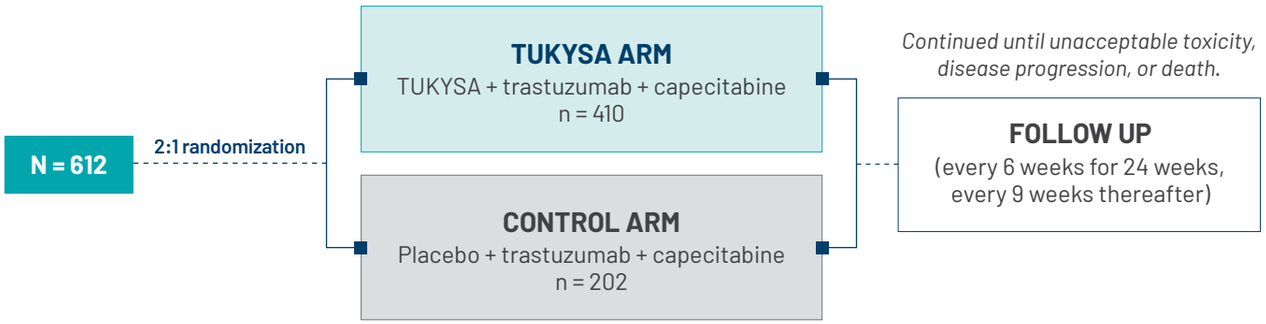
TUKYSA is indicated in combination with trastuzumab and capecitabine for treatment of adult patients with advanced unresectable or metastatic HER2-positive breast cancer, including patients with brain metastases, who have received one or more prior anti-HER2-based regimens in the metastatic setting.

TUCATINIB, TRASTUZUMAB, AND CAPECITABINE FOR HER2-POSITIVE METASTATIC BREAST CANCER

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

HER2CLIMB study methodology[1]

HER2CLIMB was a global, randomized, double-blind controlled trial of adult patients with HER2+ metastatic breast cancer (MBC), with or without brain metastases, who were previously treated with trastuzumab, pertuzumab, and ado-trastuzumab emtansine (T-DM1) separately or in combination, in the neoadjuvant, adjuvant, or metastatic setting[1]



- Dosing, repeated every 21 days: TUKYSA, 300 mg orally, twice daily, or placebo, twice daily; trastuzumab, 6 mg/kg intravenously, once every 21 days with an initial dose of 8 mg/kg (subcutaneous dosing was also allowed); capecitabine, 1000 mg/m^2 orally, twice daily, on Days 1-14
- Patients were stratified according to whether brain metastases were present (yes or no), ECOG performance status score (0 or 1), and geographic region (United States and Canada, or rest of world)

ECOG = Eastern Cooperative Oncology Group.

Select Safety Information

Warnings and Precautions

- **Diarrhea:** TUKYSA can cause severe diarrhea including dehydration, hypotension, acute kidney injury, and death. In HER2CLIMB, 81% of patients who received TUKYSA experienced diarrhea, including 12% with Grade 3 and 0.5% with Grade 4. Both patients who developed Grade 4 diarrhea subsequently died, with diarrhea as a contributor to death. Median time to onset of the first episode of diarrhea was 12 days and the median time to resolution was 8 days. Diarrhea led to TUKYSA dose reductions in 6% of patients and TUKYSA discontinuation in 1% of patients. Prophylactic use of antidiarrheal treatment was not required on HER2CLIMB.

  If diarrhea occurs, administer antidiarrheal treatment as clinically indicated. Perform diagnostic tests as clinically indicated to exclude other causes of diarrhea. Based on the severity of the diarrhea, interrupt dose, then dose reduce or permanently discontinue TUKYSA.

Please see Important Safety Information on page 10 and the accompanying full Prescribing Information.

In combination with trastuzumab + capecitabine

TUKYSA WAS EVALUATED IN A GLOBAL, RANDOMIZED DOUBLE-BLIND, CONTROLLED TRIAL

Patients in the TUKYSA arm (TUKYSA + trastuzumab + capecitabine) were compared with those in the control arm (placebo + trastuzumab + capecitabine)[1]

PRIMARY ENDPOINT[1]

- Progression-free survival (PFS), defined as the time from randomization to documented disease progression by BICR; n = 480*

KEY SECONDARY ENDPOINTS[1]

- Overall survival (OS); N = 612
- PFS in patients with brain metastases; n = 291*
- Confirmed objective response rate (ORR) for patients with measurable disease at baseline; n = 511*

- Target enrollment for HER2CLIMB was increased twice to ensure there was adequate statistical power to assess the primary endpoint and, subsequently, a key secondary endpoint
- CT, PET-CT, or MRI was performed at baseline, every 6 weeks for 24 weeks, and every 9 weeks thereafter. MRI of the head at baseline was required for all patients; those with brain metastases on the baseline scan underwent follow-up MRI of the head at the same intervals

