Abstract 1030: The Contribution of Clinical Subtype to Survival Differences among Patients with De Novo and Recurrent Metastatic Breast Cancer

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Background

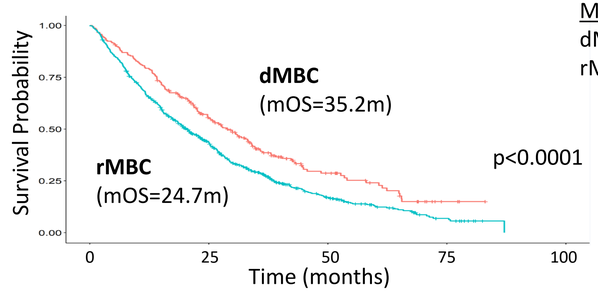
- Superior median overall survival (mOS) has been reported in patients with de novo metastatic breast cancer (dMBC) compared to recurrent (rMBC)
- Examination of survival stratified by potentially confounding variables such as clinical subtype in the modern treatment era has not been performed

Methods

- Clinicopathological data from patients diagnosed with MBC from 2011 to 2017 was obtained from the prospective University of North Carolina MBC Clinical Database
- Stratification by clinical subtype of primary tumor; pathologic staging used if available
- Exclusion criteria: >1 primary, unknown subtype, date of diagnosis or survival status
- Statistics: chi-square test for comparisons; Cox proportional hazards model for OS

Results

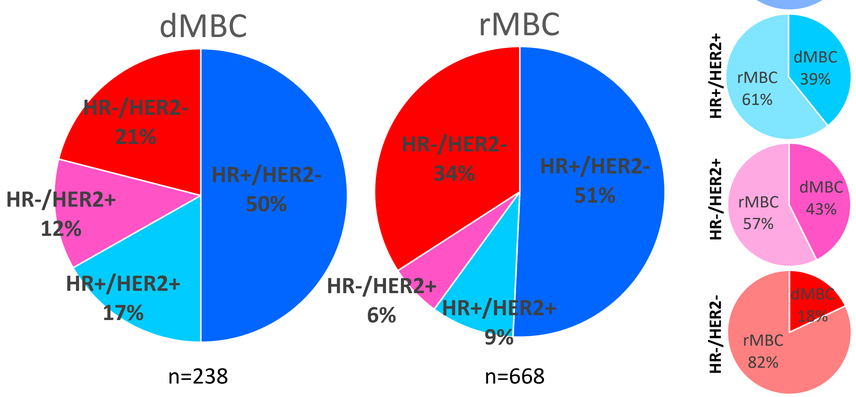
- 238 patients with dMBC and 668 patients with rMBC



Median Follow Up
dMBC: 42.3m
rMBC: 40.5m

	N	Event	Censored	Median (95% CI)
dMBC	238	157 (66%)	81 (34%)	35.2 (30.1,41.2)
rMBC	668	525 (79%)	143 (21%)	24.7 (22.2,27.9)

Clinical Subtype:



dMBC is associated with an improvement in mOS of 8.9 to 23.8 months over rMBC depending on the clinical subtype. Clinicopathological features (ie excess HER2+) and metastatic patterns partially but do not fully explain this disparity. Further investigation into biologic differences between dMBC and rMBC may clarify and help optimize treatment in both settings.

Clinicopathological Features:

Variable	dMBC (n=238)	rMBC (n=668)	p-value
Age Initial Dx			<0.01*
<35	12 (5.0%)	53 (7.9%)	
35-69	196 (82.4%)	573 (85.8%)	
70+	30 (12.6%)	42 (6.3%)	
Age Metastatic Dx			0.80
<35	12 (5.0%)	30 (4.5%)	
35-69	195 (81.9%)	560 (83.8%)	
70+	31 (13.0%)	78 (11.7%)	
Race			0.12
Caucasian	149 (62.6%)	456 (68.3%)	
African American	69 (29.0%)	148 (22.2%)	
Other	15 (6.3%)	39 (5.8%)	
Unknown	5 (2.1%)	25 (3.7%)	
Clinical Subtype			<0.01*
HR+/HER2-	119 (50.0%)	339 (50.7%)	
HR+/HER2+	40 (16.8%)	62 (9.3%)	
HR-/HER2+	29 (12.2%)	39 (5.8%)	
HR-/HER2-	50 (21.0%)	228 (34.1%)	
T Stage			<0.01*
T0/T1/T2	104 (43.7%)	476 (71.3%)	
T3/T4	112 (47.0%)	155 (23.2%)	
Tx/Unknown	22 (9.2%)	37 (5.5%)	
N Stage			<0.01*
Node negative	35 (14.7%)	230 (34.4%)	
Node positive	181 (76.1%)	408 (61.1%)	
Nx/Unknown	22 (9.2%)	30 (4.5%)	
Grade			0.03*
1	9 (3.8%)	26 (3.9%)	
2	86 (36.1%)	174 (26.0%)	
3	106 (44.5%)	343 (51.3%)	Not statistically different within each subtype
Unknown	37 (15.5%)	125 (18.7%)	

