

Current Treatment Approaches to TNBC

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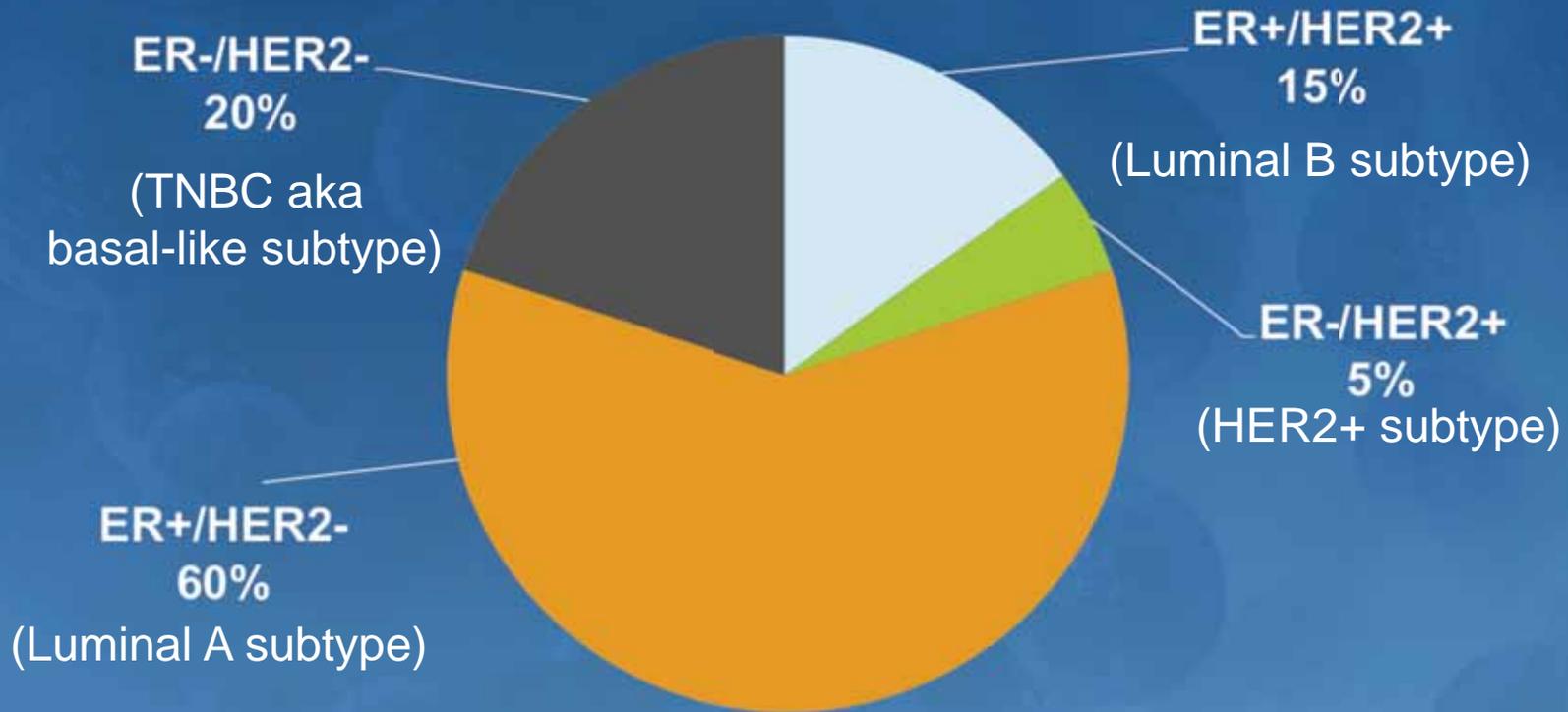
Disclosures for Kimberly L Blackwell, MD

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|--|---|
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Key Topics Discussed

- Incidence of breast cancer subsets, including TNBC
- Clinical characteristics of TNBC
- National Patterns of Care Study, October 2010

Breast Cancer Subtypes



(Assumptions: ER+ 75 percent^{a,b}; HER2+ 20%^c)

Estimated New Cancer Cases per Year in the US

| | Estimated New Cases |
|---|---------------------|
| Breast | 209,060 |
| Triple-negative subset¹ | ~31,359 |
| Pancreas | 43,140 |
| CNS | 22,020 |
| Ovarian | 21,880 |
| Gastric | 21,000 |
| Multiple myeloma | 20,180 |
| Hodgkin lymphoma | 8,490 |
| Chronic myeloid leukemia | 4,870 |

¹ Value estimated by multiplying the number of new breast cancer cases by reported 15% incidence (Stead, *Breast Cancer Res* 2009) of TNBC.

