Sacituzumab Govitecan (IMMU-132), an Anti-Trop-2-SN-38 Antibody-Drug Conjugate, as ≥3rd-line Therapeutic Option for Patients With Relapsed/Refractory Metastatic Triple-Negative Breast Cancer (mTNBC): Efficacy Results

Aditya Bardia,[1] Linda T. Vahdat,[2,†] Jennifer R. Diamond,[3] Kevin Kalinsky,[4] Joyce O'Shaughnessy,[5] Rebecca L. Moroose,[6] Steven J. Isakoff,[1] Sara M. Tolaney,[7] Alessandro D. Santin,[8] Vandana Abramson,[9] Nikita C. Shah,[6] Serengulam V. Govindan,[10] Pius Maliakal,[10] Robert M. Sharkey,[10] William A. Wegener,[10] David M. Goldenberg,[10] Ingrid A. Mayer[9]

[1]Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA; [2]Weill Cornell Medicine, New York, NY; [3]University of Colorado Cancer Center, Aurora, CO; [4]Columbia University-Herbert Irving Comprehensive Cancer Center, New York, NY; [5]Texas Oncology, Baylor University Medical Center, US Oncology, Dallas, TX; [6]UF Health Cancer Center, Orlando, FL; [7]The Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA; [8]Yale University School of Medicine, New Haven, CT; [9]Vanderbilt-Ingram Cancer Center, Nashville, TN; [10]Immunomedics, Inc., Morris Plains, NJ; [†]Current affiliation: Memorial Sloan Kettering Cancer Center, New York, NY.

Immunomedics

40 YEAR ANNIVERSARY SAN ANTONIO BREAST CANCER SYMPOSIUM®

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

Background

- Metastatic triple-negative breast cancer (mTNBC) is an aggressive disease with poor prognosis that disproportionally affects young women
  - Visceral and brain metastases are very common
- No single standard chemotherapy available for relapsed/refractory mTNBC
  - Response rates with standard chemotherapy are low (~10-15%)
  - Median progression-free survival (PFS) is ~2-3 months with standard therapies (capecitabine, cisplatin or carboplatin, eribulin, nab-paclitaxel)
- Currently, there is a large unmet need in the breast cancer community

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

Low Response Rates in Pretreated mTNBC

Drug	Phase	N	Population	ORR, %	PFS, months	OS, months	Source
1st-line treatment							
Carboplatin	III	188	1st line	31	3.1	12.4	Tutt A, SABCS 2014
Docetaxel	III	188	1st line	36	4.5	12.3	Tutt A, SABCS 2014
Cisplatin/ Carboplatin	II	86	1st line (80.2%)	26	2.9	11.0	Isakoff SJ, J Clin Oncol, 2015
≥1st-line treatment							
Ixabepilone	II (pooled analysis)	60	Resist to AC-T or just to T	6-17	1.6-2.7	--	Perez EA, Breast Cancer Res Treat 2010
Capecitabine	III (pooled analysis)	208	Prior A, T or resist to A, T	15	1.7	--	Perez EA, Breast Cancer Res Treat 2010
Eribulin	III (pooled analysis)	199	≥1 prior chemo	11	2.8	12.4	Pivot X, Ann Oncol 2016

Includes breast cancer drugs with data from Phase II/III trials with minimum mTNBC sample size ≥60; ORR and PFS data

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

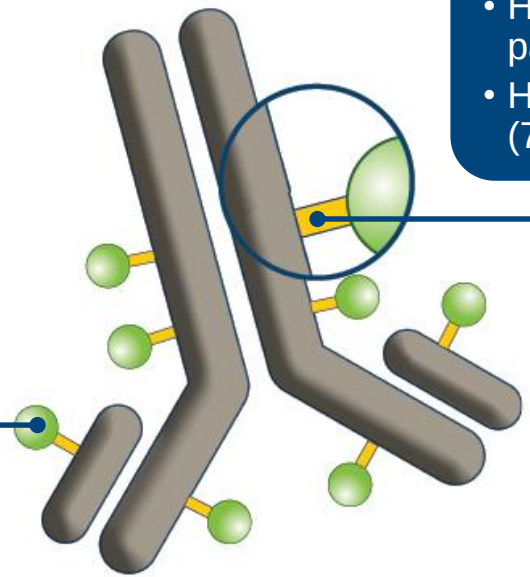
Sacituzumab Govitecan Antibody-Drug Conjugate (ADC)

