Society of Gynecologic Oncology
ANNUAL MEETING ON WOMENS' CANCER®
BUILDING BRIDGES // BREAKING BARRIERS
SGO // PHOENIX, ARIZONA // MARCH 18 – 21, 2022

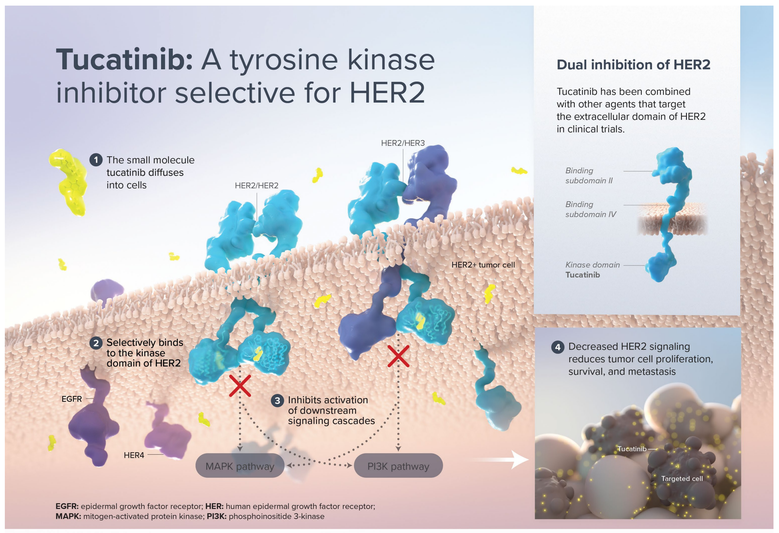
SGNTUC-019 PHASE 2 BASKET STUDY OF TUCATINIB AND TRASTUZUMAB IN SOLID TUMORS WITH HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2 ALTERATIONS: UTERINE AND CERVICAL CANCER COHORTS

Bradley J. Monk[1], Jorge Ramos[2], Sherry Tan[2], David O'Malley[3]
[1] Arizona Oncology (US Oncology Network), University of Arizona, Creighton University, Phoenix, AZ, USA; [2]Seagen Inc., Bothell, WA, USA; [3]Ohio State University, Columbus, OH, USA

BACKGROUND AND RATIONALE

- Tucatinib (TUC) is a highly selective HER2-directed TKI recently approved in multiple regions for HER2 overexpressed/amplified (HER2+) metastatic breast cancer
- In HER2+ and HER2-mutated xenograft models, dual targeting of HER2 with the combination of TUC and trastuzumab (Tras) showed superior activity compared to either agent alone[1,2]
- The prognoses of advanced cervical and uterine cancers are poor, with 5-year overall survival rates for metastatic diseases of 16% and 9%, respectively[3,4]
- HER2 overexpression and amplification occur in 21% and 0.5%–14% of cases for cervical cancer, and 18%–80% and 4%–59% of cases for uterine cancers, respectively[5]
- The SGNTUC-019 basket study (NCT04579380) is evaluating TUC in combination with Tras in patients with HER2+ or HER2-mutated solid tumors, including cohorts of patients with HER2+ cervical or uterine cancers

TUCATINIB PROPOSED MECHANISM OF ACTION



STUDY DESIGN

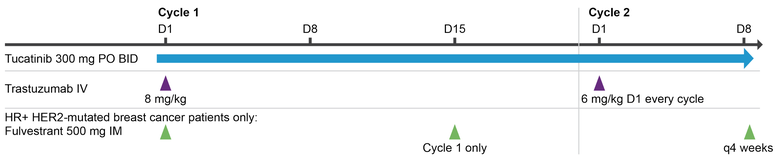
Cervical and Uterine Cancer Cohorts

- In Stage 1, 12 response-evaluable patients will be enrolled in both Cohorts 1 and 2 with HER2+ cervical and uterine cancers
- Stage 2 will be opened for both Cohorts 1 and 2 to enroll 30 response-evaluable patients total in each cohort if ≥2 responses are observed in either cohort in Stage 1
  - According to the PPoS method[6], having ≥2 responders in each cohort means it is likely the ORR exceeds 15%
- Patients with HER2-mutated cervical and uterine cancers will be enrolled in Cohort 9; specific cohorts may be opened if enrollment is sufficient

