

## Prephase rituximab/prednisone therapy and aging-related, proinflammatory cytokine milieu in older, vulnerable patients with newly diagnosed diffuse large B-cell lymphoma

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Received: March 6, 2021.

Accepted: July 12, 2021.

Pre-published: July 22, 2021.

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Supplemental Table 1. Toxicity events by stage

Characteristic	N	Stage I/II, N = 13	Stage III/IV, N = 20	p-value	q-value
Toxic events	33	8 (62%)	14 (70%)	0.7	>0.9
Severe toxic events	33	4 (31%)	8 (40%)	0.7	>0.9
G3+ nonheme toxicity / G4+ heme toxicity	33			>0.9	>0.9
At least 1 G3+ nonheme / G4+ heme toxicity		6 (46%)	10 (50%)		
No G3+ nonheme / G4+ heme toxicities		7 (54%)	10 (50%)		
G3+ nonheme toxicities	33			>0.9	>0.9
At least 1 G3+ nonheme toxicity		6 (46%)	10 (50%)		
No G3+ nonheme toxicities		7 (54%)	10 (50%)		
G3+ heme toxicities	33			<b>0.026</b>	0.2
At least 1 G3+ heme toxicity		6 (46%)	17 (85%)		
No G3+ heme toxicities		7 (54%)	3 (15%)		
G4+ heme toxicities	33			>0.9	>0.9
At least 1 G4+ heme toxicity		2 (15%)	4 (20%)		
No G4+ heme toxicities		11 (85%)	16 (80%)		

**Abbreviations:** G3, grade 3; G4, grade 4. Bold/Italic indicates significant p-value.

Supplemental Table 2. Correlations of baseline GA measures with baseline pro-inflammatory cytokine levels

GA measures	Cytokine levels	Spearman's Rho	p-value	q-value
TUG	TNF-alpha	0.65	5.92e-05	<b>0.005</b>
IADL	TNF-alpha	-0.48	8.49e-04	<b>0.024</b>
CARG score	IL-6	0.50	9.27e-04	<b>0.024</b>
% risk	TNF-alpha	0.43	1.44e-03	<b>0.024</b>
pKPS	IL-10	-0.48	1.68e-03	<b>0.024</b>
TUG	IL-2	0.54	1.78e-03	<b>0.024</b>
CARG score	TNF-alpha	0.45	1.90e-03	<b>0.024</b>
ADL	IL-10	-0.42	2.40e-03	<b>0.027</b>
pKPS	TNF-alpha	-0.46	2.68e-03	<b>0.027</b>
pKPS	IL-2	-0.58	3.36e-03	<b>0.029</b>
cKPS	IL-6	-0.45	3.91e-03	<b>0.029</b>
LDH (log level)	IL-10	0.40	4.27e-03	<b>0.029</b>
IADL	IL-10	-0.38	4.45e-03	<b>0.029</b>
LDH (log level)	TNF-alpha	0.42	4.58e-03	<b>0.029</b>
IADL	IL-2	-0.54	5.60e-03	<b>0.033</b>
cKPS	IL-2	-0.55	6.32e-03	<b>0.033</b>

## Original Article

ADL	TNF-alpha	-0.36	6.56e-03	<b>0.033</b>
% risk	IL-6	0.41	6.73e-03	<b>0.033</b>
Activity limitation	IL-6	-0.60	6.90e-03	<b>0.033</b>
IADL	IL-6	-0.42	7.68e-03	<b>0.034</b>
cKPS	TNF-alpha	-0.33	8.00e-03	<b>0.034</b>
LDH (log level)	IL-2	0.48	9.30e-03	<b>0.038</b>
TUG	IL-10	0.41	1.05e-02	<b>0.041</b>
CARG score	IL-10	0.41	1.32e-02	<b>0.049</b>

**Abbreviations:** GA, geriatric assessment; LDH, lactate dehydrogenase; cKPS, clinician-rated karnofsky performance scale; pKPS, patient-rated karnofsky performance scale; ADL, activities of daily living; IADL, instrumental activities of daily living; TUG, timed-get-up and go; CARG, cancer and aging group; IFN, interferon; IL, interleukin; TNF, tumor necrosis factor. Bold indicates significant q-value.

