# **Oncology Emergencies: Integrative Literature Review**

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Urgências e Emergências Oncológicas: Revisão Integrativa da Literatura Urgencias y Emergencias Oncológicas: Revisión Integrativa de la Literatura

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#### Abstract

Introduction: Oncological emergencies are acute conditions caused by cancer or its treatment, which require rapid intervention. Objective: To analyze and synthesize the scientific production related to patient care with emergencies and oncological emergencies. Method: Integrative literature review with PubMed, Cinahl, Embase and Lilacs queries in February 2018, with the descriptors Emergencies AND Oncology OR Neoplasm, with no time restrictions. Results: Selected 55 articles, published from 1987 to 2017; with a weak or moderate level of evidence (96.3%); 54.5% of the articles covered structural-obstructive gastrointestinal emergencies, 10.9% respiratory tract, 7.2% infections and neurological system, 5.4% cardiac, abdominal and metabolic emergencies and 3.6% hepatic emergencies. Conclusion: Oncological emergencies should be better studied, recognized and understood by the team, so that there is an improvement in the prognosis and quality of life of the patients.

Key words: Emergencies; Medical Oncology; Neoplasms; Patient Care.

#### Resumo

Introdução: Emergências oncológicas são condições agudas causadas pelo câncer, ou por seu tratamento, que requerem rápida intervenção. Objetivo: Analisar e sintetizar a produção científica relacionada à assistência ao paciente com urgências e emergências oncológicas. Método: Revisão integrativa da literatura com consultas no PubMed, Cinahl, Embase e Lilacs, em fevereiro de 2018, com os descritores Emergencies AND Oncology OR Neoplasm, sem restrições de tempo. Resultados: Selecionados 55 artigos, publicados de 1987 a 2017; com nível de evidência fraco ou moderado (96,3%); 54,5% dos artigos abordaram emergências estruturais-obstrutivas do trato gastrointestinal, 10,9% do trato respiratório, 7,2% infecções e sistema neurológico, 5,4% emergências cardíacas, abdominais e metabólicas e 3,6% emergências hepáticas. Conclusão: As emergências oncológicas devem ser mais bem estudadas, reconhecidas e entendidas pela equipe, para que haja melhora no prognóstico e na qualidade de vida dos pacientes. Palavras-chave: Emergências; Oncologia; Neoplasias; Assistência ao Paciente.

Introducción: Las emergencias oncológicas son condiciones agudas causadas por el cáncer o por su tratamiento, que requieren una rápida intervención. Objetivo: Analizar y sintetizar la producción científica relacionada a la asistencia al paciente con urgencias y emergencias oncológicas. Método: Revisión integrativa de la literatura con consultas en PubMed, Cinahl, Embase y Lilacs en febrero de 2018, con los descriptores Emergencies AND Oncology OR Neoplasm, sin restricciones de tiempo. Resultados: Seleccionados 55 artículos, publicados desde 1987 hasta 2017; con un nivel de evidencia débil o moderado (96,3%); El 54,5% de los artículos abordaron emergencias estructurais-obstructivas del tracto gastrointestinal, 10,9% tracto respiratorio, 7,2% infecciones y sistema neurológico, 5,4% emergencias cardíacas, abdominales y metabólicas y 3,6% emergencias hepáticas. Conclusión: Las emergencias oncológicas deben ser mejor estudiadas, reconocidas y entendidas por el equipo, para que haya mejoría en el pronóstico y la calidad de vida de los pacientes

Palabras clave: Urgencias Médicas; Oncología Médica; Neoplasias; Atención al Paciente.

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#### INTRODUCTION

Oncologic emergencies are acute conditions caused by cancer or its treatment, which require rapid intervention because they involve imminent risk of life or risk of permanent serious damage 1.

The care to oncology urgencies or emergencies has a key role in the reversion of cases that head to death. It should further the improvement of the quality of life and prevention of sequelae arising from the complications <sup>2</sup>.

The lengthening of the survival of the patients with cancer may lead to the evolution of the disease, which associated to comorbidities and toxicities of the treatment may increase the cases of oncologic emergencies. The evolution may be because of metastasis and has a rate of incidence of 70% of cancer cases<sup>3,4</sup>.