Select inclusion criteria[1]

- Patients aged ≥18 years with locally advanced or metastatic breast cancer confirmed to be HER2+ by central laboratory analysis
- Patients with brain metastases, including those with progressing or untreated lesions, were eligible to enroll provided they were neurologically stable and did not require immediate radiation or surgery†
  - Patients who required immediate local intervention could receive local therapy and be enrolled subsequently
- Patients with untreated brain metastases larger than 2 cm in diameter could be enrolled with approval from the medical monitor
- Prior treatment with trastuzumab, pertuzumab, and T-DM1, separately or in combination, in the neoadjuvant, adjuvant, or metastatic setting
- Prior treatment with lapatinib provided more than 12 months had elapsed before starting the trial regimen

Select exclusion criteria[1]

- Patients with leptomeningeal disease
- Prior treatment of metastatic disease with capecitabine or a HER2 targeted tyrosine kinase inhibitor, except lapatinib

*Evaluated in accordance with Response Evaluation Criteria in Solid Tumors (RECIST) criteria, version 1.1, by means of blinded independent central review (BICR).

†Prior treatment status percentages for baseline brain metastases in the total population have been revised from what is presented in the supplemental appendix; 48% of patients had brain metastases; 60% of patients with brain metastases had active brain metastases; 23% of patients with brain metastases were untreated progressing, and 37% were treated progressing.

CT = computed tomography; MRI = magnetic resonance imaging; PET-CT = positron emission tomography–computed tomography; T-DM1 = ado-trastuzumab emtansine.

Please see Important Safety Information on page 10 and the accompanying full Prescribing Information.

Baseline characteristics were balanced between treatment arms[1]

HER2CLIMB STUDIED A BROAD POPULATION OF PATIENTS WITH HER2+ MBC

	TUKYSA arm (n = 410)	Control arm (n = 202)
Median age, years	55.0	54.0
Age <65 years, n (%)	328 (80.0)	168 (83.2)
Age ≥65 years, n (%)	82 (20.0)	34 (16.8)
PRIOR THERAPIES, n (%)		
Trastuzumab	410 (100)	202 (100)
Pertuzumab	409 (99.8)	201 (99.5)
T-DM1	410 (100)	202 (100)
STAGE IV AT INITIAL DIAGNOSIS, n (%)	143 (34.9)	77 (38.1)
LOCATION OF METASTASES, n (%)		
Lung	200 (48.8)	100 (49.5)
Liver	137 (33.4)	78 (38.6)
Bone	223 (54.4)	111 (55.0)
Brain	198 (48.3)	93 (46.0)
HORMONE RECEPTOR STATUS, n (%)		
ER and/or PR positive	243 (59.3)	127 (62.9)
ER and PR negative	161 (39.3)	75 (37.1)
Other	6 (1.5)	0
ECOG PERFORMANCE STATUS, n (%)		
0	204 (49.8)	94 (46.5)
1	206 (50.2)	108 (53.5)
RACE, n (%)		
Asian	18 (4.4)	5 (2.5)
Black/African American	41 (10.0)	14 (6.9)
White	287 (70.0)	157 (77.7)
Unknown/other	64 (15.6)	26 (12.9)
REGION OF WORLD, n (%)		
US and Canada	246 (60.0)	123 (60.9)
Rest of world	164 (40.0)	79 (39.1)

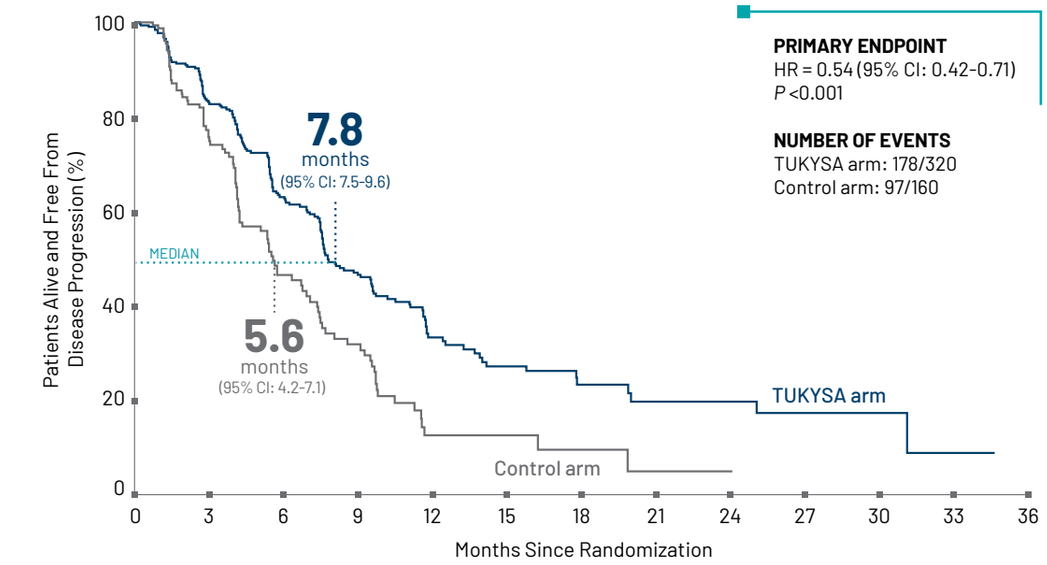
ER = estrogen receptor; PR = progesterone receptor.

