COMPLIANCE WITH THE INFECTIOUS DISEASES SOCIETY OF AMERICA GUIDELINES FOR EMERGENCY MANAGEMENT OF FEBRILE NEUTROPENIA IN CANCER PATIENTS

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ABSTRACT

***Aims**: Although the febrile neutropenia care guidelines have been available for several years, little is known regarding guideline compliance in the emergency setting.*

This study aimed to assess compliance with the 2010 updated Infectious Diseases Society of America (IDSA) Guidelines Fever and Neutropenia Guidelines in the emergency management of febrile neutropenia.

***Materials and methods**: Adult cancer patients with a diagnosis of febrile neutropenia presenting over a one-year period were observed for guideline compliant care rate of emergency care. "Guideline compliant care" was defined as: subsequent to drawing blood cultures, administration of antibiotic within 2 hours of emergency department admission, accurate disposition according to Multinational Association of Supportive Care in Cancer score and absolute neutrophil count.*

***Results**: Among 117 included febrile neutropenia patients 63 (53.8%) patients received their first dose antibiotics during emergency stay. The number of patients who received antibiotics within 120 minutes subsequent to blood sampling for cultures was 28 (23.9%). Accurate disposition was observed in 75 (64.1%) patients. The percentage of study group who received guideline-compliant care by meeting all the defined criteria in the emergency department was 19.7%. No independent factors were determined to predict compliance. Compliance was not associated with clinical outcomes (p=0.648).*

***Conclusion**: Compliance with the 2010 updated Infectious Diseases Society of America Guidelines within the emergency department was low in this study. Implementing a corporate protocol for management in the emergency department in collaboration with partners may provide awareness of febrile neutropenia among emergency staff and contribute to improved clinical outcomes.*

***Key words**: febrile neutropenia, emergency care, guideline adherence.*

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Introduction

Advances in cancer treatment have resulted in an increasing number of patients undergoing novel or experimental adjuvant and neo-adjuvant chemotherapy regimens, and a subsequent increase in the number of complications resulting from these treatments[1]. As a consequence of the expansion of ambulatory chemotherapy modalities[2], cancer patients frequently present at emergency departments with treatment- and disease-associated complications. Febrile neutropenia (FN) is a major cause of emergency department (ED) visits[3]. Considered an oncologic emergency, FN requires rapid assessment and the administration of broad-spectrum antibiotics in the ED. Moreover, emergency departments are critical points of care for the management of fluid therapy, and the site of important admission and discharge decisions that can have tremendous consequences for clinical outcomes[4].

FN is a significant cause of mortality and morbidity among cancer patients and clinical management guidelines have been developed as an evidence-based guide to FN treatment[2,5,6]. The most widely recognized international guideline is the "Infectious Diseases Society of America (IDSA) Fever and Neutropenia Guideline", updated in

2010. Although the FN care guidelines have long been available, data regarding clinical compliance is limited[7]. Oncology clinics have reported significant variability in clinical practice[7-9]. Wright et al. conducted a study of 25,231 hospitalized FN patients, reporting significant variations in the management of FN. In that study, guideline-compliant therapy was associated with reduced in-hospital mortality rates[7]. However, relatively little is known regarding FN guideline compliance in the emergency setting[10,11].

This study aimed at assessing compliance with the 2010 IDSA Fever and Neutropenia Guidelines in the ED management of patients with febrile neutropenia in an academic tertiary hospital.

Material and methods

Study design

This prospective, observational study was conducted in the ED of a university teaching hospital over a one-year period. The study design was reviewed and approved by the hospital ethics committee (Review No. KAEK 2012/132). As the study does not involve any tests or interventions, the informed consent requirement was waived.

Study setting and population

The study site is a 697-bed tertiary hospital. A 24-bed medical oncology department, 6-bed radiation oncology department, and 36-bed hematology service are available within the hospital. Approximately 2,300 medical oncology patients are treated annually. The ED serves with an annual census of 35,000. Emergency facilities include 31 beds, 16 of which have monitors. No isolation beds are available for the treatment of communicable diseases. Patient care is provided by emergency medicine residents and specialists.

