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Ipatasertib (IPAT) + paclitaxel (PAC) for PIK3CA/AKT1/PTEN-altered hormone receptor-positive (HR+) HER2-negative advanced breast cancer (aBC): Primary results from Cohort B of the IPATunity130 randomised phase III trial

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Background

PI3K/AKT pathway alterations occur in ⊠50% of HR+ breast cancers. In a phase II trial in triple-negative aBC, adding IPAT to PAC improved progression-free survival (PFS), especially in patients (pts) with *PIK3CA/AKT1/PTEN*-altered tumours [Kim 2017].

Methods

IPATunity130 Cohort B enrolled pts with HR+ HER2– *PIK3CA/AKT1/PTEN*-altered measurable aBC suitable for chemotherapy (CT). Pts with prior CT for aBC or relapse <1 y since (neo)adjuvant CT were ineligible. Pts were randomised 2:1 to IPAT (400 mg d1–21) + PAC (80 mg/m^2 d1, 8 & 15) on a 28 d cycle or placebo (PBO) + PAC until progression or unacceptable toxicity, stratified by (neo)adjuvant CT, prior PI3K/mTOR inhibitor and region. The primary endpoint was investigator-assessed PFS.

Results

146 pts were randomised to IPAT + PAC and 76 to PBO + PAC. Prior therapy was balanced between arms, with (neo)adjuvant CT in 55%, endocrine therapy for aBC in 46%, PI3K/mTOR inhibitor in 24% and CDK4/6 inhibitor in 26%. At data cut-off (17/1/20; median follow-up 12.9 mo) 21% of pts remained on therapy. Median investigator-assessed PFS was 9.3 mo in both arms (HR 1.00, 95% CI 0.71–1.40). Median PFS by independent review committee was 9.2 mo with IPAT + PAC vs. 8.5 mo with PBO + PAC (HR 0.79, 95% CI 0.56–1.13). In both arms, objective response rate was 47% and median response duration was 9.2 mo. Overall survival (OS) results are immature (deaths in 25%). Median PAC duration was 6.9 mo with IPAT + PAC vs. 8.8 mo with PBO + PAC; median duration of IPAT was 8.0 mo and PBO was 9.1 mo. IPAT + PAC was associated with more AEs leading to withdrawal of PAC (26% vs. 13%) or IPAT/PBO (11% vs. 4%). IPAT/PBO dose reductions were more common (34% vs. 8%) but PAC dose reductions (26% vs. 24%) and interruptions (53% vs. 51%) and IPAT/PBO interruptions (43% vs. 43%) were similar. No new safety signals were seen. The most common AEs were diarrhoea (85% vs. 37%; grade ≥3: 12% vs. 1%), alopecia (50% vs. 59%) and nausea (41% vs. 20%).

Conclusions

Adding IPAT to PAC did not improve efficacy in *PIK3CA/AKT1/PTEN*-altered HR+ aBC. The IPAT + PAC safety profile was consistent with known AEs of each agent. OS follow-up is ongoing.

Clinical trial identification

NCT03337724.

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