Treatment of HER2-Positive Breast Cancer Brain Metastases

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Outline

- Incidence of HER2+ Breast Cancer Brain Metastases
- Management of patients with progression limited to the CNS
- Overview of CNS-permeable approved and investigational agents
  - Overview of data with neratinib, tucatinib and trastuzumab deruxtecan
  - Appropriate sequencing of agents

Courtesy of Carey K Anders, MD

Brain metastases are a common consequence of advanced cancer

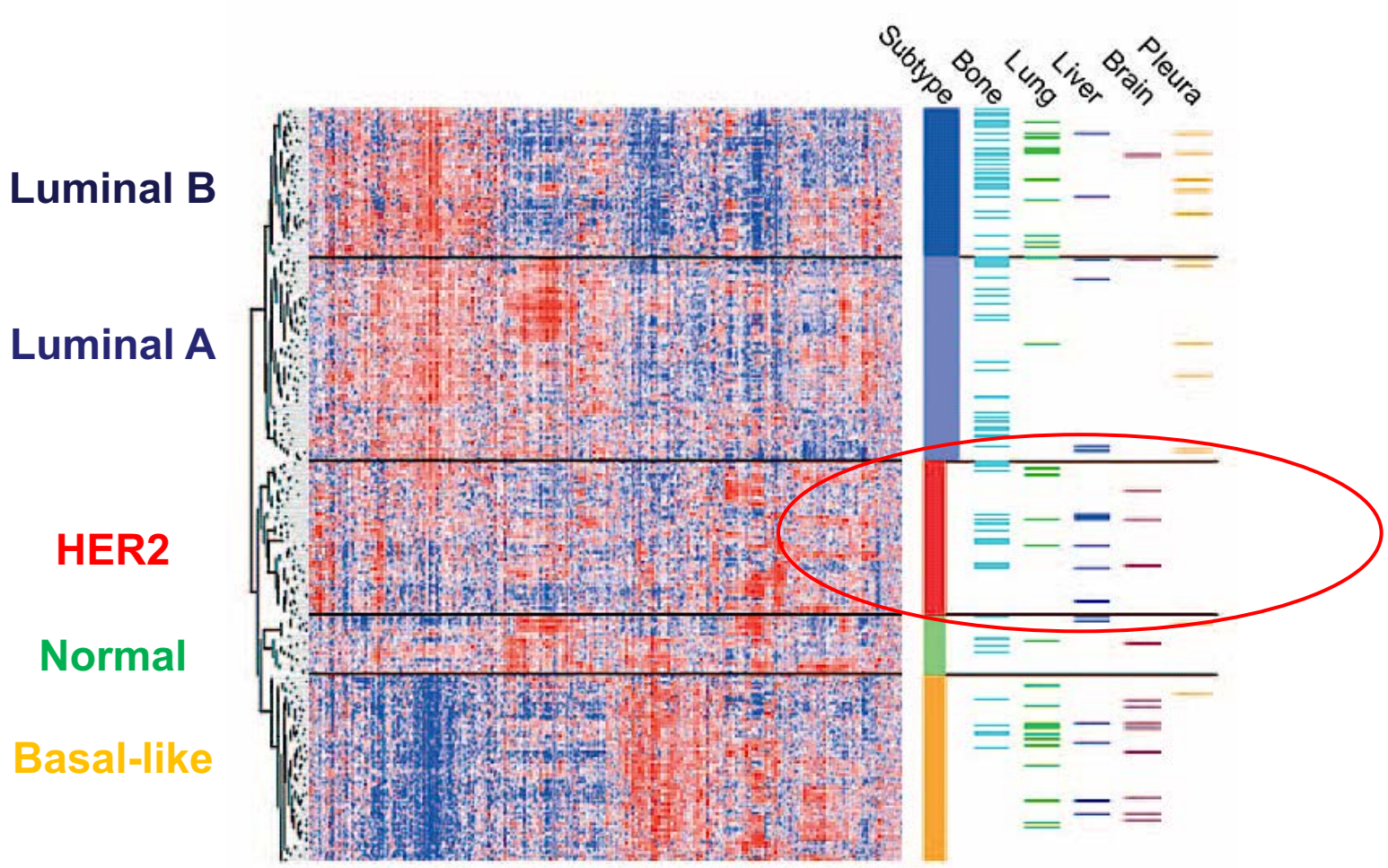
Primary site	Incidence Rates
Lung (overall)	16.3–19.9%
SCLC*	29.7% (at 5 years)
NSCLC*	12.6% (at 5 years)
Breast	10–15%
HER2 positive	25–50%
Triple negative	20%
Melanoma	6.9–7.4% → 40 – 50%
Renal	6.5–9.8%
Colorectal	3.0%

*can be up to 50–60% depending on study and disease duration

Courtesy of Carey K Anders, MD

Glitza Oliva et al. Ann Oncol 2018;29: 1509–1520
Barnholtz-Sloan et al. J. Clin Oncol. 2004;22(14):2865–72
Schouten et al. Cancer. 2002;94(10):2698–705
Chamberalin et al. Neuro-Oncology. 2017;19(1):i1–i24