Adult cancer patients with a diagnosis of FN presenting to the ED meeting the diagnostic criteria indicated by the 2010 IDSA Fever and Neutropenia Guidelines were included. Adult patients with a pathological diagnosis of solid or hematological malignancy or patients with metastatic disease were included in the study. Patients with non-malignant transient neutropenia (e.g.temporary bone marrow suppression), patients hospitalized directly and therefore not evaluated in the ED, hospitalized patients who subsequently developed FN, and patients with incomplete records were excluded from the study. In cases where FN occurred on multiple occasions, only the records of the first incident were included in the analysis. Furthermore, patients seen by the lead investigator, EA, were excluded from the study.

Study protocol

The ED doctors were asked to complete data collection forms regarding patients diagnosed with FN. These forms were designed to collect data on patient characteristics, primary tumor site, time of most recent chemotherapy treatment, ED arrival time, symptoms, findings, presence of any catheter, suspected origin of infection, laboratory results, medications and times of application, consultations, and ED disposition with ED length of stay (LOS). In an attempt to keep the ED staff blinded to the objectives of the study, FN risk factors and total Multinational Association of Supportive Care in Cancer (MASCC)[12] scores were not a component of the form and were calculated following data collection. Consulting physicians were also blinded to the study.

Body temperature measurements were obtained using a tympanic thermometer (Covidien GENIUS 2 Tympanic Thermometer - Thermometer with Base - Model 303000, Each, USA). Patient leukocyte and neutrophil counts were measured at the emergency laboratory using a cytological counter (Cell Dyn 3700, Abbot, Turkey). Tympanic body temperature greater than 38.0°C for one hour was consistent with a diagnosis of FN. Patients with an absolute neutrophil count (ANC) of<500/mm^3 or > 500/mm^3 but predicted to decrease below 500/mm^3 within 48 hours were considered neutropenic. No changes to standard emergency care were introduced during this study. Disposition decisions were at the discretion of the oncology or hematology specialists.

Time and dosage of antibiotic administrations were collected through examination of physician data forms and nursing records. The ED LOS and antibiotic administration times were expressed in minutes. FN time and duration of hospitalization were represented in days. Experience and training of the ED physicians at the time of patient admission were also recorded on the data collection form.

After the ED disposition, follow-up data were accessed through the hospital's electronic records. These data were used as clinical outcome parameters. The need for mechanical ventilation, need for antibiotics change, hospital re-admittance rate and in-hospital mortality constituted a negative out-

come. In-hospital mortality was defined as death during the hospital stay as a result of FN, while readmission to the hospital was defined as return to the ED or outpatient facility with infection and fever within 7 days of discharge.

Outcome measures

The study's primary outcome measure was the compliance rate of the ED management of FN with the "IDSA Fever and Neutropenia Management Guideline 2010 update". Given that the management of individual patients is dependent upon specific risk factors varying between patients, compliance with IDSA guidelines was evaluated according to recommendations applying to all FN patients. "Guideline compliant care" was defined as follows: subsequent to drawing blood cultures, administration of first dose antibiotic within 2 hours of ED admission, accurate hospital admission or discharge according to MASCC score and ANC.

A secondary outcome of the study was the assessment of factors influencing the ability to comply with IDSA guidelines.

Statistical analysis

All study data were analyzed by using SPSS 13.0 for Windows (SPSS Inc., Chicago, USA). Both visual (histogram) and analytical (Kolmogorov-Smirnov test) methods were used to assess the normal distribution of continuous variables. Qualitative variables were expressed as percentages and ratios and quantitative variables were expressed as mean and standard deviation (±SD) or median and interquartile range (IQR). Since guideline compliance was used as the primary outcome of this study, potentially independent variables were compared between patient who received guideline-compliant and noncompliant ED care for FN. The chi-square test was used for the comparison of categorical variables, while independent samples t-test or Mann-Whitney U test were used for the comparison of continuous variables, as appropriate. Parameters associated with guideline compliance with $p< 0.25$ were included in the logistic regression model. All measures were reported with 95% confidence interval and a p value of < 0.05 was considered as statistically significant.

