CI

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
I-Renal impairment	Mild (N=69)	
	Duration of response by subgroup, months	
	Subjects with CR/PR	44
	Subjects with events (%)	11 (25.0)
	Subjects censored (%)	33 (75.0)
	Ongoing without PD (%)	10 (22.7)
	Other (%)	23 (52.3)
	25th Percentile	10.6
	95% CI	(5.6, NE)
	Median	NE
	95% CI	(15.0, NE)
	Duration of response by subgroup at specific timepoints	
	at 6 Months (%)	89.1
	95% CI	(73.3, 95.8)
	at 12 Months (%)	70.6
	95% CI	(50.3, 83.8)
	at 24 Months (%)	NE
	95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)
I-Renal impairment	Moderate (N=25)	Duration of response by subgroup, months
		Subjects with CR/PR
		Subjects with events (%)
		Subjects censored (%)
		Ongoing without PD (%)
		Other (%)
		25th Percentile
		95% CI
		Median
		95% CI
		Duration of response by subgroup at specific timepoints
		at 6 Months (%)
		95% CI
		at 12 Months (%)
		95% CI
		at 24 Months (%)
		95% CI

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
J-Hepatic impairment Normal (N=105)	
Duration of response by subgroup, months	
Subjects with CR/PR	68
Subjects with events (%)	23 (33.8)
Subjects censored (%)	45 (66.2)
Ongoing without PD (%)	18 (26.5)
Other (%)	27 (39.7)
25th Percentile	9.7
95% CI	(5.7, 15.5)
Median	21.5
95% CI	(14.8, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	85.2
95% CI	(73.5, 92.1)
at 12 Months (%)	69.4
95% CI	(55.2, 79.9)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
J-Hepatic impairment Mild (N=76)	
Duration of response by subgroup, months	
Subjects with CR/PR	43
Subjects with events (%)	16 (37.2)
Subjects censored (%)	27 (62.8)
Ongoing without PD (%)	9 (20.9)
Other (%)	18 (41.9)
25th Percentile	5.7
95% CI	(4.2, 11.5)
Median	18.2
95% CI	(10.0, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	74.9
95% CI	(57.2, 86.1)
at 12 Months (%)	59.4
95% CI	(41.0, 73.7)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
K-Brain metastases Yes (N=24)	
Duration of response by subgroup, months	
Subjects with CR/PR	14
Subjects with events (%)	4 (28.6)
Subjects censored (%)	10 (71.4)
Ongoing without PD (%)	4 (28.6)
Other (%)	6 (42.9)
25th Percentile	16.9
95% CI	(2.0, NE)
Median	NE
95% CI	(5.7, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	76.0
95% CI	(42.2, 91.6)
at 12 Months (%)	76.0
95% CI	(42.2, 91.6)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	No (N=160)	Overall - EAS (5.4 mg/kg)
K-Brain metastases		
Duration of response by subgroup, months		
Subjects with CR/PR		98
Subjects with events (%)		35 (35.7)
Subjects censored (%)		63 (64.3)
Ongoing without PD (%)		23 (23.5)
Other (%)		40 (40.8)
25th Percentile		9.0
95% CI		(5.6, 11.5)
Median		20.8
95% CI		(14.8, NE)
Duration of response by subgroup at specific timepoints		
at 6 Months (%)		82.4
95% CI		(72.4, 89.0)
at 12 Months (%)		64.2
95% CI		(52.4, 73.9)
at 24 Months (%)		NE
95% CI		(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
L-Bone metastases Yes (N=53)	
Duration of response by subgroup, months	
Subjects with CR/PR	28
Subjects with events (%)	12 (42.9)
Subjects censored (%)	16 (57.1)
Ongoing without PD (%)	5 (17.9)
Other (%)	11 (39.3)
25th Percentile	7.9
95% CI	(4.5, 11.4)
Median	15.0
95% CI	(7.9, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	83.7
95% CI	(62.2, 93.6)
at 12 Months (%)	56.1
95% CI	(33.4, 73.7)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	No (N=131)	Overall - EAS (5.4 mg/kg)
L-Bone metastases		
Duration of response by subgroup, months		
Subjects with CR/PR		84
Subjects with events (%)		27 (32.1)
Subjects censored (%)		57 (67.9)
Ongoing without PD (%)		22 (26.2)
Other (%)		35 (41.7)
25th Percentile		9.7
95% CI		(5.6, 15.5)
Median		21.5
95% CI		(15.5, NE)
Duration of response by subgroup at specific timepoints		
at 6 Months (%)		80.7
95% CI		(69.5, 88.1)
at 12 Months (%)		69.1
95% CI		(56.4, 78.8)
at 24 Months (%)		NE
95% CI		(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
M-History of visceral disease Yes (N=169)	
Duration of response by subgroup, months	
Subjects with CR/PR	102
Subjects with events (%)	34 (33.3)
Subjects censored (%)	68 (66.7)
Ongoing without PD (%)	26 (25.5)
Other (%)	42 (41.2)
25th Percentile	9.0
95% CI	(5.6, 13.8)
Median	NE
95% CI	(15.0, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	81.0
95% CI	(71.2, 87.8)
at 12 Months (%)	66.6
95% CI	(55.2, 75.7)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
M-History of visceral disease No (N=15)	
Duration of response by subgroup, months	
Subjects with CR/PR	10
Subjects with events (%)	5 (50.0)
Subjects censored (%)	5 (50.0)
Ongoing without PD (%)	1 (10.0)
Other (%)	4 (40.0)
25th Percentile	8.3
95% CI	(2.8, 20.8)
Median	20.8
95% CI	(2.8, 21.5)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	90.0
95% CI	(47.3, 98.5)
at 12 Months (%)	54.0
95% CI	(12.7, 83.2)
at 24 Months (%)	0.0
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
N-T-DM1 last therapy	Yes (N=56)	Duration of response by subgroup, months	
		Subjects with CR/PR	37
		Subjects with events (%)	11 (29.7)
		Subjects censored (%)	26 (70.3)
		Ongoing without PD (%)	12 (32.4)
		Other (%)	14 (37.8)
		25th Percentile	11.5
		95% CI	(3.7, 20.8)
		Median	NE
		95% CI	(15.5, NE)
		Duration of response by subgroup at specific timepoints	
		at 6 Months (%)	84.9
		95% CI	(67.3, 93.4)
		at 12 Months (%)	74.7
		95% CI	(55.6, 86.5)
		at 24 Months (%)	NE
		95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
N-T-DM1 last therapy No (N=128)	
Duration of response by subgroup, months	
Subjects with CR/PR	75
Subjects with events (%)	28 (37.3)
Subjects censored (%)	47 (62.7)
Ongoing without PD (%)	15 (20.0)
Other (%)	32 (42.7)
25th Percentile	8.3
95% CI	(5.6, 10.6)
Median	18.2
95% CI	(10.6, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	79.9
95% CI	(67.8, 87.8)
at 12 Months (%)	60.7
95% CI	(46.6, 72.1)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
0-Prior treatment lines < 3 lines (N=17)	
Duration of response by subgroup, months	
Subjects with CR/PR	14
Subjects with events (%)	5 (35.7)
Subjects censored (%)	9 (64.3)
Ongoing without PD (%)	5 (35.7)
Other (%)	4 (28.6)
25th Percentile	15.5
95% CI	(2.8, NE)
Median	20.8
95% CI	(11.5, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	85.7
95% CI	(53.9, 96.2)
at 12 Months (%)	77.9
95% CI	(45.9, 92.3)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
0-Prior treatment lines >= 3 lines (N=167)	
Duration of response by subgroup, months	
Subjects with CR/PR	98
Subjects with events (%)	34 (34.7)
Subjects censored (%)	64 (65.3)
Ongoing without PD (%)	22 (22.4)
Other (%)	42 (42.9)
25th Percentile	8.3
95% CI	(5.6, 10.6)
Median	21.5
95% CI	(13.8, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	80.7
95% CI	(70.3, 87.7)
at 12 Months (%)	63.2
95% CI	(51.1, 73.1)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
P-Best Response to T-DM1 therapy	
CR/PR/SD (N=79)	
Duration of response by subgroup, months	
Subjects with CR/PR	48
Subjects with events (%)	21 (43.8)
Subjects censored (%)	27 (56.3)
Ongoing without PD (%)	11 (22.9)
Other (%)	16 (33.3)
25th Percentile	9.0
95% CI	(5.5, 11.5)
Median	18.2
95% CI	(11.4, 21.5)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	82.9
95% CI	(67.4, 91.4)
at 12 Months (%)	61.6
95% CI	(44.5, 74.9)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
P-Best Response to T-DM1 therapy	PD (N=66)
Duration of response by subgroup, months	
Subjects with CR/PR	43
Subjects with events (%)	15 (34.9)
Subjects censored (%)	28 (65.1)
Ongoing without PD (%)	9 (20.9)
Other (%)	19 (44.2)
25th Percentile	5.7
95% CI	(3.7, 14.8)
Median	NE
95% CI	(9.7, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	74.6
95% CI	(57.8, 85.5)
at 12 Months (%)	64.9
95% CI	(46.9, 78.1)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	Overall - EAS (5.4 mg/kg)
Q-Prior pertuzumab Yes (N=121)	
Duration of response by subgroup, months	
Subjects with CR/PR	78
Subjects with events (%)	27 (34.6)
Subjects censored (%)	51 (65.4)
Ongoing without PD (%)	18 (23.1)
Other (%)	33 (42.3)
25th Percentile	9.7
95% CI	(5.7, 15.0)
Median	20.8
95% CI	(15.0, NE)
Duration of response by subgroup at specific timepoints	
at 6 Months (%)	85.2
95% CI	(74.2, 91.8)
at 12 Months (%)	67.5
95% CI	(54.0, 77.8)
at 24 Months (%)	NE
95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	No (N=63)	Overall - EAS (5.4 mg/kg)
Q-Prior pertuzumab		
Duration of response by subgroup, months		
Subjects with CR/PR		34
Subjects with events (%)		12 (35.3)
Subjects censored (%)		22 (64.7)
Ongoing without PD (%)		9 (26.5)
Other (%)		13 (38.2)
25th Percentile		5.7
95% CI		(4.2, 13.8)
Median		NE
95% CI		(9.0, NE)
Duration of response by subgroup at specific timepoints		
at 6 Months (%)		73.5
95% CI		(53.8, 85.8)
at 12 Months (%)		61.9
95% CI		(41.6, 77.0)
at 24 Months (%)		NE
95% CI		(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup		Overall - EAS (5.4 mg/kg)	
R-Pertuzumab before line 3	Yes (N=51)	Duration of response by subgroup, months	
		Subjects with CR/PR	39
		Subjects with events (%)	14 (35.9)
		Subjects censored (%)	25 (64.1)
		Ongoing without PD (%)	9 (23.1)
		Other (%)	16 (41.0)
		25th Percentile	9.7
		95% CI	(2.9, 15.5)
		Median	20.8
		95% CI	(11.5, NE)
		Duration of response by subgroup at specific timepoints	
		at 6 Months (%)	81.2
		95% CI	(64.6, 90.6)
		at 12 Months (%)	67.5
		95% CI	(48.4, 80.7)
		at 24 Months (%)	NE
		95% CI	(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Table T3DOR_EST0: Duration of response by subgroup
Enrolled Analysis Set

Subgroup	No (N=133)	Overall - EAS (5.4 mg/kg)
R-Pertuzumab before line 3		
Duration of response by subgroup, months		
Subjects with CR/PR		73
Subjects with events (%)		25 (34.2)
Subjects censored (%)		48 (65.8)
Ongoing without PD (%)		18 (24.7)
Other (%)		30 (41.1)
25th Percentile		8.3
95% CI		(5.6, 13.8)
Median		21.5
95% CI		(13.8, NE)
Duration of response by subgroup at specific timepoints		
at 6 Months (%)		81.7
95% CI		(69.4, 89.5)
at 12 Months (%)		64.4
95% CI		(50.1, 75.5)
at 24 Months (%)		NE
95% CI		(NE, NE)

Table is considering only patients with response.
Brookmeyer-Crowley 95% confidence intervals were used for quantile estimates, for point estimates asymptotic normality to the
log-log transformation of rates was applied.
Source Data: adam.adtte.

Sicherheit – weitere Untersuchungen

Gesamtrate UE

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	183 (99.5)	(97.0, 100.0)
		Cycle 1	184	173 (94.0)	(89.6, 97.0)
		Cycle 2	181	133 (72.3)	(65.2, 78.6)
		Cycle 3	174	115 (62.5)	(55.1, 69.5)
		Cycle 4	169	108 (58.7)	(51.2, 65.9)
		Cycle 5	155	93 (50.5)	(43.1, 58.0)
		Cycle 6	152	83 (45.1)	(37.8, 52.6)
		Cycle 7	145	88 (47.8)	(40.4, 55.3)
		Cycle >= 8 and < 18	138	124 (67.4)	(60.1, 74.1)
		Cycle >= 18	75	69 (37.5)	(30.5, 44.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	139 (99.3) (96.1, 100.0)
		Cycle 1	140	133 (95.0) (90.0, 98.0)
		Cycle 2	138	100 (71.4) (63.2, 78.7)
		Cycle 3	132	87 (62.1) (53.6, 70.2)
		Cycle 4	128	84 (60.0) (51.4, 68.2)
		Cycle 5	116	70 (50.0) (41.4, 58.6)
		Cycle 6	113	61 (43.6) (35.2, 52.2)
		Cycle 7	109	62 (44.3) (35.9, 52.9)
		Cycle >= 8 and < 18	103	91 (65.0) (56.5, 72.9)
		Cycle >= 18	56	52 (37.1) (29.1, 45.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	44 (100.0) (92.0, 100.0)
		Cycle 1	44	40 (90.9) (78.3, 97.5)
		Cycle 2	43	33 (75.0) (59.7, 86.8)
		Cycle 3	42	28 (63.6) (47.8, 77.6)
		Cycle 4	41	24 (54.5) (38.8, 69.6)
		Cycle 5	39	23 (52.3) (36.7, 67.5)
		Cycle 6	39	22 (50.0) (34.6, 65.4)
		Cycle 7	36	26 (59.1) (43.2, 73.7)
		Cycle >= 8 and < 18	35	33 (75.0) (59.7, 86.8)
		Cycle >= 18	19	17 (38.6) (24.4, 54.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63 (100.0)	(94.3, 100.0)
		Cycle 1	58 (92.1)	(82.4, 97.4)
		Cycle 2	61 (65.1)	(52.0, 76.7)
		Cycle 3	58 (60.3)	(47.2, 72.4)
		Cycle 4	58 (47.6)	(34.9, 60.6)
		Cycle 5	55 (49.2)	(36.4, 62.1)
		Cycle 6	55 (44.4)	(31.9, 57.5)
		Cycle 7	53 (50.8)	(37.9, 63.6)
		Cycle >= 8 and < 18	49 (69.8)	(57.0, 80.8)
		Cycle >= 18	29 (41.3)	(29.0, 54.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	53 (100.0)	(93.3, 100.0)
		Cycle 1	53	52 (98.1)	(89.9, 100.0)
		Cycle 2	53	43 (81.1)	(68.0, 90.6)
		Cycle 3	52	38 (71.7)	(57.7, 83.2)
		Cycle 4	49	38 (71.7)	(57.7, 83.2)
		Cycle 5	44	29 (54.7)	(40.4, 68.4)
		Cycle 6	42	20 (37.7)	(24.8, 52.1)
		Cycle 7	40	19 (35.8)	(23.1, 50.2)
		Cycle >= 8 and < 18	39	34 (64.2)	(49.8, 76.9)
		Cycle >= 18	23	21 (39.6)	(26.5, 54.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	67 (98.5)	(92.1, 100.0)
		Cycle 1	68	63 (92.6)	(83.7, 97.6)
		Cycle 2	67	49 (72.1)	(59.9, 82.3)
		Cycle 3	64	39 (57.4)	(44.8, 69.3)
		Cycle 4	62	40 (58.8)	(46.2, 70.6)
		Cycle 5	56	33 (48.5)	(36.2, 61.0)
		Cycle 6	55	35 (51.5)	(39.0, 63.8)
		Cycle 7	52	37 (54.4)	(41.9, 66.5)
		Cycle >= 8 and < 18	50	46 (67.6)	(55.2, 78.5)
		Cycle >= 18	23	22 (32.4)	(21.5, 44.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	101 (99.0)	(94.7, 100.0)
		Cycle 1	102	94 (92.2)	(85.1, 96.6)
		Cycle 2	101	80 (78.4)	(69.2, 86.0)
		Cycle 3	100	73 (71.6)	(61.8, 80.1)
		Cycle 4	98	65 (63.7)	(53.6, 73.0)
		Cycle 5	94	60 (58.8)	(48.6, 68.5)
		Cycle 6	93	48 (47.1)	(37.1, 57.2)
		Cycle 7	88	56 (54.9)	(44.7, 64.8)
		Cycle >= 8 and < 18	86	78 (76.5)	(67.0, 84.3)
		Cycle >= 18	49	47 (46.1)	(36.2, 56.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	81 (100.0)	(95.5, 100.0)
		Cycle 1	81	78 (96.3)	(89.6, 99.2)
		Cycle 2	79	52 (64.2)	(52.8, 74.6)
		Cycle 3	73	41 (50.6)	(39.3, 61.9)
		Cycle 4	71	43 (53.1)	(41.7, 64.3)
		Cycle 5	61	33 (40.7)	(29.9, 52.2)
		Cycle 6	59	35 (43.2)	(32.2, 54.7)
		Cycle 7	57	32 (39.5)	(28.8, 51.0)
		Cycle >= 8 and < 18	52	46 (56.8)	(45.3, 67.8)
		Cycle >= 18	26	22 (27.2)	(17.9, 38.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions < 5 cm (N=73)	Any TEAE	73	73 (100.0)	(95.1, 100.0)
	Cycle 1	73	69 (94.5)	(86.6, 98.5)
	Cycle 2	72	56 (76.7)	(65.4, 85.8)
	Cycle 3	70	49 (67.1)	(55.1, 77.7)
	Cycle 4	65	44 (60.3)	(48.1, 71.5)
	Cycle 5	60	35 (47.9)	(36.1, 60.0)
	Cycle 6	59	30 (41.1)	(29.7, 53.2)
	Cycle 7	58	33 (45.2)	(33.5, 57.3)
	Cycle >= 8 and < 18	53	48 (65.8)	(53.7, 76.5)
	Cycle >= 18	33	31 (42.5)	(31.0, 54.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

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			Overall 5.4 mg/kg SAF (N=184)		
Subgroup		Time Period	N patients in cycle	n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=97)	Any TEAE	97	96 (99.0)	(94.4, 100.0)
		Cycle 1	97	90 (92.8)	(85.7, 97.0)
		Cycle 2	95	66 (68.0)	(57.8, 77.1)
		Cycle 3	90	57 (58.8)	(48.3, 68.7)
		Cycle 4	90	57 (58.8)	(48.3, 68.7)
		Cycle 5	81	49 (50.5)	(40.2, 60.8)
		Cycle 6	79	44 (45.4)	(35.2, 55.8)
		Cycle 7	74	48 (49.5)	(39.2, 59.8)
		Cycle >= 8 and < 18	72	65 (67.0)	(56.7, 76.2)
		Cycle >= 18	34	30 (30.9)	(21.9, 41.1)

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	153 (99.4)	(96.4, 100.0)
		Cycle 1	154	144 (93.5)	(88.4, 96.8)
		Cycle 2	152	116 (75.3)	(67.7, 81.9)
		Cycle 3	146	96 (62.3)	(54.2, 70.0)
		Cycle 4	141	90 (58.4)	(50.2, 66.3)
		Cycle 5	129	78 (50.6)	(42.5, 58.8)
		Cycle 6	127	69 (44.8)	(36.8, 53.0)
		Cycle 7	121	75 (48.7)	(40.6, 56.9)
		Cycle >= 8 and < 18	114	106 (68.8)	(60.9, 76.0)
		Cycle >= 18	69	63 (40.9)	(33.1, 49.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Any TEAE	28	28 (100.0) (87.7, 100.0)
		Cycle 1	28	28 (100.0) (87.7, 100.0)
		Cycle 2	27	16 (57.1) (37.2, 75.5)
		Cycle 3	26	17 (60.7) (40.6, 78.5)
		Cycle 4	26	16 (57.1) (37.2, 75.5)
		Cycle 5	24	14 (50.0) (30.6, 69.4)
		Cycle 6	23	12 (42.9) (24.5, 62.8)
		Cycle 7	22	12 (42.9) (24.5, 62.8)
		Cycle >= 8 and < 18	22	16 (57.1) (37.2, 75.5)
		Cycle >= 18	5	5 (17.9) (6.1, 36.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	92 (98.9)	(94.2, 100.0)
		Cycle 1	93	88 (94.6)	(87.9, 98.2)
		Cycle 2	92	67 (72.0)	(61.8, 80.9)
		Cycle 3	87	55 (59.1)	(48.5, 69.2)
		Cycle 4	84	57 (61.3)	(50.6, 71.2)
		Cycle 5	80	51 (54.8)	(44.2, 65.2)
		Cycle 6	78	43 (46.2)	(35.8, 56.9)
		Cycle 7	75	48 (51.6)	(41.0, 62.1)
		Cycle >= 8 and < 18	73	64 (68.8)	(58.4, 78.0)
		Cycle >= 18	34	30 (32.3)	(22.9, 42.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	88 (100.0)	(95.9, 100.0)
		Cycle 1	88	82 (93.2)	(85.7, 97.5)
		Cycle 2	86	65 (73.9)	(63.4, 82.7)
		Cycle 3	85	59 (67.0)	(56.2, 76.7)
		Cycle 4	84	51 (58.0)	(47.0, 68.4)
		Cycle 5	74	42 (47.7)	(37.0, 58.6)
		Cycle 6	73	40 (45.5)	(34.8, 56.4)
		Cycle 7	69	39 (44.3)	(33.7, 55.3)
		Cycle >= 8 and < 18	64	59 (67.0)	(56.2, 76.7)
		Cycle >= 18	41	39 (44.3)	(33.7, 55.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	50 (98.0)	(89.6, 100.0)
		Cycle 1	51	48 (94.1)	(83.8, 98.8)
		Cycle 2	50	34 (66.7)	(52.1, 79.2)
		Cycle 3	49	34 (66.7)	(52.1, 79.2)
		Cycle 4	49	28 (54.9)	(40.3, 68.9)
		Cycle 5	47	27 (52.9)	(38.5, 67.1)
		Cycle 6	46	22 (43.1)	(29.3, 57.8)
		Cycle 7	45	27 (52.9)	(38.5, 67.1)
		Cycle >= 8 and < 18	44	40 (78.4)	(64.7, 88.7)
		Cycle >= 18	21	20 (39.2)	(25.8, 53.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	125 (100.0)	(97.1, 100.0)
		Cycle 1	125	117 (93.6)	(87.8, 97.2)
		Cycle 2	123	94 (75.2)	(66.7, 82.5)
		Cycle 3	118	78 (62.4)	(53.3, 70.9)
		Cycle 4	114	77 (61.6)	(52.5, 70.2)
		Cycle 5	103	64 (51.2)	(42.1, 60.2)
		Cycle 6	101	59 (47.2)	(38.2, 56.3)
		Cycle 7	95	58 (46.4)	(37.4, 55.5)
		Cycle >= 8 and < 18	90	81 (64.8)	(55.8, 73.1)
		Cycle >= 18	52	47 (37.6)	(29.1, 46.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	96 (99.0)	(94.4, 100.0)
		Cycle 1	97	92 (94.8)	(88.4, 98.3)
		Cycle 2	96	71 (73.2)	(63.2, 81.7)
		Cycle 3	91	58 (59.8)	(49.3, 69.6)
		Cycle 4	88	58 (59.8)	(49.3, 69.6)
		Cycle 5	84	53 (54.6)	(44.2, 64.8)
		Cycle 6	82	44 (45.4)	(35.2, 55.8)
		Cycle 7	79	49 (50.5)	(40.2, 60.8)
		Cycle >= 8 and < 18	76	67 (69.1)	(58.9, 78.1)
		Cycle >= 18	36	32 (33.0)	(23.8, 43.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	83 (100.0)	(95.7, 100.0)
		Cycle 1	83	77 (92.8)	(84.9, 97.3)
		Cycle 2	81	60 (72.3)	(61.4, 81.6)
		Cycle 3	80	56 (67.5)	(56.3, 77.4)
		Cycle 4	79	50 (60.2)	(48.9, 70.8)
		Cycle 5	69	40 (48.2)	(37.1, 59.4)
		Cycle 6	68	39 (47.0)	(35.9, 58.3)
		Cycle 7	64	38 (45.8)	(34.8, 57.1)
		Cycle >= 8 and < 18	60	55 (66.3)	(55.1, 76.3)
		Cycle >= 18	38	36 (43.4)	(32.5, 54.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Normal (N=90)	Any TEAE	90	89 (98.9)	(94.0, 100.0)
		Cycle 1	90	85 (94.4)	(87.5, 98.2)
		Cycle 2	89	59 (65.6)	(54.8, 75.3)
		Cycle 3	85	53 (58.9)	(48.0, 69.2)
		Cycle 4	85	56 (62.2)	(51.4, 72.2)
		Cycle 5	76	46 (51.1)	(40.3, 61.8)
		Cycle 6	73	39 (43.3)	(32.9, 54.2)
		Cycle 7	72	43 (47.8)	(37.1, 58.6)
		Cycle >= 8 and < 18	69	59 (65.6)	(54.8, 75.3)
		Cycle >= 18	41	38 (42.2)	(31.9, 53.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	69 (100.0)	(94.8, 100.0)
		Cycle 1	69	65 (94.2)	(85.8, 98.4)
		Cycle 2	68	55 (79.7)	(68.3, 88.4)
		Cycle 3	66	47 (68.1)	(55.8, 78.8)
		Cycle 4	63	40 (58.0)	(45.5, 69.8)
		Cycle 5	59	35 (50.7)	(38.4, 63.0)
		Cycle 6	59	32 (46.4)	(34.3, 58.8)
		Cycle 7	56	34 (49.3)	(37.0, 61.6)
		Cycle >= 8 and < 18	54	51 (73.9)	(61.9, 83.7)
		Cycle >= 18	27	26 (37.7)	(26.3, 50.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	25 (100.0)	(86.3, 100.0)
		Cycle 1	25	23 (92.0)	(74.0, 99.0)
		Cycle 2	24	19 (76.0)	(54.9, 90.6)
		Cycle 3	23	15 (60.0)	(38.7, 78.9)
		Cycle 4	21	12 (48.0)	(27.8, 68.7)
		Cycle 5	20	12 (48.0)	(27.8, 68.7)
		Cycle 6	20	12 (48.0)	(27.8, 68.7)
		Cycle 7	17	11 (44.0)	(24.4, 65.1)
		Cycle >= 8 and < 18	15	14 (56.0)	(34.9, 75.6)
		Cycle >= 18	7	5 (20.0)	(6.8, 40.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	104 (99.0)	(94.8, 100.0)
		Cycle 1	105	100 (95.2)	(89.2, 98.4)
		Cycle 2	104	76 (72.4)	(62.8, 80.7)
		Cycle 3	102	69 (65.7)	(55.8, 74.7)
		Cycle 4	98	67 (63.8)	(53.9, 73.0)
		Cycle 5	90	49 (46.7)	(36.9, 56.7)
		Cycle 6	89	52 (49.5)	(39.6, 59.5)
		Cycle 7	87	53 (50.5)	(40.5, 60.4)
		Cycle >= 8 and < 18	84	77 (73.3)	(63.8, 81.5)
		Cycle >= 18	44	42 (40.0)	(30.6, 50.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	76 (100.0)	(95.3, 100.0)
		Cycle 1	76	70 (92.1)	(83.6, 97.0)
		Cycle 2	74	54 (71.1)	(59.5, 80.9)
		Cycle 3	69	44 (57.9)	(46.0, 69.1)
		Cycle 4	68	39 (51.3)	(39.6, 63.0)
		Cycle 5	63	43 (56.6)	(44.7, 67.9)
		Cycle 6	61	31 (40.8)	(29.6, 52.7)
		Cycle 7	56	34 (44.7)	(33.3, 56.6)
		Cycle >= 8 and < 18	54	47 (61.8)	(50.0, 72.8)
		Cycle >= 18	31	27 (35.5)	(24.9, 47.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	24 (100.0)	(85.8, 100.0)
		Cycle 1	24	22 (91.7)	(73.0, 99.0)
		Cycle 2	23	15 (62.5)	(40.6, 81.2)
		Cycle 3	22	13 (54.2)	(32.8, 74.4)
		Cycle 4	22	14 (58.3)	(36.6, 77.9)
		Cycle 5	19	9 (37.5)	(18.8, 59.4)
		Cycle 6	18	11 (45.8)	(25.6, 67.2)
		Cycle 7	18	15 (62.5)	(40.6, 81.2)
		Cycle >= 8 and < 18	18	18 (75.0)	(53.3, 90.2)
		Cycle >= 18	10	10 (41.7)	(22.1, 63.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	159 (99.4)	(96.6, 100.0)
		Cycle 1	160	151 (94.4)	(89.6, 97.4)
		Cycle 2	158	118 (73.8)	(66.2, 80.4)
		Cycle 3	152	102 (63.8)	(55.8, 71.2)
		Cycle 4	147	94 (58.8)	(50.7, 66.5)
		Cycle 5	136	84 (52.5)	(44.5, 60.4)
		Cycle 6	134	72 (45.0)	(37.1, 53.1)
		Cycle 7	127	73 (45.6)	(37.7, 53.7)
		Cycle >= 8 and < 18	120	106 (66.3)	(58.4, 73.5)
		Cycle >= 18	65	59 (36.9)	(29.4, 44.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	53 (100.0)	(93.3, 100.0)
		Cycle 1	53	51 (96.2)	(87.0, 99.5)
		Cycle 2	52	42 (79.2)	(65.9, 89.2)
		Cycle 3	49	29 (54.7)	(40.4, 68.4)
		Cycle 4	48	34 (64.2)	(49.8, 76.9)
		Cycle 5	43	26 (49.1)	(35.1, 63.2)
		Cycle 6	42	28 (52.8)	(38.6, 66.7)
		Cycle 7	41	30 (56.6)	(42.3, 70.2)
		Cycle >= 8 and < 18	39	37 (69.8)	(55.7, 81.7)
		Cycle >= 18	18	16 (30.2)	(18.3, 44.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	130 (99.2)	(95.8, 100.0)
		Cycle 1	131	122 (93.1)	(87.4, 96.8)
		Cycle 2	129	91 (69.5)	(60.8, 77.2)
		Cycle 3	125	86 (65.6)	(56.9, 73.7)
		Cycle 4	121	74 (56.5)	(47.6, 65.1)
		Cycle 5	112	67 (51.1)	(42.3, 60.0)
		Cycle 6	110	55 (42.0)	(33.4, 50.9)
		Cycle 7	104	58 (44.3)	(35.6, 53.2)
		Cycle >= 8 and < 18	99	87 (66.4)	(57.6, 74.4)
		Cycle >= 18	57	53 (40.5)	(32.0, 49.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	168 (99.4)	(96.7, 100.0)
		Cycle 1	169	159 (94.1)	(89.4, 97.1)
		Cycle 2	166	122 (72.2)	(64.8, 78.8)
		Cycle 3	159	103 (60.9)	(53.2, 68.3)
		Cycle 4	154	99 (58.6)	(50.8, 66.1)
		Cycle 5	142	85 (50.3)	(42.5, 58.1)
		Cycle 6	139	76 (45.0)	(37.3, 52.8)
		Cycle 7	132	81 (47.9)	(40.2, 55.7)
		Cycle >= 8 and < 18	125	112 (66.3)	(58.6, 73.4)
		Cycle >= 18	70	64 (37.9)	(30.5, 45.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	15 (100.0)	(78.2, 100.0)
		Cycle 1	15	14 (93.3)	(68.1, 99.8)
		Cycle 2	15	11 (73.3)	(44.9, 92.2)
		Cycle 3	15	12 (80.0)	(51.9, 95.7)
		Cycle 4	15	9 (60.0)	(32.3, 83.7)
		Cycle 5	13	8 (53.3)	(26.6, 78.7)
		Cycle 6	13	7 (46.7)	(21.3, 73.4)
		Cycle 7	13	7 (46.7)	(21.3, 73.4)
		Cycle >= 8 and < 18	13	12 (80.0)	(51.9, 95.7)
		Cycle >= 18	5	5 (33.3)	(11.8, 61.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	56 (100.0)	(93.6, 100.0)
		Cycle 1	56	54 (96.4)	(87.7, 99.6)
		Cycle 2	55	42 (75.0)	(61.6, 85.6)
		Cycle 3	54	36 (64.3)	(50.4, 76.6)
		Cycle 4	53	34 (60.7)	(46.8, 73.5)
		Cycle 5	49	29 (51.8)	(38.0, 65.3)
		Cycle 6	48	23 (41.1)	(28.1, 55.0)
		Cycle 7	48	27 (48.2)	(34.7, 62.0)
		Cycle >= 8 and < 18	45	39 (69.6)	(55.9, 81.2)
		Cycle >= 18	32	31 (55.4)	(41.5, 68.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	127 (99.2)	(95.7, 100.0)
		Cycle 1	128	119 (93.0)	(87.1, 96.7)
		Cycle 2	126	91 (71.1)	(62.4, 78.8)
		Cycle 3	120	79 (61.7)	(52.7, 70.2)
		Cycle 4	116	74 (57.8)	(48.8, 66.5)
		Cycle 5	106	64 (50.0)	(41.0, 59.0)
		Cycle 6	104	60 (46.9)	(38.0, 55.9)
		Cycle 7	97	61 (47.7)	(38.8, 56.7)
		Cycle >= 8 and < 18	93	85 (66.4)	(57.5, 74.5)
		Cycle >= 18	43	38 (29.7)	(21.9, 38.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	< 3 lines (N=17)	Any TEAE	17 (100.0)	(80.5, 100.0)
		Cycle 1	16 (94.1)	(71.3, 99.9)
		Cycle 2	17 (82.4)	(56.6, 96.2)
		Cycle 3	17 (64.7)	(38.3, 85.8)
		Cycle 4	17 (82.4)	(56.6, 96.2)
		Cycle 5	17 (52.9)	(27.8, 77.0)
		Cycle 6	16 (47.1)	(23.0, 72.2)
		Cycle 7	16 (52.9)	(27.8, 77.0)
		Cycle >= 8 and < 18	16 (82.4)	(56.6, 96.2)
		Cycle >= 18	14 (76.5)	(50.1, 93.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	>= 3 lines (N=167)	Any TEAE	167	166 (99.4) (96.7, 100.0)
		Cycle 1	167	157 (94.0) (89.3, 97.1)
		Cycle 2	164	119 (71.3) (63.8, 78.0)
		Cycle 3	157	104 (62.3) (54.5, 69.6)
		Cycle 4	152	94 (56.3) (48.4, 63.9)
		Cycle 5	138	84 (50.3) (42.5, 58.1)
		Cycle 6	136	75 (44.9) (37.2, 52.8)
		Cycle 7	129	79 (47.3) (39.5, 55.2)
		Cycle >= 8 and < 18	122	110 (65.9) (58.1, 73.0)
		Cycle >= 18	61	56 (33.5) (26.4, 41.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	78 (98.7)	(93.1, 100.0)
		Cycle 1	79	74 (93.7)	(85.8, 97.9)
		Cycle 2	78	57 (72.2)	(60.9, 81.7)
		Cycle 3	75	49 (62.0)	(50.4, 72.7)
		Cycle 4	73	43 (54.4)	(42.8, 65.7)
		Cycle 5	70	44 (55.7)	(44.1, 66.9)
		Cycle 6	69	37 (46.8)	(35.5, 58.4)
		Cycle 7	68	42 (53.2)	(41.6, 64.5)
		Cycle >= 8 and < 18	65	59 (74.7)	(63.6, 83.8)
		Cycle >= 18	37	35 (44.3)	(33.1, 55.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	66 (100.0) (94.6, 100.0)
		Cycle 1	66	62 (93.9) (85.2, 98.3)
		Cycle 2	66	46 (69.7) (57.1, 80.4)
		Cycle 3	64	39 (59.1) (46.3, 71.0)
		Cycle 4	61	39 (59.1) (46.3, 71.0)
		Cycle 5	55	26 (39.4) (27.6, 52.2)
		Cycle 6	53	27 (40.9) (29.0, 53.7)
		Cycle 7	51	31 (47.0) (34.6, 59.7)
		Cycle >= 8 and < 18	51	46 (69.7) (57.1, 80.4)
		Cycle >= 18	23	19 (28.8) (18.3, 41.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	121 (100.0)	(97.0, 100.0)
		Cycle 1	121	113 (93.4)	(87.4, 97.1)
		Cycle 2	120	87 (71.9)	(63.0, 79.7)
		Cycle 3	119	78 (64.5)	(55.2, 73.0)
		Cycle 4	115	78 (64.5)	(55.2, 73.0)
		Cycle 5	106	68 (56.2)	(46.9, 65.2)
		Cycle 6	103	55 (45.5)	(36.4, 54.8)
		Cycle 7	96	56 (46.3)	(37.2, 55.6)
		Cycle >= 8 and < 18	93	81 (66.9)	(57.8, 75.2)
		Cycle >= 18	54	49 (40.5)	(31.7, 49.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	62 (98.4)	(91.5, 100.0)
		Cycle 1	63	60 (95.2)	(86.7, 99.0)
		Cycle 2	61	46 (73.0)	(60.3, 83.4)
		Cycle 3	55	37 (58.7)	(45.6, 71.0)
		Cycle 4	54	30 (47.6)	(34.9, 60.6)
		Cycle 5	49	25 (39.7)	(27.6, 52.8)
		Cycle 6	49	28 (44.4)	(31.9, 57.5)
		Cycle 7	49	32 (50.8)	(37.9, 63.6)
		Cycle >= 8 and < 18	45	43 (68.3)	(55.3, 79.4)
		Cycle >= 18	21	20 (31.7)	(20.6, 44.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	51 (100.0)	(93.0, 100.0)
		Cycle 1	51	47 (92.2)	(81.1, 97.8)
		Cycle 2	50	37 (72.5)	(58.3, 84.1)
		Cycle 3	50	28 (54.9)	(40.3, 68.9)
		Cycle 4	49	34 (66.7)	(52.1, 79.2)
		Cycle 5	46	29 (56.9)	(42.2, 70.7)
		Cycle 6	44	22 (43.1)	(29.3, 57.8)
		Cycle 7	40	26 (51.0)	(36.6, 65.2)
		Cycle >= 8 and < 18	40	34 (66.7)	(52.1, 79.2)
		Cycle >= 18	24	22 (43.1)	(29.3, 57.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AA_SSI0: Incidence of TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	132 (99.2)	(95.9, 100.0)
		Cycle 1	133	126 (94.7)	(89.5, 97.9)
		Cycle 2	131	96 (72.2)	(63.7, 79.6)
		Cycle 3	124	87 (65.4)	(56.7, 73.4)
		Cycle 4	120	74 (55.6)	(46.8, 64.2)
		Cycle 5	109	64 (48.1)	(39.4, 56.9)
		Cycle 6	108	61 (45.9)	(37.2, 54.7)
		Cycle 7	105	62 (46.6)	(37.9, 55.5)
		Cycle >= 8 and < 18	98	90 (67.7)	(59.0, 75.5)
		Cycle >= 18	51	47 (35.3)	(27.3, 44.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

SUE

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	50 (27.2)	(20.9, 34.2)
		Cycle 1	184	8 (4.3)	(1.9, 8.4)
		Cycle 2	181	9 (4.9)	(2.3, 9.1)
		Cycle 3	174	6 (3.3)	(1.2, 7.0)
		Cycle 4	169	7 (3.8)	(1.5, 7.7)
		Cycle 5	155	5 (2.7)	(0.9, 6.2)
		Cycle 6	152	2 (1.1)	(0.1, 3.9)
		Cycle 7	145	4 (2.2)	(0.6, 5.5)
		Cycle >= 8 and < 18	138	17 (9.2)	(5.5, 14.4)
		Cycle >= 18	75	9 (4.9)	(2.3, 9.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

			Overall 5.4 mg/kg SAF (N=184)	
Subgroup	Time Period	N patients in cycle	n(%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	37 (26.4) (19.3, 34.5)
		Cycle 1	140	8 (5.7) (2.5, 10.9)
		Cycle 2	138	5 (3.6) (1.2, 8.1)
		Cycle 3	132	5 (3.6) (1.2, 8.1)
		Cycle 4	128	6 (4.3) (1.6, 9.1)
		Cycle 5	116	5 (3.6) (1.2, 8.1)
		Cycle 6	113	2 (1.4) (0.2, 5.1)
		Cycle 7	109	4 (2.9) (0.8, 7.2)
		Cycle >= 8 and < 18	103	11 (7.9) (4.0, 13.6)
		Cycle >= 18	56	6 (4.3) (1.6, 9.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