Humanized anti-Trop-2 antibody

- Targets Trop-2, an epithelial antigen expressed on many solid cancers, including mTNBC

Linker for SN-38

- Hydrolysable linker for payload release
- High drug-to-antibody ratio (7.5:1)



SN-38 payload

- SN-38 more potent than parent compound, irinotecan
- ADC delivers up to 136-fold more SN-38 than irinotecan *in vivo*

Immunomedics

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

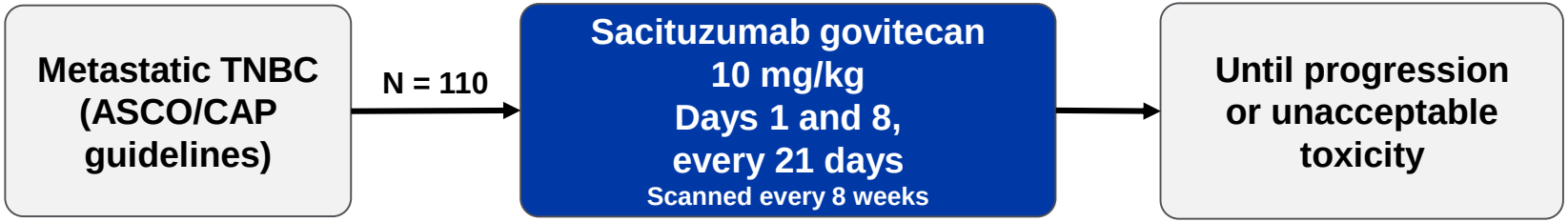
Clinical Trial Experience

- Preliminary results in 69 patients with mTNBC showed an objective response rate of 30%, which was published earlier this year in the *Journal of Clinical Oncology*[1]
- In 2016, sacituzumab govitecan was awarded breakthrough therapy designation by the FDA, and enrollment was resumed in a more defined population in ≥3rd-line setting
- 110 mTNBC patients were treated with sacituzumab govitecan 10 mg/kg on days 1 and 8 every 21 days until progression or unacceptable toxicity
  - Includes 53 of 69 patients who received ≥2 prior therapies from previously reported study

1. Bardia et al. *J Clin Oncol.* 2017;35:2141-2148.

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

Single-Arm, Open-Label Study Design



Key Eligibility Criteria

- Adults, ≥18 years of age
- ECOG 0-1
- ≥2 prior therapies in metastatic setting or >1 therapy if progressed within 12 months of (neo)adjuvant therapy
- Prior taxane therapy
- Measurable disease

Evaluations

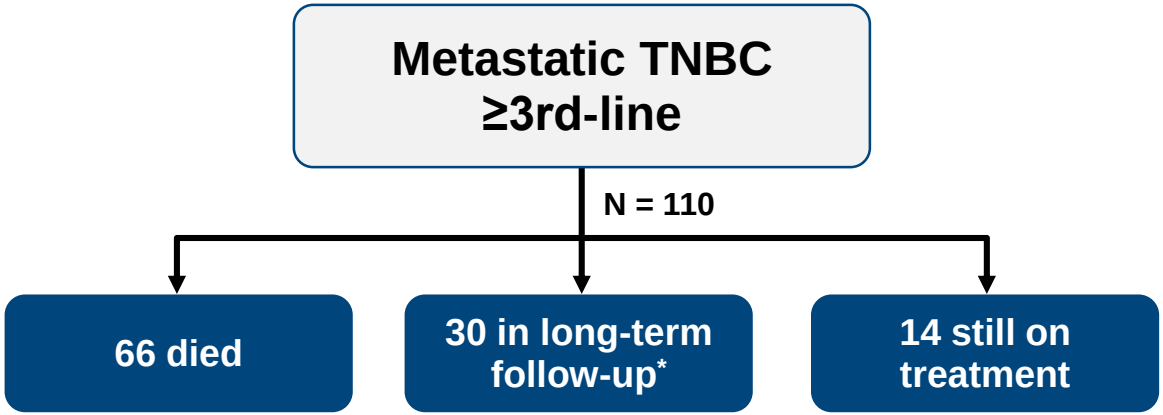
- Response evaluation by investigators
- Blinded independent central review of all CRs, PRs, and ≥20% tumor reductions
- Other evaluations: safety, immunogenicity, Trop-2 expression

