Inclusion of Older Adults in the Tesetaxel Development Program

Kevin Tang
Odonate Therapeutics, Inc.

Improving the Evidence Base for Treatment Decision-Making for Older Adults with Cancer: A Virtual Workshop

Convened by the National Cancer Policy Forum, in collaboration with the Forum on Drug Discovery, Development, and Translation, and the Forum on Aging, Disability, and Independence

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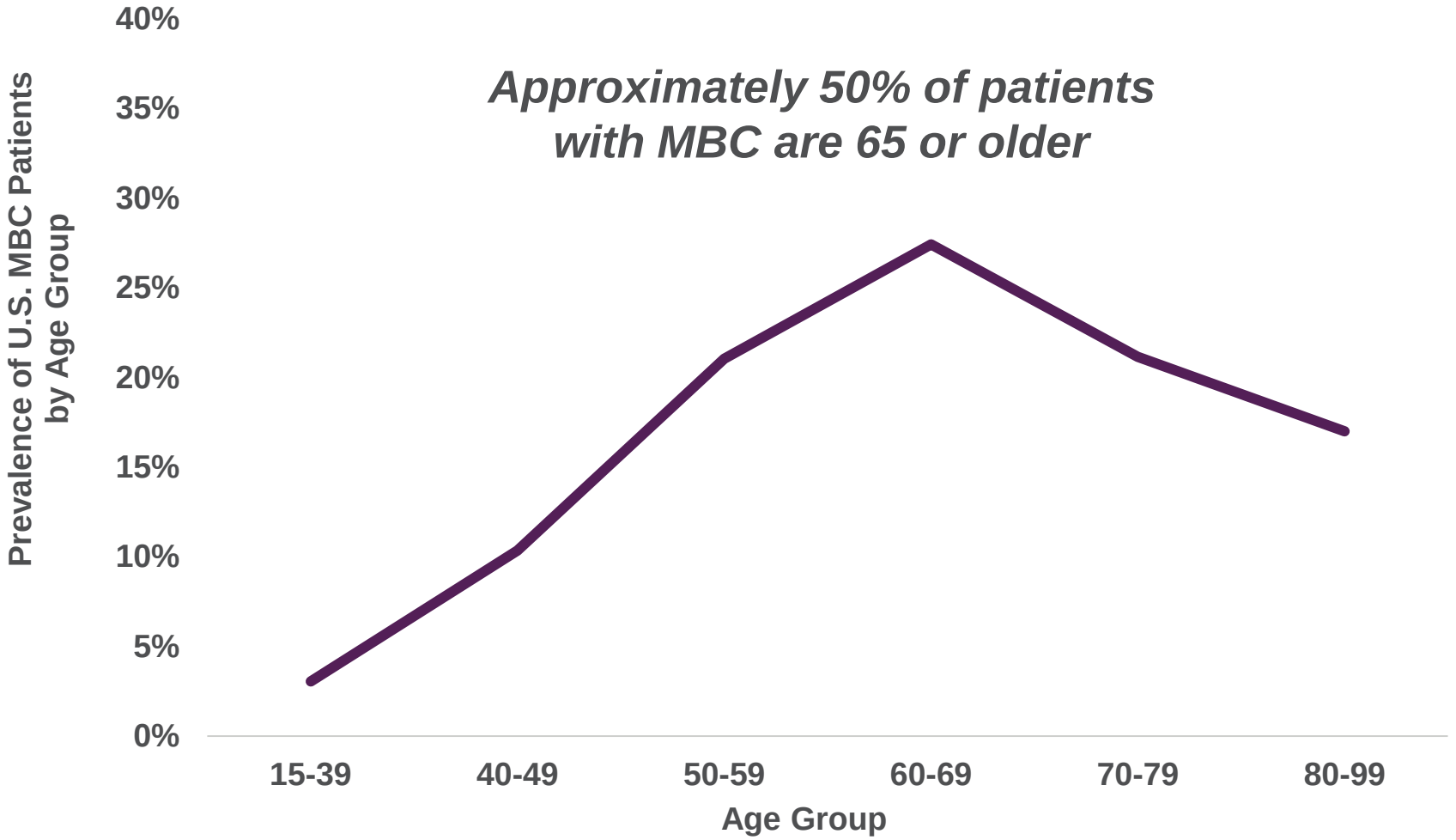
Disclosures

Kevin Tang is a board member, officer and stockholder of Odonate Therapeutics, Inc.

Older Adults Often Overlooked Population with Unmet Medical Need

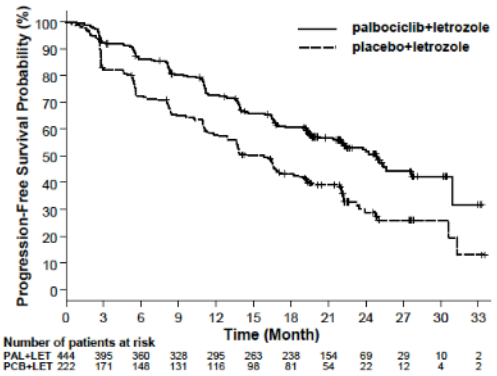
- In oncology, development strategies often focus on:
  - Tumor type
  - Molecular target (on the tumor or immune cell)
  - Line of therapy
  - Current treatment landscape
- Certain populations with unmet medical need are often overlooked:
  - Pediatric patients
  - Patients ineligible for standard therapy
  - **Older adults**

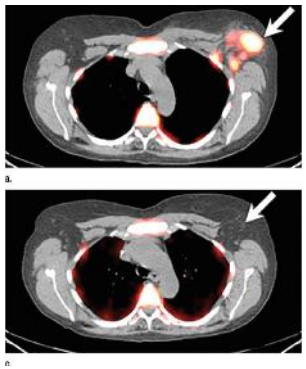
Older Adults with Metastatic Breast Cancer (MBC) Represent a Population with Unmet Medical Need[a]