			Overall 5.4 mg/kg SAF (N=184)		
Subgroup	Time Period	N patients in cycle	n(%)	95% CI	
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	13 (29.5)	(16.8, 45.2)
		Cycle 1	44	0 (0.0)	(0.0, 8.0)
		Cycle 2	43	4 (9.1)	(2.5, 21.7)
		Cycle 3	42	1 (2.3)	(0.1, 12.0)
		Cycle 4	41	1 (2.3)	(0.1, 12.0)
		Cycle 5	39	0 (0.0)	(0.0, 8.0)
		Cycle 6	39	0 (0.0)	(0.0, 8.0)
		Cycle 7	36	0 (0.0)	(0.0, 8.0)
		Cycle >= 8 and < 18	35	6 (13.6)	(5.2, 27.4)
		Cycle >= 18	19	3 (6.8)	(1.4, 18.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	11 (17.5) (9.1, 29.1)
		Cycle 1	63	1 (1.6) (0.0, 8.5)
		Cycle 2	61	2 (3.2) (0.4, 11.0)
		Cycle 3	58	1 (1.6) (0.0, 8.5)
		Cycle 4	58	1 (1.6) (0.0, 8.5)
		Cycle 5	55	0 (0.0) (0.0, 5.7)
		Cycle 6	55	2 (3.2) (0.4, 11.0)
		Cycle 7	53	0 (0.0) (0.0, 5.7)
		Cycle >= 8 and < 18	49	2 (3.2) (0.4, 11.0)
		Cycle >= 18	29	2 (3.2) (0.4, 11.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	13 (24.5)	(13.8, 38.3)
		Cycle 1	53	2 (3.8)	(0.5, 13.0)
		Cycle 2	53	2 (3.8)	(0.5, 13.0)
		Cycle 3	52	1 (1.9)	(0.0, 10.1)
		Cycle 4	49	1 (1.9)	(0.0, 10.1)
		Cycle 5	44	3 (5.7)	(1.2, 15.7)
		Cycle 6	42	0 (0.0)	(0.0, 6.7)
		Cycle 7	40	1 (1.9)	(0.0, 10.1)
		Cycle >= 8 and < 18	39	3 (5.7)	(1.2, 15.7)
		Cycle >= 18	23	3 (5.7)	(1.2, 15.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	26 (38.2)	(26.7, 50.8)
		Cycle 1	68	5 (7.4)	(2.4, 16.3)
		Cycle 2	67	5 (7.4)	(2.4, 16.3)
		Cycle 3	64	4 (5.9)	(1.6, 14.4)
		Cycle 4	62	5 (7.4)	(2.4, 16.3)
		Cycle 5	56	2 (2.9)	(0.4, 10.2)
		Cycle 6	55	0 (0.0)	(0.0, 5.3)
		Cycle 7	52	3 (4.4)	(0.9, 12.4)
		Cycle >= 8 and < 18	50	12 (17.6)	(9.5, 28.8)
		Cycle >= 18	23	4 (5.9)	(1.6, 14.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	23 (22.5)	(14.9, 31.9)
		Cycle 1	102	4 (3.9)	(1.1, 9.7)
		Cycle 2	101	4 (3.9)	(1.1, 9.7)
		Cycle 3	100	3 (2.9)	(0.6, 8.4)
		Cycle 4	98	0 (0.0)	(0.0, 3.6)
		Cycle 5	94	2 (2.0)	(0.2, 6.9)
		Cycle 6	93	1 (1.0)	(0.0, 5.3)
		Cycle 7	88	2 (2.0)	(0.2, 6.9)
		Cycle >= 8 and < 18	86	8 (7.8)	(3.4, 14.9)
		Cycle >= 18	49	4 (3.9)	(1.1, 9.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	26 (32.1)	(22.2, 43.4)
		Cycle 1	81	4 (4.9)	(1.4, 12.2)
		Cycle 2	79	5 (6.2)	(2.0, 13.8)
		Cycle 3	73	2 (2.5)	(0.3, 8.6)
		Cycle 4	71	7 (8.6)	(3.5, 17.0)
		Cycle 5	61	3 (3.7)	(0.8, 10.4)
		Cycle 6	59	1 (1.2)	(0.0, 6.7)
		Cycle 7	57	2 (2.5)	(0.3, 8.6)
		Cycle >= 8 and < 18	52	9 (11.1)	(5.2, 20.0)
		Cycle >= 18	26	5 (6.2)	(2.0, 13.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions	< 5 cm (N=73)			
	Any TEAE	73	19 (26.0)	(16.5, 37.6)
	Cycle 1	73	1 (1.4)	(0.0, 7.4)
	Cycle 2	72	3 (4.1)	(0.9, 11.5)
	Cycle 3	70	2 (2.7)	(0.3, 9.5)
	Cycle 4	65	1 (1.4)	(0.0, 7.4)
	Cycle 5	60	2 (2.7)	(0.3, 9.5)
	Cycle 6	59	0 (0.0)	(0.0, 4.9)
	Cycle 7	58	2 (2.7)	(0.3, 9.5)
	Cycle >= 8 and < 18	53	7 (9.6)	(3.9, 18.8)
	Cycle >= 18	33	5 (6.8)	(2.3, 15.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=97)			
	Any TEAE	97	27 (27.8)	(19.2, 37.9)
	Cycle 1	97	6 (6.2)	(2.3, 13.0)
	Cycle 2	95	6 (6.2)	(2.3, 13.0)
	Cycle 3	90	3 (3.1)	(0.6, 8.8)
	Cycle 4	90	5 (5.2)	(1.7, 11.6)
	Cycle 5	81	3 (3.1)	(0.6, 8.8)
	Cycle 6	79	2 (2.1)	(0.3, 7.3)
	Cycle 7	74	1 (1.0)	(0.0, 5.6)
	Cycle >= 8 and < 18	72	6 (6.2)	(2.3, 13.0)
	Cycle >= 18	34	3 (3.1)	(0.6, 8.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	42 (27.3)	(20.4, 35.0)
		Cycle 1	154	7 (4.5)	(1.8, 9.1)
		Cycle 2	152	8 (5.2)	(2.3, 10.0)
		Cycle 3	146	5 (3.2)	(1.1, 7.4)
		Cycle 4	141	7 (4.5)	(1.8, 9.1)
		Cycle 5	129	4 (2.6)	(0.7, 6.5)
		Cycle 6	127	2 (1.3)	(0.2, 4.6)
		Cycle 7	121	4 (2.6)	(0.7, 6.5)
		Cycle >= 8 and < 18	114	12 (7.8)	(4.1, 13.2)
		Cycle >= 18	69	8 (5.2)	(2.3, 10.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHCR3+ (N=28)	Any TEAE	28	7 (25.0) (10.7, 44.9)
		Cycle 1	28	1 (3.6) (0.1, 18.3)
		Cycle 2	27	1 (3.6) (0.1, 18.3)
		Cycle 3	26	1 (3.6) (0.1, 18.3)
		Cycle 4	26	0 (0.0) (0.0, 12.3)
		Cycle 5	24	1 (3.6) (0.1, 18.3)
		Cycle 6	23	0 (0.0) (0.0, 12.3)
		Cycle 7	22	0 (0.0) (0.0, 12.3)
		Cycle >= 8 and < 18	22	4 (14.3) (4.0, 32.7)
		Cycle >= 18	5	1 (3.6) (0.1, 18.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	27 (29.0)	(20.1, 39.4)
		Cycle 1	93	7 (7.5)	(3.1, 14.9)
		Cycle 2	92	8 (8.6)	(3.8, 16.2)
		Cycle 3	87	4 (4.3)	(1.2, 10.6)
		Cycle 4	84	4 (4.3)	(1.2, 10.6)
		Cycle 5	80	3 (3.2)	(0.7, 9.1)
		Cycle 6	78	0 (0.0)	(0.0, 3.9)
		Cycle 7	75	1 (1.1)	(0.0, 5.8)
		Cycle >= 8 and < 18	73	11 (11.8)	(6.1, 20.2)
		Cycle >= 18	34	3 (3.2)	(0.7, 9.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	22 (25.0)	(16.4, 35.4)
		Cycle 1	88	1 (1.1)	(0.0, 6.2)
		Cycle 2	86	1 (1.1)	(0.0, 6.2)
		Cycle 3	85	1 (1.1)	(0.0, 6.2)
		Cycle 4	84	3 (3.4)	(0.7, 9.6)
		Cycle 5	74	2 (2.3)	(0.3, 8.0)
		Cycle 6	73	2 (2.3)	(0.3, 8.0)
		Cycle 7	69	3 (3.4)	(0.7, 9.6)
		Cycle >= 8 and < 18	64	6 (6.8)	(2.5, 14.3)
		Cycle >= 18	41	6 (6.8)	(2.5, 14.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	12 (23.5)	(12.8, 37.5)
		Cycle 1	51	3 (5.9)	(1.2, 16.2)
		Cycle 2	50	3 (5.9)	(1.2, 16.2)
		Cycle 3	49	3 (5.9)	(1.2, 16.2)
		Cycle 4	49	3 (5.9)	(1.2, 16.2)
		Cycle 5	47	1 (2.0)	(0.0, 10.4)
		Cycle 6	46	0 (0.0)	(0.0, 7.0)
		Cycle 7	45	2 (3.9)	(0.5, 13.5)
		Cycle >= 8 and < 18	44	6 (11.8)	(4.4, 23.9)
		Cycle >= 18	21	1 (2.0)	(0.0, 10.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	36 (28.8)	(21.1, 37.6)
		Cycle 1	125	4 (3.2)	(0.9, 8.0)
		Cycle 2	123	6 (4.8)	(1.8, 10.2)
		Cycle 3	118	2 (1.6)	(0.2, 5.7)
		Cycle 4	114	4 (3.2)	(0.9, 8.0)
		Cycle 5	103	4 (3.2)	(0.9, 8.0)
		Cycle 6	101	2 (1.6)	(0.2, 5.7)
		Cycle 7	95	2 (1.6)	(0.2, 5.7)
		Cycle >= 8 and < 18	90	11 (8.8)	(4.5, 15.2)
		Cycle >= 18	52	8 (6.4)	(2.8, 12.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	28 (28.9)	(20.1, 39.0)
		Cycle 1	97	7 (7.2)	(3.0, 14.3)
		Cycle 2	96	8 (8.2)	(3.6, 15.6)
		Cycle 3	91	4 (4.1)	(1.1, 10.2)
		Cycle 4	88	4 (4.1)	(1.1, 10.2)
		Cycle 5	84	3 (3.1)	(0.6, 8.8)
		Cycle 6	82	0 (0.0)	(0.0, 3.7)
		Cycle 7	79	2 (2.1)	(0.3, 7.3)
		Cycle >= 8 and < 18	76	11 (11.3)	(5.8, 19.4)
		Cycle >= 18	36	3 (3.1)	(0.6, 8.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	21 (25.3)	(16.4, 36.0)
		Cycle 1	83	1 (1.2)	(0.0, 6.5)
		Cycle 2	81	1 (1.2)	(0.0, 6.5)
		Cycle 3	80	1 (1.2)	(0.0, 6.5)
		Cycle 4	79	3 (3.6)	(0.8, 10.2)
		Cycle 5	69	2 (2.4)	(0.3, 8.4)
		Cycle 6	68	2 (2.4)	(0.3, 8.4)
		Cycle 7	64	2 (2.4)	(0.3, 8.4)
		Cycle >= 8 and < 18	60	6 (7.2)	(2.7, 15.1)
		Cycle >= 18	38	6 (7.2)	(2.7, 15.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Normal (N=90)	Any TEAE	90	28 (31.1)	(21.8, 41.7)
		Cycle 1	90	3 (3.3)	(0.7, 9.4)
		Cycle 2	89	3 (3.3)	(0.7, 9.4)
		Cycle 3	85	1 (1.1)	(0.0, 6.0)
		Cycle 4	85	5 (5.6)	(1.8, 12.5)
		Cycle 5	76	5 (5.6)	(1.8, 12.5)
		Cycle 6	73	0 (0.0)	(0.0, 4.0)
		Cycle 7	72	3 (3.3)	(0.7, 9.4)
		Cycle >= 8 and < 18	69	10 (11.1)	(5.5, 19.5)
		Cycle >= 18	41	4 (4.4)	(1.2, 11.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	16 (23.2)	(13.9, 34.9)
		Cycle 1	69	4 (5.8)	(1.6, 14.2)
		Cycle 2	68	5 (7.2)	(2.4, 16.1)
		Cycle 3	66	4 (5.8)	(1.6, 14.2)
		Cycle 4	63	2 (2.9)	(0.4, 10.1)
		Cycle 5	59	0 (0.0)	(0.0, 5.2)
		Cycle 6	59	1 (1.4)	(0.0, 7.8)
		Cycle 7	56	1 (1.4)	(0.0, 7.8)
		Cycle >= 8 and < 18	54	6 (8.7)	(3.3, 18.0)
		Cycle >= 18	27	4 (5.8)	(1.6, 14.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	6 (24.0)	(9.4, 45.1)
		Cycle 1	25	1 (4.0)	(0.1, 20.4)
		Cycle 2	24	1 (4.0)	(0.1, 20.4)
		Cycle 3	23	1 (4.0)	(0.1, 20.4)
		Cycle 4	21	0 (0.0)	(0.0, 13.7)
		Cycle 5	20	0 (0.0)	(0.0, 13.7)
		Cycle 6	20	1 (4.0)	(0.1, 20.4)
		Cycle 7	17	0 (0.0)	(0.0, 13.7)
		Cycle >= 8 and < 18	15	1 (4.0)	(0.1, 20.4)
		Cycle >= 18	7	1 (4.0)	(0.1, 20.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	32 (30.5)	(21.9, 40.2)
		Cycle 1	105	3 (2.9)	(0.6, 8.1)
		Cycle 2	104	4 (3.8)	(1.0, 9.5)
		Cycle 3	102	4 (3.8)	(1.0, 9.5)
		Cycle 4	98	3 (2.9)	(0.6, 8.1)
		Cycle 5	90	2 (1.9)	(0.2, 6.7)
		Cycle 6	89	2 (1.9)	(0.2, 6.7)
		Cycle 7	87	4 (3.8)	(1.0, 9.5)
		Cycle >= 8 and < 18	84	13 (12.4)	(6.8, 20.2)
		Cycle >= 18	44	7 (6.7)	(2.7, 13.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	17 (22.4)	(13.6, 33.4)
		Cycle 1	76	5 (6.6)	(2.2, 14.7)
		Cycle 2	74	5 (6.6)	(2.2, 14.7)
		Cycle 3	69	2 (2.6)	(0.3, 9.2)
		Cycle 4	68	3 (3.9)	(0.8, 11.1)
		Cycle 5	63	3 (3.9)	(0.8, 11.1)
		Cycle 6	61	0 (0.0)	(0.0, 4.7)
		Cycle 7	56	0 (0.0)	(0.0, 4.7)
		Cycle >= 8 and < 18	54	4 (5.3)	(1.5, 12.9)
		Cycle >= 18	31	2 (2.6)	(0.3, 9.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

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Data Cut Date: 08Jun2020

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Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	5 (20.8)	(7.1, 42.2)
		Cycle 1	24	0 (0.0)	(0.0, 14.2)
		Cycle 2	23	1 (4.2)	(0.1, 21.1)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	1 (4.2)	(0.1, 21.1)
		Cycle 6	18	1 (4.2)	(0.1, 21.1)
		Cycle 7	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 8 and < 18	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 18	10	2 (8.3)	(1.0, 27.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	45 (28.1)	(21.3, 35.8)
		Cycle 1	160	8 (5.0)	(2.2, 9.6)
		Cycle 2	158	8 (5.0)	(2.2, 9.6)
		Cycle 3	152	6 (3.8)	(1.4, 8.0)
		Cycle 4	147	7 (4.4)	(1.8, 8.8)
		Cycle 5	136	4 (2.5)	(0.7, 6.3)
		Cycle 6	134	1 (0.6)	(0.0, 3.4)
		Cycle 7	127	4 (2.5)	(0.7, 6.3)
		Cycle >= 8 and < 18	120	17 (10.6)	(6.3, 16.5)
		Cycle >= 18	65	7 (4.4)	(1.8, 8.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	20 (37.7)	(24.8, 52.1)
		Cycle 1	53	5 (9.4)	(3.1, 20.7)
		Cycle 2	52	5 (9.4)	(3.1, 20.7)
		Cycle 3	49	2 (3.8)	(0.5, 13.0)
		Cycle 4	48	4 (7.5)	(2.1, 18.2)
		Cycle 5	43	2 (3.8)	(0.5, 13.0)
		Cycle 6	42	0 (0.0)	(0.0, 6.7)
		Cycle 7	41	1 (1.9)	(0.0, 10.1)
		Cycle >= 8 and < 18	39	11 (20.8)	(10.8, 34.1)
		Cycle >= 18	18	1 (1.9)	(0.0, 10.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	30 (22.9)	(16.0, 31.1)
		Cycle 1	131	3 (2.3)	(0.5, 6.5)
		Cycle 2	129	4 (3.1)	(0.8, 7.6)
		Cycle 3	125	4 (3.1)	(0.8, 7.6)
		Cycle 4	121	3 (2.3)	(0.5, 6.5)
		Cycle 5	112	3 (2.3)	(0.5, 6.5)
		Cycle 6	110	2 (1.5)	(0.2, 5.4)
		Cycle 7	104	3 (2.3)	(0.5, 6.5)
		Cycle >= 8 and < 18	99	6 (4.6)	(1.7, 9.7)
		Cycle >= 18	57	8 (6.1)	(2.7, 11.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	46 (27.2)	(20.7, 34.6)
		Cycle 1	169	8 (4.7)	(2.1, 9.1)
		Cycle 2	166	9 (5.3)	(2.5, 9.9)
		Cycle 3	159	6 (3.6)	(1.3, 7.6)
		Cycle 4	154	7 (4.1)	(1.7, 8.3)
		Cycle 5	142	5 (3.0)	(1.0, 6.8)
		Cycle 6	139	2 (1.2)	(0.1, 4.2)
		Cycle 7	132	4 (2.4)	(0.6, 5.9)
		Cycle >= 8 and < 18	125	14 (8.3)	(4.6, 13.5)
		Cycle >= 18	70	8 (4.7)	(2.1, 9.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	4 (26.7)	(7.8, 55.1)
		Cycle 1	15	0 (0.0)	(0.0, 21.8)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	3 (20.0)	(4.3, 48.1)
		Cycle >= 18	5	1 (6.7)	(0.2, 31.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	9 (16.1)	(7.6, 28.3)
		Cycle 1	56	1 (1.8)	(0.0, 9.6)
		Cycle 2	55	1 (1.8)	(0.0, 9.6)
		Cycle 3	54	1 (1.8)	(0.0, 9.6)
		Cycle 4	53	1 (1.8)	(0.0, 9.6)
		Cycle 5	49	1 (1.8)	(0.0, 9.6)
		Cycle 6	48	0 (0.0)	(0.0, 6.4)
		Cycle 7	48	0 (0.0)	(0.0, 6.4)
		Cycle >= 8 and < 18	45	2 (3.6)	(0.4, 12.3)
		Cycle >= 18	32	2 (3.6)	(0.4, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	41 (32.0)	(24.1, 40.9)
		Cycle 1	128	7 (5.5)	(2.2, 10.9)
		Cycle 2	126	8 (6.3)	(2.7, 11.9)
		Cycle 3	120	5 (3.9)	(1.3, 8.9)
		Cycle 4	116	6 (4.7)	(1.7, 9.9)
		Cycle 5	106	4 (3.1)	(0.9, 7.8)
		Cycle 6	104	2 (1.6)	(0.2, 5.5)
		Cycle 7	97	4 (3.1)	(0.9, 7.8)
		Cycle >= 8 and < 18	93	15 (11.7)	(6.7, 18.6)
		Cycle >= 18	43	7 (5.5)	(2.2, 10.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	< 3 lines (N=17)			
	Any TEAE	17	1 (5.9)	(0.1, 28.7)
	Cycle 1	17	0 (0.0)	(0.0, 19.5)
	Cycle 2	17	0 (0.0)	(0.0, 19.5)
	Cycle 3	17	0 (0.0)	(0.0, 19.5)
	Cycle 4	17	0 (0.0)	(0.0, 19.5)
	Cycle 5	17	1 (5.9)	(0.1, 28.7)
	Cycle 6	16	0 (0.0)	(0.0, 19.5)
	Cycle 7	16	0 (0.0)	(0.0, 19.5)
	Cycle >= 8 and < 18	16	0 (0.0)	(0.0, 19.5)
	Cycle >= 18	14	0 (0.0)	(0.0, 19.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	>= 3 lines (N=167)	Any TEAE	167	49 (29.3)
		Cycle 1	167	8 (4.8)
		Cycle 2	164	9 (5.4)
		Cycle 3	157	6 (3.6)
		Cycle 4	152	7 (4.2)
		Cycle 5	138	4 (2.4)
		Cycle 6	136	2 (1.2)
		Cycle 7	129	4 (2.4)
		Cycle >= 8 and < 18	122	17 (10.2)
		Cycle >= 18	61	9 (5.4)
				(2.5, 10.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	17 (21.5)	(13.1, 32.2)
		Cycle 1	79	3 (3.8)	(0.8, 10.7)
		Cycle 2	78	3 (3.8)	(0.8, 10.7)
		Cycle 3	75	1 (1.3)	(0.0, 6.9)
		Cycle 4	73	2 (2.5)	(0.3, 8.8)
		Cycle 5	70	1 (1.3)	(0.0, 6.9)
		Cycle 6	69	0 (0.0)	(0.0, 4.6)
		Cycle 7	68	0 (0.0)	(0.0, 4.6)
		Cycle >= 8 and < 18	65	6 (7.6)	(2.8, 15.8)
		Cycle >= 18	37	3 (3.8)	(0.8, 10.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	22 (33.3)	(22.2, 46.0)
		Cycle 1	66	3 (4.5)	(0.9, 12.7)
		Cycle 2	66	4 (6.1)	(1.7, 14.8)
		Cycle 3	64	3 (4.5)	(0.9, 12.7)
		Cycle 4	61	3 (4.5)	(0.9, 12.7)
		Cycle 5	55	2 (3.0)	(0.4, 10.5)
		Cycle 6	53	2 (3.0)	(0.4, 10.5)
		Cycle 7	51	2 (3.0)	(0.4, 10.5)
		Cycle >= 8 and < 18	51	7 (10.6)	(4.4, 20.6)
		Cycle >= 18	23	5 (7.6)	(2.5, 16.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	21 (17.4)	(11.1, 25.3)
		Cycle 1	121	4 (3.3)	(0.9, 8.2)
		Cycle 2	120	2 (1.7)	(0.2, 5.8)
		Cycle 3	119	3 (2.5)	(0.5, 7.1)
		Cycle 4	115	3 (2.5)	(0.5, 7.1)
		Cycle 5	106	4 (3.3)	(0.9, 8.2)
		Cycle 6	103	1 (0.8)	(0.0, 4.5)
		Cycle 7	96	1 (0.8)	(0.0, 4.5)
		Cycle >= 8 and < 18	93	5 (4.1)	(1.4, 9.4)
		Cycle >= 18	54	3 (2.5)	(0.5, 7.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	29 (46.0)	(33.4, 59.1)
		Cycle 1	63	4 (6.3)	(1.8, 15.5)
		Cycle 2	61	7 (11.1)	(4.6, 21.6)
		Cycle 3	55	3 (4.8)	(1.0, 13.3)
		Cycle 4	54	4 (6.3)	(1.8, 15.5)
		Cycle 5	49	1 (1.6)	(0.0, 8.5)
		Cycle 6	49	1 (1.6)	(0.0, 8.5)
		Cycle 7	49	3 (4.8)	(1.0, 13.3)
		Cycle >= 8 and < 18	45	12 (19.0)	(10.2, 30.9)
		Cycle >= 18	21	6 (9.5)	(3.6, 19.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

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Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	7 (13.7)	(5.7, 26.3)
		Cycle 1	51	2 (3.9)	(0.5, 13.5)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	50	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	3 (5.9)	(1.2, 16.2)
		Cycle 5	46	3 (5.9)	(1.2, 16.2)
		Cycle 6	44	0 (0.0)	(0.0, 7.0)
		Cycle 7	40	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	40	1 (2.0)	(0.0, 10.4)
		Cycle >= 18	24	1 (2.0)	(0.0, 10.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AS_SSI0: Incidence of serious TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	43 (32.3)	(24.5, 41.0)
		Cycle 1	133	6 (4.5)	(1.7, 9.6)
		Cycle 2	131	9 (6.8)	(3.1, 12.5)
		Cycle 3	124	6 (4.5)	(1.7, 9.6)
		Cycle 4	120	4 (3.0)	(0.8, 7.5)
		Cycle 5	109	2 (1.5)	(0.2, 5.3)
		Cycle 6	108	2 (1.5)	(0.2, 5.3)
		Cycle 7	105	4 (3.0)	(0.8, 7.5)
		Cycle >= 8 and < 18	98	16 (12.0)	(7.0, 18.8)
		Cycle >= 18	51	8 (6.0)	(2.6, 11.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

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Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	113 (61.4)	(54.0, 68.5)
		Cycle 1	184	37 (20.1)	(14.6, 26.6)
		Cycle 2	181	27 (14.7)	(9.9, 20.6)
		Cycle 3	174	14 (7.6)	(4.2, 12.4)
		Cycle 4	169	18 (9.8)	(5.9, 15.0)
		Cycle 5	155	10 (5.4)	(2.6, 9.8)
		Cycle 6	152	8 (4.3)	(1.9, 8.4)
		Cycle 7	145	14 (7.6)	(4.2, 12.4)
		Cycle >= 8 and < 18	138	43 (23.4)	(17.5, 30.2)
		Cycle >= 18	75	25 (13.6)	(9.0, 19.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	83 (59.3)
		Cycle 1	140	29 (20.7)
		Cycle 2	138	16 (11.4)
		Cycle 3	132	10 (7.1)
		Cycle 4	128	12 (8.6)
		Cycle 5	116	8 (5.7)
		Cycle 6	113	3 (2.1)
		Cycle 7	109	12 (8.6)
		Cycle >= 8 and < 18	103	28 (20.0)
		Cycle >= 18	56	19 (13.6)
				(8.4, 20.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	30 (68.2) (52.4, 81.4)
		Cycle 1	44	8 (18.2) (8.2, 32.7)
		Cycle 2	43	11 (25.0) (13.2, 40.3)
		Cycle 3	42	4 (9.1) (2.5, 21.7)
		Cycle 4	41	6 (13.6) (5.2, 27.4)
		Cycle 5	39	2 (4.5) (0.6, 15.5)
		Cycle 6	39	5 (11.4) (3.8, 24.6)
		Cycle 7	36	2 (4.5) (0.6, 15.5)
		Cycle >= 8 and < 18	35	15 (34.1) (20.5, 49.9)
		Cycle >= 18	19	6 (13.6) (5.2, 27.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	36 (57.1)	(44.0, 69.5)
		Cycle 1	63	14 (22.2)	(12.7, 34.5)
		Cycle 2	61	7 (11.1)	(4.6, 21.6)
		Cycle 3	58	4 (6.3)	(1.8, 15.5)
		Cycle 4	58	2 (3.2)	(0.4, 11.0)
		Cycle 5	55	3 (4.8)	(1.0, 13.3)
		Cycle 6	55	6 (9.5)	(3.6, 19.6)
		Cycle 7	53	6 (9.5)	(3.6, 19.6)
		Cycle >= 8 and < 18	49	17 (27.0)	(16.6, 39.7)
		Cycle >= 18	29	8 (12.7)	(5.6, 23.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	34 (64.2) (49.8, 76.9)
		Cycle 1	53	11 (20.8) (10.8, 34.1)
		Cycle 2	53	10 (18.9) (9.4, 32.0)
		Cycle 3	52	7 (13.2) (5.5, 25.3)
		Cycle 4	49	9 (17.0) (8.1, 29.8)
		Cycle 5	44	5 (9.4) (3.1, 20.7)
		Cycle 6	42	1 (1.9) (0.0, 10.1)
		Cycle 7	40	3 (5.7) (1.2, 15.7)
		Cycle >= 8 and < 18	39	9 (17.0) (8.1, 29.8)
		Cycle >= 18	23	8 (15.1) (6.7, 27.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	43 (63.2)	(50.7, 74.6)
		Cycle 1	68	12 (17.6)	(9.5, 28.8)
		Cycle 2	67	10 (14.7)	(7.3, 25.4)
		Cycle 3	64	3 (4.4)	(0.9, 12.4)
		Cycle 4	62	7 (10.3)	(4.2, 20.1)
		Cycle 5	56	2 (2.9)	(0.4, 10.2)
		Cycle 6	55	1 (1.5)	(0.0, 7.9)
		Cycle 7	52	5 (7.4)	(2.4, 16.3)
		Cycle >= 8 and < 18	50	17 (25.0)	(15.3, 37.0)
		Cycle >= 18	23	9 (13.2)	(6.2, 23.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	63 (61.8)	(51.6, 71.2)
		Cycle 1	102	20 (19.6)	(12.4, 28.6)
		Cycle 2	101	17 (16.7)	(10.0, 25.3)
		Cycle 3	100	10 (9.8)	(4.8, 17.3)
		Cycle 4	98	5 (4.9)	(1.6, 11.1)
		Cycle 5	94	5 (4.9)	(1.6, 11.1)
		Cycle 6	93	5 (4.9)	(1.6, 11.1)
		Cycle 7	88	6 (5.9)	(2.2, 12.4)
		Cycle >= 8 and < 18	86	21 (20.6)	(13.2, 29.7)
		Cycle >= 18	49	16 (15.7)	(9.2, 24.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	49 (60.5)	(49.0, 71.2)
		Cycle 1	81	17 (21.0)	(12.7, 31.5)
		Cycle 2	79	10 (12.3)	(6.1, 21.5)
		Cycle 3	73	3 (3.7)	(0.8, 10.4)
		Cycle 4	71	13 (16.0)	(8.8, 25.9)
		Cycle 5	61	5 (6.2)	(2.0, 13.8)
		Cycle 6	59	3 (3.7)	(0.8, 10.4)
		Cycle 7	57	8 (9.9)	(4.4, 18.5)
		Cycle >= 8 and < 18	52	22 (27.2)	(17.9, 38.2)
		Cycle >= 18	26	9 (11.1)	(5.2, 20.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions < 5 cm (N=73)	Any TEAE	73	41 (56.2)	(44.1, 67.8)
	Cycle 1	73	8 (11.0)	(4.9, 20.5)
	Cycle 2	72	12 (16.4)	(8.8, 27.0)
	Cycle 3	70	6 (8.2)	(3.1, 17.0)
	Cycle 4	65	6 (8.2)	(3.1, 17.0)
	Cycle 5	60	3 (4.1)	(0.9, 11.5)
	Cycle 6	59	1 (1.4)	(0.0, 7.4)
	Cycle 7	58	7 (9.6)	(3.9, 18.8)
	Cycle >= 8 and < 18	53	17 (23.3)	(14.2, 34.6)
	Cycle >= 18	33	11 (15.1)	(7.8, 25.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=97)			
	Any TEAE	97	62 (63.9)	(53.5, 73.4)
	Cycle 1	97	25 (25.8)	(17.4, 35.7)
	Cycle 2	95	11 (11.3)	(5.8, 19.4)
	Cycle 3	90	7 (7.2)	(3.0, 14.3)
	Cycle 4	90	12 (12.4)	(6.6, 20.6)
	Cycle 5	81	6 (6.2)	(2.3, 13.0)
	Cycle 6	79	6 (6.2)	(2.3, 13.0)
	Cycle 7	74	5 (5.2)	(1.7, 11.6)
	Cycle >= 8 and < 18	72	21 (21.6)	(13.9, 31.2)
	Cycle >= 18	34	11 (11.3)	(5.8, 19.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	97 (63.0)	(54.8, 70.6)
		Cycle 1	154	32 (20.8)	(14.7, 28.0)
		Cycle 2	152	23 (14.9)	(9.7, 21.6)
		Cycle 3	146	12 (7.8)	(4.1, 13.2)
		Cycle 4	141	15 (9.7)	(5.6, 15.6)
		Cycle 5	129	9 (5.8)	(2.7, 10.8)
		Cycle 6	127	8 (5.2)	(2.3, 10.0)
		Cycle 7	121	13 (8.4)	(4.6, 14.0)
		Cycle >= 8 and < 18	114	37 (24.0)	(17.5, 31.6)
		Cycle >= 18	69	23 (14.9)	(9.7, 21.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Any TEAE	28	14 (50.0) (30.6, 69.4)
		Cycle 1	28	5 (17.9) (6.1, 36.9)
		Cycle 2	27	4 (14.3) (4.0, 32.7)
		Cycle 3	26	2 (7.1) (0.9, 23.5)
		Cycle 4	26	3 (10.7) (2.3, 28.2)
		Cycle 5	24	1 (3.6) (0.1, 18.3)
		Cycle 6	23	0 (0.0) (0.0, 12.3)
		Cycle 7	22	1 (3.6) (0.1, 18.3)
		Cycle >= 8 and < 18	22	4 (14.3) (4.0, 32.7)
		Cycle >= 18	5	2 (7.1) (0.9, 23.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	59 (63.4)	(52.8, 73.2)
		Cycle 1	93	25 (26.9)	(18.2, 37.1)
		Cycle 2	92	18 (19.4)	(11.9, 28.9)
		Cycle 3	87	7 (7.5)	(3.1, 14.9)
		Cycle 4	84	8 (8.6)	(3.8, 16.2)
		Cycle 5	80	6 (6.5)	(2.4, 13.5)
		Cycle 6	78	3 (3.2)	(0.7, 9.1)
		Cycle 7	75	7 (7.5)	(3.1, 14.9)
		Cycle >= 8 and < 18	73	22 (23.7)	(15.5, 33.6)
		Cycle >= 18	34	10 (10.8)	(5.3, 18.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	53 (60.2)	(49.2, 70.5)
		Cycle 1	88	12 (13.6)	(7.2, 22.6)
		Cycle 2	86	9 (10.2)	(4.8, 18.5)
		Cycle 3	85	6 (6.8)	(2.5, 14.3)
		Cycle 4	84	10 (11.4)	(5.6, 19.9)
		Cycle 5	74	4 (4.5)	(1.3, 11.2)
		Cycle 6	73	5 (5.7)	(1.9, 12.8)
		Cycle 7	69	7 (8.0)	(3.3, 15.7)
		Cycle >= 8 and < 18	64	21 (23.9)	(15.4, 34.1)
		Cycle >= 18	41	15 (17.0)	(9.9, 26.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	29 (56.9)	(42.2, 70.7)
		Cycle 1	51	12 (23.5)	(12.8, 37.5)
		Cycle 2	50	7 (13.7)	(5.7, 26.3)
		Cycle 3	49	3 (5.9)	(1.2, 16.2)
		Cycle 4	49	2 (3.9)	(0.5, 13.5)
		Cycle 5	47	3 (5.9)	(1.2, 16.2)
		Cycle 6	46	1 (2.0)	(0.0, 10.4)
		Cycle 7	45	6 (11.8)	(4.4, 23.9)
		Cycle >= 8 and < 18	44	14 (27.5)	(15.9, 41.7)
		Cycle >= 18	21	7 (13.7)	(5.7, 26.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	81 (64.8)	(55.8, 73.1)
		Cycle 1	125	24 (19.2)	(12.7, 27.2)
		Cycle 2	123	19 (15.2)	(9.4, 22.7)
		Cycle 3	118	10 (8.0)	(3.9, 14.2)
		Cycle 4	114	16 (12.8)	(7.5, 20.0)
		Cycle 5	103	7 (5.6)	(2.3, 11.2)
		Cycle 6	101	7 (5.6)	(2.3, 11.2)
		Cycle 7	95	8 (6.4)	(2.8, 12.2)
		Cycle >= 8 and < 18	90	29 (23.2)	(16.1, 31.6)
		Cycle >= 18	52	18 (14.4)	(8.8, 21.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	61 (62.9)	(52.5, 72.5)
		Cycle 1	97	26 (26.8)	(18.3, 36.8)
		Cycle 2	96	20 (20.6)	(13.1, 30.0)
		Cycle 3	91	7 (7.2)	(3.0, 14.3)
		Cycle 4	88	8 (8.2)	(3.6, 15.6)
		Cycle 5	84	7 (7.2)	(3.0, 14.3)
		Cycle 6	82	3 (3.1)	(0.6, 8.8)
		Cycle 7	79	8 (8.2)	(3.6, 15.6)
		Cycle >= 8 and < 18	76	23 (23.7)	(15.7, 33.4)
		Cycle >= 18	36	10 (10.3)	(5.1, 18.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	51 (61.4)	(50.1, 71.9)
		Cycle 1	83	11 (13.3)	(6.8, 22.5)
		Cycle 2	81	7 (8.4)	(3.5, 16.6)
		Cycle 3	80	6 (7.2)	(2.7, 15.1)
		Cycle 4	79	10 (12.0)	(5.9, 21.0)
		Cycle 5	69	3 (3.6)	(0.8, 10.2)
		Cycle 6	68	5 (6.0)	(2.0, 13.5)
		Cycle 7	64	6 (7.2)	(2.7, 15.1)
		Cycle >= 8 and < 18	60	20 (24.1)	(15.4, 34.7)
		Cycle >= 18	38	15 (18.1)	(10.5, 28.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Normal (N=90)	Any TEAE	90	54 (60.0)	(49.1, 70.2)
		Cycle 1	90	17 (18.9)	(11.4, 28.5)
		Cycle 2	89	8 (8.9)	(3.9, 16.8)
		Cycle 3	85	4 (4.4)	(1.2, 11.0)
		Cycle 4	85	10 (11.1)	(5.5, 19.5)
		Cycle 5	76	7 (7.8)	(3.2, 15.4)
		Cycle 6	73	1 (1.1)	(0.0, 6.0)
		Cycle 7	72	8 (8.9)	(3.9, 16.8)
		Cycle >= 8 and < 18	69	17 (18.9)	(11.4, 28.5)
		Cycle >= 18	41	14 (15.6)	(8.8, 24.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	45 (65.2)	(52.8, 76.3)
		Cycle 1	69	16 (23.2)	(13.9, 34.9)
		Cycle 2	68	12 (17.4)	(9.3, 28.4)
		Cycle 3	66	7 (10.1)	(4.2, 19.8)
		Cycle 4	63	7 (10.1)	(4.2, 19.8)
		Cycle 5	59	2 (2.9)	(0.4, 10.1)
		Cycle 6	59	5 (7.2)	(2.4, 16.1)
		Cycle 7	56	6 (8.7)	(3.3, 18.0)
		Cycle >= 8 and < 18	54	21 (30.4)	(19.9, 42.7)
		Cycle >= 18	27	9 (13.0)	(6.1, 23.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	14 (56.0)	(34.9, 75.6)
		Cycle 1	25	4 (16.0)	(4.5, 36.1)
		Cycle 2	24	7 (28.0)	(12.1, 49.4)
		Cycle 3	23	3 (12.0)	(2.5, 31.2)
		Cycle 4	21	1 (4.0)	(0.1, 20.4)
		Cycle 5	20	1 (4.0)	(0.1, 20.4)
		Cycle 6	20	2 (8.0)	(1.0, 26.0)
		Cycle 7	17	0 (0.0)	(0.0, 13.7)
		Cycle >= 8 and < 18	15	5 (20.0)	(6.8, 40.7)
		Cycle >= 18	7	2 (8.0)	(1.0, 26.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	72 (68.6)	(58.8, 77.3)
		Cycle 1	105	21 (20.0)	(12.8, 28.9)
		Cycle 2	104	19 (18.1)	(11.3, 26.8)
		Cycle 3	102	11 (10.5)	(5.3, 18.0)
		Cycle 4	98	8 (7.6)	(3.3, 14.5)
		Cycle 5	90	5 (4.8)	(1.6, 10.8)
		Cycle 6	89	7 (6.7)	(2.7, 13.3)
		Cycle 7	87	9 (8.6)	(4.0, 15.6)
		Cycle >= 8 and < 18	84	28 (26.7)	(18.5, 36.2)
		Cycle >= 18	44	16 (15.2)	(9.0, 23.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	38 (50.0)	(38.3, 61.7)
		Cycle 1	76	15 (19.7)	(11.5, 30.5)
		Cycle 2	74	8 (10.5)	(4.7, 19.7)
		Cycle 3	69	3 (3.9)	(0.8, 11.1)
		Cycle 4	68	8 (10.5)	(4.7, 19.7)
		Cycle 5	63	5 (6.6)	(2.2, 14.7)
		Cycle 6	61	1 (1.3)	(0.0, 7.1)
		Cycle 7	56	4 (5.3)	(1.5, 12.9)
		Cycle >= 8 and < 18	54	15 (19.7)	(11.5, 30.5)
		Cycle >= 18	31	9 (11.8)	(5.6, 21.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	15 (62.5)	(40.6, 81.2)
		Cycle 1	24	5 (20.8)	(7.1, 42.2)
		Cycle 2	23	2 (8.3)	(1.0, 27.0)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	1 (4.2)	(0.1, 21.1)
		Cycle 6	18	1 (4.2)	(0.1, 21.1)
		Cycle 7	18	2 (8.3)	(1.0, 27.0)
		Cycle >= 8 and < 18	18	9 (37.5)	(18.8, 59.4)
		Cycle >= 18	10	5 (20.8)	(7.1, 42.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	98 (61.3)	(53.2, 68.8)
		Cycle 1	160	32 (20.0)	(14.1, 27.0)
		Cycle 2	158	25 (15.6)	(10.4, 22.2)
		Cycle 3	152	14 (8.8)	(4.9, 14.2)
		Cycle 4	147	18 (11.3)	(6.8, 17.2)
		Cycle 5	136	9 (5.6)	(2.6, 10.4)
		Cycle 6	134	7 (4.4)	(1.8, 8.8)
		Cycle 7	127	12 (7.5)	(3.9, 12.7)
		Cycle >= 8 and < 18	120	34 (21.3)	(15.2, 28.4)
		Cycle >= 18	65	20 (12.5)	(7.8, 18.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
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Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	38 (71.7)	(57.7, 83.2)
		Cycle 1	53	14 (26.4)	(15.3, 40.3)
		Cycle 2	52	12 (22.6)	(12.3, 36.2)
		Cycle 3	49	3 (5.7)	(1.2, 15.7)
		Cycle 4	48	6 (11.3)	(4.3, 23.0)
		Cycle 5	43	3 (5.7)	(1.2, 15.7)
		Cycle 6	42	2 (3.8)	(0.5, 13.0)
		Cycle 7	41	4 (7.5)	(2.1, 18.2)
		Cycle >= 8 and < 18	39	15 (28.3)	(16.8, 42.3)
		Cycle >= 18	18	6 (11.3)	(4.3, 23.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	75 (57.3)	(48.3, 65.9)
		Cycle 1	131	23 (17.6)	(11.5, 25.2)
		Cycle 2	129	15 (11.5)	(6.6, 18.2)
		Cycle 3	125	11 (8.4)	(4.3, 14.5)
		Cycle 4	121	12 (9.2)	(4.8, 15.5)
		Cycle 5	112	7 (5.3)	(2.2, 10.7)
		Cycle 6	110	6 (4.6)	(1.7, 9.7)
		Cycle 7	104	10 (7.6)	(3.7, 13.6)
		Cycle >= 8 and < 18	99	28 (21.4)	(14.7, 29.4)
		Cycle >= 18	57	19 (14.5)	(9.0, 21.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	105 (62.1)	(54.4, 69.5)
		Cycle 1	169	35 (20.7)	(14.9, 27.6)
		Cycle 2	166	26 (15.4)	(10.3, 21.7)
		Cycle 3	159	13 (7.7)	(4.2, 12.8)
		Cycle 4	154	17 (10.1)	(6.0, 15.6)
		Cycle 5	142	10 (5.9)	(2.9, 10.6)
		Cycle 6	139	8 (4.7)	(2.1, 9.1)
		Cycle 7	132	12 (7.1)	(3.7, 12.1)
		Cycle >= 8 and < 18	125	38 (22.5)	(16.4, 29.5)
		Cycle >= 18	70	21 (12.4)	(7.9, 18.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	8 (53.3)	(26.6, 78.7)
		Cycle 1	15	2 (13.3)	(1.7, 40.5)
		Cycle 2	15	1 (6.7)	(0.2, 31.9)
		Cycle 3	15	1 (6.7)	(0.2, 31.9)
		Cycle 4	15	1 (6.7)	(0.2, 31.9)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	2 (13.3)	(1.7, 40.5)
		Cycle >= 8 and < 18	13	5 (33.3)	(11.8, 61.6)
		Cycle >= 18	5	4 (26.7)	(7.8, 55.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	27 (48.2)	(34.7, 62.0)
		Cycle 1	56	6 (10.7)	(4.0, 21.9)
		Cycle 2	55	3 (5.4)	(1.1, 14.9)
		Cycle 3	54	3 (5.4)	(1.1, 14.9)
		Cycle 4	53	4 (7.1)	(2.0, 17.3)
		Cycle 5	49	1 (1.8)	(0.0, 9.6)
		Cycle 6	48	1 (1.8)	(0.0, 9.6)
		Cycle 7	48	4 (7.1)	(2.0, 17.3)
		Cycle >= 8 and < 18	45	10 (17.9)	(8.9, 30.4)
		Cycle >= 18	32	10 (17.9)	(8.9, 30.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	86 (67.2)	(58.3, 75.2)
		Cycle 1	128	31 (24.2)	(17.1, 32.6)
		Cycle 2	126	24 (18.8)	(12.4, 26.6)
		Cycle 3	120	11 (8.6)	(4.4, 14.9)
		Cycle 4	116	14 (10.9)	(6.1, 17.7)
		Cycle 5	106	9 (7.0)	(3.3, 12.9)
		Cycle 6	104	7 (5.5)	(2.2, 10.9)
		Cycle 7	97	10 (7.8)	(3.8, 13.9)
		Cycle >= 8 and < 18	93	33 (25.8)	(18.5, 34.3)
		Cycle >= 18	43	15 (11.7)	(6.7, 18.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	< 3 lines (N=17)			
	Any TEAE	17	10 (58.8)	(32.9, 81.6)
	Cycle 1	17	4 (23.5)	(6.8, 49.9)
	Cycle 2	17	1 (5.9)	(0.1, 28.7)
	Cycle 3	17	1 (5.9)	(0.1, 28.7)
	Cycle 4	17	3 (17.6)	(3.8, 43.4)
	Cycle 5	17	1 (5.9)	(0.1, 28.7)
	Cycle 6	16	1 (5.9)	(0.1, 28.7)
	Cycle 7	16	2 (11.8)	(1.5, 36.4)
	Cycle >= 8 and < 18	16	4 (23.5)	(6.8, 49.9)
	Cycle >= 18	14	5 (29.4)	(10.3, 56.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
0-Prior treatment lines	>= 3 lines (N=167)			
	Any TEAE	167	103 (61.7)	(53.8, 69.1)
	Cycle 1	167	33 (19.8)	(14.0, 26.6)
	Cycle 2	164	26 (15.6)	(10.4, 22.0)
	Cycle 3	157	13 (7.8)	(4.2, 12.9)
	Cycle 4	152	15 (9.0)	(5.1, 14.4)
	Cycle 5	138	9 (5.4)	(2.5, 10.0)
	Cycle 6	136	7 (4.2)	(1.7, 8.4)
	Cycle 7	129	12 (7.2)	(3.8, 12.2)
	Cycle >= 8 and < 18	122	39 (23.4)	(17.2, 30.5)
	Cycle >= 18	61	20 (12.0)	(7.5, 17.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	49 (62.0)	(50.4, 72.7)
		Cycle 1	79	18 (22.8)	(14.1, 33.6)
		Cycle 2	78	14 (17.7)	(10.0, 27.9)
		Cycle 3	75	6 (7.6)	(2.8, 15.8)
		Cycle 4	73	8 (10.1)	(4.5, 19.0)
		Cycle 5	70	4 (5.1)	(1.4, 12.5)
		Cycle 6	69	4 (5.1)	(1.4, 12.5)
		Cycle 7	68	6 (7.6)	(2.8, 15.8)
		Cycle >= 8 and < 18	65	19 (24.1)	(15.1, 35.0)
		Cycle >= 18	37	12 (15.2)	(8.1, 25.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	43 (65.2)	(52.4, 76.5)
		Cycle 1	66	14 (21.2)	(12.1, 33.0)
		Cycle 2	66	8 (12.1)	(5.4, 22.5)
		Cycle 3	64	6 (9.1)	(3.4, 18.7)
		Cycle 4	61	5 (7.6)	(2.5, 16.8)
		Cycle 5	55	3 (4.5)	(0.9, 12.7)
		Cycle 6	53	4 (6.1)	(1.7, 14.8)
		Cycle 7	51	5 (7.6)	(2.5, 16.8)
		Cycle >= 8 and < 18	51	18 (27.3)	(17.0, 39.6)
		Cycle >= 18	23	10 (15.2)	(7.5, 26.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	71 (58.7)	(49.4, 67.6)
		Cycle 1	121	24 (19.8)	(13.1, 28.1)
		Cycle 2	120	16 (13.2)	(7.8, 20.6)
		Cycle 3	119	9 (7.4)	(3.5, 13.7)
		Cycle 4	115	13 (10.7)	(5.8, 17.7)
		Cycle 5	106	7 (5.8)	(2.4, 11.6)
		Cycle 6	103	5 (4.1)	(1.4, 9.4)
		Cycle 7	96	6 (5.0)	(1.8, 10.5)
		Cycle >= 8 and < 18	93	24 (19.8)	(13.1, 28.1)
		Cycle >= 18	54	16 (13.2)	(7.8, 20.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	42 (66.7)	(53.7, 78.0)
		Cycle 1	63	13 (20.6)	(11.5, 32.7)
		Cycle 2	61	11 (17.5)	(9.1, 29.1)
		Cycle 3	55	5 (7.9)	(2.6, 17.6)
		Cycle 4	54	5 (7.9)	(2.6, 17.6)
		Cycle 5	49	3 (4.8)	(1.0, 13.3)
		Cycle 6	49	3 (4.8)	(1.0, 13.3)
		Cycle 7	49	8 (12.7)	(5.6, 23.5)
		Cycle >= 8 and < 18	45	19 (30.2)	(19.2, 43.0)
		Cycle >= 18	21	9 (14.3)	(6.7, 25.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	30 (58.8)	(44.2, 72.4)
		Cycle 1	51	11 (21.6)	(11.3, 35.3)
		Cycle 2	50	3 (5.9)	(1.2, 16.2)
		Cycle 3	50	1 (2.0)	(0.0, 10.4)
		Cycle 4	49	8 (15.7)	(7.0, 28.6)
		Cycle 5	46	3 (5.9)	(1.2, 16.2)
		Cycle 6	44	1 (2.0)	(0.0, 10.4)
		Cycle 7	40	3 (5.9)	(1.2, 16.2)
		Cycle >= 8 and < 18	40	12 (23.5)	(12.8, 37.5)
		Cycle >= 18	24	9 (17.6)	(8.4, 30.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AC_SSI0: Incidence of severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	83 (62.4)	(53.6, 70.7)
		Cycle 1	133	26 (19.5)	(13.2, 27.3)
		Cycle 2	131	24 (18.0)	(11.9, 25.6)
		Cycle 3	124	13 (9.8)	(5.3, 16.1)
		Cycle 4	120	10 (7.5)	(3.7, 13.4)
		Cycle 5	109	7 (5.3)	(2.1, 10.5)
		Cycle 6	108	7 (5.3)	(2.1, 10.5)
		Cycle 7	105	11 (8.3)	(4.2, 14.3)
		Cycle >= 8 and < 18	98	31 (23.3)	(16.4, 31.4)
		Cycle >= 18	51	16 (12.0)	(7.0, 18.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