Clinical Characteristics of TNBC

- **Risk Factors**

- Young¹
- African-American²
- BRCA1 mutation carrier³

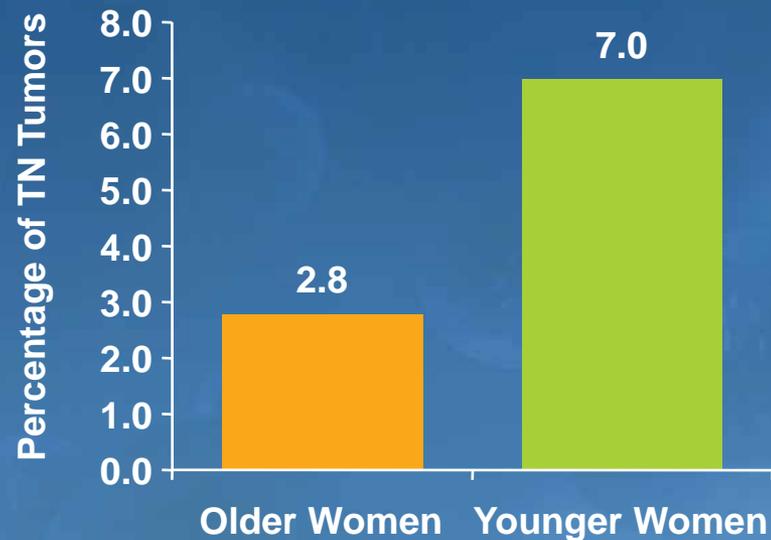
- **Relapse Pattern**

- Higher risk^{4,5}
- Earlier timing^{4,5}
- CNS metastases are more prevalent when compared to historical controls⁶

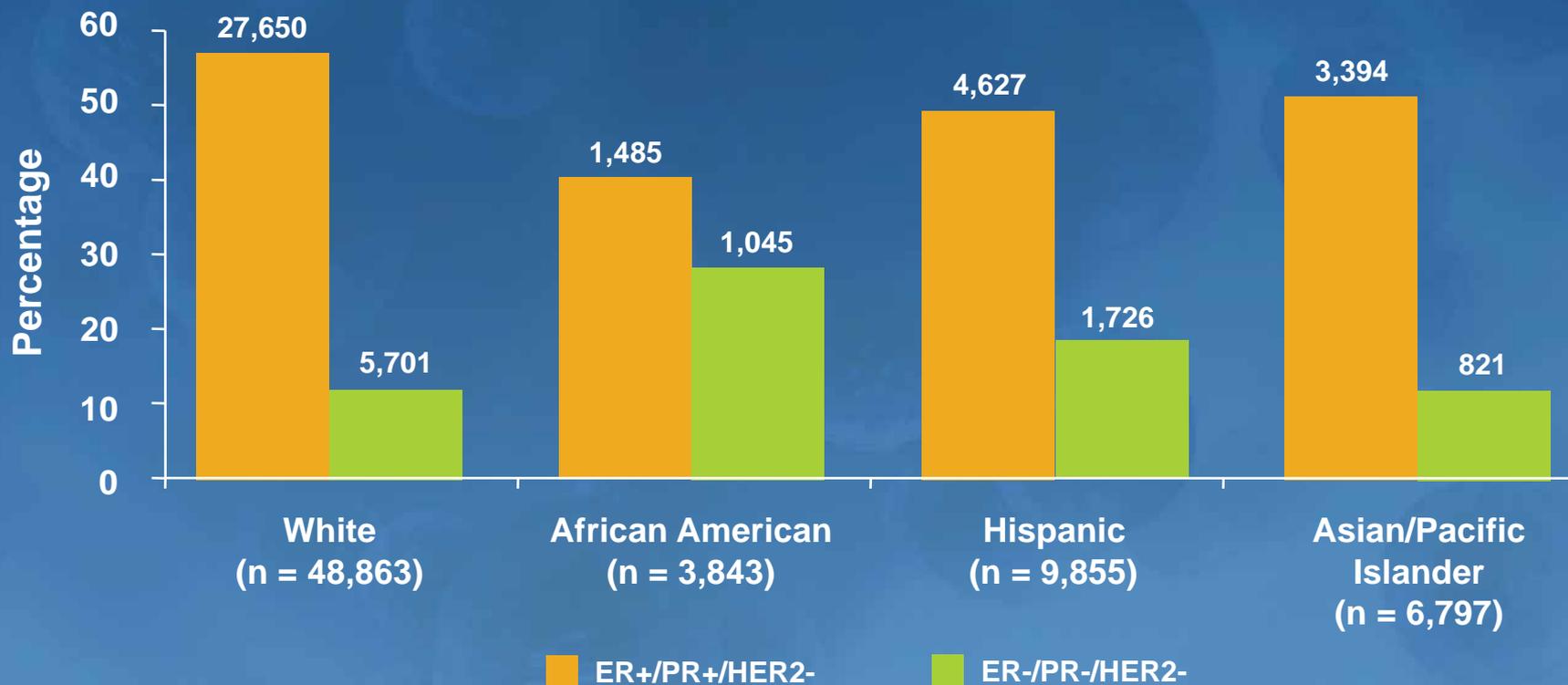
¹ Bauer KR et al. *Cancer* 2007;109(9):1721-8; ² Carey LA et al. *JAMA* 2006;295(21):2492-502; ³ Foulkes WD et al. *J Natl Cancer Inst* 2003;95(19):1482-5; ⁴ Dent R et al. *Clin Cancer Res* 2007;13(15):4429-34; ⁵ Liedtke C et al. *J Clin Oncol* 2008;26(8):1275-81; ⁶ Lin NU et al. *Cancer* 2008;113(10):2638-45.

