



Memorial Sloan Kettering
Cancer Center

Symptoms, Unmet Needs, and Quality of Life in Erdheim-Chester Disease: A Longitudinal Registry Analysis

Eli L. Diamond, MD

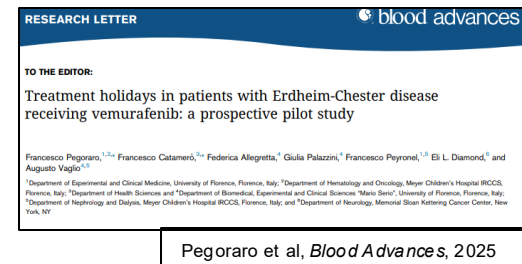
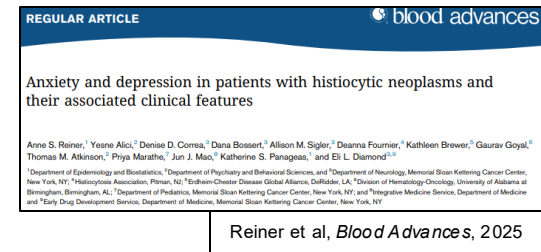
Department of Neurology / Early Drug Development Service

Memorial Sloan Kettering Cancer Center

New York, NY

Background

- Patients with ECD endure dense and widely varied symptomatology
- Physical and psychological symptoms
- HrQOL = broader construct reflecting overall satisfaction and well-being
- Unclear relationship between treatment/disease status and symptoms and HrQOL
- Unmet needs have not been examined
- Longitudinal evolution of HrQOL and its relationship to change in symptoms, unmet needs is not well understood
- Goal of present study to examine HrQOL and association with other PROs
- Provide opportunities for intervention



Methods

- Prospective registry-based cohort of patients ≥ 18 years with confirmed ECD diagnosis (MSK #17-516)
- Includes MSK and non-MSK patients
- Clinically curated database
- PROs completed at enrollment, 6 months every 12 months (assuming English fluency)
- Descriptive statistics to characterize distributions of symptoms, unmet needs, and HrQOL
- Univariable and multivariable linear regression modeling to associate PROs with
 - total FACT-G score at enrollment and 12 months
 - change in PROs over time over 12 months



PROs collected

- Pain (Brief Pain Inventory)
- Fatigue (Brief Fatigue Inventory)
- Supportive Care Needs Survey
 - Psychological
 - Health systems/information
 - Physical/daily living
 - Patient care/support
 - Sexual



ECD Symptom Scale

- Symptom inventory for ECD care and evaluation of therapies
- Rigorous focus groups designed by MSK PRO-CEL
- Generated scale with 63 disease-related symptoms in 6 categories
- Content validation in 50 patients with ECD
- 3-5 top symptoms are selected and then rated on 0-10 numerical rating scales
- Yields continuous variable of disease-related symptom severity
- Allows for different symptoms to contribute to overall symptom burden



Outcome Measure: HrQOL

- Functional Assessment of Cancer Therapy – General (FACT-G)
- 27 item questionnaire
- Measures 4 domains of HrQOL
 - Physical, social, emotional, functional well-being
- Validated in patients with cancer aged 18+
- 5-point Likert-type scale
- Recall over past 7 days
- Yields subscale scores and total score



Results – Patient Characteristics

Variable	N (%)	Mean	StDev	Min	Max
Age at ECD diagnosis (y)	159 (100)	51.2	12.3	8.1	76.9
Age at enrollment (y)	159 (100)	55.3	12.1	18.9	80
Diagnosis					
ECD	139 (87)				
Mixed ECD/LCH	15 (9)				
Mixed ECD/RDD	5 (3)				
Sex					
Female	65 (41)				
Male	94 (59)				
Length of undiagnosed ECD illness (y)	159 (100)	2.4	3.5	0	20.6
Length of diagnosed ECD illness (y)	159 (100)	6.5	6	0.08	38.8
Sites of Disease					
Bone	147 (92)				
Neurologic	108 (68)				
Brain/Parenchyma	83 (52)				
Cardiovascular	73 (46)				
Pulmonary	28 (18)				
Retroperitoneum	80 (50)				
Abdomen	28 (18)				
Skin	40 (25)				
Lymph Node	13 (8)				
Other	22 (14)				



Results – Patient Characteristics

Mutational Status	
BRAF V600E mutant	90 (57)
<i>With JAK2</i>	1 (1)
<i>With RAS</i>	1 (1)
BRAF V600E wild-type	39 (25)
<i>CSF1R</i>	1 (1)
<i>JAK2</i>	1 (1)
<i>ARAF</i>	2 (1)
<i>MAP2K1</i>	10 (6)
<i>RAS/RAF</i>	5 (4)
Non-V600E BRAF	3 (3)
Not sequenced	6 (4)
Treatment at enrollment	
None	52 (33)
Conventional	15 (9)
Targeted	92 (58)
Treatment at 12 months	
None	28 (24)
Conventional	9 (8)
Targeted	78 (49)
Other*	3 (2)
Unknown	41 (25)

