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Clinicomorphological features of gPALB2-associated breast cancer: real-world single-institution experience of NGS testing in Russia

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Background

Current Russian guidelines recommend testing for BRCA1/2 mutations for breast cancer patients, while ESMO guidelines include the analysis of germline *PALB2* (*gPALB2*) mutations for PARP inhibitor therapy. Here, we aimed to determine the frequency of *gPALB2* mutations in Russian breast cancer patients, its distribution between histological/molecular subtypes of the disease and treatment outcomes associated with *gPALB2* mutations.

Methods

Medical records of 3800 breast cancer patients treated and routinely tested via NGS ("Solo-test ABC plus" panel, OncoAtlas, Russia) for the mutations in the *BRCA1/2*, *PALB2* and other HRR genes at the N.N. Blokhin National Medical Research Center of Oncology (Moscow, Russia) in 2022–2024 were retrospectively analyzed.

Results

Germline *PALB2* mutations were observed in 39 (1.03%) patients, consistent with global data. The most common mutations were c.509_510del (p.Arg170IlefsTer14, 25.64%), c.1592del (p.Leu531CysfsTer30, 20.51%), and c.172_175del (p.Gln60ArgfsTer7, 10.3%). At diagnosis, disease stages were as follows: I – 10 (25.6%), II – 14 (35.9%), III – 12 (30.8%), IV – 3 (7.7%) patients. Invasive ductal carcinoma was the main histological type—33 (84.6%) pts (G2: 19, G3: 12, G1: 2). Invasive lobular carcinoma occurred in 5 (12.8%) patients (G2: 4, G3: 1). Metaplastic carcinoma G3 was identified in 1 (2.6%) patient. ER+ breast cancer predominated (31; 79.49%), and 4 (12.9%) of these cases were HER2+. Triple-negative phenotype was found in 7 (17.95%) patients. Contralateral breast cancer was diagnosed in 4 (10.26%) patients, all with ER+ HER2- metachronous breast cancer. Neoadjuvant chemotherapy (NAC, anthracyclines/taxanes) was administered to 9 (23.08%) patients. Morphological assessment demonstrated a pCR rate of 33.3% (3/9), RCB-I - 11.1% (1/9), RCB-II - 44.4% (4/9), RCB-III - 11.1 % (1/9).

Conclusions

In our study, 1% of breast cancer were found to carry germline *PALB2* mutations. Carriers had HR+ breast cancer, and HER2+ and triple-negative breast cancer, indicating that all testing should be performed regardless of subtype. Future directions should be focused on improving Russian guidelines in terms of germline *PALB2* testing for tailoring therapy.

Parameters	Number of patients	
	N	%
Age, years		
M ± m	49 ± 2.13	
Median	44 (range, 34 - 79)	
Distribution by stages		
Stage I	10	25.64
Stage II	14	35.9
Stage III	12	30.77
Stage IV	3	7.69
Histological subtype and degree of malignancy		
Invasive ductal carcinoma		
G1	2	5.13
G2	19	48.72
G3	12	30.77
Invasive lobular carcinoma		
G1	0	—
G2	4	10.26
G3	1	2.56
Metaplastic carcinoma		
G1	0	—
G2	0	—
G3	1	2.56
Molecular biological subtype		
luminal A	11	28.21
luminal B HER2-	16	41.02
luminal B HER2+	4	10.26
HER2+ non-luminal	1	2.56
triple-negative	7	17.95
Contralateral breast cancer (10.26%)		
synchronous	0	—
metachronous	4	10.26

Table 1 (right). Characteristics of patients (N = 39). *PALB2* mutations were found in all molecular subtypes.

