

Pegfilgrastim OBI device use for neutropenia prevention: a scoping review

Uso do dispositivo Pegfilgrastim OBI para prevenção de neutropenia: revisão de escopo

Uso del dispositivo Pegfilgrastim OBI para prevenir la neutropenia: revisión de alcance

Vivian do Prado Martins¹  <https://orcid.org/0000-0003-3850-6317>

Karina Dal Sasso Mendes¹  <https://orcid.org/0000-0003-3349-2075>

Bruna Nogueira dos Santos¹  <https://orcid.org/0000-0002-1939-6194>

Bruno Andraus Filardi²  <https://orcid.org/0000-0002-8535-0338>

Letícia Genova Vieira¹  <https://orcid.org/0000-0002-9780-4309>

Renata Cristina de Campos Pereira Silveira¹  <https://orcid.org/0000-0002-2883-3640>

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Descritores

Neutropenia; Neutropenia febril induzida por quimioterapia; Prática clínica baseada em evidências; Filgrastim; Antineoplásicos; Neoplasias

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Corresponding author

Renata Cristina de Campos Pereira Silveira
E-mail: recris@eerp.usp.br

Associate Editor (Peer review process):

Edvane Birelo Lopes De Domenico
(<https://orcid.org/0000-0001-7455-1727>)
Escola Paulista de Enfermagem, Universidade Federal de São Paulo, São Paulo, SP, Brazil

Abstract

Objective: To map the health care of Pegfilgrastim On-body Injector in neutropenia prevention in adults with cancer in home care after outpatient chemotherapy.

Methods: This is a scoping review based on the JBI methodology. Only studies with adults with cancer undergoing outpatient chemotherapy were included. The search was carried out in the Cochrane, CINAHL, EMBASE, LILACS, PubMed, Scopus, LIVIVO and Web of Science databases, in addition to gray literature ProQuest, SciELO, Database in Nursing, Google Scholar, Open Grey, drug leaflet and websites. The searches in the references of selected studies were exhausted. All identified studies were exported to the EndNote reference manager for organization and removal of duplicates. The Rayyan web application was used for evidence selection. The studies were selected by pairs independently, with conflicts resolved by a third researcher.

Results: A total of 10 articles were included, whose results were subdivided into categories: patient compliance, health team opinion, patient workload in cancer treatment and device use in clinical practice. The device has few flaws and was accepted by health care teams and patients in most studies.

Conclusion: The main health care for Pegfilgrastim On-body Injector use is related to the skin preparation technique where the device will be applied, in addition to device preparation and administration. Moreover, the importance of assessing the knowledge of patients and their family about the device is highlighted, providing all the necessary guidelines, verbally and in writing, clearly and objectively, and validating this information, making sure that patients have understood all of them and are safe.

Resumo

Objetivo: Mapear os cuidados em saúde do dispositivo *Pegfilgrastim on-body injector* na prevenção de neutropenia em adultos com câncer em assistência domiciliar após quimioterapia ambulatorial.

Métodos: Revisão de escopo baseada na metodologia do *Joanna Briggs Institute*. Foram incluídos somente estudos com adultos com câncer submetidos à quimioterapia ambulatorial. A busca foi realizada nas bases de dados Cochrane, CINAHL, EMBASE, LILACS, PubMed, Scopus, LIVIVO e Web of Science, além da literatura cinzenta ProQuest, Scielo, Banco de Dados em Enfermagem, Google Scholar, Open Grey, bula do medicamento e *websites*. Foram esgotadas as buscas nas referências dos estudos elegidos. Todos os estudos identificados foram exportados para o gerenciador de referências EndNote para organização e remoção das duplicadas. Utilizou-se o aplicativo *web* Rayyan para seleção das evidências. Os estudos foram selecionados por pares e de forma independente, sendo os conflitos solucionados por um terceiro pesquisador.

¹Escola de Enfermagem de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, Brazil.

²Department of Genetics, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, Brazil.

Conflicts of interest: nothing to declare.

Resultados: Foram incluídos 10 artigos cujos resultados foram subdivididos nas categorias: adesão do paciente, opinião da equipe de saúde, carga de trabalho do paciente em tratamento do câncer e uso do dispositivo na prática clínica. O dispositivo apresenta poucas falhas e foi aceito pelas equipes de saúde e pacientes na maioria dos estudos.

Conclusão: Os principais cuidados em saúde para o uso do dispositivo *Pegfilgrastim on-body injector* estão relacionados à técnica de preparo da pele onde o dispositivo será aplicado, o preparo e a administração do dispositivo. Além disso, salienta-se a importância da avaliação do conhecimento do paciente e seu familiar sobre o dispositivo, o fornecimento de todas as orientações necessárias, verbalmente e por escrito, de forma clara e objetiva, e a validação dessas informações, certificando-se que o paciente compreendeu todas elas e está seguro.

Resumen

Objetivo: Mapear los cuidados de la salud al utilizar el dispositivo *Pegfilgrastim on-body injector* para prevenir la neutropenia en adultos con cáncer en atención domiciliar después de quimioterapia ambulatoria.

Métodos: Revisión de alcance basada en la metodología del *Joanna Briggs Institute*. Se incluyeron solamente estudios con adultos con cáncer sometidos a quimioterapia ambulatoria. La búsqueda se realizó en las bases de datos Cochrane, CINAHL, EMBASE, LILACS, PubMed, Scopus, LIVIVO y Web of Science, además de la literatura gris ProQuest, Scielo, Banco de Datos de Enfermería, Google Scholar, Open Grey, prospecto del medicamento y sitios web. Se concluyeron las búsquedas en las referencias de los estudios seleccionados. Todos los estudios identificados se exportaron al programa de gestión de referencias EndNote para organizarlas y remover las duplicadas. Se utilizó la aplicación *web Rayyan* para seleccionar las evidencias. Se seleccionaron los estudios por pares y de forma independiente, y los conflictos se solucionaron mediante un tercer investigador.