The brain is a common site of HER2+ breast cancer metastases

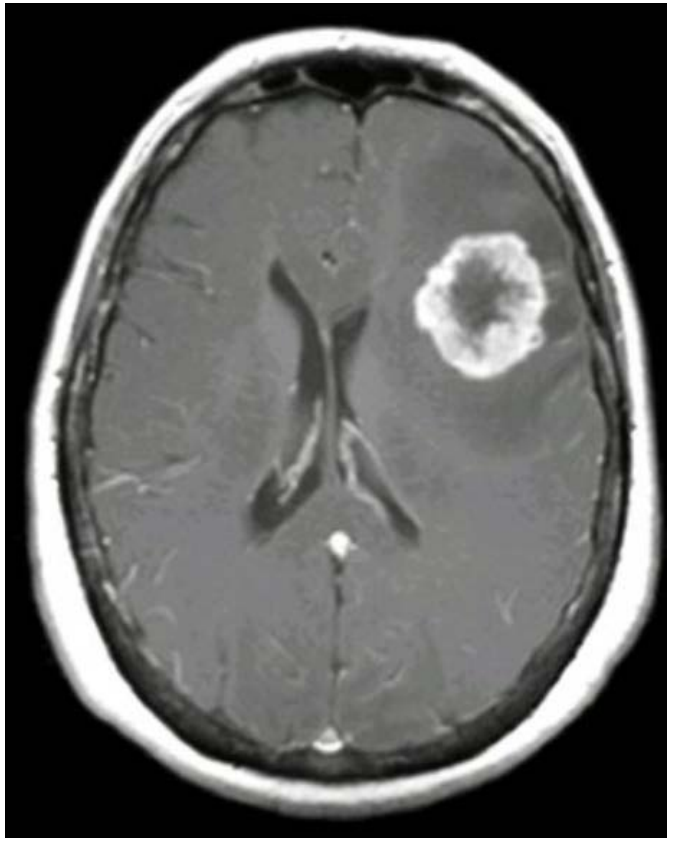


Courtesy of Carey K Anders, MD

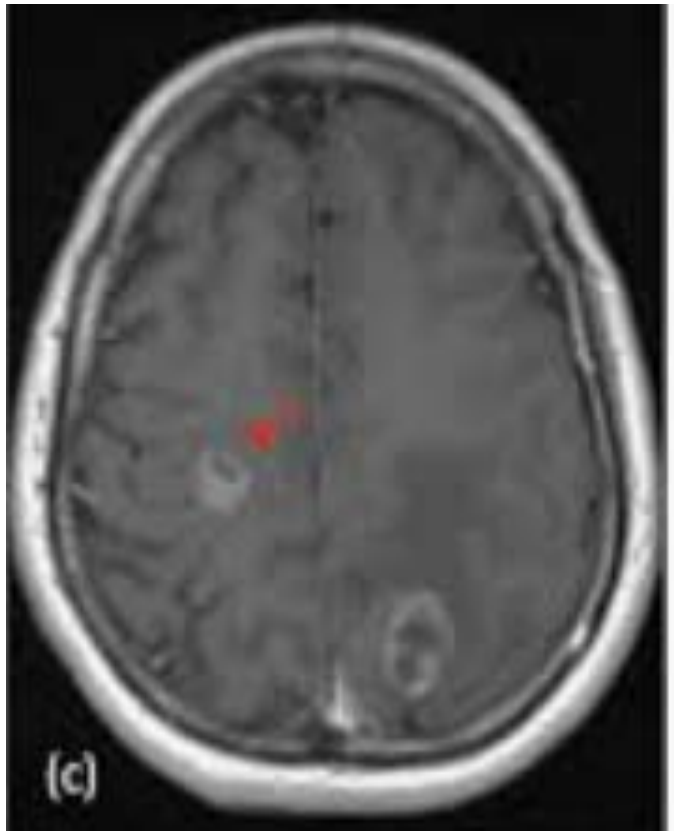
Smid et al. CCR 2008

Radiographic Images of Brain Metastases

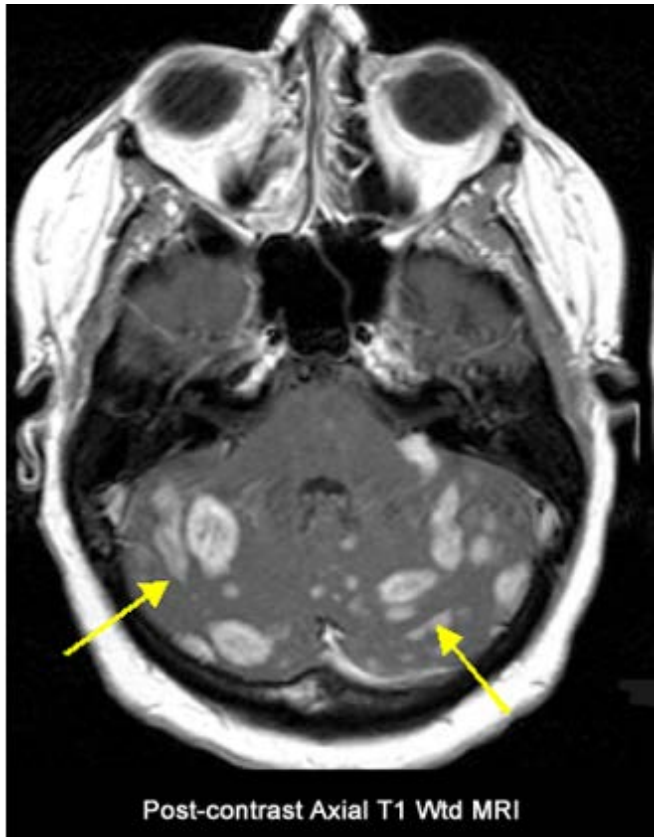
- Solitary lesion



Limited lesions

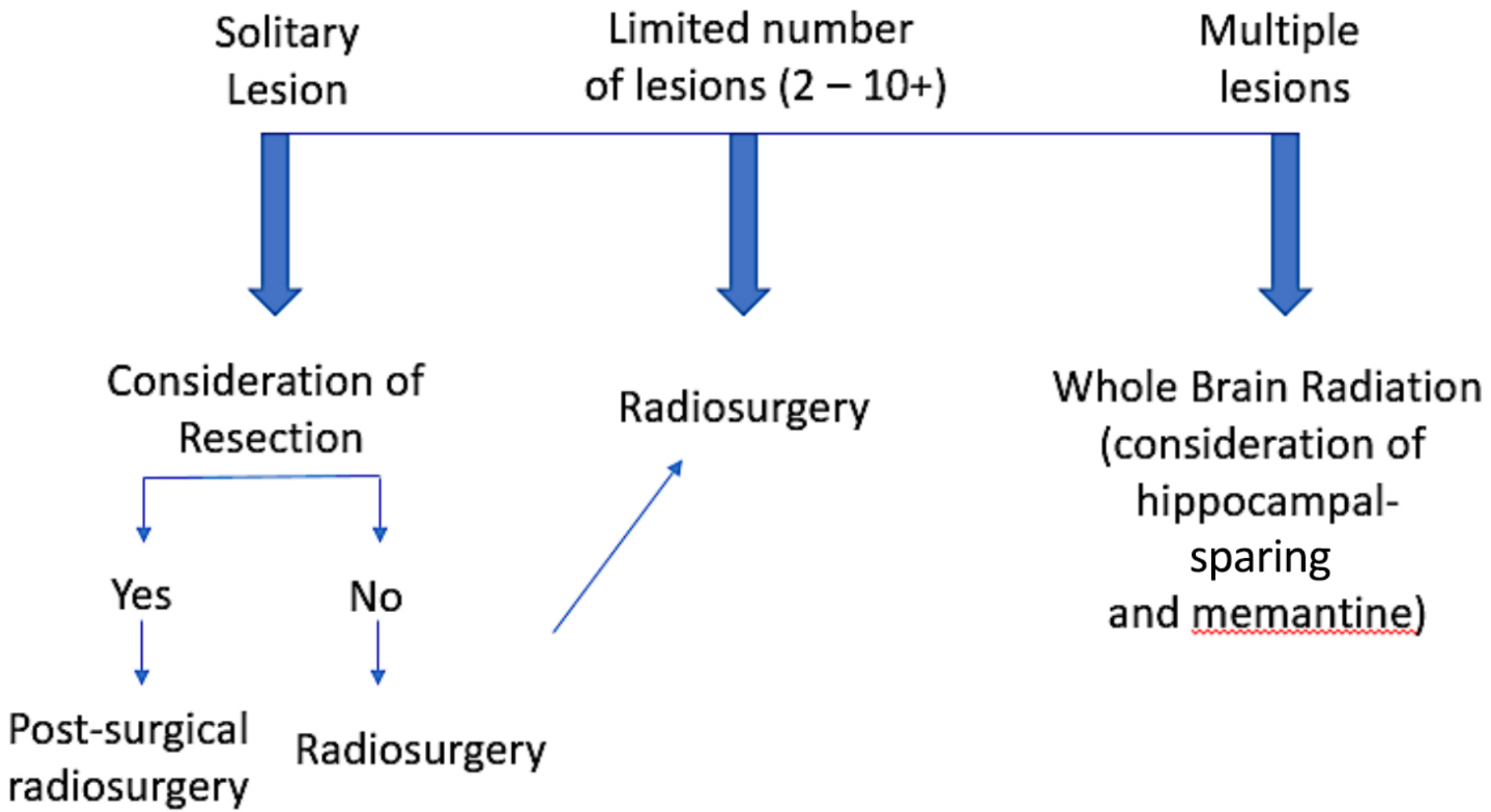


Multiple lesions



Courtesy of Carey K Anders, MD

Local Therapy for Brain Metastases: General Approach



Courtesy of Carey K Anders, MD

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ASCO SPECIAL ARTICLE

Recommendations on Disease Management for Patients With Advanced Human Epidermal Growth Factor Receptor 2–Positive Breast Cancer and Brain Metastases: ASCO Clinical Practice Guideline Update

Naren Ramakrishna, Sarah Temin, Sarat Chandarlapaty, Jennie R. Crews, Nancy E. Davidson, Francisco J. Esteva, Sharon H. Giordano, Jeffrey J. Kirshner, Ian E. Krop, Jennifer Levinson, Shanu Modi, Debra A. Patt, Jane Perlmutter, Eric P. Winer, and Nancy U. Lin

- For patients with progressive intracranial metastases despite initial radiation therapy, options include SRS, surgery, WBRT, a trial of systemic therapy, or enrollment in a clinical trial, depending on initial treatment. For patients in this group who also have diffuse recurrence, best supportive care is an additional option.
- For patients whose systemic disease is not progressive at the time of brain metastasis diagnosis, systemic therapy should not be switched.
- For patients whose systemic disease is progressive at the time of brain metastasis diagnosis, clinicians should offer HER2-targeted therapy according to the algorithms for treatment of HER2-positive metastatic breast cancer.

Courtesy of Carey K Anders, MD

NCCN: Systemic Therapy Options Expanded in 2020

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2020
Central Nervous System Cancers

PRINCIPLES OF BRAIN AND SPINAL CORD TUMOR SYSTEMIC THERAPY
BRAIN METASTASES

- Tumor agnostic[s]
  - *NTRK* gene-fusion tumors
    - ◊ Larotrectinib[113,114]
    - ◊ Entrectinib[115,116]
  - Temozolomide 5/28 schedule

- Breast Cancer[u]
  - HER2-positive
    - ◊ Capecitabine + lapatinib[117,118]
    - ◊ Capecitabine + neratinib[119,120]
    - ◊ Paclitaxel + neratinib (category 2B)[121]
    - ◊ Capecitabine (category 2B)[122-126]
    - ◊ Tucatinib + trastuzumab + capecitabine (if previously treated with 1 or more anti-HER2-based regimens)[127]
  - HER2 non-specific
    - ◊ Cisplatin (category 2B)[128,129]
    - ◊ Etoposide (category 2B)[128,129]
    - ◊ Cisplatin + etoposide (category 2B)[129,130]
    - ◊ High-dose methotrexate (category 2B)[m,131]

***Tucatinib added to list in 2020**

- Melanoma[u]
  - *BRAF* V600E positive
    - ◊ Dabrafenib[132-134]/trametinib[135]
    - ◊ Vemurafenib[136,137]/cobimetinib[t] (category 2B)
  - *BRAF* non-specific
    - ◊ Ipilimumab + nivolumab (preferred) [138-140]
    - ◊ Ipilimumab[141]
    - ◊ Nivolumab[139]
    - ◊ Pembrolizumab[142]

- Non-Small Cell Lung Cancer[u]
  - EGFR-sensitizing mutation positive
    - ◊ Osimertinib (EGFR T790M positive)[143-145]
    - ◊ Pulsatile erlotinib[146-148]
    - ◊ Afatinib (category 2B)[149]
    - ◊ Gefitinib (category 2B)[150,151]
  - ALK rearrangement positive
    - ◊ Brigatinib[152,153]
    - ◊ Alectinib[154,155]
    - ◊ Ceritinib[156]
  - ALK rearrangement positive or ROS1 positive
    - ◊ Crizotinib (category 2B)[157]
  - PD-L1 positive
    - ◊ Pembrolizumab[142,158]
    - ◊ Nivolumab[159-161]

- Small Cell Lung Cancer[u]
  - ◊ Topotecan (category 2B)

- Lymphoma[u]
  - ◊ High-dose methotrexate[162]

www.NCCN.org

Courtesy of Carey K Anders, MD

Systemic therapy for HER2+ breast cancer brain metastases

Commercially available:

- Lapatinib-capecitabine
- T-DM1
- Neratinib-capecitabine*
- Tucatinib/trastuzumab/capecitabine (HER2Climb)
- Trastuzumab deruxtecan
- Anthracyclines (e.g. trastuzumab-doxorubicin)
- Platinum salts (e.g. trastuzumab-carboplatin)

Selected completed and ongoing clinical trials:

- Neratinib + T-DM1
- T-DM1 +/- Tucatinib
- T-DM1-temozolomide s/p SRS
- Trastuzumab/pertuzumab/atezolizumab
- "High dose" trastuzumab (closed to accrual, awaiting mature data)

*2020 NCCN Guidelines on Neuro-Oncology include neratinib-capecitabine as an option for patients with HER2+ breast cancer brain metastases.

Courtesy of Carey K Anders, MD

Slide courtesy of Dr. Nancy Lin per SABCS 2018

HER2+ Breast Cancer Brain Metastases: Lapatinib

Study	N	CNS ORR	Minor response 20-50% vol ↓	TTP/PFS
Lin et al JCO 2008	39	**2.6%** (RECIST) **5.2%** (50% volumetric reduction)	10%	3.0 mo
Lin et al CCR 2008	237*	**6%** (composite criteria)	15%	2.4 mo
	50 (L+ Cape)	**20%** (optional extension)	18%	3.6 mo

Courtesy of Carey K Anders, MD

LANDSCAPE: Lapatinib/Capecitabine in XRT-*Naïve* HER2+ BCBM

Primary Endpoint: CNS volumetric response rate (>50% reduction)

CNS-OR : 29/43 = 67.4% (95% CI: 52-81)

CNS Volumetric change	n = 43 (%)	
≥ 80% Reduction	9	(20.9)
50- <80% Reduction	20	(46.5)
20- <50% Reduction	6	(14)
> 0- <20% Reduction	2	(4.7)
Progression*	6	(14)