Please see Important Safety Information on page 10 and the accompanying full Prescribing Information.

In combination with trastuzumab + capecitabine

TUKYSA REDUCED THE RISK OF DISEASE PROGRESSION OR DEATH BY 46%*

PFS by BICR in the primary endpoint population: Kaplan-Meier estimates[1]



NUMBER AT RISK

TUKYSA arm	320	235	152	98	40	29	15	10	8	4	2	1	0
Control arm	160	94	45	27	6	4	2	1	1	0	0	0	0

- Hazard ratios for PFS across subgroups† were consistent with the HR for PFS of the primary endpoint population[1]

At 12 months, the estimated PFS was 33.1% (95% CI: 26.6-39.7) in the TUKYSA arm and 12.3% (95% CI: 6.0-20.9) in the control arm.‡[1]

‡This analysis is descriptive only. HER2CLIMB was not powered to assess a statistical difference between treatment groups at this time point.

*Compared with patients in the control arm who received placebo + trastuzumab + capecitabine.

† Age (younger than 65 vs 65 and older), race (white vs nonwhite), hormone-receptor status (positive for ER, PR, or both vs negative for ER and PR), baseline brain metastases (yes vs no), ECOG performance status (0 vs 1), and geographic region (US and Canada vs rest of the world). Age and race were not prespecified subgroups, and results of the exploratory analysis should be interpreted with caution.[1]

ALT = alanine transaminase; AST = aspartate aminotransferase; CI = confidence interval; HR = hazard ratio; ULN = upper limit of normal.

Select Safety Information

- **Hepatotoxicity:** TUKYSA can cause severe hepatotoxicity. In HER2CLIMB, 8% of patients who received TUKYSA had an ALT increase >5 × ULN, 6% had an AST increase >5 × ULN, and 1.5% had a bilirubin increase >3 × ULN (Grade ≥3). Hepatotoxicity led to TUKYSA dose reductions in 8% of patients and TUKYSA discontinuation in 1.5% of patients.

  Monitor ALT, AST, and bilirubin prior to starting TUKYSA, every 3 weeks during treatment, and as clinically indicated. Based on the severity of hepatoxicity, interrupt dose, then dose reduce or permanently discontinue TUKYSA.

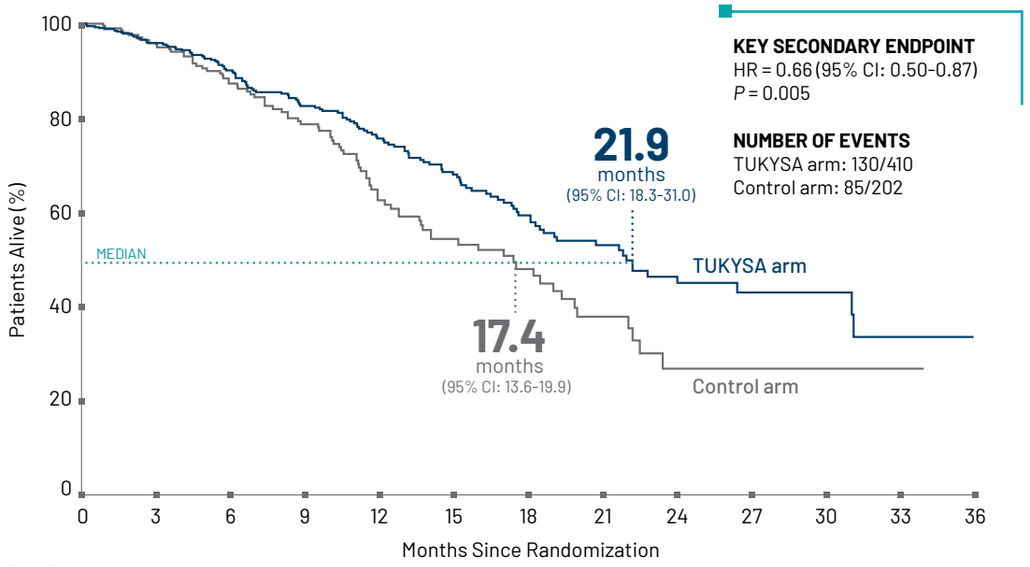
Please see Important Safety Information on page 10 and the accompanying full Prescribing Information.