Resultados: Se incluyeron diez artículos cuyos resultados fueron subdivididos en las siguientes categorías: adhesión del paciente, opinión del equipo de salud, carga de trabajo del paciente en tratamiento de cáncer y uso del dispositivo en la práctica clínica. El dispositivo presenta pocas fallos y fue aceptado por los equipos de salud y por los pacientes en la mayoría de los estudios.

Conclusión: Los principales cuidados de la salud para el uso del dispositivo *Pegfilgrastim on-body injector* se relacionan con la técnica de preparación de la piel donde se aplicará el dispositivo, la preparación y la administración del dispositivo. Además, se destaca la importancia de la evaluación de conocimientos del paciente y su familiar sobre el dispositivo, la entrega de todas las instrucciones necesarias, verbalmente y por escrito, de forma clara y objetiva, la validación de la información y la verificación de que el paciente haya comprendido todo y esté seguro.

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Introduction

Cancer is one of the main public health problems today, with an estimate of approximately 19.3 million new cases and about 10.0 million deaths in 2020.⁽¹⁾ Antineoplastic chemotherapy, the main modality of cancer treatment, is used alone or in combination with the surgical procedure and/or radiotherapy and/or immunotherapy. However, antineoplastic agents cause cell death and, consequently, toxicities in different organs and structures.⁽²⁾

Hematological toxicities arising from anti-neoplastic therapy are characterized by hematopoietic tissue myelosuppression, which occurs in the occurrence of neutropenia and leukopenia. Chemotherapy-induced neutropenia, classified by an absolute circulating neutrophil count below 2,000 cells/mm³, is the most common toxicity observed in patients undergoing antineoplastic chemotherapy.⁽³⁾

It should be noted that neutropenia is a predisposing risk factor for severe infection and has the potential to prolong hospitalization and rehospitalization, in addition to increasing the mortality of

patients with cancer, as it can cause delays or reductions in chemotherapy dose, compromising its effectiveness.⁽⁴⁾

Current guidelines in the United States of America and Europe recommend using Granulocyte Colony Stimulating Factor (G-CSF) when the risk of febrile neutropenia resulting from the chemotherapy protocol is greater than or equal to 20%. G-CSF increases proliferation and differentiation of neutrophils from committed progenitor cells, inducing maturation, enhancing the survival and function of mature neutrophils, resulting in increased neutrophils and therefore reduced occurrence, duration, and severity of neutropenia.^(5,6)

In Brazil, two presentations of G-CSF are commonly used: Filgrastim and Pegfilgrastim. Pegfilgrastim is the long-acting form of Filgrastim, i.e., it requires a single application per chemotherapy cycle. In addition to low renal clearance, clinical trials have shown that just one injection per chemotherapy cycle of Pegfilgrastim was as safe and effective as 11 daily injections of Filgrastim for reducing neutropenia and its complications in breast patients with cancer with a myelotoxic protocol.⁽⁷⁾

However, both Filgrastim and Pegfilgrastim are administered in subcutaneous applications with a pre-filled syringe, 27 hours after the end of chemotherapy and in different circumstances, such as by the oncology service itself, in other health services such as primary and secondary care or by patients and their family, after receiving training to administer the injection at home, all within the outpatient setting.⁽⁷⁾ The nursing team's work is of fundamental importance in this context, as it is responsible for application, teaching patients about management and toxicities, and adverse event monitoring.

Pegfilgrastim On-body Injector (OBI) (Neulasta® Onpro®) device was approved by the Brazilian National Health Regulatory Agency (ANVISA - *Agência Nacional de Vigilância Sanitária*) on June 29, 2020 as part of the chemotherapy regimen. It is a patch that must be applied to patients' skin. Such technology has an automatic application system of the G-CSF dose with subcutaneous injection, which starts 27 hours after the end of intravenous chemotherapy, with an application duration of approximately 40 minutes, with the end of administration announced through a message digital alarm.⁽⁷⁻⁹⁾

Given the regularization of Pegfilgrastim OBI use in the Brazilian context,⁽⁸⁾ it is necessary to compile and understand evidence in literature regarding device effectiveness, nursing care during application, teaching and patient compliance as well as of care required after using the technology, since no previous scoping review related to this innovative theme was found in the literature.

Thus, this study, based on the premise of evidence-based practice in health, with a view to promoting safety and quality of care for patients with cancer, aimed to map health care for Pegfilgrastim OBI use in neutropenia prevention in adult patients with cancer receiving home care after outpatient chemotherapy.

Methods

This is a scoping review based on the JBI⁽¹⁰⁾ methodology and reported in accordance with the guide

Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews (PRISMA-ScR).⁽¹¹⁾ The protocol of this review was registered with the Open Science Framework (OSF)⁽¹²⁾ under DOI: 10.17605/OSF.IO/E2XF5.

The guiding question of this review was: What are the health precautions for Pegfilgrastim OBI use for neutropenia prevention in adult patients with cancer in home care after outpatient chemotherapy? This question was formulated based on the PCC strategy,⁽¹⁰⁾ where P (Population): adult patients with cancer undergoing outpatient chemotherapy; C (Concept): health care for Pegfilgrastim OBI use in neutropenia prevention; and C (Context): patients in outpatient care, with home care after chemotherapy.