There are several forms of classification of these emergencies, according to tumor-related harms and those provoked by the treatment<sup>5</sup>or by structural, metabolic and secondary emergencies to the treatment<sup>4,6</sup>; others propose the division pursuant to the systems affected<sup>2</sup> and, ultimately, there are those that consider the symptoms and consequences of the harms as actual emergencies 7.

Errors or delays in care may result in death or irreversible damages. The capacitation of professionals to identify rapidly the problem and apply the proper therapy can modify the prognosis or improve significantly the quality of the life of these patients<sup>6</sup>.

The comprehension of these acute conditions is essential for the team who provides care to patients in oncologic emergency units where screening, anamnesis and physical exam are carried out in order to decide which is the best possible conduct and approach 8.

However, the education background of the healthcare team is not always adequate, which makes many professionals to feel unprepared to deal with the complexity of the oncologic harms, where clinical alterations mingle with evolutive conditions of the neoplasms and aggressive toxicities of the treatment 8.

Therefore, because of the necessity of approaching the scientific production related to oncologic emergency cases with the clinical practice, the objective is to analyze and synthetize the scientific production related to the patient care in oncologic urgencies and emergencies.

## **METHOD**

It is an integrative review of the literature, constructed from the following stages: development of the steering question, search of the primary studies in the databases, extraction of the studies data, assessment of the studies selected, analysis and synthesis of the results and presentation of the review 9.

To reach the goal, the following steering question was elaborated: What are the available scientific evidences about oncologic urgencies and emergencies associated to patient care?

The collection of the data was carried out in February 2018. The selection of the articles was made in the databases US National Library of Medicine (PubMed), Cumulative Index to Nursing and Allied Health Literature (Cinahl), Excerpta Medica Database (Embase) and Latin-American and Caribbean System on Health Sciences Information – LILACS.

The descriptors emergencies, oncology, neoplasm, were combined in different forms as seen in Table 1.

Table 1. Crossings of the descriptors selected according to the databases. Lagarto, Sergipe, Brazil, 2018

Database	Crossings	
PubMed Cinahl Embase	Emergencies AND Oncology OR Neoplasm Neoplasm AND Emergencies OR Oncology	
Lilacs	Emergencies AND Oncology OR Neoplasm	

The inclusion criteria for the pre-selections of the studies were: studies in English, Portuguese or Spanish published in journals, which approached the care to the patient in oncologic urgencies and emergencies.

The non-primary articles, as those of opinions and reviews were excluded and those that after the full reading failed to meet the objective of this review. No limits were determined in relation to the year of publication of the articles.

It was used the validated instrument 10 to collect and analyze the data that was adapted to meet the study objectives. The pre-selection of the studies was carried out through the thorough reading of titles and abstracts; the articles were fully read for the final selection.

The topics of interest approached in the instrument were: title, year of publication, idiom, origin country of the publication, database, objective, method, results, conclusions/recommendations and level of evidence.

For the level of evidence, it was used the classification suggested by Melnyk and Fineout-Overholt11, which classified the studies in seven levels: 1 - systematic review or meta-analysis of clinical trials randomized controlled; 2 - at least one well designed controlled randomized clinical trial; 3 - no randomized clinical trials well designed; 4 - well designed cohort and case-control; 5 - systematic review of qualitative and descriptive studies; 6 - unique descriptive or qualitative study; 7 - opinion of authorities and/or report by specialists committees.

Levels 1 and 2, under this classification, are considered strong evidences; 3 and 4, moderate and 5 to 7, weak.

The identification, selection and inclusion process was divided in three stages. The first stage comprehended the verification of duplicate articles, what was undetected, reaching 693 articles.

The second stage consisted in reading the titles and abstracts of the articles, under the scrutiny of the inclusion and exclusion criteria. Thus, 233 articles were chosen.

In the third stage, the 233 articles were read in full, 177 articles were removed because they failed to meet the inclusion criteria and did not answer the steering question of this review.

### **RESULTS**

The final sample consisted of 55 articles, the oldest published in 1987 and the most recent in 2017 of which, 7.2% were published between 1987 and 1989; 25.4% between 1991 and 1999; 23.6% between 2003 and 2010; and 43.6% between 2011 and 2017.

English is the idiom of 76.3% of the published articles, 14.5% in Spanish and 9% in Portuguese.