Incidence of TNBC is Higher in Younger Women

Age-Specific Differences in Percentage of Triple-Negative Tumors



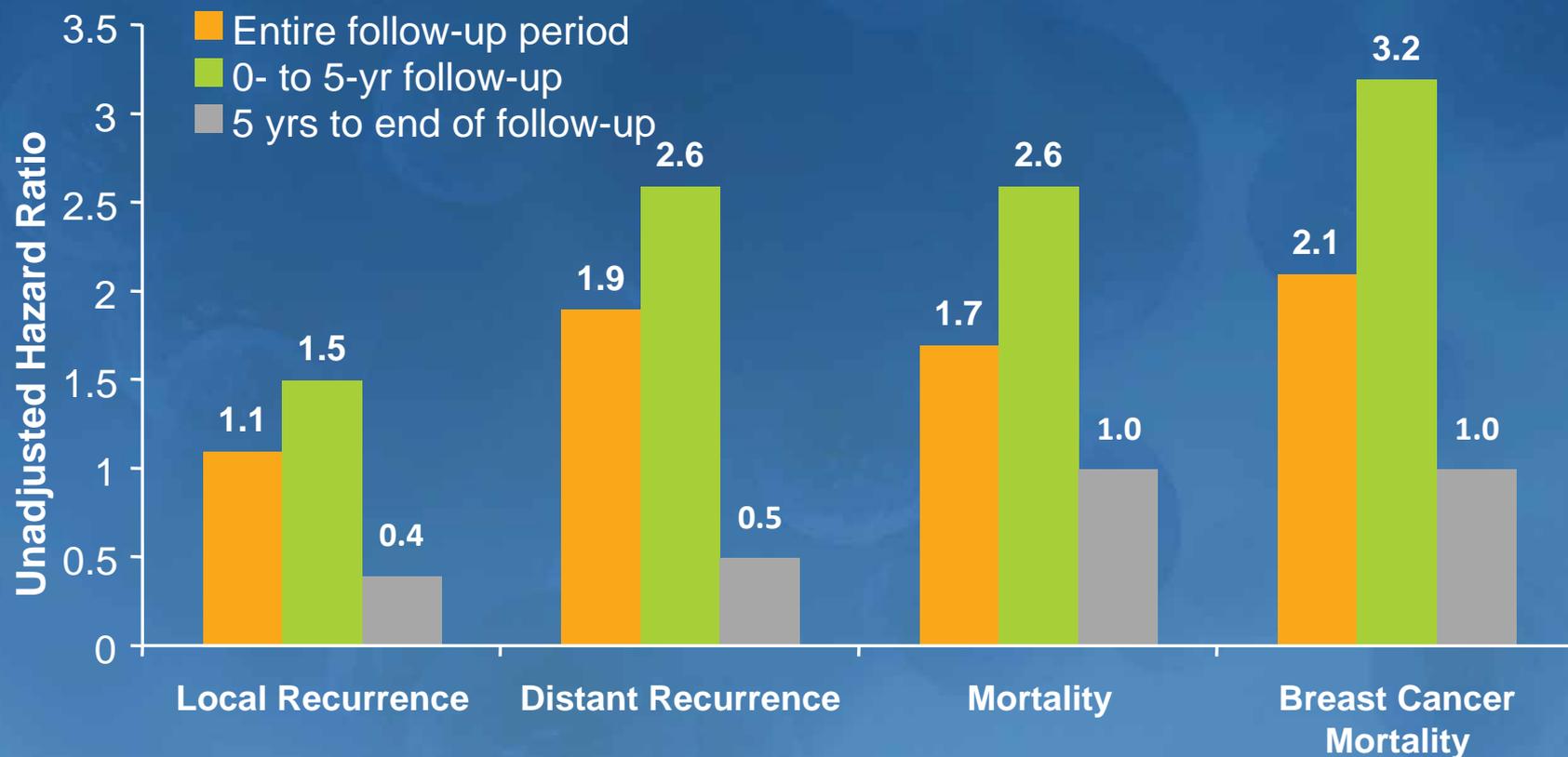
Proportion of TNBC is Higher in African American Women than Other Ethnic Groups