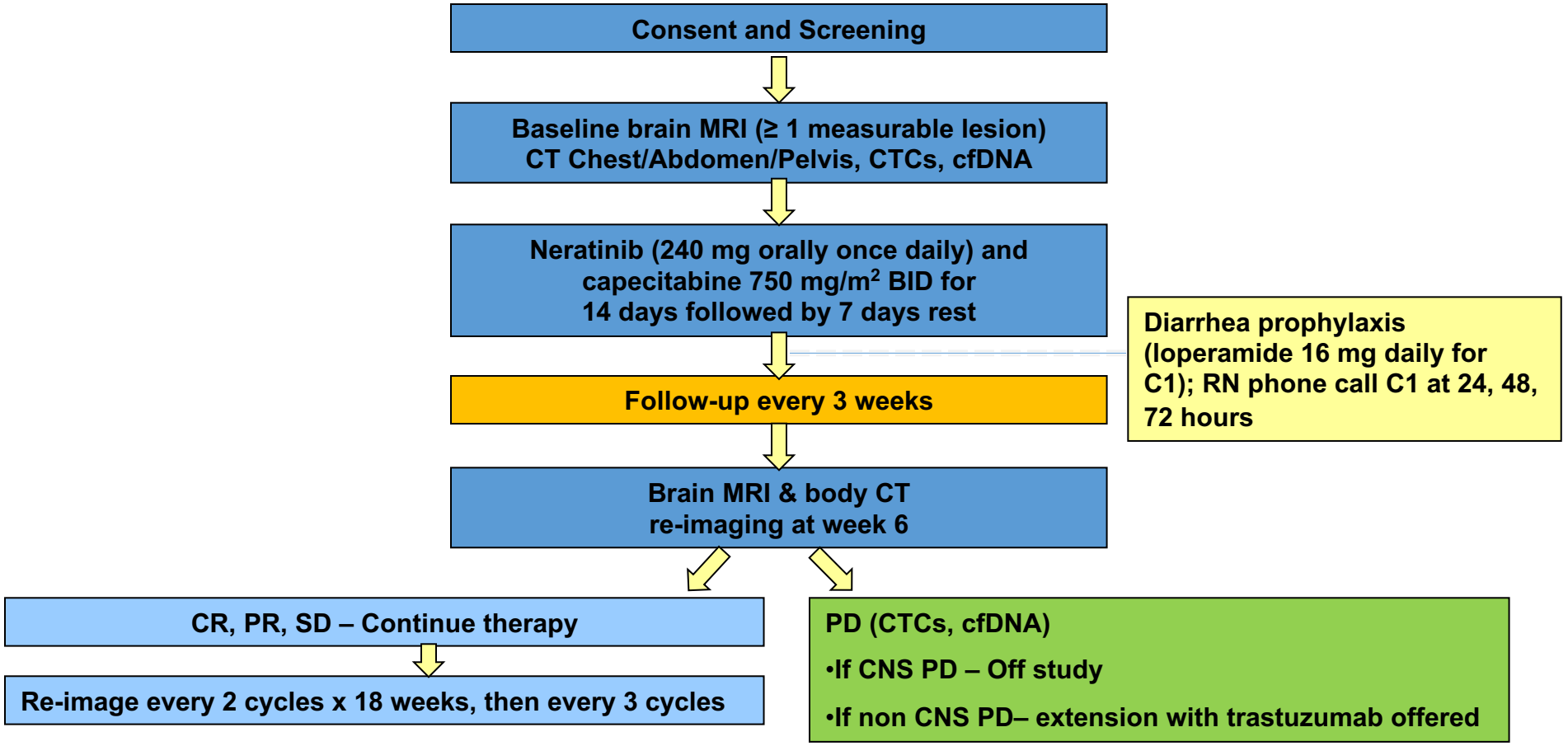
NSS improvement : 14/24 = 58.3% (95% CI: 36.6-77.9)

TTP: 5.5 months (95% CI = 4.3 – 6mos); OS: 6mos survival = 91%

Bachelot et al. ASCO 2011, Abstr # 509; Lancet Oncology 2013.

Courtesy of Carey K Anders, MD

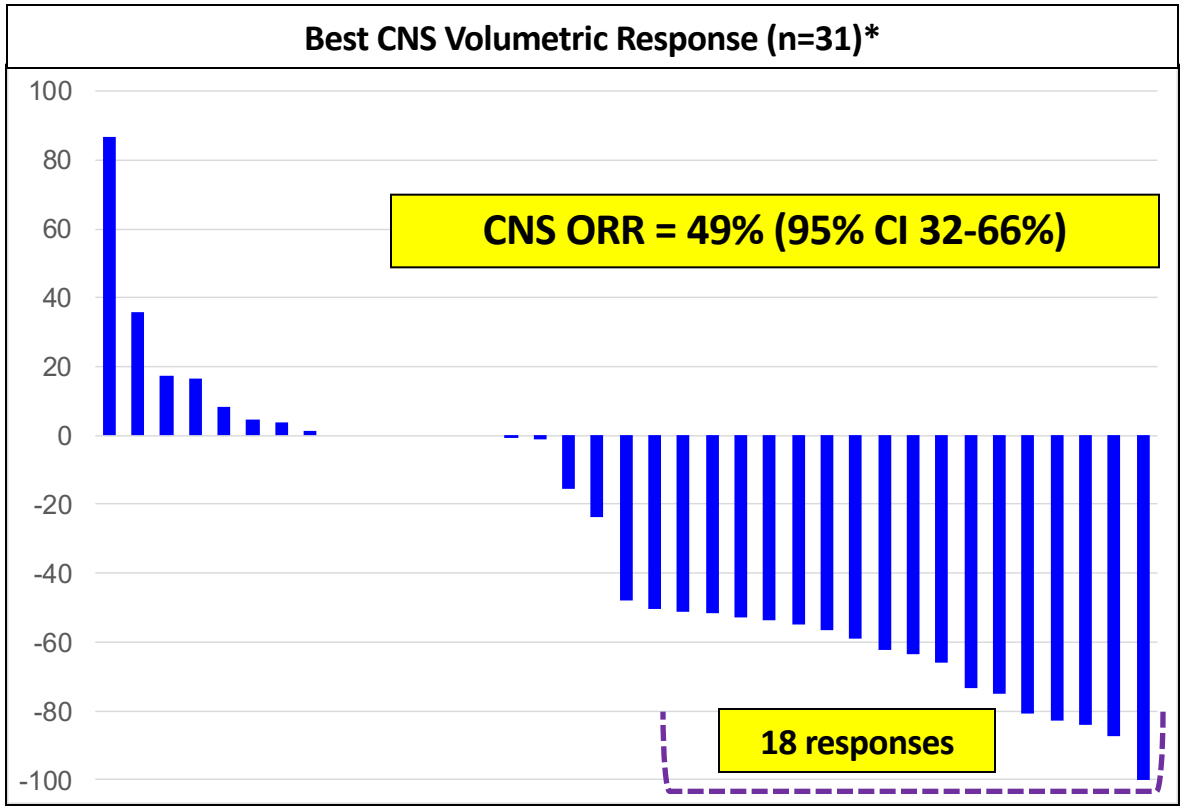
TBCRC 022 (Ph II neratinib/capecitabine): Study Design



Freedman R, et al. JCO 2019 and Clin Br Cancer 2020

Courtesy of Carey K Anders, MD

Primary Endpoint – Neratinib/Capecitabine:
CNS Volumetric Response



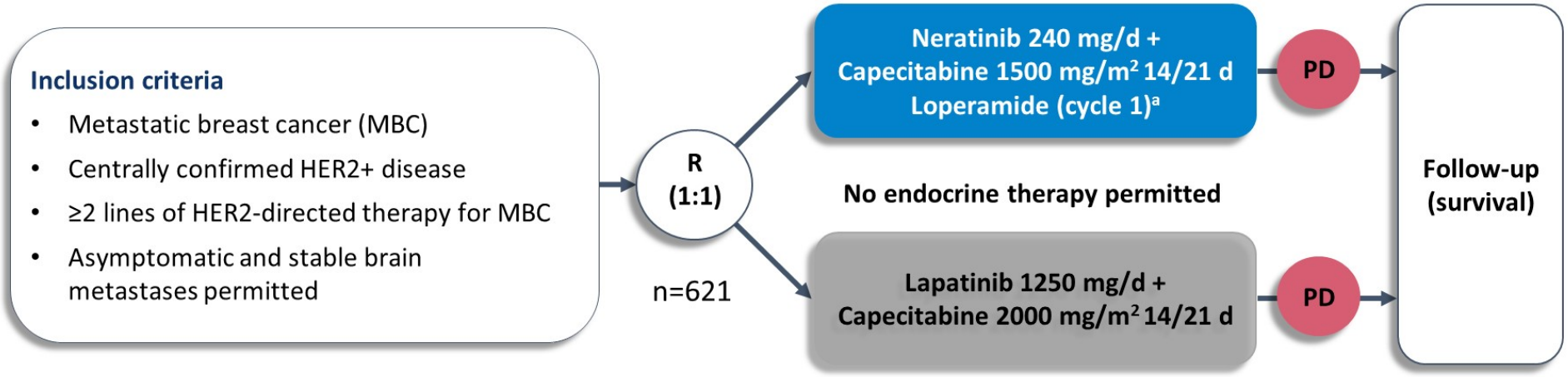
*** 6 patients did not reach first re-staging evaluation and are categorized as '0'**
┼ No patient had clear increase in steroid use, non-target lesions, non-CNS lesions, or worsening neurological symptoms at time of radiographic response

Courtesy of Carey K Anders, MD

Freedman R, et al. JCO 2019 and Clin Br Cancer 2020

Neratinib vs. lapatinib both plus capecitabine in HER2+ MBC

NALA study design



Stratification variables

- Number of prior HER2 therapies for MBC
- Disease location
- HR status
- Geographic location

Endpoints

- Co-primary: PFS (centrally confirmed) and OS
- Secondary: PFS (local), ORR, DoR, CBR, intervention for CNS metastases, safety, health outcomes