In the United States of America, 21.8% of the studies were conducted, 7.2 % in the United Kingdom and the same percent in Brazil; 5.4%, South Korea, China and Spanish each one, 3.6% in Singapore, Italy, Germany, Israel, Argentine and Chile each one; 1.8% in France, Sweden, Australia, Japan, Slovenia, The Netherlands, East Europe, Mexican, Venezuela, Peru, Canada, Ecuador and Thailand.

PubMed (54%), Lilacs (20%), Cinahl (18%) and Embase (7.2%) were the databases utilized.

The most frequent designs were retrospective longitudinal (32.7%) and case report (21.8%), followed by observational (10.9%), cohort (7.2%), case-control (5.5%), clinical trial (5.5%), mixed method (5.5%), randomized clinical trial (3.6%), prospective longitudinal (3.6%), crosssectional (1.8%) and, at last, descriptive (1.8%).

Of these, 40% had level evidence 5 (weak), 56.3%, 3 (moderate) and 3.6%, level of evidence 2 (strong).

In relation to the location of the tumor, the samples were of intestine cancer (60.8%); pancreas, head and neck, mediastinum, respiratory, rhabdomyosarcoma, lymphoma, brain and ovaries (1.8% in each one of the tumors); liver (3.6%); bone marrow (10.9%) and several organs (10.9%).

After reading the studies, they were divided in three groups: studied oncologic emergency, therapeutic or treatment implemented and endpoints.

The emergencies more studied were the obstructivestructural gastrointestinal tract (60.7%), followed by the obstruction of the airways (10.9%), superior vena cava syndrome (SVCS) (5.4%), febrile neutropenia (5.4%), hematologic emergencies (3.6%), syndrome of medullary compression (SMC) (3.6%), other neurologic emergencies (3.6%), rupture of the hepatocellular carcinoma (3.6%), lactic acidosis (1.8%) and, ultimately, tumor lysis syndrome (1.8%).

The therapies or treatment implemented were surgeries (38.1%) followed by introduction of stent as a bridge to surgery (18.1%), chemotherapy (7.2%), accurate diagnosis (5.4%), radiotherapy associated to chemotherapy (5.4%), retrograde endoscopy (3.6%), insertion of stent (3.6%), ventilatory support (3.6%), palliative care (3.6%), cricotomy (1.8%) and, ultimately, radiotherapy (1.8%)

The main endpoints, per author/year and type of oncologic emergency are described in Tables 2 to 4.

Thirty authors described the endpoint of the emergencies of the obstructive-structural gastrointestinal tract. There was a predominance of the safe use of stents for colon clearing, and if considered safe, it diminishes the necessity of colostomy, mortality and improves the quality of life.

In addition, it was described that the emergency surgery could be lethal; it could increase significantly the morbimortality and worsens the prognosis when compared to elective surgeries. Despite this, the surgery must be conducted. .

Table 3 presents the main endpoints and references of the studies for the respiratory, cardiovascular, infectious and neurologic emergencies (17 studies).

For respiratory emergencies, six studies were encountered, mainly with the description of techniques as tracheal dilatation, cricothyrotomy and prosthetics for better recovery of the ill.

In the endpoints of three cardiovascular emergencies studies, it were described the necessity of quick diagnosis and conduct in face of SVCS.

Four articles about infectious emergencies addressed the use of standard protocols to reduce the time to administer the first dose of antibiotics in case of fever and neutropenia.

The neurological emergencies were addressed in four studies where the authors emphasized the need of quick and accurate interventions to reduce the morbimortality.

Table 4 presents the main endpoints and references of the studies encountered for abdominal, hepatic and metabolic emergencies (eight studies).

The abdominal emergencies addressed in three articles describe mainly the symptoms as peritonitis and abdominal pain resulting from metastasis.