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Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	183 (99.5)	(97.0, 100.0)
		Cycle 1	184	171 (92.9)	(88.2, 96.2)
		Cycle 2	181	130 (70.7)	(63.5, 77.1)
		Cycle 3	174	114 (62.0)	(54.5, 69.0)
		Cycle 4	169	102 (55.4)	(47.9, 62.7)
		Cycle 5	155	91 (49.5)	(42.0, 56.9)
		Cycle 6	152	79 (42.9)	(35.7, 50.4)
		Cycle 7	145	85 (46.2)	(38.8, 53.7)
		Cycle >= 8 and < 18	138	121 (65.8)	(58.4, 72.6)
		Cycle >= 18	75	69 (37.5)	(30.5, 44.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	139 (99.3) (96.1, 100.0)
		Cycle 1	140	131 (93.6) (88.1, 97.0)
		Cycle 2	138	98 (70.0) (61.7, 77.4)
		Cycle 3	132	86 (61.4) (52.8, 69.5)
		Cycle 4	128	80 (57.1) (48.5, 65.5)
		Cycle 5	116	68 (48.6) (40.0, 57.2)
		Cycle 6	113	60 (42.9) (34.5, 51.5)
		Cycle 7	109	60 (42.9) (34.5, 51.5)
		Cycle >= 8 and < 18	103	89 (63.6) (55.0, 71.5)
		Cycle >= 18	56	52 (37.1) (29.1, 45.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	44 (100.0) (92.0, 100.0)
		Cycle 1	44	40 (90.9) (78.3, 97.5)
		Cycle 2	43	32 (72.7) (57.2, 85.0)
		Cycle 3	42	28 (63.6) (47.8, 77.6)
		Cycle 4	41	22 (50.0) (34.6, 65.4)
		Cycle 5	39	23 (52.3) (36.7, 67.5)
		Cycle 6	39	19 (43.2) (28.3, 59.0)
		Cycle 7	36	25 (56.8) (41.0, 71.7)
		Cycle >= 8 and < 18	35	32 (72.7) (57.2, 85.0)
		Cycle >= 18	19	17 (38.6) (24.4, 54.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63 (100.0)	(94.3, 100.0)
		Cycle 1	56 (88.9)	(78.4, 95.4)
		Cycle 2	61 (60.3)	(47.2, 72.4)
		Cycle 3	58 (60.3)	(47.2, 72.4)
		Cycle 4	28 (44.4)	(31.9, 57.5)
		Cycle 5	55 (46.0)	(33.4, 59.1)
		Cycle 6	55 (39.7)	(27.6, 52.8)
		Cycle 7	53 (46.0)	(33.4, 59.1)
		Cycle >= 8 and < 18	49 (66.7)	(53.7, 78.0)
		Cycle >= 18	29 (41.3)	(29.0, 54.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	53 (100.0)	(93.3, 100.0)
		Cycle 1	53	52 (98.1)	(89.9, 100.0)
		Cycle 2	53	43 (81.1)	(68.0, 90.6)
		Cycle 3	52	38 (71.7)	(57.7, 83.2)
		Cycle 4	49	37 (69.8)	(55.7, 81.7)
		Cycle 5	44	29 (54.7)	(40.4, 68.4)
		Cycle 6	42	19 (35.8)	(23.1, 50.2)
		Cycle 7	40	19 (35.8)	(23.1, 50.2)
		Cycle >= 8 and < 18	39	34 (64.2)	(49.8, 76.9)
		Cycle >= 18	23	21 (39.6)	(26.5, 54.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	67 (98.5)	(92.1, 100.0)
		Cycle 1	68	63 (92.6)	(83.7, 97.6)
		Cycle 2	67	49 (72.1)	(59.9, 82.3)
		Cycle 3	64	38 (55.9)	(43.3, 67.9)
		Cycle 4	62	37 (54.4)	(41.9, 66.5)
		Cycle 5	56	33 (48.5)	(36.2, 61.0)
		Cycle 6	55	35 (51.5)	(39.0, 63.8)
		Cycle 7	52	37 (54.4)	(41.9, 66.5)
		Cycle >= 8 and < 18	50	45 (66.2)	(53.7, 77.2)
		Cycle >= 18	23	22 (32.4)	(21.5, 44.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	101 (99.0)	(94.7, 100.0)
		Cycle 1	102	94 (92.2)	(85.1, 96.6)
		Cycle 2	101	78 (76.5)	(67.0, 84.3)
		Cycle 3	100	73 (71.6)	(61.8, 80.1)
		Cycle 4	98	62 (60.8)	(50.6, 70.3)
		Cycle 5	94	58 (56.9)	(46.7, 66.6)
		Cycle 6	93	45 (44.1)	(34.3, 54.3)
		Cycle 7	88	55 (53.9)	(43.8, 63.8)
		Cycle >= 8 and < 18	86	77 (75.5)	(66.0, 83.5)
		Cycle >= 18	49	47 (46.1)	(36.2, 56.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	81 (100.0)	(95.5, 100.0)
		Cycle 1	81	76 (93.8)	(86.2, 98.0)
		Cycle 2	79	51 (63.0)	(51.5, 73.4)
		Cycle 3	73	41 (50.6)	(39.3, 61.9)
		Cycle 4	71	40 (49.4)	(38.1, 60.7)
		Cycle 5	61	33 (40.7)	(29.9, 52.2)
		Cycle 6	59	34 (42.0)	(31.1, 53.5)
		Cycle 7	57	30 (37.0)	(26.6, 48.5)
		Cycle >= 8 and < 18	52	44 (54.3)	(42.9, 65.4)
		Cycle >= 18	26	22 (27.2)	(17.9, 38.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions	< 5 cm (N=73)	Any TEAE	73 (100.0)	(95.1, 100.0)
		Cycle 1	73 (93.2)	(84.7, 97.7)
		Cycle 2	72 (75.3)	(63.9, 84.7)
		Cycle 3	70 (65.8)	(53.7, 76.5)
		Cycle 4	65 (57.5)	(45.4, 69.0)
		Cycle 5	60 (47.9)	(36.1, 60.0)
		Cycle 6	59 (41.1)	(29.7, 53.2)
		Cycle 7	58 (43.8)	(32.2, 55.9)
		Cycle >= 8 and < 18	53 (63.0)	(50.9, 74.0)
		Cycle >= 18	33 (42.5)	(31.0, 54.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

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			Overall 5.4 mg/kg SAF (N=184)		
Subgroup		Time Period	N patients in cycle	n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=97)	Any TEAE	97	96 (99.0)	(94.4, 100.0)
		Cycle 1	97	89 (91.8)	(84.4, 96.4)
		Cycle 2	95	64 (66.0)	(55.7, 75.3)
		Cycle 3	90	57 (58.8)	(48.3, 68.7)
		Cycle 4	90	53 (54.6)	(44.2, 64.8)
		Cycle 5	81	47 (48.5)	(38.2, 58.8)
		Cycle 6	79	41 (42.3)	(32.3, 52.7)
		Cycle 7	74	46 (47.4)	(37.2, 57.8)
		Cycle >= 8 and < 18	72	64 (66.0)	(55.7, 75.3)
		Cycle >= 18	34	30 (30.9)	(21.9, 41.1)

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	153 (99.4)	(96.4, 100.0)
		Cycle 1	154	143 (92.9)	(87.6, 96.4)
		Cycle 2	152	113 (73.4)	(65.7, 80.2)
		Cycle 3	146	95 (61.7)	(53.5, 69.4)
		Cycle 4	141	85 (55.2)	(47.0, 63.2)
		Cycle 5	129	76 (49.4)	(41.2, 57.5)
		Cycle 6	127	65 (42.2)	(34.3, 50.4)
		Cycle 7	121	72 (46.8)	(38.7, 55.0)
		Cycle >= 8 and < 18	114	104 (67.5)	(59.5, 74.8)
		Cycle >= 18	69	63 (40.9)	(33.1, 49.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Any TEAE	28	28 (100.0) (87.7, 100.0)
		Cycle 1	28	27 (96.4) (81.7, 99.9)
		Cycle 2	27	16 (57.1) (37.2, 75.5)
		Cycle 3	26	17 (60.7) (40.6, 78.5)
		Cycle 4	26	15 (53.6) (33.9, 72.5)
		Cycle 5	24	14 (50.0) (30.6, 69.4)
		Cycle 6	23	12 (42.9) (24.5, 62.8)
		Cycle 7	22	12 (42.9) (24.5, 62.8)
		Cycle >= 8 and < 18	22	16 (57.1) (37.2, 75.5)
		Cycle >= 18	5	5 (17.9) (6.1, 36.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	92 (98.9)	(94.2, 100.0)
		Cycle 1	93	87 (93.5)	(86.5, 97.6)
		Cycle 2	92	65 (69.9)	(59.5, 79.0)
		Cycle 3	87	55 (59.1)	(48.5, 69.2)
		Cycle 4	84	55 (59.1)	(48.5, 69.2)
		Cycle 5	80	50 (53.8)	(43.1, 64.2)
		Cycle 6	78	41 (44.1)	(33.8, 54.8)
		Cycle 7	75	47 (50.5)	(40.0, 61.1)
		Cycle >= 8 and < 18	73	62 (66.7)	(56.1, 76.1)
		Cycle >= 18	34	30 (32.3)	(22.9, 42.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	88 (100.0)	(95.9, 100.0)
		Cycle 1	88	81 (92.0)	(84.3, 96.7)
		Cycle 2	86	64 (72.7)	(62.2, 81.7)
		Cycle 3	85	59 (67.0)	(56.2, 76.7)
		Cycle 4	84	47 (53.4)	(42.5, 64.1)
		Cycle 5	74	41 (46.6)	(35.9, 57.5)
		Cycle 6	73	38 (43.2)	(32.7, 54.2)
		Cycle 7	69	37 (42.0)	(31.6, 53.0)
		Cycle >= 8 and < 18	64	58 (65.9)	(55.0, 75.7)
		Cycle >= 18	41	39 (44.3)	(33.7, 55.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	50 (98.0)	(89.6, 100.0)
		Cycle 1	51	48 (94.1)	(83.8, 98.8)
		Cycle 2	50	34 (66.7)	(52.1, 79.2)
		Cycle 3	49	34 (66.7)	(52.1, 79.2)
		Cycle 4	49	27 (52.9)	(38.5, 67.1)
		Cycle 5	47	27 (52.9)	(38.5, 67.1)
		Cycle 6	46	21 (41.2)	(27.6, 55.8)
		Cycle 7	45	26 (51.0)	(36.6, 65.2)
		Cycle >= 8 and < 18	44	38 (74.5)	(60.4, 85.7)
		Cycle >= 18	21	20 (39.2)	(25.8, 53.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	125 (100.0)	(97.1, 100.0)
		Cycle 1	125	115 (92.0)	(85.8, 96.1)
		Cycle 2	123	91 (72.8)	(64.1, 80.4)
		Cycle 3	118	78 (62.4)	(53.3, 70.9)
		Cycle 4	114	72 (57.6)	(48.4, 66.4)
		Cycle 5	103	62 (49.6)	(40.5, 58.7)
		Cycle 6	101	56 (44.8)	(35.9, 54.0)
		Cycle 7	95	56 (44.8)	(35.9, 54.0)
		Cycle >= 8 and < 18	90	80 (64.0)	(54.9, 72.4)
		Cycle >= 18	52	47 (37.6)	(29.1, 46.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	96 (99.0)	(94.4, 100.0)
		Cycle 1	97	91 (93.8)	(87.0, 97.7)
		Cycle 2	96	69 (71.1)	(61.0, 79.9)
		Cycle 3	91	58 (59.8)	(49.3, 69.6)
		Cycle 4	88	56 (57.7)	(47.3, 67.7)
		Cycle 5	84	52 (53.6)	(43.2, 63.8)
		Cycle 6	82	42 (43.3)	(33.3, 53.7)
		Cycle 7	79	48 (49.5)	(39.2, 59.8)
		Cycle >= 8 and < 18	76	65 (67.0)	(56.7, 76.2)
		Cycle >= 18	36	32 (33.0)	(23.8, 43.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	83 (100.0)	(95.7, 100.0)
		Cycle 1	83	76 (91.6)	(83.4, 96.5)
		Cycle 2	81	59 (71.1)	(60.1, 80.5)
		Cycle 3	80	56 (67.5)	(56.3, 77.4)
		Cycle 4	79	46 (55.4)	(44.1, 66.3)
		Cycle 5	69	39 (47.0)	(35.9, 58.3)
		Cycle 6	68	37 (44.6)	(33.7, 55.9)
		Cycle 7	64	36 (43.4)	(32.5, 54.7)
		Cycle >= 8 and < 18	60	54 (65.1)	(53.8, 75.2)
		Cycle >= 18	38	36 (43.4)	(32.5, 54.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Normal (N=90)	Any TEAE	90	89 (98.9)	(94.0, 100.0)
		Cycle 1	90	85 (94.4)	(87.5, 98.2)
		Cycle 2	89	59 (65.6)	(54.8, 75.3)
		Cycle 3	85	53 (58.9)	(48.0, 69.2)
		Cycle 4	85	53 (58.9)	(48.0, 69.2)
		Cycle 5	76	45 (50.0)	(39.3, 60.7)
		Cycle 6	73	38 (42.2)	(31.9, 53.1)
		Cycle 7	72	42 (46.7)	(36.1, 57.5)
		Cycle >= 8 and < 18	69	57 (63.3)	(52.5, 73.2)
		Cycle >= 18	41	38 (42.2)	(31.9, 53.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69 (100.0)	(94.8, 100.0)
		Cycle 1	69 (91.3)	(82.0, 96.7)
		Cycle 2	68 (78.3)	(66.7, 87.3)
		Cycle 3	66 (68.1)	(55.8, 78.8)
		Cycle 4	63 (53.6)	(41.2, 65.7)
		Cycle 5	59 (50.7)	(38.4, 63.0)
		Cycle 6	59 (43.5)	(31.6, 56.0)
		Cycle 7	56 (46.4)	(34.3, 58.8)
		Cycle >= 8 and < 18	54 (72.5)	(60.4, 82.5)
		Cycle >= 18	27 (37.7)	(26.3, 50.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	25 (100.0)	(86.3, 100.0)
		Cycle 1	25	23 (92.0)	(74.0, 99.0)
		Cycle 2	24	17 (68.0)	(46.5, 85.1)
		Cycle 3	23	14 (56.0)	(34.9, 75.6)
		Cycle 4	21	12 (48.0)	(27.8, 68.7)
		Cycle 5	20	11 (44.0)	(24.4, 65.1)
		Cycle 6	20	11 (44.0)	(24.4, 65.1)
		Cycle 7	17	11 (44.0)	(24.4, 65.1)
		Cycle >= 8 and < 18	15	14 (56.0)	(34.9, 75.6)
		Cycle >= 18	7	5 (20.0)	(6.8, 40.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	104 (99.0)	(94.8, 100.0)
		Cycle 1	105	98 (93.3)	(86.7, 97.3)
		Cycle 2	104	74 (70.5)	(60.8, 79.0)
		Cycle 3	102	68 (64.8)	(54.8, 73.8)
		Cycle 4	98	64 (61.0)	(50.9, 70.3)
		Cycle 5	90	49 (46.7)	(36.9, 56.7)
		Cycle 6	89	48 (45.7)	(36.0, 55.7)
		Cycle 7	87	52 (49.5)	(39.6, 59.5)
		Cycle >= 8 and < 18	84	76 (72.4)	(62.8, 80.7)
		Cycle >= 18	44	42 (40.0)	(30.6, 50.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	76 (100.0)	(95.3, 100.0)
		Cycle 1	76	70 (92.1)	(83.6, 97.0)
		Cycle 2	74	53 (69.7)	(58.1, 79.8)
		Cycle 3	69	44 (57.9)	(46.0, 69.1)
		Cycle 4	68	37 (48.7)	(37.0, 60.4)
		Cycle 5	63	41 (53.9)	(42.1, 65.5)
		Cycle 6	61	31 (40.8)	(29.6, 52.7)
		Cycle 7	56	32 (42.1)	(30.9, 54.0)
		Cycle >= 8 and < 18	54	45 (59.2)	(47.3, 70.4)
		Cycle >= 18	31	27 (35.5)	(24.9, 47.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	24 (100.0)	(85.8, 100.0)
		Cycle 1	24	22 (91.7)	(73.0, 99.0)
		Cycle 2	23	15 (62.5)	(40.6, 81.2)
		Cycle 3	22	13 (54.2)	(32.8, 74.4)
		Cycle 4	22	14 (58.3)	(36.6, 77.9)
		Cycle 5	19	9 (37.5)	(18.8, 59.4)
		Cycle 6	18	11 (45.8)	(25.6, 67.2)
		Cycle 7	18	15 (62.5)	(40.6, 81.2)
		Cycle >= 8 and < 18	18	18 (75.0)	(53.3, 90.2)
		Cycle >= 18	10	10 (41.7)	(22.1, 63.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	159 (99.4)	(96.6, 100.0)
		Cycle 1	160	149 (93.1)	(88.0, 96.5)
		Cycle 2	158	115 (71.9)	(64.2, 78.7)
		Cycle 3	152	101 (63.1)	(55.1, 70.6)
		Cycle 4	147	88 (55.0)	(46.9, 62.9)
		Cycle 5	136	82 (51.3)	(43.2, 59.2)
		Cycle 6	134	68 (42.5)	(34.7, 50.6)
		Cycle 7	127	70 (43.8)	(35.9, 51.8)
		Cycle >= 8 and < 18	120	103 (64.4)	(56.4, 71.8)
		Cycle >= 18	65	59 (36.9)	(29.4, 44.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	53 (100.0)	(93.3, 100.0)
		Cycle 1	53	50 (94.3)	(84.3, 98.8)
		Cycle 2	52	40 (75.5)	(61.7, 86.2)
		Cycle 3	49	29 (54.7)	(40.4, 68.4)
		Cycle 4	48	32 (60.4)	(46.0, 73.5)
		Cycle 5	43	25 (47.2)	(33.3, 61.4)
		Cycle 6	42	27 (50.9)	(36.8, 64.9)
		Cycle 7	41	30 (56.6)	(42.3, 70.2)
		Cycle >= 8 and < 18	39	36 (67.9)	(53.7, 80.1)
		Cycle >= 18	18	16 (30.2)	(18.3, 44.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	130 (99.2)	(95.8, 100.0)
		Cycle 1	131	121 (92.4)	(86.4, 96.3)
		Cycle 2	129	90 (68.7)	(60.0, 76.5)
		Cycle 3	125	85 (64.9)	(56.1, 73.0)
		Cycle 4	121	70 (53.4)	(44.5, 62.2)
		Cycle 5	112	66 (50.4)	(41.5, 59.2)
		Cycle 6	110	52 (39.7)	(31.3, 48.6)
		Cycle 7	104	55 (42.0)	(33.4, 50.9)
		Cycle >= 8 and < 18	99	85 (64.9)	(56.1, 73.0)
		Cycle >= 18	57	53 (40.5)	(32.0, 49.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	168 (99.4)	(96.7, 100.0)
		Cycle 1	169	157 (92.9)	(87.9, 96.3)
		Cycle 2	166	119 (70.4)	(62.9, 77.2)
		Cycle 3	159	102 (60.4)	(52.6, 67.8)
		Cycle 4	154	93 (55.0)	(47.2, 62.7)
		Cycle 5	142	83 (49.1)	(41.4, 56.9)
		Cycle 6	139	72 (42.6)	(35.0, 50.4)
		Cycle 7	132	79 (46.7)	(39.0, 54.6)
		Cycle >= 8 and < 18	125	110 (65.1)	(57.4, 72.2)
		Cycle >= 18	70	64 (37.9)	(30.5, 45.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	15 (100.0)	(78.2, 100.0)
		Cycle 1	15	14 (93.3)	(68.1, 99.8)
		Cycle 2	15	11 (73.3)	(44.9, 92.2)
		Cycle 3	15	12 (80.0)	(51.9, 95.7)
		Cycle 4	15	9 (60.0)	(32.3, 83.7)
		Cycle 5	13	8 (53.3)	(26.6, 78.7)
		Cycle 6	13	7 (46.7)	(21.3, 73.4)
		Cycle 7	13	6 (40.0)	(16.3, 67.7)
		Cycle >= 8 and < 18	13	11 (73.3)	(44.9, 92.2)
		Cycle >= 18	5	5 (33.3)	(11.8, 61.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	56 (100.0)	(93.6, 100.0)
		Cycle 1	56	53 (94.6)	(85.1, 98.9)
		Cycle 2	55	41 (73.2)	(59.7, 84.2)
		Cycle 3	54	36 (64.3)	(50.4, 76.6)
		Cycle 4	53	31 (55.4)	(41.5, 68.7)
		Cycle 5	49	29 (51.8)	(38.0, 65.3)
		Cycle 6	48	23 (41.1)	(28.1, 55.0)
		Cycle 7	48	26 (46.4)	(33.0, 60.3)
		Cycle >= 8 and < 18	45	38 (67.9)	(54.0, 79.7)
		Cycle >= 18	32	31 (55.4)	(41.5, 68.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	127 (99.2)	(95.7, 100.0)
		Cycle 1	128	118 (92.2)	(86.1, 96.2)
		Cycle 2	126	89 (69.5)	(60.8, 77.4)
		Cycle 3	120	78 (60.9)	(51.9, 69.4)
		Cycle 4	116	71 (55.5)	(46.4, 64.3)
		Cycle 5	106	62 (48.4)	(39.5, 57.4)
		Cycle 6	104	56 (43.8)	(35.0, 52.8)
		Cycle 7	97	59 (46.1)	(37.2, 55.1)
		Cycle >= 8 and < 18	93	83 (64.8)	(55.9, 73.1)
		Cycle >= 18	43	38 (29.7)	(21.9, 38.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	< 3 lines (N=17)	Any TEAE	17 (100.0)	(80.5, 100.0)
		Cycle 1	16 (94.1)	(71.3, 99.9)
		Cycle 2	13 (76.5)	(50.1, 93.2)
		Cycle 3	11 (64.7)	(38.3, 85.8)
		Cycle 4	12 (70.6)	(44.0, 89.7)
		Cycle 5	9 (52.9)	(27.8, 77.0)
		Cycle 6	8 (47.1)	(23.0, 72.2)
		Cycle 7	8 (47.1)	(23.0, 72.2)
		Cycle >= 8 and < 18	16 (76.5)	(50.1, 93.2)
		Cycle >= 18	14 (76.5)	(50.1, 93.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	>= 3 lines (N=167)	Any TEAE	167	166 (99.4) (96.7, 100.0)
		Cycle 1	167	155 (92.8) (87.8, 96.2)
		Cycle 2	164	117 (70.1) (62.5, 76.9)
		Cycle 3	157	103 (61.7) (53.8, 69.1)
		Cycle 4	152	90 (53.9) (46.0, 61.6)
		Cycle 5	138	82 (49.1) (41.3, 56.9)
		Cycle 6	136	71 (42.5) (34.9, 50.4)
		Cycle 7	129	77 (46.1) (38.4, 54.0)
		Cycle >= 8 and < 18	122	108 (64.7) (56.9, 71.9)
		Cycle >= 18	61	56 (33.5) (26.4, 41.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)			
	Any TEAE	79	78 (98.7)	(93.1, 100.0)
	Cycle 1	79	72 (91.1)	(82.6, 96.4)
	Cycle 2	78	54 (68.4)	(56.9, 78.4)
	Cycle 3	75	49 (62.0)	(50.4, 72.7)
	Cycle 4	73	40 (50.6)	(39.1, 62.1)
	Cycle 5	70	42 (53.2)	(41.6, 64.5)
	Cycle 6	69	35 (44.3)	(33.1, 55.9)
	Cycle 7	68	41 (51.9)	(40.4, 63.3)
	Cycle >= 8 and < 18	65	58 (73.4)	(62.3, 82.7)
	Cycle >= 18	37	35 (44.3)	(33.1, 55.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	66 (100.0)	(94.6, 100.0)
		Cycle 1	66	62 (93.9)	(85.2, 98.3)
		Cycle 2	66	46 (69.7)	(57.1, 80.4)
		Cycle 3	64	38 (57.6)	(44.8, 69.7)
		Cycle 4	61	38 (57.6)	(44.8, 69.7)
		Cycle 5	55	26 (39.4)	(27.6, 52.2)
		Cycle 6	53	25 (37.9)	(26.2, 50.7)
		Cycle 7	51	29 (43.9)	(31.7, 56.7)
		Cycle >= 8 and < 18	51	44 (66.7)	(54.0, 77.8)
		Cycle >= 18	23	19 (28.8)	(18.3, 41.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	121 (100.0)	(97.0, 100.0)
		Cycle 1	121	112 (92.6)	(86.3, 96.5)
		Cycle 2	120	85 (70.2)	(61.3, 78.2)
		Cycle 3	119	77 (63.6)	(54.4, 72.2)
		Cycle 4	115	74 (61.2)	(51.9, 69.9)
		Cycle 5	106	68 (56.2)	(46.9, 65.2)
		Cycle 6	103	51 (42.1)	(33.2, 51.5)
		Cycle 7	96	55 (45.5)	(36.4, 54.8)
		Cycle >= 8 and < 18	93	80 (66.1)	(57.0, 74.5)
		Cycle >= 18	54	49 (40.5)	(31.7, 49.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	62 (98.4)	(91.5, 100.0)
		Cycle 1	63	59 (93.7)	(84.5, 98.2)
		Cycle 2	61	45 (71.4)	(58.7, 82.1)
		Cycle 3	55	37 (58.7)	(45.6, 71.0)
		Cycle 4	54	28 (44.4)	(31.9, 57.5)
		Cycle 5	49	23 (36.5)	(24.7, 49.6)
		Cycle 6	49	28 (44.4)	(31.9, 57.5)
		Cycle 7	49	30 (47.6)	(34.9, 60.6)
		Cycle >= 8 and < 18	45	41 (65.1)	(52.0, 76.7)
		Cycle >= 18	21	20 (31.7)	(20.6, 44.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	51 (100.0)	(93.0, 100.0)
		Cycle 1	51	46 (90.2)	(78.6, 96.7)
		Cycle 2	50	36 (70.6)	(56.2, 82.5)
		Cycle 3	50	28 (54.9)	(40.3, 68.9)
		Cycle 4	49	32 (62.7)	(48.1, 75.9)
		Cycle 5	46	29 (56.9)	(42.2, 70.7)
		Cycle 6	44	22 (43.1)	(29.3, 57.8)
		Cycle 7	40	25 (49.0)	(34.8, 63.4)
		Cycle >= 8 and < 18	40	33 (64.7)	(50.1, 77.6)
		Cycle >= 18	24	22 (43.1)	(29.3, 57.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AN_SSI0: Incidence of non-severe TEAEs overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	132 (99.2)	(95.9, 100.0)
		Cycle 1	133	125 (94.0)	(88.5, 97.4)
		Cycle 2	131	94 (70.7)	(62.2, 78.2)
		Cycle 3	124	86 (64.7)	(55.9, 72.7)
		Cycle 4	120	70 (52.6)	(43.8, 61.3)
		Cycle 5	109	62 (46.6)	(37.9, 55.5)
		Cycle 6	108	57 (42.9)	(34.3, 51.7)
		Cycle 7	105	60 (45.1)	(36.5, 54.0)
		Cycle >= 8 and < 18	98	88 (66.2)	(57.5, 74.1)
		Cycle >= 18	51	47 (35.3)	(27.3, 44.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

UE, die zum Therapieabbruch führten

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	34 (18.5)	(13.1, 24.9)
		Cycle 1	184	4 (2.2)	(0.6, 5.5)
		Cycle 2	181	2 (1.1)	(0.1, 3.9)
		Cycle 3	174	1 (0.5)	(0.0, 3.0)
		Cycle 4	169	1 (0.5)	(0.0, 3.0)
		Cycle 5	155	0 (0.0)	(0.0, 2.0)
		Cycle 6	152	3 (1.6)	(0.3, 4.7)
		Cycle 7	145	3 (1.6)	(0.3, 4.7)
		Cycle >= 8 and < 18	138	13 (7.1)	(3.8, 11.8)
		Cycle >= 18	75	8 (4.3)	(1.9, 8.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

			Overall 5.4 mg/kg SAF (N=184)	
Subgroup	Time Period	N patients in cycle	n (%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	25 (17.9) (11.9, 25.2)
		Cycle 1	140	4 (2.9) (0.8, 7.2)
		Cycle 2	138	2 (1.4) (0.2, 5.1)
		Cycle 3	132	1 (0.7) (0.0, 3.9)
		Cycle 4	128	1 (0.7) (0.0, 3.9)
		Cycle 5	116	0 (0.0) (0.0, 2.6)
		Cycle 6	113	2 (1.4) (0.2, 5.1)
		Cycle 7	109	3 (2.1) (0.4, 6.1)
		Cycle >= 8 and < 18	103	9 (6.4) (3.0, 11.9)
		Cycle >= 18	56	4 (2.9) (0.8, 7.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	9 (20.5) (9.8, 35.3)
		Cycle 1	44	0 (0.0) (0.0, 8.0)
		Cycle 2	43	0 (0.0) (0.0, 8.0)
		Cycle 3	42	0 (0.0) (0.0, 8.0)
		Cycle 4	41	0 (0.0) (0.0, 8.0)
		Cycle 5	39	0 (0.0) (0.0, 8.0)
		Cycle 6	39	1 (2.3) (0.1, 12.0)
		Cycle 7	36	0 (0.0) (0.0, 8.0)
		Cycle >= 8 and < 18	35	4 (9.1) (2.5, 21.7)
		Cycle >= 18	19	4 (9.1) (2.5, 21.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	17 (27.0) (16.6, 39.7)
		Cycle 1	63	3 (4.8) (1.0, 13.3)
		Cycle 2	61	1 (1.6) (0.0, 8.5)
		Cycle 3	58	0 (0.0) (0.0, 5.7)
		Cycle 4	58	0 (0.0) (0.0, 5.7)
		Cycle 5	55	0 (0.0) (0.0, 5.7)
		Cycle 6	55	1 (1.6) (0.0, 8.5)
		Cycle 7	53	2 (3.2) (0.4, 11.0)
		Cycle >= 8 and < 18	49	6 (9.5) (3.6, 19.6)
		Cycle >= 18	29	5 (7.9) (2.6, 17.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	6 (11.3) (4.3, 23.0)
		Cycle 1	53	0 (0.0) (0.0, 6.7)
		Cycle 2	53	0 (0.0) (0.0, 6.7)
		Cycle 3	52	0 (0.0) (0.0, 6.7)
		Cycle 4	49	1 (1.9) (0.0, 10.1)
		Cycle 5	44	0 (0.0) (0.0, 6.7)
		Cycle 6	42	2 (3.8) (0.5, 13.0)
		Cycle 7	40	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	2 (3.8) (0.5, 13.0)
		Cycle >= 18	23	1 (1.9) (0.0, 10.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	11 (16.2)	(8.4, 27.1)
		Cycle 1	68	1 (1.5)	(0.0, 7.9)
		Cycle 2	67	1 (1.5)	(0.0, 7.9)
		Cycle 3	64	1 (1.5)	(0.0, 7.9)
		Cycle 4	62	0 (0.0)	(0.0, 5.3)
		Cycle 5	56	0 (0.0)	(0.0, 5.3)
		Cycle 6	55	0 (0.0)	(0.0, 5.3)
		Cycle 7	52	1 (1.5)	(0.0, 7.9)
		Cycle >= 8 and < 18	50	5 (7.4)	(2.4, 16.3)
		Cycle >= 18	23	2 (2.9)	(0.4, 10.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	22 (21.6)	(14.0, 30.8)
		Cycle 1	102	3 (2.9)	(0.6, 8.4)
		Cycle 2	101	0 (0.0)	(0.0, 3.6)
		Cycle 3	100	1 (1.0)	(0.0, 5.3)
		Cycle 4	98	0 (0.0)	(0.0, 3.6)
		Cycle 5	94	0 (0.0)	(0.0, 3.6)
		Cycle 6	93	3 (2.9)	(0.6, 8.4)
		Cycle 7	88	1 (1.0)	(0.0, 5.3)
		Cycle >= 8 and < 18	86	9 (8.8)	(4.1, 16.1)
		Cycle >= 18	49	6 (5.9)	(2.2, 12.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	12 (14.8)	(7.9, 24.4)
		Cycle 1	81	1 (1.2)	(0.0, 6.7)
		Cycle 2	79	2 (2.5)	(0.3, 8.6)
		Cycle 3	73	0 (0.0)	(0.0, 4.5)
		Cycle 4	71	1 (1.2)	(0.0, 6.7)
		Cycle 5	61	0 (0.0)	(0.0, 4.5)
		Cycle 6	59	0 (0.0)	(0.0, 4.5)
		Cycle 7	57	2 (2.5)	(0.3, 8.6)
		Cycle >= 8 and < 18	52	4 (4.9)	(1.4, 12.2)
		Cycle >= 18	26	2 (2.5)	(0.3, 8.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions < 5 cm (N=73)	Any TEAE	73	18 (24.7)	(15.3, 36.1)
	Cycle 1	73	0 (0.0)	(0.0, 4.9)
	Cycle 2	72	1 (1.4)	(0.0, 7.4)
	Cycle 3	70	1 (1.4)	(0.0, 7.4)
	Cycle 4	65	1 (1.4)	(0.0, 7.4)
	Cycle 5	60	0 (0.0)	(0.0, 4.9)
	Cycle 6	59	0 (0.0)	(0.0, 4.9)
	Cycle 7	58	3 (4.1)	(0.9, 11.5)
	Cycle >= 8 and < 18	53	8 (11.0)	(4.9, 20.5)
	Cycle >= 18	33	4 (5.5)	(1.5, 13.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=97)	Any TEAE	97	12 (12.4) (6.6, 20.6)
		Cycle 1	97	4 (4.1) (1.1, 10.2)
		Cycle 2	95	1 (1.0) (0.0, 5.6)
		Cycle 3	90	0 (0.0) (0.0, 3.7)
		Cycle 4	90	0 (0.0) (0.0, 3.7)
		Cycle 5	81	0 (0.0) (0.0, 3.7)
		Cycle 6	79	2 (2.1) (0.3, 7.3)
		Cycle 7	74	0 (0.0) (0.0, 3.7)
		Cycle >= 8 and < 18	72	3 (3.1) (0.6, 8.8)
		Cycle >= 18	34	3 (3.1) (0.6, 8.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	29 (18.8)	(13.0, 25.9)
		Cycle 1	154	4 (2.6)	(0.7, 6.5)
		Cycle 2	152	2 (1.3)	(0.2, 4.6)
		Cycle 3	146	1 (0.6)	(0.0, 3.6)
		Cycle 4	141	1 (0.6)	(0.0, 3.6)
		Cycle 5	129	0 (0.0)	(0.0, 2.4)
		Cycle 6	127	2 (1.3)	(0.2, 4.6)
		Cycle 7	121	3 (1.9)	(0.4, 5.6)
		Cycle >= 8 and < 18	114	10 (6.5)	(3.2, 11.6)
		Cycle >= 18	69	7 (4.5)	(1.8, 9.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Any TEAE	28	4 (14.3) (4.0, 32.7)
		Cycle 1	28	0 (0.0) (0.0, 12.3)
		Cycle 2	27	0 (0.0) (0.0, 12.3)
		Cycle 3	26	0 (0.0) (0.0, 12.3)
		Cycle 4	26	0 (0.0) (0.0, 12.3)
		Cycle 5	24	0 (0.0) (0.0, 12.3)
		Cycle 6	23	1 (3.6) (0.1, 18.3)
		Cycle 7	22	0 (0.0) (0.0, 12.3)
		Cycle >= 8 and < 18	22	2 (7.1) (0.9, 23.5)
		Cycle >= 18	5	1 (3.6) (0.1, 18.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	18 (19.4)	(11.9, 28.9)
		Cycle 1	93	2 (2.2)	(0.3, 7.6)
		Cycle 2	92	1 (1.1)	(0.0, 5.8)
		Cycle 3	87	0 (0.0)	(0.0, 3.9)
		Cycle 4	84	1 (1.1)	(0.0, 5.8)
		Cycle 5	80	0 (0.0)	(0.0, 3.9)
		Cycle 6	78	2 (2.2)	(0.3, 7.6)
		Cycle 7	75	0 (0.0)	(0.0, 3.9)
		Cycle >= 8 and < 18	73	8 (8.6)	(3.8, 16.2)
		Cycle >= 18	34	5 (5.4)	(1.8, 12.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	16 (18.2)	(10.8, 27.8)
		Cycle 1	88	2 (2.3)	(0.3, 8.0)
		Cycle 2	86	1 (1.1)	(0.0, 6.2)
		Cycle 3	85	1 (1.1)	(0.0, 6.2)
		Cycle 4	84	0 (0.0)	(0.0, 4.1)
		Cycle 5	74	0 (0.0)	(0.0, 4.1)
		Cycle 6	73	1 (1.1)	(0.0, 6.2)
		Cycle 7	69	3 (3.4)	(0.7, 9.6)
		Cycle >= 8 and < 18	64	5 (5.7)	(1.9, 12.8)
		Cycle >= 18	41	3 (3.4)	(0.7, 9.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	10 (19.6)	(9.8, 33.1)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	1 (2.0)	(0.0, 10.4)
		Cycle 3	49	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	47	0 (0.0)	(0.0, 7.0)
		Cycle 6	46	1 (2.0)	(0.0, 10.4)
		Cycle 7	45	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	44	4 (7.8)	(2.2, 18.9)
		Cycle >= 18	21	4 (7.8)	(2.2, 18.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	24 (19.2)	(12.7, 27.2)
		Cycle 1	125	4 (3.2)	(0.9, 8.0)
		Cycle 2	123	1 (0.8)	(0.0, 4.4)
		Cycle 3	118	1 (0.8)	(0.0, 4.4)
		Cycle 4	114	1 (0.8)	(0.0, 4.4)
		Cycle 5	103	0 (0.0)	(0.0, 2.9)
		Cycle 6	101	2 (1.6)	(0.2, 5.7)
		Cycle 7	95	3 (2.4)	(0.5, 6.9)
		Cycle >= 8 and < 18	90	9 (7.2)	(3.3, 13.2)
		Cycle >= 18	52	4 (3.2)	(0.9, 8.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	19 (19.6)	(12.2, 28.9)
		Cycle 1	97	2 (2.1)	(0.3, 7.3)
		Cycle 2	96	1 (1.0)	(0.0, 5.6)
		Cycle 3	91	0 (0.0)	(0.0, 3.7)
		Cycle 4	88	1 (1.0)	(0.0, 5.6)
		Cycle 5	84	0 (0.0)	(0.0, 3.7)
		Cycle 6	82	2 (2.1)	(0.3, 7.3)
		Cycle 7	79	0 (0.0)	(0.0, 3.7)
		Cycle >= 8 and < 18	76	8 (8.2)	(3.6, 15.6)
		Cycle >= 18	36	6 (6.2)	(2.3, 13.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	15 (18.1)	(10.5, 28.0)
		Cycle 1	83	2 (2.4)	(0.3, 8.4)
		Cycle 2	81	1 (1.2)	(0.0, 6.5)
		Cycle 3	80	1 (1.2)	(0.0, 6.5)
		Cycle 4	79	0 (0.0)	(0.0, 4.3)
		Cycle 5	69	0 (0.0)	(0.0, 4.3)
		Cycle 6	68	1 (1.2)	(0.0, 6.5)
		Cycle 7	64	3 (3.6)	(0.8, 10.2)
		Cycle >= 8 and < 18	60	5 (6.0)	(2.0, 13.5)
		Cycle >= 18	38	2 (2.4)	(0.3, 8.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
I-Renal impairment	Normal (N=90)	Any TEAE	90	15 (16.7)	(9.6, 26.0)
		Cycle 1	90	3 (3.3)	(0.7, 9.4)
		Cycle 2	89	1 (1.1)	(0.0, 6.0)
		Cycle 3	85	0 (0.0)	(0.0, 4.0)
		Cycle 4	85	0 (0.0)	(0.0, 4.0)
		Cycle 5	76	0 (0.0)	(0.0, 4.0)
		Cycle 6	73	0 (0.0)	(0.0, 4.0)
		Cycle 7	72	1 (1.1)	(0.0, 6.0)
		Cycle >= 8 and < 18	69	7 (7.8)	(3.2, 15.4)
		Cycle >= 18	41	4 (4.4)	(1.2, 11.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	13 (18.8)	(10.4, 30.1)
		Cycle 1	69	1 (1.4)	(0.0, 7.8)
		Cycle 2	68	1 (1.4)	(0.0, 7.8)
		Cycle 3	66	0 (0.0)	(0.0, 5.2)
		Cycle 4	63	1 (1.4)	(0.0, 7.8)
		Cycle 5	59	0 (0.0)	(0.0, 5.2)
		Cycle 6	59	2 (2.9)	(0.4, 10.1)
		Cycle 7	56	1 (1.4)	(0.0, 7.8)
		Cycle >= 8 and < 18	54	5 (7.2)	(2.4, 16.1)
		Cycle >= 18	27	2 (2.9)	(0.4, 10.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	6 (24.0)	(9.4, 45.1)
		Cycle 1	25	0 (0.0)	(0.0, 13.7)
		Cycle 2	24	0 (0.0)	(0.0, 13.7)
		Cycle 3	23	1 (4.0)	(0.1, 20.4)
		Cycle 4	21	0 (0.0)	(0.0, 13.7)
		Cycle 5	20	0 (0.0)	(0.0, 13.7)
		Cycle 6	20	1 (4.0)	(0.1, 20.4)
		Cycle 7	17	1 (4.0)	(0.1, 20.4)
		Cycle >= 8 and < 18	15	1 (4.0)	(0.1, 20.4)
		Cycle >= 18	7	2 (8.0)	(1.0, 26.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
 Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	22 (21.0)	(13.6, 30.0)
		Cycle 1	105	2 (1.9)	(0.2, 6.7)
		Cycle 2	104	0 (0.0)	(0.0, 3.5)
		Cycle 3	102	1 (1.0)	(0.0, 5.2)
		Cycle 4	98	0 (0.0)	(0.0, 3.5)
		Cycle 5	90	0 (0.0)	(0.0, 3.5)
		Cycle 6	89	1 (1.0)	(0.0, 5.2)
		Cycle 7	87	1 (1.0)	(0.0, 5.2)
		Cycle >= 8 and < 18	84	11 (10.5)	(5.3, 18.0)
		Cycle >= 18	44	6 (5.7)	(2.1, 12.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
 Adverse events were coded using the MedDRA dictionary, Version 20.1.
 If a subject has more than one event per cycle, the subject is counted once at each level of summation.
 TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	11 (14.5)	(7.5, 24.4)
		Cycle 1	76	2 (2.6)	(0.3, 9.2)
		Cycle 2	74	2 (2.6)	(0.3, 9.2)
		Cycle 3	69	0 (0.0)	(0.0, 4.7)
		Cycle 4	68	1 (1.3)	(0.0, 7.1)
		Cycle 5	63	0 (0.0)	(0.0, 4.7)
		Cycle 6	61	2 (2.6)	(0.3, 9.2)
		Cycle 7	56	1 (1.3)	(0.0, 7.1)
		Cycle >= 8 and < 18	54	2 (2.6)	(0.3, 9.2)
		Cycle >= 18	31	2 (2.6)	(0.3, 9.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	4 (16.7)	(4.7, 37.4)
		Cycle 1	24	0 (0.0)	(0.0, 14.2)
		Cycle 2	23	0 (0.0)	(0.0, 14.2)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	0 (0.0)	(0.0, 14.2)
		Cycle 6	18	0 (0.0)	(0.0, 14.2)
		Cycle 7	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 8 and < 18	18	2 (8.3)	(1.0, 27.0)
		Cycle >= 18	10	2 (8.3)	(1.0, 27.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	30 (18.8)	(13.0, 25.7)
		Cycle 1	160	4 (2.5)	(0.7, 6.3)
		Cycle 2	158	2 (1.3)	(0.2, 4.4)
		Cycle 3	152	1 (0.6)	(0.0, 3.4)
		Cycle 4	147	1 (0.6)	(0.0, 3.4)
		Cycle 5	136	0 (0.0)	(0.0, 2.3)
		Cycle 6	134	3 (1.9)	(0.4, 5.4)
		Cycle 7	127	3 (1.9)	(0.4, 5.4)
		Cycle >= 8 and < 18	120	11 (6.9)	(3.5, 12.0)
		Cycle >= 18	65	6 (3.8)	(1.4, 8.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	12 (22.6)	(12.3, 36.2)
		Cycle 1	53	1 (1.9)	(0.0, 10.1)
		Cycle 2	52	0 (0.0)	(0.0, 6.7)
		Cycle 3	49	1 (1.9)	(0.0, 10.1)
		Cycle 4	48	0 (0.0)	(0.0, 6.7)
		Cycle 5	43	0 (0.0)	(0.0, 6.7)
		Cycle 6	42	1 (1.9)	(0.0, 10.1)
		Cycle 7	41	1 (1.9)	(0.0, 10.1)
		Cycle >= 8 and < 18	39	7 (13.2)	(5.5, 25.3)
		Cycle >= 18	18	2 (3.8)	(0.5, 13.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	22 (16.8)	(10.8, 24.3)
		Cycle 1	131	3 (2.3)	(0.5, 6.5)
		Cycle 2	129	2 (1.5)	(0.2, 5.4)
		Cycle 3	125	0 (0.0)	(0.0, 2.8)
		Cycle 4	121	1 (0.8)	(0.0, 4.2)
		Cycle 5	112	0 (0.0)	(0.0, 2.8)
		Cycle 6	110	2 (1.5)	(0.2, 5.4)
		Cycle 7	104	2 (1.5)	(0.2, 5.4)
		Cycle >= 8 and < 18	99	6 (4.6)	(1.7, 9.7)
		Cycle >= 18	57	6 (4.6)	(1.7, 9.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	30 (17.8)	(12.3, 24.4)
		Cycle 1	169	4 (2.4)	(0.6, 5.9)
		Cycle 2	166	2 (1.2)	(0.1, 4.2)
		Cycle 3	159	1 (0.6)	(0.0, 3.3)
		Cycle 4	154	1 (0.6)	(0.0, 3.3)
		Cycle 5	142	0 (0.0)	(0.0, 2.2)
		Cycle 6	139	3 (1.8)	(0.4, 5.1)
		Cycle 7	132	3 (1.8)	(0.4, 5.1)
		Cycle >= 8 and < 18	125	10 (5.9)	(2.9, 10.6)
		Cycle >= 18	70	7 (4.1)	(1.7, 8.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	4 (26.7)	(7.8, 55.1)
		Cycle 1	15	0 (0.0)	(0.0, 21.8)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	3 (20.0)	(4.3, 48.1)
		Cycle >= 18	5	1 (6.7)	(0.2, 31.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	9 (16.1)	(7.6, 28.3)
		Cycle 1	56	1 (1.8)	(0.0, 9.6)
		Cycle 2	55	1 (1.8)	(0.0, 9.6)
		Cycle 3	54	0 (0.0)	(0.0, 6.4)
		Cycle 4	53	0 (0.0)	(0.0, 6.4)
		Cycle 5	49	0 (0.0)	(0.0, 6.4)
		Cycle 6	48	0 (0.0)	(0.0, 6.4)
		Cycle 7	48	1 (1.8)	(0.0, 9.6)
		Cycle >= 8 and < 18	45	4 (7.1)	(2.0, 17.3)
		Cycle >= 18	32	3 (5.4)	(1.1, 14.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	25 (19.5)	(13.1, 27.5)
		Cycle 1	128	3 (2.3)	(0.5, 6.7)
		Cycle 2	126	1 (0.8)	(0.0, 4.3)
		Cycle 3	120	1 (0.8)	(0.0, 4.3)
		Cycle 4	116	1 (0.8)	(0.0, 4.3)
		Cycle 5	106	0 (0.0)	(0.0, 2.8)
		Cycle 6	104	3 (2.3)	(0.5, 6.7)
		Cycle 7	97	2 (1.6)	(0.2, 5.5)
		Cycle >= 8 and < 18	93	9 (7.0)	(3.3, 12.9)
		Cycle >= 18	43	5 (3.9)	(1.3, 8.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	< 3 lines (N=17)	Any TEAE	17	3 (17.6) (3.8, 43.4)
		Cycle 1	17	1 (5.9) (0.1, 28.7)
		Cycle 2	17	0 (0.0) (0.0, 19.5)
		Cycle 3	17	0 (0.0) (0.0, 19.5)
		Cycle 4	17	0 (0.0) (0.0, 19.5)
		Cycle 5	17	0 (0.0) (0.0, 19.5)
		Cycle 6	16	0 (0.0) (0.0, 19.5)
		Cycle 7	16	0 (0.0) (0.0, 19.5)
		Cycle >= 8 and < 18	16	0 (0.0) (0.0, 19.5)
		Cycle >= 18	14	3 (17.6) (3.8, 43.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	>= 3 lines (N=167)			
	Any TEAE	167	31 (18.6)	(13.0, 25.3)
	Cycle 1	167	3 (1.8)	(0.4, 5.2)
	Cycle 2	164	2 (1.2)	(0.1, 4.3)
	Cycle 3	157	1 (0.6)	(0.0, 3.3)
	Cycle 4	152	1 (0.6)	(0.0, 3.3)
	Cycle 5	138	0 (0.0)	(0.0, 2.2)
	Cycle 6	136	3 (1.8)	(0.4, 5.2)
	Cycle 7	129	3 (1.8)	(0.4, 5.2)
	Cycle >= 8 and < 18	122	13 (7.8)	(4.2, 12.9)
	Cycle >= 18	61	5 (3.0)	(1.0, 6.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	16 (20.3)	(12.0, 30.8)
		Cycle 1	79	2 (2.5)	(0.3, 8.8)
		Cycle 2	78	2 (2.5)	(0.3, 8.8)
		Cycle 3	75	1 (1.3)	(0.0, 6.9)
		Cycle 4	73	1 (1.3)	(0.0, 6.9)
		Cycle 5	70	0 (0.0)	(0.0, 4.6)
		Cycle 6	69	1 (1.3)	(0.0, 6.9)
		Cycle 7	68	1 (1.3)	(0.0, 6.9)
		Cycle >= 8 and < 18	65	3 (3.8)	(0.8, 10.7)
		Cycle >= 18	37	6 (7.6)	(2.8, 15.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	12 (18.2)	(9.8, 29.6)
		Cycle 1	66	1 (1.5)	(0.0, 8.2)
		Cycle 2	66	0 (0.0)	(0.0, 5.4)
		Cycle 3	64	0 (0.0)	(0.0, 5.4)
		Cycle 4	61	0 (0.0)	(0.0, 5.4)
		Cycle 5	55	0 (0.0)	(0.0, 5.4)
		Cycle 6	53	0 (0.0)	(0.0, 5.4)
		Cycle 7	51	0 (0.0)	(0.0, 5.4)
		Cycle >= 8 and < 18	51	9 (13.6)	(6.4, 24.3)
		Cycle >= 18	23	2 (3.0)	(0.4, 10.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	20 (16.5)	(10.4, 24.4)
		Cycle 1	121	2 (1.7)	(0.2, 5.8)
		Cycle 2	120	0 (0.0)	(0.0, 3.0)
		Cycle 3	119	1 (0.8)	(0.0, 4.5)
		Cycle 4	115	1 (0.8)	(0.0, 4.5)
		Cycle 5	106	0 (0.0)	(0.0, 3.0)
		Cycle 6	103	3 (2.5)	(0.5, 7.1)
		Cycle 7	96	1 (0.8)	(0.0, 4.5)
		Cycle >= 8 and < 18	93	7 (5.8)	(2.4, 11.6)
		Cycle >= 18	54	6 (5.0)	(1.8, 10.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	14 (22.2)	(12.7, 34.5)
		Cycle 1	63	2 (3.2)	(0.4, 11.0)
		Cycle 2	61	2 (3.2)	(0.4, 11.0)
		Cycle 3	55	0 (0.0)	(0.0, 5.7)
		Cycle 4	54	0 (0.0)	(0.0, 5.7)
		Cycle 5	49	0 (0.0)	(0.0, 5.7)
		Cycle 6	49	0 (0.0)	(0.0, 5.7)
		Cycle 7	49	2 (3.2)	(0.4, 11.0)
		Cycle >= 8 and < 18	45	6 (9.5)	(3.6, 19.6)
		Cycle >= 18	21	2 (3.2)	(0.4, 11.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	8 (15.7)	(7.0, 28.6)
		Cycle 1	51	1 (2.0)	(0.0, 10.4)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	50	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	1 (2.0)	(0.0, 10.4)
		Cycle 5	46	0 (0.0)	(0.0, 7.0)
		Cycle 6	44	1 (2.0)	(0.0, 10.4)
		Cycle 7	40	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	40	3 (5.9)	(1.2, 16.2)
		Cycle >= 18	24	3 (5.9)	(1.2, 16.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AT_SSI0: Incidence of TEAEs leading to discontinuation of treatment overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	26 (19.5)	(13.2, 27.3)
		Cycle 1	133	3 (2.3)	(0.5, 6.5)
		Cycle 2	131	2 (1.5)	(0.2, 5.3)
		Cycle 3	124	1 (0.8)	(0.0, 4.1)
		Cycle 4	120	0 (0.0)	(0.0, 2.7)
		Cycle 5	109	0 (0.0)	(0.0, 2.7)
		Cycle 6	108	2 (1.5)	(0.2, 5.3)
		Cycle 7	105	3 (2.3)	(0.5, 6.5)
		Cycle >= 8 and < 18	98	10 (7.5)	(3.7, 13.4)
		Cycle >= 18	51	5 (3.8)	(1.2, 8.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