The selection criteria were established based on the guiding question based on the PCC strategy. Indexed or non-indexed studies were included, such as articles, undergraduate course completion papers, congress abstracts, book chapters, books, editorials, letters to the editor, among others, carried out with (P) adults (age greater than or equal to 18 years) diagnosed with cancer undergoing outpatient chemotherapy, (C) using Pegfilgrastim OBI to prevent neutropenia, (C) assisted in an outpatient clinic and at home after chemotherapy. Studies that did not address Pegfilgrastim OBI, that did not investigate health care related to Pegfilgrastim OBI, whose abstracts were not found, and duplicate studies, were excluded, as they were considered only once.

The search was carried out in the Cochrane Central Register of Controlled Trials (Cochrane), Cumulative Index to Nursing and Allied Health (CINAHL), EMBASE (Elsevier Science), Latin American and Caribbean Literature in Health Sciences (LILACS), US National Library of Medicine (PubMed), Scopus, The Search Portal for Life Sciences (LIVIVO), SciELO, Database in Nursing – Brazilian Bibliography (BDENF) and in the main collection of Web of Science. Moreover, a search in gray literature was included, such as in ProQuest, Open Grey, Google Scholar and drug leaflet. A manual search was also carried out on non-governmental reference websites in oncology and on relevant websites with available guides and

protocols related to care with Pegfilgrastim OBI. Finally, the searches in the references of the chosen studies were exhausted.

The search strategy was developed from controlled and uncontrolled descriptors as well as keywords, present in the thesaurus of MeSH, DeCS, Titles Cinahl and Emtree. Once the terms referring to the PCC acronym were selected, several tests were carried out, with few or no records in information sources. Thus, it was decided to keep only the elements of the search strategy referring to the concept and, during the selection of title and full abstract, the population and context elements were considered, in order to identify studies relevant to the proposed review. Using the Boolean operator (OR), a unique search strategy was developed, validated by three researchers, one with expertise in the subject, another with expertise in the subject and method, and a third with expertise in the method. This strategy was adapted to the databases, according to the example of the search carried out in PubMed, described below: (“on-body injector” [all fields] OR “on-body Pegfilgrastim” [all fields] OR “Pegfilgrastim OBI” [all fields] OR “neulastim OBI” [all fields] OR “neulastim on-body injector” [all fields]). It should be noted that, during the searches, language filters or publication period were not selected. After validity and definition of the search strategy, it was carried out on April 30, 2021 and updated on June 3, 2022 by a single researcher.

All studies identified in the databases were exported to the EndNote Desktop reference manager version X7.9* (Thomson Reuters) for organization and removal of duplications.⁽¹³⁾ Then, the records were imported into the Rayyan web application for reading the titles and abstracts and selecting the studies for full reading. This step was performed by two independent researchers, in a masked manner. Conflict resolution was the responsibility of another researcher with expertise in the subject.⁽¹⁴⁾

In the second phase of selection, each eligible publication was read in full. Also, by two independent and blindly selected researchers. A third researcher, with expertise in the research theme and in

the review method, reached consensus and resolved conflicts.

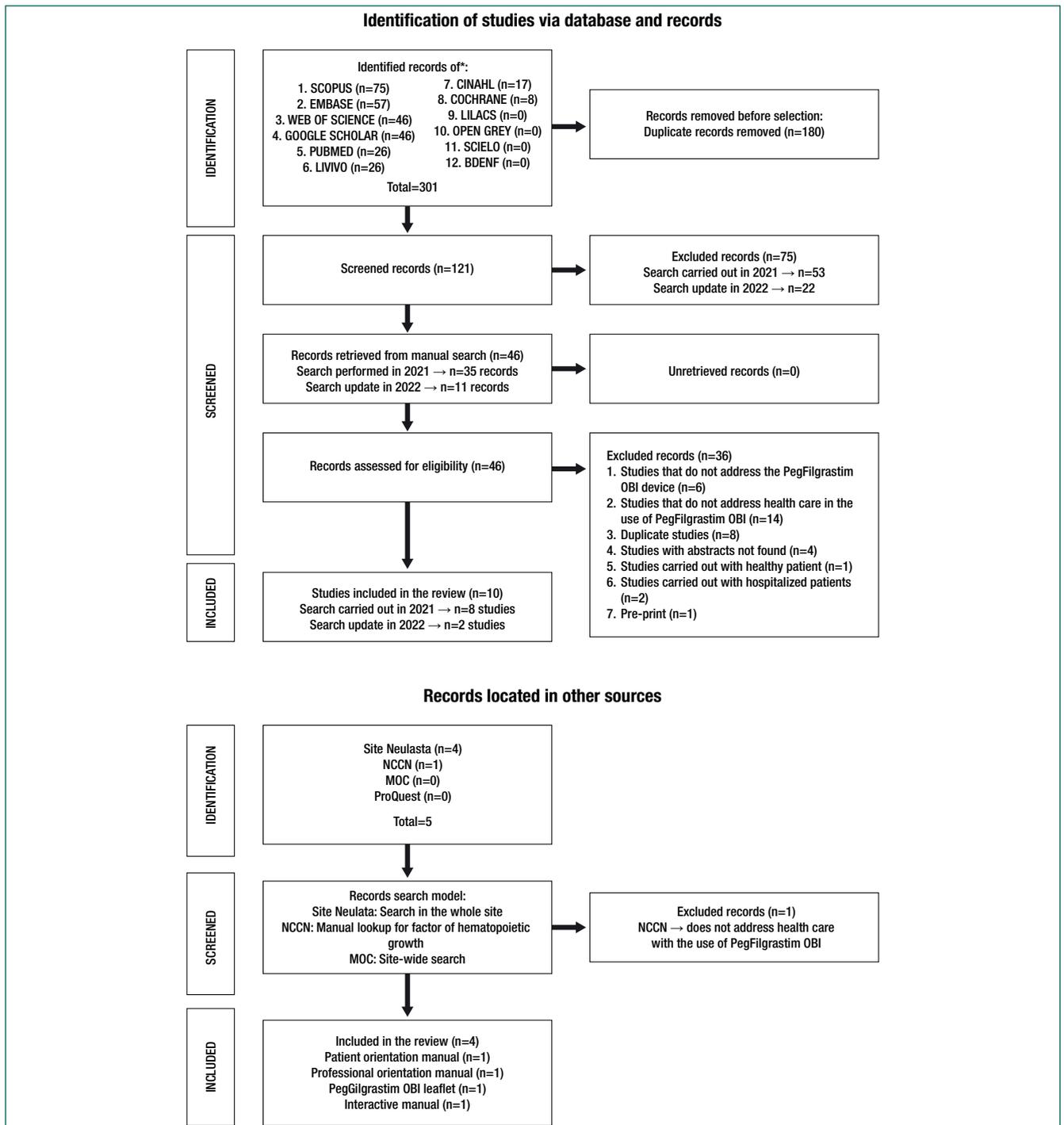
For data extraction from the included publications, an adapted script was applied, containing information such as authorship, year of publication, country of publication, study design, objective, method, main results, conclusion and information about limitations of studies. Data collection was mapped by a researcher and validated by a second reviewer. Data synthesis occurred in a descriptively.