In the hepatic emergencies, two articles were encountered about exploratory laparotomies and

Table 2. Main endpoints and references of the studies encountered for the structural-obstructive emergencies of the intestinal tract. Lagarto, Sergipe, Brazil, 2018

Authors	Main endpoints	
Arrigoni et al.¹	Acute obstruction resolved by endoscopic rechannelization (ER) in 94% of the patients of the series	
Borba et al. <sup>12</sup> ; Hequera et al. <sup>13</sup>	Urgency operated patients presented staging pT4 and elective, staging I	
Brochado et al. <sup>14</sup> ; Porta et al. <sup>15</sup>	Patients with resection and primary anastomosis, without colostomy, lower rate of mortality than the submitted to resection with exteriorization, without anastomosis	
Cauley et al. <sup>16</sup> ; Halevy et al. <sup>17</sup>	Emergency abdominal surgeries in metastatic cancer are highly lethal and many die	
Kawahara et al. <sup>18</sup>	Drainage by anastomosis is safe and minimizes the risk of intraoperatory stroke of the intestinal content, in colonic obstruction of the left side	
Kluger et al. <sup>19</sup>	Subtotal colectomy with primary ileocolonic anastomosis in obstructive carcinoma of the left colon is safe for elderly and of high risk and eliminates the colostomy	
Marano et al. <sup>20</sup>	Ages does not affect the result of the surgery of gastrointestinal stromal tumors (GIST) even in emergencies	
Meijer et al. <sup>21</sup>	Emergency surgery of acute colon cancer is safe, with primary anastomosis in the left colon	
Oliveira Filho et al. <sup>22</sup>	Emergency surgery must not be denied in oncologic patients, even for those with active disease	
Poon et al. <sup>23</sup>	Primary resection and emergency anastomosis can be conducted with favorable results in the majority of elderly with left obstructive colorectal carcinoma	
Scholefield et al. <sup>24</sup>	Screening of colorectal cancer with fecal occult blood test may reduce emergency cases of colorectal cancer	
Negoi et al. <sup>25</sup> ; Repse et al. <sup>26</sup> ; Shah et al. <sup>27</sup> ; Smothers et al. <sup>28</sup>	Emergency surgery had more odds for complication, mortality, failure and prolonged hospitalization	
Bocic et al. <sup>29</sup>	Mortatlity by intestinal cancer in emergency surgery is multifactorial, involving the baseline status of the patient, technical surgical decision and etiology of the obstruction	
Venara et al. <sup>30</sup>	Immediate removal of the nasogastric tube is indicated in case of obstruction of the large intestine	
Sabando et al. <sup>31</sup> ; Abelson et al. <sup>32</sup>	Intestinal obstruction was the majority of the cases of acute abdomen with suspected neoplasm, duodenal perforation, acute appendicitis and gastric perforation	
Frago et al. <sup>33</sup> ; Lim et al. <sup>34</sup>	Implantation of stent in patients with obstructive colorectal cancer, palliative stage IV, can be less successful than it was believed	
Ho et al. <sup>35</sup>	Elective surgery can be safer with less morbidity and mortality when compared to the current practice of urgency surgery	
Alcantara et al. <sup>36</sup> ; Young et al. <sup>37</sup> ; Ji et al. <sup>38</sup> ; Kim et al. <sup>39</sup> ; Law et al. <sup>40</sup>	Autoextensible metallic stent does not affect the rate of creation of the stroma, favors elective minimal invasive surgery and reduces post-operatory complications	

chemoembolization in the attempt to reduce mortality and complications.

The metabolic emergencies described in three articles brought up the use of chemotherapy of urgency and interventions to improve lactic acidosis, which drew the attention to the possibility of pseudo-hyperkalemia in severe leukocytosis to avoid iatrogenic hypokalemia.

## **DISCUSSION**

The results indicate that the investigation about the care provided to the patient under oncologic emergencies is not recent (1987) and the number of researches grows constantly every year, mostly between 2011 and 2017, where the rates of mortality increased substantially <sup>3</sup>.

Table 3. Main endpoints and references encountered for respiratory, cardiovascular, infectious and neurologic emergencies. Lagarto, Sergipe, Brazil, 2018