UE von besonderem Interesse – Infusionsbedingte Reaktion (IRR), unabhängig vom Schweregrad

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	18 (9.8)	(5.9, 15.0)
		Cycle 1	184	6 (3.3)	(1.2, 7.0)
		Cycle 2	181	1 (0.5)	(0.0, 3.0)
		Cycle 3	174	1 (0.5)	(0.0, 3.0)
		Cycle 4	169	2 (1.1)	(0.1, 3.9)
		Cycle 5	155	0 (0.0)	(0.0, 2.0)
		Cycle 6	152	2 (1.1)	(0.1, 3.9)
		Cycle 7	145	2 (1.1)	(0.1, 3.9)
		Cycle >= 8 and < 18	138	5 (2.7)	(0.9, 6.2)
		Cycle >= 18	75	2 (1.1)	(0.1, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

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Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	11 (7.9) (4.0, 13.6)
		Cycle 1	140	5 (3.6) (1.2, 8.1)
		Cycle 2	138	0 (0.0) (0.0, 2.6)
		Cycle 3	132	1 (0.7) (0.0, 3.9)
		Cycle 4	128	1 (0.7) (0.0, 3.9)
		Cycle 5	116	0 (0.0) (0.0, 2.6)
		Cycle 6	113	0 (0.0) (0.0, 2.6)
		Cycle 7	109	1 (0.7) (0.0, 3.9)
		Cycle >= 8 and < 18	103	3 (2.1) (0.4, 6.1)
		Cycle >= 18	56	2 (1.4) (0.2, 5.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	7 (15.9)
		Cycle 1	44	1 (2.3)
		Cycle 2	43	1 (2.3)
		Cycle 3	42	0 (0.0)
		Cycle 4	41	1 (2.3)
		Cycle 5	39	0 (0.0)
		Cycle 6	39	2 (4.5)
		Cycle 7	36	1 (2.3)
		Cycle >= 8 and < 18	35	2 (4.5)
		Cycle >= 18	19	0 (0.0)
				(0.0, 8.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	5 (7.9) (2.6, 17.6)
		Cycle 1	63	2 (3.2) (0.4, 11.0)
		Cycle 2	61	1 (1.6) (0.0, 8.5)
		Cycle 3	58	0 (0.0) (0.0, 5.7)
		Cycle 4	58	0 (0.0) (0.0, 5.7)
		Cycle 5	55	0 (0.0) (0.0, 5.7)
		Cycle 6	55	0 (0.0) (0.0, 5.7)
		Cycle 7	53	1 (1.6) (0.0, 8.5)
		Cycle >= 8 and < 18	49	0 (0.0) (0.0, 5.7)
		Cycle >= 18	29	1 (1.6) (0.0, 8.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	7 (13.2) (5.5, 25.3)
		Cycle 1	53	2 (3.8) (0.5, 13.0)
		Cycle 2	53	0 (0.0) (0.0, 6.7)
		Cycle 3	52	1 (1.9) (0.0, 10.1)
		Cycle 4	49	1 (1.9) (0.0, 10.1)
		Cycle 5	44	0 (0.0) (0.0, 6.7)
		Cycle 6	42	1 (1.9) (0.0, 10.1)
		Cycle 7	40	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	3 (5.7) (1.2, 15.7)
		Cycle >= 18	23	0 (0.0) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

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Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	6 (8.8) (3.3, 18.2)
		Cycle 1	68	2 (2.9) (0.4, 10.2)
		Cycle 2	67	0 (0.0) (0.0, 5.3)
		Cycle 3	64	0 (0.0) (0.0, 5.3)
		Cycle 4	62	1 (1.5) (0.0, 7.9)
		Cycle 5	56	0 (0.0) (0.0, 5.3)
		Cycle 6	55	1 (1.5) (0.0, 7.9)
		Cycle 7	52	1 (1.5) (0.0, 7.9)
		Cycle >= 8 and < 18	50	2 (2.9) (0.4, 10.2)
		Cycle >= 18	23	1 (1.5) (0.0, 7.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	9 (8.8) (4.1, 16.1)
		Cycle 1	102	4 (3.9) (1.1, 9.7)
		Cycle 2	101	0 (0.0) (0.0, 3.6)
		Cycle 3	100	0 (0.0) (0.0, 3.6)
		Cycle 4	98	0 (0.0) (0.0, 3.6)
		Cycle 5	94	0 (0.0) (0.0, 3.6)
		Cycle 6	93	0 (0.0) (0.0, 3.6)
		Cycle 7	88	2 (2.0) (0.2, 6.9)
		Cycle >= 8 and < 18	86	3 (2.9) (0.6, 8.4)
		Cycle >= 18	49	2 (2.0) (0.2, 6.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	8 (9.9)	(4.4, 18.5)
		Cycle 1	81	1 (1.2)	(0.0, 6.7)
		Cycle 2	79	1 (1.2)	(0.0, 6.7)
		Cycle 3	73	1 (1.2)	(0.0, 6.7)
		Cycle 4	71	2 (2.5)	(0.3, 8.6)
		Cycle 5	61	0 (0.0)	(0.0, 4.5)
		Cycle 6	59	2 (2.5)	(0.3, 8.6)
		Cycle 7	57	0 (0.0)	(0.0, 4.5)
		Cycle >= 8 and < 18	52	2 (2.5)	(0.3, 8.6)
		Cycle >= 18	26	0 (0.0)	(0.0, 4.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions	< 5 cm (N=73)			
	Any TEAE	73	7 (9.6)	(3.9, 18.8)
	Cycle 1	73	4 (5.5)	(1.5, 13.4)
	Cycle 2	72	0 (0.0)	(0.0, 4.9)
	Cycle 3	70	1 (1.4)	(0.0, 7.4)
	Cycle 4	65	0 (0.0)	(0.0, 4.9)
	Cycle 5	60	0 (0.0)	(0.0, 4.9)
	Cycle 6	59	0 (0.0)	(0.0, 4.9)
	Cycle 7	58	0 (0.0)	(0.0, 4.9)
	Cycle >= 8 and < 18	53	2 (2.7)	(0.3, 9.5)
	Cycle >= 18	33	1 (1.4)	(0.0, 7.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=97)			
	Any TEAE	97	9 (9.3)	(4.3, 16.9)
	Cycle 1	97	2 (2.1)	(0.3, 7.3)
	Cycle 2	95	1 (1.0)	(0.0, 5.6)
	Cycle 3	90	0 (0.0)	(0.0, 3.7)
	Cycle 4	90	2 (2.1)	(0.3, 7.3)
	Cycle 5	81	0 (0.0)	(0.0, 3.7)
	Cycle 6	79	2 (2.1)	(0.3, 7.3)
	Cycle 7	74	1 (1.0)	(0.0, 5.6)
	Cycle >= 8 and < 18	72	2 (2.1)	(0.3, 7.3)
	Cycle >= 18	34	0 (0.0)	(0.0, 3.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	14 (9.1)	(5.1, 14.8)
		Cycle 1	154	4 (2.6)	(0.7, 6.5)
		Cycle 2	152	1 (0.6)	(0.0, 3.6)
		Cycle 3	146	1 (0.6)	(0.0, 3.6)
		Cycle 4	141	1 (0.6)	(0.0, 3.6)
		Cycle 5	129	0 (0.0)	(0.0, 2.4)
		Cycle 6	127	2 (1.3)	(0.2, 4.6)
		Cycle 7	121	2 (1.3)	(0.2, 4.6)
		Cycle >= 8 and < 18	114	3 (1.9)	(0.4, 5.6)
		Cycle >= 18	69	2 (1.3)	(0.2, 4.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Any TEAE	28	4 (14.3)	(4.0, 32.7)
		Cycle 1	28	2 (7.1)	(0.9, 23.5)
		Cycle 2	27	0 (0.0)	(0.0, 12.3)
		Cycle 3	26	0 (0.0)	(0.0, 12.3)
		Cycle 4	26	1 (3.6)	(0.1, 18.3)
		Cycle 5	24	0 (0.0)	(0.0, 12.3)
		Cycle 6	23	0 (0.0)	(0.0, 12.3)
		Cycle 7	22	0 (0.0)	(0.0, 12.3)
		Cycle >= 8 and < 18	22	2 (7.1)	(0.9, 23.5)
		Cycle >= 18	5	0 (0.0)	(0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	8 (8.6)	(3.8, 16.2)
		Cycle 1	93	4 (4.3)	(1.2, 10.6)
		Cycle 2	92	0 (0.0)	(0.0, 3.9)
		Cycle 3	87	0 (0.0)	(0.0, 3.9)
		Cycle 4	84	0 (0.0)	(0.0, 3.9)
		Cycle 5	80	0 (0.0)	(0.0, 3.9)
		Cycle 6	78	1 (1.1)	(0.0, 5.8)
		Cycle 7	75	1 (1.1)	(0.0, 5.8)
		Cycle >= 8 and < 18	73	3 (3.2)	(0.7, 9.1)
		Cycle >= 18	34	0 (0.0)	(0.0, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	9 (10.2)	(4.8, 18.5)
		Cycle 1	88	1 (1.1)	(0.0, 6.2)
		Cycle 2	86	1 (1.1)	(0.0, 6.2)
		Cycle 3	85	1 (1.1)	(0.0, 6.2)
		Cycle 4	84	2 (2.3)	(0.3, 8.0)
		Cycle 5	74	0 (0.0)	(0.0, 4.1)
		Cycle 6	73	1 (1.1)	(0.0, 6.2)
		Cycle 7	69	1 (1.1)	(0.0, 6.2)
		Cycle >= 8 and < 18	64	2 (2.3)	(0.3, 8.0)
		Cycle >= 18	41	2 (2.3)	(0.3, 8.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	4 (7.8)	(2.2, 18.9)
		Cycle 1	51	2 (3.9)	(0.5, 13.5)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	49	1 (2.0)	(0.0, 10.4)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	47	0 (0.0)	(0.0, 7.0)
		Cycle 6	46	0 (0.0)	(0.0, 7.0)
		Cycle 7	45	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	44	2 (3.9)	(0.5, 13.5)
		Cycle >= 18	21	0 (0.0)	(0.0, 7.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	13 (10.4)	(5.7, 17.1)
		Cycle 1	125	3 (2.4)	(0.5, 6.9)
		Cycle 2	123	1 (0.8)	(0.0, 4.4)
		Cycle 3	118	0 (0.0)	(0.0, 2.9)
		Cycle 4	114	2 (1.6)	(0.2, 5.7)
		Cycle 5	103	0 (0.0)	(0.0, 2.9)
		Cycle 6	101	2 (1.6)	(0.2, 5.7)
		Cycle 7	95	2 (1.6)	(0.2, 5.7)
		Cycle >= 8 and < 18	90	3 (2.4)	(0.5, 6.9)
		Cycle >= 18	52	2 (1.6)	(0.2, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	9 (9.3)	(4.3, 16.9)
		Cycle 1	97	4 (4.1)	(1.1, 10.2)
		Cycle 2	96	0 (0.0)	(0.0, 3.7)
		Cycle 3	91	1 (1.0)	(0.0, 5.6)
		Cycle 4	88	0 (0.0)	(0.0, 3.7)
		Cycle 5	84	0 (0.0)	(0.0, 3.7)
		Cycle 6	82	1 (1.0)	(0.0, 5.6)
		Cycle 7	79	1 (1.0)	(0.0, 5.6)
		Cycle >= 8 and < 18	76	3 (3.1)	(0.6, 8.8)
		Cycle >= 18	36	0 (0.0)	(0.0, 3.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	8 (9.6)	(4.3, 18.1)
		Cycle 1	83	1 (1.2)	(0.0, 6.5)
		Cycle 2	81	1 (1.2)	(0.0, 6.5)
		Cycle 3	80	0 (0.0)	(0.0, 4.3)
		Cycle 4	79	2 (2.4)	(0.3, 8.4)
		Cycle 5	69	0 (0.0)	(0.0, 4.3)
		Cycle 6	68	1 (1.2)	(0.0, 6.5)
		Cycle 7	64	1 (1.2)	(0.0, 6.5)
		Cycle >= 8 and < 18	60	2 (2.4)	(0.3, 8.4)
		Cycle >= 18	38	2 (2.4)	(0.3, 8.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Normal (N=90)			
	Any TEAE	90	8 (8.9)	(3.9, 16.8)
	Cycle 1	90	2 (2.2)	(0.3, 7.8)
	Cycle 2	89	1 (1.1)	(0.0, 6.0)
	Cycle 3	85	1 (1.1)	(0.0, 6.0)
	Cycle 4	85	1 (1.1)	(0.0, 6.0)
	Cycle 5	76	0 (0.0)	(0.0, 4.0)
	Cycle 6	73	0 (0.0)	(0.0, 4.0)
	Cycle 7	72	1 (1.1)	(0.0, 6.0)
	Cycle >= 8 and < 18	69	2 (2.2)	(0.3, 7.8)
	Cycle >= 18	41	1 (1.1)	(0.0, 6.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	6 (8.7)	(3.3, 18.0)
		Cycle 1	69	1 (1.4)	(0.0, 7.8)
		Cycle 2	68	0 (0.0)	(0.0, 5.2)
		Cycle 3	66	0 (0.0)	(0.0, 5.2)
		Cycle 4	63	1 (1.4)	(0.0, 7.8)
		Cycle 5	59	0 (0.0)	(0.0, 5.2)
		Cycle 6	59	2 (2.9)	(0.4, 10.1)
		Cycle 7	56	1 (1.4)	(0.0, 7.8)
		Cycle >= 8 and < 18	54	2 (2.9)	(0.4, 10.1)
		Cycle >= 18	27	1 (1.4)	(0.0, 7.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	4 (16.0)	(4.5, 36.1)
		Cycle 1	25	3 (12.0)	(2.5, 31.2)
		Cycle 2	24	0 (0.0)	(0.0, 13.7)
		Cycle 3	23	0 (0.0)	(0.0, 13.7)
		Cycle 4	21	0 (0.0)	(0.0, 13.7)
		Cycle 5	20	0 (0.0)	(0.0, 13.7)
		Cycle 6	20	0 (0.0)	(0.0, 13.7)
		Cycle 7	17	0 (0.0)	(0.0, 13.7)
		Cycle >= 8 and < 18	15	1 (4.0)	(0.1, 20.4)
		Cycle >= 18	7	0 (0.0)	(0.0, 13.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	14 (13.3)	(7.5, 21.4)
		Cycle 1	105	6 (5.7)	(2.1, 12.0)
		Cycle 2	104	0 (0.0)	(0.0, 3.5)
		Cycle 3	102	1 (1.0)	(0.0, 5.2)
		Cycle 4	98	1 (1.0)	(0.0, 5.2)
		Cycle 5	90	0 (0.0)	(0.0, 3.5)
		Cycle 6	89	1 (1.0)	(0.0, 5.2)
		Cycle 7	87	2 (1.9)	(0.2, 6.7)
		Cycle >= 8 and < 18	84	3 (2.9)	(0.6, 8.1)
		Cycle >= 18	44	1 (1.0)	(0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	4 (5.3)	(1.5, 12.9)
		Cycle 1	76	0 (0.0)	(0.0, 4.7)
		Cycle 2	74	1 (1.3)	(0.0, 7.1)
		Cycle 3	69	0 (0.0)	(0.0, 4.7)
		Cycle 4	68	1 (1.3)	(0.0, 7.1)
		Cycle 5	63	0 (0.0)	(0.0, 4.7)
		Cycle 6	61	1 (1.3)	(0.0, 7.1)
		Cycle 7	56	0 (0.0)	(0.0, 4.7)
		Cycle >= 8 and < 18	54	2 (2.6)	(0.3, 9.2)
		Cycle >= 18	31	1 (1.3)	(0.0, 7.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	5 (20.8)	(7.1, 42.2)
		Cycle 1	24	1 (4.2)	(0.1, 21.1)
		Cycle 2	23	1 (4.2)	(0.1, 21.1)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	0 (0.0)	(0.0, 14.2)
		Cycle 6	18	0 (0.0)	(0.0, 14.2)
		Cycle 7	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 8 and < 18	18	2 (8.3)	(1.0, 27.0)
		Cycle >= 18	10	1 (4.2)	(0.1, 21.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	13 (8.1)	(4.4, 13.5)
		Cycle 1	160	5 (3.1)	(1.0, 7.1)
		Cycle 2	158	0 (0.0)	(0.0, 2.3)
		Cycle 3	152	1 (0.6)	(0.0, 3.4)
		Cycle 4	147	2 (1.3)	(0.2, 4.4)
		Cycle 5	136	0 (0.0)	(0.0, 2.3)
		Cycle 6	134	2 (1.3)	(0.2, 4.4)
		Cycle 7	127	2 (1.3)	(0.2, 4.4)
		Cycle >= 8 and < 18	120	3 (1.9)	(0.4, 5.4)
		Cycle >= 18	65	1 (0.6)	(0.0, 3.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	3 (5.7)	(1.2, 15.7)
		Cycle 1	53	2 (3.8)	(0.5, 13.0)
		Cycle 2	52	0 (0.0)	(0.0, 6.7)
		Cycle 3	49	0 (0.0)	(0.0, 6.7)
		Cycle 4	48	1 (1.9)	(0.0, 10.1)
		Cycle 5	43	0 (0.0)	(0.0, 6.7)
		Cycle 6	42	1 (1.9)	(0.0, 10.1)
		Cycle 7	41	0 (0.0)	(0.0, 6.7)
		Cycle >= 8 and < 18	39	1 (1.9)	(0.0, 10.1)
		Cycle >= 18	18	0 (0.0)	(0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	15 (11.5)	(6.6, 18.2)
		Cycle 1	131	4 (3.1)	(0.8, 7.6)
		Cycle 2	129	1 (0.8)	(0.0, 4.2)
		Cycle 3	125	1 (0.8)	(0.0, 4.2)
		Cycle 4	121	1 (0.8)	(0.0, 4.2)
		Cycle 5	112	0 (0.0)	(0.0, 2.8)
		Cycle 6	110	1 (0.8)	(0.0, 4.2)
		Cycle 7	104	2 (1.5)	(0.2, 5.4)
		Cycle >= 8 and < 18	99	4 (3.1)	(0.8, 7.6)
		Cycle >= 18	57	2 (1.5)	(0.2, 5.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	16 (9.5)	(5.5, 14.9)
		Cycle 1	169	4 (2.4)	(0.6, 5.9)
		Cycle 2	166	1 (0.6)	(0.0, 3.3)
		Cycle 3	159	1 (0.6)	(0.0, 3.3)
		Cycle 4	154	2 (1.2)	(0.1, 4.2)
		Cycle 5	142	0 (0.0)	(0.0, 2.2)
		Cycle 6	139	2 (1.2)	(0.1, 4.2)
		Cycle 7	132	2 (1.2)	(0.1, 4.2)
		Cycle >= 8 and < 18	125	4 (2.4)	(0.6, 5.9)
		Cycle >= 18	70	2 (1.2)	(0.1, 4.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	2 (13.3)	(1.7, 40.5)
		Cycle 1	15	2 (13.3)	(1.7, 40.5)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	1 (6.7)	(0.2, 31.9)
		Cycle >= 18	5	0 (0.0)	(0.0, 21.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	3 (5.4)	(1.1, 14.9)
		Cycle 1	56	1 (1.8)	(0.0, 9.6)
		Cycle 2	55	0 (0.0)	(0.0, 6.4)
		Cycle 3	54	0 (0.0)	(0.0, 6.4)
		Cycle 4	53	0 (0.0)	(0.0, 6.4)
		Cycle 5	49	0 (0.0)	(0.0, 6.4)
		Cycle 6	48	0 (0.0)	(0.0, 6.4)
		Cycle 7	48	0 (0.0)	(0.0, 6.4)
		Cycle >= 8 and < 18	45	2 (3.6)	(0.4, 12.3)
		Cycle >= 18	32	0 (0.0)	(0.0, 6.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	15 (11.7)	(6.7, 18.6)
		Cycle 1	128	5 (3.9)	(1.3, 8.9)
		Cycle 2	126	1 (0.8)	(0.0, 4.3)
		Cycle 3	120	1 (0.8)	(0.0, 4.3)
		Cycle 4	116	2 (1.6)	(0.2, 5.5)
		Cycle 5	106	0 (0.0)	(0.0, 2.8)
		Cycle 6	104	2 (1.6)	(0.2, 5.5)
		Cycle 7	97	2 (1.6)	(0.2, 5.5)
		Cycle >= 8 and < 18	93	3 (2.3)	(0.5, 6.7)
		Cycle >= 18	43	2 (1.6)	(0.2, 5.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	< 3 lines (N=17)			
	Any TEAE	17	1 (5.9)	(0.1, 28.7)
	Cycle 1	17	0 (0.0)	(0.0, 19.5)
	Cycle 2	17	0 (0.0)	(0.0, 19.5)
	Cycle 3	17	0 (0.0)	(0.0, 19.5)
	Cycle 4	17	0 (0.0)	(0.0, 19.5)
	Cycle 5	17	0 (0.0)	(0.0, 19.5)
	Cycle 6	16	0 (0.0)	(0.0, 19.5)
	Cycle 7	16	0 (0.0)	(0.0, 19.5)
	Cycle >= 8 and < 18	16	1 (5.9)	(0.1, 28.7)
	Cycle >= 18	14	0 (0.0)	(0.0, 19.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
O-Prior treatment lines	>= 3 lines (N=167)			
	Any TEAE	167	17 (10.2)	(6.0, 15.8)
	Cycle 1	167	6 (3.6)	(1.3, 7.7)
	Cycle 2	164	1 (0.6)	(0.0, 3.3)
	Cycle 3	157	1 (0.6)	(0.0, 3.3)
	Cycle 4	152	2 (1.2)	(0.1, 4.3)
	Cycle 5	138	0 (0.0)	(0.0, 2.2)
	Cycle 6	136	2 (1.2)	(0.1, 4.3)
	Cycle 7	129	2 (1.2)	(0.1, 4.3)
	Cycle >= 8 and < 18	122	4 (2.4)	(0.7, 6.0)
	Cycle >= 18	61	2 (1.2)	(0.1, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	8 (10.1)	(4.5, 19.0)
		Cycle 1	79	2 (2.5)	(0.3, 8.8)
		Cycle 2	78	1 (1.3)	(0.0, 6.9)
		Cycle 3	75	0 (0.0)	(0.0, 4.6)
		Cycle 4	73	1 (1.3)	(0.0, 6.9)
		Cycle 5	70	0 (0.0)	(0.0, 4.6)
		Cycle 6	69	1 (1.3)	(0.0, 6.9)
		Cycle 7	68	1 (1.3)	(0.0, 6.9)
		Cycle >= 8 and < 18	65	3 (3.8)	(0.8, 10.7)
		Cycle >= 18	37	1 (1.3)	(0.0, 6.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)			
	Any TEAE	66	7 (10.6)	(4.4, 20.6)
	Cycle 1	66	4 (6.1)	(1.7, 14.8)
	Cycle 2	66	0 (0.0)	(0.0, 5.4)
	Cycle 3	64	0 (0.0)	(0.0, 5.4)
	Cycle 4	61	0 (0.0)	(0.0, 5.4)
	Cycle 5	55	0 (0.0)	(0.0, 5.4)
	Cycle 6	53	1 (1.5)	(0.0, 8.2)
	Cycle 7	51	1 (1.5)	(0.0, 8.2)
	Cycle >= 8 and < 18	51	1 (1.5)	(0.0, 8.2)
	Cycle >= 18	23	0 (0.0)	(0.0, 5.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	12 (9.9)	(5.2, 16.7)
		Cycle 1	121	5 (4.1)	(1.4, 9.4)
		Cycle 2	120	0 (0.0)	(0.0, 3.0)
		Cycle 3	119	1 (0.8)	(0.0, 4.5)
		Cycle 4	115	1 (0.8)	(0.0, 4.5)
		Cycle 5	106	0 (0.0)	(0.0, 3.0)
		Cycle 6	103	1 (0.8)	(0.0, 4.5)
		Cycle 7	96	1 (0.8)	(0.0, 4.5)
		Cycle >= 8 and < 18	93	3 (2.5)	(0.5, 7.1)
		Cycle >= 18	54	1 (0.8)	(0.0, 4.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	6 (9.5)	(3.6, 19.6)
		Cycle 1	63	1 (1.6)	(0.0, 8.5)
		Cycle 2	61	1 (1.6)	(0.0, 8.5)
		Cycle 3	55	0 (0.0)	(0.0, 5.7)
		Cycle 4	54	1 (1.6)	(0.0, 8.5)
		Cycle 5	49	0 (0.0)	(0.0, 5.7)
		Cycle 6	49	1 (1.6)	(0.0, 8.5)
		Cycle 7	49	1 (1.6)	(0.0, 8.5)
		Cycle >= 8 and < 18	45	2 (3.2)	(0.4, 11.0)
		Cycle >= 18	21	1 (1.6)	(0.0, 8.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	3 (5.9)	(1.2, 16.2)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	50	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	1 (2.0)	(0.0, 10.4)
		Cycle 5	46	0 (0.0)	(0.0, 7.0)
		Cycle 6	44	0 (0.0)	(0.0, 7.0)
		Cycle 7	40	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	40	2 (3.9)	(0.5, 13.5)
		Cycle >= 18	24	0 (0.0)	(0.0, 7.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AI_SSI0: Incidence of infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	15 (11.3)	(6.5, 17.9)
		Cycle 1	133	6 (4.5)	(1.7, 9.6)
		Cycle 2	131	1 (0.8)	(0.0, 4.1)
		Cycle 3	124	1 (0.8)	(0.0, 4.1)
		Cycle 4	120	1 (0.8)	(0.0, 4.1)
		Cycle 5	109	0 (0.0)	(0.0, 2.7)
		Cycle 6	108	2 (1.5)	(0.2, 5.3)
		Cycle 7	105	2 (1.5)	(0.2, 5.3)
		Cycle >= 8 and < 18	98	3 (2.3)	(0.5, 6.5)
		Cycle >= 18	51	2 (1.5)	(0.2, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

UE von besonderem Interesse – Infusionsbedingte Reaktion (IRR) mit CTCAE-Grad < 3

