Identifying Treatment Patterns for Diffuse Large B-Cell Lymphoma in Real-World Data Using Unsupervised Machine Learning

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BACKGROUND

- Treatment patterns are important for identifying eligibility for further treatments like chimeric antigen receptor T-cell (CAR-T) therapy.[1]
- However, because many hematological oncology treatments delivered in practice do not precisely match treatment guidelines, researchers cannot rely on guidelines alone to identify treatment patterns and detect switches in therapy observed in real-world data.

RESEARCH OBJECTIVES

To explore whether unsupervised machine learning may be useful for identifying treatment patterns for patients with diffuse large B-cell lymphoma (DLBCL).

METHODS

Data: TriNetX Research Network electronic health records datasets (2007-2022)

Sample: 176,437 DLBCL drug records from 17,873 DLBCL patients, excluding:

- Patients with no encounters after October 18, 2017.
- Time between first and last DLBCL diagnoses is less than 30 days.
- No diagnoses earlier than the patient's first DLBCL diagnosis.
- Neither label use nor off-label use of drugs is for DLBCL or non-Hodgkin lymphomas.
- DLBCL drugs administered in visits not associated with DLBCL or associated with neoplasms other than lymphomas.

List of Drugs: National Comprehensive Cancer Network (NCCN) and American Cancer Society (ACS) guidance and the literature.

Identifying Treatment: For each patient, drugs delivered with no more than a 5-day gap between each other were grouped into multi-drug treatment regimens.

Multiple Correspondence Analysis (MCA): MCA was used to identify "dimensions" comprising weighted combinations of multiple co-occurring drugs, reducing the dimensionality of raw drug data to be used in clustering.[2]

Mini-Batch K-Means Clustering: Treatments were clustered on their MCA dimensions.[3] Suitable for large datasets.

Optimal Number of Clusters: Number of clusters was chosen to minimize the Bayesian Information Criterion (BIC).

Sensitivity Analyses: Varied "Gap" days for combining drugs into treatments, number of MCA dimensions for clustering, and criterion for determining the optimal number of clusters.