TUKYSA™ tucatinib 50 mg | 150 mg tablets

In combination with trastuzumab + capecitabine

TUKYSA EXTENDED MEDIAN OS BY 4.5 MONTHS*

OS in the total population: Kaplan-Meier estimates[1,2]



NUMBER AT RISK

TUKYSA arm	410	388	322	245	178	123	80	51	34	20	10	4	0
Control arm	202	191	160	119	77	48	32	19	7	5	2	1	0

- Hazard ratios for OS across subgroups† were consistent with the HR for OS of the total population, including patients with brain metastases (HR = 0.58 [95% CI: 0.40-0.85])[1]

At 24 months, the estimated OS was 44.9% (95% CI: 36.6-52.8) in the TUKYSA arm and 26.6% (95% CI: 15.7-38.7) in the control arm.‡[1]

‡This analysis is descriptive only. HER2CLIMB was not powered to assess a statistical difference between treatment groups at this time point.

*Compared with patients in the control arm who received placebo + trastuzumab + capecitabine.

†Age (younger than 65 vs 65 and older), race (white vs nonwhite), hormone-receptor status (positive for ER, PR, or both vs negative for ER and PR), baseline brain metastases (yes vs no), ECOG performance status (0 vs 1), and geographic region (US and Canada vs rest of the world). Age and race were not prespecified subgroups, and results of the exploratory analysis should be interpreted with caution.[1]

Select Safety Information

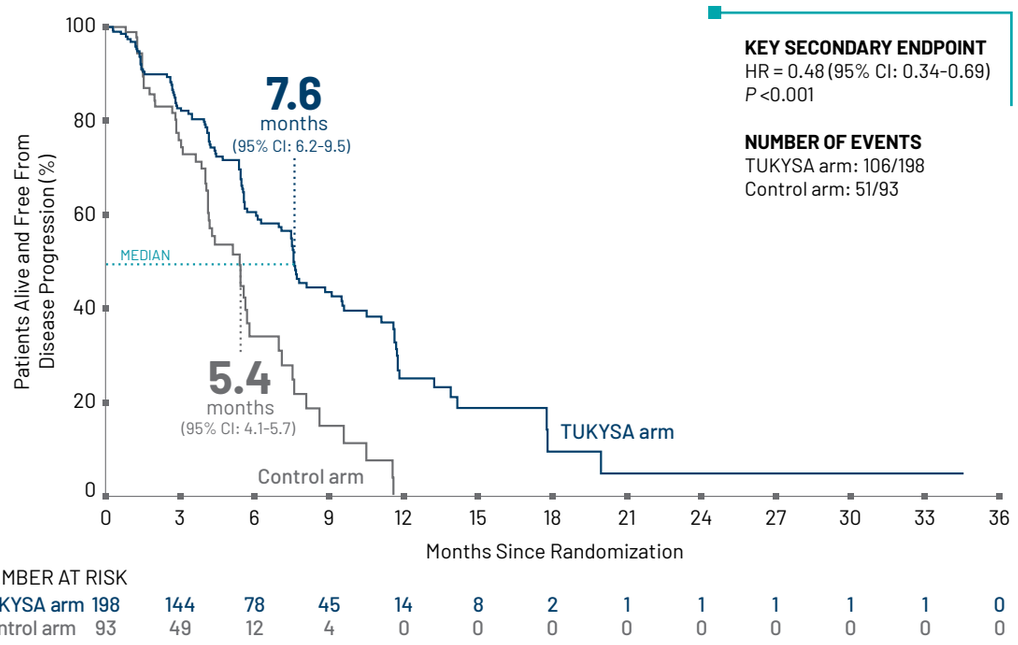
- **Embryo-Fetal Toxicity:** TUKYSA can cause fetal harm. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential, and male patients with female partners of reproductive potential, to use effective contraception during TUKYSA treatment and for at least 1 week after the last dose.

Please see Important Safety Information on page 10 and the accompanying full Prescribing Information.

In combination with trastuzumab + capecitabine

TUKYSA REDUCED THE RISK OF DISEASE PROGRESSION OR DEATH BY 52% IN PATIENTS *WITH* BRAIN METASTASES*

PFS by BICR in patients with brain metastases: Kaplan-Meier estimates†[1]



NUMBER AT RISK

TUKYSA arm	198	144	78	45	14	8	2	1	1	1	1	1	0
Control arm	93	49	12	4	0	0	0	0	0	0	0	0	0

At 12 months, the estimated PFS in patients with brain metastases was 24.9% (95% CI: 16.5-34.3) in the TUKYSA arm and 0% in the control arm.‡[1]

‡This analysis is descriptive only. HER2CLIMB was not powered to assess a statistical difference between treatment groups at this time point.

*Compared with patients in the control arm who received placebo + trastuzumab + capecitabine.

†Analysis includes patients with history or presence of parenchymal brain metastases at baseline, including target and nontarget lesions. Analysis does not include patients with dural lesions only.