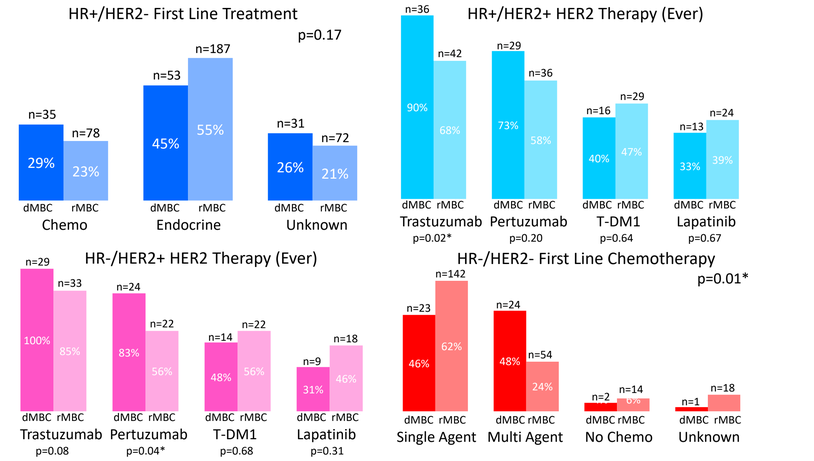
No difference in sex, body mass index, family history of breast or ovarian cancer in a first degree relative or year of metastatic diagnosis

Patterns of Metastasis:

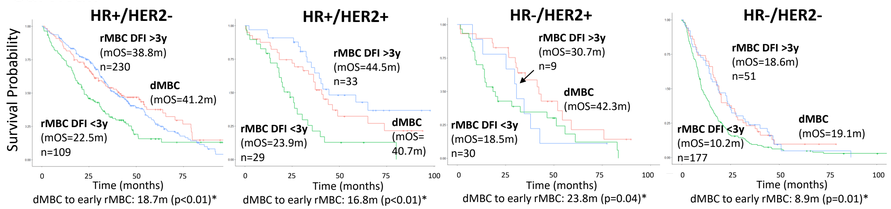
	HR+/HER2-			HR+/HER2+			HR-/HER2+			HR-/HER2-		
	dMBC n=119	rMBC n=339	p-value	dMBC n=40	rMBC n=62	p-value	dMBC n=29	rMBC n=39	p-value	dMBC n=50	rMBC n=228	p-value
Sites Dx												
Bone	89	229	0.17	31	39	0.18	16	13	0.12	22	72	0.13
Brain	9	23	0.94	2	6	0.63	3	8	0.43	3	42	0.05
Liver	27	86	0.65	20	27	0.66	12	7	0.06	19	43	0.01*
Lung	36	114	0.57	11	24	0.34	9	20	0.16	26	126	0.79t
Type			0.56			0.75			0.26			0.49
Bone	47	126		11	13		7	4		8	25	
Visceral	66	186		26	44		20	30		36	165	
Non-Vis	6	27		3	5		2	5		6	38	
# of Sites			0.42			0.75			0.15			0.37
1	56	176		14	25		8	19		20	95	
2	36	82		13	16		12	14		13	76	
3+	27	81		13	21		9	6		17	57	

Treatment:

- 29-34% of patients with dMBC underwent surgical resection within each subtype
- In HR+ subtypes, 84-90% of patients with rMBC received endocrine therapy and 78-81% received chemotherapy for localized disease
- >90% of patients with HER2+ rMBC received HER2-directed therapy for localized disease
- 95% of patients with HR-/HER2+ rMBC and 98% of patients with HR-/HER2- rMBC received chemotherapy for localized disease



Survival:



- In a multivariate analysis
  - Improved survival was associated with **dMBC** (HR 0.60, p<0.01)
  - Worse survival was associated with: **age >70 at initial diagnosis** (HR 2.26, p<0.01), **HR-/HER2- subtype** (HR 2.15, p<0.01), **grade 3** (HR 2.05, p<0.01), **2 or 3+ metastatic sites at diagnosis** (HR 1.63, 1.82, p<0.01), **metastatic diagnosis in 2017** (HR 1.55, p<0.01), **African American race** (HR 1.54, p<0.01), **T stage 3/4** (HR 1.26, p=0.01)

- **Future Directions for Research:**
  - Explore differences in response to specific treatments in dMBC and rMBC relative to prior therapy exposure and time since most recent drug in therapeutic class
  - Assess outcomes for patients with subtype switching in the metastatic setting
  - Assess for intrinsic biologic differences between dMBC, early rMBC and late rMBC

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