Results

During the study period, a total of 141 patients with suspected FN were admitted to the ED. As a result of the exclusion criteria described previously, 24 patients were excluded from the study and the final study group consisted of 117 patients diagnosed with FN. Baseline characteristics of the study subjects are summarized in table 1.

VARİABLE	N(%)
Age -- median	60
Gender	
Female	46 (39.3)
Male	71 (60.7)
ED presentation times	
Working hours (8 a.m.-4 p.m.)	42 (35.9)
Out of working hours (4 p.m.- 8 a.m.)	75 (64.1)
Any comorbidity	
No	74 (63.2)
Yes	43 (36.8)
Primary tumor site	
Solid	76 (65)
Lung	24 (20.5)
Gastrointestinal	14 (12)
Breast	12 (10.3)
Female urogenital	10 (8.5)
Male urogenital	7 (6)
Hematologic	38 (32.5)
Lymphoma	18 (15.4)
Acute leukemia	8 (6.8)
Chronic leukemia	5 (4.2)
Other hematologic	7 (6)
Without pathological diagnosis yet	3 (2.5)
Latency after chemotherapy	
Not received	11 (9.4)
Received	9
(median-days)	

Table 1: Baseline characteristics of the study subjects.

The most common primary origin of cancers observed in the study group was the lung, gastrointestinal tract and breast. The median LOS in the ED was 265 minutes (IQR: 180 - 436).

Upon the completion of emergency care 40 (34.2%) patients were discharged and 77 (65.8%) patients were hospitalized, including 3 patients requiring intensive care unit. The median duration of hospitalization was 5 days (IQR = 3-7.3).

Duration of hospital stay was similar in admitted patients receiving guideline compliant and non-compliant ED care (5 vs 5.5 days) (p = 0.953). Febrile neutropenia resulted in in-hospital mortality in 20 (17%) patients. Details of the emergency management of study patients are given in table 2.

Variable	Overall compliant N=23(%)	Non-compliant N=94 (%)
Presentation complaint		
Fever	8 (34.8)	38 (40.4)
ED LOS (min.)- Median	195	272.5
(IQR)	(150-255)	(195-470)
Obtained cultures in the ED		
Blood	23 (100)	35 (37.2)
Urine	18 (78.2)	42 (44.7)
Feces	4 (17.4)	6 (6.4)
Consultation		
Not required	1(4.3)	5 (5.3)
Required	22 (95.7)	89 (94.7)
ED disposition		
Discharged	4 (17.4)	36 (38.3)
Admitted to wards	19 (82.6)	55 (58.5)
Admitted to ICU	0	3 (3.2)

Table 2: Details of the emergency management of study patients.
LOS: length of stay ICU: intensive care unit

Sixty-three (53.8%) patients received their first dose antibiotics during ED stay. The number of patients who received their first dose antibiotics within 120 minutes was 35 (29.9%), 28 (23.9%) of whom were delivered subsequent to blood sampling for cultures. Among patients receiving their first dose of antibiotics in the ED, the median time of antibiotic administration was 110 minutes (IQR:90-188). There was a significant difference in antibiotic initiation time between patients who received compliant care and those who did not (80.7 vs 172.5 min) (p < 0.001), and between high-risk and low-risk patients (100 vs 120 min) (p = 0.038). Advanced age (>65) (p = 0.52) and the presence of comorbidities (p = 0.1) did not influence antibiotic delivery times. The most frequently prescribed antibiotics among the study group were piperacillin/tazobactam (n = 48, 76.2%), ciprofloxacin and amoxicillin/clavulanate (n = 8,12.7%) and carbapenem (n=4, 6.3%). Forty-four patients (70%) received the antibiotics appropriate to their risk group. Delays in first antibiotic administration were not associated with poorer clinical outcomes (p = 0.26) or longer length of hospital stay (p = 0.484) in the current study. Blood cultures were obtained from 58 (49.6%) of the FN patients. The number of patients who received their antibiotics subsequent to blood sampling for microbial cultures during the ED stay was 34 (66.1%). Among those 34 patients, 28 (23.9%) patients received their antibiotic treatments within 120 minutes.