Immunomedics

SAN ANTONIO BREAST CANCER SYMPOSIUM

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

Patient Disposition and Treatment



- Enrollment between Jul 2013 and Feb 2017. Data cutoff date of June 30, 2017.
- Patients received a median of 14.5 doses (range: 1-88) over a median duration of 4.9 months (range: 0.2-32.1)

*Includes 2 patients who were lost to follow up

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

Demographics and Patient Characteristics

	N = 110
Female/male, n	109/1
Median age, years (range)	55 (31-81)
Race	
White	75%
Black	7%
Asian	4%
Other	4%
Not specified	10%
ECOG performance status	
0	30%
1	70%
Median time from metastatic disease to study entry, years (range)	1.5 (0.2-9.8)
≥3rd line for metastatic disease	100%
3rd line*	41%
≥4th line	59%

	N = 110
Prior chemotherapy drugs**	
Taxanes	98%
Anthracyclines	86%
Cyclophosphamide	85%
Platinum agents	75%
Gemcitabine	57%
Fluoropyrimidine agents	51%
Eribulin	45%
Vinorelbine	15%
Prior checkpoint inhibitors	17%
Sites of metastatic disease at study entry***	
Lung/mediastinum	58%
Liver	46%
Bone	45%
Chest wall	24%

*2 patients who progressed within 12 months of (neo)adjuvant therapy only received one line in the metastatic setting;
**Used in >10% patients; ***Metastatic sites reported in >20% patients

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

Adverse Events (Regardless of Causality)

- AEs were managed with supportive medication or dose modifications
  - 25% of patients had dose modifications, predominantly to 7.5 mg/kg
- Two patients (1.8%) discontinued due to AEs (grade 3 transient infusion reaction/ grade 2 fatigue)
- There were no treatment-related deaths

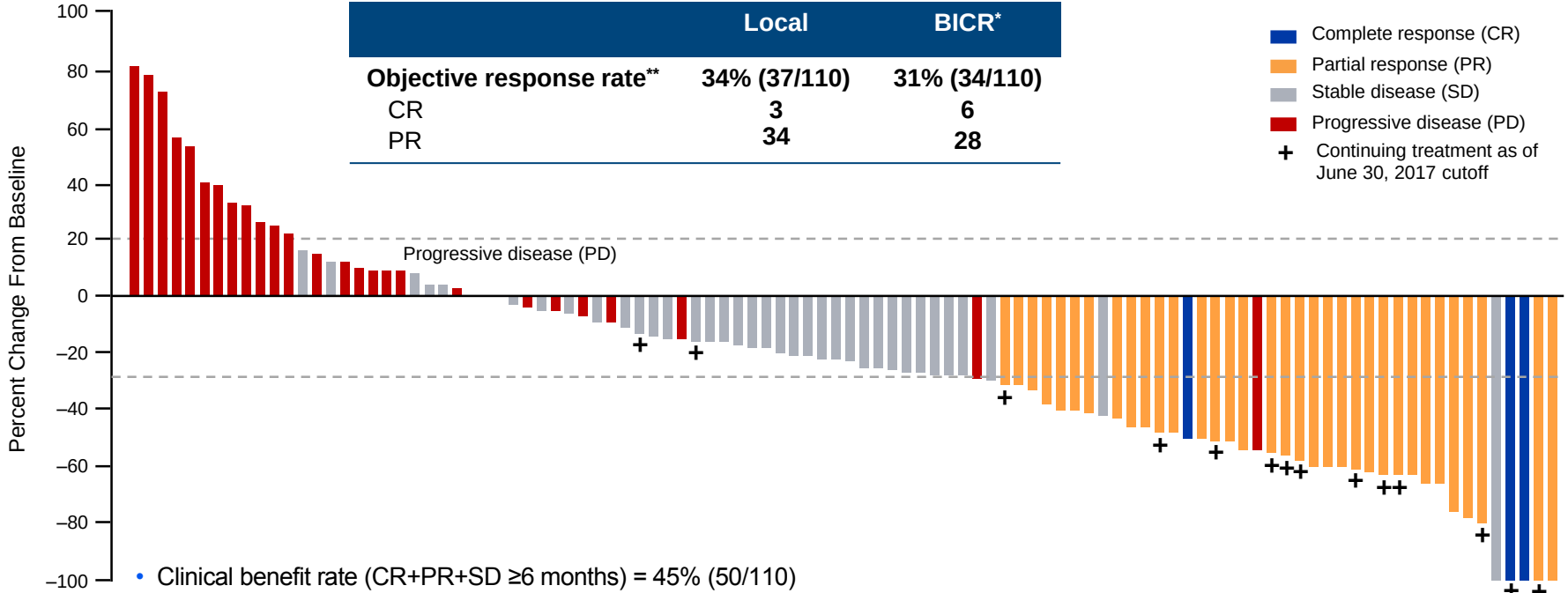
Body system	Adverse event (AE)	All grades	Grade 3 or 4
Hematologic	Neutropenia	63%	41%
	Febrile neutropenia	8%	7%
	Anemia	52%	10%
	Leukopenia	24%	14%
Gastrointestinal	Nausea	63%	5%
	Diarrhea	56%	8%
	Vomiting	46%	5%
	Constipation	32%	1%
Other	Fatigue	50%	7%
	Alopecia	36%	NA
	Decreased appetite	30%	0%
	Hyperglycemia	23%	4%
	Hypomagnesemia	21%	1%
	Hypophosphatemia	15%	8%