RESULTS

Exhibit 1. Examples of MCA Dimensions

drug	Dim 1	Dim 2	Dim 3	Dim 4	Dim 5	Dim 6	Dim 7	Dim 8
vincristine_0	0.7597942	-0.3838631	-0.0967428	-0.0356089	-0.0510617	-0.0360002	0.00440115	-0.0217944
vincristine_1	-0.7792894	0.39371244	0.09922504	0.0365226	0.05237184	0.03692395	-0.0045141	0.0223536
doxorubicin_0	0.87547107	-0.3749355	-0.0264885	-0.0684329	-0.16869	-0.1268932	-0.0198454	0.04889936
doxorubicin_1	-0.6652956	0.28492426	0.02012934	0.05200415	0.12819238	0.09642975	0.01508106	-0.03716
cyclophosphamide_0	0.75399936	-0.3991156	-0.1075565	-0.0374556	-0.0701694	-0.0917511	-0.0352103	0.01785172
cyclophosphamide_1	-0.772233	0.40876723	0.1101575	0.0383614	0.07186631	0.09396987	0.0360618	-0.0182834
rituximab_0	0.58587039	-0.481388	-0.5346825	0.47561078	0.46887686	0.42020393	0.07364681	0.02236193
rituximab_1	-0.2395181	0.19680315	0.21859124	-0.1944413	-0.1916883	-0.1717896	-0.0301086	-0.0091421
procarbazine_0	-0.0039899	0.004813	0.00326015	-0.0030651	0.02309503	0.03358327	0.02072264	-0.0428529
procarbazine_1	0.47017329	-0.5671744	-0.3841836	0.36119276	-2.72157	-3.9575285	-2.4420026	5.04988243
carboplatin_0	-0.1073494	-0.1163232	-0.0112092	0.02145552	-0.0141495	0.00389017	-0.0002529	-0.0005061
carboplatin_1	3.16070591	3.42492084	0.33003349	-0.6317181	0.4166068	-0.1145389	0.00744708	0.01490096
mesna_0	-0.1128979	-0.1354693	-0.0081716	0.01165274	-0.0206296	0.0004751	0.00514287	0.00019373
mesna_1	2.74471859	3.29346115	0.19866479	-0.2832956	0.50153714	-0.0115505	-0.1250308	-0.0047098
etoposide_0	-0.0919543	-0.2313428	0.00599728	-0.1425114	0.06173702	-0.0604041	-0.0328536	0.00427636
etoposide_1	0.49468186	1.24454237	-0.0322633	0.76666087	-0.3321234	0.32495279	0.17674099	-0.0230053
ifosfamide_0	-0.0988799	-0.117634	-0.0096397	0.01234749	-0.0144861	0.00288934	0.00497557	-0.0002982
ifosfamide_1	3.56354753	4.2394305	0.34740613	-0.4449931	0.52206595	-0.1041294	-0.1793154	0.01074763
mitoxantrone_0	-7.03E-05	-0.0001238	-2.16E-05	8.83E-05	-1.61E-05	0.00020084	0.00018527	-4.31E-05
mitoxantrone_1	1.56183748	2.75104595	0.4804376	-1.963292	0.35796007	-4.4631629	-4.11721	0.95761209
cisplatin_0	-0.0139483	0.0109753	-0.0292596	-0.0279906	0.02988441	0.00174804	-0.0042985	0.03569734
cisplatin_1	1.42114677	-1.1182358	2.98116288	2.85186207	-3.0448202	-0.1781022	0.4379566	-3.6370799
gemcitabine_0	-0.0454291	0.05567203	-0.1566314	-0.0145211	-0.0199749	-0.0157181	-0.0043884	-0.0020994
gemcitabine_1	1.22370087	-1.4996107	4.21910566	0.39114688	0.53805315	0.42339185	0.11820911	0.05655138
lenalidomide_0	-0.0570141	0.07262654	0.06759975	0.00294014	-0.093837	0.04404262	-0.015541	0.03202503
lenalidomide_1	0.97647175	-1.2438628	-1.1577697	-0.0503553	1.6071301	-0.7543108	0.26616782	-0.5484873
tafasitamab_0	-0.0076852	0.01033754	0.01095139	-0.0047762	-0.0274437	0.01864955	-0.0116174	0.03436992
tafasitamab_1	1.15022539	-1.5471963	-1.6390706	0.71484021	4.10743859	-2.7912366	1.73875329	-5.1440695
cytarabine_0	-0.0452133	0.01038307	0.02543027	-0.1511603	0.11574825	-0.0017251	0.00246883	0.01693151
