


Hi Kris,

I noticed a possible discrepancy in the NCCN Guidelines Version 4.2020 Invasive Breast Cancer NCCN Evidence Blocks™

Tucatinib/trastuzumab/capecitabine is rated as category one in the table, but equal in efficacy with better quality of evidence for Ado-trastuzumab emtansine (T-DM1). In the block chart.

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


















	National Comprehensive Cancer Network®	NCCN Guidelines Version 4.2020 Invasive Breast Cancer NCCN Evidence Blocks™	NCCN Guidelines Index Table of Contents Discussion
SYSTEMIC THERAPY REGIMENS FOR RECURRENT OR STAGE IV (M1) DISEASE^{a,b,c}			
HER2-Positive^d			
Preferred regimens		Other recommended regimens	
<ul style="list-style-type: none">• Pertuzumab + trastuzumab + docetaxel (category 1)^k• Pertuzumab + trastuzumab + paclitaxel		<ul style="list-style-type: none">• Tucatinib + trastuzumab + capecitabine (category 1)^l• Ado-trastuzumab emtansine (T-DM1)• Fam-trastuzumab deruxtecan-nxk^m• Trastuzumab + paclitaxel ± carboplatin• Trastuzumab + docetaxel^k• Trastuzumab + vinorelbine^k• Trastuzumab + capecitabine• Lapatinib + capecitabine• Trastuzumab + lapatinib (without cytotoxic therapy)• Trastuzumab + other agents^{k,n,o}• Neratinib + capecitabine• See additional targeted therapy options (BINV-R)^e	

5					E = Efficacy of Regimen/Agent
4					S = Safety of Regimen/Agent
3					Q = Quality of Evidence
2					C = Consistency of Evidence
1					A = Affordability of Regimen/Agent
	E	S	Q	C	A

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CURRENT OR STAGE IV (M1) DISEASE

HER2-Positive Disease

	Preferred regimens	
	Pertuzumab/trastuzumab/docetaxele	
	Pertuzumab/trastuzumab/paclitaxel	
	Other recommended regimens	
	Tucatinib/trastuzumab/capecitabine	
	Ado-trastuzumab emtansine (T-DM1)	
	Fam-trastuzumab deruxtecan-nxki	
	Trastuzumab/paclitaxel/carboplatin	
	Trastuzumab/paclitaxel	
	Trastuzumab/docetaxel	
	Trastuzumab/vinorelbine	
	Trastuzumab/capecitabine	
	Lapatinib/capecitabine	
	Trastuzumab/lapatinib (without cytotoxic therapy)	
	Trastuzumab/other agents	—
	Neratinib/capecitabine	

EB-1.
 Clinical trials is especially encouraged.

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BINV-Q
EB-1

Why is Tucatinib/trastuzumab/capecitabine listed as the most favored combination in the table above when it has not been directly compared with Ado-trastuzumab emtansine (T-DM1)? Should Tucatinib/trastuzumab/capecitabine be reserved for patients that have failed trastuzumab, pertuzumab, and **trastuzumab emtansine**, (1) or in patients with brain metastases? Does NCCN stand by its category one rating compared with Ado-trastuzumab emtansine (T-DM1), Fam-trastuzumab deruxtecan-nxki?

References:

1. Murthy RK, Loi S, Okines A, et al. Tucatinib, Trastuzumab, and Capecitabine for HER2-Positive Metastatic Breast Cancer. *N Engl J Med*. 2020;382(7):597-609.
2. NCCN Guidelines Version 4.2020 Invasive Breast Cancer NCCN Evidence Blocks™

Thanks,

Linda W. Wilson, M.D.