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	18 (9.8)	(5.9, 15.0)
		Cycle 1	184	6 (3.3)	(1.2, 7.0)
		Cycle 2	181	1 (0.5)	(0.0, 3.0)
		Cycle 3	174	1 (0.5)	(0.0, 3.0)
		Cycle 4	169	2 (1.1)	(0.1, 3.9)
		Cycle 5	155	0 (0.0)	(0.0, 2.0)
		Cycle 6	152	2 (1.1)	(0.1, 3.9)
		Cycle 7	145	2 (1.1)	(0.1, 3.9)
		Cycle >= 8 and < 18	138	5 (2.7)	(0.9, 6.2)
		Cycle >= 18	75	2 (1.1)	(0.1, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	11 (7.9) (4.0, 13.6)
		Cycle 1	140	5 (3.6) (1.2, 8.1)
		Cycle 2	138	0 (0.0) (0.0, 2.6)
		Cycle 3	132	1 (0.7) (0.0, 3.9)
		Cycle 4	128	1 (0.7) (0.0, 3.9)
		Cycle 5	116	0 (0.0) (0.0, 2.6)
		Cycle 6	113	0 (0.0) (0.0, 2.6)
		Cycle 7	109	1 (0.7) (0.0, 3.9)
		Cycle >= 8 and < 18	103	3 (2.1) (0.4, 6.1)
		Cycle >= 18	56	2 (1.4) (0.2, 5.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	7 (15.9) (6.6, 30.1)
		Cycle 1	44	1 (2.3) (0.1, 12.0)
		Cycle 2	43	1 (2.3) (0.1, 12.0)
		Cycle 3	42	0 (0.0) (0.0, 8.0)
		Cycle 4	41	1 (2.3) (0.1, 12.0)
		Cycle 5	39	0 (0.0) (0.0, 8.0)
		Cycle 6	39	2 (4.5) (0.6, 15.5)
		Cycle 7	36	1 (2.3) (0.1, 12.0)
		Cycle >= 8 and < 18	35	2 (4.5) (0.6, 15.5)
		Cycle >= 18	19	0 (0.0) (0.0, 8.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	5 (7.9) (2.6, 17.6)
		Cycle 1	63	2 (3.2) (0.4, 11.0)
		Cycle 2	61	1 (1.6) (0.0, 8.5)
		Cycle 3	58	0 (0.0) (0.0, 5.7)
		Cycle 4	58	0 (0.0) (0.0, 5.7)
		Cycle 5	55	0 (0.0) (0.0, 5.7)
		Cycle 6	55	0 (0.0) (0.0, 5.7)
		Cycle 7	53	1 (1.6) (0.0, 8.5)
		Cycle >= 8 and < 18	49	0 (0.0) (0.0, 5.7)
		Cycle >= 18	29	1 (1.6) (0.0, 8.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	7 (13.2) (5.5, 25.3)
		Cycle 1	53	2 (3.8) (0.5, 13.0)
		Cycle 2	53	0 (0.0) (0.0, 6.7)
		Cycle 3	52	1 (1.9) (0.0, 10.1)
		Cycle 4	49	1 (1.9) (0.0, 10.1)
		Cycle 5	44	0 (0.0) (0.0, 6.7)
		Cycle 6	42	1 (1.9) (0.0, 10.1)
		Cycle 7	40	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	3 (5.7) (1.2, 15.7)
		Cycle >= 18	23	0 (0.0) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	6 (8.8) (3.3, 18.2)
		Cycle 1	68	2 (2.9) (0.4, 10.2)
		Cycle 2	67	0 (0.0) (0.0, 5.3)
		Cycle 3	64	0 (0.0) (0.0, 5.3)
		Cycle 4	62	1 (1.5) (0.0, 7.9)
		Cycle 5	56	0 (0.0) (0.0, 5.3)
		Cycle 6	55	1 (1.5) (0.0, 7.9)
		Cycle 7	52	1 (1.5) (0.0, 7.9)
		Cycle >= 8 and < 18	50	2 (2.9) (0.4, 10.2)
		Cycle >= 18	23	1 (1.5) (0.0, 7.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	9 (8.8) (4.1, 16.1)
		Cycle 1	102	4 (3.9) (1.1, 9.7)
		Cycle 2	101	0 (0.0) (0.0, 3.6)
		Cycle 3	100	0 (0.0) (0.0, 3.6)
		Cycle 4	98	0 (0.0) (0.0, 3.6)
		Cycle 5	94	0 (0.0) (0.0, 3.6)
		Cycle 6	93	0 (0.0) (0.0, 3.6)
		Cycle 7	88	2 (2.0) (0.2, 6.9)
		Cycle >= 8 and < 18	86	3 (2.9) (0.6, 8.4)
		Cycle >= 18	49	2 (2.0) (0.2, 6.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	8 (9.9) (4.4, 18.5)
		Cycle 1	81	1 (1.2) (0.0, 6.7)
		Cycle 2	79	1 (1.2) (0.0, 6.7)
		Cycle 3	73	1 (1.2) (0.0, 6.7)
		Cycle 4	71	2 (2.5) (0.3, 8.6)
		Cycle 5	61	0 (0.0) (0.0, 4.5)
		Cycle 6	59	2 (2.5) (0.3, 8.6)
		Cycle 7	57	0 (0.0) (0.0, 4.5)
		Cycle >= 8 and < 18	52	2 (2.5) (0.3, 8.6)
		Cycle >= 18	26	0 (0.0) (0.0, 4.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions	< 5 cm (N=73)			
	Any TEAE	73	7 (9.6)	(3.9, 18.8)
	Cycle 1	73	4 (5.5)	(1.5, 13.4)
	Cycle 2	72	0 (0.0)	(0.0, 4.9)
	Cycle 3	70	1 (1.4)	(0.0, 7.4)
	Cycle 4	65	0 (0.0)	(0.0, 4.9)
	Cycle 5	60	0 (0.0)	(0.0, 4.9)
	Cycle 6	59	0 (0.0)	(0.0, 4.9)
	Cycle 7	58	0 (0.0)	(0.0, 4.9)
	Cycle >= 8 and < 18	53	2 (2.7)	(0.3, 9.5)
	Cycle >= 18	33	1 (1.4)	(0.0, 7.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=97)			
	Any TEAE	97	9 (9.3)	(4.3, 16.9)
	Cycle 1	97	2 (2.1)	(0.3, 7.3)
	Cycle 2	95	1 (1.0)	(0.0, 5.6)
	Cycle 3	90	0 (0.0)	(0.0, 3.7)
	Cycle 4	90	2 (2.1)	(0.3, 7.3)
	Cycle 5	81	0 (0.0)	(0.0, 3.7)
	Cycle 6	79	2 (2.1)	(0.3, 7.3)
	Cycle 7	74	1 (1.0)	(0.0, 5.6)
	Cycle >= 8 and < 18	72	2 (2.1)	(0.3, 7.3)
	Cycle >= 18	34	0 (0.0)	(0.0, 3.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	14 (9.1)	(5.1, 14.8)
		Cycle 1	154	4 (2.6)	(0.7, 6.5)
		Cycle 2	152	1 (0.6)	(0.0, 3.6)
		Cycle 3	146	1 (0.6)	(0.0, 3.6)
		Cycle 4	141	1 (0.6)	(0.0, 3.6)
		Cycle 5	129	0 (0.0)	(0.0, 2.4)
		Cycle 6	127	2 (1.3)	(0.2, 4.6)
		Cycle 7	121	2 (1.3)	(0.2, 4.6)
		Cycle >= 8 and < 18	114	3 (1.9)	(0.4, 5.6)
		Cycle >= 18	69	2 (1.3)	(0.2, 4.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Any TEAE	28	4 (14.3) (4.0, 32.7)
		Cycle 1	28	2 (7.1) (0.9, 23.5)
		Cycle 2	27	0 (0.0) (0.0, 12.3)
		Cycle 3	26	0 (0.0) (0.0, 12.3)
		Cycle 4	26	1 (3.6) (0.1, 18.3)
		Cycle 5	24	0 (0.0) (0.0, 12.3)
		Cycle 6	23	0 (0.0) (0.0, 12.3)
		Cycle 7	22	0 (0.0) (0.0, 12.3)
		Cycle >= 8 and < 18	22	2 (7.1) (0.9, 23.5)
		Cycle >= 18	5	0 (0.0) (0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
F-Estrogen receptors	Positive (N=93)			
	Any TEAE	93	8 (8.6)	(3.8, 16.2)
	Cycle 1	93	4 (4.3)	(1.2, 10.6)
	Cycle 2	92	0 (0.0)	(0.0, 3.9)
	Cycle 3	87	0 (0.0)	(0.0, 3.9)
	Cycle 4	84	0 (0.0)	(0.0, 3.9)
	Cycle 5	80	0 (0.0)	(0.0, 3.9)
	Cycle 6	78	1 (1.1)	(0.0, 5.8)
	Cycle 7	75	1 (1.1)	(0.0, 5.8)
	Cycle >= 8 and < 18	73	3 (3.2)	(0.7, 9.1)
	Cycle >= 18	34	0 (0.0)	(0.0, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	9 (10.2)	(4.8, 18.5)
		Cycle 1	88	1 (1.1)	(0.0, 6.2)
		Cycle 2	86	1 (1.1)	(0.0, 6.2)
		Cycle 3	85	1 (1.1)	(0.0, 6.2)
		Cycle 4	84	2 (2.3)	(0.3, 8.0)
		Cycle 5	74	0 (0.0)	(0.0, 4.1)
		Cycle 6	73	1 (1.1)	(0.0, 6.2)
		Cycle 7	69	1 (1.1)	(0.0, 6.2)
		Cycle >= 8 and < 18	64	2 (2.3)	(0.3, 8.0)
		Cycle >= 18	41	2 (2.3)	(0.3, 8.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	4 (7.8)	(2.2, 18.9)
		Cycle 1	51	2 (3.9)	(0.5, 13.5)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	49	1 (2.0)	(0.0, 10.4)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	47	0 (0.0)	(0.0, 7.0)
		Cycle 6	46	0 (0.0)	(0.0, 7.0)
		Cycle 7	45	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	44	2 (3.9)	(0.5, 13.5)
		Cycle >= 18	21	0 (0.0)	(0.0, 7.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	13 (10.4)	(5.7, 17.1)
		Cycle 1	125	3 (2.4)	(0.5, 6.9)
		Cycle 2	123	1 (0.8)	(0.0, 4.4)
		Cycle 3	118	0 (0.0)	(0.0, 2.9)
		Cycle 4	114	2 (1.6)	(0.2, 5.7)
		Cycle 5	103	0 (0.0)	(0.0, 2.9)
		Cycle 6	101	2 (1.6)	(0.2, 5.7)
		Cycle 7	95	2 (1.6)	(0.2, 5.7)
		Cycle >= 8 and < 18	90	3 (2.4)	(0.5, 6.9)
		Cycle >= 18	52	2 (1.6)	(0.2, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	9 (9.3)	(4.3, 16.9)
		Cycle 1	97	4 (4.1)	(1.1, 10.2)
		Cycle 2	96	0 (0.0)	(0.0, 3.7)
		Cycle 3	91	1 (1.0)	(0.0, 5.6)
		Cycle 4	88	0 (0.0)	(0.0, 3.7)
		Cycle 5	84	0 (0.0)	(0.0, 3.7)
		Cycle 6	82	1 (1.0)	(0.0, 5.6)
		Cycle 7	79	1 (1.0)	(0.0, 5.6)
		Cycle >= 8 and < 18	76	3 (3.1)	(0.6, 8.8)
		Cycle >= 18	36	0 (0.0)	(0.0, 3.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	8 (9.6)	(4.3, 18.1)
		Cycle 1	83	1 (1.2)	(0.0, 6.5)
		Cycle 2	81	1 (1.2)	(0.0, 6.5)
		Cycle 3	80	0 (0.0)	(0.0, 4.3)
		Cycle 4	79	2 (2.4)	(0.3, 8.4)
		Cycle 5	69	0 (0.0)	(0.0, 4.3)
		Cycle 6	68	1 (1.2)	(0.0, 6.5)
		Cycle 7	64	1 (1.2)	(0.0, 6.5)
		Cycle >= 8 and < 18	60	2 (2.4)	(0.3, 8.4)
		Cycle >= 18	38	2 (2.4)	(0.3, 8.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Normal (N=90)			
	Any TEAE	90	8 (8.9)	(3.9, 16.8)
	Cycle 1	90	2 (2.2)	(0.3, 7.8)
	Cycle 2	89	1 (1.1)	(0.0, 6.0)
	Cycle 3	85	1 (1.1)	(0.0, 6.0)
	Cycle 4	85	1 (1.1)	(0.0, 6.0)
	Cycle 5	76	0 (0.0)	(0.0, 4.0)
	Cycle 6	73	0 (0.0)	(0.0, 4.0)
	Cycle 7	72	1 (1.1)	(0.0, 6.0)
	Cycle >= 8 and < 18	69	2 (2.2)	(0.3, 7.8)
	Cycle >= 18	41	1 (1.1)	(0.0, 6.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	6 (8.7) (3.3, 18.0)
		Cycle 1	69	1 (1.4) (0.0, 7.8)
		Cycle 2	68	0 (0.0) (0.0, 5.2)
		Cycle 3	66	0 (0.0) (0.0, 5.2)
		Cycle 4	63	1 (1.4) (0.0, 7.8)
		Cycle 5	59	0 (0.0) (0.0, 5.2)
		Cycle 6	59	2 (2.9) (0.4, 10.1)
		Cycle 7	56	1 (1.4) (0.0, 7.8)
		Cycle >= 8 and < 18	54	2 (2.9) (0.4, 10.1)
		Cycle >= 18	27	1 (1.4) (0.0, 7.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	4 (16.0)	(4.5, 36.1)
		Cycle 1	25	3 (12.0)	(2.5, 31.2)
		Cycle 2	24	0 (0.0)	(0.0, 13.7)
		Cycle 3	23	0 (0.0)	(0.0, 13.7)
		Cycle 4	21	0 (0.0)	(0.0, 13.7)
		Cycle 5	20	0 (0.0)	(0.0, 13.7)
		Cycle 6	20	0 (0.0)	(0.0, 13.7)
		Cycle 7	17	0 (0.0)	(0.0, 13.7)
		Cycle >= 8 and < 18	15	1 (4.0)	(0.1, 20.4)
		Cycle >= 18	7	0 (0.0)	(0.0, 13.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	14 (13.3)	(7.5, 21.4)
		Cycle 1	105	6 (5.7)	(2.1, 12.0)
		Cycle 2	104	0 (0.0)	(0.0, 3.5)
		Cycle 3	102	1 (1.0)	(0.0, 5.2)
		Cycle 4	98	1 (1.0)	(0.0, 5.2)
		Cycle 5	90	0 (0.0)	(0.0, 3.5)
		Cycle 6	89	1 (1.0)	(0.0, 5.2)
		Cycle 7	87	2 (1.9)	(0.2, 6.7)
		Cycle >= 8 and < 18	84	3 (2.9)	(0.6, 8.1)
		Cycle >= 18	44	1 (1.0)	(0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	4 (5.3) (1.5, 12.9)
		Cycle 1	76	0 (0.0) (0.0, 4.7)
		Cycle 2	74	1 (1.3) (0.0, 7.1)
		Cycle 3	69	0 (0.0) (0.0, 4.7)
		Cycle 4	68	1 (1.3) (0.0, 7.1)
		Cycle 5	63	0 (0.0) (0.0, 4.7)
		Cycle 6	61	1 (1.3) (0.0, 7.1)
		Cycle 7	56	0 (0.0) (0.0, 4.7)
		Cycle >= 8 and < 18	54	2 (2.6) (0.3, 9.2)
		Cycle >= 18	31	1 (1.3) (0.0, 7.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	5 (20.8)	(7.1, 42.2)
		Cycle 1	24	1 (4.2)	(0.1, 21.1)
		Cycle 2	23	1 (4.2)	(0.1, 21.1)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	0 (0.0)	(0.0, 14.2)
		Cycle 6	18	0 (0.0)	(0.0, 14.2)
		Cycle 7	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 8 and < 18	18	2 (8.3)	(1.0, 27.0)
		Cycle >= 18	10	1 (4.2)	(0.1, 21.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	13 (8.1)	(4.4, 13.5)
		Cycle 1	160	5 (3.1)	(1.0, 7.1)
		Cycle 2	158	0 (0.0)	(0.0, 2.3)
		Cycle 3	152	1 (0.6)	(0.0, 3.4)
		Cycle 4	147	2 (1.3)	(0.2, 4.4)
		Cycle 5	136	0 (0.0)	(0.0, 2.3)
		Cycle 6	134	2 (1.3)	(0.2, 4.4)
		Cycle 7	127	2 (1.3)	(0.2, 4.4)
		Cycle >= 8 and < 18	120	3 (1.9)	(0.4, 5.4)
		Cycle >= 18	65	1 (0.6)	(0.0, 3.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	3 (5.7) (1.2, 15.7)
		Cycle 1	53	2 (3.8) (0.5, 13.0)
		Cycle 2	52	0 (0.0) (0.0, 6.7)
		Cycle 3	49	0 (0.0) (0.0, 6.7)
		Cycle 4	48	1 (1.9) (0.0, 10.1)
		Cycle 5	43	0 (0.0) (0.0, 6.7)
		Cycle 6	42	1 (1.9) (0.0, 10.1)
		Cycle 7	41	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	1 (1.9) (0.0, 10.1)
		Cycle >= 18	18	0 (0.0) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	15 (11.5)	(6.6, 18.2)
		Cycle 1	131	4 (3.1)	(0.8, 7.6)
		Cycle 2	129	1 (0.8)	(0.0, 4.2)
		Cycle 3	125	1 (0.8)	(0.0, 4.2)
		Cycle 4	121	1 (0.8)	(0.0, 4.2)
		Cycle 5	112	0 (0.0)	(0.0, 2.8)
		Cycle 6	110	1 (0.8)	(0.0, 4.2)
		Cycle 7	104	2 (1.5)	(0.2, 5.4)
		Cycle >= 8 and < 18	99	4 (3.1)	(0.8, 7.6)
		Cycle >= 18	57	2 (1.5)	(0.2, 5.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
M-History of visceral disease	Yes (N=169)			
	Any TEAE	169	16 (9.5)	(5.5, 14.9)
	Cycle 1	169	4 (2.4)	(0.6, 5.9)
	Cycle 2	166	1 (0.6)	(0.0, 3.3)
	Cycle 3	159	1 (0.6)	(0.0, 3.3)
	Cycle 4	154	2 (1.2)	(0.1, 4.2)
	Cycle 5	142	0 (0.0)	(0.0, 2.2)
	Cycle 6	139	2 (1.2)	(0.1, 4.2)
	Cycle 7	132	2 (1.2)	(0.1, 4.2)
	Cycle >= 8 and < 18	125	4 (2.4)	(0.6, 5.9)
	Cycle >= 18	70	2 (1.2)	(0.1, 4.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	2 (13.3)	(1.7, 40.5)
		Cycle 1	15	2 (13.3)	(1.7, 40.5)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	1 (6.7)	(0.2, 31.9)
		Cycle >= 18	5	0 (0.0)	(0.0, 21.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	3 (5.4) (1.1, 14.9)
		Cycle 1	56	1 (1.8) (0.0, 9.6)
		Cycle 2	55	0 (0.0) (0.0, 6.4)
		Cycle 3	54	0 (0.0) (0.0, 6.4)
		Cycle 4	53	0 (0.0) (0.0, 6.4)
		Cycle 5	49	0 (0.0) (0.0, 6.4)
		Cycle 6	48	0 (0.0) (0.0, 6.4)
		Cycle 7	48	0 (0.0) (0.0, 6.4)
		Cycle >= 8 and < 18	45	2 (3.6) (0.4, 12.3)
		Cycle >= 18	32	0 (0.0) (0.0, 6.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	15 (11.7)	(6.7, 18.6)
		Cycle 1	128	5 (3.9)	(1.3, 8.9)
		Cycle 2	126	1 (0.8)	(0.0, 4.3)
		Cycle 3	120	1 (0.8)	(0.0, 4.3)
		Cycle 4	116	2 (1.6)	(0.2, 5.5)
		Cycle 5	106	0 (0.0)	(0.0, 2.8)
		Cycle 6	104	2 (1.6)	(0.2, 5.5)
		Cycle 7	97	2 (1.6)	(0.2, 5.5)
		Cycle >= 8 and < 18	93	3 (2.3)	(0.5, 6.7)
		Cycle >= 18	43	2 (1.6)	(0.2, 5.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
 Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	< 3 lines (N=17)			
	Any TEAE	17	1 (5.9)	(0.1, 28.7)
	Cycle 1	17	0 (0.0)	(0.0, 19.5)
	Cycle 2	17	0 (0.0)	(0.0, 19.5)
	Cycle 3	17	0 (0.0)	(0.0, 19.5)
	Cycle 4	17	0 (0.0)	(0.0, 19.5)
	Cycle 5	17	0 (0.0)	(0.0, 19.5)
	Cycle 6	16	0 (0.0)	(0.0, 19.5)
	Cycle 7	16	0 (0.0)	(0.0, 19.5)
	Cycle >= 8 and < 18	16	1 (5.9)	(0.1, 28.7)
	Cycle >= 18	14	0 (0.0)	(0.0, 19.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
 Adverse events were coded using the MedDRA dictionary, Version 20.1.
 If a subject has more than one event per cycle, the subject is counted once at each level of summation.
 TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
O-Prior treatment lines	>= 3 lines (N=167)			
	Any TEAE	167	17 (10.2)	(6.0, 15.8)
	Cycle 1	167	6 (3.6)	(1.3, 7.7)
	Cycle 2	164	1 (0.6)	(0.0, 3.3)
	Cycle 3	157	1 (0.6)	(0.0, 3.3)
	Cycle 4	152	2 (1.2)	(0.1, 4.3)
	Cycle 5	138	0 (0.0)	(0.0, 2.2)
	Cycle 6	136	2 (1.2)	(0.1, 4.3)
	Cycle 7	129	2 (1.2)	(0.1, 4.3)
	Cycle >= 8 and < 18	122	4 (2.4)	(0.7, 6.0)
	Cycle >= 18	61	2 (1.2)	(0.1, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)			
	Any TEAE	79	8 (10.1)	(4.5, 19.0)
	Cycle 1	79	2 (2.5)	(0.3, 8.8)
	Cycle 2	78	1 (1.3)	(0.0, 6.9)
	Cycle 3	75	0 (0.0)	(0.0, 4.6)
	Cycle 4	73	1 (1.3)	(0.0, 6.9)
	Cycle 5	70	0 (0.0)	(0.0, 4.6)
	Cycle 6	69	1 (1.3)	(0.0, 6.9)
	Cycle 7	68	1 (1.3)	(0.0, 6.9)
	Cycle >= 8 and < 18	65	3 (3.8)	(0.8, 10.7)
	Cycle >= 18	37	1 (1.3)	(0.0, 6.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)			
	Any TEAE	66	7 (10.6)	(4.4, 20.6)
	Cycle 1	66	4 (6.1)	(1.7, 14.8)
	Cycle 2	66	0 (0.0)	(0.0, 5.4)
	Cycle 3	64	0 (0.0)	(0.0, 5.4)
	Cycle 4	61	0 (0.0)	(0.0, 5.4)
	Cycle 5	55	0 (0.0)	(0.0, 5.4)
	Cycle 6	53	1 (1.5)	(0.0, 8.2)
	Cycle 7	51	1 (1.5)	(0.0, 8.2)
	Cycle >= 8 and < 18	51	1 (1.5)	(0.0, 8.2)
	Cycle >= 18	23	0 (0.0)	(0.0, 5.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	12 (9.9)	(5.2, 16.7)
		Cycle 1	121	5 (4.1)	(1.4, 9.4)
		Cycle 2	120	0 (0.0)	(0.0, 3.0)
		Cycle 3	119	1 (0.8)	(0.0, 4.5)
		Cycle 4	115	1 (0.8)	(0.0, 4.5)
		Cycle 5	106	0 (0.0)	(0.0, 3.0)
		Cycle 6	103	1 (0.8)	(0.0, 4.5)
		Cycle 7	96	1 (0.8)	(0.0, 4.5)
		Cycle >= 8 and < 18	93	3 (2.5)	(0.5, 7.1)
		Cycle >= 18	54	1 (0.8)	(0.0, 4.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
Q-Prior pertuzumab	No (N=63)			
	Any TEAE	63	6 (9.5)	(3.6, 19.6)
	Cycle 1	63	1 (1.6)	(0.0, 8.5)
	Cycle 2	61	1 (1.6)	(0.0, 8.5)
	Cycle 3	55	0 (0.0)	(0.0, 5.7)
	Cycle 4	54	1 (1.6)	(0.0, 8.5)
	Cycle 5	49	0 (0.0)	(0.0, 5.7)
	Cycle 6	49	1 (1.6)	(0.0, 8.5)
	Cycle 7	49	1 (1.6)	(0.0, 8.5)
	Cycle >= 8 and < 18	45	2 (3.2)	(0.4, 11.0)
	Cycle >= 18	21	1 (1.6)	(0.0, 8.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	3 (5.9) (1.2, 16.2)
		Cycle 1	51	0 (0.0) (0.0, 7.0)
		Cycle 2	50	0 (0.0) (0.0, 7.0)
		Cycle 3	50	0 (0.0) (0.0, 7.0)
		Cycle 4	49	1 (2.0) (0.0, 10.4)
		Cycle 5	46	0 (0.0) (0.0, 7.0)
		Cycle 6	44	0 (0.0) (0.0, 7.0)
		Cycle 7	40	0 (0.0) (0.0, 7.0)
		Cycle >= 8 and < 18	40	2 (3.9) (0.5, 13.5)
		Cycle >= 18	24	0 (0.0) (0.0, 7.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AIN_SSI0: Incidence of non-severe infusion related reactions overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	15 (11.3)	(6.5, 17.9)
		Cycle 1	133	6 (4.5)	(1.7, 9.6)
		Cycle 2	131	1 (0.8)	(0.0, 4.1)
		Cycle 3	124	1 (0.8)	(0.0, 4.1)
		Cycle 4	120	1 (0.8)	(0.0, 4.1)
		Cycle 5	109	0 (0.0)	(0.0, 2.7)
		Cycle 6	108	2 (1.5)	(0.2, 5.3)
		Cycle 7	105	2 (1.5)	(0.2, 5.3)
		Cycle >= 8 and < 18	98	3 (2.3)	(0.5, 6.5)
		Cycle >= 18	51	2 (1.5)	(0.2, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

UE von besonderem Interesse – Verlängerung des QT-Intervalls, unabhängig vom Schweregrad

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 08Jun2020

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Program Name: T3AQ_SSI0.sas
Run Date: 11MAR21:15:37

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	11 (6.0)	(3.0, 10.4)
		Cycle 1	184	1 (0.5)	(0.0, 3.0)
		Cycle 2	181	2 (1.1)	(0.1, 3.9)
		Cycle 3	174	1 (0.5)	(0.0, 3.0)
		Cycle 4	169	0 (0.0)	(0.0, 2.0)
		Cycle 5	155	0 (0.0)	(0.0, 2.0)
		Cycle 6	152	3 (1.6)	(0.3, 4.7)
		Cycle 7	145	0 (0.0)	(0.0, 2.0)
		Cycle >= 8 and < 18	138	4 (2.2)	(0.6, 5.5)
		Cycle >= 18	75	4 (2.2)	(0.6, 5.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	7 (5.0) (2.0, 10.0)
		Cycle 1	140	0 (0.0) (0.0, 2.6)
		Cycle 2	138	1 (0.7) (0.0, 3.9)
		Cycle 3	132	0 (0.0) (0.0, 2.6)
		Cycle 4	128	0 (0.0) (0.0, 2.6)
		Cycle 5	116	0 (0.0) (0.0, 2.6)
		Cycle 6	113	2 (1.4) (0.2, 5.1)
		Cycle 7	109	0 (0.0) (0.0, 2.6)
		Cycle >= 8 and < 18	103	3 (2.1) (0.4, 6.1)
		Cycle >= 18	56	3 (2.1) (0.4, 6.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 08Jun2020

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Program Name: T3AQ_SSI0.sas
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Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	4 (9.1) (2.5, 21.7)
		Cycle 1	44	1 (2.3) (0.1, 12.0)
		Cycle 2	43	1 (2.3) (0.1, 12.0)
		Cycle 3	42	1 (2.3) (0.1, 12.0)
		Cycle 4	41	0 (0.0) (0.0, 8.0)
		Cycle 5	39	0 (0.0) (0.0, 8.0)
		Cycle 6	39	1 (2.3) (0.1, 12.0)
		Cycle 7	36	0 (0.0) (0.0, 8.0)
		Cycle >= 8 and < 18	35	1 (2.3) (0.1, 12.0)
		Cycle >= 18	19	1 (2.3) (0.1, 12.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

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Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	5 (7.9) (2.6, 17.6)
		Cycle 1	63	0 (0.0) (0.0, 5.7)
		Cycle 2	61	1 (1.6) (0.0, 8.5)
		Cycle 3	58	1 (1.6) (0.0, 8.5)
		Cycle 4	58	0 (0.0) (0.0, 5.7)
		Cycle 5	55	0 (0.0) (0.0, 5.7)
		Cycle 6	55	1 (1.6) (0.0, 8.5)
		Cycle 7	53	0 (0.0) (0.0, 5.7)
		Cycle >= 8 and < 18	49	3 (4.8) (1.0, 13.3)
		Cycle >= 18	29	3 (4.8) (1.0, 13.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	2 (3.8) (0.5, 13.0)
		Cycle 1	53	0 (0.0) (0.0, 6.7)
		Cycle 2	53	0 (0.0) (0.0, 6.7)
		Cycle 3	52	0 (0.0) (0.0, 6.7)
		Cycle 4	49	0 (0.0) (0.0, 6.7)
		Cycle 5	44	0 (0.0) (0.0, 6.7)
		Cycle 6	42	2 (3.8) (0.5, 13.0)
		Cycle 7	40	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	0 (0.0) (0.0, 6.7)
		Cycle >= 18	23	0 (0.0) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	4 (5.9) (1.6, 14.4)
		Cycle 1	68	1 (1.5) (0.0, 7.9)
		Cycle 2	67	1 (1.5) (0.0, 7.9)
		Cycle 3	64	0 (0.0) (0.0, 5.3)
		Cycle 4	62	0 (0.0) (0.0, 5.3)
		Cycle 5	56	0 (0.0) (0.0, 5.3)
		Cycle 6	55	0 (0.0) (0.0, 5.3)
		Cycle 7	52	0 (0.0) (0.0, 5.3)
		Cycle >= 8 and < 18	50	1 (1.5) (0.0, 7.9)
		Cycle >= 18	23	1 (1.5) (0.0, 7.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	7 (6.9) (2.8, 13.6)
		Cycle 1	102	1 (1.0) (0.0, 5.3)
		Cycle 2	101	1 (1.0) (0.0, 5.3)
		Cycle 3	100	1 (1.0) (0.0, 5.3)
		Cycle 4	98	0 (0.0) (0.0, 3.6)
		Cycle 5	94	0 (0.0) (0.0, 3.6)
		Cycle 6	93	2 (2.0) (0.2, 6.9)
		Cycle 7	88	0 (0.0) (0.0, 3.6)
		Cycle >= 8 and < 18	86	3 (2.9) (0.6, 8.4)
		Cycle >= 18	49	3 (2.9) (0.6, 8.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	4 (4.9)	(1.4, 12.2)
		Cycle 1	81	0 (0.0)	(0.0, 4.5)
		Cycle 2	79	1 (1.2)	(0.0, 6.7)
		Cycle 3	73	0 (0.0)	(0.0, 4.5)
		Cycle 4	71	0 (0.0)	(0.0, 4.5)
		Cycle 5	61	0 (0.0)	(0.0, 4.5)
		Cycle 6	59	1 (1.2)	(0.0, 6.7)
		Cycle 7	57	0 (0.0)	(0.0, 4.5)
		Cycle >= 8 and < 18	52	1 (1.2)	(0.0, 6.7)
		Cycle >= 18	26	1 (1.2)	(0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions	< 5 cm (N=73)			
	Any TEAE	73	5 (6.8)	(2.3, 15.3)
	Cycle 1	73	1 (1.4)	(0.0, 7.4)
	Cycle 2	72	1 (1.4)	(0.0, 7.4)
	Cycle 3	70	0 (0.0)	(0.0, 4.9)
	Cycle 4	65	0 (0.0)	(0.0, 4.9)
	Cycle 5	60	0 (0.0)	(0.0, 4.9)
	Cycle 6	59	0 (0.0)	(0.0, 4.9)
	Cycle 7	58	0 (0.0)	(0.0, 4.9)
	Cycle >= 8 and < 18	53	2 (2.7)	(0.3, 9.5)
	Cycle >= 18	33	1 (1.4)	(0.0, 7.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=97)			
	Any TEAE	97	5 (5.2)	(1.7, 11.6)
	Cycle 1	97	0 (0.0)	(0.0, 3.7)
	Cycle 2	95	1 (1.0)	(0.0, 5.6)
	Cycle 3	90	0 (0.0)	(0.0, 3.7)
	Cycle 4	90	0 (0.0)	(0.0, 3.7)
	Cycle 5	81	0 (0.0)	(0.0, 3.7)
	Cycle 6	79	3 (3.1)	(0.6, 8.8)
	Cycle 7	74	0 (0.0)	(0.0, 3.7)
	Cycle >= 8 and < 18	72	1 (1.0)	(0.0, 5.6)
	Cycle >= 18	34	2 (2.1)	(0.3, 7.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	10 (6.5)	(3.2, 11.6)
		Cycle 1	154	0 (0.0)	(0.0, 2.4)
		Cycle 2	152	2 (1.3)	(0.2, 4.6)
		Cycle 3	146	1 (0.6)	(0.0, 3.6)
		Cycle 4	141	0 (0.0)	(0.0, 2.4)
		Cycle 5	129	0 (0.0)	(0.0, 2.4)
		Cycle 6	127	3 (1.9)	(0.4, 5.6)
		Cycle 7	121	0 (0.0)	(0.0, 2.4)
		Cycle >= 8 and < 18	114	4 (2.6)	(0.7, 6.5)
		Cycle >= 18	69	4 (2.6)	(0.7, 6.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHCR3+ (N=28)			
	Any TEAE	28	1 (3.6)	(0.1, 18.3)
	Cycle 1	28	1 (3.6)	(0.1, 18.3)
	Cycle 2	27	0 (0.0)	(0.0, 12.3)
	Cycle 3	26	0 (0.0)	(0.0, 12.3)
	Cycle 4	26	0 (0.0)	(0.0, 12.3)
	Cycle 5	24	0 (0.0)	(0.0, 12.3)
	Cycle 6	23	0 (0.0)	(0.0, 12.3)
	Cycle 7	22	0 (0.0)	(0.0, 12.3)
	Cycle >= 8 and < 18	22	0 (0.0)	(0.0, 12.3)
	Cycle >= 18	5	0 (0.0)	(0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	6 (6.5)	(2.4, 13.5)
		Cycle 1	93	0 (0.0)	(0.0, 3.9)
		Cycle 2	92	2 (2.2)	(0.3, 7.6)
		Cycle 3	87	1 (1.1)	(0.0, 5.8)
		Cycle 4	84	0 (0.0)	(0.0, 3.9)
		Cycle 5	80	0 (0.0)	(0.0, 3.9)
		Cycle 6	78	1 (1.1)	(0.0, 5.8)
		Cycle 7	75	0 (0.0)	(0.0, 3.9)
		Cycle >= 8 and < 18	73	2 (2.2)	(0.3, 7.6)
		Cycle >= 18	34	2 (2.2)	(0.3, 7.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	5 (5.7)	(1.9, 12.8)
		Cycle 1	88	1 (1.1)	(0.0, 6.2)
		Cycle 2	86	0 (0.0)	(0.0, 4.1)
		Cycle 3	85	0 (0.0)	(0.0, 4.1)
		Cycle 4	84	0 (0.0)	(0.0, 4.1)
		Cycle 5	74	0 (0.0)	(0.0, 4.1)
		Cycle 6	73	2 (2.3)	(0.3, 8.0)
		Cycle 7	69	0 (0.0)	(0.0, 4.1)
		Cycle >= 8 and < 18	64	2 (2.3)	(0.3, 8.0)
		Cycle >= 18	41	2 (2.3)	(0.3, 8.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	2 (3.9)	(0.5, 13.5)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	1 (2.0)	(0.0, 10.4)
		Cycle 3	49	1 (2.0)	(0.0, 10.4)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	47	0 (0.0)	(0.0, 7.0)
		Cycle 6	46	0 (0.0)	(0.0, 7.0)
		Cycle 7	45	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	44	1 (2.0)	(0.0, 10.4)
		Cycle >= 18	21	1 (2.0)	(0.0, 10.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	9 (7.2)	(3.3, 13.2)
		Cycle 1	125	1 (0.8)	(0.0, 4.4)
		Cycle 2	123	1 (0.8)	(0.0, 4.4)
		Cycle 3	118	0 (0.0)	(0.0, 2.9)
		Cycle 4	114	0 (0.0)	(0.0, 2.9)
		Cycle 5	103	0 (0.0)	(0.0, 2.9)
		Cycle 6	101	3 (2.4)	(0.5, 6.9)
		Cycle 7	95	0 (0.0)	(0.0, 2.9)
		Cycle >= 8 and < 18	90	3 (2.4)	(0.5, 6.9)
		Cycle >= 18	52	3 (2.4)	(0.5, 6.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	6 (6.2)	(2.3, 13.0)
		Cycle 1	97	0 (0.0)	(0.0, 3.7)
		Cycle 2	96	2 (2.1)	(0.3, 7.3)
		Cycle 3	91	1 (1.0)	(0.0, 5.6)
		Cycle 4	88	0 (0.0)	(0.0, 3.7)
		Cycle 5	84	0 (0.0)	(0.0, 3.7)
		Cycle 6	82	1 (1.0)	(0.0, 5.6)
		Cycle 7	79	0 (0.0)	(0.0, 3.7)
		Cycle >= 8 and < 18	76	2 (2.1)	(0.3, 7.3)
		Cycle >= 18	36	2 (2.1)	(0.3, 7.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	5 (6.0)	(2.0, 13.5)
		Cycle 1	83	1 (1.2)	(0.0, 6.5)
		Cycle 2	81	0 (0.0)	(0.0, 4.3)
		Cycle 3	80	0 (0.0)	(0.0, 4.3)
		Cycle 4	79	0 (0.0)	(0.0, 4.3)
		Cycle 5	69	0 (0.0)	(0.0, 4.3)
		Cycle 6	68	2 (2.4)	(0.3, 8.4)
		Cycle 7	64	0 (0.0)	(0.0, 4.3)
		Cycle >= 8 and < 18	60	2 (2.4)	(0.3, 8.4)
		Cycle >= 18	38	2 (2.4)	(0.3, 8.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Normal (N=90)			
	Any TEAE	90	5 (5.6)	(1.8, 12.5)
	Cycle 1	90	0 (0.0)	(0.0, 4.0)
	Cycle 2	89	1 (1.1)	(0.0, 6.0)
	Cycle 3	85	0 (0.0)	(0.0, 4.0)
	Cycle 4	85	0 (0.0)	(0.0, 4.0)
	Cycle 5	76	0 (0.0)	(0.0, 4.0)
	Cycle 6	73	0 (0.0)	(0.0, 4.0)
	Cycle 7	72	0 (0.0)	(0.0, 4.0)
	Cycle >= 8 and < 18	69	2 (2.2)	(0.3, 7.8)
	Cycle >= 18	41	2 (2.2)	(0.3, 7.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	3 (4.3)	(0.9, 12.2)
		Cycle 1	69	0 (0.0)	(0.0, 5.2)
		Cycle 2	68	1 (1.4)	(0.0, 7.8)
		Cycle 3	66	1 (1.4)	(0.0, 7.8)
		Cycle 4	63	0 (0.0)	(0.0, 5.2)
		Cycle 5	59	0 (0.0)	(0.0, 5.2)
		Cycle 6	59	1 (1.4)	(0.0, 7.8)
		Cycle 7	56	0 (0.0)	(0.0, 5.2)
		Cycle >= 8 and < 18	54	1 (1.4)	(0.0, 7.8)
		Cycle >= 18	27	1 (1.4)	(0.0, 7.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	3 (12.0)	(2.5, 31.2)
		Cycle 1	25	1 (4.0)	(0.1, 20.4)
		Cycle 2	24	0 (0.0)	(0.0, 13.7)
		Cycle 3	23	0 (0.0)	(0.0, 13.7)
		Cycle 4	21	0 (0.0)	(0.0, 13.7)
		Cycle 5	20	0 (0.0)	(0.0, 13.7)
		Cycle 6	20	2 (8.0)	(1.0, 26.0)
		Cycle 7	17	0 (0.0)	(0.0, 13.7)
		Cycle >= 8 and < 18	15	1 (4.0)	(0.1, 20.4)
		Cycle >= 18	7	1 (4.0)	(0.1, 20.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	8 (7.6)	(3.3, 14.5)
		Cycle 1	105	0 (0.0)	(0.0, 3.5)
		Cycle 2	104	2 (1.9)	(0.2, 6.7)
		Cycle 3	102	1 (1.0)	(0.0, 5.2)
		Cycle 4	98	0 (0.0)	(0.0, 3.5)
		Cycle 5	90	0 (0.0)	(0.0, 3.5)
		Cycle 6	89	2 (1.9)	(0.2, 6.7)
		Cycle 7	87	0 (0.0)	(0.0, 3.5)
		Cycle >= 8 and < 18	84	4 (3.8)	(1.0, 9.5)
		Cycle >= 18	44	3 (2.9)	(0.6, 8.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	3 (3.9)	(0.8, 11.1)
		Cycle 1	76	1 (1.3)	(0.0, 7.1)
		Cycle 2	74	0 (0.0)	(0.0, 4.7)
		Cycle 3	69	0 (0.0)	(0.0, 4.7)
		Cycle 4	68	0 (0.0)	(0.0, 4.7)
		Cycle 5	63	0 (0.0)	(0.0, 4.7)
		Cycle 6	61	1 (1.3)	(0.0, 7.1)
		Cycle 7	56	0 (0.0)	(0.0, 4.7)
		Cycle >= 8 and < 18	54	0 (0.0)	(0.0, 4.7)
		Cycle >= 18	31	1 (1.3)	(0.0, 7.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	4 (16.7)	(4.7, 37.4)
		Cycle 1	24	1 (4.2)	(0.1, 21.1)
		Cycle 2	23	0 (0.0)	(0.0, 14.2)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	0 (0.0)	(0.0, 14.2)
		Cycle 6	18	2 (8.3)	(1.0, 27.0)
		Cycle 7	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 8 and < 18	18	2 (8.3)	(1.0, 27.0)
		Cycle >= 18	10	1 (4.2)	(0.1, 21.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	7 (4.4)	(1.8, 8.8)
		Cycle 1	160	0 (0.0)	(0.0, 2.3)
		Cycle 2	158	2 (1.3)	(0.2, 4.4)
		Cycle 3	152	1 (0.6)	(0.0, 3.4)
		Cycle 4	147	0 (0.0)	(0.0, 2.3)
		Cycle 5	136	0 (0.0)	(0.0, 2.3)
		Cycle 6	134	1 (0.6)	(0.0, 3.4)
		Cycle 7	127	0 (0.0)	(0.0, 2.3)
		Cycle >= 8 and < 18	120	2 (1.3)	(0.2, 4.4)
		Cycle >= 18	65	3 (1.9)	(0.4, 5.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 08Jun2020

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Program Name: T3AQ_SSI0.sas
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Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	7 (13.2)	(5.5, 25.3)
		Cycle 1	53	1 (1.9)	(0.0, 10.1)
		Cycle 2	52	2 (3.8)	(0.5, 13.0)
		Cycle 3	49	0 (0.0)	(0.0, 6.7)
		Cycle 4	48	0 (0.0)	(0.0, 6.7)
		Cycle 5	43	0 (0.0)	(0.0, 6.7)
		Cycle 6	42	2 (3.8)	(0.5, 13.0)
		Cycle 7	41	0 (0.0)	(0.0, 6.7)
		Cycle >= 8 and < 18	39	1 (1.9)	(0.0, 10.1)
		Cycle >= 18	18	1 (1.9)	(0.0, 10.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	4 (3.1)	(0.8, 7.6)
		Cycle 1	131	0 (0.0)	(0.0, 2.8)
		Cycle 2	129	0 (0.0)	(0.0, 2.8)
		Cycle 3	125	1 (0.8)	(0.0, 4.2)
		Cycle 4	121	0 (0.0)	(0.0, 2.8)
		Cycle 5	112	0 (0.0)	(0.0, 2.8)
		Cycle 6	110	1 (0.8)	(0.0, 4.2)
		Cycle 7	104	0 (0.0)	(0.0, 2.8)
		Cycle >= 8 and < 18	99	3 (2.3)	(0.5, 6.5)
		Cycle >= 18	57	3 (2.3)	(0.5, 6.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	10 (5.9)	(2.9, 10.6)
		Cycle 1	169	1 (0.6)	(0.0, 3.3)
		Cycle 2	166	2 (1.2)	(0.1, 4.2)
		Cycle 3	159	1 (0.6)	(0.0, 3.3)
		Cycle 4	154	0 (0.0)	(0.0, 2.2)
		Cycle 5	142	0 (0.0)	(0.0, 2.2)
		Cycle 6	139	3 (1.8)	(0.4, 5.1)
		Cycle 7	132	0 (0.0)	(0.0, 2.2)
		Cycle >= 8 and < 18	125	4 (2.4)	(0.6, 5.9)
		Cycle >= 18	70	3 (1.8)	(0.4, 5.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	1 (6.7)	(0.2, 31.9)
		Cycle 1	15	0 (0.0)	(0.0, 21.8)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 18	5	1 (6.7)	(0.2, 31.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	2 (3.6) (0.4, 12.3)
		Cycle 1	56	1 (1.8) (0.0, 9.6)
		Cycle 2	55	0 (0.0) (0.0, 6.4)
		Cycle 3	54	0 (0.0) (0.0, 6.4)
		Cycle 4	53	0 (0.0) (0.0, 6.4)
		Cycle 5	49	0 (0.0) (0.0, 6.4)
		Cycle 6	48	0 (0.0) (0.0, 6.4)
		Cycle 7	48	0 (0.0) (0.0, 6.4)
		Cycle >= 8 and < 18	45	0 (0.0) (0.0, 6.4)
		Cycle >= 18	32	1 (1.8) (0.0, 9.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	9 (7.0)	(3.3, 12.9)
		Cycle 1	128	0 (0.0)	(0.0, 2.8)
		Cycle 2	126	2 (1.6)	(0.2, 5.5)
		Cycle 3	120	1 (0.8)	(0.0, 4.3)
		Cycle 4	116	0 (0.0)	(0.0, 2.8)
		Cycle 5	106	0 (0.0)	(0.0, 2.8)
		Cycle 6	104	3 (2.3)	(0.5, 6.7)
		Cycle 7	97	0 (0.0)	(0.0, 2.8)
		Cycle >= 8 and < 18	93	4 (3.1)	(0.9, 7.8)
		Cycle >= 18	43	3 (2.3)	(0.5, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	< 3 lines (N=17)			
	Any TEAE	17	1 (5.9)	(0.1, 28.7)
	Cycle 1	17	0 (0.0)	(0.0, 19.5)
	Cycle 2	17	0 (0.0)	(0.0, 19.5)
	Cycle 3	17	0 (0.0)	(0.0, 19.5)
	Cycle 4	17	0 (0.0)	(0.0, 19.5)
	Cycle 5	17	0 (0.0)	(0.0, 19.5)
	Cycle 6	16	0 (0.0)	(0.0, 19.5)
	Cycle 7	16	0 (0.0)	(0.0, 19.5)
	Cycle >= 8 and < 18	16	0 (0.0)	(0.0, 19.5)
	Cycle >= 18	14	1 (5.9)	(0.1, 28.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	>= 3 lines (N=167)			
	Any TEAE	167	10 (6.0)	(2.9, 10.7)
	Cycle 1	167	1 (0.6)	(0.0, 3.3)
	Cycle 2	164	2 (1.2)	(0.1, 4.3)
	Cycle 3	157	1 (0.6)	(0.0, 3.3)
	Cycle 4	152	0 (0.0)	(0.0, 2.2)
	Cycle 5	138	0 (0.0)	(0.0, 2.2)
	Cycle 6	136	3 (1.8)	(0.4, 5.2)
	Cycle 7	129	0 (0.0)	(0.0, 2.2)
	Cycle >= 8 and < 18	122	4 (2.4)	(0.7, 6.0)
	Cycle >= 18	61	3 (1.8)	(0.4, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)			
	Any TEAE	79	3 (3.8)	(0.8, 10.7)
	Cycle 1	79	0 (0.0)	(0.0, 4.6)
	Cycle 2	78	0 (0.0)	(0.0, 4.6)
	Cycle 3	75	1 (1.3)	(0.0, 6.9)
	Cycle 4	73	0 (0.0)	(0.0, 4.6)
	Cycle 5	70	0 (0.0)	(0.0, 4.6)
	Cycle 6	69	1 (1.3)	(0.0, 6.9)
	Cycle 7	68	0 (0.0)	(0.0, 4.6)
	Cycle >= 8 and < 18	65	1 (1.3)	(0.0, 6.9)
	Cycle >= 18	37	2 (2.5)	(0.3, 8.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	5 (7.6) (2.5, 16.8)
		Cycle 1	66	0 (0.0) (0.0, 5.4)
		Cycle 2	66	2 (3.0) (0.4, 10.5)
		Cycle 3	64	0 (0.0) (0.0, 5.4)
		Cycle 4	61	0 (0.0) (0.0, 5.4)
		Cycle 5	55	0 (0.0) (0.0, 5.4)
		Cycle 6	53	1 (1.5) (0.0, 8.2)
		Cycle 7	51	0 (0.0) (0.0, 5.4)
		Cycle >= 8 and < 18	51	3 (4.5) (0.9, 12.7)
		Cycle >= 18	23	1 (1.5) (0.0, 8.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	8 (6.6) (2.9, 12.6)
		Cycle 1	121	0 (0.0) (0.0, 3.0)
		Cycle 2	120	1 (0.8) (0.0, 4.5)
		Cycle 3	119	1 (0.8) (0.0, 4.5)
		Cycle 4	115	0 (0.0) (0.0, 3.0)
		Cycle 5	106	0 (0.0) (0.0, 3.0)
		Cycle 6	103	3 (2.5) (0.5, 7.1)
		Cycle 7	96	0 (0.0) (0.0, 3.0)
		Cycle >= 8 and < 18	93	3 (2.5) (0.5, 7.1)
		Cycle >= 18	54	4 (3.3) (0.9, 8.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	3 (4.8)	(1.0, 13.3)
		Cycle 1	63	1 (1.6)	(0.0, 8.5)
		Cycle 2	61	1 (1.6)	(0.0, 8.5)
		Cycle 3	55	0 (0.0)	(0.0, 5.7)
		Cycle 4	54	0 (0.0)	(0.0, 5.7)
		Cycle 5	49	0 (0.0)	(0.0, 5.7)
		Cycle 6	49	0 (0.0)	(0.0, 5.7)
		Cycle 7	49	0 (0.0)	(0.0, 5.7)
		Cycle >= 8 and < 18	45	1 (1.6)	(0.0, 8.5)
		Cycle >= 18	21	0 (0.0)	(0.0, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	2 (3.9)	(0.5, 13.5)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	50	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	46	0 (0.0)	(0.0, 7.0)
		Cycle 6	44	0 (0.0)	(0.0, 7.0)
		Cycle 7	40	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	40	0 (0.0)	(0.0, 7.0)
		Cycle >= 18	24	2 (3.9)	(0.5, 13.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3AQ_SSI0: Incidence of QT prolongation overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	9 (6.8)	(3.1, 12.5)
		Cycle 1	133	1 (0.8)	(0.0, 4.1)
		Cycle 2	131	2 (1.5)	(0.2, 5.3)
		Cycle 3	124	1 (0.8)	(0.0, 4.1)
		Cycle 4	120	0 (0.0)	(0.0, 2.7)
		Cycle 5	109	0 (0.0)	(0.0, 2.7)
		Cycle 6	108	3 (2.3)	(0.5, 6.5)
		Cycle 7	105	0 (0.0)	(0.0, 2.7)
		Cycle >= 8 and < 18	98	4 (3.0)	(0.8, 7.5)
		Cycle >= 18	51	2 (1.5)	(0.2, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