Accuracy of disposition decisions based on ANC in conjunction with MASCC score, as recommended in IDSA Guidelines was 64.1%, as shown in table 3.

	MASCC Score + ANC	
ED disposition	Low risk	High risk
	N (%)	N (%)
Discharged	17 (47)	**23 (28.4)**
Admitted	**19 (53)**	58 (71.6)
Total	36 (100)	81 (100)

Table 3: Accuracy of ED dispositions based on ANC in conjunction with MASCC scores.
P= 0.048, MASCC: Multinational Association of Supportive Care in Cancer (MASCC) ANC: absolute neutrophil count.

The percentage of study group patients who received IDSA fever and neutropenia guideline compliant care in the ED was 19.7% (n=23).

Univariate analysis showed significant differences in body temperature, total leucocyte counts, ANC, hemoglobin levels, ED LOS and time to first dose antibiotic administration between patients who received guideline compliant and non-compliant emergency care for FN (table 4).

No statistically significant relationship between IDSA compliance and advanced age (p = 0.741), tumor type (solid-hematologic) (p = 0.409), or place of residence (urban or rural) (p = 0.082) was found. In addition, we also found no relationship between guideline compliance and time of admission (p = 0.398), experience and education of the emergency physician (p=0.202), or the presence of determined fever origin during the physical examination (p = 0.99).

No independent risk factors effective for prediction of guideline compliance was identified by

logistic regression analysis using variables with type-1 error level below 25% in the univariate analysis.

Variable	Overall Compliant N=23 Mean/ median (95%CI)	Non-compliant N=94 Mean/ median (95%CI)	P
Age	54 (47.8-60.5)	60.5 (58-64)	0.215
Systolic Blood Pressure (/mm Hg)	123.7 (113-134)	129.5 (123-135)	0.277
Pulse Rate (/min)	116 (107.6-124.5)	112 (109-116)	0.445
Respiratory Rate (/min)	26.5 (24.8-28.2)	26 (24-26)	0.961
Body Temperature (˚C)	38.5 (38.4-38.8)	38.4 (38.4-38.5)	**0.036**
MASCC	18.4 (16.4-20.3)	19.3 (18.5-20.1)	0.088
Total Leucocyte (/mm³)	535 (283-1001)	1145 (966-1300)	**0.007**
Absolute neutrophil count (/mm³)	56 (16-132)	166.5 (117-264)	**0.011**
Hemoglobin (gr/dL)	10.1 (9.5-10.6)	9.4 (9-9.9)	**0.029**
CRP (mg/dL)	18 (12-23.9)	15.9 (13.8-18)	0.378
BUN (mg/dL)	15 (9.4-26.3)	16 (15-20.4)	0.212
Creatinin (mg/dL)	0.81 (0.7-1.3)	0.81 (0.8-0.9)	0.655
AST (U/L)	20 (13.4-24	22 (18-25)	0.289
ALT (U/L)	16 (10.4-28)	20.5 (17-26)	0.236
ED LOS (/min)	195 (153.5-235)	272.5 (255-344)	**0.012**
Time to antibiotic administration (/min)	80.7 (64.5-97)	172.5 (N=40) (135-200)	**0.000**
Hospital Stay (/days)	5 (N=19) (4-7)	5.5 (N=58) (4-6)	0.953

Table 4: Univariate analysis of potential variables associated with guideline compliance.

Furthermore, our study showed no significant relationship between FN guideline compliant emergency care and clinical outcome (p = 0.648) (Table 5).

