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ORIGINALES

Chemotherapy near the end of life; assessment of the clinical practise in onco-hematological in adult patients

Quimioterapia al final de la vida; análisis de la práctica clínica en pacientes adultos onco-hematológicos con cáncer

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Abstract:

Objective: ensure a good quality of life in the last phase of onco- hematological patients should be the primary goal, despite this, we have little data at European level and published studies are contradictory. Nevertheless, most of them agree saying that administrating chemotherapy near the end of life impacts negatively in the patients quality of life. The main objective of this study is to analyze the treatment non-aggressiveness parameters in onco-hematological patients. The secondary objective is to do a describing study of the clinical variables of the patients who receive chemotherapy at the end of life and the treatments more used.
Methods: a retrospective observational study was conducted in a tertiary hospital. Both, oncological and hematological patients receiving chemotherapy (oral or intravenous) between January and December 2013 who were receiving chemotherapy in the last 90 days before death, were included.
Results: there were 823 patients that were threated between January and December of 2013. Of these 106 (13%) met the inclusion criteria to be analyzed. There were a 14.1% (n = 93) of oncological and a 8.4% (n = 13) of hematologic patients that maintained the antineoplasic treatment during the last three months before death. A 21.7% (n = 23) of the patients received chemotherapy in the last two weeks of life, 41.5% (n = 44) in the last 30 days and 78.3% (n = 83) in the last two months of life. There was a 67.9% (n = 72) of patients that had hospital admissions during their last three months of life, 47,2% (n = 50) during the last month, 33% (n = 35) during the last two weeks and 10,4% (n = 11) during the last three days of life. A 25,5% (n = 27) of patients had more than one hospital admission during their last 90 days.
Conclusions: according to the Earle et al. criteria, our population had been treated aggressively. We need more scientific evidence with consolidate date that allows us to establish a unified criteria for the selection of patients with advanced cancer who may benefit from receiving antineoplasic treatments.

Keywords: Chemotherapy, Neoplasm, Death, Hospitalization.

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Resumen:

Objetivo: garantizar una buena calidad de vida en la última fase de los pacientes onco-hematológicos debería ser nuestro principal objetivo; a pesar de ello, disponemos de pocos datos a nivel europeo y los estudios publicados son contradictorios. No obstante, la mayoría coinciden en que administrar quimioterapia en la etapa final de la vida impacta de forma negativa en la calidad de vida del paciente. El objetivo principal del estudio es analizar los indicadores de no agresividad del tratamiento en pacientes onco-hematológicos. Como objetivo secundario, realizar un estudio descriptivo de las variables clínicas de los pacientes a los que se les administra quimioterapia en la fase final de la vida y los esquemas más utilizados.
Método: se realizó un estudio observacional retrospectivo en un hospital de tercer nivel. Se incluyeron todos los pacientes oncológicos y hematológicos que recibieron quimioterapia (oral o intravenosa) entre enero y diciembre de 2013, a los que se les administró la última quimioterapia en los 90 días previos al fallecimiento.
Resultados: se analizaron 823 pacientes que recibieron tratamiento entre enero y diciembre de 2013. De ellos, 106 (13%) cumplían los criterios de inclusión. Un 14,1% (n = 93) de los pacientes oncológicos y un 8,4% (n = 13) de los hematológicos que habían recibido quimioterapia durante el último año de vida lo seguían haciendo en los últimos tres meses. Un 21,7% (n = 23) de los pacientes recibieron quimioterapia en las dos últimas semanas, 41,5% (n = 44) en los últimos 30 días y 78,3% (n = 83) en los últimos dos meses de vida. El 67,9% (n = 72) de los pacientes ingresaron en el hospital durante los últimos tres meses de vida, el 47,2% (n = 50) lo hicieron durante el último mes, el 33% (n = 35) durante las dos últimas semanas y el 10,4% (n = 11) durante los últimos tres días de vida. El 25,5% (n = 27) de los pacientes ingresaron en más de una ocasión durante los 90 días previos al fallecimiento.
Conclusiones: según los criterios establecidos por Earle et al, la población del estudio se trató de manera agresiva al final de la vida. Es necesario disponer de una evidencia científica, que todavía en la actualidad carece de una base consolidada, con la que establecer criterios para la selección de pacientes con cáncer en estadios avanzados que puedan beneficiarse de recibir tratamientos antineoplásicos.

Palabras clave: Quimioterapia, Neoplasia, Muerte, Hospitalización.

