The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

905.OUTCOMES RESEARCH-LYMPHOID MALIGNANCIES

An Examination of Aggregate Side-Effects Mapped to Therapies Experienced By Patients with Relapsed Large B-Cell Lymphomas - an Analysis from the Lymphoma Coalition's 2022 Global Patient Survey

Steve E Kalloger[1], Leandro Venturutti, PhDBSc[2], Shawn Sajkowski[1], Amanda Watson[1], Lorna Warwick[3]

[1] Lymphoma Coalition, Mississauga, Canada
[2] BC CANCER, Vancouver, Canada
[3] Lymphoma Coalition, Mississauga, CAN

Introduction
The identification of side-effects associated with a particular therapy relies on univariable assessments of incidence across treatment arms. While this approach serves to set the groundwork for the establishment of causation, it is suboptimal when the incidence is small or when novel therapeutics with limited deployment are being examined. In this study, we used a multivariate approach to aggregate multiple symptoms in order to segment our sample into those who had differing degrees of side-effect incidence. We used the resultant strata to examine the use of various therapies.
Methods
Patients with relapsed large B-cell lymphomas who responded to the Lymphoma Coalition's 2022 Global Patient Survey (N=215) were asked if they had ever been treated with a particular treatment (N = 20) and what side effects (N=32) they have ever experienced. Unsupervised hierarchical clustering utilizing Ward's algorithm was used to aggregate the incidence of side-effects (N = 32). Resultant strata from the hierarchical clustering procedure were subjected to contingency analysis with the use of 20 treatments. Differences were assessed with odds ratio's, 95% confidence intervals and p-values from the likelihood chi-square statistic as appropriate.
Results
The total number of respondents meeting the criteria for inclusion in this study was 215. The median age of respondents was 58 and ranged from 23-85 years. Females comprised 55% of the study sample. Figure 1 Illustrates the two-way clustering heat map. A subjective decision was made to segment the study sample at the first branch yielding two clusters: 1 (N = 76) and 2 (N = 139). The rationale for selecting two clusters was based upon an obvious difference in side-effect incidence. The cumulative incidence of side effects in Cluster 1 = 1570 yielding an incidence rate per patient of 11.3 which is contrasted with Cluster 2 having a cumulative side-effect incidence of 272 yielding a rate per patient of 3.6.
Table 1 illustrates the odds ratios and 95% confidence intervals derived from contingency analysis utilizing Cluster as the explanatory variable. Significantly increased odds of CAR-T (p<0.0001), steroids (0.006) and radiation therapy (p = 0.01) use were found in Cluster 1 relative to Cluster 2. We were unable to detect a significant change in the odds ratio for the other 17 treatments.
Conclusions
These results suggest that there is an association of increased side effects for those receiving CAR-T. Additionally, radiotherapy was also found to be marginally more used in those with more side-effects. The fact that steroid use was also increased in this cluster of patients makes sense since that is a routine prophylaxis strategy for patients experiencing substantial side effects. From the heat map, we can infer two things. First, there are groups of side effects that tend to cluster together which may reflect the treatment heterogeneity provided to this population. Second, it appears that about one-third of these patients experience very few side effects which supports the idea of patient heterogeneity. There are some limitations to this work which includes the use of patient reported outcomes and the fact that we were unable to explicitly map the treatment course of every individual patient. However, this study does support the idea that the diversity of the side-effect profile for CAR-T may extend well beyond the traditional phenomena of cytokine release syndrome, blood, and neurological effects. We suspect that as the use of CAR-T expands, additional side-effects will become apparent. Future studies should focus on identifying individuals who are likely to experience significant side effects and map treatment strategies to the appropriate patients.

