IMPACT OF TUCATINIB ON HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH HER2+ METASTATIC BREAST CANCER WITH AND WITHOUT BRAIN METASTASES

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Background

- Disease progression in MBC can negatively impact QoL.[1]
- For patients with HER2+ MBC previously treated with trastuzumab, pertuzumab, and T-DM1, no single regimen is considered the standard of care.[2,3]
- Up to half of patients with HER2+ MBC may develop brain metastases and effective and tolerable treatment options are needed.[4,5,6,7]
- HER2CLIMB (NCT02614794) is a pivotal, randomized trial of tucatinib (TUC) vs. placebo (Pbo) in combination with trastuzumab (Tras) and capecitabine (Cape) in patients with HER2+ MBC with and without brain metastases.[8]
- This tucatinib combination is now FDA-approved for patients with and without brain metastases who have received one or more prior anti-HER2-based regimens in the metastatic setting.

MBC: metastatic breast cancer
QoL: quality of life
T-DM1: trastuzumab emtansine

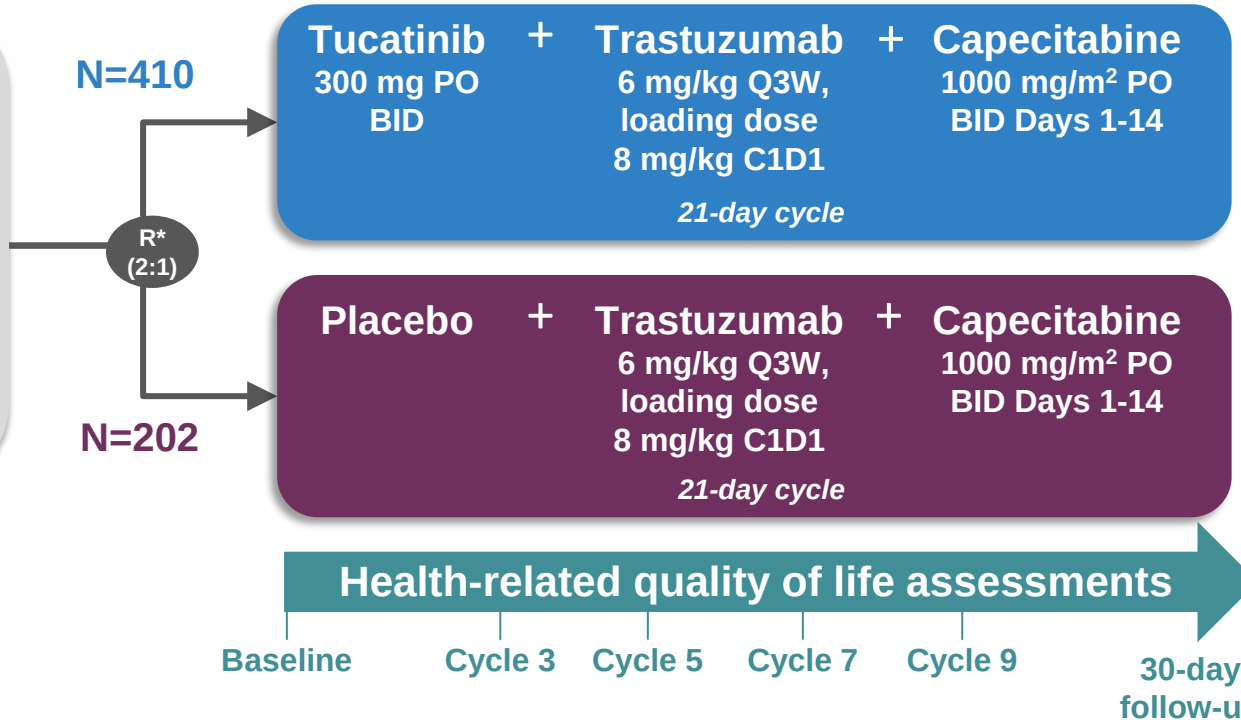
1. Mueller V, et al. *Breast* 2018;37:154-160
2. Giordano SH, et al. *J Oncol Pract* 2018;14:501-4.
3. Cardoso F, et al. *Ann Oncol* 2018;29:1634-57
4. Bendell JC, et al. *Cancer* 2003;97:2972-7.
5. Brufsky AM, et al. *Clin Cancer Res* 2011;17:4834-43.
6. Leyland-Jones B. *J Clin Oncol* 2009;27:5278-86.
7. Olson EM, et al. *Breast* 2013;22:525-31.
8. Murthy RK, et al. *N Engl J Med* 2020;382:597-609.

