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Real-world features and outcomes of young advanced breast cancer (aBC) patients (pts) from RegistEM (GEICAM/2014-03) study

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INTRODUCTION

- Breast cancer (BC) is the most incident cancer worldwide in <40 years old (y) women. A higher proportion of luminal B-like and estrogen receptor negative (ER-neg) tumors, an increased risk of early relapse, and more unfavorable long-term outcomes for young women with ER positive (ER-pos) tumors in comparison to older women, have been reported (1,2).
- In the ESME program, the median overall survival (OS) of all pts over a 9-year period was 40 mo, and in the whole cohort, older age at diagnosis of metastases had a negative prognostic impact on OS (except for TNBC) (3). Although, according to SEER data, aBC pts ≤40y have significantly a higher proportion of liver metastases, higher rates of lymph node involvement, larger tumors and more aggressive subtypes (4).
- RegistEM study provides real-world data to understand the distribution of BC subtypes in the advanced setting, being its primary objective. It is a non-interventional cohort study that includes female and male aBC pts with both recurrent BC and aBC at 1st diagnosis (*de novo* disease, which includes metastatic [MBC] and unresectable locally advanced BC [ULABC]) (ClinicalTrials.gov Identifier: NCT02819882).

OBJECTIVES OF THE CURRENT ANALYSIS

- To describe characteristics of young pts at first BC diagnosis, their types of treatment and outcomes, according to surrogate BC subtype, and compare with older pts.

MATERIAL AND METHODS

- In this analysis (**cut-off date 05/April/2023, database ongoing**), we focus on age-specific BC characterization from a real-world population-based perspective.
- **1,739 pts with aBC diagnosed between Jan-2016 and Dec-2019 were included**.
- They were split into subgroups based on **age at 1st BC diagnosis: < 40y and 40-49y**. **Comparisons with pts ≥ 50y were performed**.
- They were also classified by BC subtype (based on hormone receptor (HR) and HER2 status). The BC subtype was assessed in the most recent tumor sample (from metastasis if available or failing that from the primary tumor).
- Patients and BC characteristics, types of treatment up to 3rd-line (3L) and outcomes are described.

Age (n, %)	HR+/HER2- (n, %)	HER2+ (n, %)	TN (n, %)
< 40 y (212, 12)	(155, 73)	(37, 18)	(20, 9)
40-49 y (473, 27)	(339, 71)	(84, 18)	(50, 11)
≥ 50 y (1054, 61)	(722, 68)	(206, 20)	(126, 12)

