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Fulvestrant with or without the cyclin-dependent kinase 7 (CDK7) inhibitor samuraciclib in advanced hormone receptor positive (HR+) breast cancer after CDK4/6 inhibition: phase 2 SUMIT-BC study

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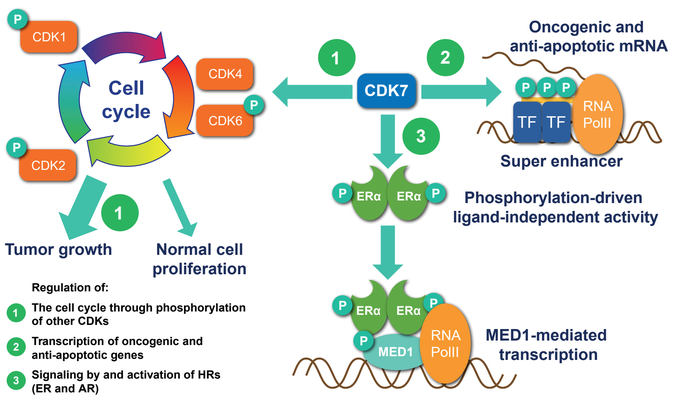
Summary

- **The CDK7 inhibitor samuraciclib has clinical activity when used in combination with fulvestrant in patients with HR+ advanced BC who have received a prior CDK4/6i[1]**
- **SUMIT-BC is a phase 2 trial (NCT05963984) comparing the efficacy, safety, PK, and QoL of samuraciclib combined with fulvestrant to those of fulvestrant alone**
- **SUMIT-BC is currently recruiting in the USA, Hungary, Mexico, Spain, and Turkey**

Introduction

- CDK7 regulates cell division, transcription, and nuclear receptor function. Its inhibition represents a novel anticancer strategy (**Figure 1**)[2]

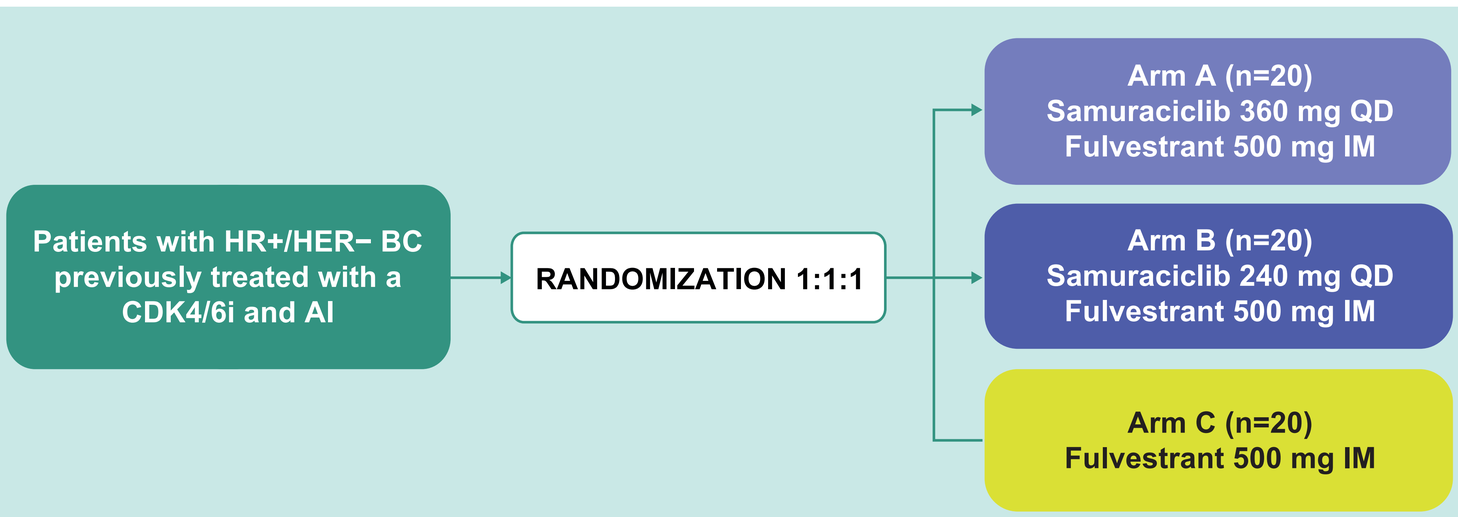
Figure 1. Role of CDK7 in cell cycle regulation and transcription and effects of CDK7 inhibition



- Samuraciclib (CT7001) is a small molecule, ATP competitive, selective oral inhibitor of CDK7 that potently inhibits key biological effects of CDK7 in cancer cells.[2] Samuraciclib selectively targets transcription to limit synthesis of mRNAs involved in tumor growth without inhibiting transcription of housekeeping genes[6]
- Clinical data suggest that samuraciclib combined with fulvestrant provides clinically meaningful anticancer activity with a favorable safety profile in patients with HR+/HER2− advanced BC previously treated with CDK4/6is[1]
- The international, multicenter, randomized, open-label, phase 2 SUMIT-BC (NCT05963984) study comparing samuraciclib combined with fulvestrant with fulvestrant alone in metastatic or locally advanced HR+/HER2− BC after prior AI and CDK4/6 inhibitor therapy is described[7]

