PS4-09-06: Retrospective evaluation of neutropenia and Duffy-Null Associated Neutrophil Counts in triple negative breast cancer patients receiving chemotherapy

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Introduction

- Duffy-Null Associated Neutrophil Count (DANC) is a non-pathologic state characterized by a low absolute neutrophil count (ANC) without increased risk of infections.
- Duffy-null phenotype is seen in about 60% of people identifying as Black, as well as in people of Middle Eastern descent and Hispanic ethnicity.[1]
- Cancer patient (pts) with DANC are often excluded from clinical trials due to low ANC and may receive inappropriate dose delays or reductions of standard chemotherapy.[2]
- Testing for Duffy-null phenotype is readily available, but no standard of care exists for management of chemotherapy dosing in breast cancer (BC) patients with DANC.
- No standard of care exists for management of chemotherapy dosing in breast cancer (BC) pts with DANC.
- There is little data assessing the impact of low baseline ANC and Duffy-null phenotype on chemotherapy dose delays and dose reductions in triple-negative breast cancer (TNBC) pts. patients.
- We evaluated baseline ANC, chemotherapy dose delays and reductions, and use of Duffy antigen testing, in TNBC pts treated at our institution, an urban academic medical center.

Methods

- Pts [n=159; 77 (48%) Black, 69 (43%) Hispanic] with Stage I to III TNBC treated with (neo)adjuvant chemotherapy without immunotherapy between 2016-2021 were identified from the Montefiore Einstein Comprehensive Cancer Center (MECCC) tumor registry.
- Baseline ANC levels, for both the entire cohort and for each race/ethnicity group, were correlated with dose reduction, delay or discontinuation of chemotherapy using logistic regression models, while controlling for stage, chemotherapy regimen, baseline white blood count and ANC, as well as race and ethnicity.

Results

- Median baseline ANC was lower in Black pts than in Hispanic or Non-Hispanic white (NHW) pts (p=0.034). (Table 1)
- No racial/ethnic differences in dose delays, reductions, early treatment discontinuation, or neutropenic fever were seen. (Table 2)
- No racial/ethnic differences in disease stage, chemotherapy regimen, or timing of chemotherapy were seen.
- Low baseline ANC for each race/ethnicity group (defined as baseline ANC below the median for each race/ethnicity group) was associated with more chemotherapy dose delays for neutropenia compared to high baseline ANC (p=0.002), and with trend to greater dose reduction for neutropenia (p=0.056). (Table 3)
- Within the low ANC group, pts with dose delays had a lower baseline ANC than pts without dose delays (p<0.001), but no correlations between baseline ANC and neutropenic fever was seen (p=0.9). (Table 4)
- Black pts had higher risk of recurrence than Hispanic or NHW pts (p=0.007).
- 3 pts had been told of low ANC prior to BC diagnosis: 1 discontinued chemotherapy early due to neutropenia, and 2 experienced dose delays and dose reductions.
- No patient received formal testing for Duffy-null phenotype.

Table 1-Demographics

Characteristics	Overall (N=159)	White (N=13)	Black (N=77)	Hispanic (N=69)	p-value
Age at diagnosis	59.0 (51.0, 68.0)	59.0 (48.0, 69.0)	61.0 (53.0, 70.0)	57.0 (50.0, 65.0)	0.081
Baseline WBC	6.4 (5.0, 7.8)	6.4 (5.5, 7.5)	6.2 (4.6, 7.7)	6.6 (5.6, 8.0)	0.277
Baseline ANC	3.6 (2.6, 4.9)	3.9 (3.5, 4.8)	3.3 (2.0, 4.6)	4.1 (2.8, 5.1)	**0.034**
cT1	65 (40.9%)	5 (38.5%)	33 (42.9%)	27 (39.1%)	0.272
cT2	59 (37.1%)	6 (46.2%)	24 (31.2%)	29 (42.0%)	
cT3	25 (15.7%)	1 (7.7%)	12 (15.6%)	12 (17.4%)	
cT4	10 (6.3%)	1 (7.7%)	8 (10.4%)	1 (1.4%)	
cN0	109 (68.6%)	8 (61.5%)	48 (62.3%)	53 (76.8%)	0.323
cN1	37 (23.3%)	5 (38.5%)	19 (24.7%)	13 (18.8%)	
cN2	7 (4.4%)	0 (0.0%)	5 (6.5%)	2 (2.9%)	
cN3	6 (3.8%)	0 (0.0%)	5 (6.5%)	1 (1.4%)	
Anthracycline + Taxane	94 (59.1%)	7 (53.8%)	40 (51.9%)	47 (68.1%)	0.246
CMF	24 (15.1%)	1 (7.7%)	15 (19.5%)	8 (11.6%)	
Taxane without anthracycline	41 (25.8%)	5 (38.5%)	22 (28.6%)	14 (20.3%)	

