Original Article

Characteristics of cancer patients with COVID-19 in a cancer hospital

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Background: Cancer patients are vulnerable to the coronavirus disease 2019 (COVID-19) given their compromised immune system. The purpose of this study was to describe the presenting symptoms, inpatient stay trajectory, and survival outcomes, for cancer patients infected with COVID-19; who presented to the emergency department (ED) of a single center during the early months of the pandemic.

Methods: We reviewed the electronic medical records of all cancer patients diagnosed with COVID-19 at our institution for demographic information, clinical presentation, laboratory findings, treatment intervention and outcomes. All patients had at least 14 days of follow-up. We determined their survival outcomes as of August 5, 2020.

Results: Twenty-eight cancer patients were diagnosed with COVID-19, and 16 (57%) presented to the ED during the study period. The median age of patients who presented to the ED was 61 years, 69% were women, and the median length of hospitalization was 11 days. There was no difference between the groups (ED *vs.* no ED visit) for demographics, treatment status or solid tumor versus hematologic malignancies or treatments. Dyspnea was a significant symptom with 67% of ED patients experiencing it versus only 17% of those that did not come to the ED (P=0.009). Do not resuscitate orders were initiated in eight patients, as early as two days from ED presentation and two of these patients died, while 88% of patients were discharged alive.

Conclusions: Most cancer patients with COVID-19 infection admitted though the ED experienced dyspnea and were discharged from the hospital. We did not notice a statistically significant difference between cancer types or type of therapy. A broad differential is of utmost importance when caring for cancer patients with COVID-19 due to the complexity of this population. Early goals of care discussion should be initiated in the ED.

Keywords: Cancer; coronavirus disease 2019 (COVID-19); SARS-CoV-2; end of life care; do not resuscitate; emergency department (ED)

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Introduction

The coronavirus disease 2019 (COVID-19), continues to increase globally with more than 33 million cases and over one million related deaths—worldwide (1). Cancer patients, who tend to be older, have comorbidities, and have deficient or compromised immune systems, are expected to be particularly vulnerable to COVID-19 (2,3). These patients' care can be complicated by the early and late toxicities of their cancer treatments. Early studies reported that patients with cancer are more likely to need mechanical ventilation, be admitted to the intensive care unit, and die than patients without cancer (3,4). Underscoring this finding, an analysis of 355 patients who died from COVID-19 in Italy showed that up to 20.3% of the patients had active cancer (5).

The most frequently reported presenting symptoms of COVID-19 are fever, cough, shortness of breath or fatigue (3,5-9). These symptoms are also common to cancer patients without COVID-19 infection presenting to the emergency department (ED). Whether specific symptoms or findings in cancer patients will suggest COVID-19 infection in ED is not clear. Recently, a risk stratification tool was proposed for use in the ED (10), but there is no specific prognostic score to assist with treatment prioritization decisions in cancer patients. This lack of understanding has important implications for oncologic emergency medicine, whose practitioners are faced with the challenge of rapidly identifying the risk profiles of cancer patients with COVID-19 and determining the appropriate timing of interventions for the disease.

Given the increasing demands on the healthcare system, it is important to understand the role of addressing end of life care early in the care of the cancer patient. The purpose of this study was to describe the clinical characteristics of cancer patients with COVID-19, including the inpatient stay, clinical outcomes, goals of care and resuscitation preferences in a tertiary cancer center over the first months of the outbreak.

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/apm-20-1447).

Methods

Study setting and patient population

This retrospective observational study included all cancer patients between March 10, 2020, and April 10, 2020, for whom reverse-transcriptase polymerase chain reaction (RT-PCR) analysis of a nasopharyngeal swab or bronchoalveolar lavage specimen revealed SARS-CoV-2 infection. The turnaround time at our institution for the RT-PCR test is approximately 24 hours, therefore results were not immediately available in the ED. All patients received an infectious disease consultation, and were followed for at least 14 days after diagnosis; we determined their survival outcomes as of August 5, 2020. Excluded patients were those without cancer or without positive SARS-CoV-2 test. This study was conducted in accordance with a clinical research protocol (# 2020-0348) approved by MD Anderson Cancer Center's Institutional Review Board, and the study conformed to the provisions of the Declaration of Helsinki (as revised in 2013). Written informed consent was waived as this was a chart review study.