Contribution to scientific literature

Quality of life in oncology patients is still one of the essential cornerstones of research in the treatment of onco-haematological patients. Despite this, there is currently little information available at European level regarding quality of life at the last stage of the disease in patients with cancer. This study analyzes some intensity parameters for antineoplastic treatments at the end of patients' lives. This analysis includes both intravenous and oral antineoplastic treatments. The inclusion of oral administration treatments represents a differentiating point from the majority of studies conducted so far, which were focused on intravenous treatments. The outcomes from our study demonstrate that the majority of patients in our population are receiving an aggressive treatment which is far from achieving the main objective of improving patients' quality of life.

Though the outcomes obtained in this study cannot be applied to other patient populations, the data presented here show the need of a higher involvement by the healthcare team regarding therapeutic decision making. To this end, it is necessary to have scientific evidence available, which currently still lacks a well-established basis, in order to determine the criteria for selecting patients with cancer in advanced stages who might benefit from receiving antineoplastic treatments. The first step in order to achieve this will be to overthrow the ill-conceived idea that antineoplastic treatments will help, under any circumstances, to improve the quality of life of patients with cancer in advanced stages.

Introduction

During the past decades, the launch of new antineoplastic agents has increased the therapeutic options and life expectancy of patients with neoplasia. Treatments with oral administration have acquired special relevance, both because they represent a therapeutic option, and due to the simplification in administration. Despite these advances, tumours are currently the first cause of death in men, the second in women, and

are responsible for 27.5% of deaths in Spain, according to data published in January, 2014 by the *Instituto Nacional de Estadística* (National Statistics Institute) [1].

Around 70% of patients with disseminated disease are receiving chemotherapy with palliative intent [2]. The decision to initiate chemotherapy depends mainly on patient's status [3], disease stage [4], and chemosensitivity5 of the tumour. Treatment interruption in the final stages of life is considered a factor determining good clinical practice [6,7]. This is due, among other causes, to the reduction in the impact on overall survival after various lines of treatment in patients on advanced stages [8,9], the development of adverse effects derived of treatment, and the cost for the healthcare system.

To ensure a good quality of life in the last stage of onco-haematological patients should be the main objective and, despite this, we have little data at European level [5,8,10], those studies published are contradictory, and the majority coincides that administering chemotherapy during the final stage of life will have a negative impact on patients' quality of life [9].

Studies published so far have used as quality of life indicators the number of hospitalizations and treatments received during the weeks before patients' death [5,11]. Earle *et al.* [7] defines the concept of treatment non-aggressiveness as chemotherapy administration below 10% during the last 14 days of life, and below 4% of patients admitted to hospital on more than one occasion during the month before death.

Other studies [12,13,14,15] have used criteria such as admission to Intensive Care Units, visits to ER, hospitalizations, or inclusion in Phase I-II clinical trials.

The main objective of this study is to analyze the indicators of treatment non-aggressiveness in onco-haematological patients. The secondary objective is to conduct a descriptive study of clinical variables in patients who are administered chemotherapy during their final stage of life, and the most widely used regimens.

Materials and methods

A retrospective observational study was conducted in a third level hospital, covering a population of approximately 310,000 inhabitants. The study included all oncologic and haematologic patients who received chemotherapy (oral or intravenous) between January and December, 2013, and who had their last chemotherapy administered in the final stage of their lives. For the purpose of analysis, the period of time considered was the 90 days previous to death. Follow-up of those patients included was continued until March, 2014.

Data collection was conducted with the computer programs used in the Hospital Pharmacy for onco-haematological patient care: Farmasyst® and Farmis-Oncofarm ®, and the computerized clinical record programs OrionClinic® and Abucasis®. The variables collected were: gender, age, prescribing hospital unit, diagnosis, disease stage, performance status, date of the latest hospitalizations, and cause of death. The variables collected associated with treatment included: time since the last administration until death, lines of treatment received, and drugs included in the last treatment administered.

With the objective of assessing the functional status of the patient, the score in the Eastern Cooperative Oncologic Group (ECOG) Scale was collected, as entered in the clinical record on the day of the last chemotherapy administered before death. The number of hospital admissions within the last three months was also assessed, and the time elapsed since the last hospital admission until patient's death.

For descriptive analysis, the statistical program Stata ® version 12.1 was used.

Outcomes

In 2013, 2,758 patients were managed in the Oncology Department, and 949 in the Haematology Department. Out of them, 24.3% (n = 669) and 16.2% (n = 154), respectively, received chemotherapy. Therefore, 823 patients who received treatment between January and December, 2013, were analyzed. Out of these, 106 (13%) met the inclusion criteria.