UE von besonderem Interesse – Interstitielle Lungenerkrankung (ILD), unabhängig vom Schweregrad

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	28 (15.2)	(10.4, 21.2)
		Cycle 1	184	0 (0.0)	(0.0, 2.0)
		Cycle 2	181	1 (0.5)	(0.0, 3.0)
		Cycle 3	174	1 (0.5)	(0.0, 3.0)
		Cycle 4	169	1 (0.5)	(0.0, 3.0)
		Cycle 5	155	2 (1.1)	(0.1, 3.9)
		Cycle 6	152	5 (2.7)	(0.9, 6.2)
		Cycle 7	145	2 (1.1)	(0.1, 3.9)
		Cycle >= 8 and < 18	138	13 (7.1)	(3.8, 11.8)
		Cycle >= 18	75	6 (3.3)	(1.2, 7.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	18 (12.9)	(7.8, 19.6)
		Cycle 1	0 (0.0)	(0.0, 2.6)
		Cycle 2	1 (0.7)	(0.0, 3.9)
		Cycle 3	1 (0.7)	(0.0, 3.9)
		Cycle 4	0 (0.0)	(0.0, 2.6)
		Cycle 5	1 (0.7)	(0.0, 3.9)
		Cycle 6	4 (2.9)	(0.8, 7.2)
		Cycle 7	2 (1.4)	(0.2, 5.1)
		Cycle >= 8 and < 18	8 (5.7)	(2.5, 10.9)
		Cycle >= 18	3 (2.1)	(0.4, 6.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	10 (22.7) (11.5, 37.8)
		Cycle 1	44	0 (0.0) (0.0, 8.0)
		Cycle 2	43	0 (0.0) (0.0, 8.0)
		Cycle 3	42	0 (0.0) (0.0, 8.0)
		Cycle 4	41	1 (2.3) (0.1, 12.0)
		Cycle 5	39	1 (2.3) (0.1, 12.0)
		Cycle 6	39	1 (2.3) (0.1, 12.0)
		Cycle 7	36	0 (0.0) (0.0, 8.0)
		Cycle >= 8 and < 18	35	5 (11.4) (3.8, 24.6)
		Cycle >= 18	19	3 (6.8) (1.4, 18.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	15 (23.8)	(14.0, 36.2)
		Cycle 1	63	0 (0.0)	(0.0, 5.7)
		Cycle 2	61	0 (0.0)	(0.0, 5.7)
		Cycle 3	58	0 (0.0)	(0.0, 5.7)
		Cycle 4	58	1 (1.6)	(0.0, 8.5)
		Cycle 5	55	1 (1.6)	(0.0, 8.5)
		Cycle 6	55	3 (4.8)	(1.0, 13.3)
		Cycle 7	53	1 (1.6)	(0.0, 8.5)
		Cycle >= 8 and < 18	49	7 (11.1)	(4.6, 21.6)
		Cycle >= 18	29	4 (6.3)	(1.8, 15.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Daiichi Sankyo, Inc.
Value Dossier Analysis: DS8201-A-U201
Data Cut Date: 08Jun2020

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Program Name: T3ILD_SSI0.sas
Run Date: 11MAR21:15:37

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	4 (7.5) (2.1, 18.2)
		Cycle 1	53	0 (0.0) (0.0, 6.7)
		Cycle 2	53	0 (0.0) (0.0, 6.7)
		Cycle 3	52	0 (0.0) (0.0, 6.7)
		Cycle 4	49	0 (0.0) (0.0, 6.7)
		Cycle 5	44	0 (0.0) (0.0, 6.7)
		Cycle 6	42	2 (3.8) (0.5, 13.0)
		Cycle 7	40	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	1 (1.9) (0.0, 10.1)
		Cycle >= 18	23	1 (1.9) (0.0, 10.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	9 (13.2) (6.2, 23.6)
		Cycle 1	68	0 (0.0) (0.0, 5.3)
		Cycle 2	67	1 (1.5) (0.0, 7.9)
		Cycle 3	64	1 (1.5) (0.0, 7.9)
		Cycle 4	62	0 (0.0) (0.0, 5.3)
		Cycle 5	56	1 (1.5) (0.0, 7.9)
		Cycle 6	55	0 (0.0) (0.0, 5.3)
		Cycle 7	52	1 (1.5) (0.0, 7.9)
		Cycle >= 8 and < 18	50	5 (7.4) (2.4, 16.3)
		Cycle >= 18	23	1 (1.5) (0.0, 7.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	21 (20.6)	(13.2, 29.7)
		Cycle 1	102	0 (0.0)	(0.0, 3.6)
		Cycle 2	101	1 (1.0)	(0.0, 5.3)
		Cycle 3	100	1 (1.0)	(0.0, 5.3)
		Cycle 4	98	1 (1.0)	(0.0, 5.3)
		Cycle 5	94	2 (2.0)	(0.2, 6.9)
		Cycle 6	93	4 (3.9)	(1.1, 9.7)
		Cycle 7	88	1 (1.0)	(0.0, 5.3)
		Cycle >= 8 and < 18	86	8 (7.8)	(3.4, 14.9)
		Cycle >= 18	49	5 (4.9)	(1.6, 11.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	7 (8.6)	(3.5, 17.0)
		Cycle 1	81	0 (0.0)	(0.0, 4.5)
		Cycle 2	79	0 (0.0)	(0.0, 4.5)
		Cycle 3	73	0 (0.0)	(0.0, 4.5)
		Cycle 4	71	0 (0.0)	(0.0, 4.5)
		Cycle 5	61	0 (0.0)	(0.0, 4.5)
		Cycle 6	59	1 (1.2)	(0.0, 6.7)
		Cycle 7	57	1 (1.2)	(0.0, 6.7)
		Cycle >= 8 and < 18	52	5 (6.2)	(2.0, 13.8)
		Cycle >= 18	26	1 (1.2)	(0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
D-Baseline sum of diameters of target lesions	< 5 cm (N=73)	Any TEAE	73	15 (20.5)	(12.0, 31.6)
		Cycle 1	73	0 (0.0)	(0.0, 4.9)
		Cycle 2	72	1 (1.4)	(0.0, 7.4)
		Cycle 3	70	1 (1.4)	(0.0, 7.4)
		Cycle 4	65	0 (0.0)	(0.0, 4.9)
		Cycle 5	60	1 (1.4)	(0.0, 7.4)
		Cycle 6	59	1 (1.4)	(0.0, 7.4)
		Cycle 7	58	2 (2.7)	(0.3, 9.5)
		Cycle >= 8 and < 18	53	7 (9.6)	(3.9, 18.8)
		Cycle >= 18	33	4 (5.5)	(1.5, 13.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=97)	Any TEAE	97	8 (8.2) (3.6, 15.6)
		Cycle 1	97	0 (0.0) (0.0, 3.7)
		Cycle 2	95	0 (0.0) (0.0, 3.7)
		Cycle 3	90	0 (0.0) (0.0, 3.7)
		Cycle 4	90	1 (1.0) (0.0, 5.6)
		Cycle 5	81	0 (0.0) (0.0, 3.7)
		Cycle 6	79	3 (3.1) (0.6, 8.8)
		Cycle 7	74	0 (0.0) (0.0, 3.7)
		Cycle >= 8 and < 18	72	3 (3.1) (0.6, 8.8)
		Cycle >= 18	34	1 (1.0) (0.0, 5.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	25 (16.2)	(10.8, 23.0)
		Cycle 1	154	0 (0.0)	(0.0, 2.4)
		Cycle 2	152	1 (0.6)	(0.0, 3.6)
		Cycle 3	146	1 (0.6)	(0.0, 3.6)
		Cycle 4	141	1 (0.6)	(0.0, 3.6)
		Cycle 5	129	2 (1.3)	(0.2, 4.6)
		Cycle 6	127	4 (2.6)	(0.7, 6.5)
		Cycle 7	121	2 (1.3)	(0.2, 4.6)
		Cycle >= 8 and < 18	114	12 (7.8)	(4.1, 13.2)
		Cycle >= 18	69	5 (3.2)	(1.1, 7.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Any TEAE	28	3 (10.7) (2.3, 28.2)
		Cycle 1	28	0 (0.0) (0.0, 12.3)
		Cycle 2	27	0 (0.0) (0.0, 12.3)
		Cycle 3	26	0 (0.0) (0.0, 12.3)
		Cycle 4	26	0 (0.0) (0.0, 12.3)
		Cycle 5	24	0 (0.0) (0.0, 12.3)
		Cycle 6	23	1 (3.6) (0.1, 18.3)
		Cycle 7	22	0 (0.0) (0.0, 12.3)
		Cycle >= 8 and < 18	22	1 (3.6) (0.1, 18.3)
		Cycle >= 18	5	1 (3.6) (0.1, 18.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	15 (16.1)	(9.3, 25.2)
		Cycle 1	93	0 (0.0)	(0.0, 3.9)
		Cycle 2	92	0 (0.0)	(0.0, 3.9)
		Cycle 3	87	0 (0.0)	(0.0, 3.9)
		Cycle 4	84	0 (0.0)	(0.0, 3.9)
		Cycle 5	80	2 (2.2)	(0.3, 7.6)
		Cycle 6	78	2 (2.2)	(0.3, 7.6)
		Cycle 7	75	0 (0.0)	(0.0, 3.9)
		Cycle >= 8 and < 18	73	8 (8.6)	(3.8, 16.2)
		Cycle >= 18	34	4 (4.3)	(1.2, 10.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	13 (14.8)	(8.1, 23.9)
		Cycle 1	88	0 (0.0)	(0.0, 4.1)
		Cycle 2	86	1 (1.1)	(0.0, 6.2)
		Cycle 3	85	1 (1.1)	(0.0, 6.2)
		Cycle 4	84	1 (1.1)	(0.0, 6.2)
		Cycle 5	74	0 (0.0)	(0.0, 4.1)
		Cycle 6	73	3 (3.4)	(0.7, 9.6)
		Cycle 7	69	2 (2.3)	(0.3, 8.0)
		Cycle >= 8 and < 18	64	5 (5.7)	(1.9, 12.8)
		Cycle >= 18	41	2 (2.3)	(0.3, 8.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	10 (19.6)	(9.8, 33.1)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	49	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	47	2 (3.9)	(0.5, 13.5)
		Cycle 6	46	1 (2.0)	(0.0, 10.4)
		Cycle 7	45	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	44	4 (7.8)	(2.2, 18.9)
		Cycle >= 18	21	4 (7.8)	(2.2, 18.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	18 (14.4)	(8.8, 21.8)
		Cycle 1	125	0 (0.0)	(0.0, 2.9)
		Cycle 2	123	1 (0.8)	(0.0, 4.4)
		Cycle 3	118	1 (0.8)	(0.0, 4.4)
		Cycle 4	114	1 (0.8)	(0.0, 4.4)
		Cycle 5	103	0 (0.0)	(0.0, 2.9)
		Cycle 6	101	4 (3.2)	(0.9, 8.0)
		Cycle 7	95	2 (1.6)	(0.2, 5.7)
		Cycle >= 8 and < 18	90	9 (7.2)	(3.3, 13.2)
		Cycle >= 18	52	2 (1.6)	(0.2, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	16 (16.5)	(9.7, 25.4)
		Cycle 1	97	0 (0.0)	(0.0, 3.7)
		Cycle 2	96	0 (0.0)	(0.0, 3.7)
		Cycle 3	91	0 (0.0)	(0.0, 3.7)
		Cycle 4	88	0 (0.0)	(0.0, 3.7)
		Cycle 5	84	2 (2.1)	(0.3, 7.3)
		Cycle 6	82	2 (2.1)	(0.3, 7.3)
		Cycle 7	79	0 (0.0)	(0.0, 3.7)
		Cycle >= 8 and < 18	76	8 (8.2)	(3.6, 15.6)
		Cycle >= 18	36	5 (5.2)	(1.7, 11.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	12 (14.5)	(7.7, 23.9)
		Cycle 1	83	0 (0.0)	(0.0, 4.3)
		Cycle 2	81	1 (1.2)	(0.0, 6.5)
		Cycle 3	80	1 (1.2)	(0.0, 6.5)
		Cycle 4	79	1 (1.2)	(0.0, 6.5)
		Cycle 5	69	0 (0.0)	(0.0, 4.3)
		Cycle 6	68	3 (3.6)	(0.8, 10.2)
		Cycle 7	64	2 (2.4)	(0.3, 8.4)
		Cycle >= 8 and < 18	60	5 (6.0)	(2.0, 13.5)
		Cycle >= 18	38	1 (1.2)	(0.0, 6.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
I-Renal impairment	Normal (N=90)	Any TEAE	90	10 (11.1)	(5.5, 19.5)
		Cycle 1	90	0 (0.0)	(0.0, 4.0)
		Cycle 2	89	0 (0.0)	(0.0, 4.0)
		Cycle 3	85	0 (0.0)	(0.0, 4.0)
		Cycle 4	85	0 (0.0)	(0.0, 4.0)
		Cycle 5	76	1 (1.1)	(0.0, 6.0)
		Cycle 6	73	0 (0.0)	(0.0, 4.0)
		Cycle 7	72	1 (1.1)	(0.0, 6.0)
		Cycle >= 8 and < 18	69	5 (5.6)	(1.8, 12.5)
		Cycle >= 18	41	3 (3.3)	(0.7, 9.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	9 (13.0)	(6.1, 23.3)
		Cycle 1	69	0 (0.0)	(0.0, 5.2)
		Cycle 2	68	0 (0.0)	(0.0, 5.2)
		Cycle 3	66	0 (0.0)	(0.0, 5.2)
		Cycle 4	63	0 (0.0)	(0.0, 5.2)
		Cycle 5	59	1 (1.4)	(0.0, 7.8)
		Cycle 6	59	2 (2.9)	(0.4, 10.1)
		Cycle 7	56	0 (0.0)	(0.0, 5.2)
		Cycle >= 8 and < 18	54	6 (8.7)	(3.3, 18.0)
		Cycle >= 18	27	1 (1.4)	(0.0, 7.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	9 (36.0)	(18.0, 57.5)
		Cycle 1	25	0 (0.0)	(0.0, 13.7)
		Cycle 2	24	1 (4.0)	(0.1, 20.4)
		Cycle 3	23	1 (4.0)	(0.1, 20.4)
		Cycle 4	21	1 (4.0)	(0.1, 20.4)
		Cycle 5	20	0 (0.0)	(0.0, 13.7)
		Cycle 6	20	3 (12.0)	(2.5, 31.2)
		Cycle 7	17	1 (4.0)	(0.1, 20.4)
		Cycle >= 8 and < 18	15	2 (8.0)	(1.0, 26.0)
		Cycle >= 18	7	2 (8.0)	(1.0, 26.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	21 (20.0)	(12.8, 28.9)
		Cycle 1	105	0 (0.0)	(0.0, 3.5)
		Cycle 2	104	1 (1.0)	(0.0, 5.2)
		Cycle 3	102	1 (1.0)	(0.0, 5.2)
		Cycle 4	98	1 (1.0)	(0.0, 5.2)
		Cycle 5	90	2 (1.9)	(0.2, 6.7)
		Cycle 6	89	2 (1.9)	(0.2, 6.7)
		Cycle 7	87	1 (1.0)	(0.0, 5.2)
		Cycle >= 8 and < 18	84	10 (9.5)	(4.7, 16.8)
		Cycle >= 18	44	5 (4.8)	(1.6, 10.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	7 (9.2)	(3.8, 18.1)
		Cycle 1	76	0 (0.0)	(0.0, 4.7)
		Cycle 2	74	0 (0.0)	(0.0, 4.7)
		Cycle 3	69	0 (0.0)	(0.0, 4.7)
		Cycle 4	68	0 (0.0)	(0.0, 4.7)
		Cycle 5	63	0 (0.0)	(0.0, 4.7)
		Cycle 6	61	3 (3.9)	(0.8, 11.1)
		Cycle 7	56	1 (1.3)	(0.0, 7.1)
		Cycle >= 8 and < 18	54	3 (3.9)	(0.8, 11.1)
		Cycle >= 18	31	1 (1.3)	(0.0, 7.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	6 (25.0)	(9.8, 46.7)
		Cycle 1	24	0 (0.0)	(0.0, 14.2)
		Cycle 2	23	0 (0.0)	(0.0, 14.2)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	1 (4.2)	(0.1, 21.1)
		Cycle 6	18	1 (4.2)	(0.1, 21.1)
		Cycle 7	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 8 and < 18	18	3 (12.5)	(2.7, 32.4)
		Cycle >= 18	10	1 (4.2)	(0.1, 21.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	22 (13.8)	(8.8, 20.1)
		Cycle 1	160	0 (0.0)	(0.0, 2.3)
		Cycle 2	158	1 (0.6)	(0.0, 3.4)
		Cycle 3	152	1 (0.6)	(0.0, 3.4)
		Cycle 4	147	1 (0.6)	(0.0, 3.4)
		Cycle 5	136	1 (0.6)	(0.0, 3.4)
		Cycle 6	134	4 (2.5)	(0.7, 6.3)
		Cycle 7	127	2 (1.3)	(0.2, 4.4)
		Cycle >= 8 and < 18	120	10 (6.3)	(3.0, 11.2)
		Cycle >= 18	65	5 (3.1)	(1.0, 7.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	11 (20.8)	(10.8, 34.1)
		Cycle 1	53	0 (0.0)	(0.0, 6.7)
		Cycle 2	52	1 (1.9)	(0.0, 10.1)
		Cycle 3	49	1 (1.9)	(0.0, 10.1)
		Cycle 4	48	0 (0.0)	(0.0, 6.7)
		Cycle 5	43	1 (1.9)	(0.0, 10.1)
		Cycle 6	42	2 (3.8)	(0.5, 13.0)
		Cycle 7	41	1 (1.9)	(0.0, 10.1)
		Cycle >= 8 and < 18	39	6 (11.3)	(4.3, 23.0)
		Cycle >= 18	18	1 (1.9)	(0.0, 10.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	17 (13.0)	(7.7, 20.0)
		Cycle 1	131	0 (0.0)	(0.0, 2.8)
		Cycle 2	129	0 (0.0)	(0.0, 2.8)
		Cycle 3	125	0 (0.0)	(0.0, 2.8)
		Cycle 4	121	1 (0.8)	(0.0, 4.2)
		Cycle 5	112	1 (0.8)	(0.0, 4.2)
		Cycle 6	110	3 (2.3)	(0.5, 6.5)
		Cycle 7	104	1 (0.8)	(0.0, 4.2)
		Cycle >= 8 and < 18	99	7 (5.3)	(2.2, 10.7)
		Cycle >= 18	57	5 (3.8)	(1.3, 8.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	25 (14.8)	(9.8, 21.1)
		Cycle 1	169	0 (0.0)	(0.0, 2.2)
		Cycle 2	166	1 (0.6)	(0.0, 3.3)
		Cycle 3	159	1 (0.6)	(0.0, 3.3)
		Cycle 4	154	1 (0.6)	(0.0, 3.3)
		Cycle 5	142	2 (1.2)	(0.1, 4.2)
		Cycle 6	139	5 (3.0)	(1.0, 6.8)
		Cycle 7	132	2 (1.2)	(0.1, 4.2)
		Cycle >= 8 and < 18	125	11 (6.5)	(3.3, 11.3)
		Cycle >= 18	70	5 (3.0)	(1.0, 6.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	3 (20.0)	(4.3, 48.1)
		Cycle 1	15	0 (0.0)	(0.0, 21.8)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	2 (13.3)	(1.7, 40.5)
		Cycle >= 18	5	1 (6.7)	(0.2, 31.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	6 (10.7)	(4.0, 21.9)
		Cycle 1	56	0 (0.0)	(0.0, 6.4)
		Cycle 2	55	0 (0.0)	(0.0, 6.4)
		Cycle 3	54	0 (0.0)	(0.0, 6.4)
		Cycle 4	53	0 (0.0)	(0.0, 6.4)
		Cycle 5	49	0 (0.0)	(0.0, 6.4)
		Cycle 6	48	1 (1.8)	(0.0, 9.6)
		Cycle 7	48	1 (1.8)	(0.0, 9.6)
		Cycle >= 8 and < 18	45	3 (5.4)	(1.1, 14.9)
		Cycle >= 18	32	2 (3.6)	(0.4, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	22 (17.2)	(11.1, 24.9)
		Cycle 1	128	0 (0.0)	(0.0, 2.8)
		Cycle 2	126	1 (0.8)	(0.0, 4.3)
		Cycle 3	120	1 (0.8)	(0.0, 4.3)
		Cycle 4	116	1 (0.8)	(0.0, 4.3)
		Cycle 5	106	2 (1.6)	(0.2, 5.5)
		Cycle 6	104	4 (3.1)	(0.9, 7.8)
		Cycle 7	97	1 (0.8)	(0.0, 4.3)
		Cycle >= 8 and < 18	93	10 (7.8)	(3.8, 13.9)
		Cycle >= 18	43	4 (3.1)	(0.9, 7.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	< 3 lines (N=17)			
	Any TEAE	17	2 (11.8)	(1.5, 36.4)
	Cycle 1	17	0 (0.0)	(0.0, 19.5)
	Cycle 2	17	0 (0.0)	(0.0, 19.5)
	Cycle 3	17	0 (0.0)	(0.0, 19.5)
	Cycle 4	17	0 (0.0)	(0.0, 19.5)
	Cycle 5	17	0 (0.0)	(0.0, 19.5)
	Cycle 6	16	0 (0.0)	(0.0, 19.5)
	Cycle 7	16	0 (0.0)	(0.0, 19.5)
	Cycle >= 8 and < 18	16	0 (0.0)	(0.0, 19.5)
	Cycle >= 18	14	2 (11.8)	(1.5, 36.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	>= 3 lines (N=167)			
	Any TEAE	167	26 (15.6)	(10.4, 22.0)
	Cycle 1	167	0 (0.0)	(0.0, 2.2)
	Cycle 2	164	1 (0.6)	(0.0, 3.3)
	Cycle 3	157	1 (0.6)	(0.0, 3.3)
	Cycle 4	152	1 (0.6)	(0.0, 3.3)
	Cycle 5	138	2 (1.2)	(0.1, 4.3)
	Cycle 6	136	5 (3.0)	(1.0, 6.8)
	Cycle 7	129	2 (1.2)	(0.1, 4.3)
	Cycle >= 8 and < 18	122	13 (7.8)	(4.2, 12.9)
	Cycle >= 18	61	4 (2.4)	(0.7, 6.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	12 (15.2)	(8.1, 25.0)
		Cycle 1	79	0 (0.0)	(0.0, 4.6)
		Cycle 2	78	1 (1.3)	(0.0, 6.9)
		Cycle 3	75	1 (1.3)	(0.0, 6.9)
		Cycle 4	73	0 (0.0)	(0.0, 4.6)
		Cycle 5	70	1 (1.3)	(0.0, 6.9)
		Cycle 6	69	1 (1.3)	(0.0, 6.9)
		Cycle 7	68	0 (0.0)	(0.0, 4.6)
		Cycle >= 8 and < 18	65	5 (6.3)	(2.1, 14.2)
		Cycle >= 18	37	5 (6.3)	(2.1, 14.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	12 (18.2)	(9.8, 29.6)
		Cycle 1	66	0 (0.0)	(0.0, 5.4)
		Cycle 2	66	0 (0.0)	(0.0, 5.4)
		Cycle 3	64	0 (0.0)	(0.0, 5.4)
		Cycle 4	61	1 (1.5)	(0.0, 8.2)
		Cycle 5	55	1 (1.5)	(0.0, 8.2)
		Cycle 6	53	1 (1.5)	(0.0, 8.2)
		Cycle 7	51	0 (0.0)	(0.0, 5.4)
		Cycle >= 8 and < 18	51	8 (12.1)	(5.4, 22.5)
		Cycle >= 18	23	1 (1.5)	(0.0, 8.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	20 (16.5)	(10.4, 24.4)
		Cycle 1	121	0 (0.0)	(0.0, 3.0)
		Cycle 2	120	1 (0.8)	(0.0, 4.5)
		Cycle 3	119	1 (0.8)	(0.0, 4.5)
		Cycle 4	115	1 (0.8)	(0.0, 4.5)
		Cycle 5	106	2 (1.7)	(0.2, 5.8)
		Cycle 6	103	5 (4.1)	(1.4, 9.4)
		Cycle 7	96	1 (0.8)	(0.0, 4.5)
		Cycle >= 8 and < 18	93	7 (5.8)	(2.4, 11.6)
		Cycle >= 18	54	5 (4.1)	(1.4, 9.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	8 (12.7)	(5.6, 23.5)
		Cycle 1	63	0 (0.0)	(0.0, 5.7)
		Cycle 2	61	0 (0.0)	(0.0, 5.7)
		Cycle 3	55	0 (0.0)	(0.0, 5.7)
		Cycle 4	54	0 (0.0)	(0.0, 5.7)
		Cycle 5	49	0 (0.0)	(0.0, 5.7)
		Cycle 6	49	0 (0.0)	(0.0, 5.7)
		Cycle 7	49	1 (1.6)	(0.0, 8.5)
		Cycle >= 8 and < 18	45	6 (9.5)	(3.6, 19.6)
		Cycle >= 18	21	1 (1.6)	(0.0, 8.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	7 (13.7)	(5.7, 26.3)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	50	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	46	1 (2.0)	(0.0, 10.4)
		Cycle 6	44	1 (2.0)	(0.0, 10.4)
		Cycle 7	40	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	40	3 (5.9)	(1.2, 16.2)
		Cycle >= 18	24	2 (3.9)	(0.5, 13.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILD_SSI0: Incidence of interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	21 (15.8)	(10.0, 23.1)
		Cycle 1	133	0 (0.0)	(0.0, 2.7)
		Cycle 2	131	1 (0.8)	(0.0, 4.1)
		Cycle 3	124	1 (0.8)	(0.0, 4.1)
		Cycle 4	120	1 (0.8)	(0.0, 4.1)
		Cycle 5	109	1 (0.8)	(0.0, 4.1)
		Cycle 6	108	4 (3.0)	(0.8, 7.5)
		Cycle 7	105	2 (1.5)	(0.2, 5.3)
		Cycle >= 8 and < 18	98	10 (7.5)	(3.7, 13.4)
		Cycle >= 18	51	4 (3.0)	(0.8, 7.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

UE von besonderem Interesse – Interstitielle Lungenerkrankung (ILD) mit CTCAE-Grad < 3

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	23 (12.5)	(8.1, 18.2)
		Cycle 1	184	0 (0.0)	(0.0, 2.0)
		Cycle 2	181	1 (0.5)	(0.0, 3.0)
		Cycle 3	174	1 (0.5)	(0.0, 3.0)
		Cycle 4	169	1 (0.5)	(0.0, 3.0)
		Cycle 5	155	2 (1.1)	(0.1, 3.9)
		Cycle 6	152	5 (2.7)	(0.9, 6.2)
		Cycle 7	145	1 (0.5)	(0.0, 3.0)
		Cycle >= 8 and < 18	138	11 (6.0)	(3.0, 10.4)
		Cycle >= 18	75	4 (2.2)	(0.6, 5.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	15 (10.7)	(6.1, 17.1)
		Cycle 1	0 (0.0)	(0.0, 2.6)
		Cycle 2	1 (0.7)	(0.0, 3.9)
		Cycle 3	1 (0.7)	(0.0, 3.9)
		Cycle 4	0 (0.0)	(0.0, 2.6)
		Cycle 5	1 (0.7)	(0.0, 3.9)
		Cycle 6	4 (2.9)	(0.8, 7.2)
		Cycle 7	1 (0.7)	(0.0, 3.9)
		Cycle >= 8 and < 18	7 (5.0)	(2.0, 10.0)
		Cycle >= 18	56	2 (1.4) (0.2, 5.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	8 (18.2) (8.2, 32.7)
		Cycle 1	44	0 (0.0) (0.0, 8.0)
		Cycle 2	43	0 (0.0) (0.0, 8.0)
		Cycle 3	42	0 (0.0) (0.0, 8.0)
		Cycle 4	41	1 (2.3) (0.1, 12.0)
		Cycle 5	39	1 (2.3) (0.1, 12.0)
		Cycle 6	39	1 (2.3) (0.1, 12.0)
		Cycle 7	36	0 (0.0) (0.0, 8.0)
		Cycle >= 8 and < 18	35	4 (9.1) (2.5, 21.7)
		Cycle >= 18	19	2 (4.5) (0.6, 15.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	15 (23.8) (14.0, 36.2)
		Cycle 1	63	0 (0.0) (0.0, 5.7)
		Cycle 2	61	0 (0.0) (0.0, 5.7)
		Cycle 3	58	0 (0.0) (0.0, 5.7)
		Cycle 4	58	1 (1.6) (0.0, 8.5)
		Cycle 5	55	1 (1.6) (0.0, 8.5)
		Cycle 6	55	3 (4.8) (1.0, 13.3)
		Cycle 7	53	1 (1.6) (0.0, 8.5)
		Cycle >= 8 and < 18	49	7 (11.1) (4.6, 21.6)
		Cycle >= 18	29	4 (6.3) (1.8, 15.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	3 (5.7) (1.2, 15.7)
		Cycle 1	53	0 (0.0) (0.0, 6.7)
		Cycle 2	53	0 (0.0) (0.0, 6.7)
		Cycle 3	52	0 (0.0) (0.0, 6.7)
		Cycle 4	49	0 (0.0) (0.0, 6.7)
		Cycle 5	44	0 (0.0) (0.0, 6.7)
		Cycle 6	42	2 (3.8) (0.5, 13.0)
		Cycle 7	40	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	1 (1.9) (0.0, 10.1)
		Cycle >= 18	23	0 (0.0) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	5 (7.4) (2.4, 16.3)
		Cycle 1	68	0 (0.0) (0.0, 5.3)
		Cycle 2	67	1 (1.5) (0.0, 7.9)
		Cycle 3	64	1 (1.5) (0.0, 7.9)
		Cycle 4	62	0 (0.0) (0.0, 5.3)
		Cycle 5	56	1 (1.5) (0.0, 7.9)
		Cycle 6	55	0 (0.0) (0.0, 5.3)
		Cycle 7	52	0 (0.0) (0.0, 5.3)
		Cycle >= 8 and < 18	50	3 (4.4) (0.9, 12.4)
		Cycle >= 18	23	0 (0.0) (0.0, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	17 (16.7)	(10.0, 25.3)
		Cycle 1	102	0 (0.0)	(0.0, 3.6)
		Cycle 2	101	1 (1.0)	(0.0, 5.3)
		Cycle 3	100	1 (1.0)	(0.0, 5.3)
		Cycle 4	98	1 (1.0)	(0.0, 5.3)
		Cycle 5	94	2 (2.0)	(0.2, 6.9)
		Cycle 6	93	4 (3.9)	(1.1, 9.7)
		Cycle 7	88	0 (0.0)	(0.0, 3.6)
		Cycle >= 8 and < 18	86	7 (6.9)	(2.8, 13.6)
		Cycle >= 18	49	3 (2.9)	(0.6, 8.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	6 (7.4) (2.8, 15.4)
		Cycle 1	81	0 (0.0) (0.0, 4.5)
		Cycle 2	79	0 (0.0) (0.0, 4.5)
		Cycle 3	73	0 (0.0) (0.0, 4.5)
		Cycle 4	71	0 (0.0) (0.0, 4.5)
		Cycle 5	61	0 (0.0) (0.0, 4.5)
		Cycle 6	59	1 (1.2) (0.0, 6.7)
		Cycle 7	57	1 (1.2) (0.0, 6.7)
		Cycle >= 8 and < 18	52	4 (4.9) (1.4, 12.2)
		Cycle >= 18	26	1 (1.2) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
D-Baseline sum of diameters of target lesions < 5 cm (N=73)	Any TEAE	73	11 (15.1)	(7.8, 25.4)
	Cycle 1	73	0 (0.0)	(0.0, 4.9)
	Cycle 2	72	1 (1.4)	(0.0, 7.4)
	Cycle 3	70	1 (1.4)	(0.0, 7.4)
	Cycle 4	65	0 (0.0)	(0.0, 4.9)
	Cycle 5	60	1 (1.4)	(0.0, 7.4)
	Cycle 6	59	1 (1.4)	(0.0, 7.4)
	Cycle 7	58	1 (1.4)	(0.0, 7.4)
	Cycle >= 8 and < 18	53	6 (8.2)	(3.1, 17.0)
	Cycle >= 18	33	2 (2.7)	(0.3, 9.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=97)			
	Any TEAE	97	8 (8.2)	(3.6, 15.6)
	Cycle 1	97	0 (0.0)	(0.0, 3.7)
	Cycle 2	95	0 (0.0)	(0.0, 3.7)
	Cycle 3	90	0 (0.0)	(0.0, 3.7)
	Cycle 4	90	1 (1.0)	(0.0, 5.6)
	Cycle 5	81	0 (0.0)	(0.0, 3.7)
	Cycle 6	79	3 (3.1)	(0.6, 8.8)
	Cycle 7	74	0 (0.0)	(0.0, 3.7)
	Cycle >= 8 and < 18	72	3 (3.1)	(0.6, 8.8)
	Cycle >= 18	34	1 (1.0)	(0.0, 5.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	21 (13.6)	(8.6, 20.1)
		Cycle 1	154	0 (0.0)	(0.0, 2.4)
		Cycle 2	152	1 (0.6)	(0.0, 3.6)
		Cycle 3	146	1 (0.6)	(0.0, 3.6)
		Cycle 4	141	1 (0.6)	(0.0, 3.6)
		Cycle 5	129	2 (1.3)	(0.2, 4.6)
		Cycle 6	127	4 (2.6)	(0.7, 6.5)
		Cycle 7	121	1 (0.6)	(0.0, 3.6)
		Cycle >= 8 and < 18	114	10 (6.5)	(3.2, 11.6)
		Cycle >= 18	69	4 (2.6)	(0.7, 6.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHCR3+ (N=28)			
	Any TEAE	28	2 (7.1)	(0.9, 23.5)
	Cycle 1	28	0 (0.0)	(0.0, 12.3)
	Cycle 2	27	0 (0.0)	(0.0, 12.3)
	Cycle 3	26	0 (0.0)	(0.0, 12.3)
	Cycle 4	26	0 (0.0)	(0.0, 12.3)
	Cycle 5	24	0 (0.0)	(0.0, 12.3)
	Cycle 6	23	1 (3.6)	(0.1, 18.3)
	Cycle 7	22	0 (0.0)	(0.0, 12.3)
	Cycle >= 8 and < 18	22	1 (3.6)	(0.1, 18.3)
	Cycle >= 18	5	0 (0.0)	(0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	12 (12.9)	(6.8, 21.5)
		Cycle 1	93	0 (0.0)	(0.0, 3.9)
		Cycle 2	92	0 (0.0)	(0.0, 3.9)
		Cycle 3	87	0 (0.0)	(0.0, 3.9)
		Cycle 4	84	0 (0.0)	(0.0, 3.9)
		Cycle 5	80	2 (2.2)	(0.3, 7.6)
		Cycle 6	78	2 (2.2)	(0.3, 7.6)
		Cycle 7	75	0 (0.0)	(0.0, 3.9)
		Cycle >= 8 and < 18	73	6 (6.5)	(2.4, 13.5)
		Cycle >= 18	34	3 (3.2)	(0.7, 9.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	11 (12.5)	(6.4, 21.3)
		Cycle 1	88	0 (0.0)	(0.0, 4.1)
		Cycle 2	86	1 (1.1)	(0.0, 6.2)
		Cycle 3	85	1 (1.1)	(0.0, 6.2)
		Cycle 4	84	1 (1.1)	(0.0, 6.2)
		Cycle 5	74	0 (0.0)	(0.0, 4.1)
		Cycle 6	73	3 (3.4)	(0.7, 9.6)
		Cycle 7	69	1 (1.1)	(0.0, 6.2)
		Cycle >= 8 and < 18	64	5 (5.7)	(1.9, 12.8)
		Cycle >= 18	41	1 (1.1)	(0.0, 6.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	9 (17.6)	(8.4, 30.9)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	49	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	47	2 (3.9)	(0.5, 13.5)
		Cycle 6	46	1 (2.0)	(0.0, 10.4)
		Cycle 7	45	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	44	4 (7.8)	(2.2, 18.9)
		Cycle >= 18	21	3 (5.9)	(1.2, 16.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	14 (11.2)	(6.3, 18.1)
		Cycle 1	125	0 (0.0)	(0.0, 2.9)
		Cycle 2	123	1 (0.8)	(0.0, 4.4)
		Cycle 3	118	1 (0.8)	(0.0, 4.4)
		Cycle 4	114	1 (0.8)	(0.0, 4.4)
		Cycle 5	103	0 (0.0)	(0.0, 2.9)
		Cycle 6	101	4 (3.2)	(0.9, 8.0)
		Cycle 7	95	1 (0.8)	(0.0, 4.4)
		Cycle >= 8 and < 18	90	7 (5.6)	(2.3, 11.2)
		Cycle >= 18	52	1 (0.8)	(0.0, 4.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	13 (13.4)	(7.3, 21.8)
		Cycle 1	97	0 (0.0)	(0.0, 3.7)
		Cycle 2	96	0 (0.0)	(0.0, 3.7)
		Cycle 3	91	0 (0.0)	(0.0, 3.7)
		Cycle 4	88	0 (0.0)	(0.0, 3.7)
		Cycle 5	84	2 (2.1)	(0.3, 7.3)
		Cycle 6	82	2 (2.1)	(0.3, 7.3)
		Cycle 7	79	0 (0.0)	(0.0, 3.7)
		Cycle >= 8 and < 18	76	6 (6.2)	(2.3, 13.0)
		Cycle >= 18	36	4 (4.1)	(1.1, 10.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	10 (12.0)	(5.9, 21.0)
		Cycle 1	83	0 (0.0)	(0.0, 4.3)
		Cycle 2	81	1 (1.2)	(0.0, 6.5)
		Cycle 3	80	1 (1.2)	(0.0, 6.5)
		Cycle 4	79	1 (1.2)	(0.0, 6.5)
		Cycle 5	69	0 (0.0)	(0.0, 4.3)
		Cycle 6	68	3 (3.6)	(0.8, 10.2)
		Cycle 7	64	1 (1.2)	(0.0, 6.5)
		Cycle >= 8 and < 18	60	5 (6.0)	(2.0, 13.5)
		Cycle >= 18	38	0 (0.0)	(0.0, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Normal (N=90)			
	Any TEAE	90	6 (6.7)	(2.5, 13.9)
	Cycle 1	90	0 (0.0)	(0.0, 4.0)
	Cycle 2	89	0 (0.0)	(0.0, 4.0)
	Cycle 3	85	0 (0.0)	(0.0, 4.0)
	Cycle 4	85	0 (0.0)	(0.0, 4.0)
	Cycle 5	76	1 (1.1)	(0.0, 6.0)
	Cycle 6	73	0 (0.0)	(0.0, 4.0)
	Cycle 7	72	0 (0.0)	(0.0, 4.0)
	Cycle >= 8 and < 18	69	3 (3.3)	(0.7, 9.4)
	Cycle >= 18	41	2 (2.2)	(0.3, 7.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	9 (13.0)	(6.1, 23.3)
		Cycle 1	69	0 (0.0)	(0.0, 5.2)
		Cycle 2	68	0 (0.0)	(0.0, 5.2)
		Cycle 3	66	0 (0.0)	(0.0, 5.2)
		Cycle 4	63	0 (0.0)	(0.0, 5.2)
		Cycle 5	59	1 (1.4)	(0.0, 7.8)
		Cycle 6	59	2 (2.9)	(0.4, 10.1)
		Cycle 7	56	0 (0.0)	(0.0, 5.2)
		Cycle >= 8 and < 18	54	6 (8.7)	(3.3, 18.0)
		Cycle >= 18	27	1 (1.4)	(0.0, 7.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	8 (32.0)	(14.9, 53.5)
		Cycle 1	25	0 (0.0)	(0.0, 13.7)
		Cycle 2	24	1 (4.0)	(0.1, 20.4)
		Cycle 3	23	1 (4.0)	(0.1, 20.4)
		Cycle 4	21	1 (4.0)	(0.1, 20.4)
		Cycle 5	20	0 (0.0)	(0.0, 13.7)
		Cycle 6	20	3 (12.0)	(2.5, 31.2)
		Cycle 7	17	1 (4.0)	(0.1, 20.4)
		Cycle >= 8 and < 18	15	2 (8.0)	(1.0, 26.0)
		Cycle >= 18	7	1 (4.0)	(0.1, 20.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	16 (15.2)	(9.0, 23.6)
		Cycle 1	105	0 (0.0)	(0.0, 3.5)
		Cycle 2	104	1 (1.0)	(0.0, 5.2)
		Cycle 3	102	1 (1.0)	(0.0, 5.2)
		Cycle 4	98	1 (1.0)	(0.0, 5.2)
		Cycle 5	90	2 (1.9)	(0.2, 6.7)
		Cycle 6	89	2 (1.9)	(0.2, 6.7)
		Cycle 7	87	0 (0.0)	(0.0, 3.5)
		Cycle >= 8 and < 18	84	8 (7.6)	(3.3, 14.5)
		Cycle >= 18	44	3 (2.9)	(0.6, 8.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	7 (9.2) (3.8, 18.1)
		Cycle 1	76	0 (0.0) (0.0, 4.7)
		Cycle 2	74	0 (0.0) (0.0, 4.7)
		Cycle 3	69	0 (0.0) (0.0, 4.7)
		Cycle 4	68	0 (0.0) (0.0, 4.7)
		Cycle 5	63	0 (0.0) (0.0, 4.7)
		Cycle 6	61	3 (3.9) (0.8, 11.1)
		Cycle 7	56	1 (1.3) (0.0, 7.1)
		Cycle >= 8 and < 18	54	3 (3.9) (0.8, 11.1)
		Cycle >= 18	31	1 (1.3) (0.0, 7.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	6 (25.0)	(9.8, 46.7)
		Cycle 1	24	0 (0.0)	(0.0, 14.2)
		Cycle 2	23	0 (0.0)	(0.0, 14.2)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	1 (4.2)	(0.1, 21.1)
		Cycle 6	18	1 (4.2)	(0.1, 21.1)
		Cycle 7	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 8 and < 18	18	3 (12.5)	(2.7, 32.4)
		Cycle >= 18	10	1 (4.2)	(0.1, 21.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	17 (10.6)	(6.3, 16.5)
		Cycle 1	160	0 (0.0)	(0.0, 2.3)
		Cycle 2	158	1 (0.6)	(0.0, 3.4)
		Cycle 3	152	1 (0.6)	(0.0, 3.4)
		Cycle 4	147	1 (0.6)	(0.0, 3.4)
		Cycle 5	136	1 (0.6)	(0.0, 3.4)
		Cycle 6	134	4 (2.5)	(0.7, 6.3)
		Cycle 7	127	1 (0.6)	(0.0, 3.4)
		Cycle >= 8 and < 18	120	8 (5.0)	(2.2, 9.6)
		Cycle >= 18	65	3 (1.9)	(0.4, 5.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	9 (17.0)	(8.1, 29.8)
		Cycle 1	53	0 (0.0)	(0.0, 6.7)
		Cycle 2	52	1 (1.9)	(0.0, 10.1)
		Cycle 3	49	1 (1.9)	(0.0, 10.1)
		Cycle 4	48	0 (0.0)	(0.0, 6.7)
		Cycle 5	43	1 (1.9)	(0.0, 10.1)
		Cycle 6	42	2 (3.8)	(0.5, 13.0)
		Cycle 7	41	1 (1.9)	(0.0, 10.1)
		Cycle >= 8 and < 18	39	4 (7.5)	(2.1, 18.2)
		Cycle >= 18	18	1 (1.9)	(0.0, 10.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	14 (10.7)	(6.0, 17.3)
		Cycle 1	131	0 (0.0)	(0.0, 2.8)
		Cycle 2	129	0 (0.0)	(0.0, 2.8)
		Cycle 3	125	0 (0.0)	(0.0, 2.8)
		Cycle 4	121	1 (0.8)	(0.0, 4.2)
		Cycle 5	112	1 (0.8)	(0.0, 4.2)
		Cycle 6	110	3 (2.3)	(0.5, 6.5)
		Cycle 7	104	0 (0.0)	(0.0, 2.8)
		Cycle >= 8 and < 18	99	7 (5.3)	(2.2, 10.7)
		Cycle >= 18	57	3 (2.3)	(0.5, 6.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	21 (12.4)	(7.9, 18.4)
		Cycle 1	169	0 (0.0)	(0.0, 2.2)
		Cycle 2	166	1 (0.6)	(0.0, 3.3)
		Cycle 3	159	1 (0.6)	(0.0, 3.3)
		Cycle 4	154	1 (0.6)	(0.0, 3.3)
		Cycle 5	142	2 (1.2)	(0.1, 4.2)
		Cycle 6	139	5 (3.0)	(1.0, 6.8)
		Cycle 7	132	1 (0.6)	(0.0, 3.3)
		Cycle >= 8 and < 18	125	9 (5.3)	(2.5, 9.9)
		Cycle >= 18	70	4 (2.4)	(0.6, 5.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	2 (13.3)	(1.7, 40.5)
		Cycle 1	15	0 (0.0)	(0.0, 21.8)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	2 (13.3)	(1.7, 40.5)
		Cycle >= 18	5	0 (0.0)	(0.0, 21.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	6 (10.7)	(4.0, 21.9)
		Cycle 1	56	0 (0.0)	(0.0, 6.4)
		Cycle 2	55	0 (0.0)	(0.0, 6.4)
		Cycle 3	54	0 (0.0)	(0.0, 6.4)
		Cycle 4	53	0 (0.0)	(0.0, 6.4)
		Cycle 5	49	0 (0.0)	(0.0, 6.4)
		Cycle 6	48	1 (1.8)	(0.0, 9.6)
		Cycle 7	48	1 (1.8)	(0.0, 9.6)
		Cycle >= 8 and < 18	45	3 (5.4)	(1.1, 14.9)
		Cycle >= 18	32	2 (3.6)	(0.4, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	17 (13.3)	(7.9, 20.4)
		Cycle 1	128	0 (0.0)	(0.0, 2.8)
		Cycle 2	126	1 (0.8)	(0.0, 4.3)
		Cycle 3	120	1 (0.8)	(0.0, 4.3)
		Cycle 4	116	1 (0.8)	(0.0, 4.3)
		Cycle 5	106	2 (1.6)	(0.2, 5.5)
		Cycle 6	104	4 (3.1)	(0.9, 7.8)
		Cycle 7	97	0 (0.0)	(0.0, 2.8)
		Cycle >= 8 and < 18	93	8 (6.3)	(2.7, 11.9)
		Cycle >= 18	43	2 (1.6)	(0.2, 5.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	< 3 lines (N=17)			
	Any TEAE	17	2 (11.8)	(1.5, 36.4)
	Cycle 1	17	0 (0.0)	(0.0, 19.5)
	Cycle 2	17	0 (0.0)	(0.0, 19.5)
	Cycle 3	17	0 (0.0)	(0.0, 19.5)
	Cycle 4	17	0 (0.0)	(0.0, 19.5)
	Cycle 5	17	0 (0.0)	(0.0, 19.5)
	Cycle 6	16	0 (0.0)	(0.0, 19.5)
	Cycle 7	16	0 (0.0)	(0.0, 19.5)
	Cycle >= 8 and < 18	16	0 (0.0)	(0.0, 19.5)
	Cycle >= 18	14	2 (11.8)	(1.5, 36.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
O-Prior treatment lines	>= 3 lines (N=167)			
	Any TEAE	167	21 (12.6)	(8.0, 18.6)
	Cycle 1	167	0 (0.0)	(0.0, 2.2)
	Cycle 2	164	1 (0.6)	(0.0, 3.3)
	Cycle 3	157	1 (0.6)	(0.0, 3.3)
	Cycle 4	152	1 (0.6)	(0.0, 3.3)
	Cycle 5	138	2 (1.2)	(0.1, 4.3)
	Cycle 6	136	5 (3.0)	(1.0, 6.8)
	Cycle 7	129	1 (0.6)	(0.0, 3.3)
	Cycle >= 8 and < 18	122	11 (6.6)	(3.3, 11.5)
	Cycle >= 18	61	2 (1.2)	(0.1, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	9 (11.4)	(5.3, 20.5)
		Cycle 1	79	0 (0.0)	(0.0, 4.6)
		Cycle 2	78	1 (1.3)	(0.0, 6.9)
		Cycle 3	75	1 (1.3)	(0.0, 6.9)
		Cycle 4	73	0 (0.0)	(0.0, 4.6)
		Cycle 5	70	1 (1.3)	(0.0, 6.9)
		Cycle 6	69	1 (1.3)	(0.0, 6.9)
		Cycle 7	68	0 (0.0)	(0.0, 4.6)
		Cycle >= 8 and < 18	65	4 (5.1)	(1.4, 12.5)
		Cycle >= 18	37	3 (3.8)	(0.8, 10.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)			
	Any TEAE	66	11 (16.7)	(8.6, 27.9)
	Cycle 1	66	0 (0.0)	(0.0, 5.4)
	Cycle 2	66	0 (0.0)	(0.0, 5.4)
	Cycle 3	64	0 (0.0)	(0.0, 5.4)
	Cycle 4	61	1 (1.5)	(0.0, 8.2)
	Cycle 5	55	1 (1.5)	(0.0, 8.2)
	Cycle 6	53	1 (1.5)	(0.0, 8.2)
	Cycle 7	51	0 (0.0)	(0.0, 5.4)
	Cycle >= 8 and < 18	51	7 (10.6)	(4.4, 20.6)
	Cycle >= 18	23	1 (1.5)	(0.0, 8.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	18 (14.9)	(9.1, 22.5)
		Cycle 1	121	0 (0.0)	(0.0, 3.0)
		Cycle 2	120	1 (0.8)	(0.0, 4.5)
		Cycle 3	119	1 (0.8)	(0.0, 4.5)
		Cycle 4	115	1 (0.8)	(0.0, 4.5)
		Cycle 5	106	2 (1.7)	(0.2, 5.8)
		Cycle 6	103	5 (4.1)	(1.4, 9.4)
		Cycle 7	96	1 (0.8)	(0.0, 4.5)
		Cycle >= 8 and < 18	93	6 (5.0)	(1.8, 10.5)
		Cycle >= 18	54	4 (3.3)	(0.9, 8.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
Q-Prior pertuzumab	No (N=63)			
	Any TEAE	63	5 (7.9)	(2.6, 17.6)
	Cycle 1	63	0 (0.0)	(0.0, 5.7)
	Cycle 2	61	0 (0.0)	(0.0, 5.7)
	Cycle 3	55	0 (0.0)	(0.0, 5.7)
	Cycle 4	54	0 (0.0)	(0.0, 5.7)
	Cycle 5	49	0 (0.0)	(0.0, 5.7)
	Cycle 6	49	0 (0.0)	(0.0, 5.7)
	Cycle 7	49	0 (0.0)	(0.0, 5.7)
	Cycle >= 8 and < 18	45	5 (7.9)	(2.6, 17.6)
	Cycle >= 18	21	0 (0.0)	(0.0, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	7 (13.7)	(5.7, 26.3)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	50	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	46	1 (2.0)	(0.0, 10.4)
		Cycle 6	44	1 (2.0)	(0.0, 10.4)
		Cycle 7	40	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	40	3 (5.9)	(1.2, 16.2)
		Cycle >= 18	24	2 (3.9)	(0.5, 13.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDN_SSI0: Incidence of non-severe interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	16 (12.0)	(7.0, 18.8)
		Cycle 1	133	0 (0.0)	(0.0, 2.7)
		Cycle 2	131	1 (0.8)	(0.0, 4.1)
		Cycle 3	124	1 (0.8)	(0.0, 4.1)
		Cycle 4	120	1 (0.8)	(0.0, 4.1)
		Cycle 5	109	1 (0.8)	(0.0, 4.1)
		Cycle 6	108	4 (3.0)	(0.8, 7.5)
		Cycle 7	105	1 (0.8)	(0.0, 4.1)
		Cycle >= 8 and < 18	98	8 (6.0)	(2.6, 11.5)
		Cycle >= 18	51	2 (1.5)	(0.2, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