Discussion

The present study evaluates compliance with the IDSA Fever and Neutropenia Guideline 2010 update for the treatment of FN at the ED of a university hospital in Turkey. Blood cultures were obtained from half of the patients. Sixty-three (53.8%) patients received their first dose antibiotics during ED stay. Only one third of the FN patients were delivered their first dose antibiotics within 120 minutes. Accuracy of disposition based on ANC and MASCC scores was 64.1%. The overall compliance rate meeting all compliance criteria was low (19.7%). However, compliance with the guidelines was not associated with worse composite clinical outcomes (p = 0.648).

Clinical outcome	Overall compliant N(%)	Non-compliant N(%)	P value
In-hospital mortality	4 (17.4)	16 (17.02)	1
Need for mechanical ventilation	2 (8.7)	4 (4.3)	0.336
Need for antibiotic change	3 (13.1)	9 (9.6)	0.702
Hospital re-admittance	2 (8.7)	11 (11.7)	1
Total	11 (47.8)	40 (42.6)	0.648

Table 5: Distribution of clinical outcomes among patients receiving guideline compliant and non-compliant emergency care .

The IDSA fever and neutropenia 2010 guidelines recommend to obtain two sets of blood cultures from all patients. In this study, blood culture samples were obtained in only 49.6% of patients. Previous studies have reported blood culture guideline compliance as high as 93-100%[10,4], and the absence of blood culture samples in this study group is a significant obstacle to compliance with IDSA guidelines. The association between blood culture guideline compliance and clinical outcome has not been previously examined in the literature[4,10]. This study also did not investigate the impact of culture results on treatment strategy and antibiotic choice.

While current guidelines do not set a clear time limit for the initiation of antibiotic therapy, patients with FN have an obvious and urgent need for antibiotics and should be identified immediately. Despite the importance of the first antibiotic dose in the treatment of FN, the time to antibiotic treatment varies widely in the available literature (145 - 300 min), with the present study reporting a relatively shorter time to treatment[4,11]. Although the rate of antibiotic administration within the first 2 hours of admission was relatively high in this study compared to previous reports (30% vs. 6%)[11], the results must be considered negative given the total

number of patients received their first dose in the ED. There are no established causes of delayed antibiotic therapy. Previous reports suggest that delays are more common among elderly and patients with comorbidities[13,14].

In the present study, advanced age and the presence of comorbidities did not significantly alter the timing of antibiotic administration. An evaluation by Lim et al. has determined that the mean duration of triage to medical care was 65 minutes. In the same study, introduction of electronic clinical guidelines for the management of FN resulted in the reduction of time to antibiotic treatment from 4.9 to 3.9 hours[10]. In the present study triage-physician time was not measured due to technical limitations. However, the ED experienced relatively low patient volume and minimal crowding during the study period, preventing unnecessary delays. Sammut et al. have compared the time to first antibiotic treatment in an oncology unit and ED (66 min. vs. 154 min.), suggesting that delays in the ED may be attributable to poor prioritization of FN patients in the ED[1].

In the present study, only 8 out of 40 FN patients discharged from the ED received their first antibiotic dose within the emergency department. Therefore, the relatively low rate of antibiotic treatment within the ED was attributed to a lack of awareness and experience among the emergency physicians. Ultimately, the results of this study suggest an urgent need for educational emphasis on FN treatment for improvement in the emergency care of these patients. The development of written protocols for FN treatment in the ED can improve awareness among physicians, accelerate laboratory work, and reduce delays in nursing practice and the application of medications.

In this study, the selection of risk group-appropriate antibiotic agents among those who received their first dose in the ED was 70%, lower than previously reported rates (Natsch et al. 82%; Courtney et al. 91% and Sammut et al. 100%)[14, 4, 1]. Wright et al. reported a risk-appropriate antibiotic selection rate of 79% in hospitalized FN patients. They suggested that FN case volume had the strongest association with guideline adherence[7]. Considering much less case volume together with time and clinical data restraints in an emergency setting, the risk-appropriate antibiotic selection of the current study may be interpreted as reasonable.