Results

The database search identified 301 records. After a peer selection process, 10 included articles were selected, as described in Figure 1.

The results of the sources of evidence were described separately, in order to corroborate the heterogeneity of identified data. The first description refers to the results from the studies derived from the databases, which are described in Chart 1. The second part of results originates from other sources, such as websites, package inserts and manuals, and is presented in Chart 2, in order to contribute with relevant information for users of this treatment technology (patients) and for care in device application. Ten studies from the databases were included in this review (Chart 1) and divided into four categories: patient compliance with device use and their experience with Pegfilgrastim OBI use; health team’s opinion (physicians and nurses) about the device use, both in terms of effectiveness and in organization of service; workload of patients undergoing cancer treatment; and device use in clinical practice.

Of the included studies, 80% (n=8) were published in the United States of America^(15,16,19-24) and 20% (n=2) in Germany.^(17,18) This distribution shows that the source of knowledge in the area of neutropenia, such as toxicity of chemotherapy treatment, is mostly North American and that no Brazilian study on Pegfilgrastim OBI use was published during this knowledge synthesis. A synthesis of evidence from the Pegfilgrastim OBI package



Source: Prepared by the author, adapted from Tricco et al. (2018).⁽¹¹⁾

Figure 1. Study selection diagram according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews (PRISMA- ScR) Checklist

insert,⁽²⁵⁾ the official website,⁽²⁶⁾ the health care professional manual⁽²⁷⁾ and the patient manual⁽²⁸⁾ are presented in Chart 2, in order to provide immediate access and didactically compile the information found in this study.

Discussion

Since it is an innovative theme and still little explored in the literature, this scoping review was able to synthesize several types of evidence related to

