

Background and Methods

Background: The phosphatidylinositol 3-kinase (PI3K) gene encoding the catalytic component p110, PIK3CA, is one of the most frequently mutated genes in breast cancer.1 PIK3CA mutational status and prevalence have been studied in various clinical trial settings but not sufficiently studied in the community setting. In the SOLAR-1 trial, PIK3CA mutations were detected in approximately 40% of hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer patients where the mutation rate in exon 20 was similar to that in exon 9 (33.7% vs 29.9%).2,3 In other HER2-positive breast cancer trials, the PIK3CA mutation rate was 21.4% in the GeparStudies, 22.5% in NeoALTTO, and 20.4% in the CHERLOB study, where mutations in exon 20 were twice as high as in exon 9 (14.5% vs 7.2%).4-6

Methods: An unselected female cohort of 1281 patients with advanced stage HR-positive, HER2-negative breast cancer seen in the community setting was included in this study, with an average age of 62.9 years. Age groups by the decade ranged from < 30 years old to > 80 years old respectively: 6, 46, 124, 274, 390, 332, 109 patients. The breast tumor tissues used in this study were formalin-fixed, paraffin-embedded (FFPE). Mutational status was determined by an U.S. Food & Drug Administration (FDA) cleared test kit, and processed in accordance with the labeling instructions.7,8 This PIK3CA kit was a real-time qualitative PCR test for the detection of 11 mutations in the PIK3CA gene (Exon 7: C420R; Exon 9: E542K, E545A, E545D [1635G>T only], E545G, E545K, Q546E, Q546R; and Exon 20: H1047L, H1047R, H1047Y) using genomic DNA (gDNA) extracted from (FFPE) breast tumor tissue.

Results: 37.5% Mutation Rate. Increases with Age



Age Group	Mutation Detected	Mutation Count	Rate
<30	NEGATIVE	5	83.3%
<30	POSITIVE	1	16.7%
30 s	NEGATIVE	38	82.6%
30 s	POSITIVE	8	17.4%
40 s	NEGATIVE	77	62.1%
40 s	POSITIVE	47	37.9%
50s	NEGATIVE	189	69.0%
50s	POSITIVE	85	31.0%
60s	NEGATIVE	229	58.7%
60s	POSITIVE	161	41.3%
70 s	NEGATIVE	202	60.8%
70 s	POSITIVE	130	39.2%
>80	NEGATIVE	60	55.0%
>80	POSITIVE	49	45.0%
Overall	POSITIVE	481	37.5%

A large study of PIK3CA mutations in the community setting identifies varying degree of mutation positivity rates across age groups in advanced HR+, HER2- breast cancer patients using an FDA RT-PCR cleared test

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Background: PIK3CA Domains and Mutation



>	80

Results: Age Group 50s or Older had mutations across all detectable hotspots

Mutation Hatenat	-20							
initiation notspot	<30	30 s	40 s	50 s	60s	70 s	>80	Grand Total
p.H1047R		1	17	35	55	63	22	193
p.E545K	1	5	12	17	42	32	8	117
p.E543K		2	12	17	28	21	9	89
p.H1047L			4	7	17	9	2	39
p.C420R			2	2	3		1	8
E542K and H1047R				2	3		3	8
p.E545G				1	4	1	1	7
p.E545A				1	4	2		7
p.E545D				1	3		1	5
p.546R				1	1		1	3
p.H1047Y					1	1		2
p.Q546R, p.C420R, and p.H1047R							1	1
E545D and H1047Y						1		1
mutations at codon p.E545				1				1
Grand Total	1	8	47	85	161	130	49	481

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F542K			(
E545K	H1047R		
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Conclusion

PIK3CA is one of the most frequently mutated genes in breast cancer. This study marks the first large cohort assessment of PIK3CA mutation status within the community setting using an FDA-cleared assay. In this study, the mutation positivity rate of 37.5% in the community setting is similar to the ~40% in clinical trial settings.

References

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