Select Safety Information

Adverse Reactions

Serious adverse reactions occurred in 26% of patients who received TUKYSA; those occurring in ≥2% of patients were diarrhea (4%), vomiting (2.5%), nausea (2%), abdominal pain (2%), and seizure (2%). Fatal adverse reactions occurred in 2% of patients who received TUKYSA including sudden death, sepsis, dehydration, and cardiogenic shock.

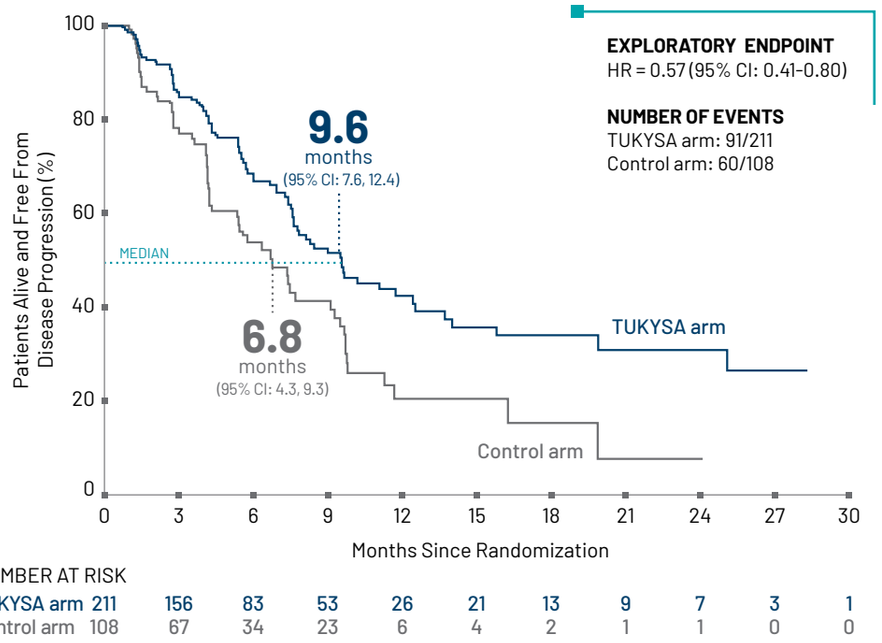
Please see Important Safety Information on page 10 and the accompanying full Prescribing Information.

TUKYSA™ tucatinib 50 mg | 150 mg tablets

In combination with trastuzumab + capecitabine

TUKYSA REDUCED THE RISK OF DISEASE PROGRESSION OR DEATH BY 43% IN PATIENTS *WITHOUT* BRAIN METASTASES*

PFS by BICR in patients without brain metastases: Kaplan-Meier estimates[1,3]



NUMBER AT RISK

TUKYSA arm	211	156	83	53	26	21	13	9	7	3	1
Control arm	108	67	34	23	6	4	2	1	1	0	0

This exploratory analysis was not controlled for a type 1 error and HER2CLIMB was not powered to test this endpoint. Results are descriptive only and are not contained in the approved product labeling.

Confirmed ORR by BICR in all patients with measurable disease at baseline

- Confirmed ORR was **40.6%** in the TUKYSA arm (n = 340; CR = 0.9%; PR = 39.7%; 95% CI: 35.3-46.0) vs **22.8%** in the control arm (n = 171; CR = 1.2%; PR = 21.6%; 95% CI: 16.7-29.8); *P* = 0.00008[1]
- Median duration of response: 8.3 months (95% CI: 6.2- 9.7) in the TUKYSA arm vs 6.3 months (95% CI: 5.8-8.9) in the control arm[2]
- Median time to response was 1.4 months in the TUKYSA arm†[4]

†Results of this exploratory analysis are descriptive only and are not contained in the approved product labeling.

*Compared with patients in the control arm who received placebo + trastuzumab + capecitabine.
CR = complete response; PR = partial response.

Select Safety Information

Adverse reactions led to treatment discontinuation in 6% of patients who received TUKYSA; those occurring in ≥1% of patients were hepatotoxicity (1.5%) and diarrhea (1%). Adverse reactions led to dose reduction in 21% of patients who received TUKYSA; those occurring in ≥2% of patients were hepatotoxicity (8%) and diarrhea (6%).

The most common adverse reactions in patients who received TUKYSA (≥20%) were diarrhea, palmar-plantar erythrodysesthesia, nausea, fatigue, hepatotoxicity, vomiting, stomatitis, decreased appetite, abdominal pain, headache, anemia, and rash.

Please see Important Safety Information on page 10 and the accompanying full Prescribing Information.