cytarabine_1	0.78968386	-0.1813478	-0.4441581	2.64012336	-2.0216271	0.03013063	-0.0431199	-0.2957211
bendamustine_0	-0.0282545	0.0287047	0.00715703	0.09812948	0.08081423	-0.0007687	-0.0281562	0.02339525
bendamustine_1	0.91243909	-0.9269792	-0.2311264	-3.1689575	-2.6097851	0.02482273	0.90926512	-0.7555176
polatuzumab_vedotin_0	2.10E-30	-1.99E-30	4.77E-30	-7.41E-25	7.39E-25	-8.44E-24	6.19E-25	-1.05E-24
oxaliplatin_0	-0.0253228	0.03645612	-0.1036292	0.00104754	-0.0257128	-0.0107531	-0.0022132	-0.0185468
oxaliplatin_1	1.32260731	-1.9041009	5.41254876	-0.0547128	1.34297577	0.56163139	0.11559661	0.9687001
ibrutinib_0	-0.0221758	0.02394828	0.02460174	0.00857948	0.00013883	-0.0206063	0.01832785	-0.0530247
ibrutinib_1	1.04569994	-1.1292792	-1.1600932	-0.4045647	-0.0065466	0.97168952	-0.8642484	2.50037783
bortezomib_0	-0.0054378	0.00512896	0.00972155	-0.0110506	-0.0065778	-0.036214	-0.0346025	-0.0275945
bortezomib_1	0.70127404	-0.6614411	-1.2537105	1.4251126	0.84828606	4.67023511	4.46240944	3.55864541
copanlisib_0	-0.0004044	0.00052229	0.00059651	-0.0004165	-0.0011676	0.00068543	-0.0006337	0.00302968
copanlisib_1	1.05680554	-1.3650193	-1.5589969	1.08866052	3.05142736	-1.7913993	1.65613167	-7.9181534
obinutuzumab_0	-0.0085585	0.00962175	0.00865996	0.01895235	0.00775751	-0.0424719	0.03244734	0.01974604
obinutuzumab_1	1.16190166	-1.3062483	-1.1756758	-2.5729706	-1.0531591	5.76598402	-4.4050513	-2.6807226
bleomycin_0	-2.19E-05	-0.0002082	-0.0006028	-0.0004026	-0.0010494	-0.0017666	-0.0008098	0.00049329
bleomycin_1	0.03353997	0.31888264	0.9232646	0.61665362	1.60735906	2.70582641	1.24033339	-0.7555496
pembrolizumab_0	-0.0051894	0.0054428	0.00525138	-0.0015726	-0.008411	-0.001054	0.00317935	-0.0083014
pembrolizumab_1	1.11449629	-1.1689083	-1.1277975	0.33773485	1.80636757	0.22636304	-0.682803	1.78282167
acalabrutinib_0	-0.0027433	0.00364883	0.00377827	-0.0009019	-0.00385	-0.0028544	0.00465446	-0.017154
acalabrutinib_1	0.87446573	-1.163109	-1.2043704	0.28748201	1.22724128	0.90987887	-1.4836667	5.46804875
brentuximab_vedotin_0	2.10E-30	-1.98E-30	4.76E-30	-7.41E-25	7.39E-25	-8.44E-24	6.39E-25	-1.01E-24
duvelisib_0	-0.0004446	-8.99E-05	0.00066171	-0.0032683	8.32E-05	-0.0050814	-0.0031026	-0.0002018
duvelisib_1	0.70527111	0.14257656	-1.0497341	5.18483161	-0.1319676	8.06107002	4.92197436	0.32010245
chlorambucil_0	-0.0001646	0.0002225	0.00028748	0.00065282	0.00016158	-0.004546	0.00574823	0.00184255
chlorambucil_1	1.21914392	-1.6480191	-2.1293342	-4.8353522	-1.196769	33.6714287	-42.57621	-13.647431
ofatumumab_0	-0.0014568	-6.80E-05	0.00140796	0.0090813	0.00701948	-0.0092393	-0.0210458	-0.0002249
ofatumumab_1	1.11490392	0.05204345	-1.0775513	-6.9501691	-5.372204	7.07108849	16.1069003	0.17211992
vinorelbine_0	-0.0010595	2.85E-05	-0.0025743	-0.0002249	-0.002929	-0.0023363	0.00070577	-0.0013578
vinorelbine_1	2.35362134	-0.0632677	5.71839344	0.49952924	6.50633637	5.18969582	-1.5677555	3.01618362