Data collection

Data obtained from the electronic medical record included: demographics; symptoms leading to COVID-19 testing; comorbidities; cancer diagnoses and treatment; vital signs at presentation to the ED; radiographic and laboratory test results; clinical outcomes. All laboratory values were obtained from the day of presentation/admission.

Chart reviews and data abstraction were independently conducted by two trained investigators (DNL and MTCC), who resolved any disagreements through discussion. A third, monitored investigator (JT) reviewed 20% of the charts for accuracy and consistency. A standardized abstraction form to guide data collection as well as precise definitions of variables were provided to avoid misclassification bias.

Statistical analysis

Descriptive statistics were used to summarize the sociodemographic and clinical characteristics of the study population. Continuous variables were reported as medians and interquartile ranges, or means and standard deviations, while categorical values were analyzed as counts and percentages. Differences between patients presenting to the ED and those getting outpatient testing were assessed using independent *t*-test, Student Pearson's chi-squared test, or Fisher's exact test where appropriate. Statistical Package for Social Sciences (SPSS) statistical software 24 was used for all analyses (IBM, Armonk, NY, USA).

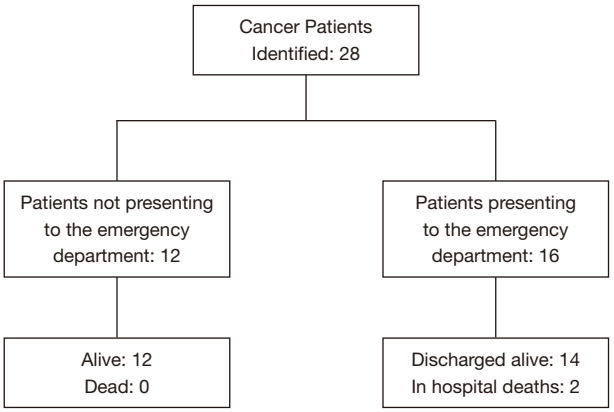

Figure 1 Flowchart of patient selection and outcomes.

Clinical definitions

For this study, we defined "severe outcome" as death, needing vasopressor support or mechanical ventilation. Furthermore, patients who developed hypoxemia were initially given supplemental oxygen by nasal cannula; those who required oxygen at a rate of more than 6 L/min were switched to a non-rebreather mask. Tocilizumab (8 mg/kg), a monoclonal antibody that competitively inhibits the binding of interleukin-6 to its receptor, was administered to any patient on nasal cannula who required more than 3 L O_2/min to maintain an O_2 saturation of >92%; if no clinical improvement was detected within 24 h, a second dose of tocilizumab was administered. In a few cases, the decision to give tocilizumab was based on treating physician discretion.

Results

Demographics and clinical characteristics

Twenty-eight cancer patients tested positive for SARS-CoV-2. Of those, 16 (57%) presented to the ED during the study period for a total of 18 ED encounters, while 12 (43%) did not visit the ED. Fifteen of the 16 patients that presented to the ED were hospitalized due to COVID-19, and only two of those died (*Figure 1*). The patients' demographics and clinical characteristics are summarized in *Table 1*, there was no statistically significant difference between the ED and no ED visit groups. Further breakdown of the disease stage and specific treatment for each patient is listed in Table S1. The most common type of malignancies were multiple myeloma (18%), gastrointestinal tumors (18%) and breast cancer (14%), and there was no difference between solid organ tumors and hematological malignancies. Patients on active treatment also did not significantly differ when compared to those who had not received treatment in the 30 days prior to COVID-19 testing.

Symptoms are detailed in *Table 2*, and shortness of breath was the only symptom that significantly varied (P=0.009) between the two groups (ED versus non-ED).

Laboratory and radiologic findings

The ED patients' laboratory values are given in *Table 3*. Patients who received tocilizumab during their hospitalization had a lower absolute lymphocyte count at presentation (2.77±1.86 versus 4.70±2.34) than those who did not get this intervention. Lymphopenia was noted in 44% of all encounters. Additionally, abnormal findings were present in 89% of chest radiographs ordered and 100% of computed tomography scans ordered.

All patients' swab specimens were negative for other respiratory viruses. One patient whose nasopharyngeal swab specimens tested negative for SARS-CoV-2 on two occasions had a bronchoalveolar lavage specimen positive for the virus.

