Patterns of Care in Medical Oncology

Treatment of HER2-Positive Metastatic Disease

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Clinical Scenario 17: A 60-year-old woman with a 2.2-cm, ER-positive, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. After completing trastuzumab and while receiving an adjuvant AI it is discovered that the patient has bone and lung metastases that are asymptomatic.

Which of the following initial treatments would you most likely recommend for this patient if the bone and lung metastases were discovered at the following points after completion of trastuzumab?

	Point after completion of trastuzumab		
Treatment	**6 months**	**18 months**	**3 years**
Lapatinib + capecitabine	**30%**	**12%**	**9%**
Switch endocrine therapy + lapatinib	**21%**	**6%**	**2%**

Clinical Scenario 17: A 60-year-old woman with a 2.2-cm, ER-positive, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. After completing trastuzumab and while receiving an adjuvant AI it is discovered that the patient has bone and lung metastases that are asymptomatic. (Continued)

Which of the following initial treatments would you most likely recommend for this patient if the bone and lung metastases were discovered at the following points after completion of trastuzumab?

	Point after completion of trastuzumab		
Treatment	**6 months**	**18 months**	**3 years**
Trastuzumab + chemotherapy	**16%**	**40%**	**41%**
Switch endocrine therapy + trastuzumab	**13%**	**28%**	**30%**

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Clinical Scenario 17: A 60-year-old woman with a 2.2-cm, ER-positive, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. After completing trastuzumab and while receiving an adjuvant AI it is discovered that the patient has bone and lung metastases that are asymptomatic. (Continued)

Which of the following initial treatments would you most likely recommend for this patient if the bone and lung metastases were discovered at the following points after completion of trastuzumab?

	Point after completion of trastuzumab		
Treatment	**6 months**	**18 months**	**3 years**
Lapatinib + other chemotherapy	**5%**	**3%**	**0%**
Trastuzumab + lapatinib + chemotherapy	**5%**	**2%**	**5%**

Clinical Scenario 17: A 60-year-old woman with a 2.2-cm, ER-positive, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. After completing trastuzumab and while receiving an adjuvant AI it is discovered that the patient has bone and lung metastases that are asymptomatic. (Continued)

Which of the following initial treatments would you most likely recommend for this patient if the bone and lung metastases were discovered at the following points after completion of trastuzumab?

	Point after completion of trastuzumab		
Treatment	**6 months**	**18 months**	**3 years**
Lapatinib alone	**5%**	**3%**	**4%**
Trastuzumab alone	**3%**	**3%**	**4%**

Clinical Scenario 17: A 60-year-old woman with a 2.2-cm, ER-positive, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. After completing trastuzumab and while receiving an adjuvant AI it is discovered that the patient has bone and lung metastases that are asymptomatic. (Continued)

Which of the following initial treatments would you most likely recommend for this patient if the bone and lung metastases were discovered at the following points after completion of trastuzumab?

	Point after completion of trastuzumab		
Treatment	**6 months**	**18 months**	**3 years**
Switch endocrine therapy alone	**1%**	**3%**	**5%**
Other	**1%**	**0%**	**0%**

Clinical Scenario 18: ***A fit and otherwise healthy woman with a 2.2-cm, ER-positive, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. Three years after completing trastuzumab and while receiving an adjuvant AI it is discovered that the patient has bone and lung metastases that are asymptomatic.***

Which of the following initial treatments would you most likely recommend if the patient's age was:

Treatment	75 years	85 years
Switch endocrine therapy + trastuzumab	35%	37%
Trastuzumab + chemotherapy	29%	13%
Lapatinib + capecitabine	15%	7%
Trastuzumab alone	7%	12%
Switch endocrine therapy + lapatinib	5%	9%

Clinical Scenario 18: ***A fit and otherwise healthy woman with a 2.2-cm, ER-positive, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. Three years after completing trastuzumab and while receiving an adjuvant AI it is discovered that the patient has bone and lung metastases that are asymptomatic. (Continued)***

Which of the following initial treatments would you most likely recommend if the patient's age was:

Treatment	75 years	85 years
Switch endocrine therapy alone	4%	9%
Lapatinib alone	2%	8%
Trastuzumab + lapatinib	1%	4%
Other	2%	1%

Clinical Scenario 19: A 60-year-old woman with a 2.2-cm, ER-positive, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. After completing trastuzumab and while receiving an adjuvant AI it is discovered that the patient has bone and lung metastases that are very symptomatic (pain and dyspnea).

Which of the following initial treatments would you most likely recommend for this patient if the bone and lung metastases were discovered at the following points after completion of trastuzumab?