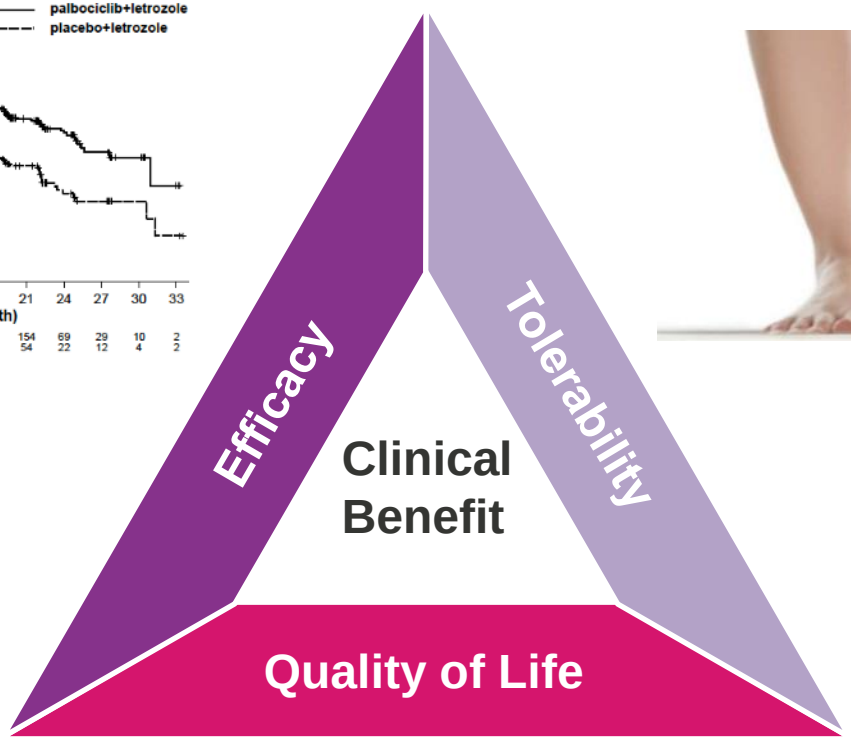


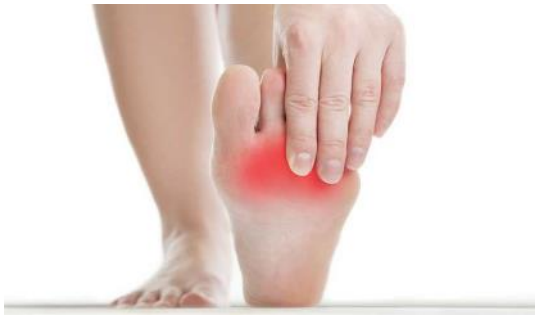
[a] Mariotto et al, *Cancer Epidemiol Biomarkers Prev.* 2017; 26:809-815

Balance of Efficacy, Tolerability and Quality of Life Is Particularly Important in Older Adults



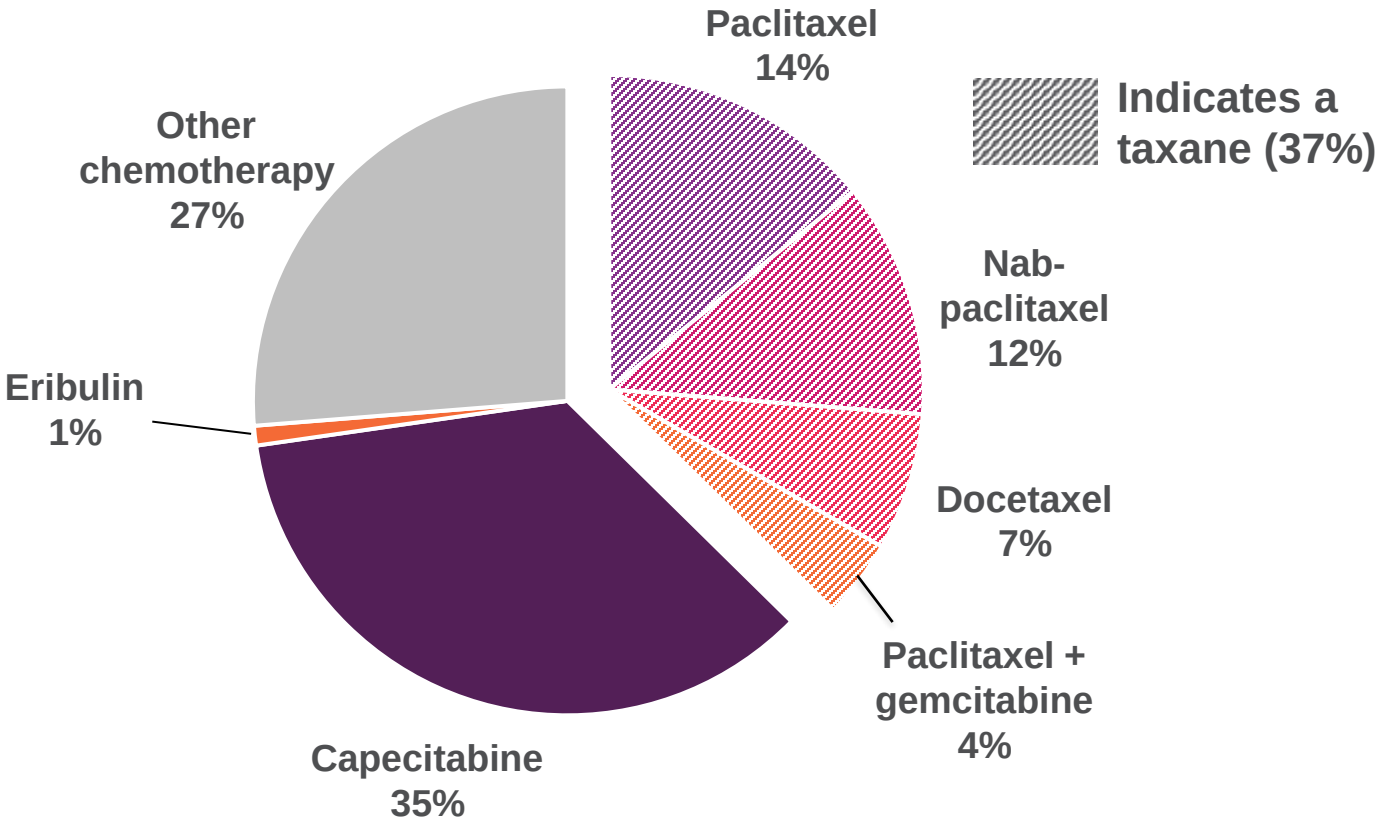






Taxanes and Capecitabine Are Commonly Used Chemotherapy Options in MBC

Physician-reported Preferences for First-line Chemotherapy for Patients with HR-Positive, HER2-Negative MBC