ED interventions

The most common ED intervention, initiated at the time of evaluation and before the SARS-CoV-2 test was resulted, was intravenous antibiotics (78%). The most commonly used antibiotics were the combination of cefepime and vancomycin (56%) followed by cefepime and linezolid (16%). Most patients received supplemental oxygen via a nasal cannula or non-rebreather mask, and one patient required intubation in the ED.

Inpatient interventions

Among the 15 patients who were hospitalized (*Table 4*) the most common medications administered included azithromycin (93%), hydroxychloroquine (73%), and tocilizumab (53%). Half of the patients who received tocilizumab required mechanical ventilation and seven out of eight were discharged. We also noticed that patients with severe COVID-19 who required ventilatory support and developed acute respiratory distress syndrome (ARDS) had durable responses to intravenous steroids.

Table 1 Study population demographics

Characteristic*	Total patients (N=28)	ED visit (N=16)	No ED visit (N=12)
Age, years, median (range)	61 [31–83]	60.5 [37–83]	62.5 [31–80]
Gender			
Female	18 (64%)	11 (69%)	7 (58%)
Male	10 (36%)	5 (31%)	5 (42%)
Race			
White	13 (46%)	7 (44%)	6 (50%)
Black	13 (46%)	9 (56%)	4 (33%)
Asian	2 (7%)	0	2 (17%)
Ethnicity			
Hispanic	1 (4%)	1 (6%)	0
Non-Hispanic	27 (96%)	15 (94%)	12 (100%)
BMI, kg/m^2			
<30	16 (57%)	7 (44%)	10 (83%)
≥30	12 (43%)	9 (56%)	3 (25%)
Comorbidities			
Hypertension	16 (57%)	11 (69%)	5 (42%)
Diabetes	11 (39%)	7 (44%)	4 (33%)
Obstructive sleep apnea	8 (29%)	6 (38%)	2 (17%)
History of VTE	5 (18%)	3 (19%)	2 (17%)
Underlying lung disease	6 (21%)	5 (31%)	1 (8%)
Exposure history			
Travel history	4 (14%)	3 (19%)	1 (8%)
Known exposure to COVID-19	5 (18%)	1 (6%)	4 (33%)
Solid organ tumor≠			
Gastrointestinal cancer	5 (18%)	1 (6%)	4 (33%)
Breast cancer	4 (14%)	2 (13%)	2 (17%)
Lung cancer	2 (7%)	2 (13%)	0
Gynecological cancer	1 (4%)	1 (6%)	0
Prostate	1 (4%)	0	1 (8%)
Sarcoma	1 (4%)	0	1 (8%)
Neuroendocrine tumor	1 (4%)	1 (6%)	0
Skin	1 (4%)	0	1 (8%)
Hematological malignancies			
Multiple myeloma	5 (18%)	5 (31%)	0
Lymphoma	3 (11%)	1 (6%)	2 (17%)
Myelofibrosis	2 (7%)	2 (13%)	0
Leukemia	2 (7%)	1 (6%)	1 (8%)

Table 1 (*continued*)

Table 1 (*continued*)

Characteristic*	Total patients (N=28)	ED visit (N=16)	No ED visit (N=12)
Disease status			
Active	18 (64%)	11 (69%)	7 (58%)
No active disease	10 (36%)	5 (31%)	5 (42%)
Active treatment within 30 days[€]	16 (57%)	10 (63%)	6 (50%)

*, no statistically significant difference was found for any of the variables. [≠], analyses by grouping on hematological versus solid tumors was non-significant. [€], one patient was only receiving radiation. ED, emergency department; BMI, body mass index; COVID-19, coronavirus disease 2019; VTE, venous thromboembolism.

Table 2 Symptoms leading to testing and duration of symptoms

Symptoms	ED visit (N=18)[#]	No ED visit (N=12)
Symptoms leading to testing		
Fever	12 (67%)	7 (58%)
Shortness of breath*	12 (67%)	2 (17%)
Cough	9 (50%)	8 (67%)
Fatigue	5 (28%)	3 (25%)
Headache	4 (22%)	1 (8%)
Diarrhea	3 (17%)	1 (8%)
Congestion	2 (11%)	0
Sore throat	1 (6%)	2 (17%)
Confusion	1 (6%)	0
Sleepiness	1 (6%)	0
Runny nose	1 (6%)	4 (33%)
Lethargy	1 (6%)	0 (0%)
Anosmia	0	3 (25%)
Dysgeusia	0	1 (8%)
Duration of symptoms prior to testing, median [range], days[1]	4 [1–23]	4 [0–20]

*, P=0.009. [#], 16 patients presented to the ED for a total of 18 ED visits, with two patients presenting twice. [1], patients who were asymptomatic were coded as "0" days. ED, emergency department.