Prevalence of *BRCA1* and *BRCA2* Mutations

| | Percentage of Patients | |
|------------------|--------------------------------------|--------------------------------------|
| Ethnicity | Prevalence of <i>BRCA1</i> Mutations | Prevalence of <i>BRCA2</i> Mutations |
| African American | 1.3-1.4 | 2.6 |
| Caucasian | 2.2-2.9 | 2.1 |
| Ashkenazi Jewish | 8.3-10.2 | — |

Higher Percentages of TNBC Recurrences Occur Within the First 5 Years



Sites of Distant Recurrence and Clinical Outcomes in Patients with Metastatic Triple-Negative Breast Cancer – High Incidence of Central Nervous System Metastases

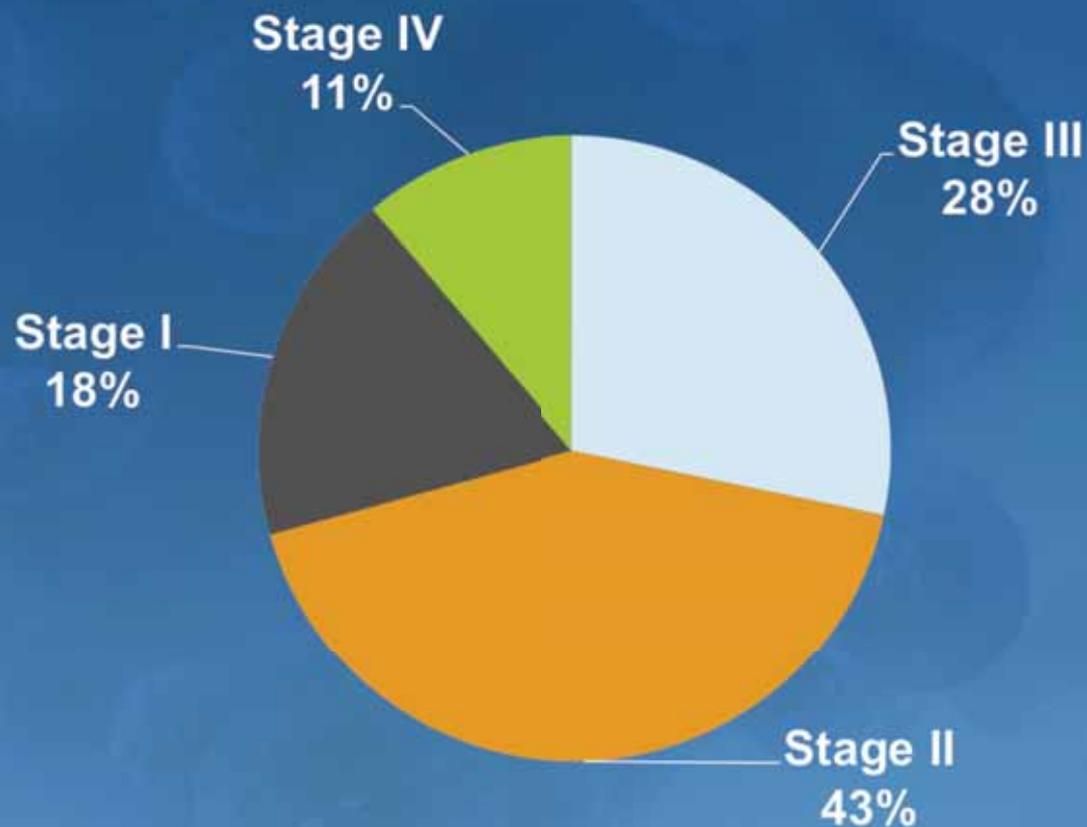
Lin NU et al.