Chart 1. Synthesis of results of studies from the databases

Category 1- Patient experience and opinion regarding Pegfilgrastim OBI use				
Author	Objective	Method	Population	Results
Lisa S. (2016) ⁽¹⁵⁾ USA	Test the safety and efficacy of Pegfilgrastim OBI in an infusion center and educate the nursing team to manage the device.	Pilot study. Nursing team training with a practical demonstration on how to handle the device. Patients received an information leaflet to read, watched a video and were followed up 48 hours after OBI infusion to ensure the success of the injector. Laboratory tests were obtained one week later.	25 patients on outpatient chemotherapy.	The injector was successful in all participants. An incomplete dose was delivered to one patient and three patients were hospitalized within a week of Neulasta injection. None of these events were considered injector related.
Saif et al. (2019) ⁽¹⁶⁾ USA	Assess the acceptance of the Onpro kit among patients undergoing chemotherapy.	Descriptive, retrospective study with patients who received the Onpro kit within 1 hour of completion of systemic chemotherapy. Nursing notes and pharmacy records were reviewed to identify patients who refused the Onpro kit and to discern reasons for refusal, including racial reason.	Patients with gastrointestinal tumors undergoing G-CSF.	Five of 68 patients refused the kit (22%), of which 87% were Asian. Reasons for refusal included: aversion to bulky compliance with the skin, understanding about unwitnessed medication administration, fear of reaction, disposal at home, fear of pain, and lack of confirmation of proper dose administration.
Category 2: Patient and health team experience and opinions regarding Pegfilgrastim OBI use				
Author	Objective	Method	Population	Results
Brett Hauber et al. (2018) ⁽¹⁷⁾ Germany	Estimate patient and physician preferences Pegfilgrastim administration options and the relative importance of the resources associated with these options to determine systematic variations in physicians' preferences according to patients' profile.	Cross-sectional. Application of a multiple-choice data collection instrument about Pegfilgrastim administration options.	200 patients and 200 physicians prescribing G-CSF	Most patients (77.5%) preferred to receive application at the clinic and 16% of patients chose the OBI. Patients generally preferred the administration option with which they had experience: 48.5% of patients who received prior injections at the clinic chose this route and 56.8% with prior OBI administration preferred this option. For the most clinically committed patient with a longer travel distance to the clinic, 37.5% of physicians preferred in-clinic application and 49.5% preferred the OBI. For the less clinically committed patient and with the shortest travel distance to the clinic, 55.5% of physicians preferred application in the clinic, and 28%, the OBI.
Metz et al. (2021) ⁽¹⁸⁾ Germany	Assess patient, nurse, and physician preferences as well as health care economics, for administering Pegfilgrastim with OBI or manually using a pre-filled syringe (OS).	Randomized, crossover, non-blinded, two-arm clinical trial. Patients with breast cancer x patients with non-Hodgkin's lymphoma, 1:1, were randomized to receive Pegfilgrastim for four consecutive cycles of chemotherapy in an alternating sequence, starting with OBI or pre-filled syringe. The primary outcome was patient preference assessed by questionnaires.	308 patients with early-stage breast cancer receiving anthracycline/ cyclophosphamide or taxane-based chemotherapy, and patients with non-Hodgkin's lymphoma receiving first-line R-CHOP.	Patients preferred OBI over pre-filled syringe (OBI 43.2%; vs. pre-filled syringe 36.0%), but the difference was not statistically significant. Among patients with preference for OBI, saving time was the main reason for preference. Both arms of the study showed the same results, indicating that patients' preference is independent of application sequence. Study nurses slightly preferred the pre-filled syringe (n = 19, 46.3%) over the OBI (n = 18, 43.9%) Physicians clearly preferred the pre-filled syringe (n = 24, 58.8%) over the OBI (n = 15, 36.6%).
Mahler et al. (2017) ⁽¹⁹⁾ USA	Monitor the execution Onpro delivery system in an oncology clinic.	A satisfaction survey was carried out with patients.	38 patients with cancer using Pegfilgrastim OBI and nursing staff from the oncology clinic.	Of 38 participants, 6 reported a problem using the OBI. On a scale of 1 (not satisfied) to 5 (extremely satisfied), 32 patients rated their satisfaction as 4 or 5, and only 2 were dissatisfied with the OBI. Nurses had no difficulties in placing the device. Failed devices were returned by patients and replaced under the Amgen® refund program. There was an improvement in the clinic's workflow.
Yucel et al. (2021) ⁽²⁰⁾ USA	Develop a Satisfaction and Experience Questionnaire for G-CSF (SEQ-G-CSF) to help understand perspectives and patient satisfaction with different G-CSF options.	Descriptive study with a qualitative approach. All patients were receiving prophylaxis with G-CSF via injection or OBI. The sample was divided into 2 groups, with group 1 comprising 20 participants with previous experience using Pegfilgrastim OBI and group 2 comprising 20 participants with no prior experience. Both participated in focus groups conducted by video with online calls and semi-structured discussions.	Three oncology nurses and 40 adult patients with cancer, 10 with breast cancer, 10 with lung cancer, 10 with non-Hodgkin's lymphoma and 10 with prostate cancer.	Discussing their experience and satisfaction with the G-CSF, 53% of patients and 29% of participants highlighted the benefits of using the OBI, including convenience, ease of use, available support, and reduced travel and time overhead. The most cited negative experiences were adverse events (lethargy and fatigue) and the need to undergo additional treatment. The SEQ-G-CSF included five domains involving overall satisfaction (one item), treatment burden (four items), travel burden (two items), time burden (four items), and compliance with treatment (two items). Nurses reported that patients tend to tolerate adverse treatment events when they see improvement or if their quality of life is not significantly impacted.
Category 3 - Workload of patients undergoing cancer treatment				
Author	Objective	Method	Population	Results
Cheng et al. (2019) ⁽²¹⁾ USA.	Assess dimensions of treatment workload related to outpatient visits, commuting, and admissions.	Descriptive, quantitative study. The authors developed measures to measure the workload of the days when patients go to the health service for treatment and their displacement. They then applied these methods to two populations of breast patients with cancer to determine whether the measures were sensitive to differences in disease stage and treatment protocols.	Women at different stages and undergoing treatment for breast cancer.	Patients with more advanced cancers experienced a greater treatment workload. In the first 18 months after diagnosis, patients with stage III disease spent a median of 81 hours in outpatient clinics, 61 hours in commuting time, and spent \$1,432 in commuting costs. In contrast, patients with stage I disease spent an average of 29 hours in the clinic, 34 hours in travel time, and \$834 in travel costs. Authors emphasize that Pegfilgrastim OBI was effective in reducing some dimensions of the workload for these patients, such as, for example, the time in days that patients stay in the clinic and the need for additional visits.

Continue...

Continuation.