HER2CLIMB Study Design

48% of patients had brain metastases at baseline
including previously untreated, treated stable, and treated and progressing

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



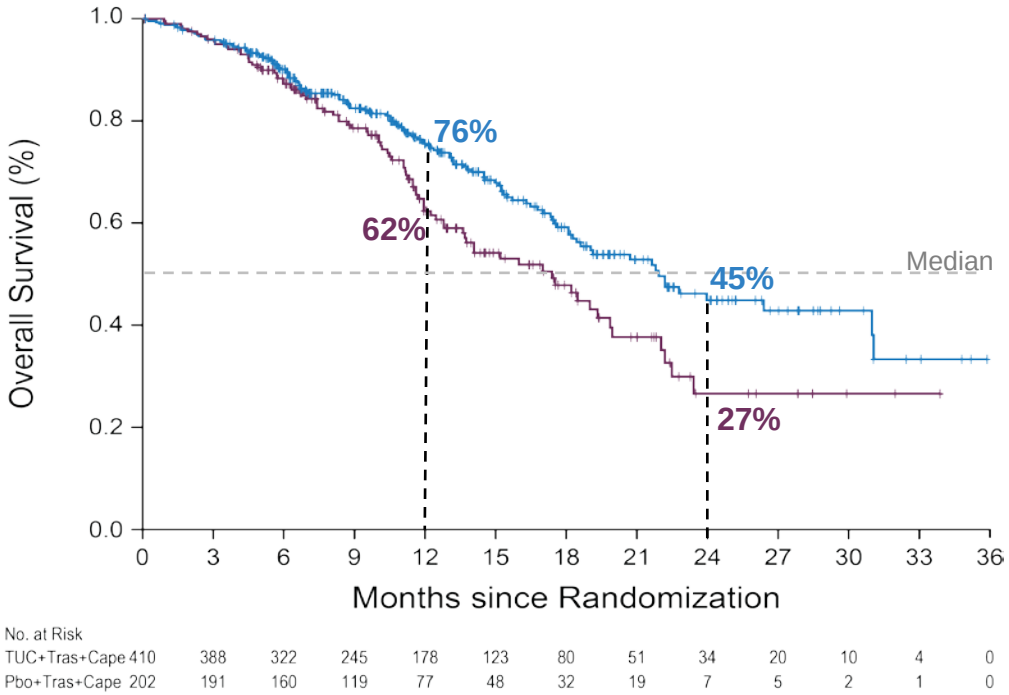
*Stratification factors:
- Presence of brain metastases (yes/no)
- ECOG status (0 or 1)
- Region (US or Canada or rest of world)

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

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

Overall Survival in the Total Study Population

- Alpha-controlled secondary endpoint in the HER2CLIMB trial



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

	Events N=612	HR (95% CI)	P Value
TUC+Tras+Cape	130/410	0.66 (0.50, 0.88)	0.005
Pbo+Tras+Cape	85/202		

Risk of death was reduced by 34% in the total population

Two-year OS (95% CI):	
TUC+Tras+Cape	Pbo+Tras+Cape
45% (37, 53)	27% (16, 39)
Median OS (95% CI):	
21.9 months (18.3, 31.0)	17.4 months (13.6, 19.9)

Prespecified efficacy boundary for PFS-brain metastases (P=0.0080) was met at the first interim analysis. Data cut off: Sep 4, 2019

HER2CLIMB Primary Analysis Results

- The HER2CLIMB trial met all primary and alpha-controlled secondary endpoints at the first interim analysis
- Benefit was observed in patients with and without brain metastases
- Median duration of exposure: TUC 7.3 months (<0.1–35.1), Pbo 4.4 months (<0.1– 24.0)

PFS by BICR
N=480*

Risk of progression or death was reduced by

46%

95% CI: 0.42 to 0.71, P<0.001

Overall Survival
N=612

Risk of death was reduced by

34%

95% CI, 0.50 to 0.88, P=0.005

PFS by BICR in patients with brain metastases
N=291

Risk of progression or death was reduced by

52%

95% CI, 0.34 to 0.69, P<0.001

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

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Treatment-Related Adverse Events Resulting in Hospitalization in ≥1% of Patients in the Tucatinib Arm