TUKYSA™ tucatinib 50 mg | 150 mg tablets

TUKYSA SAFETY PROFILE

Of the most common adverse events in the TUKYSA arm, a majority were Grade 1 or 2

Adverse reactions in ≥10% of patients and at ≥5% higher incidence in the TUKYSA arm[2]

	TUKYSA + trastuzumab + capecitabine (n = 404)			Placebo + trastuzumab + capecitabine (n = 197)		
	All Grades %	Grade 3 %	Grade 4 %	All Grades %	Grade 3 %	Grade 4 %
GASTROINTESTINAL DISORDERS						
Diarrhea	81	12	0.5	53	9	0
Nausea	58	3.7	0	44	3	0
Vomiting	36	3	0	25	3.6	0
Stomatitis*	32	2.5	0	21	0.5	0
SKIN AND SUBCUTANEOUS TISSUE DISORDERS						
PPE syndrome	63	13	0	53	9	0
Rash†	20	0.7	0	15	0.5	0
HEPATOBILIARY DISORDERS						
Hepatotoxicity‡	42	9	0.2	24	3.6	0
METABOLISM AND NUTRITION DISORDERS						
Decreased appetite	25	0.5	0	20	0	0
BLOOD AND LYMPHATIC SYSTEM DISORDERS						
Anemia§	21	3.7	0	13	2.5	0
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS						
Arthralgia	15	0.5	0	4.6	0.5	0
INVESTIGATIONS						
Creatinine increased¶	14	0	0	1.5	0	0
Weight decreased	13	1	0	6	0.5	0
NERVOUS SYSTEM DISORDERS						
Peripheral neuropathy**	13	0.5	0	7	1	0
RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS						
Epistaxis	12	0	0	5	0	0

- Serious adverse reactions occurred in 26% of TUKYSA-treated patients; the most common serious adverse reactions (≥2%) were[2]:
  - diarrhea (4%)
  - vomiting (2.5%)
  - nausea (2%)
  - abdominal pain (2%)
  - seizure (2%)
- There was low incidence (<5%) of alopecia in HER2CLIMB (4.7% TUKYSA arm vs 3.6% control arm)[4]

PPE = palmar-plantar erythrodysesthesia.

*Stomatitis includes stomatitis, oropharyngeal pain, oropharyngeal discomfort, mouth ulceration, oral pain, lip ulceration, glossodynia, tongue blistering, lip blister, oral dysesthesia, tongue ulceration, and aphthous ulcer.

†Rash includes rash maculo-papular, rash, dermatitis acneiform, erythema, rash macular, rash papular, rash pustular, rash pruritic, rash erythematous, skin exfoliation, urticaria, dermatitis allergic, palmar erythema, plantar erythema, skin toxicity, and dermatitis.

‡Hepatotoxicity includes hyperbilirubinemia, blood bilirubin increased, bilirubin conjugated increased, alanine aminotransferase increased, transaminases increased, hepatotoxicity, aspartate aminotransferase increased, liver function test increased, liver injury, and hepatocellular injury.

§Anemia includes anemia, hemoglobin decreased, and normocytic anemia.

¶Due to inhibition of renal tubular transport of creatinine without affecting glomerular function.

**Peripheral neuropathy includes peripheral sensory neuropathy, neuropathy peripheral, peripheral motor neuropathy, and peripheral sensorimotor neuropathy.

Please see Important Safety Information on page 10 and the accompanying full Prescribing Information.

DISCONTINUATION OF TUKYSA DUE TO ADVERSE EVENTS WAS INFREQUENT (6%)

Adverse events leading to discontinuation*[2,4]

AGENT DISCONTINUED	TUKYSA + trastuzumab + capecitabine (n = 404)	Placebo + trastuzumab + capecitabine (n = 197)
TUKYSA/placebo	6%	3%
Trastuzumab	5%	3%
Capecitabine	10%	9%

*Discontinuation rates are descriptive data that are not intended to provide conclusions about safety and should be interpreted with caution.

- Adverse reactions leading to treatment discontinuation of TUKYSA in ≥1% of patients were hepatotoxicity (1.5%) and diarrhea (1%)[2]
- Adverse reactions leading to dose reduction occurred in 21% of patients treated with TUKYSA[2]
- Adverse reactions leading to dose reduction of TUKYSA in ≥2% of patients were hepatotoxicity (8%) and diarrhea (6%)[2]

Diarrhea observed in HER2CLIMB

- Prophylactic support to manage diarrhea was not required per HER2CLIMB protocol[2]
- 81% of patients who received TUKYSA experienced diarrhea, including 12% with Grade 3 and 0.5% with Grade 4[2]
- The median time to onset of any grade diarrhea was 12 days, and the median time to resolution was 8 days[2]
- The median duration of antidiarrheal use was 3 days for each 21-day repeating regimen[1]
- If diarrhea occurs, as clinically indicated, administer antidiarrheal treatment and perform diagnostic tests to exclude other causes; based on the severity, interrupt dose then dose reduce or permanently discontinue TUKYSA[2]

For dose modifications of TUKYSA, please refer to the accompanying full Prescribing Information. For dose modifications of trastuzumab and capecitabine, please refer to the respective Prescribing Information for each agent.[2]

Please see Important Safety Information on page 10 and the accompanying full Prescribing Information.

