Evaluating the impact of neighborhood deprivation on CDK4/6 inhibitor use, outcomes, and circulating tumor DNA (ctDNA) alterations in patients with metastatic breast cancer

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Background

- Area Deprivation Index (ADI) is a **validated measure** used to determine **neighborhood-level** deprivation using 9-digit zip codes
- Includes education, poverty, employment, housing
- A higher ADI means higher neighborhood-level social and economic disadvantage[1,2]
- We previously showed differences in PI3K inhibitor use and overall survival in MBC by ADI[3]
- Here we explore whether there are differences by ADI in **use of CDK4/6 inhibitors** (CDK4/6i), **prognostic associations** in patients on CDK4/6i, and outcomes in patients with MBC

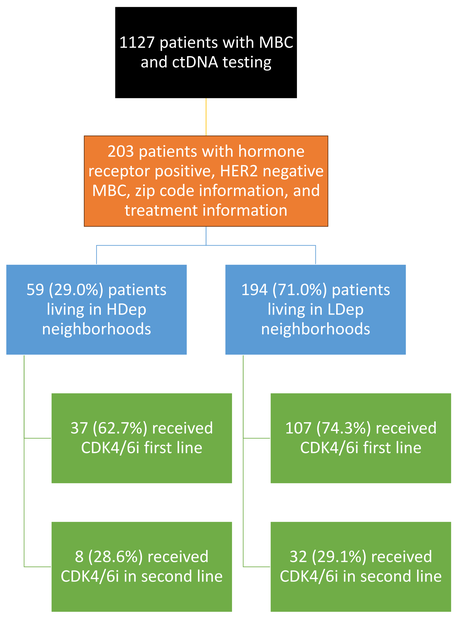
Methods

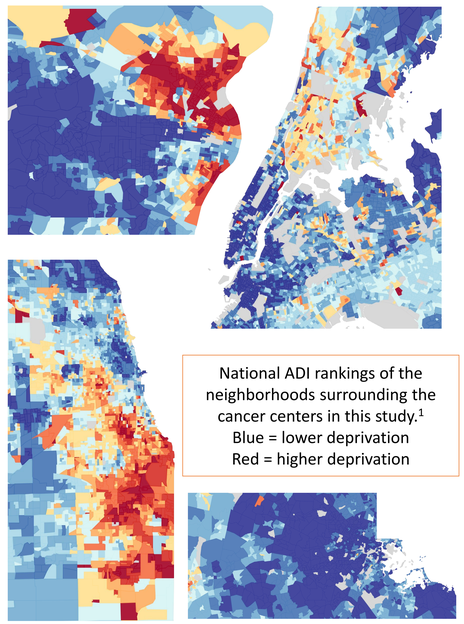
- **Sites:** Washington University (N=634), Massachusetts General Hospital (N=313), Weill Cornell (N=109), and Northwestern University (N=71)
- **Retrospective cohort:** 1127 patients with MBC and ctDNA results from the commercially-available Guardant360 test, 2015-2024
- **Methods:**
  - Patient-reported 9-digit zip codes were extracted from the electronic medical record
  - Zip codes converted to national ADI rankings using 2022 ADI data
  - Patients were divided into living in high deprivation areas (HDep, national ADI ≥60) and low deprivation areas (LDep, ADI <60)
- **Analysis:**
  - Evaluated for use of CDK4/6i in the first and second line by ADI
  - Progression free survival evaluated in first line by CDK4/6i and ADI
  - Multivariate models designed to determine prognostic differences in somatic mutations by ADI

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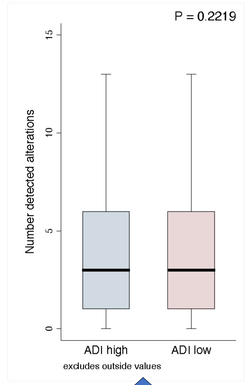
Patients with MBC living in **higher deprivation areas** by Area Deprivation Index were **equally likely to receive CDK4/6 inhibitors** as those living in less economically deprived areas and had **similar PFS.**

Patients living in **wealthier areas** were **more likely to have disease progression on CDK4/6 inhibitors** if they had an ***ESR1*** **mutation.**





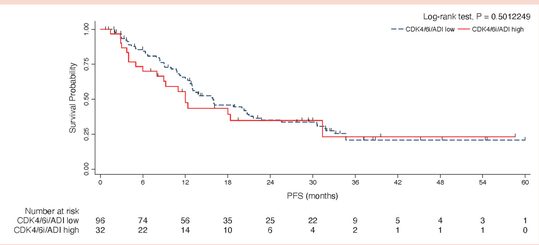
National ADI rankings of the neighborhoods surrounding the cancer centers in this study.[1]
Blue = lower deprivation
Red = higher deprivation



Patients living in high and low ADI neighborhoods had similar numbers of detected alterations by ctDNA

Results

- Patients living in LDep and HDep neighborhoods with MBC on CDK4/6i had **statistically similar PFS** when adjusting for line of therapy



- Patients living in LDep neighborhoods were more likely to **progress on CDK4/6i** if they had a **baseline *ESR1* single nucleotide variation (snv)** on ctDNA profiling (Hazard ratio [HR] 2.22, 95% confidence interval [CI] 1.08-4.54, p=0.03) **despite equal incidence** (7.5% in LDep, 8.1% in HDep).
- Patients living in HDep neighborhoods were more likely to progress on CDK4/6i if they had an *ERBB2* snv on ctDNA profiling (HR 8.20, 95% CI 1.57 – 42.93, p=0.013)

Future directions

- This data is reassuring, but we will need **larger datasets** with greater numbers of patients with MBC to validate the findings
- This work suggests more **equitable use** of treatment that **does not require a molecular target**
- Next steps:
  - Assess whether patients in high and low deprivation areas are receiving similar **endocrine therapy** choices and duration – could this be driving the *ESR1* finding?
  - Assess **choice of CDK4/6i** in patients across ADI

[1] Kind AJH et al. *New England Journal of Medicine*, 2018. DOI: 10.1056/NEJMp1802313 [2]University of Wisconsin School of Medicine and Public Health. 2022 Area Deprivation Index. Downloaded from https://www.neighborhoodatlas.medicine.wisc.edu in May 2025 [3]Podany EL et al. Differences in genomic profiles, targeted treatment use, and overall survival in patients with metastatic breast cancer by Area Deprivation Index. *J Clin Oncol* 43, 1046-1046(2025).