Clinical outcomes

One patient was evaluated and discharged from the ED the same day. A second patient was initially discharged from the ED and returned requiring hospitalization, while a third patient returned to the ED after hospital discharge and was discharged home the same day from the ED. There was only one admission from the cohort that did not present to the ED, and it was for an elective procedure. This patient was tested in preparation for the procedure and found to be positive for SARS-CoV-2 infection.

DNR orders were initiated for eight patients as early as two days after their presentation to the ED. Two of these patients died; one patient died three days after the initiation of the DNR order, and the other patient died four days after the initiation of the DNR order. Three out of four patients that developed ARDS and needed ventilatory support had a

Table 3 Vital signs and laboratory findings of 16 patients with 18 ED encounters

Parameters	Numbers
Vital signs	
Pulse oximetry ≤95%	12 (67%)
Pulse oximetry %, median [range]	95 [91–97]
Heart rate ≥100 beats per minute	8 (44%)
Heart rate bpm, median [range]	99 [87–110]
Temperature ≥100.4 °F	5 (28%)
Respiratory rate ≥20 breaths per minute	5 (28%)
Blood pressure ≤90/60 mm/Hg	1 (6%)
Laboratory values	
WBC elevated (>11.0 k/μL)	3 (17%)
WBC decreased (<4.0 k/μL)	3 (17%)
ANC elevated (>7.30 k/μL)	3 (17%)
ANC decreased (<1.70 k/μL)	3 (17%)
Hgb decreased [<12.0 g/dL (women); <14.0 g/dL (men)]	12 (67%)
Platelet count decreased (<140 k/μL)	6 (33%)
LDH elevated (>225 U/L)[a]	8/10 (80%)
ALC decreased (<1.0 k/μL)	10 (56%)
ALC elevated (>4.8 k/μL)	1 (6%)
AST elevated (>33 U/L)	7 (39%)
ALT elevated (>32 U/L)	7 (39%)
Creatinine elevated (>0.95 mg/dL)	9 (50%)
D-dimer elevated (>0.50 mcg/mL FEU)[a]	8/14 (57%)
CRP elevated (>10 mg/L)[a]	8/10 (80%)
Procalcitonin elevated (>0.08 ng/mL)[a]	4/8 (50%)
Troponin T elevated (>19 ng/L)[a]	1/9 (11%)

[a], data are for the indicated number of ordered tests only. ED, emergency department; ANC, absolute neutrophil count; ALC, absolute lymphocyte count; ALT, alkaline phosphatase; AST, aspartate aminotransferase; CRP, C-reactive protein; FEU, fibrinogen equivalent units; Hgb, hemoglobin; LDH, lactate dehydrogenase; WBC, white blood cell count.

DNR order placed after initiation of mechanical ventilation. All of the patients that required mechanical ventilation were eventually discharged home. Of the 16 patients that presented to the ED 14 survived.

Table 4 Inpatient management of 15 patients at least 14 days after admission

Management data	Number
Systemic agents	
Antimicrobials*	15 (100%)
Hydroxychloroquine	11 (73%)
Tocilizumab	8 (53%)
Vitamin C	6 (40%)
Corticosteroids	5 (33%)
Anakinra	3 (20%)
Zinc	3 (20%)
Inpatient interventions	
Intubation	4 (27%)
Mean time to intubation ± SD, days	2.00±1.41
Mean time to vasopressor use ± SD, days	3.33±3.215
Outcomes	
Mean time from presentation to DNR initiation ± SD, days[a]	2.38±1.4
Mean time from DNR initiation to death ± SD, days[b]	3.5±0.70
Mean hospitalization time ± SD (range), days	10.9±10.7 [2–39]
Mean time to death ± SD, days[b]	5.5±7.0

*, azithromycin 14 (93%), other antimicrobial 13 (87%). [a], data are for 8 patients for whom DNR orders were initiated during the study period. [b], data are for 2 patients who died during the study period. DNR, do-not-resuscitate order; SD, standard deviation.