- All other events that led to hospitalization were <1%
- The addition of tucatinib did not increase the percentage of patients requiring hospitalization

Adverse Event, n (%)	HER2CLIMB Safety Analysis Population[a]	
	TUC+Tras+Cape (n=404)	Pbo+Tras+Cape (n=197)
Patients with any event	83 (21)	45 (23)
Diarrhea	10 (3)	4 (2)
Vomiting	7 (2)	2 (1)
Seizure	6 (2)	2 (1)
Dyspnea	5 (1)	4 (2)

a. Safety assessed in all patients who received at least one dose of study treatment (N=601)

Health-Related Quality of Life (HRQoL) Methods

Total Study Population

612 patients randomized 2:1 February 2016 to May 2019

HRQoL Study Population

Assessments initiated in August 2017

Patients who had a baseline assessment and could be included in the analysis:

- 218/410 (53%) patients in the TUC arm
- 113/202 (56%) patients in the Pbo arm

HRQoL Data Collection

EQ-5D-5L collected at baseline, Cycles 3, 5, 7, 9, and 30-day follow-up

HRQoL Assessments

- Overall health status: visual analog scale (VAS)
- Time to deterioration of QoL: defined as decrease of 7 points on VAS[1]
- Change from baseline on individual patient-reported items
  - Mobility, self-care, usual activities, pain/discomfort, and anxiety/depression
  - Each dimension has 5 levels: no, slight, moderate, severe, or extreme problems