Cancer 2008;113(10):2638-45.

Dana-Farber Cross-Sectional Series of TNBC Cases

- 116 patients treated with chemotherapy for metastatic TNBC (mTNBC) between January 2000 and June 2006
- Median age at initial diagnosis: 46 years
- 84/116 (72%) received prior adjuvant chemotherapy
- 107/116 (92%) had Grade 3 invasive ductal carcinomas
- Median survival from mTNBC diagnosis: 13.3 mos

Initial Stage at Diagnosis in 116 Patients Receiving Chemotherapy for Metastatic TNBC



Dana-Farber Triple-Negative Series – *Recurrence Sites*

| Site(s) of Metastatic Disease at Diagnosis of Metastasis | Patients (n = 116) | |
|--|--------------------|----|
| | N | % |
| Lung/pleura | 48 | 41 |
| Liver | 34 | 29 |
| Bone | 28 | 24 |
| Breast/chest wall | 28 | 24 |
| Soft tissue/distant lymph nodes | 25 | 22 |
| Regional lymph nodes | 17 | 15 |
| CNS | 16 | 14 |

Dana-Farber Triple-Negative Series – *CNS Disease*

- 16 patients (14%) diagnosed with CNS involvement at mTNBC diagnosis
- 46% of patients diagnosed with CNS metastases before death
- Median survival after diagnosis of CNS metastases: 4.9 mos
- 3/53 (6%) of patients with brain metastases had stable or responsive systemic disease

Dana-Farber Triple-Negative Series – *CNS Disease Site and Therapy*

| Site of CNS Metastasis | Patients (n = 53) | |
|--------------------------------|-------------------|----|
| | N | % |
| Parenchymal only | 40 | 75 |
| Leptomeningeal only | 8 | 15 |
| Parenchymal and leptomeningeal | 5 | 9 |
| CNS-Directed Therapy | | |
| WBRT | 47 | 89 |
| SRS | 7 | 13 |
| IT chemotherapy | 6 | 11 |
| Craniotomy | 5 | 9 |

WBRT = whole-brain radiotherapy; SRS = stereotactic radiosurgery; IT = intrathecal

Are there Specific Guidelines for the Management of TNBC?