Trial design

Figure 2. Study schema



Fulvestrant is administered on day 1 every 4 weeks, with an additional dose on day 15 of Cycle 1

- A total of 60 patients will be randomized 1:1:1 to one of three arms as shown in **Figure 2**
  - An instant release capsule formulation was used in the initial clinical evaluation of samuraciclib, requiring patients to take multiple capsules that release material high in the GI tract; in SUMIT-BC, a novel single tablet formulation, which may enhance GI tolerability, will be administered in preparation for phase 3 trials[8]
  - Evaluation of two doses of samuraciclib is consistent with the principles of the FDA Oncology Center of Excellence Project OPTIMUS initiative[9]
- Baseline Guardant360 ctDNA evaluation of *TP53* mutation status for all patients will permit prospective evaluation of its potential as a predictive biomarker
- Tumors will be evaluated using RECIST v1.1 at baseline, every 8 weeks until week 48, then every 12 weeks
- AEs will be collected until at least 28 days after final study drug administration
- The PK of samuraciclib and fulvestrant will be studied during the first 6 months of the study

Eligibility

- Patients will be stratified by the presence of *TP53* mutations and/or liver metastases
  - If at any time during the study the number of patients with tumor *TP53* mutations exceeds ≈30%, no additional patients with *TP53* mutations will be enrolled
  - As patients with liver metastases tend to have poorer prognosis than those without, enrollment may be capped to ≤40% of participants with liver metastases

Table 1. Key eligibility criteria

Key inclusion criteria	Key exclusion criteria
Histologically confirmed BC with evidence of metastatic or locally advanced disease not amenable to resection or radiation therapy with curative intent	Prior treatment with: • A SERD or similar agent in the advanced/metastatic setting • >1 line of endocrine treatment for locally advanced or metastatic disease • Chemotherapy for locally advanced or metastatic disease
Documentation of ER positivity ± PgR positivity, HER2 negativity, and *TP53* mutation status	Inflammatory BC
RECIST version 1.1 measurable disease or bone-only disease, which can be measurable or non-measurable	Unresolved toxicity (except alopecia, peripheral neuropathy, arthralgia, or other toxicities not considered a safety risk for the participant per the investigator's judgment) from prior therapy of Grade ≥2 according to NCI CTCAE version 5.0

Objectives and endpoints

Table 2. Objectives and endpoints

Objectives	Endpoints
Primary	
To evaluate the efficacy of 2 doses of samuraciclib in combination with fulvestrant	Clinical benefit response (complete response, partial response, or stable disease [≥24 weeks after randomization])
Secondary	
To further characterize the efficacy of samuraciclib in combination with fulvestrant (includes *TP53* correlation)	Progression-free survival, objective response rate, duration of response
To characterize the safety and tolerability of samuraciclib in combination with fulvestrant	AEs and laboratory abnormalities as graded by NCI CTCAE v5.0
To evaluate the PK of samuraciclib and fulvestrant	Samuraciclib: C_{max} and C_{trough}; fulvestrant: C_{trough}

Statistical analysis

- The primary analysis will be performed by 24 weeks after randomization, and final analyses will be performed 48 weeks after randomization

References

1. Coombes RC, et al. Nat Commun 2023;14:4444
2. Patel H, et al. Mol Cancer Ther 2018;17:1156–1166
3. Guarducci C, et al. Cancer Res 2019;79:PD7-12
4. Rugo HS, et al. J Clin Oncol 2016;34:3069–3103
5. Cardoso F, et al. Ann Oncol 2018;29:1634–1657
6. Diab S, et al. J Med Chem 2020;63:7458–7474
7. Clinicaltrials.gov. https://clinicaltrials.gov/study/NCT05963984. Accessed April 15, 2024
8. Bardia A, et al. J Clin Oncol 2021;39:1360–1370
9. FDA. https://www.fda.gov/about-fda/oncology-center-excellence/project-optimus. Accessed April 15, 2024

Abbreviations

AE, adverse event; AI, aromatase inhibitor; AR, androgen receptor; BC, breast cancer; CDK, cyclin-dependent kinase; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; ctDNA, circulating tumor DNA; ECOG, Eastern Cooperative Oncology Group; ER, estrogen receptor; GI, gastrointestinal; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IM, intramuscular; LHRH, luteinizing hormone releasing hormone; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; PK, pharmacokinetics; PgR, progesterone receptor; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors; SERD, selective estrogen receptor degrader

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Disclosures

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Further information

hello@carricktherapeutics.com; https://clinicaltrials.gov/study/NCT05963984