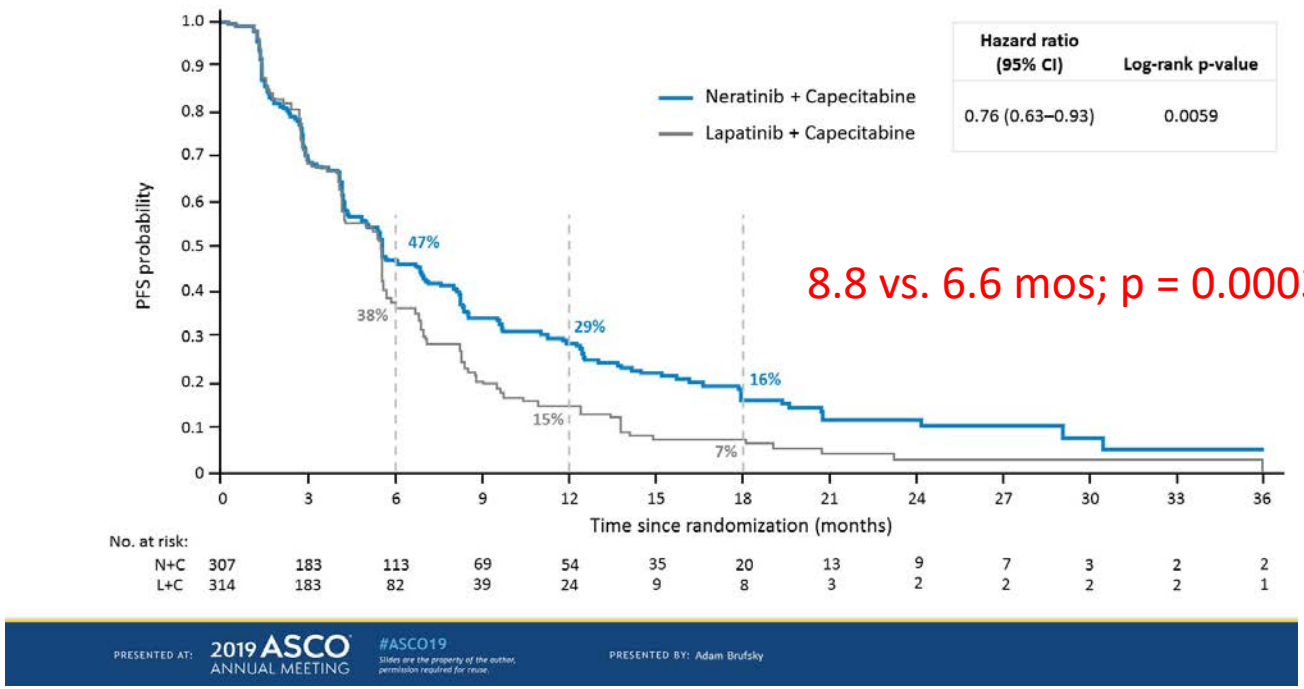
Loperamide 4 mg with first dose of neratinib, followed by 2 mg every 4 h for first 3 d, then loperamide 2 mg every 6–8 h until end of Cycle 1. Thereafter as needed

Courtesy of Carey K Anders, MD

Presented By Cristina Saura at 2019 ASCO Annual Meeting and Saura et al. JCO 2020.

Centrally confirmed PFS (co-primary endpoint)

NALA



8.8 vs. 6.6 mos; p = 0.0003

Time to intervention for CNS Mets:
- Neratinib/cape = 22%
- Lapatinib/cape = 29%

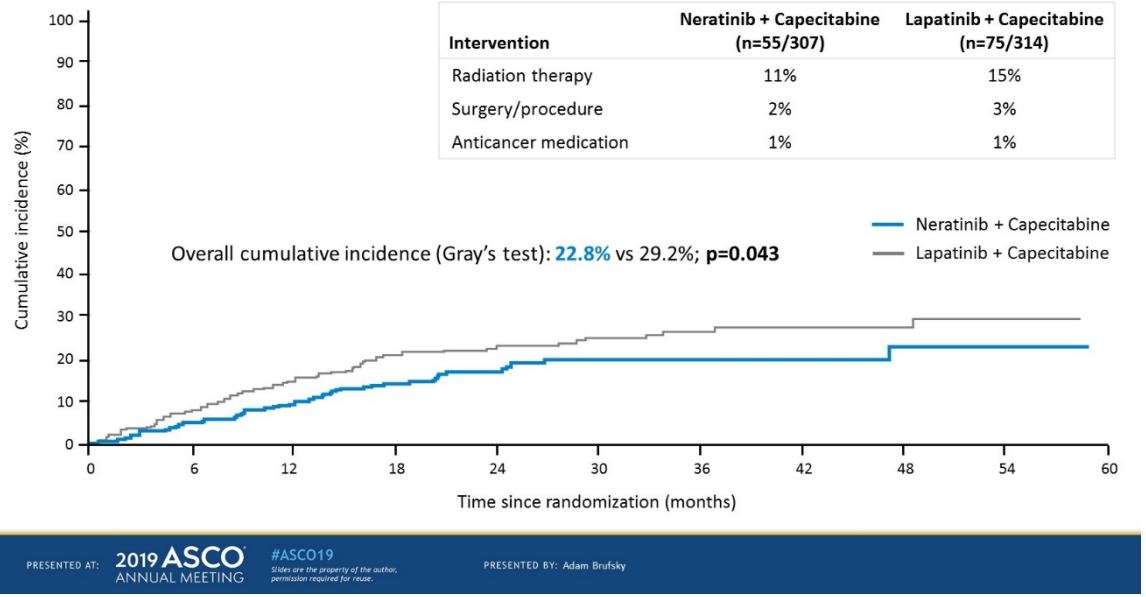
p = 0.043

30% of patients had received prior trastuzumab, pertuzumab and T-DM1

70% had 2 prior lines of therapy
30% had 3 prior lines of therapy

Time to intervention for CNS metastases

Intervention	Neratinib + Capecitabine (n=55/307)	Lapatinib + Capecitabine (n=75/314)
Radiation therapy	11%	15%
Surgery/procedure	2%	3%
Anticancer medication	1%	1%



Courtesy of Carey K Anders, MD

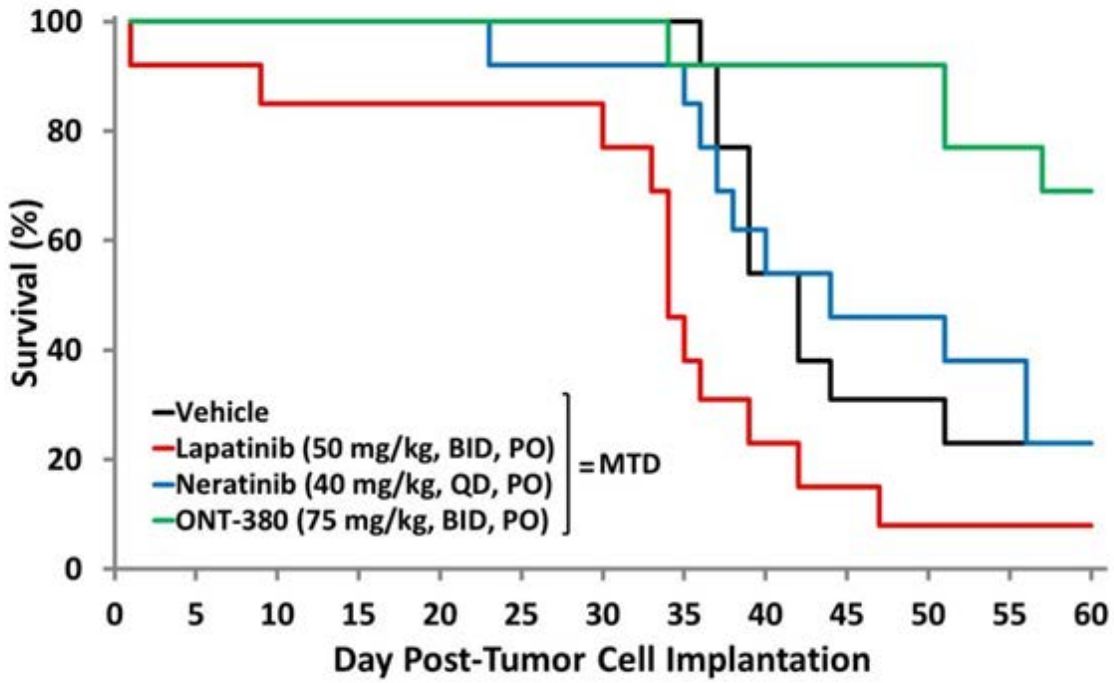
Presented By Cristina Saura at 2019 ASCO Annual Meeting and Saura et al. JCO 2020.

Tucatinib (ONT-380) in metastatic HER2+ breast cancer

Highly selective to HER2

Compound	Cellular Selectivity Data	
	HER2 IC_{50} (nM)	EGFR IC_{50} (nM)
tucatinib (ONT-380)	**8**	**>1000**
Neratinib	7	8
Lapatinib	49	31

Preclinical data in intracranial HER2+ BCBM models (BT-474)



Courtesy of Carey K Anders, MD

HER2CLIMB: Background

- Up to half of patients with HER2+ metastatic breast cancer may develop brain metastases and effective and tolerable treatment options are needed.[1-4]
- Tucatinib is an oral TKI, recently approved by the FDA, that is highly selective for the kinase domain of HER2 with minimal inhibition of EGFR.[5-6]

HER2CLIMB Randomized, Double-blind, Pivotal Trial

Key Eligibility Criteria

- HER2+ metastatic breast cancer
- Prior treatment with trastuzumab, pertuzumab, and T-DM1
- ECOG performance status 0 or 1
- Brain MRI at baseline

*Stratification factors: presence of brain metastases (yes/no), ECOG status (0 or 1), and region (US or Canada or rest of world)

R* (2:1)

N=410

Tucatinib 300 mg PO BID + **Trastuzumab** 6 mg/kg Q3W, loading dose 8 mg/kg C1D1 + **Capecitabine** 1000 mg/m² PO BID Days 1-14

21-day cycle

N=202

Placebo + **Trastuzumab** 6 mg/kg Q3W, loading dose 8 mg/kg C1D1 + **Capecitabine** 1000 mg/m² PO BID Days 1-14

21-day cycle

https://clinicaltrials.gov/ct2/show/NCT02614794

1. Bendell JC, et al. Cancer 2003;97:2972-7.
2. Brufsky AM, et al. Clin Cancer Res 2011;17:4834-43.
3. Leyland-Jones B. J Clin Oncol 2009;27:5278-86.
4. Olson EM, et al. Breast 2013;22:525-31.
5. Moulder SL, et al. Clin Cancer Res 2017;23:3529-36.
6. Pheneger T, et al. Cancer Research 2009;69:1795.

TKI: tyrosine kinase inhibitor

PRESENTED BY: Nancy Lin, nlin@partners.org

Courtesy of Carey K Anders, MD

HER2CLIMB Primary Analysis Results – SABCS 2019

- The HER2CLIMB trial met all primary and alpha-controlled secondary endpoints at the first interim analysis.
- Importantly, the secondary endpoint of PFS in patients with brain metastases was met.