UE von besonderem Interesse – Interstitielle Lungenerkrankung (ILD), unabhängig vom Schweregrad, Bewertung durch AC

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	30 (16.3)	(11.3, 22.5)
		Cycle 1	184	0 (0.0)	(0.0, 2.0)
		Cycle 2	181	2 (1.1)	(0.1, 3.9)
		Cycle 3	174	2 (1.1)	(0.1, 3.9)
		Cycle 4	169	2 (1.1)	(0.1, 3.9)
		Cycle 5	155	2 (1.1)	(0.1, 3.9)
		Cycle 6	152	4 (2.2)	(0.6, 5.5)
		Cycle 7	145	1 (0.5)	(0.0, 3.0)
		Cycle >= 8 and < 18	138	14 (7.6)	(4.2, 12.4)
		Cycle >= 18	75	5 (2.7)	(0.9, 6.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	21 (15.0) (9.5, 22.0)
		Cycle 1	140	0 (0.0) (0.0, 2.6)
		Cycle 2	138	2 (1.4) (0.2, 5.1)
		Cycle 3	132	2 (1.4) (0.2, 5.1)
		Cycle 4	128	1 (0.7) (0.0, 3.9)
		Cycle 5	116	1 (0.7) (0.0, 3.9)
		Cycle 6	113	3 (2.1) (0.4, 6.1)
		Cycle 7	109	1 (0.7) (0.0, 3.9)
		Cycle >= 8 and < 18	103	10 (7.1) (3.5, 12.7)
		Cycle >= 18	56	2 (1.4) (0.2, 5.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	9 (20.5) (9.8, 35.3)
		Cycle 1	44	0 (0.0) (0.0, 8.0)
		Cycle 2	43	0 (0.0) (0.0, 8.0)
		Cycle 3	42	0 (0.0) (0.0, 8.0)
		Cycle 4	41	1 (2.3) (0.1, 12.0)
		Cycle 5	39	1 (2.3) (0.1, 12.0)
		Cycle 6	39	1 (2.3) (0.1, 12.0)
		Cycle 7	36	0 (0.0) (0.0, 8.0)
		Cycle >= 8 and < 18	35	4 (9.1) (2.5, 21.7)
		Cycle >= 18	19	3 (6.8) (1.4, 18.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	63	13 (20.6) (11.5, 32.7)
		Cycle 1	63	0 (0.0) (0.0, 5.7)
		Cycle 2	61	0 (0.0) (0.0, 5.7)
		Cycle 3	58	0 (0.0) (0.0, 5.7)
		Cycle 4	58	1 (1.6) (0.0, 8.5)
		Cycle 5	55	1 (1.6) (0.0, 8.5)
		Cycle 6	55	2 (3.2) (0.4, 11.0)
		Cycle 7	53	0 (0.0) (0.0, 5.7)
		Cycle >= 8 and < 18	49	6 (9.5) (3.6, 19.6)
		Cycle >= 18	29	4 (6.3) (1.8, 15.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	4 (7.5) (2.1, 18.2)
		Cycle 1	53	0 (0.0) (0.0, 6.7)
		Cycle 2	53	0 (0.0) (0.0, 6.7)
		Cycle 3	52	0 (0.0) (0.0, 6.7)
		Cycle 4	49	0 (0.0) (0.0, 6.7)
		Cycle 5	44	0 (0.0) (0.0, 6.7)
		Cycle 6	42	2 (3.8) (0.5, 13.0)
		Cycle 7	40	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	1 (1.9) (0.0, 10.1)
		Cycle >= 18	23	1 (1.9) (0.0, 10.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	13 (19.1)	(10.6, 30.5)
		Cycle 1	68	0 (0.0)	(0.0, 5.3)
		Cycle 2	67	2 (2.9)	(0.4, 10.2)
		Cycle 3	64	2 (2.9)	(0.4, 10.2)
		Cycle 4	62	1 (1.5)	(0.0, 7.9)
		Cycle 5	56	1 (1.5)	(0.0, 7.9)
		Cycle 6	55	0 (0.0)	(0.0, 5.3)
		Cycle 7	52	1 (1.5)	(0.0, 7.9)
		Cycle >= 8 and < 18	50	7 (10.3)	(4.2, 20.1)
		Cycle >= 18	23	0 (0.0)	(0.0, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	20 (19.6)	(12.4, 28.6)
		Cycle 1	102	0 (0.0)	(0.0, 3.6)
		Cycle 2	101	1 (1.0)	(0.0, 5.3)
		Cycle 3	100	1 (1.0)	(0.0, 5.3)
		Cycle 4	98	1 (1.0)	(0.0, 5.3)
		Cycle 5	94	2 (2.0)	(0.2, 6.9)
		Cycle 6	93	4 (3.9)	(1.1, 9.7)
		Cycle 7	88	1 (1.0)	(0.0, 5.3)
		Cycle >= 8 and < 18	86	8 (7.8)	(3.4, 14.9)
		Cycle >= 18	49	4 (3.9)	(1.1, 9.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	9 (11.1) (5.2, 20.0)
		Cycle 1	81	0 (0.0) (0.0, 4.5)
		Cycle 2	79	1 (1.2) (0.0, 6.7)
		Cycle 3	73	0 (0.0) (0.0, 4.5)
		Cycle 4	71	1 (1.2) (0.0, 6.7)
		Cycle 5	61	0 (0.0) (0.0, 4.5)
		Cycle 6	59	0 (0.0) (0.0, 4.5)
		Cycle 7	57	0 (0.0) (0.0, 4.5)
		Cycle >= 8 and < 18	52	6 (7.4) (2.8, 15.4)
		Cycle >= 18	26	1 (1.2) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions < 5 cm (N=73)	Any TEAE	73	15 (20.5)	(12.0, 31.6)
	Cycle 1	73	0 (0.0)	(0.0, 4.9)
	Cycle 2	72	2 (2.7)	(0.3, 9.5)
	Cycle 3	70	2 (2.7)	(0.3, 9.5)
	Cycle 4	65	0 (0.0)	(0.0, 4.9)
	Cycle 5	60	1 (1.4)	(0.0, 7.4)
	Cycle 6	59	0 (0.0)	(0.0, 4.9)
	Cycle 7	58	1 (1.4)	(0.0, 7.4)
	Cycle >= 8 and < 18	53	7 (9.6)	(3.9, 18.8)
	Cycle >= 18	33	3 (4.1)	(0.9, 11.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=97)			
	Any TEAE	97	10 (10.3)	(5.1, 18.1)
	Cycle 1	97	0 (0.0)	(0.0, 3.7)
	Cycle 2	95	0 (0.0)	(0.0, 3.7)
	Cycle 3	90	0 (0.0)	(0.0, 3.7)
	Cycle 4	90	2 (2.1)	(0.3, 7.3)
	Cycle 5	81	0 (0.0)	(0.0, 3.7)
	Cycle 6	79	3 (3.1)	(0.6, 8.8)
	Cycle 7	74	0 (0.0)	(0.0, 3.7)
	Cycle >= 8 and < 18	72	4 (4.1)	(1.1, 10.2)
	Cycle >= 18	34	1 (1.0)	(0.0, 5.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	27 (17.5)	(11.9, 24.5)
		Cycle 1	154	0 (0.0)	(0.0, 2.4)
		Cycle 2	152	2 (1.3)	(0.2, 4.6)
		Cycle 3	146	2 (1.3)	(0.2, 4.6)
		Cycle 4	141	2 (1.3)	(0.2, 4.6)
		Cycle 5	129	2 (1.3)	(0.2, 4.6)
		Cycle 6	127	3 (1.9)	(0.4, 5.6)
		Cycle 7	121	1 (0.6)	(0.0, 3.6)
		Cycle >= 8 and < 18	114	12 (7.8)	(4.1, 13.2)
		Cycle >= 18	69	5 (3.2)	(1.1, 7.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHCR3+ (N=28)	Any TEAE	28	2 (7.1) (0.9, 23.5)
		Cycle 1	28	0 (0.0) (0.0, 12.3)
		Cycle 2	27	0 (0.0) (0.0, 12.3)
		Cycle 3	26	0 (0.0) (0.0, 12.3)
		Cycle 4	26	0 (0.0) (0.0, 12.3)
		Cycle 5	24	0 (0.0) (0.0, 12.3)
		Cycle 6	23	1 (3.6) (0.1, 18.3)
		Cycle 7	22	0 (0.0) (0.0, 12.3)
		Cycle >= 8 and < 18	22	1 (3.6) (0.1, 18.3)
		Cycle >= 18	5	0 (0.0) (0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	16 (17.2)	(10.2, 26.4)
		Cycle 1	93	0 (0.0)	(0.0, 3.9)
		Cycle 2	92	1 (1.1)	(0.0, 5.8)
		Cycle 3	87	0 (0.0)	(0.0, 3.9)
		Cycle 4	84	0 (0.0)	(0.0, 3.9)
		Cycle 5	80	2 (2.2)	(0.3, 7.6)
		Cycle 6	78	2 (2.2)	(0.3, 7.6)
		Cycle 7	75	0 (0.0)	(0.0, 3.9)
		Cycle >= 8 and < 18	73	9 (9.7)	(4.5, 17.6)
		Cycle >= 18	34	3 (3.2)	(0.7, 9.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	13 (14.8)	(8.1, 23.9)
		Cycle 1	88	0 (0.0)	(0.0, 4.1)
		Cycle 2	86	1 (1.1)	(0.0, 6.2)
		Cycle 3	85	1 (1.1)	(0.0, 6.2)
		Cycle 4	84	2 (2.3)	(0.3, 8.0)
		Cycle 5	74	0 (0.0)	(0.0, 4.1)
		Cycle 6	73	2 (2.3)	(0.3, 8.0)
		Cycle 7	69	1 (1.1)	(0.0, 6.2)
		Cycle >= 8 and < 18	64	5 (5.7)	(1.9, 12.8)
		Cycle >= 18	41	2 (2.3)	(0.3, 8.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	10 (19.6)	(9.8, 33.1)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	1 (2.0)	(0.0, 10.4)
		Cycle 3	49	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	47	2 (3.9)	(0.5, 13.5)
		Cycle 6	46	1 (2.0)	(0.0, 10.4)
		Cycle 7	45	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	44	4 (7.8)	(2.2, 18.9)
		Cycle >= 18	21	3 (5.9)	(1.2, 16.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	18 (14.4)	(8.8, 21.8)
		Cycle 1	125	0 (0.0)	(0.0, 2.9)
		Cycle 2	123	1 (0.8)	(0.0, 4.4)
		Cycle 3	118	1 (0.8)	(0.0, 4.4)
		Cycle 4	114	2 (1.6)	(0.2, 5.7)
		Cycle 5	103	0 (0.0)	(0.0, 2.9)
		Cycle 6	101	3 (2.4)	(0.5, 6.9)
		Cycle 7	95	1 (0.8)	(0.0, 4.4)
		Cycle >= 8 and < 18	90	9 (7.2)	(3.3, 13.2)
		Cycle >= 18	52	2 (1.6)	(0.2, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	17 (17.5)	(10.6, 26.6)
		Cycle 1	97	0 (0.0)	(0.0, 3.7)
		Cycle 2	96	1 (1.0)	(0.0, 5.6)
		Cycle 3	91	0 (0.0)	(0.0, 3.7)
		Cycle 4	88	0 (0.0)	(0.0, 3.7)
		Cycle 5	84	2 (2.1)	(0.3, 7.3)
		Cycle 6	82	2 (2.1)	(0.3, 7.3)
		Cycle 7	79	0 (0.0)	(0.0, 3.7)
		Cycle >= 8 and < 18	76	9 (9.3)	(4.3, 16.9)
		Cycle >= 18	36	4 (4.1)	(1.1, 10.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	12 (14.5)	(7.7, 23.9)
		Cycle 1	83	0 (0.0)	(0.0, 4.3)
		Cycle 2	81	1 (1.2)	(0.0, 6.5)
		Cycle 3	80	1 (1.2)	(0.0, 6.5)
		Cycle 4	79	2 (2.4)	(0.3, 8.4)
		Cycle 5	69	0 (0.0)	(0.0, 4.3)
		Cycle 6	68	2 (2.4)	(0.3, 8.4)
		Cycle 7	64	1 (1.2)	(0.0, 6.5)
		Cycle >= 8 and < 18	60	5 (6.0)	(2.0, 13.5)
		Cycle >= 18	38	1 (1.2)	(0.0, 6.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
I-Renal impairment	Normal (N=90)	Any TEAE	90	13 (14.4)	(7.9, 23.4)
		Cycle 1	90	0 (0.0)	(0.0, 4.0)
		Cycle 2	89	1 (1.1)	(0.0, 6.0)
		Cycle 3	85	0 (0.0)	(0.0, 4.0)
		Cycle 4	85	1 (1.1)	(0.0, 6.0)
		Cycle 5	76	1 (1.1)	(0.0, 6.0)
		Cycle 6	73	0 (0.0)	(0.0, 4.0)
		Cycle 7	72	1 (1.1)	(0.0, 6.0)
		Cycle >= 8 and < 18	69	7 (7.8)	(3.2, 15.4)
		Cycle >= 18	41	2 (2.2)	(0.3, 7.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	8 (11.6) (5.1, 21.6)
		Cycle 1	69	0 (0.0) (0.0, 5.2)
		Cycle 2	68	0 (0.0) (0.0, 5.2)
		Cycle 3	66	0 (0.0) (0.0, 5.2)
		Cycle 4	63	0 (0.0) (0.0, 5.2)
		Cycle 5	59	1 (1.4) (0.0, 7.8)
		Cycle 6	59	2 (2.9) (0.4, 10.1)
		Cycle 7	56	0 (0.0) (0.0, 5.2)
		Cycle >= 8 and < 18	54	5 (7.2) (2.4, 16.1)
		Cycle >= 18	27	1 (1.4) (0.0, 7.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	9 (36.0)	(18.0, 57.5)
		Cycle 1	25	0 (0.0)	(0.0, 13.7)
		Cycle 2	24	1 (4.0)	(0.1, 20.4)
		Cycle 3	23	2 (8.0)	(1.0, 26.0)
		Cycle 4	21	1 (4.0)	(0.1, 20.4)
		Cycle 5	20	0 (0.0)	(0.0, 13.7)
		Cycle 6	20	2 (8.0)	(1.0, 26.0)
		Cycle 7	17	0 (0.0)	(0.0, 13.7)
		Cycle >= 8 and < 18	15	2 (8.0)	(1.0, 26.0)
		Cycle >= 18	7	2 (8.0)	(1.0, 26.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	24 (22.9)	(15.2, 32.1)
		Cycle 1	105	0 (0.0)	(0.0, 3.5)
		Cycle 2	104	1 (1.0)	(0.0, 5.2)
		Cycle 3	102	2 (1.9)	(0.2, 6.7)
		Cycle 4	98	2 (1.9)	(0.2, 6.7)
		Cycle 5	90	2 (1.9)	(0.2, 6.7)
		Cycle 6	89	2 (1.9)	(0.2, 6.7)
		Cycle 7	87	1 (1.0)	(0.0, 5.2)
		Cycle >= 8 and < 18	84	12 (11.4)	(6.0, 19.1)
		Cycle >= 18	44	4 (3.8)	(1.0, 9.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	6 (7.9) (3.0, 16.4)
		Cycle 1	76	0 (0.0) (0.0, 4.7)
		Cycle 2	74	1 (1.3) (0.0, 7.1)
		Cycle 3	69	0 (0.0) (0.0, 4.7)
		Cycle 4	68	0 (0.0) (0.0, 4.7)
		Cycle 5	63	0 (0.0) (0.0, 4.7)
		Cycle 6	61	2 (2.6) (0.3, 9.2)
		Cycle 7	56	0 (0.0) (0.0, 4.7)
		Cycle >= 8 and < 18	54	2 (2.6) (0.3, 9.2)
		Cycle >= 18	31	1 (1.3) (0.0, 7.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	5 (20.8)	(7.1, 42.2)
		Cycle 1	24	0 (0.0)	(0.0, 14.2)
		Cycle 2	23	0 (0.0)	(0.0, 14.2)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	1 (4.2)	(0.1, 21.1)
		Cycle 6	18	1 (4.2)	(0.1, 21.1)
		Cycle 7	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 8 and < 18	18	2 (8.3)	(1.0, 27.0)
		Cycle >= 18	10	1 (4.2)	(0.1, 21.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	25 (15.6)	(10.4, 22.2)
		Cycle 1	160	0 (0.0)	(0.0, 2.3)
		Cycle 2	158	2 (1.3)	(0.2, 4.4)
		Cycle 3	152	2 (1.3)	(0.2, 4.4)
		Cycle 4	147	2 (1.3)	(0.2, 4.4)
		Cycle 5	136	1 (0.6)	(0.0, 3.4)
		Cycle 6	134	3 (1.9)	(0.4, 5.4)
		Cycle 7	127	1 (0.6)	(0.0, 3.4)
		Cycle >= 8 and < 18	120	12 (7.5)	(3.9, 12.7)
		Cycle >= 18	65	4 (2.5)	(0.7, 6.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	12 (22.6)	(12.3, 36.2)
		Cycle 1	53	0 (0.0)	(0.0, 6.7)
		Cycle 2	52	1 (1.9)	(0.0, 10.1)
		Cycle 3	49	1 (1.9)	(0.0, 10.1)
		Cycle 4	48	1 (1.9)	(0.0, 10.1)
		Cycle 5	43	1 (1.9)	(0.0, 10.1)
		Cycle 6	42	1 (1.9)	(0.0, 10.1)
		Cycle 7	41	0 (0.0)	(0.0, 6.7)
		Cycle >= 8 and < 18	39	7 (13.2)	(5.5, 25.3)
		Cycle >= 18	18	1 (1.9)	(0.0, 10.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	18 (13.7)	(8.4, 20.8)
		Cycle 1	131	0 (0.0)	(0.0, 2.8)
		Cycle 2	129	1 (0.8)	(0.0, 4.2)
		Cycle 3	125	1 (0.8)	(0.0, 4.2)
		Cycle 4	121	1 (0.8)	(0.0, 4.2)
		Cycle 5	112	1 (0.8)	(0.0, 4.2)
		Cycle 6	110	3 (2.3)	(0.5, 6.5)
		Cycle 7	104	1 (0.8)	(0.0, 4.2)
		Cycle >= 8 and < 18	99	7 (5.3)	(2.2, 10.7)
		Cycle >= 18	57	4 (3.1)	(0.8, 7.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	27 (16.0)	(10.8, 22.4)
		Cycle 1	169	0 (0.0)	(0.0, 2.2)
		Cycle 2	166	2 (1.2)	(0.1, 4.2)
		Cycle 3	159	2 (1.2)	(0.1, 4.2)
		Cycle 4	154	2 (1.2)	(0.1, 4.2)
		Cycle 5	142	2 (1.2)	(0.1, 4.2)
		Cycle 6	139	4 (2.4)	(0.6, 5.9)
		Cycle 7	132	1 (0.6)	(0.0, 3.3)
		Cycle >= 8 and < 18	125	12 (7.1)	(3.7, 12.1)
		Cycle >= 18	70	4 (2.4)	(0.6, 5.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	3 (20.0)	(4.3, 48.1)
		Cycle 1	15	0 (0.0)	(0.0, 21.8)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	2 (13.3)	(1.7, 40.5)
		Cycle >= 18	5	1 (6.7)	(0.2, 31.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	6 (10.7) (4.0, 21.9)
		Cycle 1	56	0 (0.0) (0.0, 6.4)
		Cycle 2	55	1 (1.8) (0.0, 9.6)
		Cycle 3	54	0 (0.0) (0.0, 6.4)
		Cycle 4	53	0 (0.0) (0.0, 6.4)
		Cycle 5	49	0 (0.0) (0.0, 6.4)
		Cycle 6	48	0 (0.0) (0.0, 6.4)
		Cycle 7	48	0 (0.0) (0.0, 6.4)
		Cycle >= 8 and < 18	45	3 (5.4) (1.1, 14.9)
		Cycle >= 18	32	2 (3.6) (0.4, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	24 (18.8)	(12.4, 26.6)
		Cycle 1	128	0 (0.0)	(0.0, 2.8)
		Cycle 2	126	1 (0.8)	(0.0, 4.3)
		Cycle 3	120	2 (1.6)	(0.2, 5.5)
		Cycle 4	116	2 (1.6)	(0.2, 5.5)
		Cycle 5	106	2 (1.6)	(0.2, 5.5)
		Cycle 6	104	4 (3.1)	(0.9, 7.8)
		Cycle 7	97	1 (0.8)	(0.0, 4.3)
		Cycle >= 8 and < 18	93	11 (8.6)	(4.4, 14.9)
		Cycle >= 18	43	3 (2.3)	(0.5, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	< 3 lines (N=17)	Any TEAE	17	2 (11.8) (1.5, 36.4)
		Cycle 1	17	0 (0.0) (0.0, 19.5)
		Cycle 2	17	0 (0.0) (0.0, 19.5)
		Cycle 3	17	0 (0.0) (0.0, 19.5)
		Cycle 4	17	0 (0.0) (0.0, 19.5)
		Cycle 5	17	0 (0.0) (0.0, 19.5)
		Cycle 6	16	0 (0.0) (0.0, 19.5)
		Cycle 7	16	0 (0.0) (0.0, 19.5)
		Cycle >= 8 and < 18	16	0 (0.0) (0.0, 19.5)
		Cycle >= 18	14	2 (11.8) (1.5, 36.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	>= 3 lines (N=167)			
	Any TEAE	167	28 (16.8)	(11.4, 23.3)
	Cycle 1	167	0 (0.0)	(0.0, 2.2)
	Cycle 2	164	2 (1.2)	(0.1, 4.3)
	Cycle 3	157	2 (1.2)	(0.1, 4.3)
	Cycle 4	152	2 (1.2)	(0.1, 4.3)
	Cycle 5	138	2 (1.2)	(0.1, 4.3)
	Cycle 6	136	4 (2.4)	(0.7, 6.0)
	Cycle 7	129	1 (0.6)	(0.0, 3.3)
	Cycle >= 8 and < 18	122	14 (8.4)	(4.7, 13.7)
	Cycle >= 18	61	3 (1.8)	(0.4, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)	Any TEAE	79	12 (15.2)	(8.1, 25.0)
		Cycle 1	79	0 (0.0)	(0.0, 4.6)
		Cycle 2	78	2 (2.5)	(0.3, 8.8)
		Cycle 3	75	1 (1.3)	(0.0, 6.9)
		Cycle 4	73	0 (0.0)	(0.0, 4.6)
		Cycle 5	70	1 (1.3)	(0.0, 6.9)
		Cycle 6	69	1 (1.3)	(0.0, 6.9)
		Cycle 7	68	0 (0.0)	(0.0, 4.6)
		Cycle >= 8 and < 18	65	5 (6.3)	(2.1, 14.2)
		Cycle >= 18	37	4 (5.1)	(1.4, 12.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	14 (21.2)	(12.1, 33.0)
		Cycle 1	66	0 (0.0)	(0.0, 5.4)
		Cycle 2	66	0 (0.0)	(0.0, 5.4)
		Cycle 3	64	1 (1.5)	(0.0, 8.2)
		Cycle 4	61	1 (1.5)	(0.0, 8.2)
		Cycle 5	55	1 (1.5)	(0.0, 8.2)
		Cycle 6	53	1 (1.5)	(0.0, 8.2)
		Cycle 7	51	0 (0.0)	(0.0, 5.4)
		Cycle >= 8 and < 18	51	9 (13.6)	(6.4, 24.3)
		Cycle >= 18	23	1 (1.5)	(0.0, 8.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	19 (15.7)	(9.7, 23.4)
		Cycle 1	121	0 (0.0)	(0.0, 3.0)
		Cycle 2	120	1 (0.8)	(0.0, 4.5)
		Cycle 3	119	2 (1.7)	(0.2, 5.8)
		Cycle 4	115	1 (0.8)	(0.0, 4.5)
		Cycle 5	106	2 (1.7)	(0.2, 5.8)
		Cycle 6	103	4 (3.3)	(0.9, 8.2)
		Cycle 7	96	0 (0.0)	(0.0, 3.0)
		Cycle >= 8 and < 18	93	6 (5.0)	(1.8, 10.5)
		Cycle >= 18	54	5 (4.1)	(1.4, 9.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	11 (17.5)	(9.1, 29.1)
		Cycle 1	63	0 (0.0)	(0.0, 5.7)
		Cycle 2	61	1 (1.6)	(0.0, 8.5)
		Cycle 3	55	0 (0.0)	(0.0, 5.7)
		Cycle 4	54	1 (1.6)	(0.0, 8.5)
		Cycle 5	49	0 (0.0)	(0.0, 5.7)
		Cycle 6	49	0 (0.0)	(0.0, 5.7)
		Cycle 7	49	1 (1.6)	(0.0, 8.5)
		Cycle >= 8 and < 18	45	8 (12.7)	(5.6, 23.5)
		Cycle >= 18	21	0 (0.0)	(0.0, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	7 (13.7)	(5.7, 26.3)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	50	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	46	1 (2.0)	(0.0, 10.4)
		Cycle 6	44	1 (2.0)	(0.0, 10.4)
		Cycle 7	40	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	40	3 (5.9)	(1.2, 16.2)
		Cycle >= 18	24	2 (3.9)	(0.5, 13.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDA_SSI0: Incidence of adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	23 (17.3)	(11.3, 24.8)
		Cycle 1	133	0 (0.0)	(0.0, 2.7)
		Cycle 2	131	2 (1.5)	(0.2, 5.3)
		Cycle 3	124	2 (1.5)	(0.2, 5.3)
		Cycle 4	120	2 (1.5)	(0.2, 5.3)
		Cycle 5	109	1 (0.8)	(0.0, 4.1)
		Cycle 6	108	3 (2.3)	(0.5, 6.5)
		Cycle 7	105	1 (0.8)	(0.0, 4.1)
		Cycle >= 8 and < 18	98	11 (8.3)	(4.2, 14.3)
		Cycle >= 18	51	3 (2.3)	(0.5, 6.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

UE von besonderem Interesse – Interstitielle Lungenerkrankung (ILD), SUE, Bewertung durch AC

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	10 (5.4)	(2.6, 9.8)
		Cycle 1	184	0 (0.0)	(0.0, 2.0)
		Cycle 2	181	0 (0.0)	(0.0, 2.0)
		Cycle 3	174	1 (0.5)	(0.0, 3.0)
		Cycle 4	169	1 (0.5)	(0.0, 3.0)
		Cycle 5	155	1 (0.5)	(0.0, 3.0)
		Cycle 6	152	0 (0.0)	(0.0, 2.0)
		Cycle 7	145	1 (0.5)	(0.0, 3.0)
		Cycle >= 8 and < 18	138	5 (2.7)	(0.9, 6.2)
		Cycle >= 18	75	1 (0.5)	(0.0, 3.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	8 (5.7) (2.5, 10.9)
		Cycle 1	140	0 (0.0) (0.0, 2.6)
		Cycle 2	138	0 (0.0) (0.0, 2.6)
		Cycle 3	132	1 (0.7) (0.0, 3.9)
		Cycle 4	128	1 (0.7) (0.0, 3.9)
		Cycle 5	116	1 (0.7) (0.0, 3.9)
		Cycle 6	113	0 (0.0) (0.0, 2.6)
		Cycle 7	109	1 (0.7) (0.0, 3.9)
		Cycle >= 8 and < 18	103	4 (2.9) (0.8, 7.2)
		Cycle >= 18	56	0 (0.0) (0.0, 2.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	2 (4.5) (0.6, 15.5)
		Cycle 1	44	0 (0.0) (0.0, 8.0)
		Cycle 2	43	0 (0.0) (0.0, 8.0)
		Cycle 3	42	0 (0.0) (0.0, 8.0)
		Cycle 4	41	0 (0.0) (0.0, 8.0)
		Cycle 5	39	0 (0.0) (0.0, 8.0)
		Cycle 6	39	0 (0.0) (0.0, 8.0)
		Cycle 7	36	0 (0.0) (0.0, 8.0)
		Cycle >= 8 and < 18	35	1 (2.3) (0.1, 12.0)
		Cycle >= 18	19	1 (2.3) (0.1, 12.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)			
	Any TEAE	63	0 (0.0)	(0.0, 5.7)
	Cycle 1	63	0 (0.0)	(0.0, 5.7)
	Cycle 2	61	0 (0.0)	(0.0, 5.7)
	Cycle 3	58	0 (0.0)	(0.0, 5.7)
	Cycle 4	58	0 (0.0)	(0.0, 5.7)
	Cycle 5	55	0 (0.0)	(0.0, 5.7)
	Cycle 6	55	0 (0.0)	(0.0, 5.7)
	Cycle 7	53	0 (0.0)	(0.0, 5.7)
	Cycle >= 8 and < 18	49	0 (0.0)	(0.0, 5.7)
	Cycle >= 18	29	0 (0.0)	(0.0, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	2 (3.8) (0.5, 13.0)
		Cycle 1	53	0 (0.0) (0.0, 6.7)
		Cycle 2	53	0 (0.0) (0.0, 6.7)
		Cycle 3	52	0 (0.0) (0.0, 6.7)
		Cycle 4	49	0 (0.0) (0.0, 6.7)
		Cycle 5	44	0 (0.0) (0.0, 6.7)
		Cycle 6	42	0 (0.0) (0.0, 6.7)
		Cycle 7	40	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	1 (1.9) (0.0, 10.1)
		Cycle >= 18	23	1 (1.9) (0.0, 10.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

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Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	8 (11.8) (5.2, 21.9)
		Cycle 1	68	0 (0.0) (0.0, 5.3)
		Cycle 2	67	0 (0.0) (0.0, 5.3)
		Cycle 3	64	1 (1.5) (0.0, 7.9)
		Cycle 4	62	1 (1.5) (0.0, 7.9)
		Cycle 5	56	1 (1.5) (0.0, 7.9)
		Cycle 6	55	0 (0.0) (0.0, 5.3)
		Cycle 7	52	1 (1.5) (0.0, 7.9)
		Cycle >= 8 and < 18	50	4 (5.9) (1.6, 14.4)
		Cycle >= 18	23	0 (0.0) (0.0, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	5 (4.9) (1.6, 11.1)
		Cycle 1	102	0 (0.0) (0.0, 3.6)
		Cycle 2	101	0 (0.0) (0.0, 3.6)
		Cycle 3	100	0 (0.0) (0.0, 3.6)
		Cycle 4	98	0 (0.0) (0.0, 3.6)
		Cycle 5	94	1 (1.0) (0.0, 5.3)
		Cycle 6	93	0 (0.0) (0.0, 3.6)
		Cycle 7	88	1 (1.0) (0.0, 5.3)
		Cycle >= 8 and < 18	86	2 (2.0) (0.2, 6.9)
		Cycle >= 18	49	1 (1.0) (0.0, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	4 (4.9) (1.4, 12.2)
		Cycle 1	81	0 (0.0) (0.0, 4.5)
		Cycle 2	79	0 (0.0) (0.0, 4.5)
		Cycle 3	73	0 (0.0) (0.0, 4.5)
		Cycle 4	71	1 (1.2) (0.0, 6.7)
		Cycle 5	61	0 (0.0) (0.0, 4.5)
		Cycle 6	59	0 (0.0) (0.0, 4.5)
		Cycle 7	57	0 (0.0) (0.0, 4.5)
		Cycle >= 8 and < 18	52	3 (3.7) (0.8, 10.4)
		Cycle >= 18	26	0 (0.0) (0.0, 4.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions	< 5 cm (N=73)			
	Any TEAE	73	7 (9.6)	(3.9, 18.8)
	Cycle 1	73	0 (0.0)	(0.0, 4.9)
	Cycle 2	72	0 (0.0)	(0.0, 4.9)
	Cycle 3	70	1 (1.4)	(0.0, 7.4)
	Cycle 4	65	0 (0.0)	(0.0, 4.9)
	Cycle 5	60	1 (1.4)	(0.0, 7.4)
	Cycle 6	59	0 (0.0)	(0.0, 4.9)
	Cycle 7	58	1 (1.4)	(0.0, 7.4)
	Cycle >= 8 and < 18	53	3 (4.1)	(0.9, 11.5)
	Cycle >= 18	33	1 (1.4)	(0.0, 7.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=97)			
	Any TEAE	97	1 (1.0)	(0.0, 5.6)
	Cycle 1	97	0 (0.0)	(0.0, 3.7)
	Cycle 2	95	0 (0.0)	(0.0, 3.7)
	Cycle 3	90	0 (0.0)	(0.0, 3.7)
	Cycle 4	90	1 (1.0)	(0.0, 5.6)
	Cycle 5	81	0 (0.0)	(0.0, 3.7)
	Cycle 6	79	0 (0.0)	(0.0, 3.7)
	Cycle 7	74	0 (0.0)	(0.0, 3.7)
	Cycle >= 8 and < 18	72	0 (0.0)	(0.0, 3.7)
	Cycle >= 18	34	0 (0.0)	(0.0, 3.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	8 (5.2) (2.3, 10.0)
		Cycle 1	154	0 (0.0) (0.0, 2.4)
		Cycle 2	152	0 (0.0) (0.0, 2.4)
		Cycle 3	146	1 (0.6) (0.0, 3.6)
		Cycle 4	141	1 (0.6) (0.0, 3.6)
		Cycle 5	129	1 (0.6) (0.0, 3.6)
		Cycle 6	127	0 (0.0) (0.0, 2.4)
		Cycle 7	121	1 (0.6) (0.0, 3.6)
		Cycle >= 8 and < 18	114	3 (1.9) (0.4, 5.6)
		Cycle >= 18	69	1 (0.6) (0.0, 3.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHCR3+ (N=28)			
	Any TEAE	28	1 (3.6)	(0.1, 18.3)
	Cycle 1	28	0 (0.0)	(0.0, 12.3)
	Cycle 2	27	0 (0.0)	(0.0, 12.3)
	Cycle 3	26	0 (0.0)	(0.0, 12.3)
	Cycle 4	26	0 (0.0)	(0.0, 12.3)
	Cycle 5	24	0 (0.0)	(0.0, 12.3)
	Cycle 6	23	0 (0.0)	(0.0, 12.3)
	Cycle 7	22	0 (0.0)	(0.0, 12.3)
	Cycle >= 8 and < 18	22	1 (3.6)	(0.1, 18.3)
	Cycle >= 18	5	0 (0.0)	(0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
F-Estrogen receptors	Positive (N=93)			
	Any TEAE	93	5 (5.4)	(1.8, 12.1)
	Cycle 1	93	0 (0.0)	(0.0, 3.9)
	Cycle 2	92	0 (0.0)	(0.0, 3.9)
	Cycle 3	87	0 (0.0)	(0.0, 3.9)
	Cycle 4	84	0 (0.0)	(0.0, 3.9)
	Cycle 5	80	1 (1.1)	(0.0, 5.8)
	Cycle 6	78	0 (0.0)	(0.0, 3.9)
	Cycle 7	75	0 (0.0)	(0.0, 3.9)
	Cycle >= 8 and < 18	73	4 (4.3)	(1.2, 10.6)
	Cycle >= 18	34	0 (0.0)	(0.0, 3.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	4 (4.5)	(1.3, 11.2)
		Cycle 1	88	0 (0.0)	(0.0, 4.1)
		Cycle 2	86	0 (0.0)	(0.0, 4.1)
		Cycle 3	85	0 (0.0)	(0.0, 4.1)
		Cycle 4	84	1 (1.1)	(0.0, 6.2)
		Cycle 5	74	0 (0.0)	(0.0, 4.1)
		Cycle 6	73	0 (0.0)	(0.0, 4.1)
		Cycle 7	69	1 (1.1)	(0.0, 6.2)
		Cycle >= 8 and < 18	64	1 (1.1)	(0.0, 6.2)
		Cycle >= 18	41	1 (1.1)	(0.0, 6.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
G-Progesterone receptors	Positive (N=51)			
	Any TEAE	51	2 (3.9)	(0.5, 13.5)
	Cycle 1	51	0 (0.0)	(0.0, 7.0)
	Cycle 2	50	0 (0.0)	(0.0, 7.0)
	Cycle 3	49	0 (0.0)	(0.0, 7.0)
	Cycle 4	49	0 (0.0)	(0.0, 7.0)
	Cycle 5	47	1 (2.0)	(0.0, 10.4)
	Cycle 6	46	0 (0.0)	(0.0, 7.0)
	Cycle 7	45	0 (0.0)	(0.0, 7.0)
	Cycle >= 8 and < 18	44	1 (2.0)	(0.0, 10.4)
	Cycle >= 18	21	0 (0.0)	(0.0, 7.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	7 (5.6) (2.3, 11.2)
		Cycle 1	125	0 (0.0) (0.0, 2.9)
		Cycle 2	123	0 (0.0) (0.0, 2.9)
		Cycle 3	118	0 (0.0) (0.0, 2.9)
		Cycle 4	114	1 (0.8) (0.0, 4.4)
		Cycle 5	103	0 (0.0) (0.0, 2.9)
		Cycle 6	101	0 (0.0) (0.0, 2.9)
		Cycle 7	95	1 (0.8) (0.0, 4.4)
		Cycle >= 8 and < 18	90	4 (3.2) (0.9, 8.0)
		Cycle >= 18	52	1 (0.8) (0.0, 4.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	5 (5.2)	(1.7, 11.6)
		Cycle 1	97	0 (0.0)	(0.0, 3.7)
		Cycle 2	96	0 (0.0)	(0.0, 3.7)
		Cycle 3	91	0 (0.0)	(0.0, 3.7)
		Cycle 4	88	0 (0.0)	(0.0, 3.7)
		Cycle 5	84	1 (1.0)	(0.0, 5.6)
		Cycle 6	82	0 (0.0)	(0.0, 3.7)
		Cycle 7	79	0 (0.0)	(0.0, 3.7)
		Cycle >= 8 and < 18	76	4 (4.1)	(1.1, 10.2)
		Cycle >= 18	36	0 (0.0)	(0.0, 3.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	4 (4.8)	(1.3, 11.9)
		Cycle 1	83	0 (0.0)	(0.0, 4.3)
		Cycle 2	81	0 (0.0)	(0.0, 4.3)
		Cycle 3	80	0 (0.0)	(0.0, 4.3)
		Cycle 4	79	1 (1.2)	(0.0, 6.5)
		Cycle 5	69	0 (0.0)	(0.0, 4.3)
		Cycle 6	68	0 (0.0)	(0.0, 4.3)
		Cycle 7	64	1 (1.2)	(0.0, 6.5)
		Cycle >= 8 and < 18	60	1 (1.2)	(0.0, 6.5)
		Cycle >= 18	38	1 (1.2)	(0.0, 6.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