Includes all events >20% (all grades) or >5% (grade 3 or 4); NA = not applicable.

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

Tumor Response to Treatment

	Local	BICR*
Objective response rate**	**34% (37/110)**	**31% (34/110)**
CR	**3**	**6**
PR	**34**	**28**



- Clinical benefit rate (CR+PR+SD ≥6 months) = 45% (50/110)
- 74% (75/102) of patients with at least one CT response assessment had reduction of target lesions (sum of diameters)***
- 102 patients had ≥1 scheduled CT response assessment. 8 patients withdrew prior to assessment (4 PD, 4 MRI brain metastases)

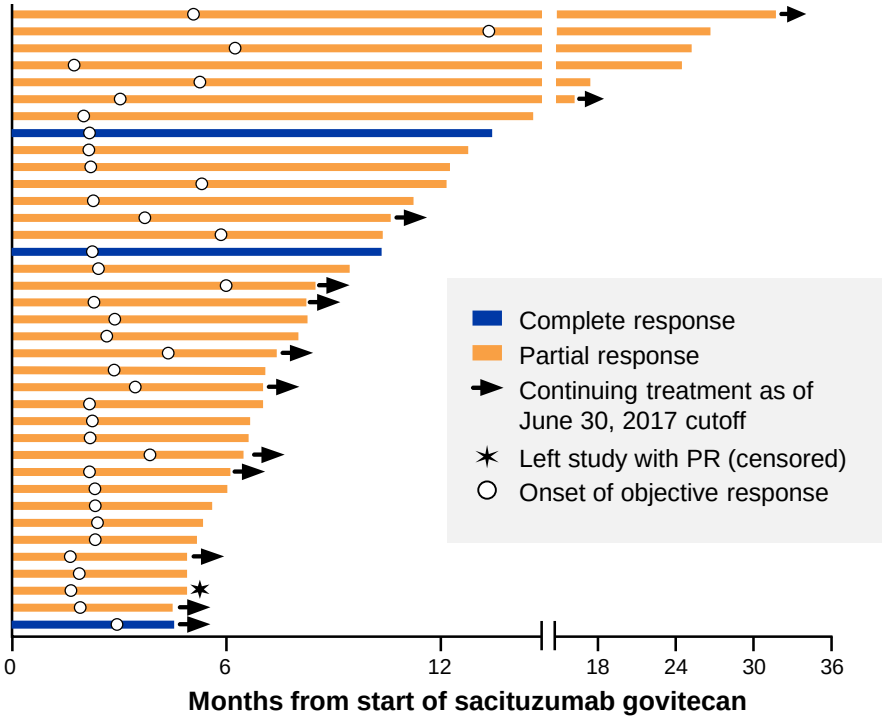
*Patients with at least 20% tumor reduction (n = 56) were reviewed; **Confirmed objective response rate per RECIST; ***Waterfall is based on local assessment; BICR = Blinded Independent Adjudicated Central Review.