RESULTS

TABLE 1. DEMOGRAPHIC CHARACTERISTICS BY SUBTYPE

Subtype	HR+ HER2- n=1216 (70%)			HER2+ n=327 (19%)			TN n=196 (11%)		
Age-specific	**< 40y***	**40-49y**	**≥ 50y**	**< 40y***	**40-49y**	**≥ 50y**	**< 40y***	**40-49y**	**≥ 50y**
	n=155	**n=339**	**n=722**	**n=37**	**n=84**	**n=206**	**n=20**	**n=50**	**n=126**
Age at ABC diagnosis, years									
Median (min;max)	41 (26;74)	49 (40;84)	68 (50;95)	39 (31;57)	47 (40;75)	65 (50;89)	37 (30;72)	48 (41;54)	65 (50;89)
Menopausal status at EBC diagnosis, n (%)									
Postmenopausal	7 (5)	20 (8)	340 (79)	0	4 (7)	87 (87)	1 (6)	0	78 (83)
Premenopausal	128 (95)	217 (91)	84 (20)	29 (100)	50 (93)	13 (13)	15 (94)	39 (100)	15 (16)
Menopausal status at ABC diagnosis, n (%)									
Postmenopausal	52 (34)	153 (45)	652 (90)	11 (30)	27 (32)	181 (88)	4 (20)	10 (20)	110 (87)
Premenopausal	99 (64)	182 (54)	47 (7)	25 (68)	55 (66)	16 (8)	16 (80)	34 (68)	10 (8)
TNM stage at first diagnosis, n (%)									
I	20 (13)	32 (9)	56 (8)	4 (11)	8 (10)	9 (4)	2 (10)	5 (10)	16 (12)
II	67 (43)	117 (35)	207 (29)	18 (48)	26 (31)	48 (23)	7 (35)	22 (44)	38 (30)
III	33 (21)	71 (21)	153 (21)	6 (16)	18 (21)	40 (20)	6 (30)	11 (22)	35 (28)
IV (*de novo*)	20 (13)	101 (30)	282 (39)	8 (22)	30 (36)	103 (50)	3 (15)	11 (22)	31 (25)
UK	15 (10)	18 (5)	24 (3)	1 (3)	2 (2)	6 (3)	2 (10)	1 (2)	6 (5)
Histological grade (G), n (%)									
G 1	9 (6)	31 (9)	76 (11)	0	7 (8)	6 (3)	0	2 (4)	5 (3)
G 2	74 (48)	155 (46)	355 (49)	11 (30)	34 (40)	81 (39)	3 (15)	11 (22)	30 (24)
G 3	40 (26)	78 (23)	143 (20)	18 (49)	33 (39)	84 (41)	14 (70)	29 (58)	76 (60)
Time to distant recurrence, years (EBC patients), n (%)									
≤ 1	3 (2)	7 (3)	23 (5)	0	5 (9)	9 (9)	0	2 (5)	12 (13)
> 1 to ≤ 3	22 (16)	29 (12)	72 (16)	7 (24)	16 (30)	27 (26)	10 (59)	22 (56)	42 (44)
> 3 to ≤ 5	33 (24)	67 (28)	103 (23)	9 (31)	15 (28)	28 (27)	1 (6)	11 (28)	24 (25)
> 5 to ≤ 9	29 (21)	47 (20)	107 (24)	5 (17)	8 (15)	20 (19)	1 (6)	2 (5)	8 (8)
> 9	48 (36)	88 (37)	127 (29)	8 (28)	10 (19)	16 (16)	4 (24)	2 (5)	8 (8)
Most frequent / relevant metastatic locations, n (%)**									
Bone	106 (68)	234 (69)	505 (70)	17 (46)	50 (60)	100 (49)	4 (20)	22 (44)	38 (30)
Lymph nodes	59 (38)	148 (44)	309 (43)	15 (41)	43 (51)	113 (55)	11 (55)	31 (62)	61 (48)
Liver	46 (30)	95 (28)	148 (21)	15 (41)	35 (42)	69 (34)	4 (20)	9 (18)	33 (26)
Brain	5 (3)	11 (3)	15 (2)	4 (11)	5 (6)	16 (8)	2 (10)	4 (8)	16 (13)
Nº of metastatic locations*, n (%)**									
≤ 2	97 (63)	200 (59)	406 (56)	25 (68)	44 (52)	95 (46)	14 (70)	34 (68)	69 (55)
≥ 3	58 (37)	139 (41)	314 (44)	12 (32)	40 (48)	111 (54)	6 (30)	16 (32)	57 (45)
Family history of BC and/or ovarian cancer, n (%)									
Yes	56 (36)	106 (31)	188 (26)	15 (41)	32 (38)	55 (27)	6 (30)	17 (34)	50 (40)
Pts. with any genetic testing for hereditary risk, n (%)									
Yes	77 (51)	106 (33)	142 (21)	17 (47)	21 (26)	42 (21)	13 (68)	20 (43)	45 (38)
Pts. with specific genetic tests mutated**, n (%)**									
BRCA1/2	14 (27)	7 (17)	5 (17)	0	0	2 (33)	6 (54)	3 (27)	1 (6)
PALB2	1 (9)	0	0	0	0	0	0	0	0
CHEK2	1 (12)	1 (10)	0	0	1 (50)	0	0	0	0

