Pathologic Complete Response in Germline Mutation Carriers: A Comparison Study Between a Safety-Net and Academic Population

Ethan L. Low[1], Nicole Nyamongo[1], Aliya Lackan[1], Cynthia Gonzalez[1], Kevin Hoffman[1], Nikhita Kunta[1], Samantha Sarlin[1], Shaun Bulsara[1], Susan Hilsenbeck[1], Todd Snow[1], Cathy Sullivan[1] , Georgiann Garza[1], Ahmed Elkhanany[1], Natalie Chen[1], C. Kent Osborne[1], Mothaffar Rimawi[1], Sidrah Shah[1], Julie Nangia[1]

BACKGROUND

- Pathologic complete response (pCR) after neoadjuvant chemotherapy is defined as no residual invasive disease in the breast or axillary nodes.
- pCR is a strong prognostic marker in locally advanced breast cancer and is associated with improved event-free and overall survival, particularly in triple-negative breast cancer (TNBC) and HER2-positive disease.
- Germline pathogenic/likely pathogenic variants (P/LPV) in hereditary cancer genes (HCGs) such as BRCA1/2 and PALB2, may add additional prognostic value beyond biomarker subtype
- Racial and ethnic minorities, including Latina/Latino patients, are underrepresented in hereditary cancer research.
- We retrospectively compared pCR rates among patients stage I-III breast cancer patients with germline P/LPV in HCGs at a majority-Latina/Latino safety net clinic vs. a majority-White academic center.

METHODS

- At Smith Clinic (SC, safety-net clinic) and Baylor St. Luke's Medical Center (BSLMC, academic clinic), all NCCN guideline eligible patients with breast cancer were offered germline testing.
- We identified 118 patients with germline P/LPV in HCGs from October 1, 2009 to September 30, 2019 (SC n=71; BSLMC n=47).
- Included patients had stage I-III breast cancer, a germline P/LPV, and received neoadjuvant chemotherapy followed by lumpectomy or mastectomy.
- pCR was defined as no residual invasive cancer in breast or axillary nodes on surgical pathology
- Residual Cancer Burden (RCB) scores were calculated when sufficient pathologic data were available, and descriptive statistics were used to summarize the cohort.

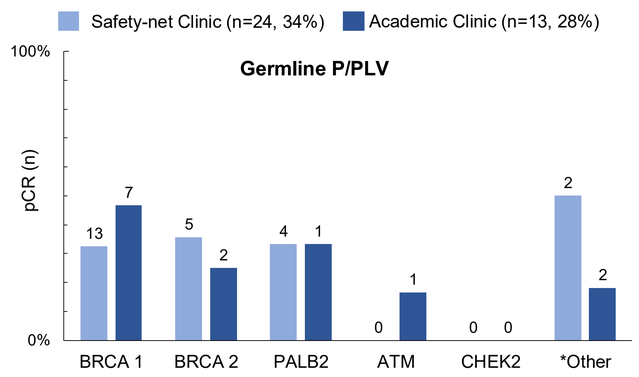
RESULTS

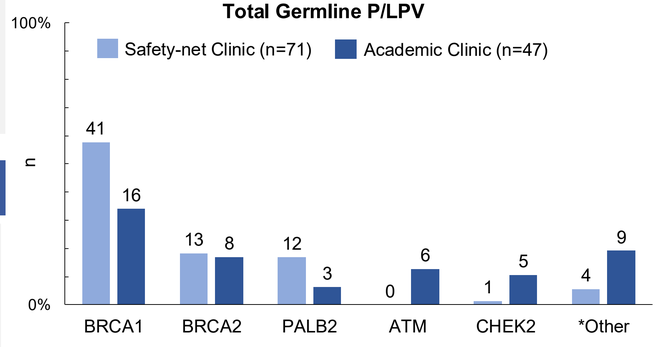
Demographics

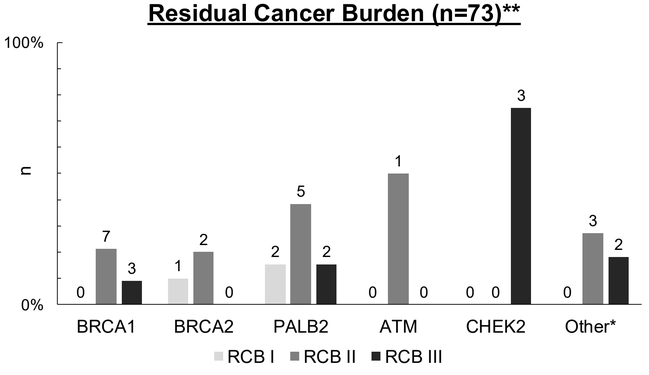
Median age (IQR): Safety-net clinic: 42 (36,54); Academic Clinic: 44 (36,52)