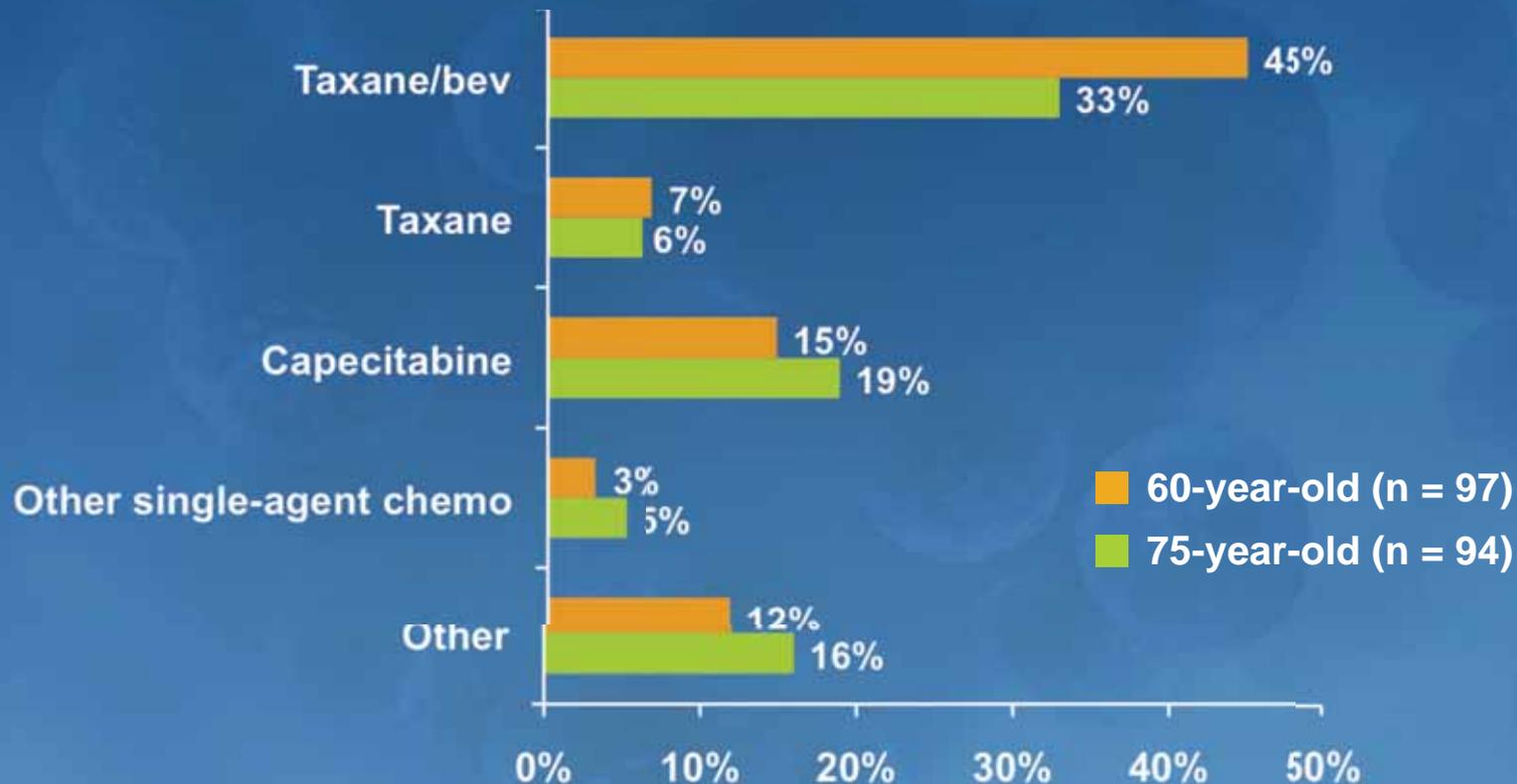
Published Guidelines for the Management of TNBC

- **NCCN: No specific algorithm**
 - NCCN Guidelines 2010, v.2
- **ESMO: No specific algorithm**
 - Cardoso F et al. *Ann Oncol* 2010;21(Suppl):v15-v19;
 - Aebi S et al. *Ann Oncol* 2010(Suppl):v9-v14;
 - Balmana J et al. *Ann Oncol* 2010;21(Suppl):v20-v22.
- **St Gallen: No specific algorithm**
 - Goldhirsch A et al. *Ann Oncol* 2009;20:1319-29.