Recent survey of 201 U.S. community-based oncologists from Lin et al, *Cancer Medicine* 2016;5(2):209-220

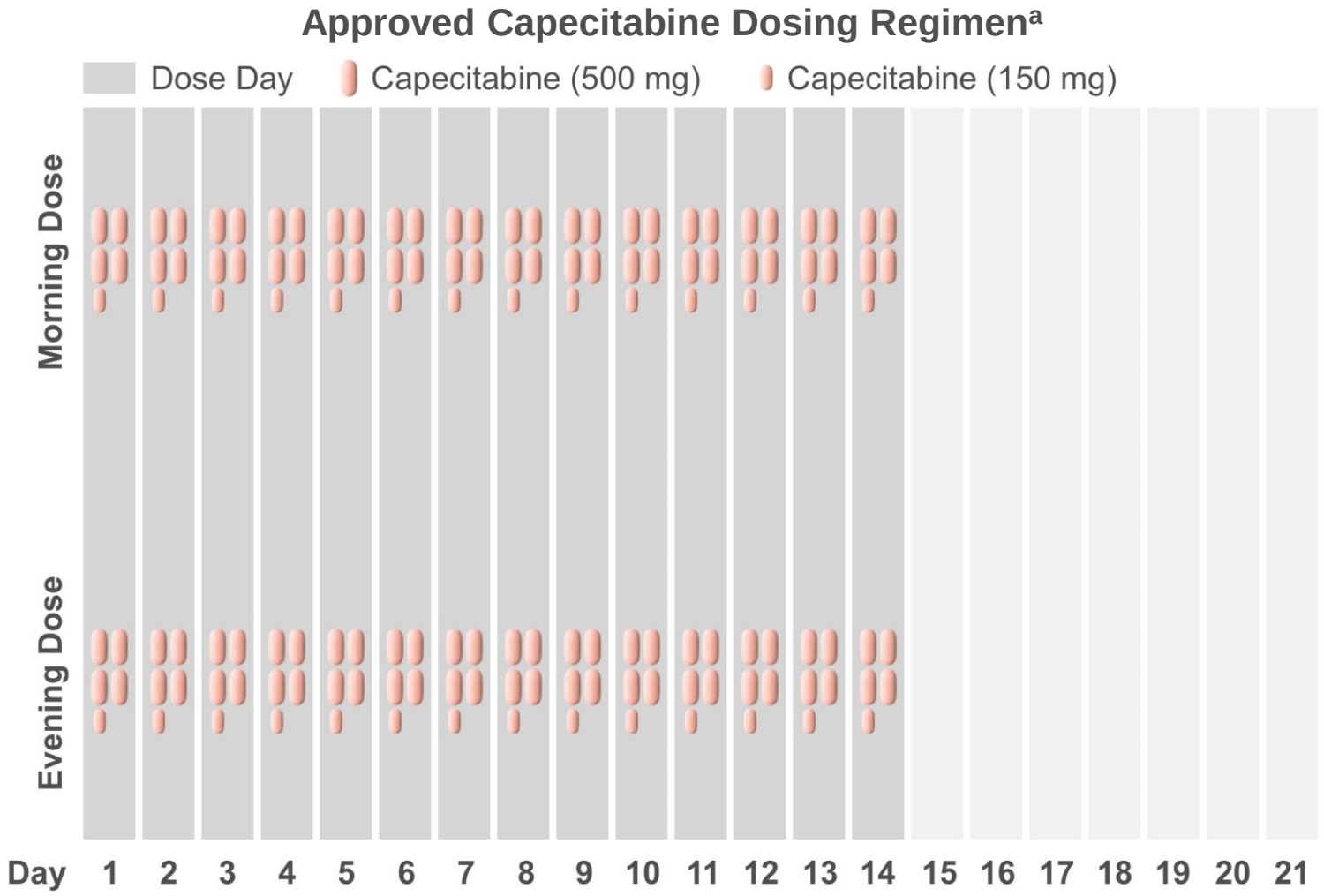
Currently Available Taxanes (Paclitaxel, Nab-paclitaxel and Docetaxel) All Are Administered Intravenously

Therapies that must be given intravenously at an infusion center often are associated with[a]:

- Fear of needles and complications associated with venous access
- Anxiety, including institutional-triggered side effects such as nausea and vomiting
- Heightened awareness of life-threatening disease presence
- Disruption of daily activities

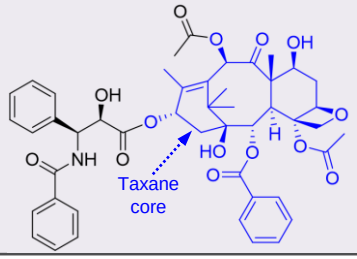
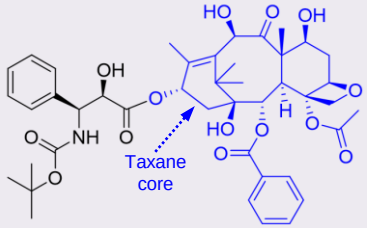
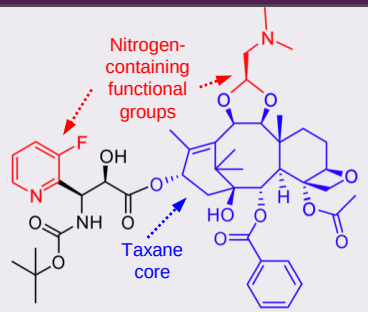
[a] Gornas et al, *European Journal of Cancer Care* 2010;19(1):131-136; Schott et al, *BMC Cancer* 2011;11:129

Capecitabine Is Administered Orally with a Significant Pill Burden



[a] Illustration for patients with body surface area of 1.66-1.77 m^2 (most common body surface area range) based on Xeloda (capecitabine) FDA prescribing information