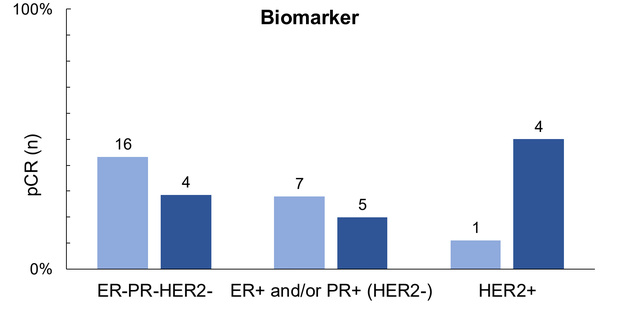
	Safety-net Clinic (n=71)		Academic Clinic (n=47)	
	n	%	n	%
Race				
Non-Hispanic White	3	4.2	20	42.6
Hispanic	50	70.4	15	31.9
Non-Hispanic Black	11	15.5	8	17.0
Asian/Pacific Islander	1	1.4	2	4.3
Other	6	8.5	2	4.3
Stage at diagnosis		0.0		0.0
I	3	4.2	7	14.9
II	30	42.3	23	48.9
III	35	49.3	17	36.2
X	3	4.2	0	0.0
Biomarker		0.0		0.0
ER-/PR-/HER2-	37	52.1	14	29.8
ER+/PR+ (HER2-)	25	35.2	25	53.2
ER+/HER2+	7	9.9	7	14.9
ER-/HER2+	2	2.8	1	2.1

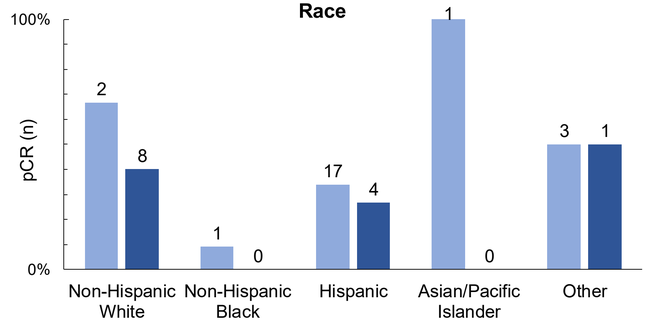
pCR rates











Corresponding Author: Ethan.low@bcm.edu
[1]Lester and Sue Smith Breast Center, Dan L Duncan Comprehensive Cancer Center, Baylor College of Medicine, Houston, TX

DISCUSSION/CONCLUSIONS

- High-risk P/LPV of HCGs (BRCA1, BRCA2, PALB2) were more common in the majority-Latina safety-net cohort than in the academic cohort.
- Despite a more stage III disease in the safety-net population, pCR rates were similar or higher, suggesting that high-risk HCG tumor biology may partially offset worse stage at presentation.
- Across both sites, carriers of high-risk HCG variants had the highest pCR rates to neoadjuvant chemotherapy.
- Across all germline carriers, HR+/HER2- tumors showed appreciable pCR rates, suggesting increased chemosensitivity in this group.
- Germline HCG status may complement standard biomarker subtype for patient counseling on response and prognosis, particularly in diverse and safety-net populations.

LIMITATIONS

- Retrospective study within a single health system with modest sample size.
- Only P/LPV included; limiting inference about absolute pCR differences vs. wild type.
- Chemotherapy regimens were heterogenous and not fully adjusted in our analysis.
- Residual Cancer Burden (RCB) could be calculated in only a small subset of patients (n=73), precluding detailed analysis.

FUTURE DIRECTIONS

- Expand the cohort to include patients without germline mutations to compare absolute pCR differences between mutations carriers vs. wild type
- Increase number of patients by continually updating our database

**Other included RAD51C, PMS2, EPCAM, RAD50 (2), MUTYH, NTHL1, PIK3CA, SMARCA, MSHS6, HOXB13, PMS2, RAD51D, TP53, APC (3), CDKN2A, BARD1*

***Residual cancer burden scores of both populations were combined and reported as an aggregate percentage. Patients with residual disease but did not have RCB reported on surgical pathology were excluded*