The rates of admission and discharge are important components of guideline compliance. When classifying patients according to MASCC score and profound neutropenia, we identified 81 high-risk patients who were expected to be treated in the hospital, of whom 23 (28.4%) had been discharged. FN patients are typically hospitalized and treated with parenteral antibiotics. However, with the increase in the incidence of cancer and chemotherapy modalities, outpatient treatment of FN can now be safely recommended[15,16]. The IDSA Fever and Neutropenia 2010 guidelines hold that outpatient oral therapy is appropriate for low-risk patients. A meta-analysis by Teuffel et al. concluded that outpatient FN treatment was an efficient and reliable approach[17]. Outpatient or inpatient oral antibiotic treatment for appropriate low-risk FN patients is a component of evidence based management strategy[18,19].

However, at present there are no recommendations regarding outpatient treatment of high-risk patients. Hospitalization costs[16,20] and resource limitations may necessitate outpatient treatment of some high-risk patients. In this study, disposition decision was at the discretion of the specialists other than emergency physicians. Physicians whose primary specialization is oncology are able to monitor these patients closely, taking stage of the disease and past fungal infections into account when determining prognosis of the current malignancy. In some cases, physicians may prescribe daily follow up appointment with outpatient FN patients. Hospitalization of patients with fever and prolonged neutropenia may be the most effective utilization of resources. Our hospital utilizes an outpatient parenteral treatment unit connected to the infectious disease department. This unit could be used to facilitate the scheduled parenteral treatment of the aforementioned group of patients. These factors might have contributed to disposition decisions. Consideration of patient related factors that are not components of MASCC score is also crucial when interpreting adherence rates. Thirty-two patients from our study group with low MASCC scores were hospitalized. Thirteen of these patients had severe neutropenia (ANC of <100). The remaining 19 patients were hospitalized for reasons not included in the MASCC score (mucositis, vomiting, etc.), hypoxemia, need for transfusion, lack of social support, or incompatibility with oral therapy.

In the present study, clinical outcome did not vary significantly between patients discharged inappropriately and those who were treated according to the risk-appropriate recommendations. This finding

supports the recommendation of clinical reasoning through the best choice for an individual in the era of evidence-based medicine[21].

Although a large amount of data is available for oncology and infectious disease departments regarding the treatment of FN, the recommendations for emergency care are limited[22]. Nevertheless, several previous studies have reported low compliance with guidelines for hospitalized FN patients[7,23]. In 2008, Zuckermann et al. reported an FN guideline compliance rate of 21.6%[23]. After the National Chemotherapy Advisory Group recommended door-to-antibiotic times < 1 hour for neutropenic patients, Clarke et al. reported compliance rates as low as 26%[24]. Another study evaluating hospitalized hematology and oncology patients with neutropenia and fever, reported 56.7% adherence to institutional FN management protocols. The most common source of non-adherence was the use of parenteral antibiotics by low-risk patients, who might otherwise have been prescribed oral antibiotics[25]. Sammut et al. reported significantly lower FN guideline compliance within the emergency department relative to an oncology department[1].

In the present study, compliance with FN treatment guidelines within the emergency department occurred at a rate of 19.7%. Given the differences between local protocols and international guidelines, low compliance was indeed anticipated. Potential causes of non-compliance were discussed above. However, in general we believe that the emergency setting and physician-associated factors are the most important obstacles of guideline compliance. FN is relatively rare to the emergency physician who treats various types of diseases with limited patient data, time and resources. Therefore, emergency physicians are likely to have limited experience with this condition. Our findings clearly implicate lack of awareness, poor risk assessment, and delayed initiation of antibiotic therapy as reasons for non-compliance. It is crucial the emergency physicians consider the risk of complications even among FN patients with good vital signs and generally good appearance.

