The INAVO120 phase 3 trial has opened a new chapter in the first-line management of hormone receptor–positive (HR+), HER2-negative metastatic breast cancer (mBC) harboring a PIK3CA mutation. In this double-blind, randomized study, patients who experienced disease recurrence during or within 12 months after adjuvant endocrine therapy were treated with **inavolisib plus palbociclib and fulvestrant**, or **placebo plus palbociclib and fulvestrant**.

With a median follow-up of over 34 months, **inavolisib-based therapy demonstrated a clinically meaningful and statistically significant improvement in overall survival**—34.0 months versus 27.0 months with placebo (HR = 0.67; 95% CI, 0.48–0.94; P = 0.02). The updated **progression-free survival (PFS) benefit remained robust** (HR = 0.42; 95% CI, 0.32–0.55), and the **objective response rate more than doubled** (62.7% vs. 28.0%; P < 0.001).

The safety profile was consistent with the known class effects of PI3K inhibitors, with higher incidences of **hyperglycemia, stomatitis, gastrointestinal, and ocular adverse events**, though treatment discontinuation due to AEs remained low (6.8%).

These findings reinforce **inavolisib as a next-generation, highly selective PI3Kα inhibitor** that delivers not only durable disease control but also a significant survival advantage in the first-line setting for PIK3CA-mutated HR+ mBC. As a result, **the integration of targeted therapy at the genomic level marks a transformative step forward**—reshaping the treatment landscape toward more personalized, mechanism-driven strategies for endocrine-resistant disease.