PFS by BICR N=480*	Overall Survival N=612	PFS by BICR in patients with brain metastases N=291
Risk of progression or death was reduced by **46%**	Risk of death was reduced by **34%**	Risk of progression or death was reduced by **52%**
95% CI: 0.42 to 0.71, P<0.001	95% CI, 0.50 to 0.88, P=0.005	95% CI, 0.34 to 0.69, P<0.001

PFS: progression-free survival; BICR: blinded independent central review
*The primary endpoint of PFS was assessed in the first 480 patients enrolled.

Murthy RK, et al. *N Engl J Med* 2020;382:597-609.

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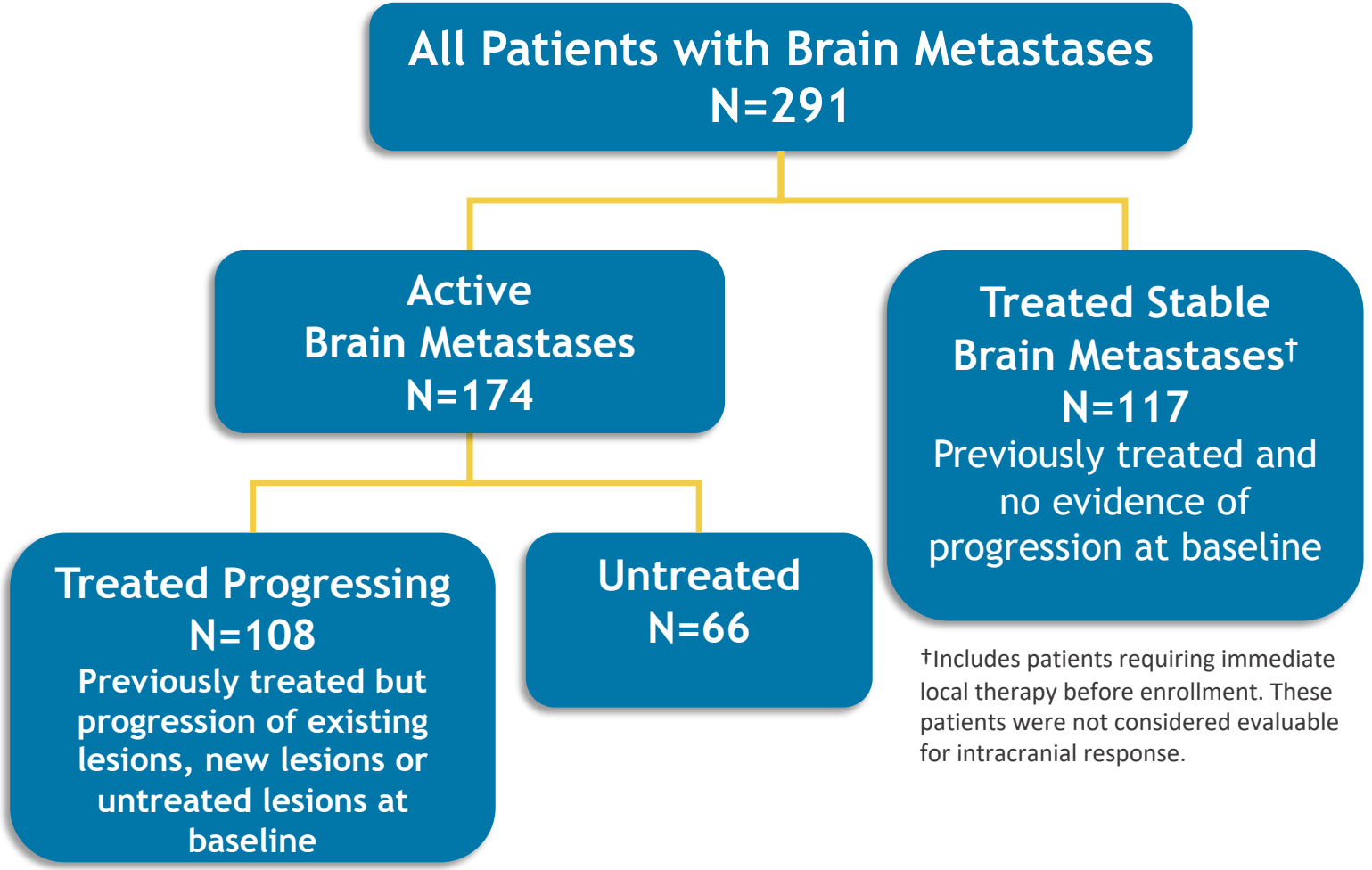
Courtesy of Carey K Anders, MD

HER2CLIMB Analysis of Patients with Brain Metastases

- Brain MRI at baseline for all patients
- Brain MRI for brain metastases patients every 6 weeks in first 24 weeks, every 9 weeks thereafter
- Eligible brain metastases patients:
  - Not requiring immediate local therapy
  - Requiring local therapy during screening could be eligible after washout*



†Includes patients requiring immediate local therapy before enrollment. These patients were not considered evaluable for intracranial response.

*These patients were included in the Treated Stable group for analysis.

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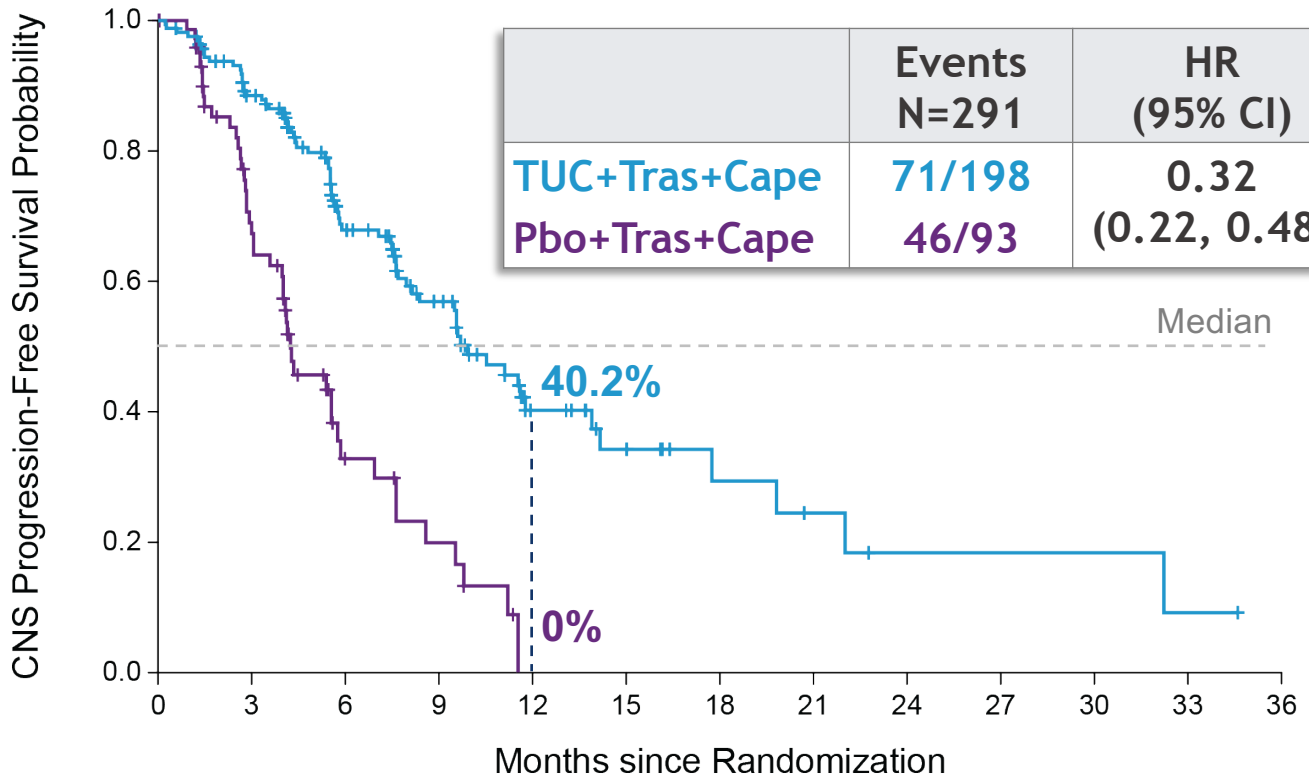
HER2CLIMB: CNS-PFS Benefit in Patients with Brain Metastases



	Events N=291	HR (95% CI)	P Value
TUC+Tras+Cape	71/198	0.32 (0.22, 0.48)	<0.00001
Pbo+Tras+Cape	46/93		

No. at Risk													
TUC+Tras+Cape	198	132	74	45	18	11	6	4	2	2	2	1	0
Pbo+Tras+Cape	93	41	11	6	0	0	0	0	0	0	0	0	0

Risk of CNS progression or death was reduced by 68% in patients with brain metastases

One-year CNS-PFS (95% CI):

TUC+Tras+Cape	Pbo+Tras+Cape
40.2% (29.5, 50.6)	0%

Median CNS-PFS (95% CI):

TUC+Tras+Cape	Pbo+Tras+Cape
9.9 months (8.0, 13.9)	4.2 months (3.6, 5.7)

Stable BrMets:	13.9 mos	5.6 mos
Active BrMets:	9.5 mos	4.1 mos

CNS-PFS: time from randomization to disease progression in the brain or death by investigator assessment.
HR: hazard ratio computed from Cox proportional hazards model using stratification factors (ECOG performance status: 0/1, and Region of world: North America/Rest of World) at randomization. All P values are nominal.