Exhibit 2. MCA Reduced 30 Single Drugs to 23 Dimensions for Clustering Analysis

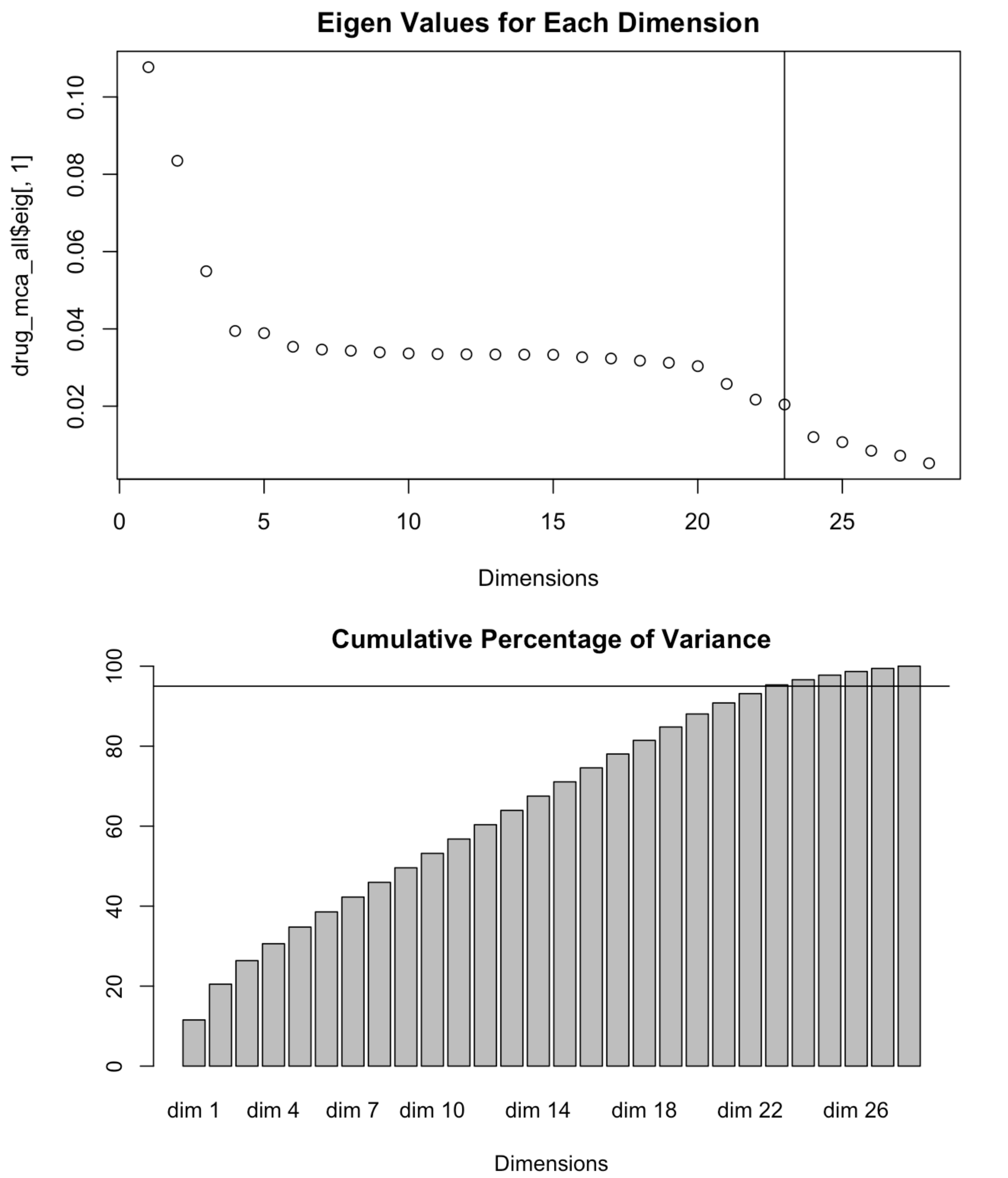

Exhibit 3. Examples of MCA Factor Maps

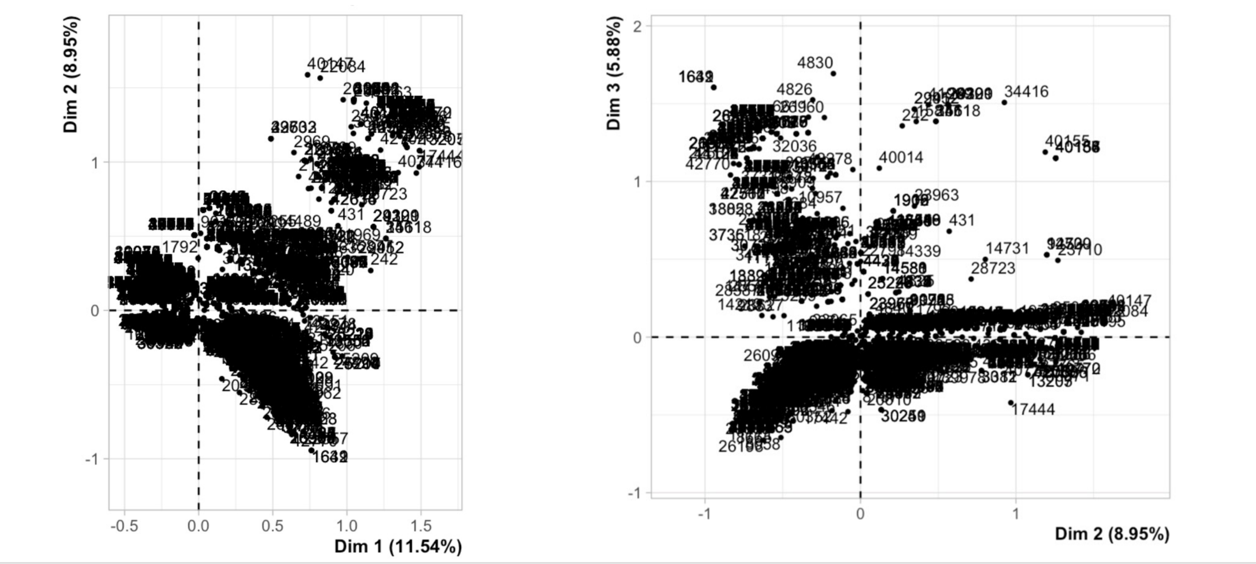

Exhibit 4. Bayesian Information Criterion Determined the Optimal Number of Clusters to be 20

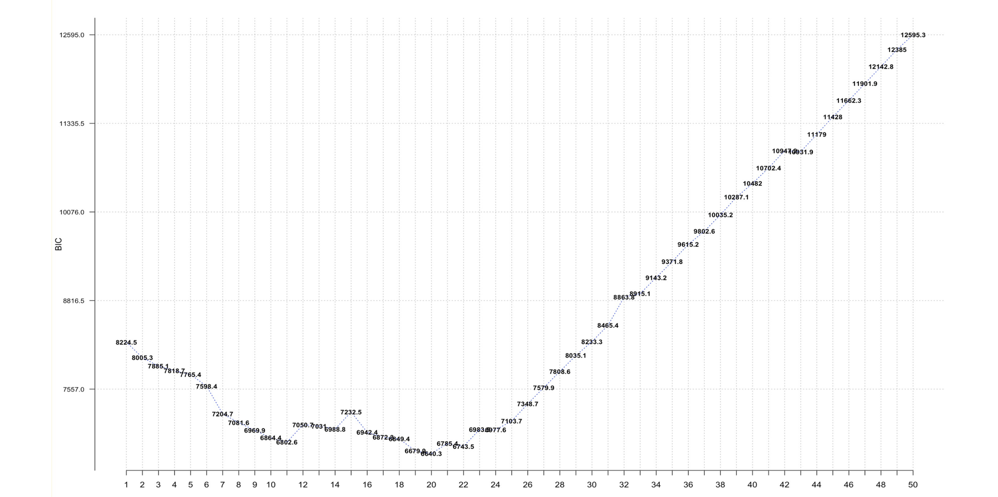

Exhibit 5. Examples of Clusters

cluster	TX	vincristine	doxorubicin	cyclophosphamide	rituximab	procarbazine	carboplatin	mesna	etoposide	ifosfamide	mitoxantrone	cisplatin	gemcitabine	lenalidomide	tafasitamab	cytarabine	bendamustine	polatuzumab_vedotin	oxaliplatin	ibrutinib	bortezomib	copanlisib	obinutuzumab	bleomycin	pembrolizumab	acalabrutinib	brentuximab_vedotin	duvelisib	chlorambucil	ofatumumab	vinorelbine
20	RCHOP	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20	RCDOP	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	1	1	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	1	1	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	0	1	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20	RGCVP	1	0	1	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		0	1	1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	1	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	1	1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	1	1	1	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	1	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	1	1	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	0	1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		0	1	1	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		0	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	0	1	1	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20		1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
20		1	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