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

Response Onset and Durability (n = 37)

	Local	BICR*
Median duration of response, months (95% CI)	**7.6** (4.8, 11.3)	**9.1** (4.1, 14.3)

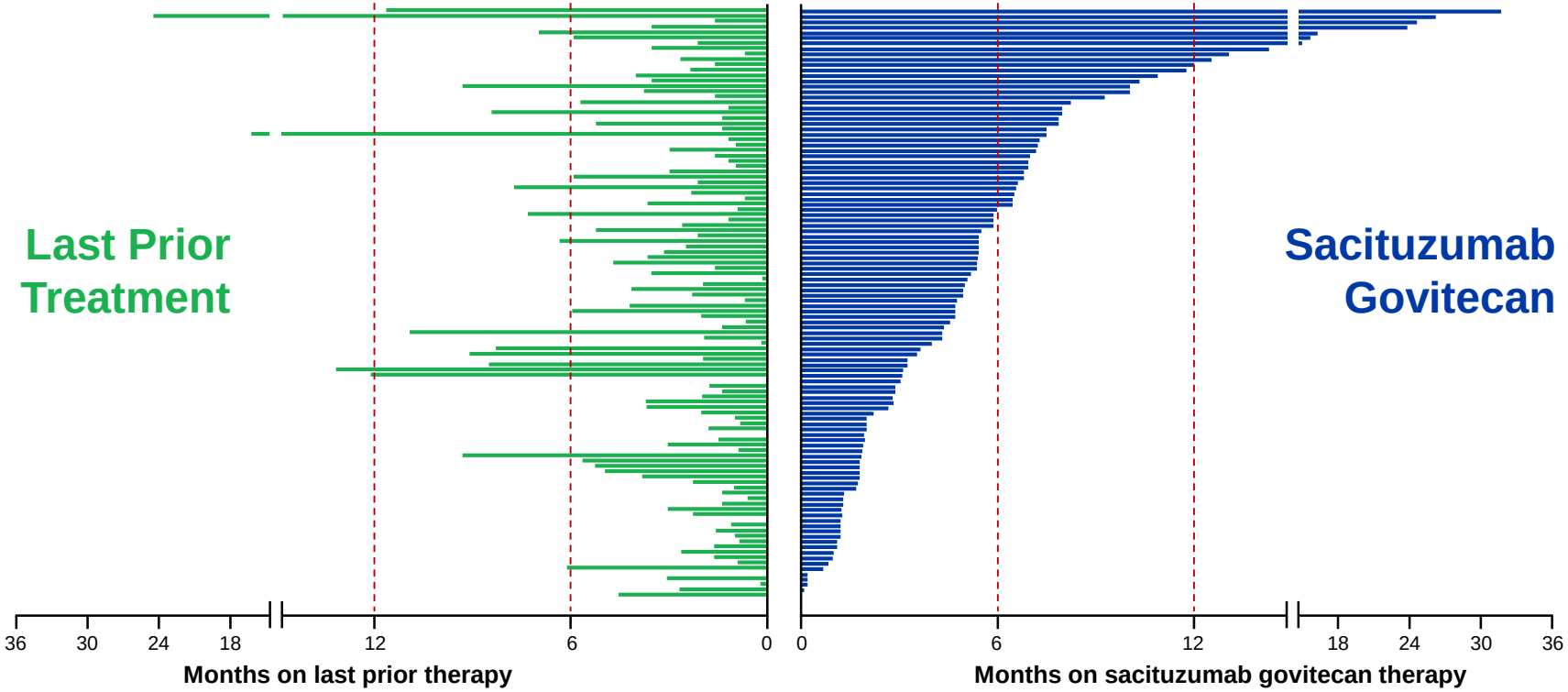
- Median time to onset of response: 2.0 months (range: 1.5-13.4)
- 9 long-term responders were progression free for >1 year from start of treatment (4 responders >2 years)
- 12 responders were still receiving sacituzumab govitecan at time of data cutoff, June 30, 2017



*Patients with at least 20% tumor reduction (n = 56) were reviewed; BICR = Blinded Independent Adjudicated Central Review. 1 patient left study with PR due to clinical progression.