Authors	Studied Emergencies	Main endpoints
Piastra et al. <sup>41</sup>	Ventilatory difficulty	Intensive therapy is essential for the recovery of the patient with severe neoplasm of the mediastinum, in addition to anti-neoplasm therapy
Aneeshkumar et al. <sup>42</sup>		Cricothyrotomy opens a safe and rapid airway, with little trauma
Godbout et al. <sup>43</sup>		There was no difference in the survival with the administration of the "distress protocol" (sedation for palliative care) among those who received and those who did not receive
Nicolai et al. <sup>44</sup>	Airway obstruction	The endoscopic dilatation of the balloon through an endotracheal tube with implantation of stent succeeded, it allowed extubation and release of the child from ICU
Tasci et al. <sup>45</sup>		Bronchoscopy is the golden standard to confirm the etiology subjacent to the central airway obstruction
Wassermann et al.46		Setting of unidirectional and bifurcated prosthesis in advanced tumor of the central airway is viable, efficient and ethically justifiable
Bonetto et al. <sup>47</sup>		The superior vena cava syndrome is an oncologic emergency that requires diagnosis and immediate treatment to improve the results
Davis et al. <sup>48</sup>	Superior vena cava syndrome	The superior vena cava syndrome is rare in children with cancer requires immediate treatment, demanding clear guidelines of conduct
Ferreira et al. <sup>49</sup>		There were no advantage of the treatment combined with chemotherapy and radiotherapy in this series
Cash et al. <sup>50</sup>	Echrila nautranania	The use of the standard process reduces the time for the first dose of antibiotic in case of fever and neutropenia
Pakakasama et al. <sup>51</sup>	Febrile neutropenia	Guidelines for children with cancer and fever result in reduction of the adverse effects and improvement of survival
Valdespino-Gómez et al. <sup>52</sup>	Severe neutropenia, septic shock	Not effective analgesia was associated to inadequate prescription or insufficient intake of opioid analgesic
Kane et al. <sup>53</sup>	Hematologic emergency	Admission in urgency unit presents worse endpoints than those with clinical characteristics similar through other routes of admission
Pack et al. <sup>54</sup>	Neurologic: syndrome of	Rapid and accurate intervention in children with neurologic complications can reduce the progression of signs and symptoms and death
Sánchez et al. <sup>55</sup>	medullary compression	Diagnosis and treatment should be the short as possible to minimize the sequelae
Aberger <sup>56</sup>		Palliative care can be the best action for the family and for the patient in terminal state
Berkeley et al. <sup>57</sup>	Neurologic	Treatment includes early removal of the teratoma, intravenous immunoglobulin, methylprednisolone or plasmapheresis

The world estimate shows that in 2012, there were 14.1 million new cases of cancer and 8.2 million of deaths. It was observed a discreet predominance of male cases in the incidence (53%) and mortality (57%) 66.

Overall, it were observed higher incidence rates in the developed countries (North America, East Europe, Japan, South Korea, Australia and New Zealand). Intermediate rates are seen in South and Central America, East Europe and in great part of Southeast Asia (including China). The lower rates are found in great part of Africa, Southern and West Asia (including India) 66.

Table 4. Main endpoints and references of the studies encountered for the abdominal, hepatic and metabolic emergencies. Lagarto, Sergipe	٥,
Brazil, 2018	

Authors	Studied Emergencies	Main endpoints
Löhr <sup>58</sup>	Abdominal pain, diabetes	Pancreas cancer needs an effective approach with rapid diagnosis and multiprofessional approach
Lee et al. <sup>59</sup>	Peritonitis, anemia, hypoalbuminemia,	Urgency surgery of peritonitis because of cancer, pre-operatory anemia and pre-operatory hypoalbuminemia exhibit high mortality
Albinagorta et al.60	Commitment of the digestive tract	Radical surgical approach offers better possibilities for these patients
Parekh et al. <sup>61</sup>	Rupture of the hepatocellular carcinoma	Open laparotomy was replaced by transarterial embolization with rates equivalent to hemostasis, reduction of mortality in 30 days
Chen et al.62	Rupture of the hepatic carcinoma	Emergency chemoembolization did not improve the endpoint and was associated to higher rates of mortality and complications
Gardner et al. <sup>63</sup>	Lactic acidosis	Emergency chemotherapy was well succeeded in the reduction of lactate levels. The venous hemofiltration did not have effect in the reduction of lactic acidosis
Alhaj et al. <sup>64</sup>	Pseudo- hyperkalemia in one leukocytosis	It should consider the pseudo-hyperkalemia in cases of severe leukocytosis to avoid iatrogenic hypokalemia
Maloney et al. <sup>65</sup>	Tumoral lysis syndrome	The understanding of the risk factors for the tumoral lysis syndrome gives oncologic nurses a base for its prevention

The majority of the studies (92.8%) was produced internationally, which shows the reduced production of national studies on the subject. The level of evidence for 56.3% was moderate. The studies reached similar approaches in what concerns recommendations for oncologic emergencies.

