Evaluating Patient Count Vs Hospitalization Risk for Common Clinical Trial Eligibility Criteria: A Case Study for Relapsed/Refractory Lymphoma/Leukemia

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Background

-Clinical trials remain essential for generating medical evidence

-Within the same disease domain, common eligibility criteria (CEC) patterns can be observed as many of the same criteria might be applied for safety reasons and/or reducing study population heterogeneity, but at the expense of reducing available patients who might benefit from participation

-**Objective:** To assess the tradeoff in patient count vs hospitalization risk when using different CEC sets, by using adult relapsed/refractory (r/r) lymphoma/leukemia trials as a case study

Methods

General Procedure | **Details**

Data Sources

-23 trials available for r/r lymphoma/leukemia

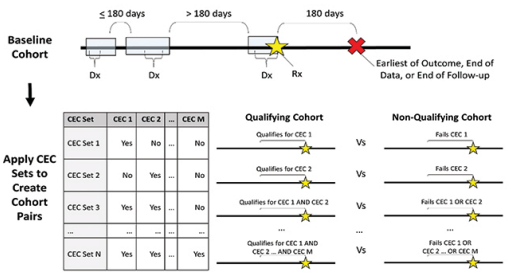
-Provides candidate eligibility criteria

-Provides patient data (from a large academic medical center) for cohort construction

CEC Identification

-Select concepts appearing in at least 25% of all trials
-Remove concepts if too vague or not reasonably captured in EHR
-Manually cross-check concepts to original ClinicalTrials.gov source text

Cohort Construction



-Rx = portion of relevant chemotherapy or corticosteroid
-Dx = lymphoma or leukemia diagnosis
-Outcome = hospitalization (length of stay > 1 day)

Analysis

-Perform power calculations to identify powered CEC sets
-Create scatterplot between CEC patient count and hospitalization risk for each powered CEC set
-Apply k-means clustering to identify CEC patterns

Results

-There were 9 CEC found, with no prior malignancy found to be the most restrictive

CEC Label	CEC Description	Number of Trials N (%)	Patient Count N (%)
Start	N/A	23 (100)	623 (100)
No HIV	No HIV within the past 365 days	20 (86.96)	614 (98.56)
No HBV/HCV	No HBV/HCV within the past 365 days	19 (82.61)	613 (98.39)
Not pregnant	No evidence of current pregnancy within the past 60 days	19 (82.61)	622 (99.84)
No prior chemo/rad	No prior chemotherapy or radiotherapy within the past 14 days (excludes index)	18 (78.26)	590 (94.70)
No prior malignancy	No prior malignancy (beside lymphoma, leukemia, non-melanoma skin cancer, melanoma in situ, carcinoma in situ of the cervix, benign tumor, or lipomatous tumor) within the past 1095 days	17 (73.91)	313 (50.24)
Adequate eGFR	Most recent eGFR measure within the past 180 days > 30 mL/min/1.73m^2 (per MDRD equation)	11 (47.83)	525 (84.27)
No infection	No active infection within the past 30 days	10 (43.48)	604 (96.95)
Adequate ANC	Most recent ANC measure within the past 180 days > 1000/mm3	9 (39.13)	587 (94.22)
No corticosteroid	No prior corticosteroid use within the past 7 days (excludes index)	9 (39.13)	612 (98.23)

-Of 511 possible CEC sets, only 256 (50%) were powered; all included the CEC of no prior malignancy

-Combining no infection and no prior chemo/rad suggests the lowest hospitalization risk, but at the expense of the smallest available number of patients to recruit (i.e. Cluster 5)

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Cluster 6
N of CEC Sets	33	22	58	52	48	43
No HIV	8 (24%)	2 (9%)	22 (38%)	22 (42%)	40 (83%)	34 (79%)
No HBV/HCV	12 (36%)	12 (55%)	28 (48%)	25 (48%)	24 (50%)	27 (63%)
Not pregnant	17 (52%)	11 (50%)	29 (50%)	27 (52%)	24 (50%)	20 (47%)
No prior chemo/rad	0 (0%)	0 (0%)	24 (41%)	24 (46%)	40 (83%)	40 (93%)
No prior malignancy	33 (100%)	22 (100%)	58 (100%)	52 (100%)	48 (100%)	43 (100%)
Adequate eGFR	13 (39%)	8 (36%)	24 (41%)	25 (48%)	32 (67%)	26 (60%)
No infection	0 (0%)	22 (100%)	58 (100%)	0 (0%)	48 (100%)	0 (0%)
Adequate ANC	9 (27%)	4 (18%)	28 (48%)	29 (56%)	32 (67%)	26 (60%)
No corticosteroid	13 (39%)	14 (64%)	26 (45%)	32 (62%)	24 (50%)	19 (44%)

Conclusions

-This procedure demonstrates a possible approach for better estimating and addressing the effect of eligibility criteria on patient counts and safety risk

-Trial sample and EHR data can greatly impact results, so CEC found to have muted effects from this analysis might not necessarily hold in other environments or different data sources

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