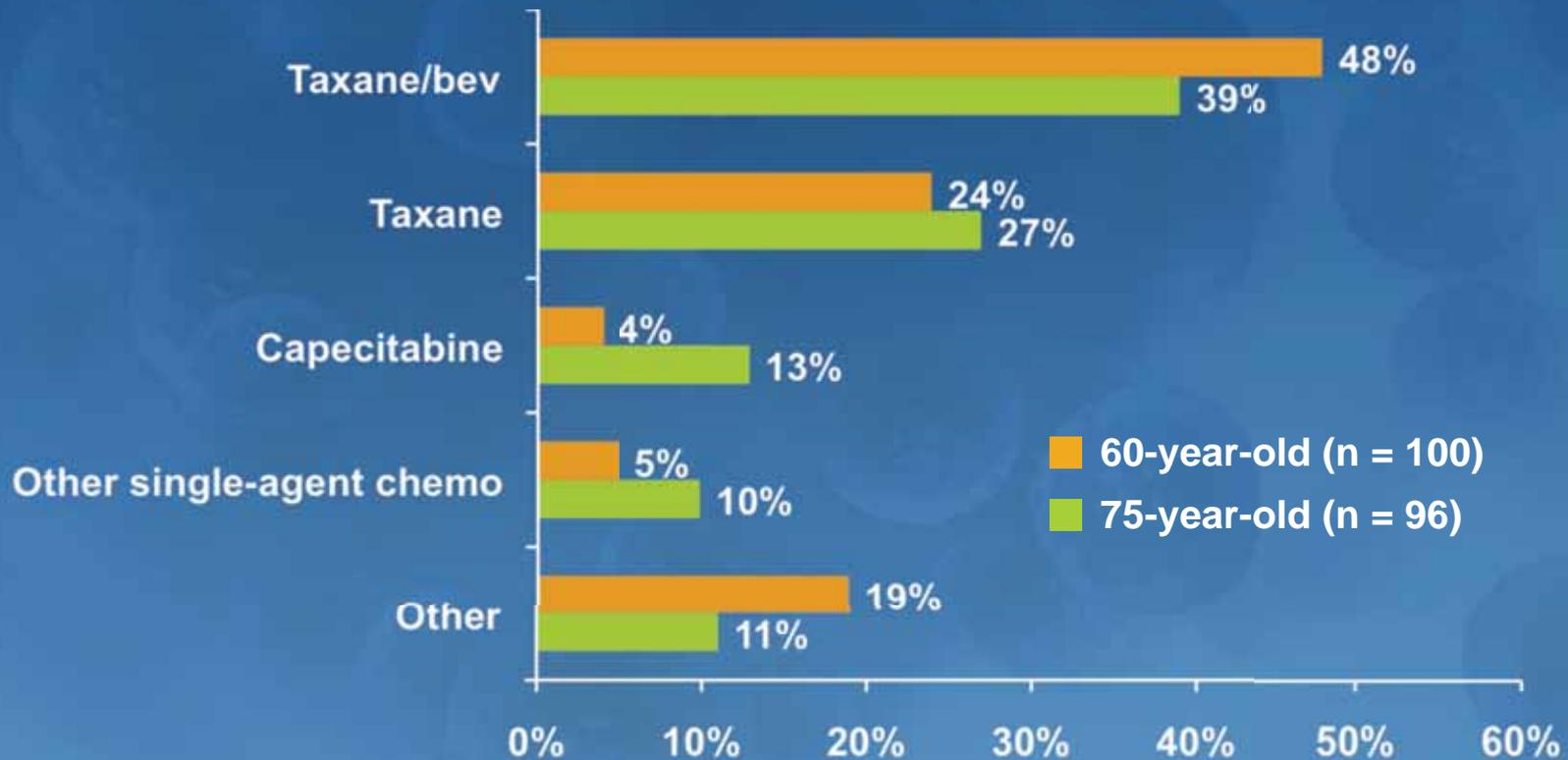
National Patterns of Care Study in Breast Cancer

- Launched October 2010
- 100 US-based community oncologists surveyed
- Proportion of patients/office visits with breast cancer: 30% (median)
- New patients with breast cancer seen per month: 15 (median)

A 60 (75) yo woman with TNBC and asymptomatic bone mets 2 years after adjuvant dd AC → T. Which chemotherapy would you recommend?



A 60 (75) yo woman with TNBC and symptomatic bone mets 2 years after adjuvant dd AC → T. Which chemotherapy would you recommend?