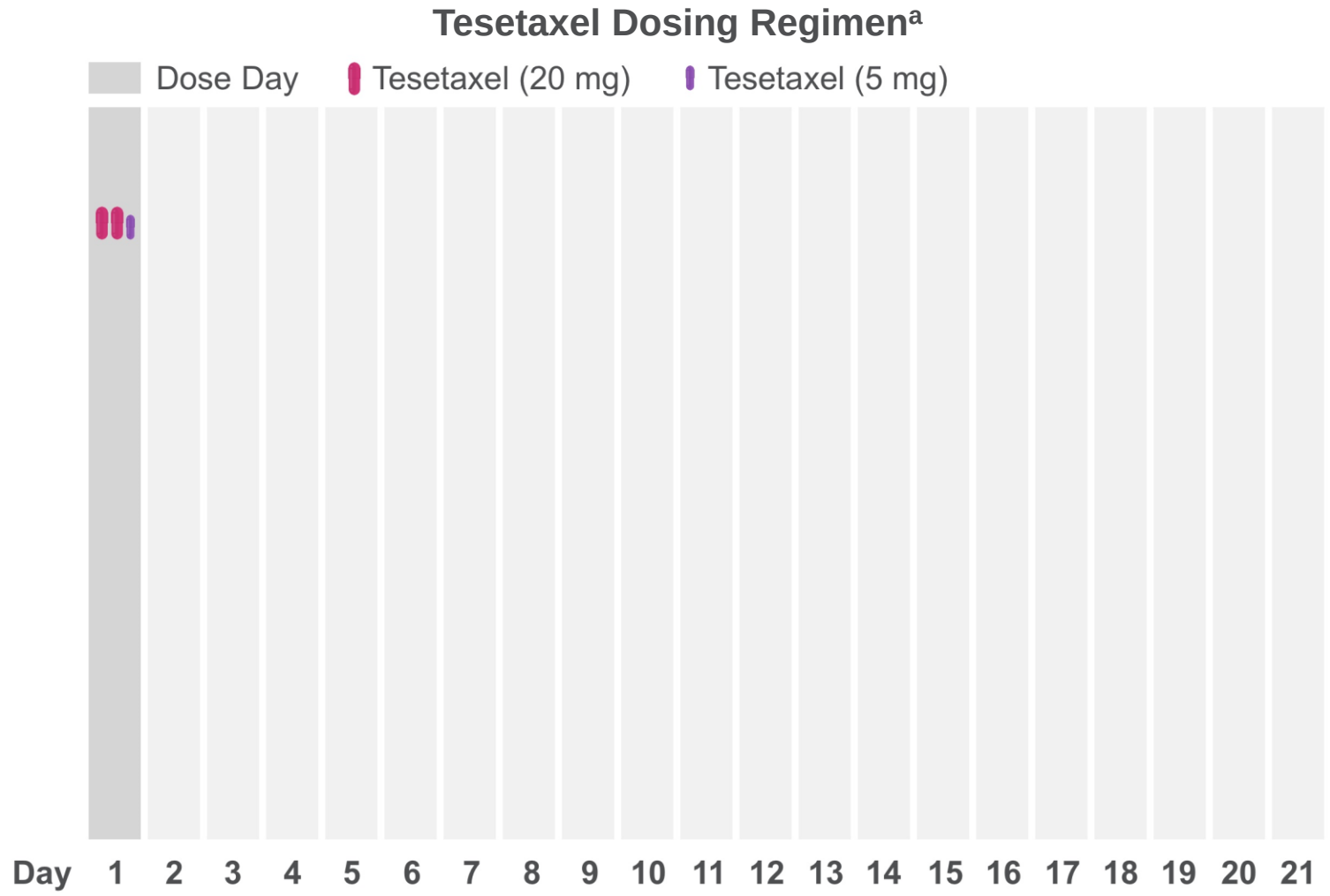
Tesetaxel: An Orally Administered Taxane with Unique Pharmacologic Properties

Molecule	Paclitaxel	Docetaxel	Tesetaxel
Structure			
Substantially effluxed by P-gp pump*	Yes	Yes	No
Oral bioavailability in preclinical studies	8%[a]	18%[b]	**56%**
Solubility (µg/mL)[c]	0.3[d]	0.5[e]	41,600
Terminal plasma half-life in humans ($t_{1/2}$)	0.5 days[f]	0.5 days[g]	**8 days[h]**

*The P-glycoprotein (P-gp) efflux pump mediates gastric absorption as well as chemotherapy resistance

[a] Shanmugam et al, *Drug Development and Industrial Pharmacy* 2015;41(11):1864-1876
[b] McEntee et al, *Veterinary and Comparative Oncology* 2003;1(2):105-112
[c] At pH conditions similar to gastric fluid
[d] Montaseri, *Taxol: Solubility, Stability and Bioavailability* 1997
[e] Bharate et al, *Bioorganic & Medicinal Chemistry Letters* 2015;25(7):1561-1567
[f] Tan et al, *British Journal of Cancer* 2014;110(11):2647-54
[g] Taxotere (docetaxel) FDA prescribing information
[h] Pharmacokinetic data from Studies 927A-PRT001, 927E-PRT003, 927E-PRT005, 927A-PRT006 and 927E-PRT007

Tesetaxel Is Administered Orally as 2-5 Capsules Once Every 3 Weeks



[a] Illustration for patients with body surface area of 1.57-1.75 m^2 (most common body surface area range) based on CONTESSA, CONTESSA 2 and CONTESSA TRIO

2018 ASCO® ANNUAL MEETING

Activity of Tesetaxel, an Oral Taxane, Given as a Single-agent in Patients with HER2-, Hormone Receptor + (HR+) Metastatic Breast Cancer (MBC) in a Phase 2 Study