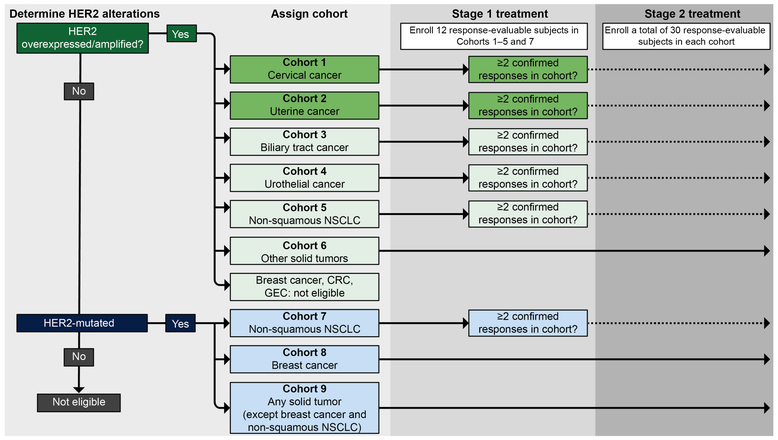
DISCLOSURES
This study is sponsored by Seagen Inc., Bothell, WA, USA in collaboration with Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA. The development of this presentation was funded by Seagen Inc. Natalie Pizzimenti, MS (MMS Holdings, Canton, MI), provided medical writing and editorial support in accordance with Good Publication Practice (GPP3) guidelines. DO has consultancy for Abbvie, Agenus, Ambry, Amgen, Arquer, AstraZeneca, Celsion, Clovis, Corcept, Eisai, Elevar, Genentech/Roche, GOG Fnd, Immunogen, Inxmed, Iovance, Janssen, Johnson&Johnson, Merck, Mersana, Myriad, Novartis Novocure, Regeneron, Roche, Rubis, SDPOnc, Seagen Inc. Sorrento, Takeda, Tesaro/GSK, and Toray; and has research funding from Abbvie, Agenus, Ajinomoto, Amgen, Array, AstraZeneca, BMS, Cerulean, Clovis, Eisai, EMD Serono, Ergomed, Genentech/Roche, GenMab, GOG Found, Immunogen, Inc Research, InVentiv Health, Iovance, Janssen, Johnson&Johnson, Ludwig Cancer Research, Merck, Mersana, New Mexico CCA, Novocure, PRA Int'l, Regeneron, SDPOnc, Seagen, Serono, Stemcentrx, Tarveda, Tesaro/GSK, Tracon Pharma, VentiRx, and Yale University. ST is employed by Seagen Inc.; and has equity and ownership in Seagen Inc. JR is employed by Seagen Inc.; and has equity and ownership in Seagen Inc. BM has consultancy for Abbvie, Advaxis, Agenus, Akeso, Amgen, Aravive, AstraZeneca, Asymmetric, Boston Bio, ChemoCare, ChemoID, Clovis, Deciphera, Eisai, Geistlich, Genmab/Seagen, GOG Found, Gradalis, Immunogen, Immunomedics, Incyte, Iovance, Karyopharm, Laekna, Merck, Mersana, Myriad, Novocure, Nucana, Oncomed, Oncoquest, Oncosec, Perthera, Pfizer, Puma, Regeneron, Roche/Genentech, Senti, Sorrento, Takeda, Tarveda, TESARO/GSK, Vavotar, Vascular, and Vigeo; honoraria from Abbvie, Advaxis, Agensys, Akeso, Amgen, Aravive, AstraZeneca, Asymmetric, Boston Bio, Chemoid, Clovis, Deciphera, Eisai, Elevar, Geistlich, Genmab/Seagen, GOG Found, Gradalis, Immunogen, Immunomedics, Incyte, Iovance, Karyopharm, Laekna, Mersana, Myriad, Novocure, Nucana, Oncomed, Oncoquest, Oncosec, Perthera, Pfizer, Puma, Regeneron, Roche/Genentech, Senti, Starton, Tarveda, Tesaro/GSK, Vascular Biogenics, Vavotar, and Vigeo; and research funding from Advaxis, Amgen, Array, AstraZeneca, Genentech, Immunogen, Janssen, Lilly, Morphotek, Novartis, Nucana, Pfizer, Regeneron, and Tesaro.

STUDY TREATMENT

- Patients will receive TUC 300 mg PO BID and Tras 8 mg/kg IV on Cycle 1 Day 1 and 6 mg/kg every 21 days thereafter
- Patients with hormone receptor-positive HER2-mutated breast cancer will also receive fulvestrant 500 mg IM once every 4 weeks and on Cycle 1 Day 15



STUDY SCHEMA



a. If a sufficient number of patients with a particular tumor type are enrolled in Cohorts 6 or 9, the sponsor may evaluate that tumor type in a separate cohort, drawn from optional Cohorts 10 to 15.

OBJECTIVES

Primary Objective	Endpoints
To evaluate the antitumor activity of TUC combined with Tras	**Primary endpoint:** Confirmed ORR according to RECIST v1.1 per investigator assessment **Secondary endpoints:** DCR, DOR, PFS per investigator assessment, and OS
Secondary Objective	**Endpoints**
To evaluate the safety and tolerability of TUC combined with Tras (and with fulvestrant in HR+ HER2-mutated breast cancer)	• Incidence, severity, and relatedness of AEs and SAEs • Incidence and severity of laboratory abnormalities • Frequency of dose modifications due to AEs • Other relevant safety variables including AESIs
To evaluate the PK of TUC	Plasma concentrations of TUC
Exploratory Objectives	**Endpoints**
To determine concordance of HER2 alterations by tissue and blood assay	Concordance of HER2 alterations as detected by different testing methodologies
To identify somatic alterations that are associated with resistance to TUC	Identify tumor-specific alterations that are associated with resistance to TUC
To evaluate PROs	Change from baseline in HRQoL, as assessed by the EQ-5D-5L

REFERENCES
1. Kulukian A et al, Mol Cancer Ther. 2020 Apr;19(4):976–987.
2. Peterson S et al, AACR. 2020; Abstract 4222.
3. NIH, SEER Cancer Stat Facts: Cervical Cancer. https://seer.cancer.gov/statfacts/html/cervix.html. Accessed Sep. 30, 2021.
4. NIH, SEER Cancer Stat Facts: Uterine Cancer. https://seer.cancer.gov/statfacts/html/corp.html. Accessed Oct. 1, 2021.
5. Oh DY et al, HER2-targeted therapies - a role beyond breast cancer. Nat Rev Clin Oncol. 2020;17(1):33-48.
6. Lee JJ et al, Clin Trials. 2008; 5(2):93–106.