TUKYSA™ tucatinib 50 mg | 150 mg tablets

Important Safety Information

Warnings and Precautions

- **Diarrhea:** TUKYSA can cause severe diarrhea including dehydration, hypotension, acute kidney injury, and death. In HER2CLIMB, 81% of patients who received TUKYSA experienced diarrhea, including 12% with Grade 3 and 0.5% with Grade 4. Both patients who developed Grade 4 diarrhea subsequently died, with diarrhea as a contributor to death. Median time to onset of the first episode of diarrhea was 12 days and the median time to resolution was 8 days. Diarrhea led to TUKYSA dose reductions in 6% of patients and TUKYSA discontinuation in 1% of patients. Prophylactic use of antidiarrheal treatment was not required on HER2CLIMB.

  If diarrhea occurs, administer antidiarrheal treatment as clinically indicated. Perform diagnostic tests as clinically indicated to exclude other causes of diarrhea. Based on the severity of the diarrhea, interrupt dose, then dose reduce or permanently discontinue TUKYSA.
- **Hepatotoxicity:** TUKYSA can cause severe hepatotoxicity. In HER2CLIMB, 8% of patients who received TUKYSA had an ALT increase >5 × ULN, 6% had an AST increase >5 × ULN, and 1.5% had a bilirubin increase >3 × ULN (Grade ≥3). Hepatotoxicity led to TUKYSA dose reductions in 8% of patients and TUKYSA discontinuation in 1.5% of patients.

  Monitor ALT, AST, and bilirubin prior to starting TUKYSA, every 3 weeks during treatment, and as clinically indicated. Based on the severity of hepatoxicity, interrupt dose, then dose reduce or permanently discontinue TUKYSA.
- **Embryo-Fetal Toxicity:** TUKYSA can cause fetal harm. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential, and male patients with female partners of reproductive potential, to use effective contraception during TUKYSA treatment and for at least 1 week after the last dose.

Adverse Reactions

Serious adverse reactions occurred in 26% of patients who received TUKYSA; those occurring in ≥2% of patients were diarrhea (4%), vomiting (2.5%), nausea (2%), abdominal pain (2%), and seizure (2%). Fatal adverse reactions occurred in 2% of patients who received TUKYSA including sudden death, sepsis, dehydration, and cardiogenic shock.

Adverse reactions led to treatment discontinuation in 6% of patients who received TUKYSA; those occurring in ≥1% of patients were hepatotoxicity (1.5%) and diarrhea (1%). Adverse reactions led to dose reduction in 21% of patients who received TUKYSA; those occurring in ≥2% of patients were hepatotoxicity (8%) and diarrhea (6%).

The most common adverse reactions in patients who received TUKYSA (≥20%) were diarrhea, palmar-plantar erythrodysesthesia, nausea, fatigue, hepatotoxicity, vomiting, stomatitis, decreased appetite, abdominal pain, headache, anemia, and rash.

Lab Abnormalities

In HER2CLIMB, Grade ≥3 laboratory abnormalities reported in ≥5% of patients who received TUKYSA were decreased phosphate, increased ALT, decreased potassium, and increased AST.

The mean increase in serum creatinine was 32% within the first 21 days of treatment with TUKYSA. The serum creatinine increases persisted throughout treatment and were reversible upon treatment completion. Consider alternative markers of renal function if persistent elevations in serum creatinine are observed.

Drug Interactions

- **Strong CYP3A/Moderate CYP2C8 Inducers:** Concomitant use may decrease TUKYSA activity. Avoid concomitant use of TUKYSA.
- **Strong or Moderate CYP2C8 Inhibitors:** Concomitant use of TUKYSA with a strong CYP2C8 inhibitor may increase the risk of TUKYSA toxicity; avoid concomitant use. Increase monitoring for TUKYSA toxicity with moderate CYP2C8 inhibitors.
- **CYP3A Substrates:** Concomitant use may increase the toxicity associated with a CYP3A substrate. Avoid concomitant use of TUKYSA where minimal concentration changes may lead to serious or life-threatening toxicities. If concomitant use is unavoidable, decrease the CYP3A substrate dosage.
- **P-gp Substrates:** Concomitant use may increase the toxicity associated with a P-gp substrate. Consider reducing the dosage of P-gp substrates where minimal concentration changes may lead to serious or life-threatening toxicity.

Use in Specific Populations

- **Lactation:** Advise women not to breastfeed while taking TUKYSA and for at least 1 week after the last dose.
- **Renal Impairment:** Use of TUKYSA in combination with capecitabine and trastuzumab is not recommended in patients with severe renal impairment (CLcr < 30 mL/min), because capecitabine is contraindicated in patients with severe renal impairment.
- **Hepatic Impairment:** Reduce the dose of TUKYSA for patients with severe (Child-Pugh C) hepatic impairment.