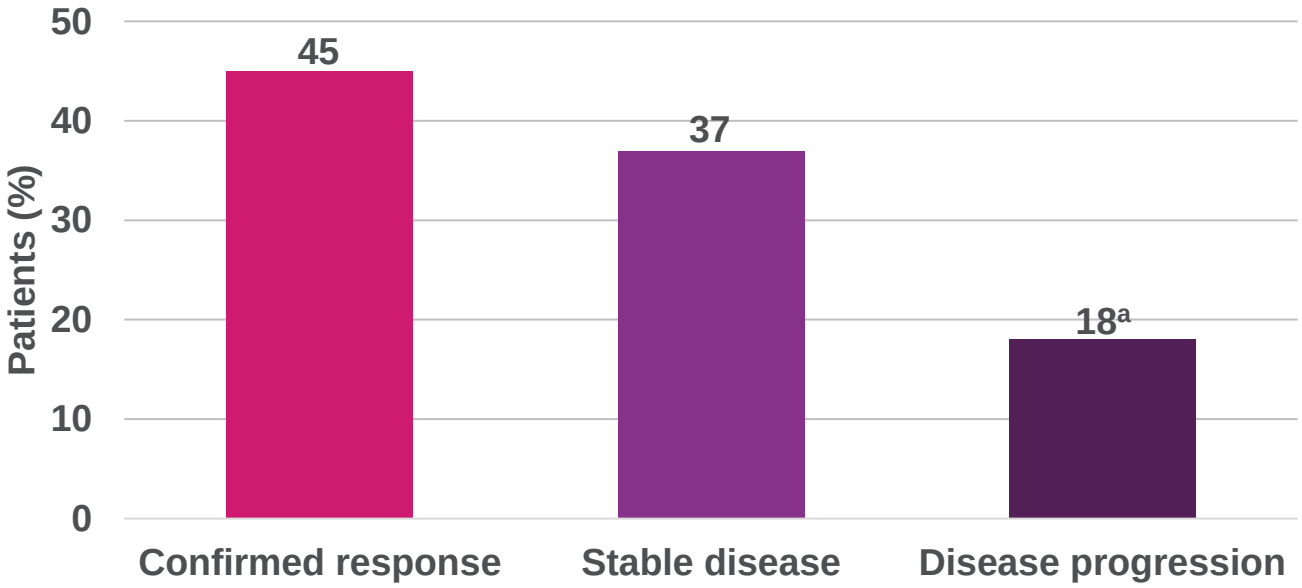
Andrew Seidman[1], Lee Schwartzberg[2], Vinay Gudena[3], Peter Rubin[4], Stew Kroll[5], Joseph O'Connell[5], Kevin Tang[5], Joyce O'Shaughnessy[6]

[1]Memorial Sloan Kettering Cancer Center, New York, NY; [2]West Cancer Center, Memphis, TN; [3]Cone Health Cancer Center, Greensboro, NC; [4]SMHC Cancer Care and Blood Disorders, Biddeford, ME; [5]Odonate Therapeutics, Inc., San Diego, CA; [6]Texas Oncology-Baylor Charles A. Sammons Cancer Center, US Oncology, Dallas, TX

Source: Seidman et al, 2018 ASCO Annual Meeting

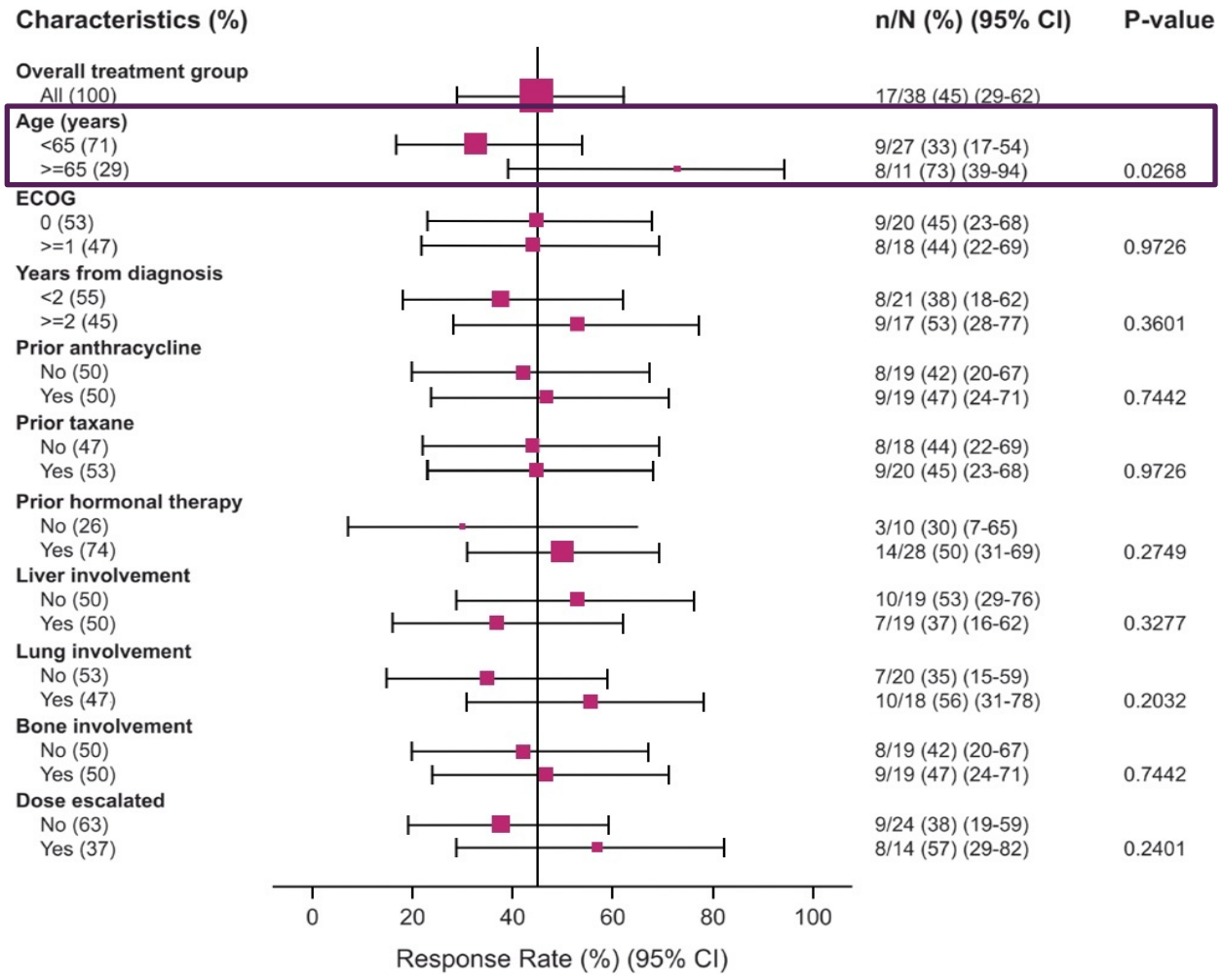
Response

- All 38 enrolled patients are included in the efficacy analysis
- 45% (95% CI: 29%-62%) of patients achieved a confirmed response
- Median duration of response was 10.9 months (95% CI: 4.3-13.6 months)
- Median progression-free survival (PFS) was 5.4 months (95% CI: 3.8-9.8 months)



CI=confidence interval
[a] Includes 1 patient who was not evaluated for response
Source: Seidman et al, 2018 ASCO Annual Meeting