ABBREVIATIONS
AE, adverse event; AESI, AE of special interest; BID, twice daily; CBC, complete blood count; CNS, central nervous system; CR, complete response; CRC, colorectal cancer; ctDNA, circulating tumor DNA; D, day; DCR, disease control rate (CR or PR or stable disease as best objective response); DOR, duration of response; ECG, electrocardiogram; ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; eGFR, estimated glomerular filtration rate; EOT, end of treatment; EQ-5D-5L, European Quality of Life 5-Dimension 5-Level; GEC, gastric or gastroesophageal junction adenocarcinoma; HBV, hepatitis B virus; HCV, hepatitis C virus; HER2, human epidermal growth factor receptor 2; HER2+, HER2 overexpression or amplification; HIV, human immunodeficiency virus; HR+, hormone receptor positive; HRQoL, health-related quality of life; IHC, immunohistochemistry; IM, intramuscular; ISH, in situ hybridization; IV, intravenous; LVEF, left ventricular ejection fraction; MAPK, mitogen-activated protein kinase; NGS, next generation sequencing; NSCLC, non-small cell lung cancer; ORR, objective response rate (CR or PR); OS, overall survival; PK, pharmacokinetics; PFS, progression-free survival; PI3K, phosphoinositide 3-kinase; PO, orally; PPoS, predicted probability of success; PR, partial response; PRO, patient-reported outcomes; q, every; RECIST, Response Evaluation Criteria in Solid Tumors; SAE, serious adverse event; SMC, safety monitoring committee; TKI, tyrosine kinase inhibitor; Tras, trastuzumab; TUC, tucatinib; US, United States.

ELIGIBILITY

Key Inclusion Criteria

- Histologically or cytologically confirmed, locally-advanced unresectable or metastatic, HER2+ or HER2-mutated solid tumors, including primary brain tumors
- Must have progressed during or after ≥1 prior line of systemic therapy for locally advanced unresectable or metastatic disease
  - Patients with metastatic cervical cancer must have received platinum-based chemotherapy with or without bevacizumab in the metastatic setting
- Progression during or after, or intolerance of, the most recent line of systemic therapy
- HER2 alterations demonstrated by one of the following:
  - HER2 overexpression (3+ IHC)
  - HER2 amplification in tumor tissue by pre-study ISH (signal ratio ≥2.0 or gene copy number >6)
  - HER2 amplification or activating mutations in a pre-study or on-study NGS assay of ctDNA or pre-study tissue NGS assay
- ≥18 years of age
- ECOG performance status 0 or 1
- Adequate hepatic, renal, and hematologic, and LVEF ≥50%

Key Exclusion Criteria

- HER2+ breast cancer, CRC, or gastric or gastroesophageal junction adenocarcinoma
- Prior HER2 directed therapy; patients with uterine serous carcinoma or HER2-mutated gastric or gastroesophageal junction adenocarcinoma without HER2-overexpression/amplification may have received prior Tras
- Myocardial infarction or unstable angina within 6 months, or clinically significant cardiopulmonary disease
- Known active HBV, HCV, or HIV infection or chronic liver disease
- Active CNS lesions >2 cm unless approved by medical monitor

ASSESSMENTS

- Disease assessments per RECIST v1.1: q6 weeks for 24 weeks, then q12 weeks. For patients without disease progression at treatment discontinuation, assessments continue until disease progression, withdrawal of consent, death, loss to follow-up, or study closure
- Safety assessments: AEs, SAEs, AESIs, treatment modifications, laboratory assessments (metabolic panel, CBC with differential, and eGFR), vital signs, LVEF every 12 weeks, and ECG at baseline and EOT
  - An SMC will monitor safety at regular intervals
- PK assessments in all patients: Trough TUC concentrations on Cycles 2–6 Day 1 and peak concentrations on Cycle 3 Day 1
- Exploratory biomarker assessments: HER2 status by NGS of ctDNA and tissue IHC/ISH and NGS assays
- EQ-5D-5L questionnaires are administered every 2 cycles during study treatment

SUMMARY

- SGNTUC-019 is a basket study evaluating TUC in combination with Tras in previously treated patients with HER2 overexpressed/amplified or HER2-mutated solid tumors, including cohorts of patients with locally-advanced unresectable or metastatic cervical or uterine cancers
- Approximately 75 sites are planned for the US, Asia-Pacific, and Europe. The study is open and enrolling in all regions

Abstract ID: 11938