Please see the full Prescribing Information.

TUKYSA™ tucatinib
50 mg | 150 mg tablets

TUCATINIB, TRASTUZUMAB, AND CAPECITABINE FOR HER2-POSITIVE METASTATIC BREAST CANCER

Murthy RK, Loi S, Okines A, et al.

Results from the HER2CLIMB study published in the *New England Journal of Medicine*, including links to the full trial protocol and an expansive supplementary appendix.

Please visit TUKYSAhcp.com/resources for additional product information and resources

Conclusions

- In this double-blind, randomized, controlled trial, the addition of TUKYSA to capecitabine and trastuzumab significantly reduced the risk of disease progression or death and extended OS in patients with HER2+ MBC compared with those treated with placebo + trastuzumab + capecitabine[1]
- The most common adverse reactions in patients who received TUKYSA (≥20%) were diarrhea, palmar-plantar erythrodysesthesia, nausea, fatigue, hepatotoxicity, vomiting, stomatitis, decreased appetite, abdominal pain, headache, anemia, and rash[1,2]

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;382:597-609. **2.** TUKYSA [Prescribing Information]. Bothell, WA: Seattle Genetics, Inc. April 2020. **3.** Murthy RK, Loi S, Okines A, et al. Supplemental appendix for: Tucatinib, trastuzumab, and capecitabine for HER2-positive metastatic breast cancer. *N Engl J Med.* 2020;382:597-609. **4.** Data on file. Seattle Genetics, Inc. 2020.

Please see Important Safety Information on page 10 and the accompanying full Prescribing Information.

TUKYSA in combination with trastuzumab + capecitabine*

PROVEN SURVIVAL BENEFIT IN A BROAD RANGE OF PATIENTS WITH HER2+ MBC†

Patients were previously treated with trastuzumab, pertuzumab, and T-DM1, separately or in combination, in the neoadjuvant, adjuvant, or metastatic setting[1]

Reduced risk of disease progression or death by 46%[1]

- HR = 0.54 (95% CI: 0.42-0.71); *P* <0.001
- Median PFS by BICR: 7.8 months (95% CI: 7.5-9.6) in the TUKYSA arm vs 5.6 months (95% CI: 4.2-7.1) in the control arm
- Data from the first 480 patients who underwent randomization; primary endpoint

Increased median OS by 4.5 months[1]

- Median OS: 21.9 months (95% CI: 18.3-31.0) in the TUKYSA arm vs 17.4 months (95% CI: 13.6-19.9) in the control arm
- Reduced risk of death: HR = 0.66 (95% CI: 0.50-0.87); *P* = 0.005
- Data from the total population of 612 patients; key secondary endpoint

Reduced risk of disease progression or death in patients with brain metastases by 52%[1,3]

- HR = 0.48 (95% CI: 0.34-0.69); *P* <0.001
- Median PFS: 7.6 months (95% CI: 6.2-9.5) in the TUKYSA arm vs 5.4 months (95% CI: 4.1-5.7) in the control arm
- PFS by BICR data from the 291 (47.5%) patients *with* brain metastases at baseline
- 43% lower risk of disease progression or death in patients *without* brain metastases (prespecified exploratory analysis of PFS by BICR; HR = 0.57 [95% CI: 0.41-0.80]; median PFS: 9.6 months [95% CI: 7.6-12.4] in the TUKYSA arm vs 6.8 months [95% CI: 4.3-9.3] months in the control arm‡

The most common adverse reactions in patients who received TUKYSA (≥20%) were diarrhea, palmar-plantar erythrodysesthesia, nausea, fatigue, hepatotoxicity, vomiting, stomatitis, decreased appetite, abdominal pain, headache, anemia, and rash[1,2]

- Of the most common adverse events in the TUKYSA arm, a majority were Grade 1 or 2

*In HER2CLIMB, patients in the TUKYSA arm (TUKYSA + trastuzumab + capecitabine) were compared with those in the control arm (placebo + trastuzumab + capecitabine).

†Efficacy results were consistent across patient subgroups defined by stratification factors (presence or history of brain metastases, Eastern Cooperative Oncology Group [ECOG] performance status [0 vs 1], and region [US, Canada, or rest of world]) and hormone receptor status.

‡This exploratory analysis was not controlled for a type 1 error, and HER2CLIMB was not powered to test this endpoint. Results are descriptive only and are not contained in the approved product labeling.

Indication

TUKYSA is indicated in combination with trastuzumab and capecitabine for treatment of adult patients with advanced unresectable or metastatic HER2-positive breast cancer, including patients with brain metastases, who have received one or more prior anti-HER2-based regimens in the metastatic setting.

SeattleGenetics®

Please see Important Safety Information on page 10 and the accompanying full Prescribing Information.

TUKYSA™ tucatinib 50 mg | 150 mg tablets