Confirmed Response Rate by Subgroups



Source: Seidman et al, 2018 ASCO Annual Meeting

Results from CONTESSA: A Phase 3 study of tesetaxel plus a reduced dose of capecitabine versus capecitabine alone in patients with HER2-, hormone receptor + (HR+) metastatic breast cancer (MBC) who have previously received a taxane

Joyce O'Shaughnessy, Lee Schwartzberg, Martine Piccart, Hope S. Rugo, Denise A. Yardley, Javier Cortes, Michael Untch, Nadia Harbeck, Gail S. Wright, Igor Bondarenko, John Glaspy, Zbigniew Nowecki, Fadi Kayali, Arlene Chan, Christelle Levy, Mei-Ching Liu, Sung-Bae Kim, Julie Lemieux, Alexey Manikhas, Sara Tolaney, Elaine Lim, Andrea Gombos, Agostina Stradella, Mark Pegram, Peter Fasching, Laszlo Mangel, Vladimir Semiglazov, Veronique Dieras, Luca Gianni, Michael A. Danso, Jeff Vacirca, Stew Kroll, Joseph O'Connell, Kevin Tang, Thomas Wei and Andrew Seidman

Source: O'Shaughnessy et al, 2020 SABCS

Study Design

Key Eligibility Criteria

- HR-positive, HER2-negative MBC
- At least 18 years of age (no upper limit)
- 0-1 prior chemotherapy regimens for MBC
- Prior taxane in the neoadjuvant or adjuvant setting required
- Any number of prior endocrine or targeted therapies

Multinational, Multicenter, Randomized

1:1 Randomization

Tesetaxel
27 mg/m² PO
Day 1 of a 21-day cycle

+

Capecitabine
1,650 mg/m² PO
(825 mg/m² BID)
Evening Day 1 to Morning Day 15 of a 21-day cycle

Treat until progressive disease or unacceptable toxicity

Capecitabine
2,500 mg/m² PO
(1,250 mg/m² BID)
Evening Day 1 to Morning Day 15 of a 21-day cycle

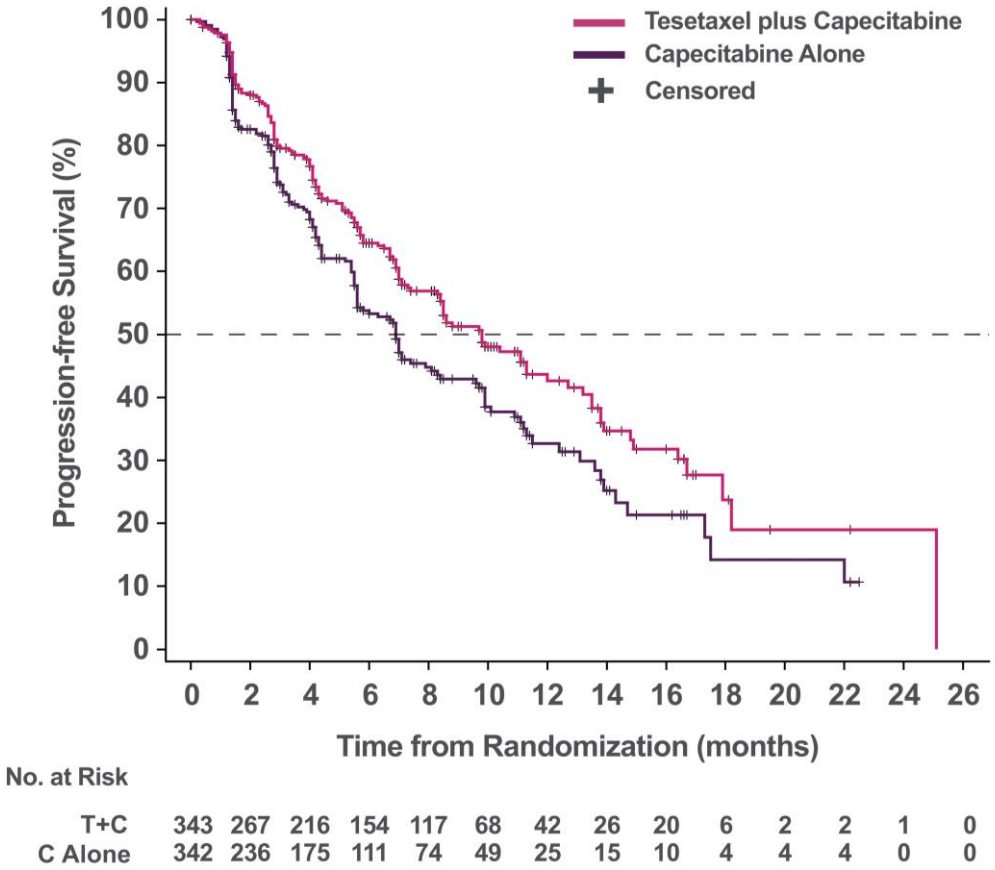
BID=twice per day; PO=oral dosing

Primary Endpoint: PFS as assessed by the Independent Radiologic Review Committee (IRC)

Secondary Endpoints: Overall survival (OS), objective response rate (ORR) as assessed by IRC[a] and disease control rate (DCR) [ORR or stable disease of ≥24 weeks] as assessed by IRC[a]