1. Pickard AS, Neary MP, and Cella D. *Health Qual Life Outcomes*. 2007;5:70.

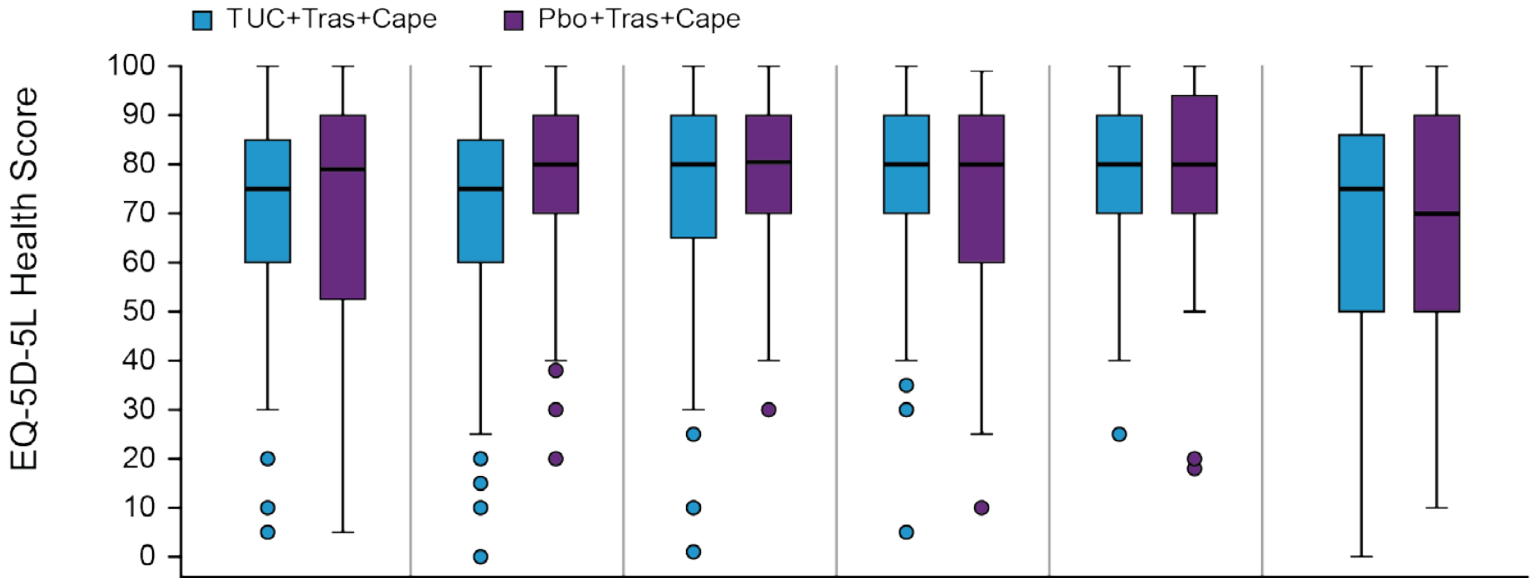
Baseline Patient Characteristics

- Characteristics were similar between the total and HRQoL populations

		Total Study Population		HRQoL Population	
		TUC+Tras+Cape (n=410)	Pbo+Tras+Cape (n=202)	TUC+Tras+Cape (n=218)	Pbo+Tras+Cape (n=113)
Age in years, median (range)		55.0 (22, 80)	54.0 (25, 82)	55.0 (22, 79)	54.0 (25, 76)
Female, n (%)		407 (99)	200 (99)	217 (99)	111 (98)
ECOG PS, n (%)	0	204 (50)	94 (47)	106 (49)	52 (46)
	1	206 (50)	108 (54)	112 (51)	61 (54)
Stage IV at initial diagnosis, n (%)		143 (35)	77 (39)	77 (35)	40 (35)
Histology, n (%)	ER and/or PR positive	243 (60)	127 (63)	135 (62)	71 (63)
	ER and PR negative	161 (40)	75 (37)	79 (36)	42 (37)
Prior lines of therapy, median (range)	Overall	4.0 (2, 14)	4.0 (2,17)	4.0 (2, 11)	4.0 (2, 12)
	Metastatic setting	3.0 (1, 14)	3.0 (1, 13)	3.0 (1, 11)	3.0 (1, 11)
Presence/history of brain metastases		198 (48)	93 (46)	107 (49)	57 (50)

Overall HRQoL

- HRQoL was maintained throughout treatment and was not different between treatment arms