Regardless of the reasons for non-compliance, it is appropriate to suggest improvements based on our study results. As a result of this study, in accordance with the recommendations of the current guidelines and recommendations[5,26] we suggest developing a corporate Emergency Department Febrile Neutropenia Management Algorithm in collaboration with associate clinics. We also suggest integration of this algorithm into hospital computer systems and recommend regular evaluation by internal quality control personnel. We believe that such initiatives have the potential to enhance physician awareness, strengthen inter-unit relations, improve laboratory and consultation response times, decrease time in the ED, and improve clinical outcomes.

Limitations

The study was conducted at a single center and the relatively small number of patients included in the study might have limited our statistical analysis. Need for vasopressors, suggesting sepsis, was not evaluated in our analysis of clinical outcome. However, the primary outcome measure of our study was compliance with the guideline, and the absence of this factor did not limit interpretation of our findings. Following ED care, data regarding the addition of granulocyte colony stimulating factors during early treatment was not included in the analysis. Similarly, we did not include data regarding the prophylactic use of antibiotics prior to the ED presentation, a factor that may have influenced selection and timing of antibiotic application. In this study, we did not record and analyze the patients according to tumor stage due to difficulties obtaining the relevant clinical records. Tumor stage is not a component of the MASCC scoring system for assessing risk of complications in FN, and this limitation is unlikely to have had a significant effect on our conclusions. Finally, even though emergency physicians were blinded to study they were aware of data collection; a critical reader will note the possible influence of the Hawthorne effect.

In conclusion, compliance with the IDSA Fever and Neutropenia Guideline 2010 Update in the treatment of FN within the ED was low in this study. Nevertheless, non-compliance with IDSA guidelines was not associated with negative clinical outcomes.

Preparing and implementing a corporate protocol for FN management in the ED in collaboration with partner clinics will improve awareness of FN among emergency physicians and contribute to improved clinical results and the efficient use of resources. Large studies evaluating the impact of local protocols according to international guidelines on clinical outcomes may support this recommendation.