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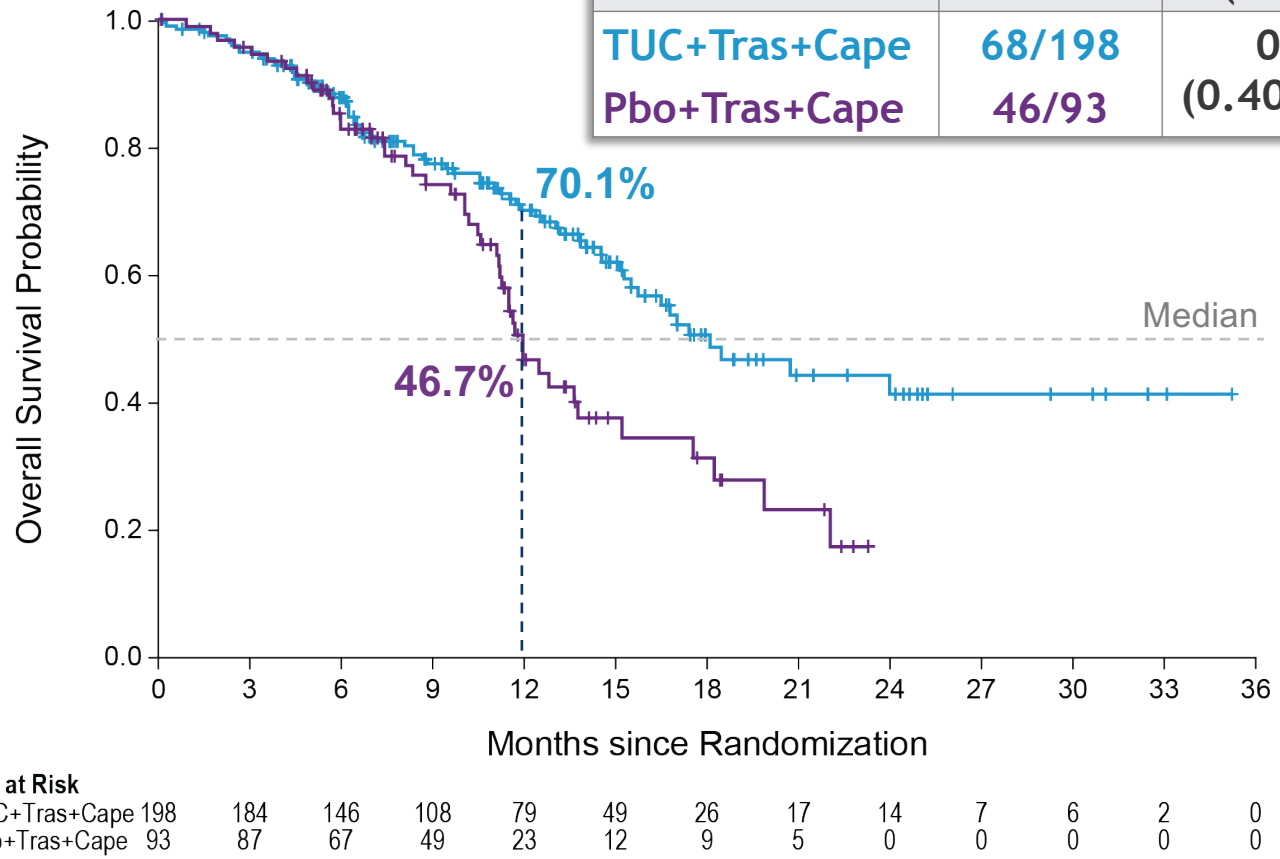
Courtesy of Carey K Anders, MD

HER2CLIMB: OS Benefit in Patients with Brain Metastases

	Events N=291	HR (95% CI)	P Value
TUC+Tras+Cape	68/198	0.58 (0.40, 0.85)	0.005
Pbo+Tras+Cape	46/93		



Risk of death was reduced by 42% in patients with brain metastases

One-year OS (95% CI):	
TUC+Tras+Cape	Pbo+Tras+Cape
70.1% (62.1, 76.7)	46.7% (33.9, 58.4)
Median OS (95% CI):	
18.1 months (15.5, NE)	12.0 months (11.2, 15.2)

NE: not estimable

Stable BrMets:	15.7 mos	13.6 mos
Active BrMets:	20.7 mos	11.6 mos

HR: hazard ratio computed from Cox proportional hazards model using stratification factors (ECOG performance status: 0/1, and Region of world: North America/Rest of World) at randomization. All P values are nominal.

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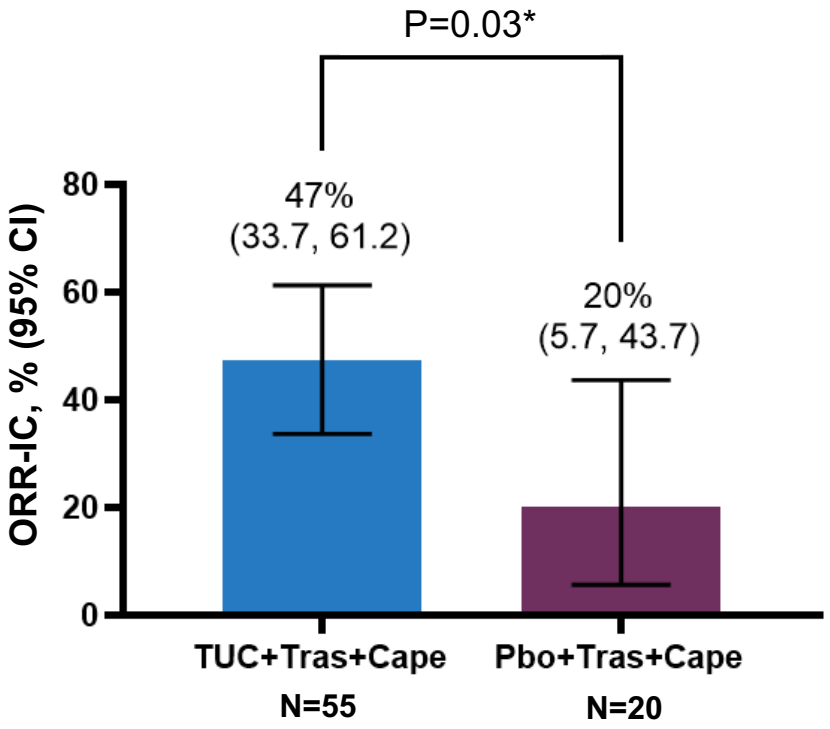
HER2CLIMB: Intracranial Response Rate (ORR-IC) in Patients with Active Brain Metastases and Measurable Intracranial Lesions at Baseline

Confirmed Objective Response Rate (RECIST 1.1)



*Stratified Cochran-Mantel-Haenszel P value

	TUC+Tras+Cape (N=55)	Pbo+Tras+Cape (N=20)
Best Overall Intracranial Response[a], n (%)		
Complete Response (CR)	3 (5.5)	1 (5.0)
Partial Response (PR)	23 (41.8)	3 (15.0)
Stable Disease (SD)	24 (43.6)	16 (80.0)
Progressive Disease (PD)	2 (3.6)	0
Not Available[b]	3 (5.5)	0
Subjects with Objective Response of Confirmed CR or PR, n	26	4
Duration of Intracranial Response (DOR-IC)[e] (95% CI)[f], months	6.8 (5.5, 16.4)	3.0 (3.0, 10.3)

(a) Confirmed Best overall response assessed per RECIST 1.1. (b) Subjects with no post-baseline response assessments. (c) Two-sided 95% exact confidence interval, computed using the Clopper-Pearson method (1934). (d Cochran-Mantel-Haenszel test controlling for stratification factors (ECOG performance status: 0/1, and Region of world: North America/Rest of World) at randomization. (e) As estimated using Kaplan-Meier methods. (f) Calculated using the complementary log-log transformation method (Collett, 1994).

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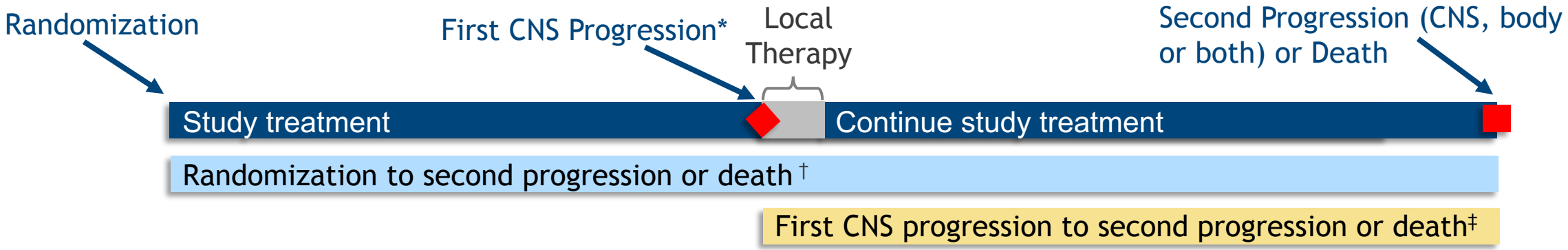
HER2CLIMB: PFS in Patients with Isolated Progression in the Brain Who Continued with Assigned Study Treatment



	Median time from randomization to second progression or death	HR	Median time from first CNS progression to second progression or death	HR
TUC+Tras+Cap N=21	15.9 months (11.7, 28.2)	0.292 (0.11, 0.77) P=0.009	7.6 months (3.9, 11.3)	0.332 (0.13, 0.85) P=0.02
Pbo+Tras+Cap N=9	9.7 months (4.9, 12.0)		3.1 months (1.2, 4.1)	

*Note: First CNS progression was captured as a PFS event in the primary analysis.
† Time from randomization to second progression or death among patients who received local therapy and continued study treatment after isolated CNS progression.
‡Time from first isolated CNS progression to second progression or death among patients who received local therapy and continued study treatment after isolated CNS progression.

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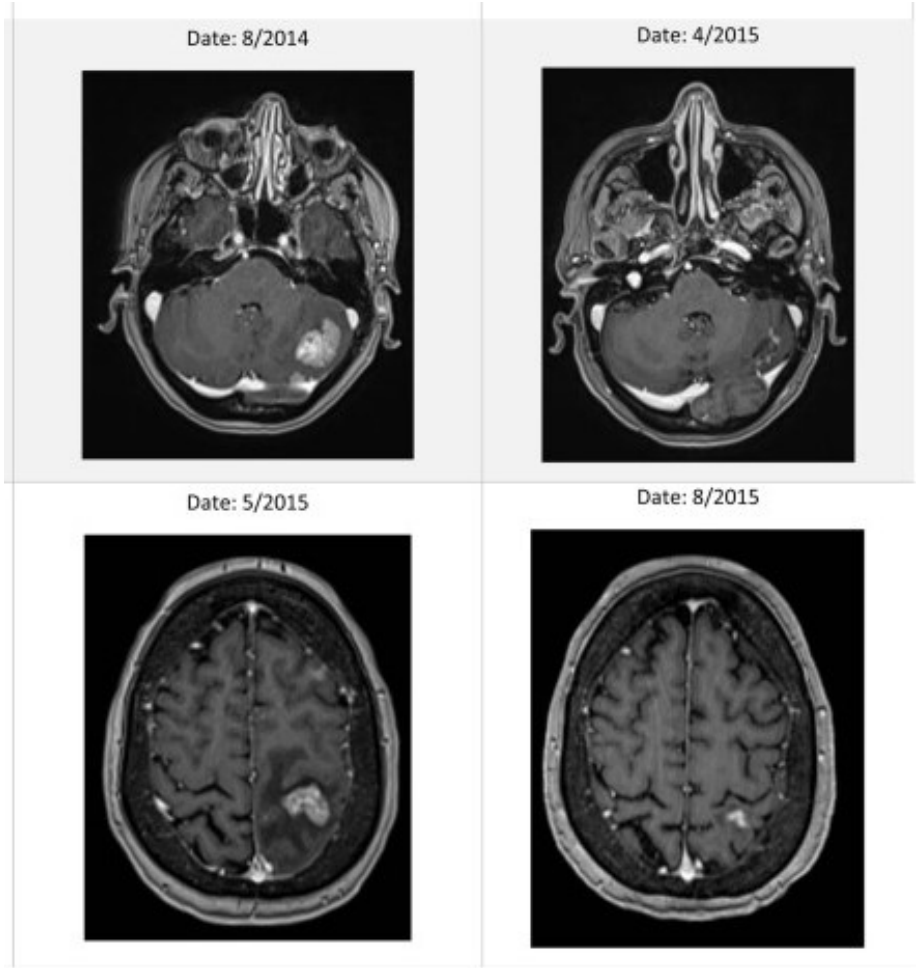
T-DM1 activity in HER2+ brain metastases: UNC experience and case reports



Case report of n = 10 pts illustrated
PFS of 5.5 mos; OS 8.5 mos

Four patients treated at UNC with durable responses, one over 16 mos.