Supplemental Table 3. Baseline and change in GA measures by stage

GA measures	N	Stage I/II, N = 13 (median, IQR)	Stage III/IV, N = 20 (median, IQR)	p-value	q-value
Baseline LOG LDH	33	5.48 (5.26, 5.58)	5.77 (5.54, 6.02)	<b>0.010</b>	0.089
Baseline cKPS	33	90 (70, 90)	70 (60, 90)	0.11	0.2
Baseline pKPS	33	90 (80, 100)	80 (60, 90)	<b>0.037</b>	0.13
Baseline ADL	33	85 (45, 100)	42 (18, 80)	<b>0.021</b>	0.094
Baseline IADL	33	14.00 (13.00, 14.00)	12.00 (7.75, 14.00)	0.068	0.2
Baseline Activity limitation	33	56 (50, 62)	44 (41, 62)	0.6	0.6
Baseline TUG	31	9 (9, 11)	14 (11, 20)	<b>0.009</b>	0.089
Baseline CARG score	33	9.00 (7.00, 11.00)	10.50 (10.00, 13.25)	<b>0.045</b>	0.14
Baseline % risk	33	54 (54, 77)	54 (54, 89)	0.3	0.4
$\Delta$ in LOG LDH	30	0.00 (-0.20, 0.24)	0.01 (-0.25, 0.10)	0.3	0.4
$\Delta$ in cKPS	32	0 (0, 0)	10 (0, 15)	0.3	0.4
$\Delta$ in pKPS	32	0 (0, 10)	0 (-10, 10)	0.3	0.4
$\Delta$ in ADL	30	2 (-5, 6)	0 (-12, 10)	0.6	0.6
$\Delta$ in IADL	31	0.00 (-0.25, 0.00)	0.00 (-0.50, 0.50)	0.6	0.6
$\Delta$ in Activity limitation	31	0 (-12, 6)	0 (-17, 0)	0.2	0.3

## Original Article

$\Delta$ in TUG	29	-1.0 (-1.2, 1.0)	-0.7 (-3.8, 1.0)	0.6	0.6
$\Delta$ in CARG score	32	0.00 (0.00, 2.00)	-1.00 (-3.00, 0.00)	<b>0.016</b>	0.094
$\Delta$ in % risk	32	0 (0, 0)	0 (-8, 0)	0.2	0.3

**Abbreviations:** IQR, interquartile range; LDH, lactate dehydrogenase; cKPS, clinician-rated karnofsky performance scale; pKPS, patient-rated karnofsky performance scale; ADL, activities of daily living; IADL, instrumental activities of daily living; TUG, timed-get-up and go; CARG, cancer and aging group. Bold/Italic indicates significant p-value.

Supplemental Table 4. Baseline and change in cytokine levels by stage

Cytokine levels	N	Stage I/II, N = 13 (median, IQR)	Stage III/IV, N = 20 (median, IQR)	p-value	q-value
Baseline LOG IFN-gamma	32	1.81 (1.35, 2.31)	2.93 (2.14, 3.82)	<b>0.010</b>	0.2
Baseline LOG IL-10	32	-0.29 (-0.81, 1.41)	0.09 (-0.32, 2.65)	0.12	0.5
Baseline LOG IL-12	32	-1.81 (-2.39, -1.32)	-1.86 (-2.50, -1.36)	0.8	0.8
Baseline LOG IL-13	32	-1.11 (-4.41, -0.88)	-0.81 (-1.65, -0.37)	0.2	0.5
Baseline LOG IL-1-beta	32	-5.30 (-5.30, -5.30)	-5.30 (-5.30, -5.30)	0.6	0.7
Baseline LOG IL-2	31	-5.30 (-5.30, -1.95)	-2.43 (-4.51, -1.03)	0.057	0.4
Baseline LOG IL-4	32	-3.35 (-3.58, -3.04)	-3.15 (-4.17, -2.59)	0.8	0.8
Baseline LOG IL-6	32	0.73 (-0.32, 1.18)	1.07 (0.59, 1.81)	0.2	0.5
Baseline LOG IL-8	30	2.44 (2.20, 2.94)	2.81 (2.50, 3.05)	0.5	0.7
Baseline LOG TNF-alpha	32	0.87 (0.56, 1.69)	1.77 (1.53, 2.29)	<b>0.020</b>	0.2
$\Delta$ in LOG IFN-gamma	30	0.51 (-0.55, 1.30)	-0.88 (-1.72, 0.50)	0.2	0.5
$\Delta$ in LOG IL-10	30	-0.33 (-1.00, 0.10)	-0.72 (-2.19, 0.20)	0.6	0.7
$\Delta$ in LOG IL-12	30	-0.12 (-0.47, 0.11)	-0.03 (-0.30, 0.36)	0.4	0.7
$\Delta$ in LOG IL-13	30	0.62 (-1.09, 2.74)	-0.06 (-1.12, 0.49)	0.5	0.7
$\Delta$ in LOG IL-1-beta	30	0.03 (0.00, 2.74)	0.00 (0.00, 0.00)	0.11	0.5