Category 4 - Pegfilgrastim OBI use in clinical practice				
Author	Objective	Method	Population	Results
Patel et al. (2019) ⁽²²⁾ USA	Assess the incidence of febrile neutropenia in patients receiving Pegfilgrastim OBI.	Observational, descriptive and quantitative study. A retrospective review of electronic medical records of adult patients with cancer who received chemotherapy and Pegfilgrastim OBI was performed. Before a patient receives the OBI device, the nursing staff has been educated and trained. The primary outcome was the development of febrile neutropenia. Secondary outcomes included Pegfilgrastim OBI device failure and treatment delays or dose modifications secondary to febrile neutropenia or neutropenia event. Patients were followed for up to 30 days after the last chemotherapy administration to assess the occurrence of any study parameters.	28 adult patients with cancer on myelosuppressive chemotherapy.	Pegfilgrastim OBI were administered during the study period. All patients received Pegfilgrastim OBI as primary prophylaxis and none of the participants developed febrile neutropenia. There were no treatment delays or changes in chemotherapy dose secondary to a febrile neutropenia or neutropenia event. - There were two device failures (1.92%). Failure 1: A patient observed a malfunction in the device's indicator light, yet received the full dose. Failure 2: The Pegfilgrastim dose was not administered correctly, and it was reported that the Pegfilgrastim leaked down patients' arm. One case of anaphylaxis has been reported after receiving Pegfilgrastim OBI.
Mahtani et al. (2022) ⁽²³⁾ USA	Assess the incidence of febrile neutropenia in patients who received treatment with curative intent, patients undergoing chemotherapy with delays or dose reduction and compliance with the device.	Prospective, multicenter cohort study. Patients were followed from baseline until death, discontinuation of chemotherapy, withdrawal of consent, loss to follow-up, or termination of the study.	Patients with cancer receiving myelosuppressive chemotherapy treatment and at high risk of developing febrile neutropenia.	In all cycles, the incidence of febrile neutropenia was lower in patients receiving Pegfilgrastim OBI (4.4% [95% CI, 3.3-5.6%]) compared to those who received other options (7.4% [95% CI 5.3-9.6%]). The OBI group had a lower incidence of febrile neutropenia in each cycle. In patients receiving treatment with curative intent, the incidence of febrile neutropenia in all cycles was lower in those receiving Pegfilgrastim OBI (4.6% [95% CI, 3.4-5.8%]); across all cycles, the percentage of patients on chemotherapy with delays or dose reductions was 4.7% (95% CI, 3.5-5.9%) for the OBI group and 4.7% (95% CI, 2.9-6.4%) for the other group. Adherence to G-CSF was higher in patients receiving Pegfilgrastim OBI (93.8% [CI 95%, 92.5-95.2%]) compared to those receiving other options (69.8% [CI 95%, 66.1-73.6%]).
McBride et al. (2021) ⁽²⁴⁾ USA	Compare effectiveness and economic outcomes of Pegfilgrastim in pre-filled versus OBI presentations.	Retrospective cohort study. A propensity score was used to match pre-filled syringe cohort 1:1 to OBI. The results were compared between the matched cohorts using estimation equations.	3,152 patients with breast diagnosis cancer or non-Hodgkin's lymphoma that received myelosuppressive chemotherapy and prophylactic use of Pegfilgrastim via pre-filled syringe or OBI.	1088 patients received prophylaxis with Pegfilgrastim OBI and 2064 received pre-filled syringe. Rates of febrile neutropenia within each Pegfilgrastim cohort were low. During the first cycle of chemotherapy, there was no statistically significant difference in the incidence of febrile neutropenia between the OBI or pre-filled syringe cohorts (1.01% [95% CI = 0.56-1.82] versus 1.48% [95% CI = 0.91-2.39], respectively; $p = 0.336$). When considering all chemotherapy cycles (total cycles = 7,467), there was also no difference in the incidence of febrile neutropenia between the OBI or pre-filled syringe cohorts (0.91% [95% CI = 0.64-1.30] vs 1.22% [95% CI = 0.90-1.64], respectively; $p = 0.214$).

the Pegfilgrastim OBI device. It was noted that patients' opinion, workload and quality of life, health professionals' opinion and clinical practice are essential factors to guarantee safe and quality care for the clientele under chemotherapy care with a view to preventing neutropenia.

Observational studies describe the efficacy and implications for clinical practice of using Pegfilgrastim OBI. A retrospective study of 104 patients identified two failures in the Pegfilgrastim OBI device (1.9%), one of which was a malfunction of the indicator light, although patients received the full dose, and in another patient, Pegfilgrastim OBI was not administered correctly due to drug leakage. This study also reported a serious adverse event in a patient who presented anaphylaxis, 15 minutes after receiving the injection, with glottis edema, tachypnea and abdominal pain. Pegfilgrastim OBI was discontinued and

patients received G-CSF in a pre-filled syringe for the remainder of their treatment regimen without any further complications.⁽²²⁾ Even though such negative outcomes were statistically insignificant, these events need to be better understood and followed up to ensure patient safety.

In a multicenter prospective cohort, the incidence of febrile neutropenia was lower in patients receiving Pegfilgrastim OBI compared to those receiving other treatment options. The percentage of patients with chemotherapy dose delays or reductions was similar for both groups. Finally, compliance with prophylaxis was higher in patients receiving Pegfilgrastim OBI compared to other therapies.⁽²³⁾

Another retrospective cohort identified low rates of febrile neutropenia, with no difference in incidence between the OBI and pre-filled syringe groups ($p=0.214$). Pegfilgrastim OBI administra-

Chart 2. Synthesis of evidence from the package insert for Pegfilgrastim OBI,⁽²⁵⁾ the official website,⁽²⁶⁾ the manual for health professionals⁽²⁷⁾ and the manual for patients⁽²⁸⁾