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

Time on Treatment for All Patients (N = 110)

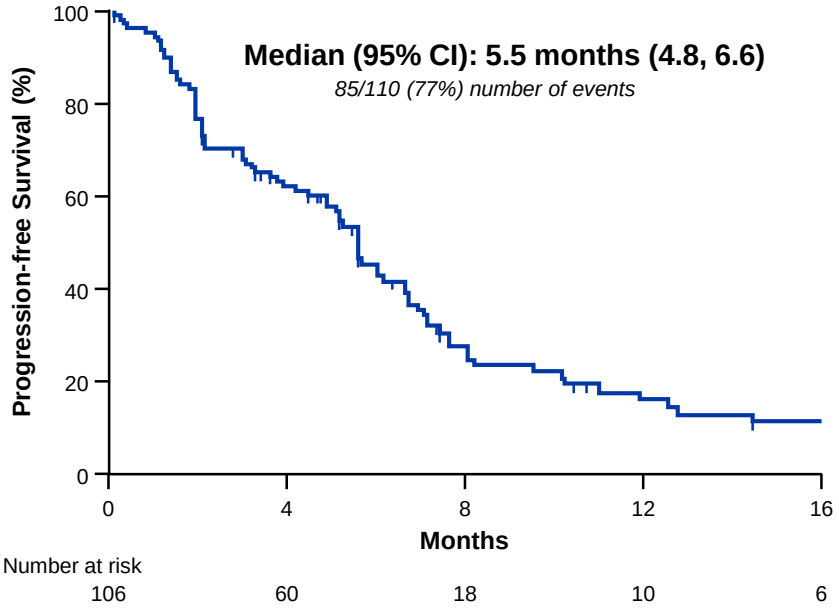


Last prior time on treatment calculated as last dose date – first dose date. Sacituzumab govitecan time on treatment calculated as (date off study or data cut off date) – first dose date. If more than 1 agent is given in the last prior regimen, the time of treatment is taken as the longest time for any one of the agents used

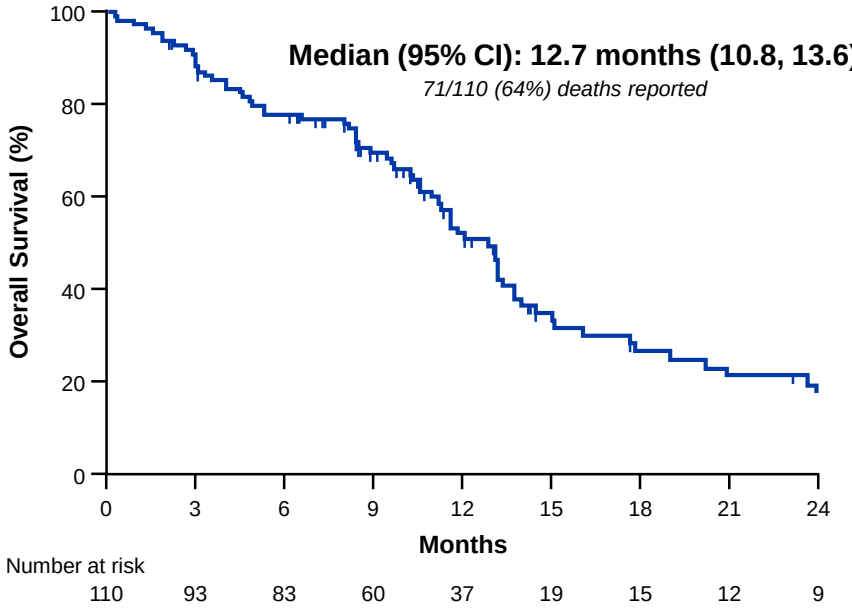
This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

Progression-Free and Overall Survival

Progression-free survival



Overall survival



Based on local assessment

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

Response to Sacituzumab Govitecan in Subgroups

	ORR, % (n/N)
Overall	34% (37/110)
Age	
<55	37% (20/54)
≥55	30% (17/56)
Onset of metastatic disease	
<1.5 years	29% (16/55)
≥1.5 years	38% (21/55)
Prior regimens for metastatic disease	
3rd line	36% (16/45)
≥4th line	32% (21/65)