For tumor location, intestine cancer was the most studied. The most incident types of cancer in the world were lung (1.8 million), breast (1.7 million), intestine (1.4 million) and prostate (1.1 million)<sup>66</sup>.

The obstructive-structural of the gastrointestinal tract stood out among the oncologic emergencies, the intestinal obstruction was predominant. These are relatively common in patients with advanced cancer, the major causes being ovary carcinoma and rectum 67.

The obstruction can be structural or pseudostructural as consequence of tumoral infiltration of the mesentery or smooth muscle, involvement of the celiac plexus or paraneoplastic neuropathy in patients with lung cancer of small cells and expansive lesion of tumors located in the region <sup>67</sup>.

The emergency surgeries showed a poor diagnosis when compared to elective surgeries 12,15,16,24,25,29. But, the emergency surgery should not be denied or delayed for oncologic patients who need immediate intervention, even for those with the active disease 21.

The emergency surgery for left and right colon cancer presented in the studies selected a better prognosis when performed in a stage with resection and primary anastomosis, without colostomy, not showing counterindications in elderly patients 14,18,21,23,26.

Several studies demonstrated that stent implantation is quite safe and little invasive, with less morbidity and mortality when compared to emergency surgeries 11,35-38,40. However, it was not beneficial for stage IV colorectal obstructive cancer and if not implanted, it is anticipated a poor diagnosis when compared to those where stent was implanted successfully or to emergency surgery <sup>33,34</sup>.

Concerning airway obstruction in respiratory emergencies, cricothyrotomy is an agile form to obtain a safer airway in an emergency situation<sup>42</sup>. Bronchoscopy was described as the golden standard to confirm the etiology of the obstruction 45.

SVCS requires immediate treatment and diagnosis to obtain a better prognosis, it is necessary to have clear guidelines conduct to improve the agility and efficacy of the treatment 47,48.

The infectious emergencies describe guidelines to treat febrile neutropenia that can evolve to septic shock. The recommendation is to have a standard protocol to reduce the adverse effects and the improvement of survival 50,52.

The neurologic emergencies as the SCM and raise of the intracranial pressure have a poor prognosis and should be diagnosed and treated as partial or total loss of the motor and sensitive function of the posterior part of the spinal medulla of the neoplasm-affected region, as shown in the complete neurological exam of the sensitive and motor function, which is the first step of the diagnosis of this emergency 54,55.

Usually, the abdominal oncologic emergencies are late diagnosed, it is common that the diagnosis is done in the emergency. Because of a poor prognosis with a reduced survival time, as in pancreas cancer, these oncologic emergencies are addressed in but a few studies for diagnosis and new methods of intervention<sup>58</sup>.

So, if possible, the surgical treatment is always recommended and waiting time for the procedure may be associated to adjuvant chemotherapy to stabilize the tumor<sup>58,60</sup>.

In hepatic emergencies, the researchers discussed the exploratory laparotomies and chemoembolization to control the tumor, there were no improvement of the rates of complications and mortality<sup>61,62</sup>.

The metabolic emergencies ponder about the use of urgency chemotherapy and interventions to improve the lactic acidosis and hyperkalemia considering pseudohyperkalemia in cases of severe leukocytosis postoncologic treatment 64,65.

#### CONCLUSION

The oncologic emergencies related scientific production had a substantial expansion in the last years, a consequence of the development of antineoplastic treatments that enabled a major survival to the oncologic patients and high incidence of acute manifestations of the disease.

The majority of the studies presented weak or moderate level of evidence. In this way, it is perceived the necessity of studies with more substantial evidence to favor better conducts towards oncologic urgencies.

In this study, the oncologic emergencies caused diverse disorders, mainly in the neurologic and gastrointestinal systems. These are important and should be acknowledged and understood by the team to improve the diagnosis and quality of life of the patients.

#### CONTRIBUTIONS

All the authors participated of the study conception and design, analysis and interpretation of the data, wording and review and approval of the final version.

#### **DECLARATION OF CONFLICT OF INTERESTS**

No conflicts of interest to declare.

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None.

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