The median age of patients included was 64.6 years (range 21.9-92.5) (Fig. 1); 68.9% (n = 73) were male and 31.1% (n = 33) were female.

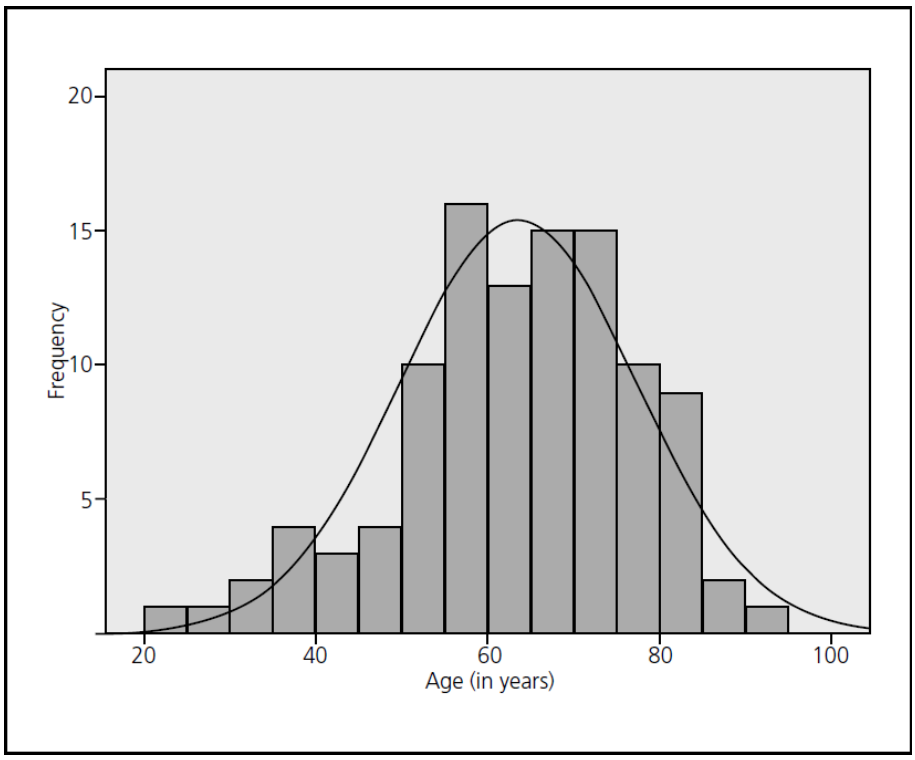

FIGURE 1
Distribution of patient age.

The hospital unit of origin of said patients was Haematology for 12.3% (n = 13) and Oncology for 87.7% of cases (n = 93).

Both intravenous and oral administration drugs were included in the treatment. A 14.1% (n = 93) of oncological patients and 8.4% (n = 13) of haematological patients who had received chemotherapy during their last year of life continued receiving it during their last three months.

The distribution of patients who received antineoplastic drugs in their last 90 days of life appears in figure 2.

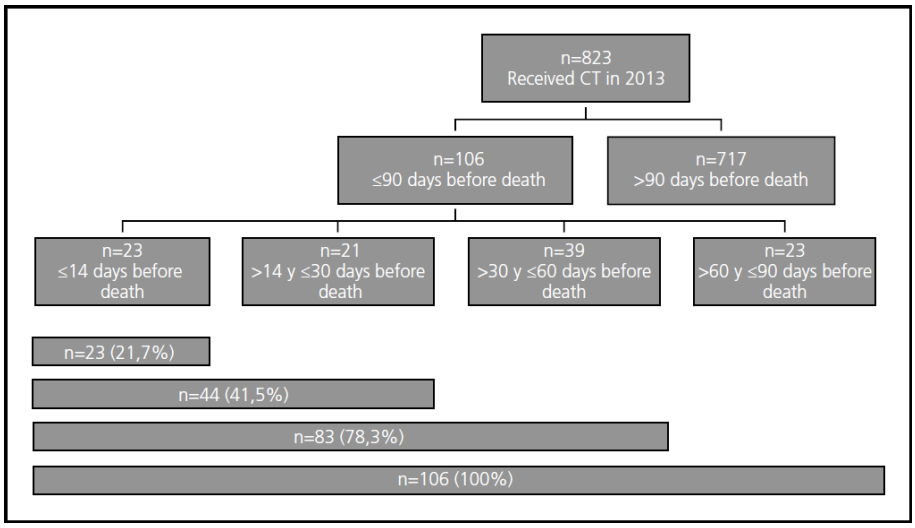

FIGURE 2
Distribution of patients according to the time when they received chemotherapy before death.