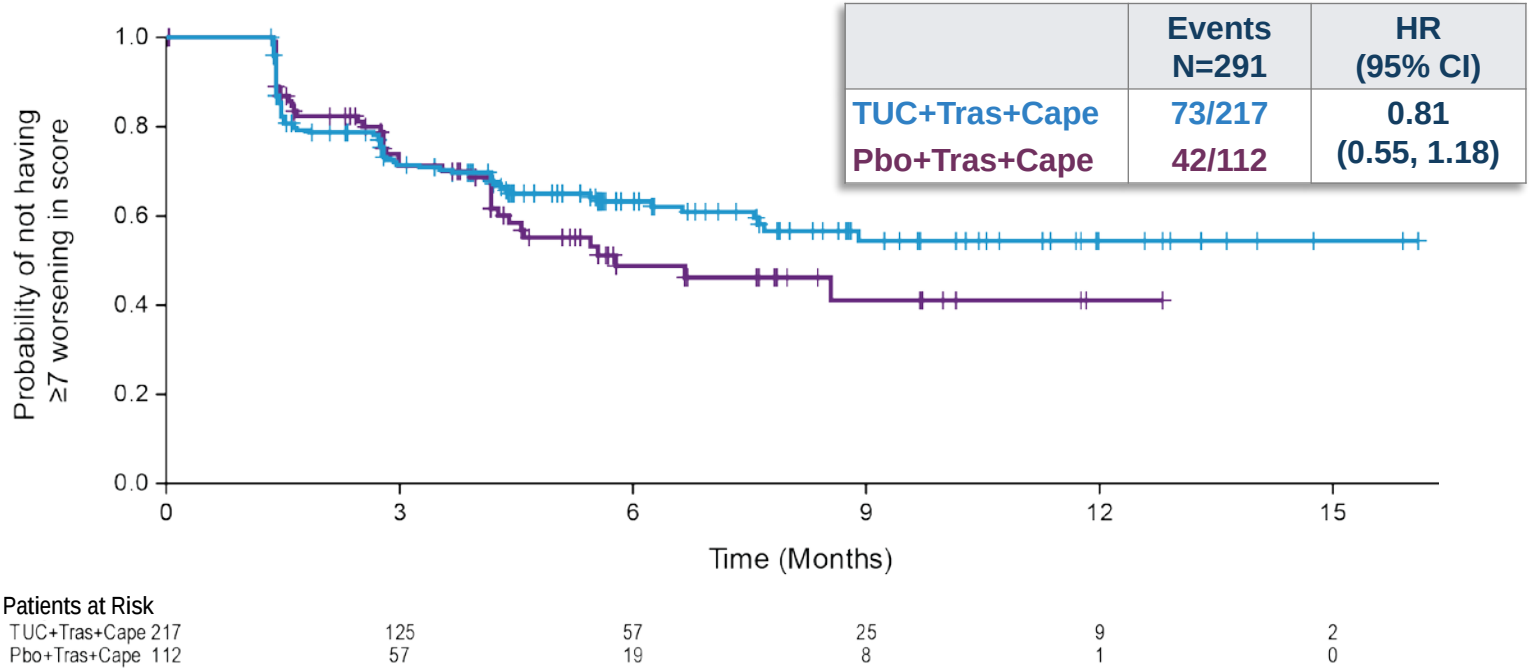


	Baseline	Cycle 3	Cycle 5	Cycle 7	Cycle 9	30 Day Follow Up
TUC+Tras+Cape (n/N)	217/217	183/200	157/194	134/182	90/178	76/188
Pbo+Tras+Cape (n/N)	112/112	91/102	70/88	54/84	39/83	45/93

Numerator is # of patients who completed the HRQoL survey in that cycle. Denominator is # of patients who completed the baseline survey and were still on treatment.

Time to Meaningful Worsening (≥ 7 Points) in EQ-5D-5L Health Score

- The addition of tucatinib did not increase time to worsening of EQ-5D-5L Health Score[1]



	Events N=291	HR (95% CI)
TUC+Tras+Cape	73/217	0.81 (0.55, 1.18)
Pbo+Tras+Cape	42/112	

Patients at Risk

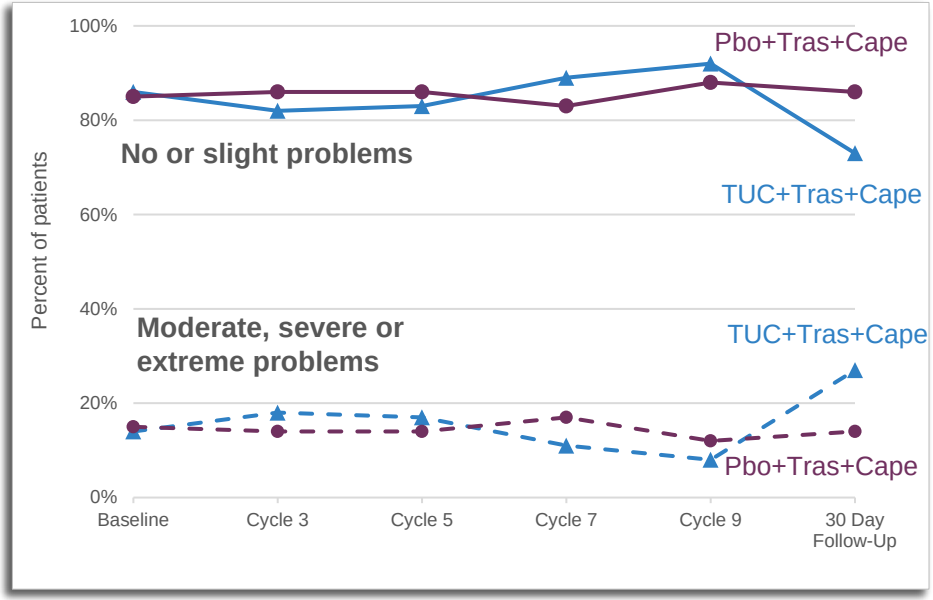
TUC+Tras+Cape 217	125	57	25	9	2
Pbo+Tras+Cape 112	57	19	8	1	0