Discussion

Cancer patients are thought to have an increased vulnerability to COVID-19 due to their compromised immune system, and have been reported to have high mortality rates (3-5). Our study showed that although 57% of the patients presented to the ED, most of these patients were discharged, which suggests better outcomes than previously reported in the literature. Symptoms leading up to the diagnosis of COVID-19 were similar to those reported in the general population (3,5-9). and in cancer patients without COVID-19 infection (11). However, the presence of dyspnea, hypoxemia and characteristic radiologic findings may facilitate prompt identification of those infected and may trigger early goals of care discussion.

In our cohort only one of the patients with a severe outcome, was noted to have metastatic disease. Active cancer treatment and stage of disease have been previously associated with worse outcomes (5). This is an important aspect to consider in cancer patients as therapies for COVID-19 may have potential interactions with commonly used antineoplastic drugs (12). Both patients who died were on chemotherapy, had hypertension, and obstructive sleep apnea. Consistent with previous studies' findings (5,13). our findings suggest that active cancer treatment and hypertension increases patients' vulnerability to COVID-19 (14-18). The role of hormone therapy in SARS-CoV-2 infections has been previously discussed as a having potentially protective effects in cancer patients with COVID-19 (19). However, we did not feel this contributed to our slightly female predominant sample.

We did not find a difference in COVID-19 disease severity when comparing patients with solid tumors versus those with hematologic malignancies. However, all five patients with multiple myeloma required hospitalizations (20). In multiple myeloma patients, plasma cells—terminally differentiated B cells that have an essential function in adaptive immunity (21)—aberrantly accumulate in the bone marrow, causing secondary hypogammaglobulinemia and increasing the risk of infection (22). This immunodeficiency can be aggravated by anti-myeloma treatments; in fact, all the multiple myeloma patients in our series were receiving anti-myeloma treatment at the time of admission to the ED (23,24). Deficiencies in acquired immunity, paired with the negative effects of anti-myeloma therapy, may increase the risk of SARS-CoV-2 infection in myeloma patients.

Co-infections with other pathogens in COVID-19 patients have also been reported (25). Thus, ED physicians in an oncologic setting should consider synchronous infections, including those from opportunistic pathogens (such as *Pneumocystis Jorovecci*, *Nocardia*, and fungal infections). Most patients in our cohort received intravenous antibiotics in the ED for presumed bacterial pneumonia. Radiographic imaging may be helpful in narrowing the differential, and chest CT has been recommended as the standard method for diagnosing COVID-19 (26). Using RT-PCR findings as a reference, Caruso and associates reported that chest CT has a sensitivity of 97% but a specificity of only 56% in detecting COVID-19 (27). Radiological findings may be atypical, and ground glass opacities may point to a diagnosis other than COVID-19 (28). In cancer patients, other etiologies should be considered including drug-induced pneumonitis, radiation pneumonitis, and metastatic disease (29,30).

Over half of the hospitalized patients had a DNR order written, but three of four patients requiring ventilatory and vasopressor support were made DNR after the patient was intubated. While all four of these patients were discharged, the importance of a goals of care discussion antecedent to the development of a critical illness is paramount (31). When addressed earlier, the patient's wishes may be respected, and the burden of decision making on family members can be alleviated. None of the patients had goals of care discussion in the ED. Thus, especially in those with pre-existing condition such as cancer, the discussion of code status should be initiated early, or at least introduced.

In addition to age, other factors such as disease stage, prognosis, and symptoms should be considered prior to intubation. In those with an established DNR order, the focus of care in the ED should be shifted to symptom management. Oxygen, opioids, and steroids are good interventions for the palliation of dyspnea. Frequent communication with family members using telemedicine modalities should be encouraged. Patients and their family members should be referred to palliative care services, which can provide counseling that can ease the pain of loss and help in the bereavement process.

Limitations

This study was limited by the small sample size obtained from a single center, which limits its generalizability to larger, more diverse patient population and prevents meaningful inferences from being made. The data was obtained from retrospective chart review, which may present its own inherent limitation, such as possibly missing data (e.g., missing lab values); however, the use of the electronic medical record minimized loss of information. We noticed a slightly higher percentage of females in our cohort, but we attribute this to the small sample size and not the type of malignancy. Our sample size may also be limited due to our institution's swift response in encouraging social distancing, as well as the adherence of cancer patients to these safety precautions. We believe this series highlights the complexities associated with the evaluation pf cancer patients including end of life discussion.