Information for patients using the Pegfilgrastim OBI device	Precautions when applying the Pegfilgrastim OBI device for health professionals
ABOUT THE DEVICE	ASSESSMENT
<p>Pegfilgrastim OBI (NEULASTA) is a smart device placed on your skin (belly or upper arm) that delivers the exact dose of its medication automatically and at the correct time. After your chemotherapy infusion is finished, nurses will stick the device to your skin and you can go home. After 27 hours, the prescribed dose will be applied automatically.</p>	<p>Knowledge assessment: Assess what patient and family member know about the device; Assess conditions of sanitation and personal hygiene; Have an enlightening conversation about device care. skin assessment Do not apply to scars, wounds and moles; in case of excess hair, trim with scissors before application; Do not fix close to ostomies and/or hernias.</p>
AT THE CLINIC PREPARATION AND TRAINING	PREPARATION
<p>Nurses will prep your skin and glue the pre-filled device. It is critical that you have a full view of the device, and if it is taped behind your arm, you need a caregiver who can watch it at all times. Nurses will train you, explaining the precautions and the light and sound signals that the device emits: Status light: Flashing Green: Body injector is working properly, do not remove. Steady green: the medication has been injected, check if the volume is set to "empty". Flashing red: Device error. Contact the infusion clinic and talk to nurses. Volume indicator: Shows the amount of medication inside the device (full or empty).</p>	<p>Preparing the medication: 1. Remove the medication from the refrigerator (it must be stored under refrigeration at 2°C to 8°C). Wait 30 minutes and remove the syringe from the wrapper; 2. Remove the needle cap; 3. Insert the needle at a 90° angle into the medication port and push the plunger until all the contents are deposited in the device. CAUTION: During inflation, a "beep" will sound and the body injector will activate. After activation, you have 3 minutes to: complete steps 4, 5 and 6 and apply to patients; 4. Check if the marker is in "full"; 5. Remove the blue security seal; 6. Peel off the two patches and prepare to attach to patients. The device is ready to be applied to properly assessed and prepared skin.</p>
AT THE CLINIC BEFORE YOU GO HOME:	APPLICATION
<p>Have the contact of the clinic/health team so that you can call immediately with any questions or errors. When should I call my physician/nurse? <ul style="list-style-type: none"> If you have any allergic reaction at the site of fixation; If you feel any reaction during/after application, such as: redness in the body, shortness of breath, dizziness, swelling in the lips and eyes, excessive sweating, racing heart, itching or fever; If you feel pain in the upper left part of your stomach or at the tip of your left shoulder; If the team does not answer you quickly, look for the emergency service </p>	<p>1. Choose location: The device can be applied on the left and right sides of the abdomen at a distance of 5 cm from the navel or on the back of the arm, as long as you have a caregiver/family member to observe the site. 2. Prepare the skin: After choosing the location, perform skin antiseptics with cotton and 70% alcohol, ensuring that the site is clean. Wait for it to dry before adhering the device. 3. Apply the device: On the back of the upper arm, the status light should face down. On the abdomen, the status light should be facing the navel. 4. Make sure it is correct: A beep will inform you that the cannula is about to be inserted. A long beep will sound and the status light will turn green. This means the cannula has been inserted.</p>
AT HOME APPLICATION, WITHDRAWAL AND IMPORTANT CARE:	MONITORING
<ul style="list-style-type: none"> 26 hours after placement of Neulasta, find a comfortable place to wait for application; At the 27th hour prepare for application; When starting application, the device will emit a sound warning and a green light will "flash"; For 45 minutes the medicine will be administered; When finished, you will hear a "BEEP" sound and the green light will stop flashing; Check if the tag is on "empty". If so, everything worked. Wait for another 1 hour to ensure complete application. That is it, you can now remove the device and throw it in the specific trash that was delivered to you. <p>If the device beeps and emits a RED light and/or remains "full". CALL YOUR NURSE OR PHYSICIAN.</p> <ul style="list-style-type: none"> Do not rub the device (blouse/belt); Do not stay in temperatures lower than 5°C or higher than 40°C; Do not expose the device directly to the sun; Do not sleep on top of the device; Do not remove the adhesive before application; Do not apply creams and perfumes near the site; Do not expose the device to: radiotherapy, tomography, magnetic resonance imaging, ultrasound and X-ray; Keep the device 10 cm away from electronics and microwaves; Traveling by plane: No problem, as long as you are not flying at the time of application (between the 24th hour and 1 hour after the end). The device must not pass through the metal detector. Ask your physician for a report and TSA card. <p>Taking a shower: Do not take a bath in the bathtub, sauna or swimming pools. Shower within the first 24 hours after putting on the device to allow time for the dressing to dry during application.</p>	<ul style="list-style-type: none"> Error or failure when applying: If it beeps continuously for 5 minutes and the status light is flashing red, remove the On -body Injector from patients and attach another one. In all occurrences of error, it is important that patients flag it and you speak with the Amgen representative in your region who will assist you and provide the refund. End care and navigation in oncology Deliver in writing to patients the final time at which the injector was applied in the body, what is the expected start and end time of application; Provide the telephone number of the clinic/physician/nurse; Reinforce in which situations patients should seek the emergency unit; If possible, contact the emergency team where patients are referred and explain about the device; Review each step of patient care guidelines; Give patients instructions to take home; Before patients go home, make sure they understand all the information and are safe; Monitor patients via teleservice the next day to find out how the device is being fixed and reinforce care; Perform a teleservice on the second day to check if the dose has been delivered. This step is essential for patient safety.

Source: Neulasta® (Pegfilgrastim). [Bulletin]. Juncos – Puerto Rico: Amgen Manufacturing Limited. AMGEN. Neulasta Onpro Health Professionals [Internet]. Thousand Oaks, California: Amgen Inc; 2022 [access on 17 Sep. 2022]. Available at: <https://www.neulastahcp.com/>. 29. AMGEN. Neulasta® (pegfilgrastim) Onpro™ kit health provider instructions for use [Internet]. Thousand Oaks, California: Amgen Inc; 2021 [accessed on 17 Sep. 2022]. Available at: https://pi.amgen.com/~/media/amgen/repositorysites/pi-amgen-com/neulasta/neulasta_ifu_hcp_pt_old_english.pdf. AMGEN. Neulasta® (pegfilgrastim) On-Body Injector patients' instructions for use [Internet]. Thousand Oaks, California: Amgen Inc; 2020 [accessed on 17 Sept. 2022]. Available from: https://www.pi.amgen.com/united_states/neulasta/neulasta_patient_ifu_obi.pdf. (26-29)

tion was identified as the highest degree of convenience, as it is an administration method that reduces the need for patients to return to the clinic.⁽²⁴⁾