1. Pickard AS, Neary MP, and Cella D. *Health Qual Life Outcomes*. 2007;5:70.

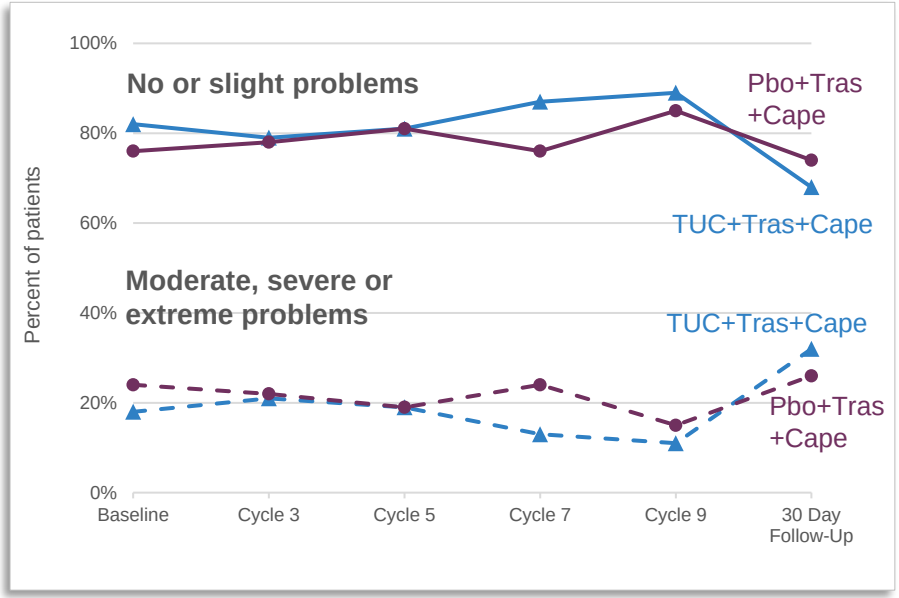
EQ-5D-5L Mobility and Usual Activities Subscale Responses at Baseline and Up to 30 Days Follow-Up