	Point after completion of trastuzumab		
Treatment	**6 months**	**18 months**	**3 years**
Lapatinib + capecitabine	**47%**	**18%**	**10%**
Trastuzumab + chemotherapy	**27%**	**68%**	**70%**

Clinical Scenario 19: A 60-year-old woman with a 2.2-cm, ER-positive, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. After completing trastuzumab and while receiving an adjuvant AI it is discovered that the patient has bone and lung metastases that are very symptomatic (pain and dyspnea). (Continued)

Which of the following initial treatments would you most likely recommend for this patient if the bone and lung metastases were discovered at the following points after completion of trastuzumab?

	Point after completion of trastuzumab		
Treatment	**6 months**	**18 months**	**3 years**
Lapatinib + other chemotherapy	**11%**	**3%**	**3%**
Trastuzumab + lapatinib + chemotherapy	**5%**	**5%**	**6%**

Clinical Scenario 19: A 60-year-old woman with a 2.2-cm, ER-positive, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. After completing trastuzumab and while receiving an adjuvant AI it is discovered that the patient has bone and lung metastases that are very symptomatic (pain and dyspnea). (Continued)

Which of the following initial treatments would you most likely recommend for this patient if the bone and lung metastases were discovered at the following points after completion of trastuzumab?

	Point after completion of trastuzumab		
Treatment	**6 months**	**18 months**	**3 years**
Trastuzumab alone	**3%**	**2%**	**3%**
Lapatinib alone	**3%**	**1%**	**1%**

Clinical Scenario 19: A 60-year-old woman with a 2.2-cm, ER-positive, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. After completing trastuzumab and while receiving an adjuvant AI it is discovered that the patient has bone and lung metastases that are very symptomatic (pain and dyspnea). (Continued)

Which of the following initial treatments would you most likely recommend for this patient if the bone and lung metastases were discovered at the following points after completion of trastuzumab?

	Point after completion of trastuzumab		
Treatment	**6 months**	**18 months**	**3 years**
Switch endocrine therapy + trastuzumab	**0%**	**3%**	**7%**
Other	**4%**	**0%**	**0%**

***Clinical Scenario 20:* A fit and otherwise healthy woman with a 2.2-cm, ER-positive, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. Three years after completing trastuzumab and while receiving an adjuvant AI it is discovered that the patient has bone and lung metastases that are very symptomatic (pain and dyspnea).**

Which treatment would you most likely recommend for this patient, in addition to endocrine therapy, if the patient's age was:

Treatment	75 years	85 years
Trastuzumab + chemotherapy	56%	34%
Lapatinib + capecitabine	17%	12%
Switch endocrine therapy + trastuzumab	8%	17%
Trastuzumab alone	6%	15%

Clinical Scenario 20: ***A fit and otherwise healthy woman with a 2.2-cm, ER-positive, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. Three years after completing trastuzumab and while receiving an adjuvant AI it is discovered that the patient has bone and lung metastases that are very symptomatic (pain and dyspnea). (Continued)***

Which treatment would you most likely recommend for this patient, in addition to endocrine therapy, if the patient's age was:

Treatment	75 years	85 years
Trastuzumab + lapatinib + chemotherapy	4%	1%
Trastuzumab + lapatinib	3%	3%
Switch endocrine therapy + lapatinib	2%	8%
Lapatinib alone	2%	8%

Clinical Scenario 20: ***A fit and otherwise healthy woman with a 2.2-cm, ER-positive, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. Three years after completing trastuzumab and while receiving an adjuvant AI it is discovered that the patient has bone and lung metastases that are very symptomatic (pain and dyspnea). (Continued)***

Which treatment would you most likely recommend for this patient, in addition to endocrine therapy, if the patient's age was:

Treatment	75 years	85 years
Other	2%	2%

Combined aromatase inhibitor and HER2-targeted treatments for postmenopausal patients with HER2-positive, ER-positive metastatic breast cancer

	TAnDEM			EGF30008		
	Anastrozole + trastuzumab	Anastrozole	*p*-value	Letrozole + lapatinib	Letrozole	*p*-value
Median PFS	4.8 mo	2.4 mo	0.0016	8.2 mo	3.0 mo	0.019
Median OS	28.5 mo	23.9 mo	0.325	33.3 mo	32.3 mo	0.113
CBR	42.7%	27.9%	0.026	48%	29%	0.003

PFS = progression-free survival; OS = overall survival; CBR = objective response + stable disease

Johnston S et al. San Antonio Breast Cancer Symposium 2008;Abstract 46;
Mackey JR et al. San Antonio Breast Cancer Symposium 2006;Abstract 3.