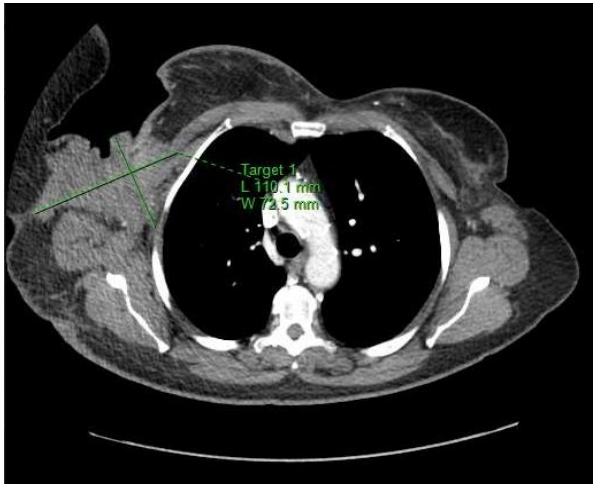
	ORR, % (n/N)
Visceral involvement at study entry	
Yes	30% (26/88)
No	50% (11/22)
Trop-2 IHC (n = 62)	
0-1 (weak, absent)	0% (0/5)
2-3 (moderate, strong)	40% (23/57)
No Trop-2 IHC	29% (14/48)
Prior checkpoint inhibitors	47% (9/19)

Based on local assessment

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

Clinical Response to Sacituzumab Govitecan

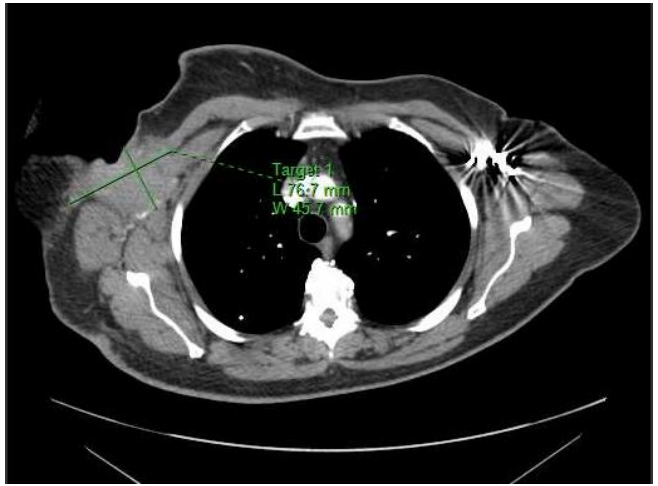
- Patient with mTNBC seen for management of fungating chest-wall/axillary mass
- 7 prior regimens for MBC including carboplatin, capecitabine, doxorubicin, paclitaxel, vinorelbine, ixabepilone, and eribulin



Pretreatment

After 2 cycles

Target lesion size reduced from 110x73 mm to 77x46 mm



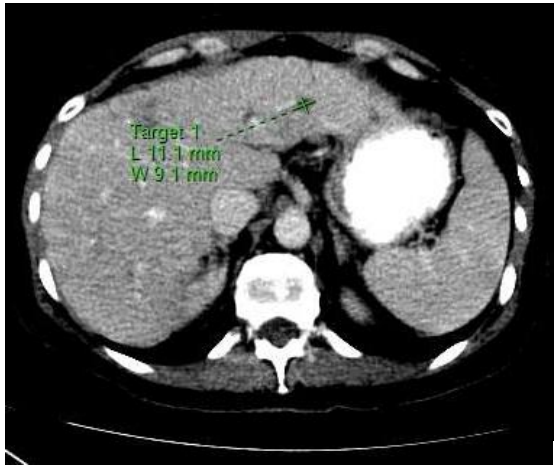
On treatment

Immunomedics

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

Clinical Response to Sacituzumab Govitecan

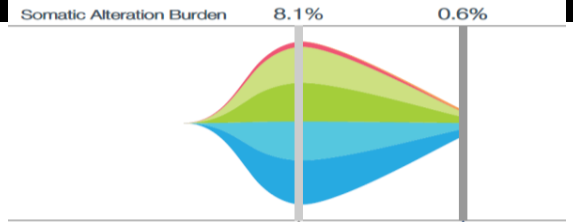
- Patient with mTNBC, including metastasis to liver
- 2 prior regimens including paclitaxel and carboplatin