- Mobility and usual activities were maintained throughout the treatment course

Mobility



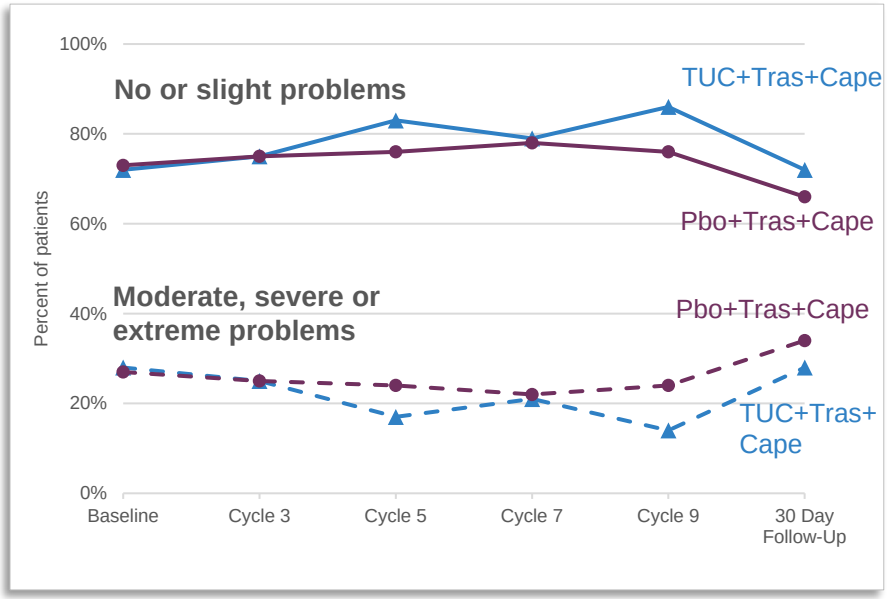
Usual Activities



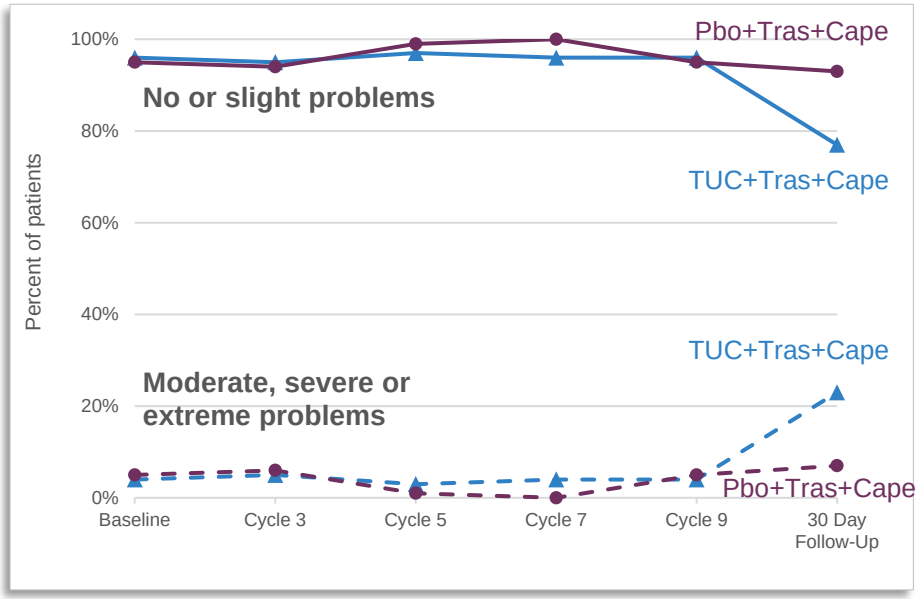
EQ-5D-5L Pain and Self Care Subscale Responses at Baseline and Up to 30 Days Follow-Up

- There was no change in pain and self care categories throughout the treatment course

Pain

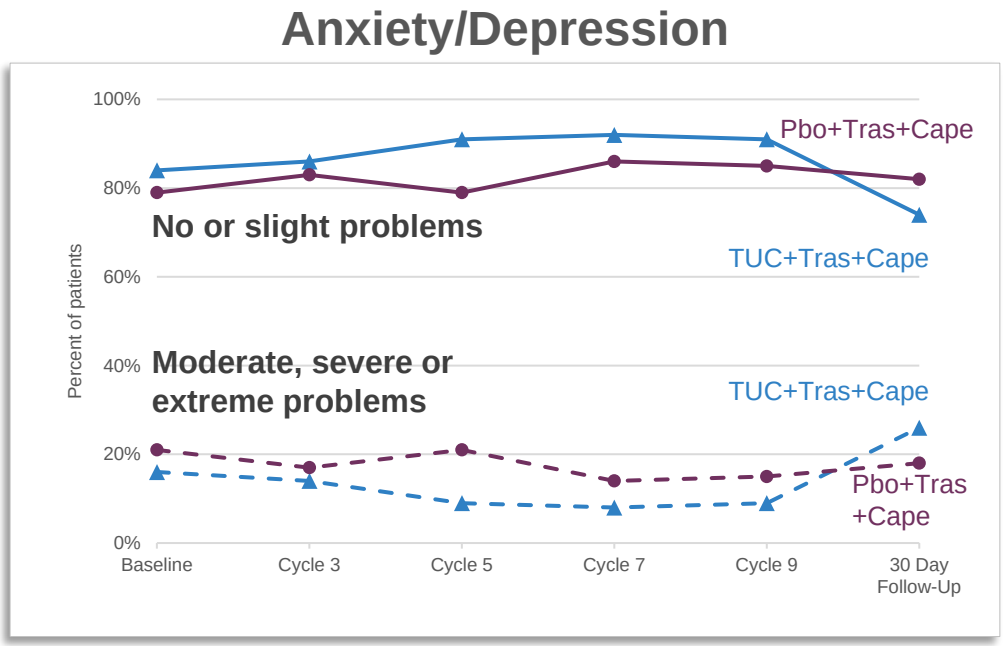


Self Care



EQ-5D-5L Anxiety/Depression Subscale Responses at Baseline and Up to 30 Days Follow-Up

- There was no change in the anxiety/depression category throughout the course of treatment



Conclusions

- In patients with HER2+ MBC with or without brain metastases, tucatinib in combination with trastuzumab and capecitabine significantly improved PFS and OS.
- The addition of tucatinib to trastuzumab and capecitabine does not negatively impact HRQoL in patients with or without brain metastases, and there is no difference in AE-related hospitalization rate when compared to trastuzumab and capecitabine alone.
- Patients treated with tucatinib, trastuzumab, and capecitabine maintain HRQoL throughout the treatment period, which was longer compared to patients treated with only trastuzumab and capecitabine.[1]
- These results, together with the HER2CLIMB primary analysis, demonstrate that this regimen not only provides significant and clinically meaningful activity but also maintains QoL in patients with and without brain metastases.

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