Data regarding ECOG scale scores at treatment initiation was available in 87.7% of those patients analyzed. The majority (67% n = 71) presented a 0-1 score in the ECOG scale; 18.9% (n = 20) presented a score of 2, and a minority (1.9%, n = 2) had ECOG 3.

The majority of patients (77.6%, n = 76) presented Stage IV disease at the time of their death, which was secondary to their basal disease. A 28.3% of patients (n = 30) presented complications secondary to treatment as cause of death (Fig. 3).

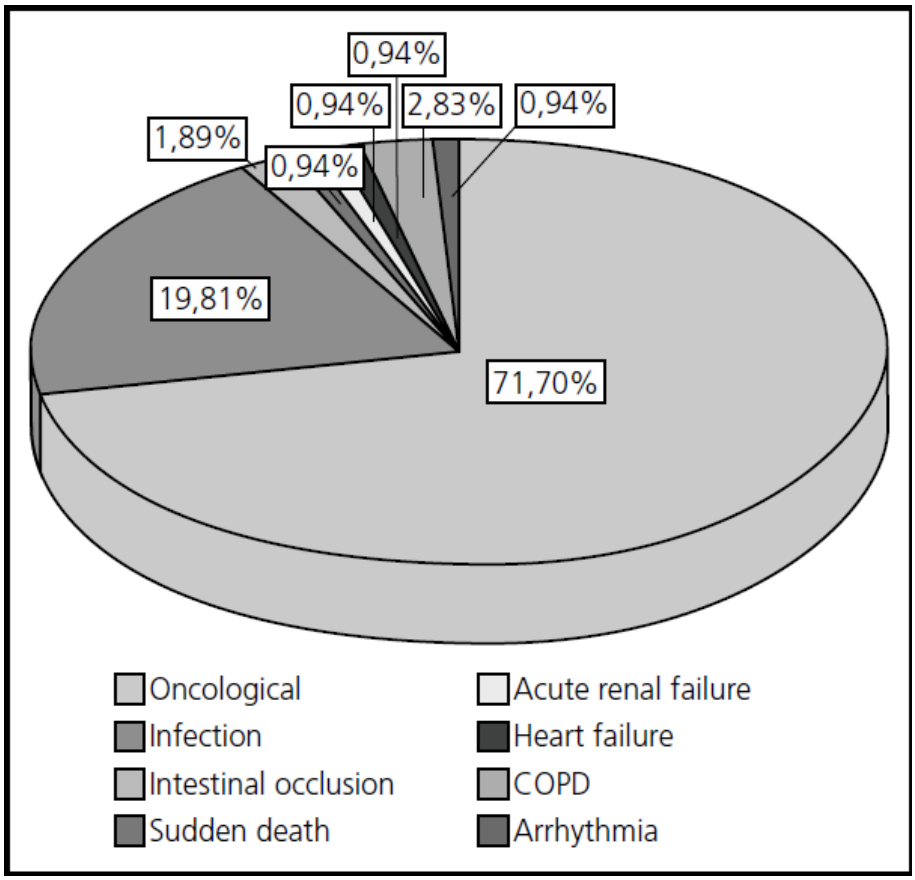

FIGURE 3
Causes of Death.

The distribution of the tumours suffered by patients included in the study appears in figure 4. The highest percentage of tumours had intermediate sensitivity to treatment, according to the classification by Martoni *et al.* [5] (Fig. 5)