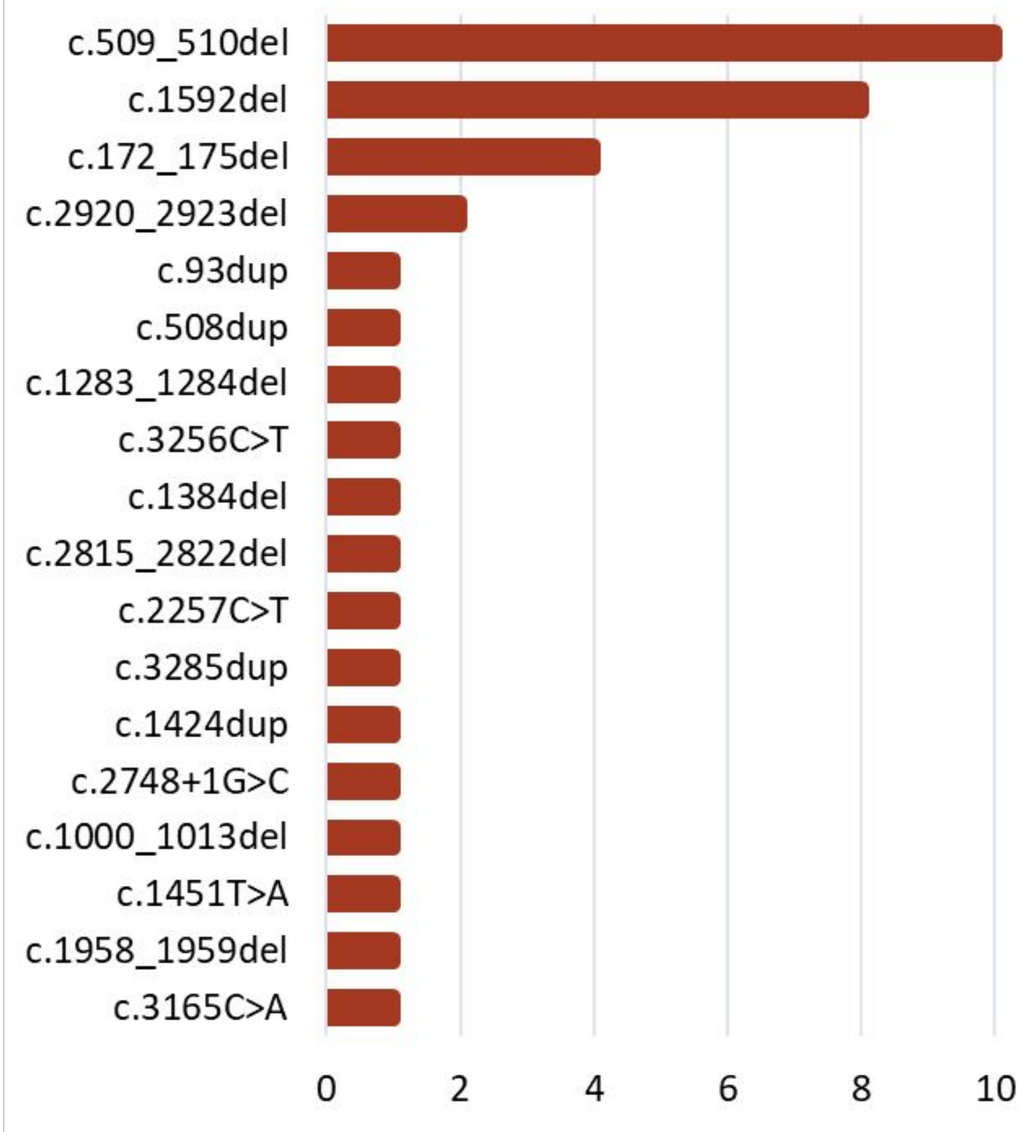

Figure 1 (top). Types of germline mutations in the *PALB2* gene in patients with breast cancer observed in our cohort.

	Molecular biological subtype		Total	%
RCB 0	Luminal B HER2+	1/3	3	33.3%
	Triple-negative	2/3		
RCB I	Luminal B HER2-	1/2	1	11.1%
RCB II	Luminal B HER2+	2/3	4	44.5%
	HER2+ non-luminal	1/1		
	Triple-negative	1/3		
RCB III	Luminal B HER2-	1/2	1	11.1%
Total			9	100%

Table 2 (top). Characteristics of patients with breast cancer who received neoadjuvant chemotherapy (NAC, anthracyclines/taxanes) (N = 9).

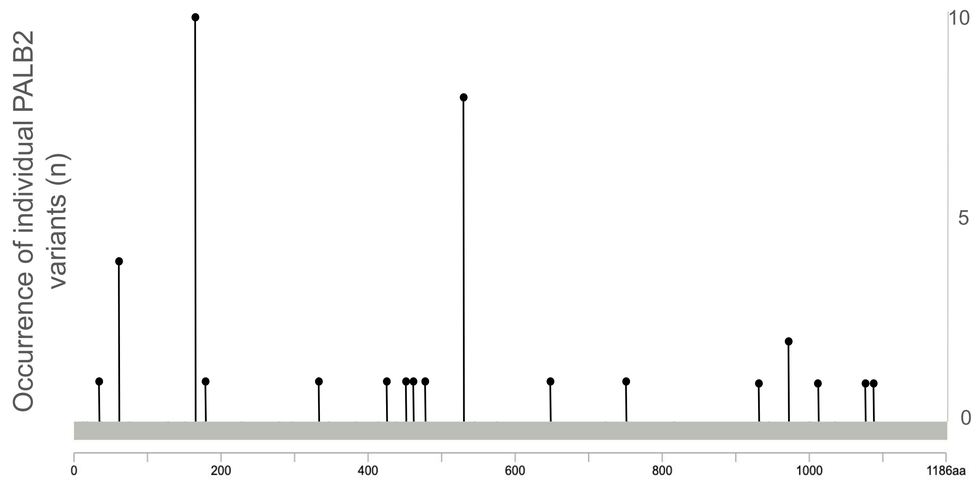

Figure 2 (top). Occurrence of individual *PALB2* variants.
Although recurrent germline *PALB2* mutations were identified, unique mutations affecting different genomic locations were observed, highlighting the need for NGS-based analysis.