Ph II study of T-DM1 plus neratinib in HER2+ BCBM activated through TBCRC 022

(PI R. Freedman)

R. Bartsch,et al, Clin.Exp.Metastasis 2015.

Keith, K et al. Cancer Treat Comm 2016.

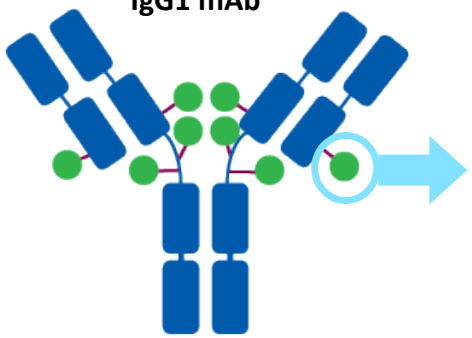
Courtesy of Carey K Anders, MD

Trastuzumab Deruxtecan (DS-8201) Is a Novel ADC Designed to Deliver an Optimal Antitumor Effect

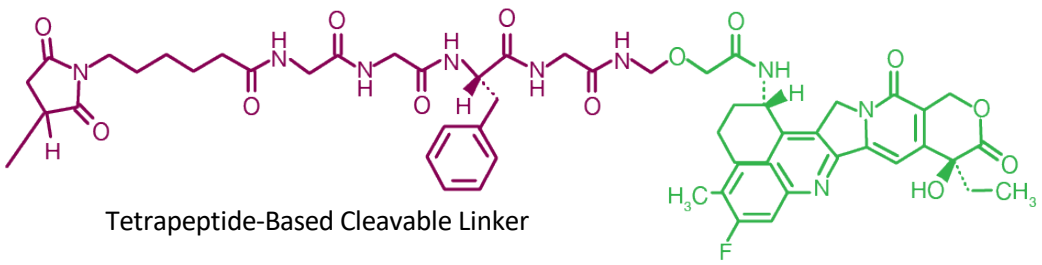
Trastuzumab deruxtecan is an ADC composed of 3 components:

- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload, an exatecan derivative
- A tetrapeptide-based cleavable linker

Humanized anti-HER2 IgG1 mAb[1-3]



Deruxtecan[1,2]



Tetrapeptide-Based Cleavable Linker

Topoisomerase I Inhibitor payload (DXd)

- Payload MOA: topoisomerase I inhibitor
- High potency of payload
- High drug to antibody ratio ≈ 8
- Payload with short systemic half-life
- Stable linker-payload
- Tumor-selective cleavable linker
- Membrane-permeable payload

The clinical relevance of these features is under investigation.

ADC, antibody-drug conjugate; MOA, mechanism of action.

1. Nakada T, et al. Chem Pharm Bull (Tokyo). 2019;67(3):173-185. 2. Ogitani Y, et al. Clin Cancer Res. 2016;22(20):5097-5108. 3. Trail PA, et al. Pharmacol Ther. 2018;181:126-142. 4. Ogitani Y, et al. Cancer Sci. 2016;107(7):1039-1046.

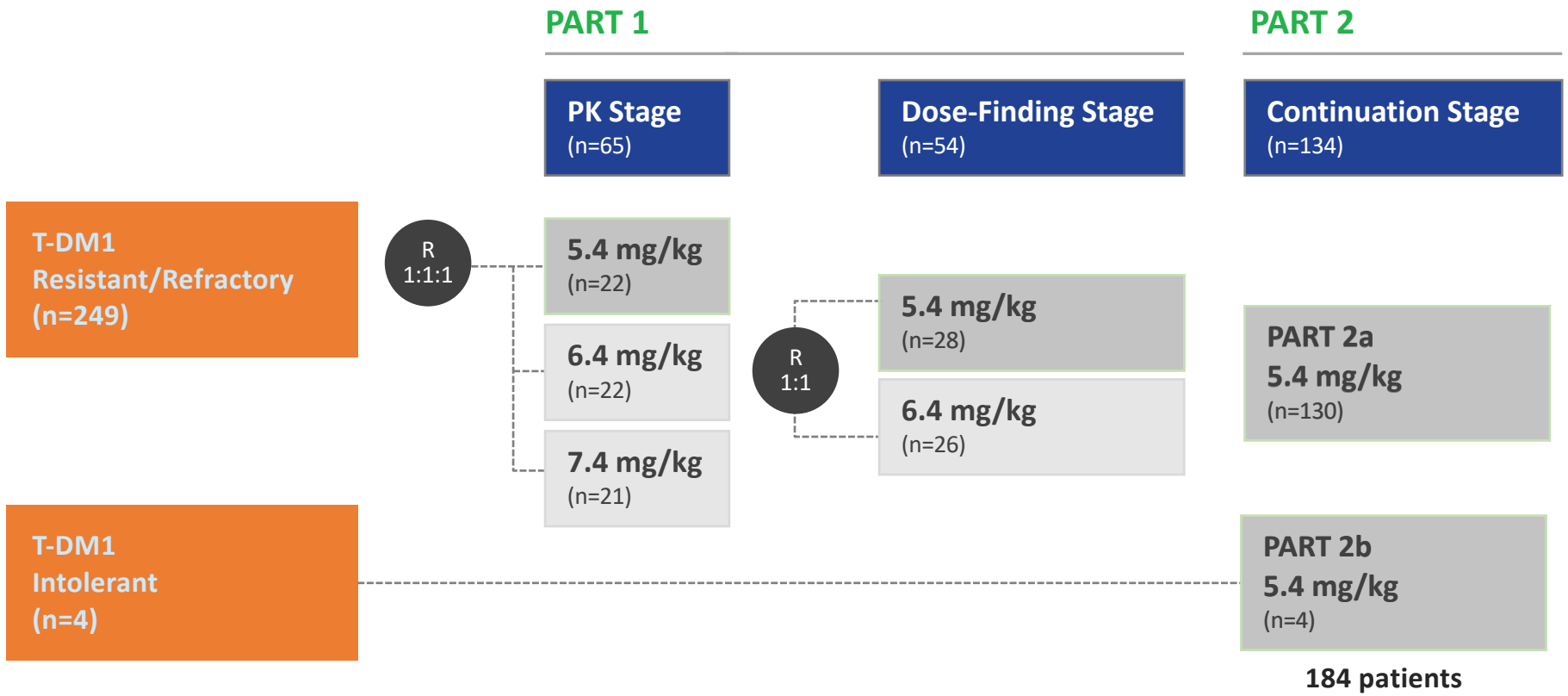
Courtesy of Carey K Anders, MD

DESTINY-Breast01 Study Design:

An Open-Label, Multicenter, Phase 2 Study

Population

- ≥18 years of age
- Unresectable and/or metastatic BC
- HER2-positive (centrally confirmed on archival tissue)
- Prior T-DM1
- Excluded patients with history of significant ILD
- Stable, treated brain metastases were allowed



184 patients enrolled at 5.4 mg/kg

Endpoints

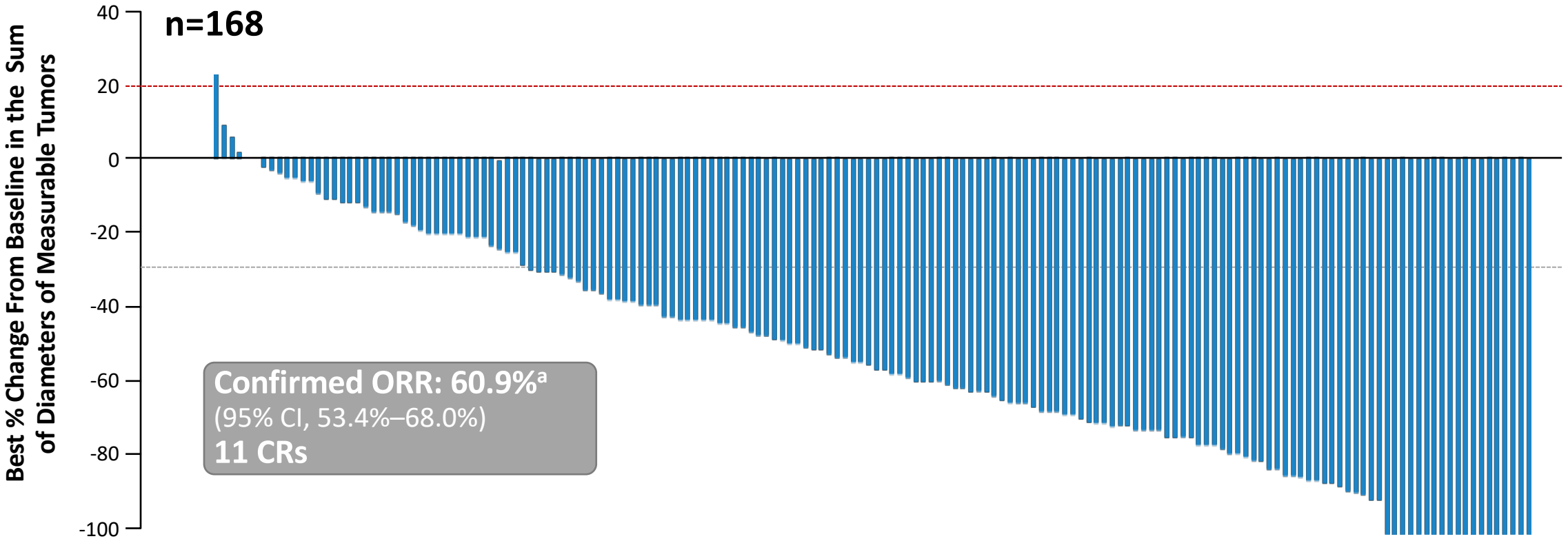
- **Primary:** confirmed ORR by independent central imaging facility review per RECIST v1.1
- **Secondary:** investigator-assessed ORR, DCR, DOR, CBR, PFS, OS, PK and safety

Data Cutoff: August 1, 2019

- **79 patients** (42.9%) are ongoing
- **105 patients** (57.1%) discontinued, primarily for progressive disease (28.8%)

Courtesy of Carey K Anders, MD

DESTINY-Breast01: Best Change in Tumor Size



By independent central review.

