INTRODUCTION
Incorrect use of colony stimulating factors (CSF) can add unnecessary cost to cancer treatments and advance side to patients. We conducted an epidemiological study to assess the correlation between CSF use recommendations issued by the Brazilian Regulatory Agency of Health (ANS) and technical recommendations established by international guidelines. We also analyzed the main reasons for not recommending the use of CSF, in patients during chemotherapy.

METHODS: Data on patients treated with CSF during 2014 was retrieved from Evidências – Kantar Health database of administrative claims, which comprises more than 4 million people and 68 Private Health Insurance Companies (PHI) in Brazil. Demographic assessment, type of tumor, number of patients, treatment purpose, technical recommendations, ANS recommendation, reasons for not recommending and class of requested CSF were assessed.

RESULTS: We retrieved 440 CSF requests corresponding to 322 patients. 188 requests were recommended both technically and supported by AHS. In 160 CSF use was not recommended either with guidelines or ANS and only 30 claims were in discordance, if CSF was use was recommended by guidelines but not by ANS. Reasons for technical non-recommendation were: requests for primary prophylaxis on chemotherapy regimens with risk of febrile neutropenia below 20%, and complicated neutropenia (FN) in palliative care setting or request based on complete blood count (CBC) collected at the route of chemotherapy.

CONCLUSIONS: Administrative-recommendations from ANS are in close agreement with the scientific literature. Nevertheless, despite clear international guidelines and ANS recommendations, these findings indicate the need for further education and training interventions for CSF. Continual medical education on this topic should emphasize the following of protocols to ensure proper CSF use.

RESULTS

General Aspects
In the aforementioned period, 440 requests for CSF corresponding to 322 patients were retrieved from Evidências – Kantar Health database of administrative claims, which comprise more than 4 million people and 68 Private Health Insurance Companies (PHI) in Brazil. The goal of the present study was to evaluate the patterns of CSF use in the Private Healthcare System (PHS) in Brazil.

Types of Data Collected:
- Demographics, geographic origin of the patients, number of CSF requests input on the database, types of tumor, number of patients, treatment purpose (adjunct, neoadjuvant, palliative, for bone marrow transplantation), etc.
- Technical recommendation: if the treatment was supported by international guidelines
- ANS recommendation: if the CSF indication was supported by the Regulatory Agency
- Reasons for not recommending the treatment
- Class of CSF requested

Origin
Regarding requests according to geographical region, there were: 143 from the South, 205 (50%), 63 (12%) from the Southeast, 20 (5%) from the Northeast and none from the North Region (see Figure 3).

Tumor Types
All the tumor types, CSF was requested mainly for breast cancer (80 requests), non-Hodgkin’s lymphoma (47), leukemia (45) and myelodysplastic syndrome/myeloma (46).

CSF was also requested for patients diagnosed with: gynecological tumors (28 requests), Hodgkin’s lymphoma (25), colon cancer (25), Ewing’s sarcoma (13), engrafted/grafted tumors (11) and urological cancers (28). Forty-four requests were distributed among other types of cancer (see Table 1 and Figure 3).

Treatment Purpose
Regarding the purpose of chemotherapy treatments in which CSF were added: 104 were aggressive therapies, 164 adjuvant therapies, 164 palliative, 164 transplantation, 32 hematological (hematological treatments) and 21 bone marrow transplantations (see Figure 4).

Agreement with Guidelines and ANS
Except for requests linked to bone marrow transplantations, which are not regulated by INSS, all the other ones were assessed:
- 168 were recommended by ANS and supported by the literature
- 80 were not recommended neither by guidelines nor ANS supported by the literature
- 30 were not recommended by ANS but were supported by the literature

Reasons for Pre-autorization Denial
- Request of CSF for patients in chemotherapy with less than 20% risk of febrile neutropenia and no complications (79 requests), 7% of denials
- First measure of treatment for neutropenic patients in palliative chemotherapy (32 requests), 20% of denials.
- Complete blood count (CBC) collected on chemotherapy’s route (17 to 30 days post infusion) to justify the need for CSF (24 requests, 20% of all denials). That was a regular practice in the PHS.
- CBC without signs of neutropenia (neutrophils were ≥ 2,500 cells/mm^3) (9 requests, 4.5% of denials).
- Treatment of uncomplicated low-risk neutropenia (10 requests, 5% of denials).
- CSF requested for patients who were not receiving chemotherapy or were about to be submitted to orthopedic surgery (9 requests, 2% of denials).

Table 1. Number of Requests According to Tumor Type

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Number of Requests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer</td>
<td>80</td>
</tr>
<tr>
<td>Non-Hodgkin’s Lymphoma</td>
<td>85</td>
</tr>
<tr>
<td>Hodgkin’s Lymphoma</td>
<td>25</td>
</tr>
<tr>
<td>Colon Cancer</td>
<td>25</td>
</tr>
<tr>
<td>Ewing’s Sarcoma</td>
<td>19</td>
</tr>
<tr>
<td>Graft/Engrafted/Grafted Tumors</td>
<td>31</td>
</tr>
<tr>
<td>Myelodyplastic/Hodgkin’s Lymphoma</td>
<td>22</td>
</tr>
<tr>
<td>Others</td>
<td>87</td>
</tr>
<tr>
<td>Total</td>
<td>440</td>
</tr>
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CONCLUSION
Three real-world data allowed us to identify that there is still an important knowledge gap regarding the correct use of CSF. The most common misconceptions or uncoordinated practices were:
- Incorrect timing to collect CBC in the course of chemotherapy
- Lack of knowledge on which chemotherapy regimens need prophylaxis
- Tendency to use CSF as first measure of treatment in patients on palliative therapy
- Uncertainty about the correct level of neutrophils that justify a request for CSF
- Misuse of CSF to treat uncomplicated, low-risk febrile neutropenia

We also observed that there is a high rate of agreement between the regulatory recommendations (ANS) and the scientific literature (medical and surgical guidelines).

Almost three quarters of the requests are for one specific brand of CSF.

Despite the vast amount of information on febrile neutropenia available both in printing and online, there is need for further educational activities on this topic. Continual medical education programs must address this gap, to avoid damage to patients and waste of healthcare systems.

REFERENCES