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Report

Ls Which drugs interact with PIK3CA, and is there evidence of sensitivity to these drugs in breast cancer

I'll search for drug interactions with PIK3CA and evidence of sensitivity in breast cancer using the specialized databases.

L get\_drug\_interactions\_for\_gene\_list

Now let me search for clinical evidence specifically regarding PIK3CA and drug sensitivity in breast cancer using the CIViC database.

L get\_variant\_evidence

Let me also check for any formal assertions (higher-level clinical guidelines) regarding PIK3CA and breast cancer sensitivity.

L get\_variant\_assertions

Now I have comprehensive information. Here's a summary of drugs that interact with PIK3CA and the clinical evidence for sensitivity in breast cancer:

## Drugs Interacting with PIK3CA

Based on drug-gene interaction databases, several **FDA-approved drugs** interact with PIK3CA:

### PI3K Inhibitors (Direct PIK3CA Targeting)

Drug	Interaction Type	Approval Status
Inavolisib	Inhibitor (PI3Ka-selective)	FDA-approved
Alpelisib	Inhibitor (PI3Ka-selective)	FDA-approved
Copanlisib	Inhibitor (pan-PI3K)	FDA-approved
Idelalisib	Inhibitor	FDA-approved

## mTOR/AKT Pathway Inhibitors

Drug	Notes
Capivasertib	AKT inhibitor
Everolimus	mTOR inhibitor
Temsirolimus	mTOR inhibitor

## Other Interacting Drugs

Cetuximab, Neratinib, and Doxorubicin Liposome also show interactions, though mechanisms vary.

## Clinical Evidence for Sensitivity in Breast Cancer

There is **strong Level A evidence** (validated clinical trials) supporting PIK3CA mutation as a predictive biomarker for drug sensitivity in **HR+/HER2- breast cancer**:

### 1. Alpelisib + Fulvestrant (SOLAR-1 Trial)

- **Evidence Level:** A (Phase 3 trial) | **Rating:** 5/5
- **Key Finding:** In PIK3CA-mutated HR+/HER2- breast cancer, median PFS was **11 months** with alpelisib-fulvestrant vs. **5.7 months** with placebo-fulvestrant (HR 0.65, p<0.001)
- **Response Rate:** 26.6% vs. 12.8%
- **Sensitive Mutations:** E542K, E545X variants, H1047X variants, C420R, Q546E/R
- **Source:** [PMID: 31091374](#) | [CIViC EID:7313](#)

### 2. Capivasertib + Fulvestrant (CAPItello-291 Trial)

- **Evidence Level:** A (Phase 3 trial) | **Rating:** 3/5
- **Key Finding:** In patients with PIK3CA/AKT1/PTEN alterations, median PFS was **7.3 months** with capivasertib-fulvestrant vs. **3.1 months** with placebo-fulvestrant (HR 0.50)
- **Source:** [PMID: 37256976](#) | [CIViC EID:12020](#)

### 3. Inavolisib + Palbociclib + Fulvestrant (INAVO120 Trial)

- **Evidence Level:** A (Phase 3 trial) | **Rating:** 3/5

- **Key Finding:** In endocrine-resistant PIK3CA-mutated HR+/HER2- breast cancer, median PFS was **15.0 months** with inavolisib triplet vs. **7.3 months** with control (HR 0.43, p<0.0001)
- **Response Rate:** 58% vs. 25%
- **Sensitive Mutations:** H1047X variants, E545X variants, and other hotspot mutations
- **Source:** [PMID: 40845250](#) | [CIViC EID:12533](#)

## Summary

**Yes, there is robust clinical evidence** that PIK3CA mutations in HR+/HER2- breast cancer predict sensitivity to PI3K pathway inhibitors, particularly:

- **Alpelisib** (FDA-approved for PIK3CA-mutated breast cancer)
- **Inavolisib** (FDA-approved for PIK3CA-mutated breast cancer)
- **Capivasertib** (AKT inhibitor, approved for PIK3CA/AKT1/PTEN-altered breast cancer)

The most commonly tested hotspot mutations include **H1047R/L/Y, E545K/A/G/D, E542K, and C420R**. These mutations consistently show improved progression-free survival when treated with targeted PI3K pathway inhibitors in combination with endocrine therapy.

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