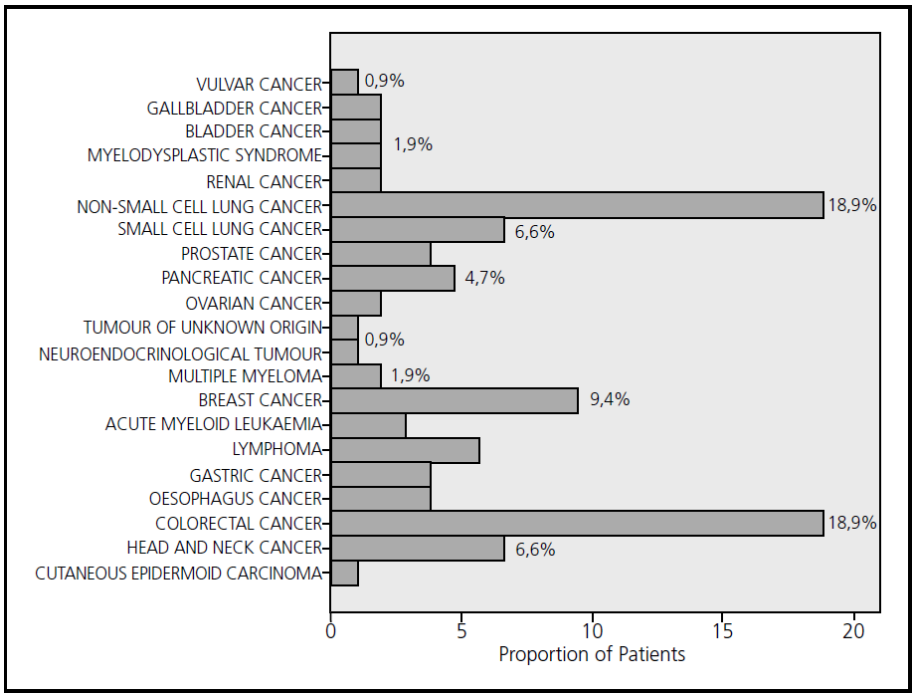

FIGURE 4
Distribution of number of patients according to type of tumour.

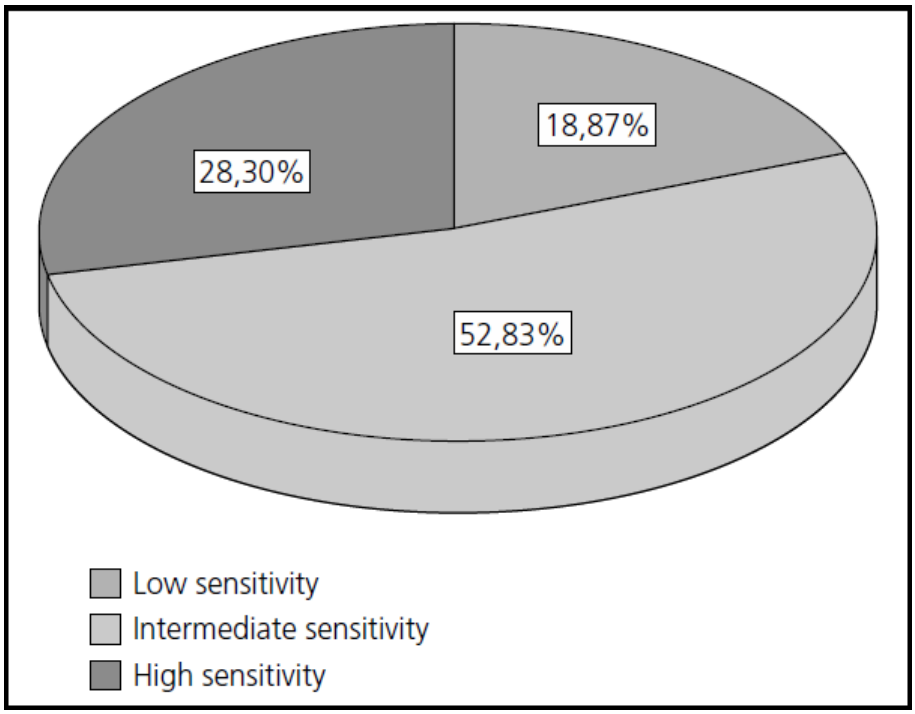

FIGURE 5
Tumour sensitivity to chemotherapy.

The most widely used therapeutic regimen was capecitabine as monotherapy, administered in 6 patients, as well as the capecitabine + oxaliplatin combination. Topotecan was administered to 5 patients. The following treatments were received by 4 patients each: abiraterone, docetaxel, gemcitabine, azacitidine, cetuximab, doxorubicin, erlotinib, as well as the following combinations: bevacizumab + capecitabine + oxaliplatin; carboplatin + etoposide; carboplatin + paclitaxel, and cetuximab + paclitaxel. Capecitabine was the drug

received by the highest number of patients: 18.9% (n = 20), followed by oxaliplatin: 12.2% (n = 13) and gemcitabine: 9.4% (n = 10) (Fig. 6).