[a] In patients with measurable disease
Source: O'Shaughnessy et al, 2020 SABCS

PFS as Assessed by IRC

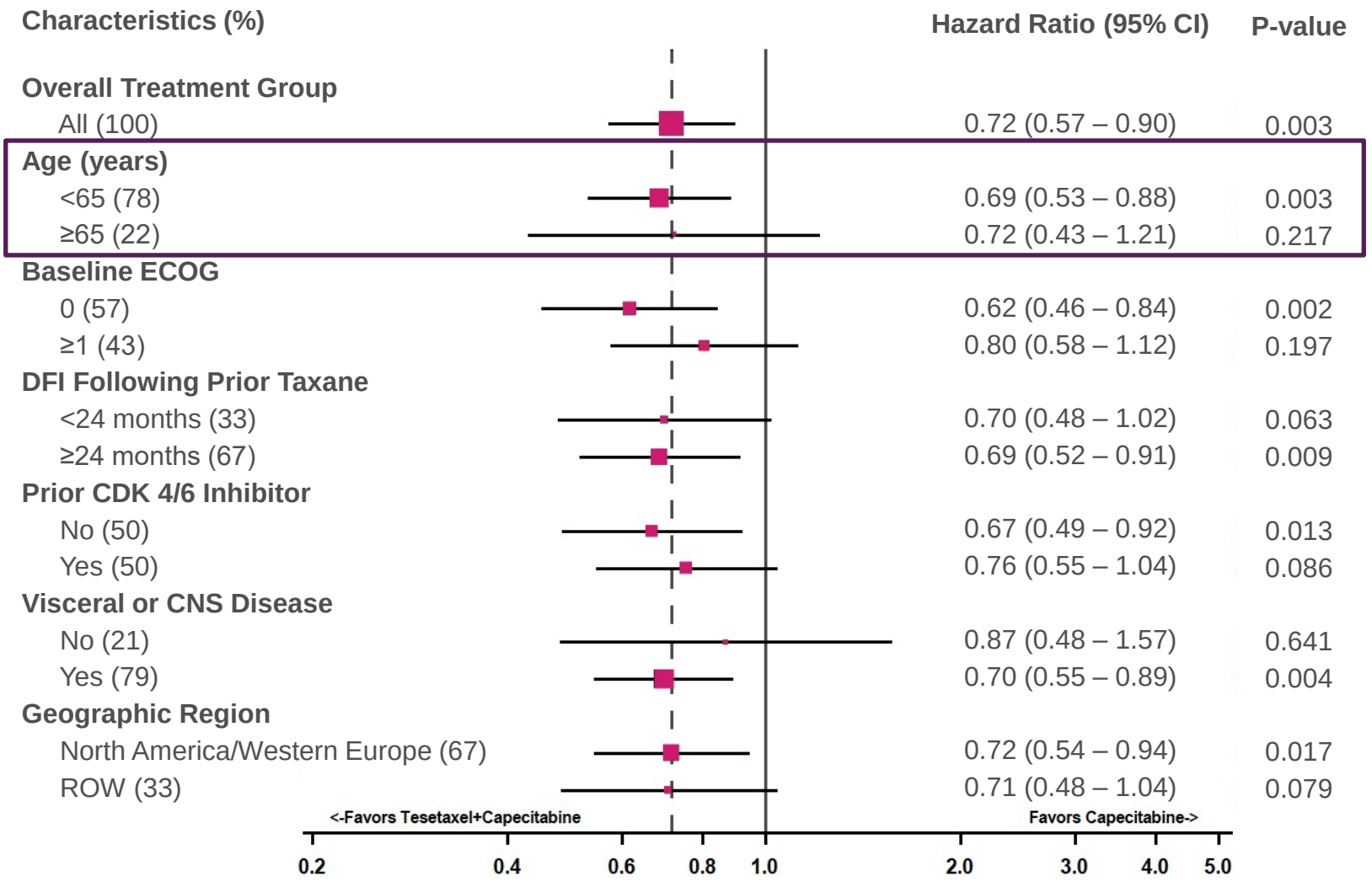


	Tesetaxel plus Capecitabine (N=343)	Capecitabine Alone (N=342)
Events	155	169
Median Months (95% CI)	9.8 (8.4 – 12.0)	6.9 (5.6 – 8.3)
	2.9-Month Improvement	
Hazard Ratio (95% CI)	0.716 (0.573 – 0.895)	
P-value	0.003	

CI=confidence interval

Source: O'Shaughnessy et al, 2020 SABCS

PFS as Assessed by IRC by Protocol-Specified Subgroups



Source: O'Shaughnessy et al, 2020 SABCS

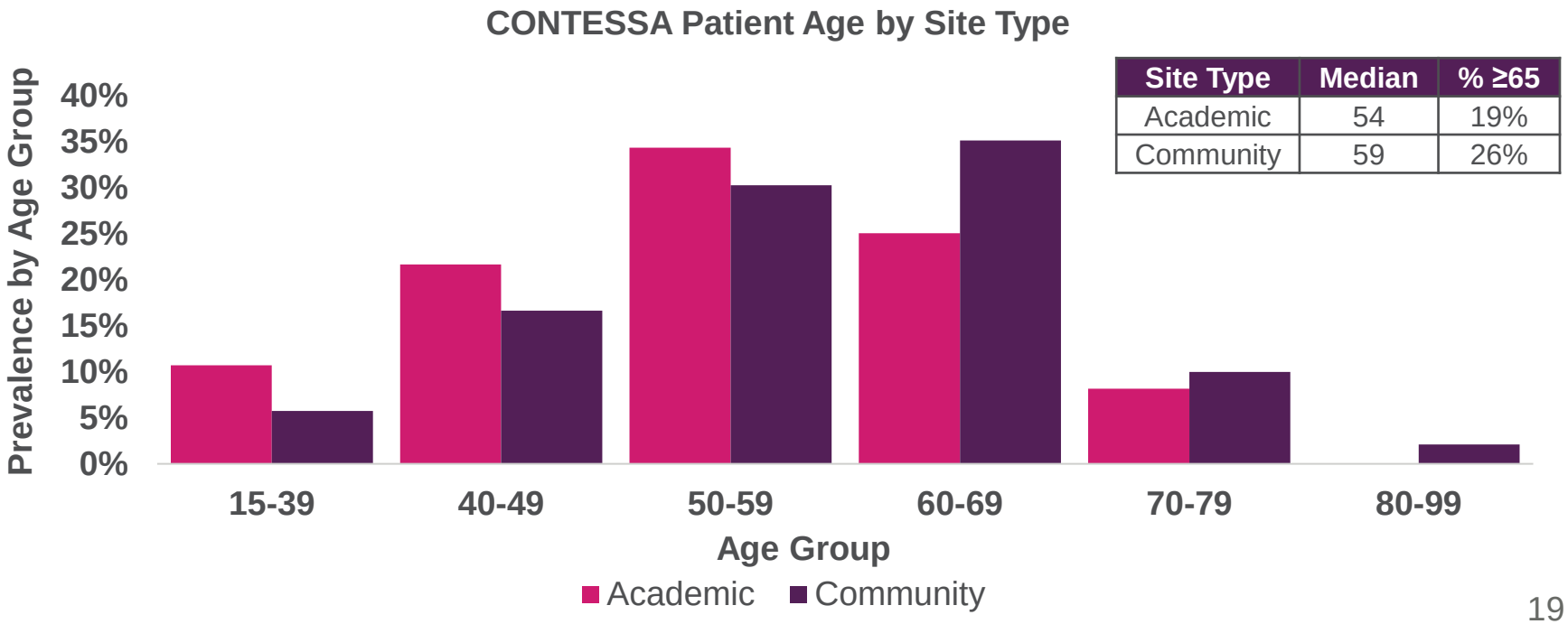
Tesetaxel plus Capecitabine All Grade Treatment Emergent Adverse Events (TEAEs) of Interest