- Fairly representative cohort
- 57% BRAF V600E
- Few conventional therapies
- Increasing unknowns over time for treatment status



Results – Health-related QOL

PRO assessment	Enrollment					12-months				
	N (%)	Mean Score	StDev	Min	Max	N (%)	Mean Score	StDev	Min	Max
FACT-G: physical well being	158 (99.4)	18.8	6.5	0	28	126 (79.2)	20.5	5.6	5	28
FACT-G: emotional well being	158 (99.4)	16.6	4.5	3	24	126 (79.2)	17.6	4	4	24
FACT-G: social well being	158 (99.4)	19.7	6.1	1	28	126 (79.2)	20.2	5.7	2.8	28
FACT-G: functional well being	158 (99.4)	15.7	6.7	0	28	126 (79.2)	16.8	6	0	28
FACT-G: total	158 (99.4)	70.8	19	22	105	126 (79.2)	75.2	16.8	31	104

Disease Type	Mean FACT-G Score
ECD	71-75
Advanced stage ovarian cancer	80-90
NHL	83
AML 60+ years with HSCT	80



Results – Health-related QOL, age deciles

	Age Deciles					
	18-<30 (N=7)	30-<40 (N=8)	40-<50 (N=31)	50-<60 (N=54)	60-<70 (N=43)	70+ (N=16)
FACT-G Scale	20.1	19.3	17.5	20	16.5	22.8
Physical	16.4	18	15.8	16.4	16.3	18.7
Emotional	16.3	19.5	14	16.2	14.1	19
Functional	18.4	22.2	18.6	19.8	18.9	23
Social	71.3	79	65.9	72.4	65.8	83.5
Total						

Table 2b

Quality of life values in the general population, as measured by the FACT-G subscales, including

	Range	18–29 n = 106	30–39 n = 210	40–49 n = 180	50–59 n = 166	60–69 n = 136	> 70 n = 128
FACT-G subscales[#]							
Physical well-being	0–28	25.7	25.1	25.4	24.6	24.8	23.9
Emotional well-being	0–28	20.5	20.1	19.3	19.2	19.3	18.9
Functional well-being	0–24	22.4	22.3	21.8	21.2	21.2	19.3
Social well-being	0–28	22.3	21.4	20.4	20.0	19.0	17.9
Total	0–108	90.9	89.1	87.1	84.9	84.7	80.5

[#]Higher scores indicate better quality of life.

*ANCOVA with adjustment for gender and education

Results – Symptom Burden

PRO assessment	Enrollment		12-months	
	N (%)	Mean Score	N (%)	Mean Score
BPI: severity	154 (96.9)	2.3	123 (77.4)	1.9
BPI: interference	154 (96.9)	2.4	123 (77.4)	1.9
BPI: total	154 (96.9)	2.4	124 (78)	2
Clinically-relevant pain	75 (49)		52 (42)	
BFI: severity	154 (96.9)	4.1	122 (76.7)	3.6
BFI: interference	154 (96.9)	3.5	122 (76.7)	3
BFI: total	154 (96.9)	3.7	122 (76.7)	3.2
Clinically-relevant fatigue	110 (71)		72 (59)	
Top 3 ECDSS Symptoms: Severity	154 (96.9)	6.7	122 (76.7)	5.5
Top 5 ECDSS Symptoms: Severity	154 (96.9)	6.4	122 (76.7)	5.2
Top ECDSS Symptom: Other	52 (33)		30 (34)	
Top ECDSS Symptom: Neurological	58 (37)		34 (39)	
Top ECDSS Symptom: GI	10 (6)		7 (8)	
Top ECDSS Symptom: Pain	27 (17)		11 (13)	
Top ECDSS Symptom: Vision	5 (3)		2 (2)	
Top ECDSS Symptom: Respiratory	6 (4)		3 (3)	



Results – Unmet Needs

PRO assessment	Enrollment					12-months				
	N (%)	Mean Score	StDev	Min	Max	N (%)	Mean Score	StDev	Min	Max
Unmet health care service needs	58 (38)					33 (28)				
Unmet psychological/emotional needs	90 (57)					56 (45)				
Unmet physical and daily health needs	90 (57)					63 (50)				
Unmet care and support needs	37 (23)					19 (15)				
Unmet sexual needs	37 (23)					26 (22)				
Number of Unmet needs	159 (100)	7	7.4	0	29	125 (78.6)	5	6.2	0	31
3+ Unmet needs	100 (63)					64 (51)				
5+ Unmet needs	79 (50)					49 (39)				
10+ Unmet needs	48 (30)					26 (21)				

- Abundance of unmet needs across domains
- Physical / daily health, psychological emotional most common
- Support needs same as sexual needs
- 30% with 10 or more unmet needs at enrollment
- Overall decrease over time



Results – Unmet Needs

- Higher frequency of unmet needs compared to diverse other cancer types

Disease Type	Unmet Psych/Emotional Needs	Unmet Physical/Daily Health Needs	Unmet Sexual Needs
ECD	58%	57%	25%
Head and neck cancer	43%	21%	9%
Colorectal cancer	26%	35%	0%
Hematologic cancer	30%	30%	8%