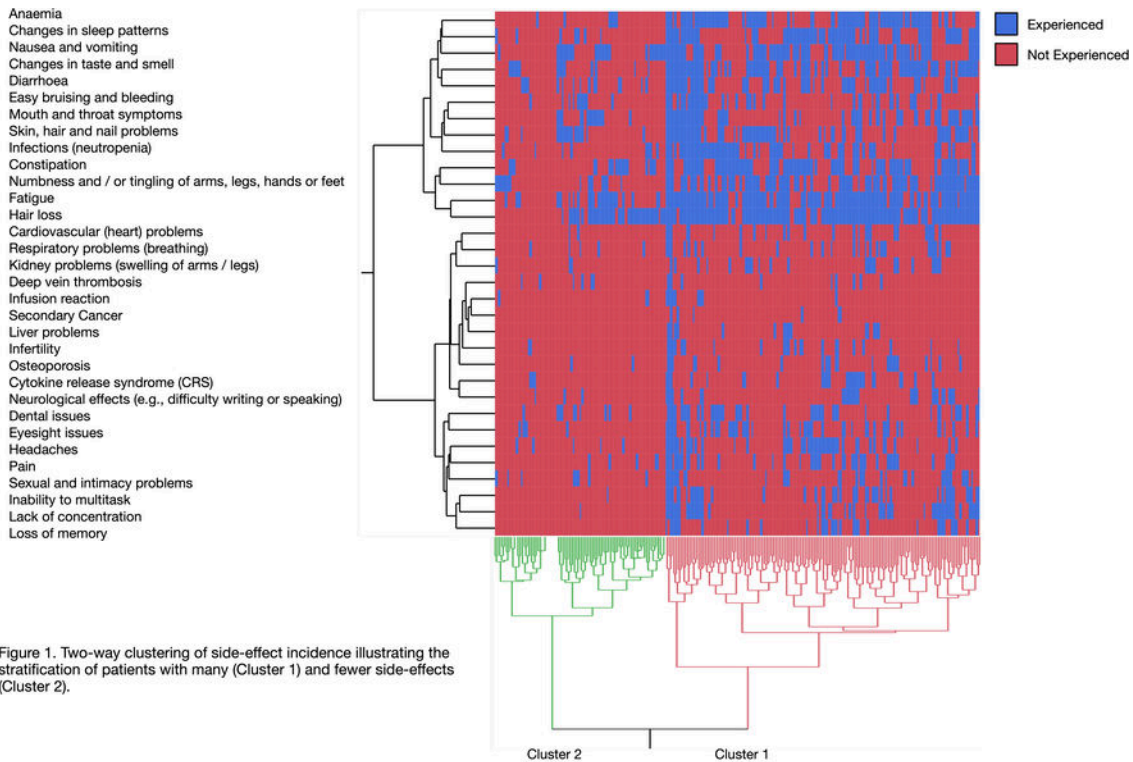**Disclosures** No relevant conflicts of interest to declare.

Figure 1. Two-way clustering of side-effect incidence illustrating the stratification of patients with many (Cluster 1) and fewer side-effects (Cluster 2).

Table 1. Odds ratios (OR) for Cluster 1 receiving a treatment relative to Cluster 2. Confidence intervals that do not include 1 are considered statistically significant at an alpha = 0.05. OR's equal to zero represent a situation where one or both clusters had no incidence of treatment with a particular therapy.

Treatment	OR	Lower 95% CI	Upper 95% CI
Chimeric antigen receptor T cell therapy (CAR-T) (e.g., axicabtagene ciloleucel (YESCARTA®), Kymriah® or tisagenlecleucel)	8.83	2.62	29.73
Complementary and alternative medicine (CAM) (e.g., acupuncture, supplements)	7.09	0.90	55.59
Targeted therapy (e.g., Idelalisib (Zydelig®) Copanlisib (ALIQOPA®), Bortezomib (Velcade), Ibrutinib)	5.81	0.73	46.32
Steroids (e.g., dexamethansone, methylprednisolone (Medrol®))	3.07	1.29	7.33
Radiation therapy	2.26	1.15	4.46
Skin creams and ointments	2.09	0.57	7.74
Chemo-immunotherapy (e.g., R-CHOP, BR-Bendamustine rituximab)	1.77	0.92	3.40
Chemotherapy alone (e.g., CHOP, chlorambucil, Bendamustine, ABVD)	1.22	0.59	2.53
Autologous or allogeneic stem cell transplant (bone marrow transplant)	1.20	0.68	2.12
Immunotherapy only (e.g., Rituximab (rituxan®); Obinutuzumab (Gazya™), mogamulizumab (Poteligeo) d Brentuximab vedotin (Adcetris), Lenalidomide (Revlimid®))	1.01	0.48	2.12
Extracorporeal Photopheresis (ECP)	0	-	-
Light therapy (phototherapy)	0	-	-
Radioimmunotherapy (e.g., Ibritumomab (Zevalin®))	0	-	-
Targeted electron beam	0	-	-
Total skin electron beam	0	-	-
Topical gel (e.g., topical nitrogen mustard, Valchor / Ladaga)	0	-	-
Topical retinoids (e.g., Bexaratene, istretinoin)	0	-	-
Topical steroid creams	0	-	-
Psoralen with UVA light (PUVA)	0	-	-
UVB light	0	-	-

Figure 1