Clinical Scenario 21: ***A 60-year-old woman with a 2.2-cm, ER-negative, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. Eighteen months after completing trastuzumab it is discovered that the patient has bone and lung metastases.***

Which treatment would you most likely recommend if the patient was:

Treatment	Asymptomatic	Very symptomatic with pain and dyspnea
Trastuzumab + chemotherapy	55%	60%
Lapatinib + capecitabine	20%	18%
Trastuzumab alone	9%	1%
Lapatinib alone	8%	4%

***Clinical Scenario 21:* A 60-year-old woman with a 2.2-cm, ER-negative, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. Eighteen months after completing trastuzumab it is discovered that the patient has bone and lung metastases. (Continued)**

Which treatment would you most likely recommend if the patient was:

Treatment	Asymptomatic	Very symptomatic with pain and dyspnea
Trastuzumab + lapatinib	3%	0%
Trastuzumab + lapatinib + chemotherapy	3%	11%
Lapatinib + other chemotherapy	2%	6%

Approximately what percent of your patients with HER2-positive metastatic disease develop brain metastases at some point in the course of their disease?

Median	**20%**

Have you observed any patients with HER2-positive brain metastases who experienced an objective CNS tumor response to systemic anti-HER2 treatment?

Yes	**40%**
No	**60%**

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With which of the following agents have you observed an objective CNS tumor response to systemic anti-HER2 treatment? (May have more than 1 response)

Lapatinib	87%
Trastuzumab	33%
T-DM1 (on protocol)	8%
Lapatinib + capecitabine	3%

n = 39

Clinical Scenario 22: A woman with a 2.2-cm, ER-negative, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. Eighteen months after completing trastuzumab it is discovered that the patient has bone and lung metastases that are asymptomatic. The patient receives capecitabine and trastuzumab and has stable disease for 4 months, after which the disease progresses but no new sites of disease are evident and the patient is still asymptomatic.

Which treatment would you most likely recommend if the patient's age was:

Treatment	60 years	75 years	85 years
Trastuzumab + chemotherapy	40%	35%	22%
Lapatinib + other chemotherapy	22%	20%	11%
Lapatinib + capecitabine	19%	19%	12%
Trastuzumab + lapatinib	7%	13%	17%

Clinical Scenario 22: A woman with a 2.2-cm, ER-negative, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. Eighteen months after completing trastuzumab it is discovered that the patient has bone and lung metastases that are asymptomatic. The patient receives capecitabine and trastuzumab and has stable disease for 4 months, after which the disease progresses but no new sites of disease are evident and the patient is still asymptomatic. (Continued)

Which treatment would you most likely recommend if the patient's age was:

Treatment	60 years	75 years	85 years
Trastuzumab + lapatinib + chemotherapy	6%	1%	0%
Lapatinib alone	4%	11%	29%
Trastuzumab alone	2%	1%	9%

Clinical Scenario 23: ***A woman with a 2.2-cm, ER-negative, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. Eighteen months after completing trastuzumab it is discovered that the patient has bone and lung metastases that are asymptomatic. The patient receives capecitabine and trastuzumab and has stable disease for 4 months, after which the disease progresses but no new sites of disease are evident and the patient is still asymptomatic. The patient receives trastuzumab/vinorelbine and experiences a minor response that lasts 9 months but then develops disease progression in the same sites and experiences moderate symptoms (bone pain, asthenia).***

Which treatment would you most likely recommend if the patient's age was:

Treatment	60 years	75 years	85 years
Lapatinib + capecitabine	27%	26%	18%
Lapatinib + other chemotherapy	27%	23%	12%

Clinical Scenario 23: ***A woman with a 2.2-cm, ER-negative, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. Eighteen months after completing trastuzumab it is discovered that the patient has bone and lung metastases that are asymptomatic. The patient receives capecitabine and trastuzumab and has stable disease for 4 months, after which the disease progresses but no new sites of disease are evident and the patient is still asymptomatic. The patient receives trastuzumab/vinorelbine and experiences a minor response that lasts 9 months but then develops disease progression in the same sites and experiences moderate symptoms (bone pain, asthenia). (Continued)***

Which treatment would you most likely recommend if the patient's age was:

Treatment	60 years	75 years	85 years
Trastuzumab + chemotherapy	16%	12%	7%
Trastuzumab + lapatinib + chemotherapy	13%	9%	4%