References

1) Sammut SJ, Mazhar D. *Management of febrile neutropenia in an acute oncology service*. Q J Med 2012; 105: *327-36*
2) *National Confidential Enquiry Into Patient Outcome And Death. Systemic anti-cancer therapy report 2008: For better, for worse, A review of the care of patients who died within 30 days of receiving systemic anti-cancer therapy. http://www.ncepod.org.uk/2008sact.htm. access date: 30/10/2013*.
3) Vandyk AD, Harrison MB, Macartney G, Ross-White A, Stacey D. *Emergency department visits for symptoms experienced by oncology patients: a systematic review*. Support Care Cancer 2012; 20: *1589-99*
4) Courtney DM, AldeenAZ, GormanSM, HandlerJA, TrifilioSM, et al. *Cancer associated neutropenic fever: clinical outcome and economic costs of emergency department care*. Oncologist 2007; 12: *1019-26*
5) Freifeld AG, Bow EJ, Sepkowitz KA, Boeckh MJ, Ito J I, et al. *Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America*. Clin Infect Dis 2011;5 2: *56-93*
6) Flowers C R, Seidenfeld J, Bow EJ, Karten C, Gleason C, et al. *Antimicrobial prophylaxis and outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology Clinical Practice Guideline*. J Clin Oncol 2013; 31: *794-810*.
7) Wright JD, Neugut AI, Ananth CV, Lewin SN, Wilde ET, et al. *Deviations from Guideline-Based Therapy for Febrile Neutropenia in Cancer Patients and Their Impact on Outcomes*. JAMA Intern Med 2013; 173: *559-68*.
8) Danova M, Rosti G, De Placido S, Bencardino K, Venturini M. *Use of granulocyte colony-stimulating factor: survey among Italian medical oncologists*. Oncol Rep. 2005; 14: *1405-12*.
9) Freifeld A, Sankaranarayanan J, Ullrich F, Sun J. *Clinical practice patterns of managing low-risk adult febrile neutropenia during cancer chemotherapy in the USA*. Support Care Cancer. 2008; 16: *181-91*.
10) Lim C, Bawden J, Wing A, Villa-Roel C, Meurer D. P, et al. *Febrile neutropenia in EDs: the role of an electronic clinical practice guideline*. Am J Emerg Med. 2012; 30: *5-11*.
11) Szwajcer D, Czaykowski P, Turner D. *Assessment and management of febrile neutropenia in emergency departments within a regional health authority-a benchmark analysis*. Curr Oncol. 2011; 18: *280-4*.
12) Klastersky J, Paesmans M, Rubenstein EB, Boyer M, Elting L, et al. *The Multinational Association for Supportive Care in Cancer risk index: a multinational scoring system for identifying low-risk febrile neutropenic patients*. J Clin Oncol 2000; 18: *3038-51*.
13) Nirenberg A, Mulhearn L, Lin S, Larson *E. Emergency department waiting times for patients with cancer with febrile neutropenia: a pilot study*. Oncol Nurs Forum 2004;3 *1: 711-15*.
14) Natsch S, Kullberg BJ, van der Meer JW, Meis JF. *Delay in administering the first dose of antibiotics in patients admitted to hospital with serious infections*. Eur J Clin Microbiol Infect Dis 1998; 17: *681-4*.
15) Malik IA, Abbas Z, Karim M. *Randomised comparison of oral ofloxacin alone with combination of parenteral antibiotics in neutropenic febrile patients*. Lancet 1992; 339: *1092-6*.
16) Elting LS, Lu C, Escalante CP, Giordano SH, Trent JC, et al. *Outcomes and cost of outpatient or inpatient management of 712 patients with febrile neutropenia*. J Clin Oncol 2008; 26: *606-11*.
17) Teuffel O, Ethier MC, Alibhai SM, Beyene J, Sung L. *Outpatient management of cancer patients with febrile neutropenia: A systematic review and meta-analysis*. Ann Oncol 2011; 22: *2358-65*.
18) Debey C, Meert AP, Berghmans T, Thomas JM, Sculier JP. *Febrile neutropenia at the emergency department of a cancer hospital]*. Rev Med Brux 2011; 32: *74-82*. [abstract].
19) Lingaratnam S, Slavin MA, Mileshkin L, Solomon B, Burbury K, et al. *An Australian survey of clinical practices in management of neutropenic fever in adult cancer patients 2009*. Intern Med J 2011; 41: *110-20*.
20) Caggiano V, Weiss RV, Rickert TS, Linde-Zwirble WT. *Incidence, cost, and mortality of neutropenia hospitalization associated with chemotherapy*. Cancer 2005; 103: *1916-24*.
21) Sniderman AD, LaChapelle KJ, Rachon NA, Furberg CD. *The necessity for clinical reasoning in the era of evidence-based medicine*. Mayo Clin Proc 2013; 88: 1*108-14*
22) Perrone J, Hollander JE, Datner EM. *Emergency Department evaluation of patients with fever and chemotherapy-induced neutropenia*. J Emerg Med 2004; 27: *115-9*.
23) Zuckermann J, Moreira LB, Stoll P, Moreira LM, Kuchenbecker RS, Polanczyk CA. *Compliance with a critical pathway for the management of febrile neutropenia and impact on clinical outcomes*. Ann Hematol 2008; 87: *139-45*.
24) Clarke RT, Warnick J, Stretton K, Littlewood TJ. *Improving the immediate management of neutropenic sepsis in the UK: lessons from an ational audit*. Br J Haematol 2011; 153: *773-9*.
25) Jin J, Lee YM, Ding Y, Koh LP, Lim SE, Lim R, et al. *Prospective audit of febrile neutropenia management at a tertiary university hospital in Singapore*. Ann Acad Med Singapore 2010; 39: *453-9*.
26) *NCAG. Chemotherapy Services in England: Ensuring quality and safety A Report from the National Chemotherapy Advisory Group. UK: Department of Health,2009http://webarchive.nationalarchives.gov.uk/+/www.dh.go.uk/en/publicationsandstatistics/publications/dh_104500*

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