Conclusions

The majority of cancer patients with COVID-19 infection admitted to the hospital through the ED had good survival.

We did not notice a difference between cancer types, and active therapy might be a risk factor for more severe disease. A broad differential is important when caring for cancer patients with COVID-19, for infection may co-exist with other concomitant processes. Finally, goals of care discussion should become part of the ED encounter in case further decompensation ensues.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/apm-20-1447

Data Sharing Statement: Available at http://dx.doi.org/10.21037/apm-20-1447

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with a clinical research protocol (# 2020-0348) approved by MD Anderson Cancer Center's Institutional Review Board and the study conformed to the provisions of the Declaration of Helsinki (as revised in 2013). Written informed consent was waived as this was a chart review study.

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Supplementary

Table S1 Stage of disease and cancer treatment for 28 cancer patients with COVID-19

Malignancy class	Cancer treatment at the time of SARS-CoV-2 diagnosis*	Cancer type	Cancer status	Hospitalization	Days of hospitalization	Death related to SARS-CoV-2
Solid tumor						
Lung cancer						
Patient 1	None	Adenocarcinoma of lung	Remission	Yes	2	No
Patient 2	None	Adenocarcinoma of lung	Stage IA	No	0	No
Breast cancer						
Patient 1	None	Invasive ductal carcinoma	Remission	Yes	39	No
Patient 2	Bevacizumab	Invasive ductal carcinoma	Metastatic	Yes	6	No
Patient 3	Capecitabine	Infiltrating carcinoma of breast	Metastatic	No	0	No
Patient 4	Pertuzumab , trastuzumab, tamoxifen	Infiltrating carcinoma of breast	Stage IA	No	0	No
Gastrointestinal tumor						
Patient 1	None	Rectal cancer	Metastatic	Yes	6	Yes
Patient 2	None	Adenocarcinoma of the pancreas	Stage IIB	No	0	No
Patient 3	None	Adenocarcinoma of the cecum	Stage IIB	No	0	No
Patient 4	Bevacizumab with irinotecan, leucovorin, 5-flourouracil	Adenocarcinoma of the sigmoid colon	Metastatic	No	0	No
Patient 5	None	Liver cell carcinoma	Stage IB	No	0	No
Gynecologic cancer						
Patient 1	Cisplatin, radiation therapy	Mixed endometrial cancer	Stage IIIB	Yes	5	Yes
Prostate cancer						
Patient 1	None	Prostate cancer	Remission	No	0	No
Neuroendocrine tumor						
Patient 1	None	Neuroendocrine tumor of nasal cavity	Remission	Yes	5	No
Sarcoma						
Patient 1	Stereotactic body radiation therapy	Leiomyosarcoma of retroperitoneum	Stage IIIB	No	0	No
Skin cancer						
Patient 1	None	Basal cell carcinoma of skin	Remission	No	0	No
Hematologic malignancies						
Myelofibrosis						
Patient 1	Jakafi	Myeloproliferative neoplasm	Active—new diagnosis	Yes	9	No
Patient 2	Ruxolitinib and Aranesp	Myelodysplastic/myeloproliferative neoplasm	Active	Yes	19	No
Multiple myeloma						
Patient 1	Bortezomib, dexamethasone, cisplatin, doxorubicin, cyclophosphamide and etoposide	IgA kappa	Relapsed	Yes	5	No
Patient 2	Revlimid	IgG lambda	Remission	Yes	9	No
Patient 3	Carfilzomib, pomalidomide and dexamethasone	IgG kappa	Relapsed	Yes	28	No
Patient 4	Daratumumab, carfilzomib, cyclophosphamide, dexamethasone	IgA kappa	Relapsed	Yes	3	No
Patient 5	Daratumumab, lenalidomide and dexamethasone	IgG kappa	Relapsed	Yes	13	No
Leukemia						
Patient 1	None	Chronic lymphoid leukemia	Remission	Yes	28	
Patient 2	Ibrutinib	Chronic lymphoid leukemia	Relapsed	No	0	No
Lymphoma						
Patient 1	None	Hodgkin lymphoma	Remission	Yes	4	No
Patient 2	Rituximab and Ibrutinib	Mantle cell lymphoma	Active	No	0	No
Patient 3	None	Diffuse large B-cell lymphoma	Active—new diagnosis	No	0	No

*, treatment within 30 days prior to diagnosis.

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