Clinical Scenario 23: ***A woman with a 2.2-cm, ER-negative, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. Eighteen months after completing trastuzumab it is discovered that the patient has bone and lung metastases that are asymptomatic. The patient receives capecitabine and trastuzumab and has stable disease for 4 months, after which the disease progresses but no new sites of disease are evident and the patient is still asymptomatic. The patient receives trastuzumab/vinorelbine and experiences a minor response that lasts 9 months but then develops disease progression in the same sites and experiences moderate symptoms (bone pain, asthenia). (Continued)***

Which treatment would you most likely recommend if the patient's age was:

Treatment	60 years	75 years	85 years
Trastuzumab + lapatinib	11%	17%	22%
Lapatinib alone	3%	11%	29%

Clinical Scenario 23: ***A woman with a 2.2-cm, ER-negative, HER2-positive, node-positive IDC (1 sentinel node) receives TCH followed by trastuzumab for 1 year. Eighteen months after completing trastuzumab it is discovered that the patient has bone and lung metastases that are asymptomatic. The patient receives capecitabine and trastuzumab and has stable disease for 4 months, after which the disease progresses but no new sites of disease are evident and the patient is still asymptomatic. The patient receives trastuzumab/vinorelbine and experiences a minor response that lasts 9 months but then develops disease progression in the same sites and experiences moderate symptoms (bone pain, asthenia). (Continued)***

Which treatment would you most likely recommend if the patient's age was:

Treatment	60 years	75 years	85 years
Trastuzumab alone	2%	1%	6%
Other	1%	1%	2%

A Phase III randomized comparison of lapatinib (L) with capecitabine (C) versus capecitabine alone for women with advanced breast cancer that has progressed on trastuzumab

	C (n = 201)	C + L (n = 198)	Hazard ratio	*p*-value
Median TTP	18.6 wk	27.1 wk	0.57	<0.001
Median OS	66.6 wk	67.7 wk	0.78	0.177

TTP = time to progression; OS = overall survival

Cameron D et al. *Breast Cancer Res Treat* 2008;112(3):533-43.

Trastuzumab beyond progression in HER2-positive advanced breast cancer: A German Breast Group 26/ Breast International Group 03-05 study of capecitabine (C) with or without trastuzumab (H)

	C (n = 78)	C + H (n = 78)	Hazard ratio	*p*-value
Median TTP	5.64 mo	8.16 mo	0.685	0.0338
Median OS	20.39 mo	25.48 mo	0.763	0.2570

TTP = time to progression; OS = overall survival

Von Minckwitz G et al. *J Clin Oncol* 2009;27(12):1999-2006.

EGF104900: A randomized Phase III study of lapatinib (L) versus lapatinib with trastuzumab (T) for patients with HER2-positive, trastuzumab-refractory metastatic breast cancer

	L (n = 145)	L + T (n = 146)	Hazard ratio	*p*-value
Median PFS	8.1 wk	12.0 wk	0.73	0.008
Median OS	9.5 mo	14 mo	0.74	0.026

PFS = progression-free survival; OS = overall survival
Median number of prior trastuzumab regimens for metastatic breast cancer: 3

"This study demonstrated that lapatinib in combination with trastuzumab offers a chemotherapy-free option that has an acceptable tolerability profile and, versus lapatinib alone, reduced the risk of disease progression by 27% (P = .008). The efficacy benefits arose in a treatment setting that lacked many of the well-known chemotherapy-related toxicities."

Blackwell KL et al. *J Clin Oncol* 2010;28(7):1124-30; Blackwell KL et al. San Antonio Breast Cancer Symposium 2009;Abstract 61.

Are you familiar with the agent T-DM1?

Yes	67%
No	33%
If T-DM1 were available off protocol, how would you use it?	
After first trastuzumab progression	48%
After progression on both trastuzumab and lapatinib	40%
Instead of trastuzumab	12%
To how many of your current patients would you offer T-DM1 if it were available?	
Median*	5

* Excludes 18 respondents who answered “I don’t know”
n = 67

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Phase II trial of T-DM1 for patients with HER2-positive metastatic breast cancer who experienced disease progression on prior HER2-directed therapy

	Investigator		Independent review	
	All (N = 112)	HER2 centrally confirmed (N = 74)	All (N = 112)	HER2 centrally confirmed (N = 74)
Overall response rate	**37.5%**	**47.3%**	**25.9%**	**33.8%**
Clinical benefit rate (CBR)*	**76.8%**	**NR**	**75%**	**NR**

* CBR = complete response + partial response + stable disease ≥ 6 months;
NR = not reported

Burris HA et al. *J Clin Oncol* 2011;29(4):398-405.