*23 pts were < 30y (14 in luminal-like group, 6 in HER2+, and 1 in TN). 12 male pts were included, only 1 was < 50y, the rest of them were ≥ 50y. **Visceral involvement was the most frequent in all age groups and BC subtypes, highlighting statistical differences (p=0.022) between < 50y (54%) vs. ≥ 50y (71%) pts, only in TN subtype. Brain disease was more likely present at aBC diagnosis in TN (11%) and HER2+ (8%) than in luminal-like HER2-neg (3%). ***The presence of > 2 metastatic locations was statistically different in HER2+ pts between the three subgroups ≥ 50y (54%) vs.< 40y (32%) vs. 40-49y (48%) (p=0,0498). ****Percentages obtained over the total pts with the specific genetic test performed.

FIGURE 1. MOST FREQUENT TREATMENTS IN 1– 3 LINES

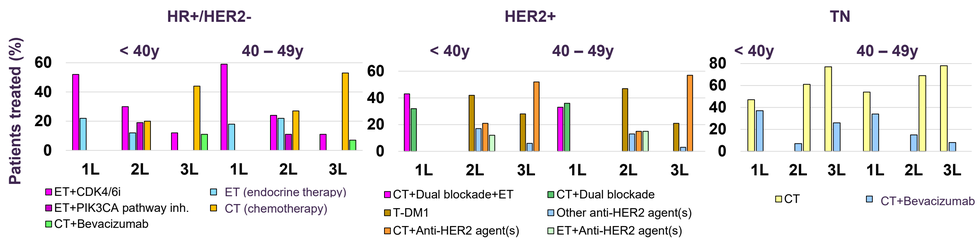
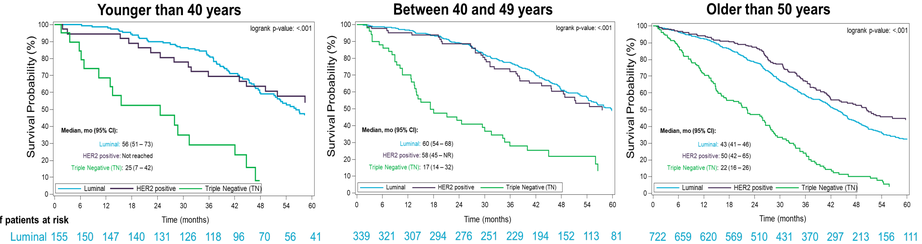


TABLE 2. TIME-RELATED OUTCOMES BY LINE FROM aBC DIAGNOSIS

	HR+/HER2-						HER2+						TN					
	< 40y			40-49y			< 40y			40-49y			< 40y			40-49y		
Line	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
n	155	107	90	339	225	169	37	24	18	84	57	40	20	15	8	50	32	23
Pts. on next L, %	69	84	77	67	75	72	65	75	61	68	70	68	79	53	75	68	72	48
Pts. on current L, %	25	10	10	28	15	10	24	17	17	24	12	15	10	7	0	15	0	4
Deaths, %	5	5	12	4	9	17	11	8	22	6	16	15	10	40	25	15	28	48
Treatment duration, mo	19	8	5	22	7	5	21	6	5	17	6	6	3	2	2	5	3	3
PFS median & 95% CI, mo	21 17,24	8 6,9	5 4,6	24 21,27	8 6,9	6 5,7	25 10,43	8 5,9	5 2,6	19 14,28	8 4,11	7 4,9	4 3,7	2 1,6	2 1,3	8 5,10	3 2,4	3 2,5

Data from ≥ 50y pts are similar to data from 40-49y pts at different lines and for all subtypes in terms of treatment duration and PFS.

FIGURE 2. SURVIVAL FROM aBC DIAGNOSIS



CONCLUSIONS

- **There are no relevant discrepancies between younger and older pts' groups, but statistical differences were identified in visceral involvement in TN and >2 metastatic locations in HER2+, against older subgroup.**
- **Young pts have the highest proportion of BRCA1/2 mutations.**
- **TNBC pts experienced the shortest median time to recurrence and the highest mortality rate regardless of age.**

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