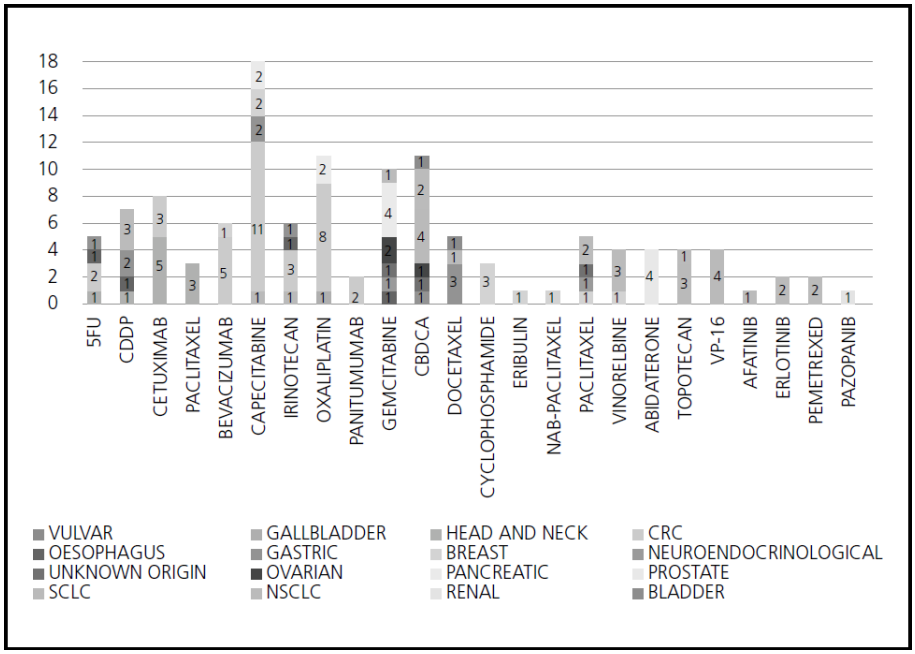

FIGURE 6
Distribution of drugs based on type of cancer.

The median number of treatment regimens received was 2 (range 1-7). There were 10 patients who received more than 3 different regimens.

A 67.9% (n = 72) of patients were admitted to hospital during their last three months of life; 47.2% (n = 50) during their last month; 33% (n = 35) during their last two weeks, and 10.4% (n = 11) during their last 3 days of life. A 25.5% (n = 27) of patients were admitted in more than one occasion throughout the 90 days previous to their death.

Discussion

The use of chemotherapy during the last stages of life of cancer patients is a controversial issue, which Emanuel *et al.* [11] dealt with over a decade ago, and that continues being studied nowadays. The outcomes of our study show that the proportion of patients in the Oncology Department who receive chemotherapy at the last stage of their lives is similar to the one by Earle *et al.* [13].

Regarding the use of chemotherapy during the final stages of life, relative to the total number of patients who are treated with this type of drugs, 5.8% received chemotherapy during their last month of life. This value is close to the 6.2% published by Wright *et al.* [16], but appears far from the 22.7% published by Angelo *et al.* [5].

The latest studies published about the use of chemotherapy in the final stage of life [9] and of the disease, demonstrate this is damaging for the quality of life of patients receiving it, regardless of their performance status at treatment initiation. Adverse reactions derived of treatment can be an additional factor for a worsening in the quality of life of patients with antineoplastic treatment. The prescription to the patients in the study of capecitabine instead of 5-fluorouracil was probably considered with the aim of minimizing the development of adverse reactions [17,18].

Regarding hospitalizations at the end of life, our patients were admitted in a higher proportion than those in other studies [19,20]. According to the criteria by Earle *et al.* [7], our patients received aggressive treatment

at the end of their lives. In order to improve clinical practice and decision making regarding chemotherapy administration at the end of life, it is considered necessary to conduct further studies to define the criteria for establishing the conditions that ensure an improvement in quality of life for patients with advanced stage cancer.

The inclusion of treatments with oral administration represents a differentiating point from the majority of studies conducted so far, which are focused on intravenous treatments. The outcomes obtained in our study demonstrate that the majority of patients in our population are receiving an aggressive treatment which is far from achieving the primary goal of improving the quality of life of patients.

A higher involvement by the healthcare team in therapeutic decision making is required. For this aim, it is necessary to have scientific evidence, which currently still lacks a solid basis [21], in order to determine the criteria for the selection of patients with advanced stage cancer who might benefit from receiving antineoplastic treatments. The first step in order to achieve this will be to overthrow the ill-conceived idea that antineoplastic treatments, under any circumstances, will help to improve the quality of life of patients with advanced stage cancer [9].

The limitations of this study are that this is a retrospective study which analyzed the sample in a single centre during one year, and therefore it cannot be applied to other populations.

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