The line at 20% indicates progressive disease; the line at −30% indicates partial response.

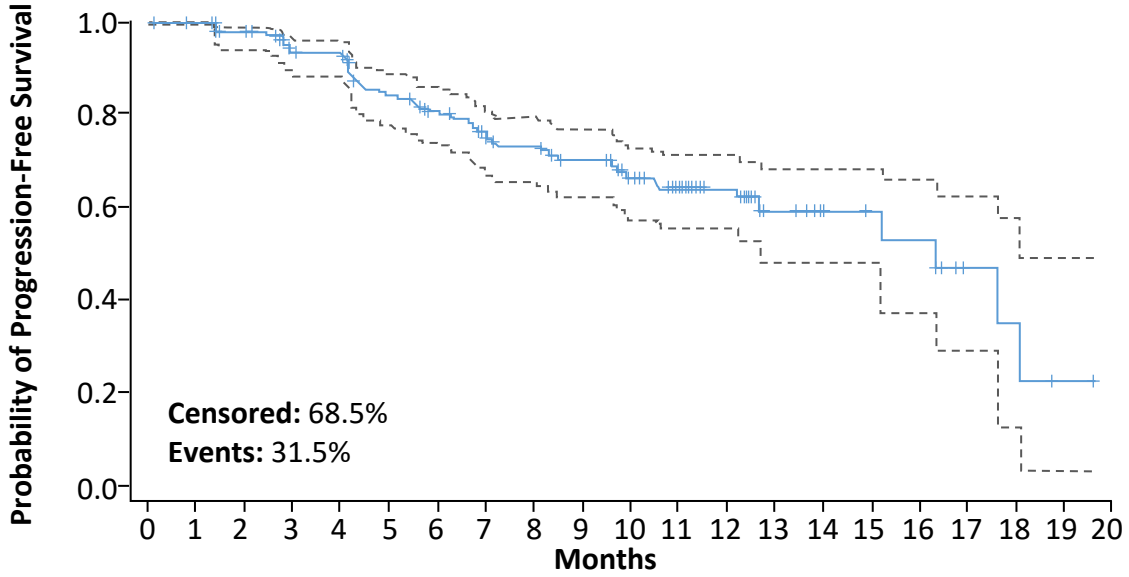
[a] Includes all patients who received T-DXd 5.4 mg/kg (intent-to-treat analysis; N=184).

Courtesy of Carey K Anders, MD

DESTINY-Breast01: Progression-Free and Overall Survival

Progression-Free Survival

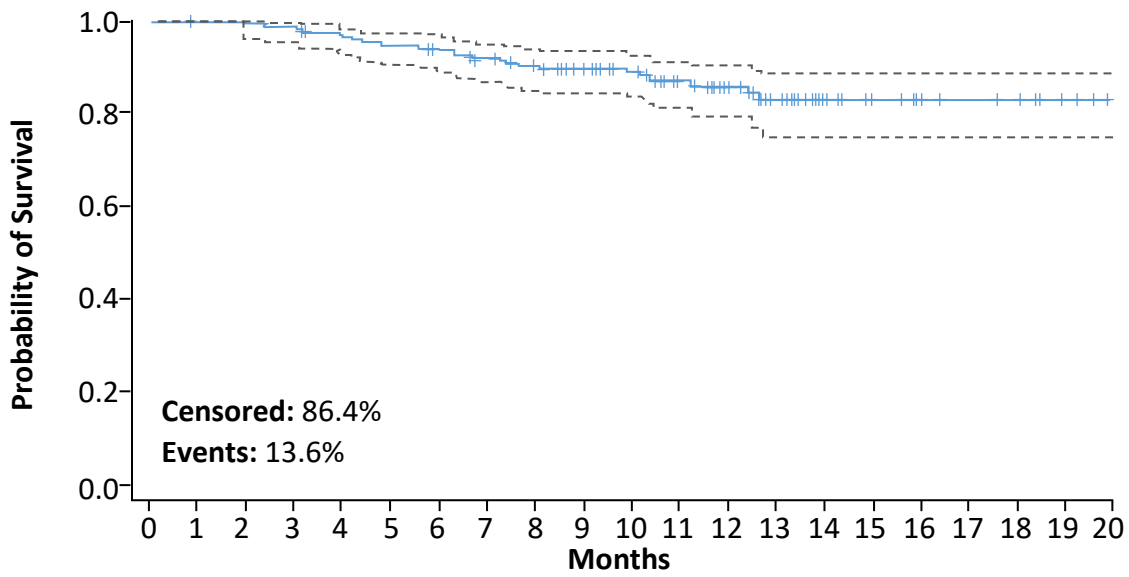
Median: 16.4 months (95% CI, 12.7-NE)



No. at risk: 184 182 174 155 153 135 121 107 103 94 69 54 38 17 11 10 9 4 3 1 0

Overall Survival

Median: Not reached (95% CI, NE-NE)



No. at risk: 184 183 182 179 174 171 167 161 155 147 133 101 66 36 21 16 12 9 8 4 0

- Median follow-up, 11.1 months (range, 0.7-19.9 months)
- Median PFS in the 24 patients with brain metastases was 18.1 months (95% CI, 6.7-18.1 months)

Patients who received T-DXd 5.4 mg/kg.
CI, confidence interval; NE, not estimable.

Courtesy of Carey K Anders, MD

DESTINY-Breast01: PFS for patients with stable brain metastases treated with trastuzumab deruxtecan

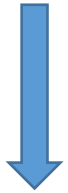
The median response duration was 14.8 months (95% CI, 13.8 to 16.9) (Figure 3A). The median duration of progression-free survival was 16.4 months (95% CI, 12.7 to not reached) among all patients and 18.1 months (95% CI, 6.7 to 18.1) among the 24 patients who were enrolled with treated and asymptomatic brain metastases. Estimated overall survival was 93.9% (95% CI, 89.3 to 96.6) at 6 months and 86.2% (95% CI, 79.8 to 90.7) at 12 months; the median overall survival was not reached at the time of this report (Fig. S2).

Courtesy of Carey K Anders, MD

Modi et al. NEJM 2020;382(7):610-21

How do we synthesize this data into a practical clinical algorithm?

Post-CNS radiation systemic therapy considerations



HER2-targeted therapy algorithms for HER2+ metastatic breast cancer

- **1st line: THP**
- **2nd line: T-DM1**
- **3rd line: Current options:**
  - **Trastuzumab-deruxtecan (Stable BrM)**
  - **(Progressive BrM)**
    - **Tucatinib/Trastuzumab/Capecitabine**
    - **Neratinib/Capecitabine**
    - **Lapatinib/Capecitabine**

Many outstanding questions:

1. **Would incorporating tucatinib earlier in the treatment for patients with brain metastases be of benefit?**

2. **Would combining tucatinib with H/P or T-DM1 be of benefit to patients with brain metastases?**

3. **Would combining tucatinib with trastuzumab deruxtecan be of benefit to patients with brain metastases?**

4. **Would switching therapy to tucatinib regimen post-CNS XRT be of benefit to patients with brain metastases?**

5. **Many more…..?**

Courtesy of Carey K Anders, MD

Question #1:

46 yr old female presents to your clinic for systemic therapy recommendations for metastatic hormone receptor negative, HER2-positive breast cancer metastatic to brain. She was initially diagnosed with *de novo* metastatic breast cancer to the liver 2.5 years prior and initially received paclitaxel/trastuzumab pertuzumab. At her visit, she had been on T-DM1 for 8 months, and had radiosurgery to 3 brain metastases 4 months prior; T-DM1 was continued post-SRS as her liver lesions were stable. She now has intracranial progression with 5 new lesions that are all sub-cm. Her performance status remains excellent and she is hopeful to avoid additional radiation to the brain. Based on the available literature, you advise her that the next best step is:

A. Vinorelbine/trastuzumab

B. Tucatinib/trastuzumab/capecitabine

C. Trastuzumab deruxtecan

D. Abemaciclib/trastuzumab

Answer: The answer is B based on the HER2CLIMB data.

Courtesy of Carey K Anders, MD

Question #2:

47 yr old female with a known ER/PR negative, HER2-positive breast cancer to the liver who has previously progressed on taxane/trastuzumab/pertuzumab, and was on T-DM1 when she developed 3 supratentorial brain metastases that were treated with SRS. She continued on T-DM1 for 6 months following SRS when her LFT's started to rise and she developed RUQ pain. Her brain lesions remain stable. You recommend which of the following in hopes to achieving highest response in her liver metastases?

A. Vinorelbine/trastuzumab

B. Tucatinib/trastuzumab/capecitabine

C. Trastuzumab deruxtecan

D. Neratinib/capecitabine

Answer: The answer is C based on the DESTINY-Breast01 study with an ORR of 61% which is higher than any other combination therapy.

Courtesy of Carey K Anders, MD

Question #3:

You are meeting with a 62 yr old female who has progressive HER2+ brain metastases and discussing the risks and benefits of tucatinib/trastuzumab/capecitabine (HER2CLIMB regimen). She asks what the expected intracranial response rate is from the phase 3 study. You reply:

A. 10%

B. 30%

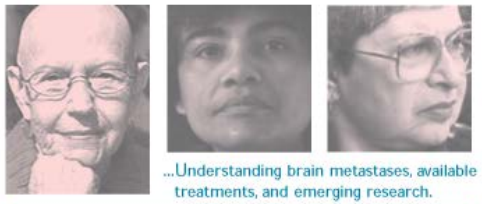
C. 45%

D. 80%

Answer: The answer is C based on the HER2CLIMB study.

Courtesy of Carey K Anders, MD

BRAINMETSBC.ORG



...Understanding brain metastases, available treatments, and emerging research.

Thanks and Questions!