Only one randomized clinical trial has assessed the safety of Pegfilgrastim OBI. However, this clinical study was carried out with healthy subjects. In this series, it was concluded that Pegfilgrastim OBI administration resulted in a pharmacokinetic profile comparable to that observed with manual injection using the pre-filled syringe. Although Pegfilgrastim OBI administration was associated with a higher incidence of adverse events, including contact dermatitis, headache and local reaction, none of these were serious and all could be easily managed. Subjects' experience with the OBI device was considered favorable, highlighting the potential to improve patient compliance with primary prophylaxis with Pegfilgrastim.⁽²⁹⁾

It is important to consider that the lack of scientific evidence on the Pegfilgrastim OBI product can contribute to non-compliance by the health team. A clinical trial showed that nurses and physicians slightly preferred the pre-filled syringe over the OBI, due to greater control in administration, lower incidence of adverse events and shorter working time.⁽¹⁸⁾

It is worth noting that physicians vary the choice of treatment according to patients' profile. For those clinically compromised and/or with greater distance from their home to the clinic, the OBI was the preferred choice. As for patients who are clinically less compromised and/or with a shorter distance to the clinic, most physicians choose application at the clinic.⁽¹⁷⁾

Regarding patient propensity, the clinical trial assessed 308 participants who opted for the OBI instead of pre-filled syringe ($p=0.159$), although statistically without significance. The time saving factor was the main reason for predilection (53.4%).⁽¹⁸⁾

Another study applied a five-point scale to assess patients' opinion using the device, and of the 38 patients interviewed, 32 classified their satisfaction at level 4 or 5 (1 being the lowest level of dissatisfaction and 5 the highest). Only two participants were dissatisfied with the OBI. Older patients reported the absence of the need to travel to the clinic

for manual injection as an advantage. In the same direction, younger patients explained the benefit of not having to be absent from work or being able to stay at home taking care of their children.⁽¹⁹⁾

In another investigation with 68 patients with gastrointestinal tumors, 22% refused Pegfilgrastim OBI for reasons such as aversion to bulky compliance with the skin, understanding about unwitting drug administration, fear of drug reaction, disposal at home, fear of pain and lack of confirming administration of the proper dose.⁽¹⁶⁾

In Brazil, in several public and private health services, G-CSF is dispensed by the pharmacy to patients who perform application at home, often without receiving the proper guidelines for handling, application and storage. Thus, ensuring that medication is administered and stored correctly is a challenge for the health team.

Faced with the high demand from patients and deficiencies in human resources in health services, Pegfilgrastim OBI seems to be an interesting choice, since it promises to reduce the time dedicated to applications in the clinic. However, it is important to point out that patients using Pegfilgrastim OBI need to be monitored by the nursing team to ensure application success. In case of failure, it must return to the infusion center for manual application.^(19,28)

Interestingly, an American study assessed the measure of workload and financial expenditure on patient transport during cancer treatment and showed that the high number of hours spent by patients in oncology outpatient clinics and monetary losses with transport can make it more patients' experience during treatment is costly. In this context, Pegfilgrastim OBI use has its justified benefits.⁽²¹⁾

Considering the above, given the need for training health teams to provide robust and objective information to Pegfilgrastim OBI users, the results of this study sought to facilitate and mediate the construction of knowledge. In this regard, it is essential that the institution has a permanent education program in health so that that institution's reality is understood and, from then on, tools are implemented to understand how to handle the device by the team as well as teaching actions for patients. The health education process and patient care using this tech-

nology require navigation in oncology. It is with this tool that oncology nurse will be able to follow the process completely and guarantee Pegfilgrastim OBI administration safety.

A limitation of this scoping review is that a significant portion of included studies was funded by Amgen*, a fact that may result in methodological biases due to possible conflicts of interest.

Publications on neutropenia and Pegfilgrastim OBI use are mostly from the United States of America. As Brazil does not have any publications in journals on the subject, it is important to carry out studies with Brazilian participants to investigate factors such as compliance, health team management, cost-effectiveness and effectiveness, since using the device may suffer cultural influences and life habits. Thus, the present study could contribute to the advancement of knowledge on the subject in Brazil, seeking to promote the construction of knowledge to support nurses' clinical practice in oncology and, therefore, patient care improvement.

Finally, it is critical that further controlled clinical studies on Pegfilgrastim OBI be performed. As mentioned, the only clinical trial performed was a phase I trial in healthy participants. Thus, even though the medication Pegfilgrastim is consolidated with phase III clinical trials, the delivery method is new and requires controlled clinical studies to assess its safety.

Conclusion

The main health precautions for using Pegfilgrastim OBI are related to the skin preparation technique where the device will be applied, correct device preparation and administration so that it works properly at home. Moreover, the importance of assessing patients' and their family's knowledge about the device is highlighted, providing all the necessary guidelines, verbally and in writing, in a clear and objective way, and validating this information, making sure that patients have understood all of them and are safe. The final time at which the injector was applied to the body and the expected start and end time of application must be delivered in

writing; advise on the light and sound signals that the device emits; explain the situations in which patients should contact the team or look for the emergency unit; provide the telephone contact of the clinic and the team; in addition to periodic follow-up via call center. The synthesis of knowledge about the main health care for Pegfilgrastim OBI contributes to the clinical practice of professionals who care for patients with cancer, in addition to encouraging autonomy and patient self-care as well as facilitating the teaching-learning process of nurses in their practice.

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