Table 1: Demographics and Clinical Stage/Chemotherapy Regimen by Race/Ethnicity

Table 2-Correlations based on racial/ethnic differences

Characteristics	Overall (N=159)	White (N=13)	Black (N=77)	Hispanic (N=69)	p-value
Lowest WBC during planned tx	3.6 (2.5, 4.9)	3.5 (2.7, 5.0)	3.6 (2.7, 4.6)	3.6 (2.5, 4.8)	0.966
Lowest ANC during planned tx	1.7 (1.0,2.6)	1.6 (1.0,2.3)	1.6 (1.0,2.5)	1.8 (1.1,2.7)	0.581
Stopped chemo early: Y	48 (30.2%)	3 (23.1%)	25 (32.5%)	20 (29.0%)	0.838
Stopped chemo early: N	111 (69.8%)	10 (76.9%)	52 (67.5%)	49 (71.0%)	
Dose delays: Y	87 (54.7%)	7 (53.8%)	42 (54.5%)	38 (55.1%)	0.996
Dose delays: N	72 (45.3%)	6 (46.2%)	35 (45.5%)	31 (44.9%)	
Dose delay due to neutropenia: Y	43 (27.0%)	4 (30.8%)	22 (28.6%)	17 (24.6%)	0.826
Dose delay due to neutropenia: N	116 (73.0%)	9 (69.2%)	55 (71.4%)	52 (75.4%)	
Dose reduction Y	20 (12.6%)	3 (23.1%)	11 (14.3%)	6 (8.7%)	0.229
Dose reduction : N	139 (87.4%)	10 (76.9%)	66 (85.7%)	63 (91.3%)	
Extra GCSF: Y	45 (28.3%)	4 (30.8%)	23 (29.9%)	18 (26.1%)	0.831
Extra GCSF: N	114 (71.7%)	9 (69.2%)	54 (70.1%)	51 (73.9%)	
Disease recurrence: Y	42 (26.4%)	2 (15.4%)	29 (37.7%)	11 (15.9%)	**0.007**
Disease recurrence: N	117 (73.6%)	11 (84.6%)	48 (62.3%)	58 (84.1%)	

Table 2: Chemotherapy dose modifications and results based on racial/ethnic differences

Table 3-Correlations based on median baseline ANC

Characteristics	Overall (N=159)	High ANC (N=81)	Low ANC (N=78)	p-value
Stopped chemo early: Y	48 (30%)	21 (26%)	27 (35%)	0.3
Stopped chemo early: N	111 (70%)	60 (74%)	51 (65%)	
Dose delays: Y	43 (27%)	13 (16%)	30 (38%)	**0.002**
Dose delays: N	116 (73%)	68 (84%)	48 (62%)	
Dose reduction: Y	20 (13%)	6 (7.4%)	14 (18%)	**0.056**
Dose reduction: N	139 (87%)	75 (93%)	64 (82%)	
Hospitalized due to fever: Y	17 (11%)	6 (7.4%)	11 (14%)	0.2
Hospitalized due to fever: N	142 (89%)	75 (93%)	67 (86%)	
Disease recurrence: Y	42 (26%)	18 (22%)	24 (31%)	0.3
Disease recurrence: N	117 (74%)	63 (78%)	54 (69%)	

Table 3: Chemotherapy dose modifications and results based on median baseline ANC

Table 4- Association within low ANC group

Low ANC Group	N	Median ANC (Q1, Q3)	p-value
Stopped chemotherapy early: Y	27	2.10 (1.70, 3.20)	0.3
Stopped chemotherapy early: N	51	2.70 (2.00, 3.10)	
Dose delays: Y	30	1.70 (1.60, 2.90)	**<0.001**
Dose delays: N	48	2.70 (2.25, 3.35)	
Dose reductions: Y	14	1.90 (1.60, 2.90)	0.14
Dose reductions: N	64	2.70 (2.00, 3.15)	

Table 4: Chemotherapy dose modifications within Low ANC group

Conclusions

- In our diverse cohort of TNBC BC pts, Black pts had lower baseline ANC than Hispanic or NHW pts, but did not have more chemotherapy dose delays or reductions for neutropenia and did not have higher risk of neutropenic fever.
- Lower baseline ANC, regardless of race or ethnicity, was associated with greater likelihood of chemotherapy dose delays and reductions for neutropenia, but not with higher risk of neutropenic fever.
- Formal testing for Duffy-null phenotype in pts with low ANC was not utilized, even in pts who reported a history of low ANC that predated their cancer diagnosis
- Despite similar stage and chemotherapy use and dose intensity, Black pts had higher rates of recurrence of TNBC than Hispanic or NHW pts.

Implications

- Duffy antigen testing of TNBC pts with low ANC may reduce unwarranted chemotherapy dose reductions or delays.
- Prospective evaluation of the utility of Duffy antigen testing in BC pts is warranted, and testing should not be limited to Black pts.
- Guidelines for management of chemotherapy dosing in BC pts with DANC should be developed.
- Additional studies evaluating potential etiologies of outcome disparities between Black and non-Black TNBC pts are warranted.

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References

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