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Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Normal (N=90)			
	Any TEAE	90	8 (8.9)	(3.9, 16.8)
	Cycle 1	90	0 (0.0)	(0.0, 4.0)
	Cycle 2	89	0 (0.0)	(0.0, 4.0)
	Cycle 3	85	0 (0.0)	(0.0, 4.0)
	Cycle 4	85	1 (1.1)	(0.0, 6.0)
	Cycle 5	76	1 (1.1)	(0.0, 6.0)
	Cycle 6	73	0 (0.0)	(0.0, 4.0)
	Cycle 7	72	1 (1.1)	(0.0, 6.0)
	Cycle >= 8 and < 18	69	5 (5.6)	(1.8, 12.5)
	Cycle >= 18	41	0 (0.0)	(0.0, 4.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Mild (N=69)			
	Any TEAE	69	0 (0.0)	(0.0, 5.2)
	Cycle 1	69	0 (0.0)	(0.0, 5.2)
	Cycle 2	68	0 (0.0)	(0.0, 5.2)
	Cycle 3	66	0 (0.0)	(0.0, 5.2)
	Cycle 4	63	0 (0.0)	(0.0, 5.2)
	Cycle 5	59	0 (0.0)	(0.0, 5.2)
	Cycle 6	59	0 (0.0)	(0.0, 5.2)
	Cycle 7	56	0 (0.0)	(0.0, 5.2)
	Cycle >= 8 and < 18	54	0 (0.0)	(0.0, 5.2)
	Cycle >= 18	27	0 (0.0)	(0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	2 (8.0) (1.0, 26.0)
		Cycle 1	25	0 (0.0) (0.0, 13.7)
		Cycle 2	24	0 (0.0) (0.0, 13.7)
		Cycle 3	23	1 (4.0) (0.1, 20.4)
		Cycle 4	21	0 (0.0) (0.0, 13.7)
		Cycle 5	20	0 (0.0) (0.0, 13.7)
		Cycle 6	20	0 (0.0) (0.0, 13.7)
		Cycle 7	17	0 (0.0) (0.0, 13.7)
		Cycle >= 8 and < 18	15	0 (0.0) (0.0, 13.7)
		Cycle >= 18	7	1 (4.0) (0.1, 20.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	10 (9.5)	(4.7, 16.8)
		Cycle 1	105	0 (0.0)	(0.0, 3.5)
		Cycle 2	104	0 (0.0)	(0.0, 3.5)
		Cycle 3	102	1 (1.0)	(0.0, 5.2)
		Cycle 4	98	1 (1.0)	(0.0, 5.2)
		Cycle 5	90	1 (1.0)	(0.0, 5.2)
		Cycle 6	89	0 (0.0)	(0.0, 3.5)
		Cycle 7	87	1 (1.0)	(0.0, 5.2)
		Cycle >= 8 and < 18	84	5 (4.8)	(1.6, 10.8)
		Cycle >= 18	44	1 (1.0)	(0.0, 5.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
J-Hepatic impairment	Mild (N=76)			
	Any TEAE	76	0 (0.0)	(0.0, 4.7)
	Cycle 1	76	0 (0.0)	(0.0, 4.7)
	Cycle 2	74	0 (0.0)	(0.0, 4.7)
	Cycle 3	69	0 (0.0)	(0.0, 4.7)
	Cycle 4	68	0 (0.0)	(0.0, 4.7)
	Cycle 5	63	0 (0.0)	(0.0, 4.7)
	Cycle 6	61	0 (0.0)	(0.0, 4.7)
	Cycle 7	56	0 (0.0)	(0.0, 4.7)
	Cycle >= 8 and < 18	54	0 (0.0)	(0.0, 4.7)
	Cycle >= 18	31	0 (0.0)	(0.0, 4.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	1 (4.2)	(0.1, 21.1)
		Cycle 1	24	0 (0.0)	(0.0, 14.2)
		Cycle 2	23	0 (0.0)	(0.0, 14.2)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	1 (4.2)	(0.1, 21.1)
		Cycle 6	18	0 (0.0)	(0.0, 14.2)
		Cycle 7	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 8 and < 18	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 18	10	0 (0.0)	(0.0, 14.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
 Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	9 (5.6)	(2.6, 10.4)
		Cycle 1	160	0 (0.0)	(0.0, 2.3)
		Cycle 2	158	0 (0.0)	(0.0, 2.3)
		Cycle 3	152	1 (0.6)	(0.0, 3.4)
		Cycle 4	147	1 (0.6)	(0.0, 3.4)
		Cycle 5	136	0 (0.0)	(0.0, 2.3)
		Cycle 6	134	0 (0.0)	(0.0, 2.3)
		Cycle 7	127	1 (0.6)	(0.0, 3.4)
		Cycle >= 8 and < 18	120	5 (3.1)	(1.0, 7.1)
		Cycle >= 18	65	1 (0.6)	(0.0, 3.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
 Adverse events were coded using the MedDRA dictionary, Version 20.1.
 If a subject has more than one event per cycle, the subject is counted once at each level of summation.
 TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	6 (11.3)	(4.3, 23.0)
		Cycle 1	53	0 (0.0)	(0.0, 6.7)
		Cycle 2	52	0 (0.0)	(0.0, 6.7)
		Cycle 3	49	0 (0.0)	(0.0, 6.7)
		Cycle 4	48	1 (1.9)	(0.0, 10.1)
		Cycle 5	43	1 (1.9)	(0.0, 10.1)
		Cycle 6	42	0 (0.0)	(0.0, 6.7)
		Cycle 7	41	0 (0.0)	(0.0, 6.7)
		Cycle >= 8 and < 18	39	4 (7.5)	(2.1, 18.2)
		Cycle >= 18	18	0 (0.0)	(0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	4 (3.1)	(0.8, 7.6)
		Cycle 1	131	0 (0.0)	(0.0, 2.8)
		Cycle 2	129	0 (0.0)	(0.0, 2.8)
		Cycle 3	125	1 (0.8)	(0.0, 4.2)
		Cycle 4	121	0 (0.0)	(0.0, 2.8)
		Cycle 5	112	0 (0.0)	(0.0, 2.8)
		Cycle 6	110	0 (0.0)	(0.0, 2.8)
		Cycle 7	104	1 (0.8)	(0.0, 4.2)
		Cycle >= 8 and < 18	99	1 (0.8)	(0.0, 4.2)
		Cycle >= 18	57	1 (0.8)	(0.0, 4.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	9 (5.3)	(2.5, 9.9)
		Cycle 1	169	0 (0.0)	(0.0, 2.2)
		Cycle 2	166	0 (0.0)	(0.0, 2.2)
		Cycle 3	159	1 (0.6)	(0.0, 3.3)
		Cycle 4	154	1 (0.6)	(0.0, 3.3)
		Cycle 5	142	1 (0.6)	(0.0, 3.3)
		Cycle 6	139	0 (0.0)	(0.0, 2.2)
		Cycle 7	132	1 (0.6)	(0.0, 3.3)
		Cycle >= 8 and < 18	125	5 (3.0)	(1.0, 6.8)
		Cycle >= 18	70	0 (0.0)	(0.0, 2.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	1 (6.7)	(0.2, 31.9)
		Cycle 1	15	0 (0.0)	(0.0, 21.8)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 18	5	1 (6.7)	(0.2, 31.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)			
	Any TEAE	56	0 (0.0)	(0.0, 6.4)
	Cycle 1	56	0 (0.0)	(0.0, 6.4)
	Cycle 2	55	0 (0.0)	(0.0, 6.4)
	Cycle 3	54	0 (0.0)	(0.0, 6.4)
	Cycle 4	53	0 (0.0)	(0.0, 6.4)
	Cycle 5	49	0 (0.0)	(0.0, 6.4)
	Cycle 6	48	0 (0.0)	(0.0, 6.4)
	Cycle 7	48	0 (0.0)	(0.0, 6.4)
	Cycle >= 8 and < 18	45	0 (0.0)	(0.0, 6.4)
	Cycle >= 18	32	0 (0.0)	(0.0, 6.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	10 (7.8)	(3.8, 13.9)
		Cycle 1	128	0 (0.0)	(0.0, 2.8)
		Cycle 2	126	0 (0.0)	(0.0, 2.8)
		Cycle 3	120	1 (0.8)	(0.0, 4.3)
		Cycle 4	116	1 (0.8)	(0.0, 4.3)
		Cycle 5	106	1 (0.8)	(0.0, 4.3)
		Cycle 6	104	0 (0.0)	(0.0, 2.8)
		Cycle 7	97	1 (0.8)	(0.0, 4.3)
		Cycle >= 8 and < 18	93	5 (3.9)	(1.3, 8.9)
		Cycle >= 18	43	1 (0.8)	(0.0, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	< 3 lines (N=17)			
	Any TEAE	17	0 (0.0)	(0.0, 19.5)
	Cycle 1	17	0 (0.0)	(0.0, 19.5)
	Cycle 2	17	0 (0.0)	(0.0, 19.5)
	Cycle 3	17	0 (0.0)	(0.0, 19.5)
	Cycle 4	17	0 (0.0)	(0.0, 19.5)
	Cycle 5	17	0 (0.0)	(0.0, 19.5)
	Cycle 6	16	0 (0.0)	(0.0, 19.5)
	Cycle 7	16	0 (0.0)	(0.0, 19.5)
	Cycle >= 8 and < 18	16	0 (0.0)	(0.0, 19.5)
	Cycle >= 18	14	0 (0.0)	(0.0, 19.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	>= 3 lines (N=167)			
	Any TEAE	167	10 (6.0)	(2.9, 10.7)
	Cycle 1	167	0 (0.0)	(0.0, 2.2)
	Cycle 2	164	0 (0.0)	(0.0, 2.2)
	Cycle 3	157	1 (0.6)	(0.0, 3.3)
	Cycle 4	152	1 (0.6)	(0.0, 3.3)
	Cycle 5	138	1 (0.6)	(0.0, 3.3)
	Cycle 6	136	0 (0.0)	(0.0, 2.2)
	Cycle 7	129	1 (0.6)	(0.0, 3.3)
	Cycle >= 8 and < 18	122	5 (3.0)	(1.0, 6.8)
	Cycle >= 18	61	1 (0.6)	(0.0, 3.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)			
	Any TEAE	79	2 (2.5)	(0.3, 8.8)
	Cycle 1	79	0 (0.0)	(0.0, 4.6)
	Cycle 2	78	0 (0.0)	(0.0, 4.6)
	Cycle 3	75	0 (0.0)	(0.0, 4.6)
	Cycle 4	73	0 (0.0)	(0.0, 4.6)
	Cycle 5	70	0 (0.0)	(0.0, 4.6)
	Cycle 6	69	0 (0.0)	(0.0, 4.6)
	Cycle 7	68	0 (0.0)	(0.0, 4.6)
	Cycle >= 8 and < 18	65	1 (1.3)	(0.0, 6.9)
	Cycle >= 18	37	1 (1.3)	(0.0, 6.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	6 (9.1) (3.4, 18.7)
		Cycle 1	66	0 (0.0) (0.0, 5.4)
		Cycle 2	66	0 (0.0) (0.0, 5.4)
		Cycle 3	64	1 (1.5) (0.0, 8.2)
		Cycle 4	61	0 (0.0) (0.0, 5.4)
		Cycle 5	55	1 (1.5) (0.0, 8.2)
		Cycle 6	53	0 (0.0) (0.0, 5.4)
		Cycle 7	51	0 (0.0) (0.0, 5.4)
		Cycle >= 8 and < 18	51	4 (6.1) (1.7, 14.8)
		Cycle >= 18	23	0 (0.0) (0.0, 5.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	4 (3.3)	(0.9, 8.2)
		Cycle 1	121	0 (0.0)	(0.0, 3.0)
		Cycle 2	120	0 (0.0)	(0.0, 3.0)
		Cycle 3	119	1 (0.8)	(0.0, 4.5)
		Cycle 4	115	0 (0.0)	(0.0, 3.0)
		Cycle 5	106	1 (0.8)	(0.0, 4.5)
		Cycle 6	103	0 (0.0)	(0.0, 3.0)
		Cycle 7	96	0 (0.0)	(0.0, 3.0)
		Cycle >= 8 and < 18	93	1 (0.8)	(0.0, 4.5)
		Cycle >= 18	54	1 (0.8)	(0.0, 4.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	6 (9.5)	(3.6, 19.6)
		Cycle 1	63	0 (0.0)	(0.0, 5.7)
		Cycle 2	61	0 (0.0)	(0.0, 5.7)
		Cycle 3	55	0 (0.0)	(0.0, 5.7)
		Cycle 4	54	1 (1.6)	(0.0, 8.5)
		Cycle 5	49	0 (0.0)	(0.0, 5.7)
		Cycle 6	49	0 (0.0)	(0.0, 5.7)
		Cycle 7	49	1 (1.6)	(0.0, 8.5)
		Cycle >= 8 and < 18	45	4 (6.3)	(1.8, 15.5)
		Cycle >= 18	21	0 (0.0)	(0.0, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	1 (2.0)	(0.0, 10.4)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	50	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	46	1 (2.0)	(0.0, 10.4)
		Cycle 6	44	0 (0.0)	(0.0, 7.0)
		Cycle 7	40	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	40	0 (0.0)	(0.0, 7.0)
		Cycle >= 18	24	0 (0.0)	(0.0, 7.0)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAS_SSI0: Incidence of serious adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	9 (6.8)	(3.1, 12.5)
		Cycle 1	133	0 (0.0)	(0.0, 2.7)
		Cycle 2	131	0 (0.0)	(0.0, 2.7)
		Cycle 3	124	1 (0.8)	(0.0, 4.1)
		Cycle 4	120	1 (0.8)	(0.0, 4.1)
		Cycle 5	109	0 (0.0)	(0.0, 2.7)
		Cycle 6	108	0 (0.0)	(0.0, 2.7)
		Cycle 7	105	1 (0.8)	(0.0, 4.1)
		Cycle >= 8 and < 18	98	5 (3.8)	(1.2, 8.6)
		Cycle >= 18	51	1 (0.8)	(0.0, 4.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

UE von besonderem Interesse – Interstitielle Lungenerkrankung (ILD), mit CTCAE-Grad < 3, Bewertung durch AC

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
Overall	Overall (N=184)	Any TEAE	184	23 (12.5)	(8.1, 18.2)
		Cycle 1	184	0 (0.0)	(0.0, 2.0)
		Cycle 2	181	2 (1.1)	(0.1, 3.9)
		Cycle 3	174	1 (0.5)	(0.0, 3.0)
		Cycle 4	169	1 (0.5)	(0.0, 3.0)
		Cycle 5	155	2 (1.1)	(0.1, 3.9)
		Cycle 6	152	4 (2.2)	(0.6, 5.5)
		Cycle 7	145	0 (0.0)	(0.0, 2.0)
		Cycle >= 8 and < 18	138	11 (6.0)	(3.0, 10.4)
		Cycle >= 18	75	4 (2.2)	(0.6, 5.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
A-Age classification 1	< 65 years (N=140)	Any TEAE	140	16 (11.4) (6.7, 17.9)
		Cycle 1	140	0 (0.0) (0.0, 2.6)
		Cycle 2	138	2 (1.4) (0.2, 5.1)
		Cycle 3	132	1 (0.7) (0.0, 3.9)
		Cycle 4	128	0 (0.0) (0.0, 2.6)
		Cycle 5	116	1 (0.7) (0.0, 3.9)
		Cycle 6	113	3 (2.1) (0.4, 6.1)
		Cycle 7	109	0 (0.0) (0.0, 2.6)
		Cycle >= 8 and < 18	103	8 (5.7) (2.5, 10.9)
		Cycle >= 18	56	2 (1.4) (0.2, 5.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
A-Age classification 1	>= 65 years (N=44)	Any TEAE	44	7 (15.9) (6.6, 30.1)
		Cycle 1	44	0 (0.0) (0.0, 8.0)
		Cycle 2	43	0 (0.0) (0.0, 8.0)
		Cycle 3	42	0 (0.0) (0.0, 8.0)
		Cycle 4	41	1 (2.3) (0.1, 12.0)
		Cycle 5	39	1 (2.3) (0.1, 12.0)
		Cycle 6	39	1 (2.3) (0.1, 12.0)
		Cycle 7	36	0 (0.0) (0.0, 8.0)
		Cycle >= 8 and < 18	35	3 (6.8) (1.4, 18.7)
		Cycle >= 18	19	2 (4.5) (0.6, 15.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	Asia (N=63)	Any TEAE	13 (20.6)	(11.5, 32.7)
		Cycle 1	0 (0.0)	(0.0, 5.7)
		Cycle 2	0 (0.0)	(0.0, 5.7)
		Cycle 3	0 (0.0)	(0.0, 5.7)
		Cycle 4	1 (1.6)	(0.0, 8.5)
		Cycle 5	1 (1.6)	(0.0, 8.5)
		Cycle 6	2 (3.2)	(0.4, 11.0)
		Cycle 7	0 (0.0)	(0.0, 5.7)
		Cycle >= 8 and < 18	6 (9.5)	(3.6, 19.6)
		Cycle >= 18	4 (6.3)	(1.8, 15.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	North America (N=53)	Any TEAE	53	3 (5.7) (1.2, 15.7)
		Cycle 1	53	0 (0.0) (0.0, 6.7)
		Cycle 2	53	0 (0.0) (0.0, 6.7)
		Cycle 3	52	0 (0.0) (0.0, 6.7)
		Cycle 4	49	0 (0.0) (0.0, 6.7)
		Cycle 5	44	0 (0.0) (0.0, 6.7)
		Cycle 6	42	2 (3.8) (0.5, 13.0)
		Cycle 7	40	0 (0.0) (0.0, 6.7)
		Cycle >= 8 and < 18	39	1 (1.9) (0.0, 10.1)
		Cycle >= 18	23	0 (0.0) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
B-Region	EU (N=68)	Any TEAE	68	7 (10.3) (4.2, 20.1)
		Cycle 1	68	0 (0.0) (0.0, 5.3)
		Cycle 2	67	2 (2.9) (0.4, 10.2)
		Cycle 3	64	1 (1.5) (0.0, 7.9)
		Cycle 4	62	0 (0.0) (0.0, 5.3)
		Cycle 5	56	1 (1.5) (0.0, 7.9)
		Cycle 6	55	0 (0.0) (0.0, 5.3)
		Cycle 7	52	0 (0.0) (0.0, 5.3)
		Cycle >= 8 and < 18	50	4 (5.9) (1.6, 14.4)
		Cycle >= 18	23	0 (0.0) (0.0, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
C-ECOG performance status	Status 0 (N=102)	Any TEAE	102	17 (16.7)	(10.0, 25.3)
		Cycle 1	102	0 (0.0)	(0.0, 3.6)
		Cycle 2	101	1 (1.0)	(0.0, 5.3)
		Cycle 3	100	1 (1.0)	(0.0, 5.3)
		Cycle 4	98	1 (1.0)	(0.0, 5.3)
		Cycle 5	94	2 (2.0)	(0.2, 6.9)
		Cycle 6	93	4 (3.9)	(1.1, 9.7)
		Cycle 7	88	0 (0.0)	(0.0, 3.6)
		Cycle >= 8 and < 18	86	7 (6.9)	(2.8, 13.6)
		Cycle >= 18	49	3 (2.9)	(0.6, 8.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
C-ECOG performance status	Status 1 (N=81)	Any TEAE	81	6 (7.4) (2.8, 15.4)
		Cycle 1	81	0 (0.0) (0.0, 4.5)
		Cycle 2	79	1 (1.2) (0.0, 6.7)
		Cycle 3	73	0 (0.0) (0.0, 4.5)
		Cycle 4	71	0 (0.0) (0.0, 4.5)
		Cycle 5	61	0 (0.0) (0.0, 4.5)
		Cycle 6	59	0 (0.0) (0.0, 4.5)
		Cycle 7	57	0 (0.0) (0.0, 4.5)
		Cycle >= 8 and < 18	52	4 (4.9) (1.4, 12.2)
		Cycle >= 18	26	1 (1.2) (0.0, 6.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
D-Baseline sum of diameters of target lesions < 5 cm (N=73)	Any TEAE	73	10 (13.7)	(6.8, 23.8)
	Cycle 1	73	0 (0.0)	(0.0, 4.9)
	Cycle 2	72	2 (2.7)	(0.3, 9.5)
	Cycle 3	70	1 (1.4)	(0.0, 7.4)
	Cycle 4	65	0 (0.0)	(0.0, 4.9)
	Cycle 5	60	1 (1.4)	(0.0, 7.4)
	Cycle 6	59	0 (0.0)	(0.0, 4.9)
	Cycle 7	58	0 (0.0)	(0.0, 4.9)
	Cycle >= 8 and < 18	53	5 (6.8)	(2.3, 15.3)
	Cycle >= 18	33	2 (2.7)	(0.3, 9.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
D-Baseline sum of diameters of target lesions	>= 5 cm (N=97)			
	Any TEAE	97	9 (9.3)	(4.3, 16.9)
	Cycle 1	97	0 (0.0)	(0.0, 3.7)
	Cycle 2	95	0 (0.0)	(0.0, 3.7)
	Cycle 3	90	0 (0.0)	(0.0, 3.7)
	Cycle 4	90	1 (1.0)	(0.0, 5.6)
	Cycle 5	81	0 (0.0)	(0.0, 3.7)
	Cycle 6	79	3 (3.1)	(0.6, 8.8)
	Cycle 7	74	0 (0.0)	(0.0, 3.7)
	Cycle >= 8 and < 18	72	4 (4.1)	(1.1, 10.2)
	Cycle >= 18	34	1 (1.0)	(0.0, 5.6)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
E-HER2 Status	IHC3+ (N=154)	Any TEAE	154	21 (13.6)	(8.6, 20.1)
		Cycle 1	154	0 (0.0)	(0.0, 2.4)
		Cycle 2	152	2 (1.3)	(0.2, 4.6)
		Cycle 3	146	1 (0.6)	(0.0, 3.6)
		Cycle 4	141	1 (0.6)	(0.0, 3.6)
		Cycle 5	129	2 (1.3)	(0.2, 4.6)
		Cycle 6	127	3 (1.9)	(0.4, 5.6)
		Cycle 7	121	0 (0.0)	(0.0, 2.4)
		Cycle >= 8 and < 18	114	10 (6.5)	(3.2, 11.6)
		Cycle >= 18	69	4 (2.6)	(0.7, 6.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
E-HER2 Status	ISH+ EXCEPT IHC3+ (N=28)	Any TEAE	28	2 (7.1) (0.9, 23.5)
		Cycle 1	28	0 (0.0) (0.0, 12.3)
		Cycle 2	27	0 (0.0) (0.0, 12.3)
		Cycle 3	26	0 (0.0) (0.0, 12.3)
		Cycle 4	26	0 (0.0) (0.0, 12.3)
		Cycle 5	24	0 (0.0) (0.0, 12.3)
		Cycle 6	23	1 (3.6) (0.1, 18.3)
		Cycle 7	22	0 (0.0) (0.0, 12.3)
		Cycle >= 8 and < 18	22	1 (3.6) (0.1, 18.3)
		Cycle >= 18	5	0 (0.0) (0.0, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
F-Estrogen receptors	Positive (N=93)	Any TEAE	93	13 (14.0)	(7.7, 22.7)
		Cycle 1	93	0 (0.0)	(0.0, 3.9)
		Cycle 2	92	1 (1.1)	(0.0, 5.8)
		Cycle 3	87	0 (0.0)	(0.0, 3.9)
		Cycle 4	84	0 (0.0)	(0.0, 3.9)
		Cycle 5	80	2 (2.2)	(0.3, 7.6)
		Cycle 6	78	2 (2.2)	(0.3, 7.6)
		Cycle 7	75	0 (0.0)	(0.0, 3.9)
		Cycle >= 8 and < 18	73	6 (6.5)	(2.4, 13.5)
		Cycle >= 18	34	3 (3.2)	(0.7, 9.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
F-Estrogen receptors	Negative (N=88)	Any TEAE	88	10 (11.4)	(5.6, 19.9)
		Cycle 1	88	0 (0.0)	(0.0, 4.1)
		Cycle 2	86	1 (1.1)	(0.0, 6.2)
		Cycle 3	85	1 (1.1)	(0.0, 6.2)
		Cycle 4	84	1 (1.1)	(0.0, 6.2)
		Cycle 5	74	0 (0.0)	(0.0, 4.1)
		Cycle 6	73	2 (2.3)	(0.3, 8.0)
		Cycle 7	69	0 (0.0)	(0.0, 4.1)
		Cycle >= 8 and < 18	64	5 (5.7)	(1.9, 12.8)
		Cycle >= 18	41	1 (1.1)	(0.0, 6.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
G-Progesterone receptors	Positive (N=51)	Any TEAE	51	9 (17.6)	(8.4, 30.9)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	1 (2.0)	(0.0, 10.4)
		Cycle 3	49	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	47	2 (3.9)	(0.5, 13.5)
		Cycle 6	46	1 (2.0)	(0.0, 10.4)
		Cycle 7	45	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	44	3 (5.9)	(1.2, 16.2)
		Cycle >= 18	21	3 (5.9)	(1.2, 16.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
G-Progesterone receptors	Negative (N=125)	Any TEAE	125	13 (10.4)	(5.7, 17.1)
		Cycle 1	125	0 (0.0)	(0.0, 2.9)
		Cycle 2	123	1 (0.8)	(0.0, 4.4)
		Cycle 3	118	1 (0.8)	(0.0, 4.4)
		Cycle 4	114	1 (0.8)	(0.0, 4.4)
		Cycle 5	103	0 (0.0)	(0.0, 2.9)
		Cycle 6	101	3 (2.4)	(0.5, 6.9)
		Cycle 7	95	0 (0.0)	(0.0, 2.9)
		Cycle >= 8 and < 18	90	7 (5.6)	(2.3, 11.2)
		Cycle >= 18	52	1 (0.8)	(0.0, 4.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
H-Hormone receptors	Positive (N=97)	Any TEAE	97	14 (14.4)	(8.1, 23.0)
		Cycle 1	97	0 (0.0)	(0.0, 3.7)
		Cycle 2	96	1 (1.0)	(0.0, 5.6)
		Cycle 3	91	0 (0.0)	(0.0, 3.7)
		Cycle 4	88	0 (0.0)	(0.0, 3.7)
		Cycle 5	84	2 (2.1)	(0.3, 7.3)
		Cycle 6	82	2 (2.1)	(0.3, 7.3)
		Cycle 7	79	0 (0.0)	(0.0, 3.7)
		Cycle >= 8 and < 18	76	6 (6.2)	(2.3, 13.0)
		Cycle >= 18	36	4 (4.1)	(1.1, 10.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
H-Hormone receptors	Negative (N=83)	Any TEAE	83	9 (10.8)	(5.1, 19.6)
		Cycle 1	83	0 (0.0)	(0.0, 4.3)
		Cycle 2	81	1 (1.2)	(0.0, 6.5)
		Cycle 3	80	1 (1.2)	(0.0, 6.5)
		Cycle 4	79	1 (1.2)	(0.0, 6.5)
		Cycle 5	69	0 (0.0)	(0.0, 4.3)
		Cycle 6	68	2 (2.4)	(0.3, 8.4)
		Cycle 7	64	0 (0.0)	(0.0, 4.3)
		Cycle >= 8 and < 18	60	5 (6.0)	(2.0, 13.5)
		Cycle >= 18	38	0 (0.0)	(0.0, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
I-Renal impairment	Normal (N=90)			
	Any TEAE	90	8 (8.9)	(3.9, 16.8)
	Cycle 1	90	0 (0.0)	(0.0, 4.0)
	Cycle 2	89	1 (1.1)	(0.0, 6.0)
	Cycle 3	85	0 (0.0)	(0.0, 4.0)
	Cycle 4	85	0 (0.0)	(0.0, 4.0)
	Cycle 5	76	1 (1.1)	(0.0, 6.0)
	Cycle 6	73	0 (0.0)	(0.0, 4.0)
	Cycle 7	72	0 (0.0)	(0.0, 4.0)
	Cycle >= 8 and < 18	69	4 (4.4)	(1.2, 11.0)
	Cycle >= 18	41	2 (2.2)	(0.3, 7.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Mild (N=69)	Any TEAE	69	8 (11.6)	(5.1, 21.6)
		Cycle 1	69	0 (0.0)	(0.0, 5.2)
		Cycle 2	68	0 (0.0)	(0.0, 5.2)
		Cycle 3	66	0 (0.0)	(0.0, 5.2)
		Cycle 4	63	0 (0.0)	(0.0, 5.2)
		Cycle 5	59	1 (1.4)	(0.0, 7.8)
		Cycle 6	59	2 (2.9)	(0.4, 10.1)
		Cycle 7	56	0 (0.0)	(0.0, 5.2)
		Cycle >= 8 and < 18	54	5 (7.2)	(2.4, 16.1)
		Cycle >= 18	27	1 (1.4)	(0.0, 7.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
I-Renal impairment	Moderate (N=25)	Any TEAE	25	7 (28.0)	(12.1, 49.4)
		Cycle 1	25	0 (0.0)	(0.0, 13.7)
		Cycle 2	24	1 (4.0)	(0.1, 20.4)
		Cycle 3	23	1 (4.0)	(0.1, 20.4)
		Cycle 4	21	1 (4.0)	(0.1, 20.4)
		Cycle 5	20	0 (0.0)	(0.0, 13.7)
		Cycle 6	20	2 (8.0)	(1.0, 26.0)
		Cycle 7	17	0 (0.0)	(0.0, 13.7)
		Cycle >= 8 and < 18	15	2 (8.0)	(1.0, 26.0)
		Cycle >= 18	7	1 (4.0)	(0.1, 20.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
J-Hepatic impairment	Normal (N=105)	Any TEAE	105	17 (16.2)	(9.7, 24.7)
		Cycle 1	105	0 (0.0)	(0.0, 3.5)
		Cycle 2	104	1 (1.0)	(0.0, 5.2)
		Cycle 3	102	1 (1.0)	(0.0, 5.2)
		Cycle 4	98	1 (1.0)	(0.0, 5.2)
		Cycle 5	90	2 (1.9)	(0.2, 6.7)
		Cycle 6	89	2 (1.9)	(0.2, 6.7)
		Cycle 7	87	0 (0.0)	(0.0, 3.5)
		Cycle >= 8 and < 18	84	9 (8.6)	(4.0, 15.6)
		Cycle >= 18	44	3 (2.9)	(0.6, 8.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
J-Hepatic impairment	Mild (N=76)	Any TEAE	76	6 (7.9) (3.0, 16.4)
		Cycle 1	76	0 (0.0) (0.0, 4.7)
		Cycle 2	74	1 (1.3) (0.0, 7.1)
		Cycle 3	69	0 (0.0) (0.0, 4.7)
		Cycle 4	68	0 (0.0) (0.0, 4.7)
		Cycle 5	63	0 (0.0) (0.0, 4.7)
		Cycle 6	61	2 (2.6) (0.3, 9.2)
		Cycle 7	56	0 (0.0) (0.0, 4.7)
		Cycle >= 8 and < 18	54	2 (2.6) (0.3, 9.2)
		Cycle >= 18	31	1 (1.3) (0.0, 7.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
K-Brain metastases	Yes (N=24)	Any TEAE	24	5 (20.8)	(7.1, 42.2)
		Cycle 1	24	0 (0.0)	(0.0, 14.2)
		Cycle 2	23	0 (0.0)	(0.0, 14.2)
		Cycle 3	22	0 (0.0)	(0.0, 14.2)
		Cycle 4	22	0 (0.0)	(0.0, 14.2)
		Cycle 5	19	1 (4.2)	(0.1, 21.1)
		Cycle 6	18	1 (4.2)	(0.1, 21.1)
		Cycle 7	18	0 (0.0)	(0.0, 14.2)
		Cycle >= 8 and < 18	18	2 (8.3)	(1.0, 27.0)
		Cycle >= 18	10	1 (4.2)	(0.1, 21.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
K-Brain metastases	No (N=160)	Any TEAE	160	18 (11.3)	(6.8, 17.2)
		Cycle 1	160	0 (0.0)	(0.0, 2.3)
		Cycle 2	158	2 (1.3)	(0.2, 4.4)
		Cycle 3	152	1 (0.6)	(0.0, 3.4)
		Cycle 4	147	1 (0.6)	(0.0, 3.4)
		Cycle 5	136	1 (0.6)	(0.0, 3.4)
		Cycle 6	134	3 (1.9)	(0.4, 5.4)
		Cycle 7	127	0 (0.0)	(0.0, 2.3)
		Cycle >= 8 and < 18	120	9 (5.6)	(2.6, 10.4)
		Cycle >= 18	65	3 (1.9)	(0.4, 5.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
L-Bone metastases	Yes (N=53)	Any TEAE	53	8 (15.1)	(6.7, 27.6)
		Cycle 1	53	0 (0.0)	(0.0, 6.7)
		Cycle 2	52	1 (1.9)	(0.0, 10.1)
		Cycle 3	49	1 (1.9)	(0.0, 10.1)
		Cycle 4	48	0 (0.0)	(0.0, 6.7)
		Cycle 5	43	1 (1.9)	(0.0, 10.1)
		Cycle 6	42	1 (1.9)	(0.0, 10.1)
		Cycle 7	41	0 (0.0)	(0.0, 6.7)
		Cycle >= 8 and < 18	39	4 (7.5)	(2.1, 18.2)
		Cycle >= 18	18	1 (1.9)	(0.0, 10.1)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
L-Bone metastases	No (N=131)	Any TEAE	131	15 (11.5)	(6.6, 18.2)
		Cycle 1	131	0 (0.0)	(0.0, 2.8)
		Cycle 2	129	1 (0.8)	(0.0, 4.2)
		Cycle 3	125	0 (0.0)	(0.0, 2.8)
		Cycle 4	121	1 (0.8)	(0.0, 4.2)
		Cycle 5	112	1 (0.8)	(0.0, 4.2)
		Cycle 6	110	3 (2.3)	(0.5, 6.5)
		Cycle 7	104	0 (0.0)	(0.0, 2.8)
		Cycle >= 8 and < 18	99	7 (5.3)	(2.2, 10.7)
		Cycle >= 18	57	3 (2.3)	(0.5, 6.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
M-History of visceral disease	Yes (N=169)	Any TEAE	169	21 (12.4)	(7.9, 18.4)
		Cycle 1	169	0 (0.0)	(0.0, 2.2)
		Cycle 2	166	2 (1.2)	(0.1, 4.2)
		Cycle 3	159	1 (0.6)	(0.0, 3.3)
		Cycle 4	154	1 (0.6)	(0.0, 3.3)
		Cycle 5	142	2 (1.2)	(0.1, 4.2)
		Cycle 6	139	4 (2.4)	(0.6, 5.9)
		Cycle 7	132	0 (0.0)	(0.0, 2.2)
		Cycle >= 8 and < 18	125	9 (5.3)	(2.5, 9.9)
		Cycle >= 18	70	4 (2.4)	(0.6, 5.9)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
M-History of visceral disease	No (N=15)	Any TEAE	15	2 (13.3)	(1.7, 40.5)
		Cycle 1	15	0 (0.0)	(0.0, 21.8)
		Cycle 2	15	0 (0.0)	(0.0, 21.8)
		Cycle 3	15	0 (0.0)	(0.0, 21.8)
		Cycle 4	15	0 (0.0)	(0.0, 21.8)
		Cycle 5	13	0 (0.0)	(0.0, 21.8)
		Cycle 6	13	0 (0.0)	(0.0, 21.8)
		Cycle 7	13	0 (0.0)	(0.0, 21.8)
		Cycle >= 8 and < 18	13	2 (13.3)	(1.7, 40.5)
		Cycle >= 18	5	0 (0.0)	(0.0, 21.8)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
N-T-DM1 last therapy	Yes (N=56)	Any TEAE	56	6 (10.7)	(4.0, 21.9)
		Cycle 1	56	0 (0.0)	(0.0, 6.4)
		Cycle 2	55	1 (1.8)	(0.0, 9.6)
		Cycle 3	54	0 (0.0)	(0.0, 6.4)
		Cycle 4	53	0 (0.0)	(0.0, 6.4)
		Cycle 5	49	0 (0.0)	(0.0, 6.4)
		Cycle 6	48	0 (0.0)	(0.0, 6.4)
		Cycle 7	48	0 (0.0)	(0.0, 6.4)
		Cycle >= 8 and < 18	45	3 (5.4)	(1.1, 14.9)
		Cycle >= 18	32	2 (3.6)	(0.4, 12.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
N-T-DM1 last therapy	No (N=128)	Any TEAE	128	17 (13.3)	(7.9, 20.4)
		Cycle 1	128	0 (0.0)	(0.0, 2.8)
		Cycle 2	126	1 (0.8)	(0.0, 4.3)
		Cycle 3	120	1 (0.8)	(0.0, 4.3)
		Cycle 4	116	1 (0.8)	(0.0, 4.3)
		Cycle 5	106	2 (1.6)	(0.2, 5.5)
		Cycle 6	104	4 (3.1)	(0.9, 7.8)
		Cycle 7	97	0 (0.0)	(0.0, 2.8)
		Cycle >= 8 and < 18	93	8 (6.3)	(2.7, 11.9)
		Cycle >= 18	43	2 (1.6)	(0.2, 5.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n(%)	95% CI
O-Prior treatment lines	< 3 lines (N=17)	Any TEAE	17	2 (11.8)
		Cycle 1	17	0 (0.0)
		Cycle 2	17	0 (0.0)
		Cycle 3	17	0 (0.0)
		Cycle 4	17	0 (0.0)
		Cycle 5	17	0 (0.0)
		Cycle 6	16	0 (0.0)
		Cycle 7	16	0 (0.0)
		Cycle >= 8 and < 18	16	0 (0.0)
		Cycle >= 18	14	2 (11.8)
				(1.5, 36.4)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
O-Prior treatment lines	>= 3 lines (N=167)			
	Any TEAE	167	21 (12.6)	(8.0, 18.6)
	Cycle 1	167	0 (0.0)	(0.0, 2.2)
	Cycle 2	164	2 (1.2)	(0.1, 4.3)
	Cycle 3	157	1 (0.6)	(0.0, 3.3)
	Cycle 4	152	1 (0.6)	(0.0, 3.3)
	Cycle 5	138	2 (1.2)	(0.1, 4.3)
	Cycle 6	136	4 (2.4)	(0.7, 6.0)
	Cycle 7	129	0 (0.0)	(0.0, 2.2)
	Cycle >= 8 and < 18	122	11 (6.6)	(3.3, 11.5)
	Cycle >= 18	61	2 (1.2)	(0.1, 4.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup	Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
			n (%)	95% CI
P-Best Response to T-DM1 therapy	CR/PR/SD (N=79)			
	Any TEAE	79	10 (12.7)	(6.2, 22.0)
	Cycle 1	79	0 (0.0)	(0.0, 4.6)
	Cycle 2	78	2 (2.5)	(0.3, 8.8)
	Cycle 3	75	1 (1.3)	(0.0, 6.9)
	Cycle 4	73	0 (0.0)	(0.0, 4.6)
	Cycle 5	70	1 (1.3)	(0.0, 6.9)
	Cycle 6	69	1 (1.3)	(0.0, 6.9)
	Cycle 7	68	0 (0.0)	(0.0, 4.6)
	Cycle >= 8 and < 18	65	4 (5.1)	(1.4, 12.5)
	Cycle >= 18	37	3 (3.8)	(0.8, 10.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
P-Best Response to T-DM1 therapy	PD (N=66)	Any TEAE	66	11 (16.7)	(8.6, 27.9)
		Cycle 1	66	0 (0.0)	(0.0, 5.4)
		Cycle 2	66	0 (0.0)	(0.0, 5.4)
		Cycle 3	64	0 (0.0)	(0.0, 5.4)
		Cycle 4	61	1 (1.5)	(0.0, 8.2)
		Cycle 5	55	1 (1.5)	(0.0, 8.2)
		Cycle 6	53	1 (1.5)	(0.0, 8.2)
		Cycle 7	51	0 (0.0)	(0.0, 5.4)
		Cycle >= 8 and < 18	51	7 (10.6)	(4.4, 20.6)
		Cycle >= 18	23	1 (1.5)	(0.0, 8.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
Q-Prior pertuzumab	Yes (N=121)	Any TEAE	121	16 (13.2)	(7.8, 20.6)
		Cycle 1	121	0 (0.0)	(0.0, 3.0)
		Cycle 2	120	1 (0.8)	(0.0, 4.5)
		Cycle 3	119	1 (0.8)	(0.0, 4.5)
		Cycle 4	115	1 (0.8)	(0.0, 4.5)
		Cycle 5	106	2 (1.7)	(0.2, 5.8)
		Cycle 6	103	4 (3.3)	(0.9, 8.2)
		Cycle 7	96	0 (0.0)	(0.0, 3.0)
		Cycle >= 8 and < 18	93	5 (4.1)	(1.4, 9.4)
		Cycle >= 18	54	4 (3.3)	(0.9, 8.2)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
Q-Prior pertuzumab	No (N=63)	Any TEAE	63	7 (11.1)	(4.6, 21.6)
		Cycle 1	63	0 (0.0)	(0.0, 5.7)
		Cycle 2	61	1 (1.6)	(0.0, 8.5)
		Cycle 3	55	0 (0.0)	(0.0, 5.7)
		Cycle 4	54	0 (0.0)	(0.0, 5.7)
		Cycle 5	49	0 (0.0)	(0.0, 5.7)
		Cycle 6	49	0 (0.0)	(0.0, 5.7)
		Cycle 7	49	0 (0.0)	(0.0, 5.7)
		Cycle >= 8 and < 18	45	6 (9.5)	(3.6, 19.6)
		Cycle >= 18	21	0 (0.0)	(0.0, 5.7)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n(%)	95% CI
R-Pertuzumab before line 3	Yes (N=51)	Any TEAE	51	7 (13.7)	(5.7, 26.3)
		Cycle 1	51	0 (0.0)	(0.0, 7.0)
		Cycle 2	50	0 (0.0)	(0.0, 7.0)
		Cycle 3	50	0 (0.0)	(0.0, 7.0)
		Cycle 4	49	0 (0.0)	(0.0, 7.0)
		Cycle 5	46	1 (2.0)	(0.0, 10.4)
		Cycle 6	44	1 (2.0)	(0.0, 10.4)
		Cycle 7	40	0 (0.0)	(0.0, 7.0)
		Cycle >= 8 and < 18	40	3 (5.9)	(1.2, 16.2)
		Cycle >= 18	24	2 (3.9)	(0.5, 13.5)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae

Table T3ILDAN_SSI0: Incidence of non-severe adjudicated interstitial lung disease overall and by subgroup
Safety Analysis Set

Subgroup		Time Period	N patients in cycle	Overall 5.4 mg/kg SAF (N=184)	
				n (%)	95% CI
R-Pertuzumab before line 3	No (N=133)	Any TEAE	133	16 (12.0)	(7.0, 18.8)
		Cycle 1	133	0 (0.0)	(0.0, 2.7)
		Cycle 2	131	2 (1.5)	(0.2, 5.3)
		Cycle 3	124	1 (0.8)	(0.0, 4.1)
		Cycle 4	120	1 (0.8)	(0.0, 4.1)
		Cycle 5	109	1 (0.8)	(0.0, 4.1)
		Cycle 6	108	3 (2.3)	(0.5, 6.5)
		Cycle 7	105	0 (0.0)	(0.0, 2.7)
		Cycle >= 8 and < 18	98	8 (6.0)	(2.6, 11.5)
		Cycle >= 18	51	2 (1.5)	(0.2, 5.3)

Notes: Percents are based on the number of subjects in the Safety Analysis Set within the specified subgroup.
Adverse events were coded using the MedDRA dictionary, Version 20.1.
If a subject has more than one event per cycle, the subject is counted once at each level of summation.
TEAE = Treatment Emergent Adverse Event

Source Data: adam.adae