Results – Symptoms, needs, HrQOL

Associations between symptoms and HrQOL in patients with ECD at enrollment and 12 months

Enrollment Variable	Enrollment		12 months	
	Change Estimate	P-value	Change Estimate	P-value
Enrollment BPI Total	-3.42	<0.0001	-2.91	<0.0001
Any clinically relevant pain	-14.83	<0.0001	-10.86	0.0003
Enrollment BFI Total	-4.71	<0.0001	-3.43	<0.0001
Any clinically relevant fatigue	-21.25	<0.0001	-16.87	<0.0001
Top 3 ECDSS Symptoms: Severity	-5.00	<0.0001	-4.15	<0.0001
Top 5 ECDSS Symptoms: Severity	-5.02	<0.0001	-4.28	<0.0001
Top ECDSS Symptom: Neurological	-8.33	0.02	-7.30	0.04
Top ECDSS Symptom: GI	-4.06	0.54	-1.23	0.87
Top ECDSS Symptom: Pain	-7.46	0.10	-4.98	0.25
Top ECDSS Symptom: Vision	-13.68	0.12	1.78	0.82
Top ECDSS Symptom: Respiratory	-5.43	0.51	5.78	0.46
Unmet health care service needs	-12.31	<0.0001	-17.32	<0.0001
Unmet psychological/emotional needs	-19.54	<0.0001	-17.88	<0.0001
Unmet physical and daily health needs	-22.99	<0.0001	-16.63	<0.0001
Unmet care and support needs	-17.15	<0.0001	-14.94	0.0003
Unmet sexual needs	-14.76	<0.0001	-11.32	0.002
Number of Unmet needs	-1.71	<0.0001	-1.90	<0.0001
3+ Unmet needs	-20.24	<0.0001	-20.91	<0.0001
5+ Unmet needs	-21.86	<0.0001	-21.44	<0.0001
10+ Unmet needs	-22.02	<0.0001	-23.45	<0.0001

Change in PROs, HrQOL over 12 months

Univariable regression of symptoms/unmet needs and FACT-G HrQOL change

Change from Enrollment to 12 month timepoint	Change Estimate	P-value
BPI Total	-1.42	0.0002
Clinically Relevant Pain	-6.70	0.03
BFI Total	-1.69	<0.0001
Clinically Relevant Fatigue	-5.55	0.10
Top 3 ECDSS Symptoms: Severity	-1.92	<0.0001
Top 5 ECDSS Symptoms: Severity	-1.84	0.0001
Met health care service needs	5.31	0.04
Met psychological/emotional needs	5.76	0.02
Met physical and daily health needs	7.20	0.008
Met care and support needs	6.32	0.02
Met sexual needs	-0.33	0.91
Increasing Number of Unmet Needs	-0.79	<0.0001



Change in PROs, HrQOL over 12 months

Multivariable regression of symptoms/unmet needs and FACT-G HrQOL change, adjusted for age at diagnosis, length of ECD diagnosis, brain involvement

Change Variable (12mo-Enrollment)	N	Estimate ^a	P-value ^a
BPI Total	119	-1.41	0.0002
Change to Clinically Relevant Pain	126	-6.72	0.04
BFI Total	118	-1.70	<0.0001
Change to Clinically Relevant Fatigue	126	-5.49	0.11
Top 3 ECDSS Symptoms: Severity	118	-1.93	<0.0001
Top 5 ECDSS Symptoms: Severity	118	-1.85	0.0001
Sustained Unmet health care service needs	126	2.41	0.37
Sustained Unmet psychological/emotional needs	126	2.66	0.21
Sustained Unmet physical and daily health needs	126	1.22	0.56
Sustained Unmet care and support needs	126	2.47	0.51
Sustained Unmet sexual needs	126	4.14	0.21
Change to Met health care service needs	126	5.20	0.052
Change to Met psychological/emotional needs	126	5.76	0.02
Change to Met physical and daily health needs	126	7.26	0.008
Change to Met care and support needs	126	6.47	0.02
Change to Met sexual needs	126	-0.20	0.95
Increasing Number of Unmet Needs	125	-0.79	<0.0001



Results – Change Over Time

- Alleviating **clinically relevant pain** improves HrQOL
- Improving **fatigue** improves HrQOL
- Improving **symptom burden** improves HrQOL
- Meeting **any previously unmet needs** (aside from sexual needs) is associated with significant improvement in HrQOL



Conclusions / limitations

- Constellation of unmet needs, symptom burden, and diminished quality of life in ECD
- Diminished even in comparison to other cancers
- Nihilism is not appropriate mindset!
- Several opportunities for intervention to improve HrQOL
- Did not examine interventions in this cohort (dose reduction, supportive medications, integrative interventions, social support)
- Invites intervention study on one or many factors



Acknowledgements

Research Team

Priya Marathe

Katherine Panageas

Anne Reiner

Allison Sigler

Dana Bossert

Frame Family Fund

Joy Family West Foundation

Applebaum Foundation

NIH/NCI: R37CA259260 (Diamond)



HISTIOCYTOSIS  ASSOCIATION®
A Rare Community



Memorial Sloan Kettering
Cancer Center