Association of Body Mass Index (BMI) and Outcomes in Relapsed and Refractory Aggressive Lymphomas Treated with Salvage Chemotherapy - Analysis of the Canadian Cancer Trials Group (CCTG) LY. 12 Trial

Aera Y Jung, Bingshu E Chen, Annette E Hay, Lois E Shepherd, Marina Djurfeldt, Ralph Meyer, Michael Crump, and Tara Baetz

Background:

Obesity has been associated with an increased incidence of different malignancies, including Hodgkin and Non-Hodgkin lymphomas. Paradoxically, some studies have shown an association between higher BMI and favorable clinical outcomes in lymphoma patients. These studies have examined the association of BMI and outcomes in newly diagnosed Hodgkin and non-Hodgkin lymphomas treated with conventional first line chemotherapy. The aim of this analysis is to examine the prognostic significance of BMI in relapsed or refractory (R/R) aggressive lymphomas treated with salvage chemotherapy prior to autologous stem cell transplant (ASCT).

Methods:

We performed a retrospective analysis of the CCTG LY.12 trial, a multicenter randomized phase III trial of 619 patients diagnosed with R/R aggressive non-Hodgkin lymphoma assigned to treatment with either gemcitabine, dexamethasone, and cisplatin (GDP) or to dexamethasone, cytarabine, and cisplatin (DHAP) prior to ASCT. Patients with B-cell lymphoma also received rituximab. Trial results demonstrated that GDP was non-inferior to DHAP in terms of response rate with a similar transplantation rate, event-free, and overall survival, less toxicity and superior quality of life. We divided all patients with recorded BMI data (614 patients) into BMI groups as defined by the World Health Organization. Only 18 patients were underweight (BMI <18.5) and they were combined with normal weight patients (BMI 18.5-25). The three groups were underweight to normal (BMI <25 kg/m^2), overweight (BMI 25-30 kg/m^2), and obese (BMI >30 kg/m^2). BMI was also analyzed as a continuous variable. Response rate, transplantation rate and survival were assessed based on the BMI of the patients.

Results:

Baseline characteristics of the 3 groups were compared (Table 1). There were 226 patients who were underweight to normal weight (N), 221 who were overweight (OW) and 167 who were obese (OB). Higher BMI was associated with higher mean and median body surface area (BSA). The N group had a higher proportion of patients with stage IV disease and a higher International Prognostic Index score at randomization but this difference was not statistically significant.

There was no association between BMI and overall response rate to salvage therapy for N vs OW vs OB (RR 43.4% vs 46.2% vs 45.5%). However, overall survival at 48 months was significantly improved in the OB vs N patients (45% vs 35%, p=0.04) (Figure 1). Elevated BMI was associated with higher transplantation rates, though this was not significant (45.1% vs 51.1% vs 55.7%; p= 0.11). There was no association between higher BMI and increased progression free survival at 48 months in the OB vs N patients (28% vs 24%, p= 0.07). BMI as a continuous variable in a multivariable model was a positive predicator of survival with each one unit increase in BMI resulting in a decreased hazard ratio of death by 2% (p =0.021). There was no difference in treatment related mortality (during salvage therapy or 1 year post ASCT) between the groups.

Conclusion:

In the R/R aggressive LY.12 lymphoma population a higher BMI is independently related to improved overall survival using both BMI as a discrete and a continuous variable. Alterable factors associated with BMI could impact on outcomes in this disease but requires confirmation in larger datasets.

TABLE 1	BMI <25	25-30	30+	Total
Age				
n	226	221	167	614
Median	53.4	56.1	55.4	54.85
Range	18.7 - 74.3	23.3 - 70.0	22.6 - 71.2	18.7 - 74.3
Weight (kg)				
n	226	221	167	614
Median	63.3	79.5	95.0	77.3
Range	40.0 - 90.0	55.9 - 110.0	67.5 - 181.2	40.0 - 181.2
Body surface area				
n	226	219	162	607
Median	1.72	1.91	2.065	1.89
Range	1.33 - 2.20	1.40 - 2.45	1.61 - 2.68	1.33 - 2.68
Disease stage on study Chisq p=(0.056)				
I	20 (8.8)	20 (9.0)	11 (6.6)	51 (8.3)
II	55 (24.3)	47 (21.3)	39 (23.4)	141 (23.0)
III	39 (17.3)	62 (28.1)	51 (30.5)	152 (24.8)
IV	112 (49.6)	92 (41.6)	66 (39.5)	270 (44.0)
Histology Chisq p=(0.941)				
Diffuse large B-cell lymphoma	158 (69.9%)	150 (67.9%)	118 (70.7%)	426 (69.4%)
Other B or T cell lymphoma	68 (30.1%)	71 (32.1%)	48 (28.7%)	187 (30.5%)
Missing	0 (0%)	0 (0%)	1 (0.6%)	1 (0.2%)
rIPI score baseline Chisq p=(0.814)				
0, 1	82 (36.3)	80 (36.2)	66 (39.5)	228 (37.1)
2	62 (27.4)	69 (31.2)	46 (27.5)	177 (28.8)
>=3	82 (36.3)	72 (32.6)	55 (32.9)	209 (34.0)
B symptoms Exact p=(0.778)				
Missing	11 (4.9)	6 (2.7)	9 (5.4)	26 (4.2)
N	132 (58.4)	139 (62.9)	101 (60.5)	372 (60.6)
Y	83 (36.7)	76 (34.4)	57 (34.1)	216 (35.2)
Response at baseline Chisq p=(0.359)				
Partial response	100 (44.2)	86 (38.9)	71 (42.5)	257 (41.9)

Complete response	52 (23.0)	62 (28.1)	51 (30.5)	165 (26.9)
No response	74 (32.7)	73 (33.0)	45 (26.9)	192 (31.3)
Salvage treatment Chisq p=(0.933)				
DHAP +/- R	114 (50.4%)	109 (49.3%)	78 (46.7%)	301 (49.0%)
GDP +/- R	109 (48.2%)	108 (48.9%)	88 (52.7%)	305 (49.7%)
No TRT	2 (0.9%)	3 (1.4%)	1 (0.6%)	6 (1.0%)
R only	1 (0.4%)	1 (0.5%)	0 (0%)	2 (0.3%)

Figure 1.