## Original Article

$\Delta$ in LOG IL-2	29	0.67 (-0.08, 1.92)	0.00 (-0.82, 1.28)	0.2	0.5
$\Delta$ in LOG IL-4	30	-0.19 (-0.52, 0.19)	-0.34 (-0.99, 0.10)	0.9	0.9
$\Delta$ in LOG IL-6	30	-0.22 (-1.29, 0.29)	-1.02 (-1.77, -0.35)	0.2	0.5
$\Delta$ in LOG IL-8	28	0.27 (-1.75, 1.69)	-0.38 (-0.75, 0.24)	0.5	0.7
$\Delta$ in LOG TNF-alpha	30	-1.18 (-1.55, 0.02)	-0.35 (-1.01, -0.03)	0.6	0.7

**Abbreviations:** IQR, interquartile range; IFN, interferon; IL, interleukin; TNF, tumor necrosis factor. Bold/Italic indicates significant p-value.



Supplemental Table 5. Association of baseline and change in cytokine levels with toxicity events

Characteristic (IQR)	N	At least 1 toxic event, N = 22	No toxic events, N = 11	p-value	q-value
Baseline LOG IFN-GAMMA	32	2.42 (1.81, 3.39)	2.28 (1.43, 2.99)	0.3	0.7
Baseline LOG IL10	32	1.50 (-0.38, 2.29)	-0.29 (-0.87, 0.00)	<b>0.012</b>	0.12
Baseline LOG IL12	32	-1.58 (-2.35, -1.33)	-2.28 (-2.51, -1.74)	0.059	0.3
Baseline LOG IL13	32	-0.72 (-1.11, -0.34)	-3.47 (-5.30, -0.95)	<b>0.006</b>	0.12
Baseline LOG IL1-BETA	32	-5.30 (-5.30, -5.30)	-5.30 (-5.30, -5.30)	0.4	0.8
Baseline LOG IL2	31	-2.64 (-5.30, -1.52)	-4.07 (-5.30, -2.25)	0.2	0.7
Baseline LOG IL4	32	-3.32 (-3.54, -2.41)	-3.54 (-4.40, -3.08)	0.068	0.3
Baseline LOG IL6	32	1.17 (0.37, 1.81)	0.66 (-0.31, 1.02)	0.09	0.3
Baseline LOG IL8	30	2.80 (2.29, 2.95)	2.75 (2.44, 3.25)	0.6	0.8
Baseline LOG TNF-ALPHA	32	1.80 (0.87, 2.31)	1.45 (0.82, 1.65)	0.067	0.3
Δ in LOG IFN-GAMMA	30	-15 (-75, 77)	4 (-35, 32)	0.6	0.8
Δ in LOG IL10	30	-51 (-96, -1)	-39 (-792, 38)	0.9	0.9
Δ in LOG IL12	30	1 (-37, 17)	-10 (-15, 9)	0.5	0.8
Δ in LOG IL13	30	-24 (-214, 78)	0 (-235, 53)	0.7	0.8
Δ in LOG IL1-BETA	30	0 (0, 37)	0 (0, 1)	0.5	0.8
Δ in LOG IL2	29	20 (-32, 40)	0 (-9, 35)	0.3	0.7
Δ in LOG IL4	30	-9 (-27, -0)	-7 (-32, 9)	0.7	0.8
Δ in LOG IL6	30	-46 (-118, -12)	-55 (-173, 23)	0.6	0.8
Δ in LOG IL8	28	-13 (-30, 24)	-4 (-32, 47)	0.5	0.8
Δ in LOG TNF-ALPHA	30	-40 (-95, 18)	-34 (-56, -17)	0.8	0.8

**Abbreviations:** IQR, interquartile range; IFN, interferon; IL, interleukin; TNF, tumor necrosis factor.

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### Figure Legend.

**Supplemental Figure 1:** Changes in individual pro-inflammatory cytokine levels (log-transformed) pre- and post-prephase therapy with q-value indicated. **Abbreviations:** IL, interleukin; TNF, tumor necrosis factor.

Supplemental Figure 1. Changes in cytokine levels from pre- to post-prephase therapy