cluster	TX	vincristine	doxorubicin	cyclophosphamide	rituximab	procarbazine	carboplatin	mesna	etoposide	ifosfamide	mitoxantrone	cisplatin	gemcitabine	lenalidomide	tafasitamab	cytarabine	bendamustine	polatuzumab_vedotin	oxaliplatin	ibrutinib	bortezomib	copanlisib	obinutuzumab	bleomycin	pembrolizumab	acalabrutinib	brentuximab_vedotin	duvelisib	chlorambucil	ofatumumab	vinorelbine
8	RGEMOX	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8	GEMOX	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		0	0	0	0	0	0	1	0	1	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		0	0	0	1	0	0	0	0	0	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		0	0	0	1	0	0	0	0	0	0	0	1	1	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
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8		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0
8		0	0	0	1	0	0	0	0	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0
8	RDHAX	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		1	0	0	0	0	0	1	0	1	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		0	0	0	1	0	0	0	0	0	0	0	1	0	0	1	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0
8		0	0	0	1	0	0	1	0	1	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		1	1	1	1	0	0	0	1	0	0	0	1	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		0	0	0	1	0	0	0	1	0	0	0	1	0	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		0	0	1	1	0	0	0	0	0	0	0	1	1	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		0	0	0	1	0	0	0	0	0	0	0	0	1	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		1	0	0	1	0	0	1	0	1	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
8		0	0	0	1	0	0	0	0	0	0	0	1	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0

Exhibit 6. Treatments of the same "line" clustered together.

Types of treatment	Number of treatments	Cluster number
First-line only	3	20
Second-line only	6	6, 8, 9, 11, 15, 17
First or second line	19	1

Exhibit 7. Example of an Individual Patient Treatment Flow

patient_id	MinDate	MaxDate	cluster_5_20	tx	tx_duration	tx_10more	vincristine	doxorubicin	cyclophosphamide	rituximab	procarbazine	carboplatin	mesna	etoposide	ifosfamide	mitoxantrone	cisplatin	gemcitabine	lenalidomide	tafasitamab	cytarabine	bendamustine	polatuzumab_vedotin	oxaliplatin	ibrutinib	bortezomib	copanlisib	obinutuzumab	bleomycin	pembrolizumab	acalabrutinib	brentuximab_vedotin	duvelisib	chlorambucil	ofatumumab	vinorelbine
xxxxx	Day 1	Day 8	20	RCHOP	8	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 16	Day 16	20	RCHOP	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 27	Day 27	20	RCHOP	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 48	Day 48	20	RCHOP	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 68	Day 68	20	RCHOP	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 89	Day 89	20	RCHOP	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 110	Day 110	20	RCHOP	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 125	Day 127	17	NA	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 139	Day 141	17	NA	2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 153	Day 156	17	NA	3	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 167	Day 173	9	NA	6	0	0	0	1	1	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 181	Day 187	9	NA	6	0	0	0	1	1	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 204	Day 207	9	NA	3	0	0	0	1	1	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 225	Day 230	9	NA	5	0	0	0	1	1	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 244	Day 244	9	R-ICE	0	0	0	0	0	1	0	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 275	Day 275	17	NA	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 281	Day 309	17	NA	28	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 317	Day 317	17	NA	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 345	Day 352	17	NA	7	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
xxxxx	Day 361	Day 361	17	R	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

CONCLUSION

Unsupervised machine learning is a promising approach for identifying meaningful treatment patterns. However, results are sensitive to learning parameters and require careful consideration.

LIMITATIONS

- Generalizability (only multi-center datasets)
- The results need further confirmation from clinicians
- Potential left and right censoring issues

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