60 yo woman: 1.0-cm sentinel node-negative IDC. Which adjuvant chemotherapy treatment would you recommend?

| Tumor Subtype | Anthra → Taxane | TC | AC | Other | None |
|--|----------------------------|-----------|-----------|--------------|-------------|
| Triple-negative | 31% | 57% | 5% | 1% | 6% |
| ER+/HER2-neg, would order Oncotype (n = 82) | | | | | |
| High RS | 30% | 60% | 6% | 4% | 0 |
| Intermediate RS | 7% | 62% | 4% | 1% | 26% |
| Low RS | 0 | 4% | 0 | 3% | 93% |
| ER+/HER2-neg, would not order Oncotype (n = 18) | 0 | 6% | 0 | 6% | 88% |

75 yo woman: 1.0-cm sentinel node-negative IDC. Which adjuvant chemotherapy treatment would you recommend?

| Tumor Subtype | Anthra → Taxane | TC | AC | Other | None |
|---|-----------------|-----|-----|-------|------|
| Triple-negative | 7% | 53% | 7% | 7% | 26% |
| ER+/HER2-neg, would order Oncotype (n = 46) | | | | | |
| High RS | 22% | 63% | 11% | 2% | 2% |
| Intermediate RS | 3% | 37% | 4% | 4% | 52% |
| Low RS | 0 | 4% | 0 | 2% | 94% |
| ER+/HER2-neg, would not order Oncotype (n = 54) | 0 | 11% | 0 | 4% | 85% |

60 yo woman: 3.4-cm sentinel node-negative IDC. Which adjuvant chemotherapy treatment would you recommend?

| Tumor Subtype | Anthra → Taxane | TC | AC | Other | None |
|--|----------------------------|-----------|-----------|--------------|-------------|
| Triple-negative | 57% | 35% | 4% | 3% | 1% |
| ER+/HER2-neg, would order <i>Oncotype</i> (n = 64) | | | | | |
| High RS | 38% | 53% | 6% | 2% | 2% |
| Intermediate RS | 11% | 72% | 6% | 2% | 9% |
| Low RS | 3% | 11% | 2% | 2% | 82% |
| ER+/HER2-neg, would not order <i>Oncotype</i> (n = 36) | 33% | 42% | 11% | 6% | 8% |

75 yo woman: 3.4-cm sentinel node-negative IDC. Which adjuvant chemotherapy treatment would you recommend?

| Tumor Subtype | Anthra → Taxane | TC | AC | Other | None |
|--|--------------------|-----|----|-------|------|
| Triple-negative | 18% | 65% | 6% | 5% | 6% |
| ER+/HER2-neg, would order Oncotype (n = 61) | | | | | |
| High RS | 16% | 69% | 5% | 7% | 3% |
| Intermediate RS | 3% | 46% | 3% | 5% | 43% |
| Low RS | 2% | 6% | 2% | 5% | 85% |
| ER+/HER2-neg, would not order Oncotype (n = 39) | 5% | 41% | 5% | 13% | 36% |

**60 yo woman: 1.0-cm IDC (2 positive nodes).
Which adjuvant chemotherapy treatment would you recommend?**

| Tumor Subtype | Anthra → Taxane | TC | AC | Other | None |
|--|----------------------------|-----------|-----------|--------------|-------------|
| Triple-negative | 73% | 17% | 3% | 6% | 1% |
| ER+/HER2-neg, would order Oncotype (n = 24) | | | | | |
| High RS | 38% | 50% | 4% | 4% | 4% |
| Intermediate RS | 29% | 58% | 0 | 0 | 13% |
| Low RS | 8% | 8% | 4% | 4% | 76% |
| ER+/HER2-neg, would not order Oncotype (n = 76) | 58% | 24% | 7% | 6% | 5% |

**75 yo woman: 1.0-cm IDC (2 positive nodes).
Which adjuvant chemotherapy treatment would you recommend?**

| Tumor Subtype | Anthra → Taxane | TC | AC | Other | None |
|--|----------------------------|-----------|-----------|--------------|-------------|
| Triple-negative | 40% | 48% | 5% | 4% | 3% |
| ER+/HER2-neg, would order Oncotype (n = 44) | | | | | |
| High RS | 25% | 57% | 5% | 11% | 2% |
| Intermediate RS | 11% | 50% | 0 | 9% | 30% |
| Low RS | 0 | 12% | 2% | 2% | 84% |
| ER+/HER2-neg, would not order Oncotype (n = 56) | 32% | 34% | 7% | 9% | 18% |

DNA Repair Signature and Anthracycline Response in TNBC