- Neutropenia was the most frequent grade ≥3 TEAE
- Grade ≥3 neuropathy was low (5.9%)
- Grade 2 alopecia (hair loss) was low (8.0%)
- No treatment-related hypersensitivity reactions

Source: O'Shaughnessy et al, 2020 SABCS

Study Design Features That May Increase Older Adult Participation

- At-home administration
- Replacement of select clinic visits with telemedicine and/or local lab assessments
- Site selection



Site Type	Median	% ≥65
Academic	54	19%
Community	59	26%

CONTESSA TRIO Cohort 2 Exclusively Enrolled Older Adults

Cohort 2: Multicenter (N=60)

Key Eligibility Criteria

- Elderly (≥65 years old) patients with HER2-negative MBC
- 0 prior chemotherapy regimens for MBC
- Any number of prior endocrine or targeted therapies

Cohort 3: Multicenter (N=60)

Key Eligibility Criteria

- Non-Elderly (≥18 to <65 years old) patients with HER2-negative MBC
- 0 prior chemotherapy regimens for MBC
- Any number of prior endocrine or targeted therapies

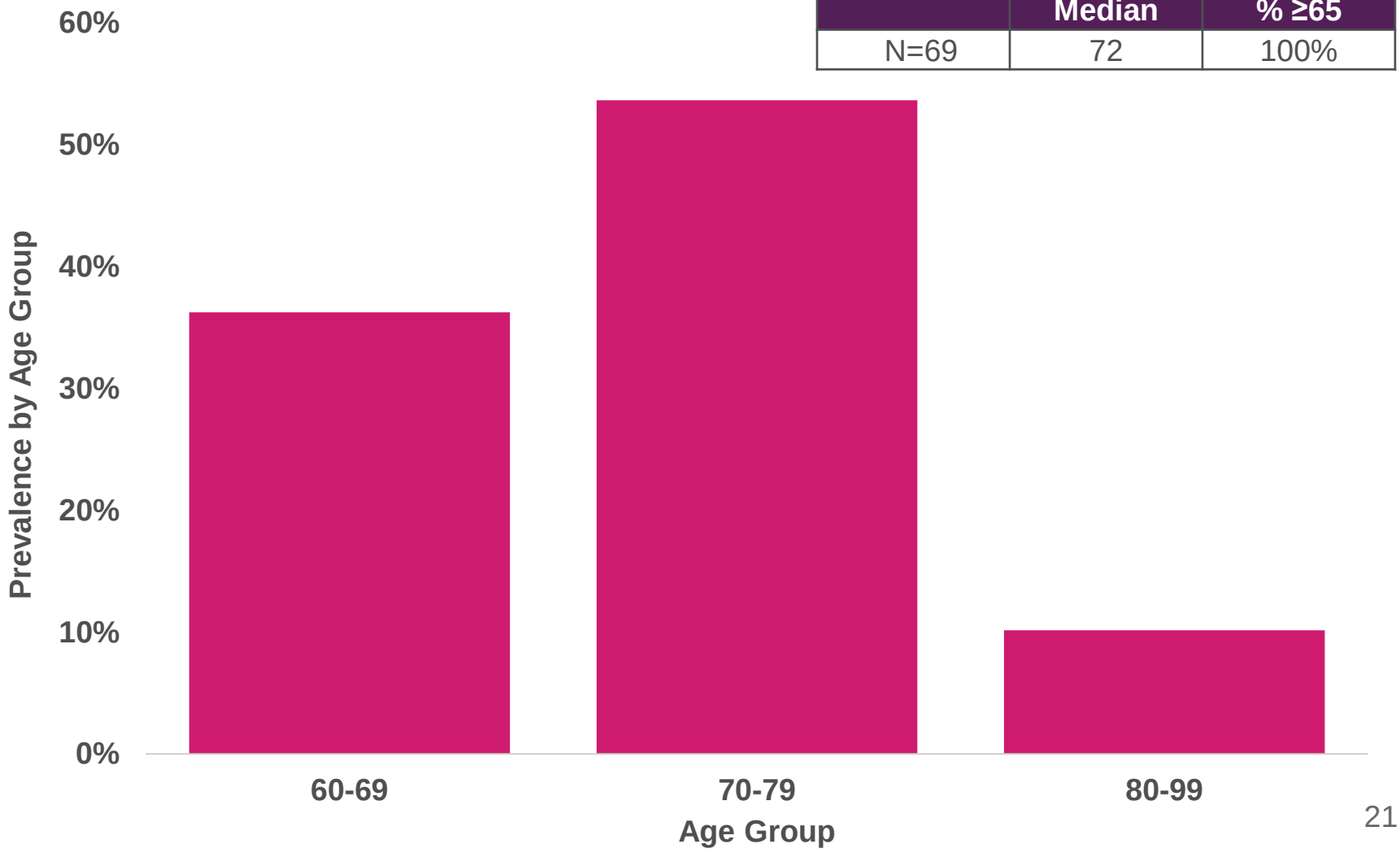
Tesetaxel Monotherapy
27 mg/m^2 once every 3 weeks

Primary Endpoints: ORR and PFS in patients with HR-positive, HER2-negative disease

Secondary Endpoints: ORR and PFS in patients with triple-negative disease, duration of response and OS

CONTESSA TRIO Cohort 2 Patient Age

	Median	% ≥65
N=69	72	100%



Summary

- Older adults often represent an overlooked population with unmet medical need
  - Approximately 50% of patients with MBC are 65 or older
- The tesetaxel development program was designed to provide evidence of tesetaxel's benefit-risk profile in older adults:
  - Phase 2 study suggested attractive profile in older adults
  - Phase 3 study included older adults
  - Additional Phase 2 study conducted exclusively in older adults
- Strategies employed to increase enrollment of older adults included:
  - At-home administration/alternatives to clinic visits
  - Inclusion of community oncology sites

Thank You