

Supplementary tables

Ipatasertib plus paclitaxel for *PIK3CA/AKT1/PTEN*-altered hormone receptor-positive HER2-negative advanced breast cancer: primary results from cohort B of the IPATunity130 randomized, phase 3 trial

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Journal: Breast Cancer Research and Treatment

Supplementary Table S1. Definition of *PIK3CA/AKT1/PTEN*-altered status

PIK3CA/AKT1/PTEN altered defined as the presence of one or more of the following:

AKT1 missense mutations that result in amino acid substitution at the following

Residues: E17, L52 or Q79

PIK3CA missense mutations that result in amino acid substitution at the following

Residues: R88, G106, K111, G118, N345, C420, E453, E542, E545, Q546, M1043, H1047 or G1049

PTEN alterations that meet any of the following criteria:

- Homozygous deletion (copy number of 0)
 - Dominant negative short variant (eg, C124S, G129E, R130X)
 - Loss of heterozygosity (LOH) with copy number of 1 without concomitant single-nucleotide variants
 - One deleterious short variant (including insertions and deletions; classification criteria provided below) with a concomitant loss of the non-mutant *PTEN* allele defined by LOH with copy number of 1 or LOH with copy number ≥ 1 :
 - Any protein-truncating mutations, including nonsense mutations and frameshift insertions and deletions
 - Any mutations in the consensus splice donor and acceptor sequence that disrupts the consensus, including insertions and deletions
 - Any missense or non-frameshift mutation that has been confirmed somatic as described in the COSMIC database
 - If there are two or more deleterious short variants under LOH, the patient will not be eligible for the study
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Supplementary Table S2. Summary of selected adverse events (safety population)

Adverse event, <i>n</i> (%)	Placebo + paclitaxel (<i>n</i> = 75)		Ipatasertib + paclitaxel (<i>n</i> = 145)	
	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Diarrhea	28 (37)	1 (1)	123 (85)	17 (12)
Peripheral neuropathy ^a	48 (64)	6 (8)	93 (64)	15 (10)
Neutropenia ^b	33 (44)	11 (15)	59 (41)	26 (18)
Asthenia/fatigue	30 (40)	4 (5)	53 (37)	2 (1)
Nausea	15 (20)	0	60 (41)	2 (1)
Erythropenia ^c	16 (21)	0	44 (30)	1 (1)
Rash ^d	15 (20)	0	44 (30)	5 (3)
Vomiting	5 (7)	0	42 (29)	3 (2)
Hepatotoxicity ^e	21 (28)	3 (4)	22 (15)	9 (6)
Oral mucositis ^f	9 (12)	0	27 (19)	0
Hyperglycemia ^g	9 (12)	0	23 (16)	3 (2)
Hyperlipidemia ^h	7 (9)	1 (1)	15 (10)	1 (1)
Pneumonia	3 (4)	1 (1)	5 (3)	1 (1)
Pneumonitis	0	0	6 (4)	1 (1)
Thrombocytopenia ⁱ	1 (1)	0	3 (2)	1 (1)
Erythema multiforme	0	0	1 (1)	1 (1)
Colitis ^j	0	0	2 (1)	1 (1)

^aIncludes neuropathy peripheral, peripheral sensory neuropathy, paresthesia, polyneuropathy, muscular weakness, neurotoxicity, hypoesthesia, peripheral motor neuropathy, dysesthesia, gait disturbance, hypotonia, neuritis; ^bIncludes neutropenia, neutrophil count decreased, febrile neutropenia; ^cIncludes anemia, hemoglobin decreased, hematocrit decreased; ^dIncludes rash, rash maculo-papular, erythema, dermatitis, drug eruption, folliculitis, dermatitis allergic, dermatitis bullous, rash erythematous, rash papular, rash pruritic; ^eIncludes alanine aminotransferase increased, aspartate aminotransferase

increased, blood alkaline phosphatase increased, hyperbilirubinemia, gamma-glutamyl transferase increased, blood bilirubin increased, cholestasis, hepatic function abnormal, hepatocellular injury, transaminases increased; ^fIncludes Stomatitis, mucosal inflammation, mouth ulceration; ^gIncludes hyperglycemia, blood glucose increased, diabetes mellitus, glycosylated hemoglobin increased, type 2 diabetes mellitus; ^hIncludes blood cholesterol increased, hypertriglyceridemia, hypercholesterolemia, blood triglycerides increased, hyperlipidemia; ⁱIncludes thrombocytopenia, platelet count decreased; ^jIncludes enterocolitis