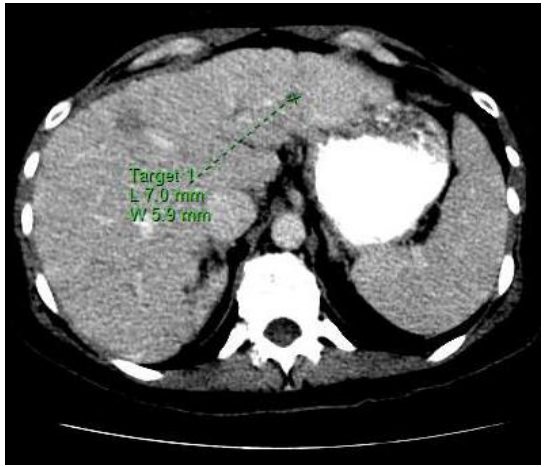


Pretreatment

After 5 cycles

Target lesion size reduced from 11x9 mm to 7x6 mm





On treatment

Immunomedics

SAN ANTONIO BREAST CANCER SYMPOSIUM

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

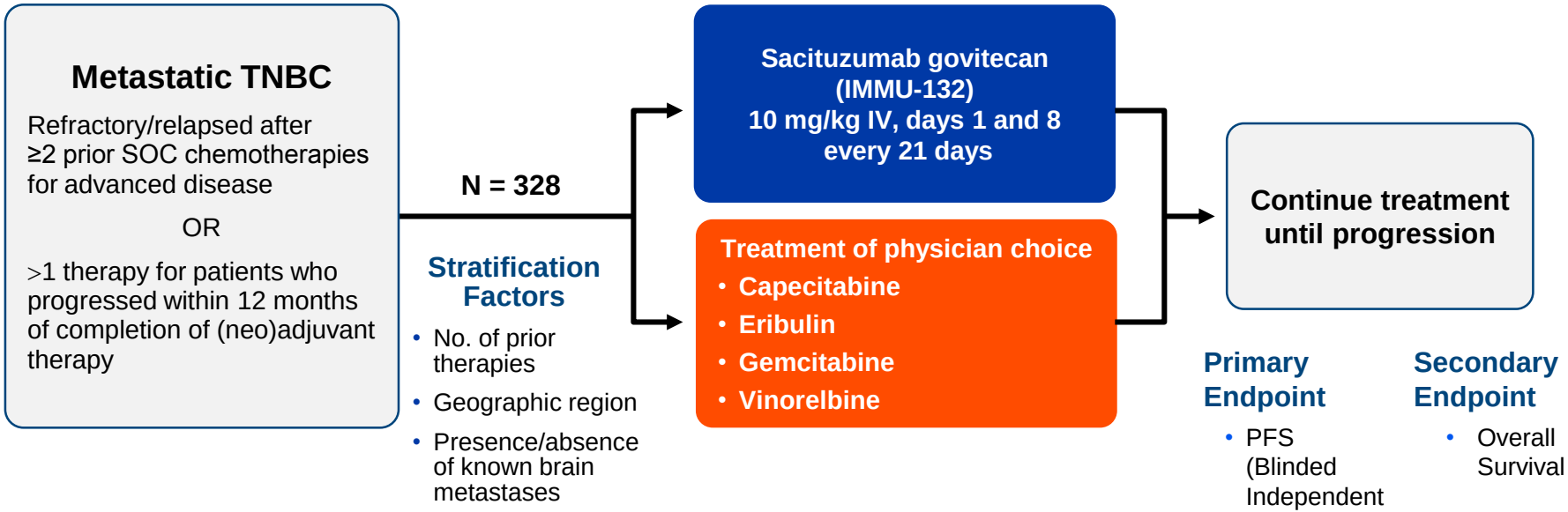
Conclusions

- Sacituzumab govitecan as a single agent demonstrated significant clinical activity as ≥3rd-line therapy in patients with relapsed/refractory mTNBC
  - Confirmed ORR*: 34%
  - Clinical benefit rate (6 months)*: 45%
  - The responses were durable (estimated median duration of response was 7.6 months based on local assessment)
  - All data consistent with central review
- Results suggest that sacituzumab govitecan has a predictable and manageable safety profile
- Additional studies including rational combinations are currently being evaluated for mTNBC and other breast cancer subsets

*Based on local assessment

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.

ASCENT Phase III Trial is Recruiting



- Now enrolling in the US; European enrollment to begin in first half of 2018
- Clinical trials number: NCT02574455
- Presented at: New Agents and Strategies; December 7, 2017; 5:00-7:00 PM, Hall 1 (abstract# 733), SABCS

This presentation is the intellectual property of the author/presenter. Contact Bardia.Aditya@mgh.harvard.edu for permission to reprint and/or distribute.