# CANCER-ASSOCIATED THROMBOSIS (CAT), A NEGLECTED CAUSE OF CANCER DEATH: ACTIONS NEEDED TO INCREASE HEALTH OUTCOMES AND REDUCE MORTALITY

Report summarising the findings of an Expert Steering Group meeting in Belgium



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# Glossary: list of definitions of words and phrases used in this report

## Cancer-associated thrombosis (CAT)

The formation of a blood clot inside a blood vessel that is associated with cancer

## Deep vein thrombosis (DVT)

Formation of a blood clot in the deep veins of a limb, usually the leg

## Low molecular weight heparin (LMWH)

An anticoagulant, currently recommended for the prevention and treatment of thrombosis, administered subcutaneously

## Pulmonary Embolism (PE)

Blockage of an artery in the lung by a blood clot arriving from the veins in the lower- or upper limbs

## Quality of Life (QoL)

The general well-being of the individual and usually determined by applying one of a number of validated questionnaires

## Venous thromboembolism (VTE)

Blood clots in the venous system that includes deep vein thrombosis (DVT) and pulmonary embolism (PE)

## World Thrombosis Day (WTD)

A global campaign of educational events taking place each year on 13 October (birthday of Rudolf Virchow, a pioneer on the pathophysiology of thrombosis); its aim is to increase awareness of the "often overlooked and misunderstood condition of thrombosis"



Across the EU, cancer is a leading cause of death, and the European Commission has set goals for reducing cancerrelated deaths by 15% in 2020. Thrombosis is an often overlooked cause of death in cancer patients that can be readily prevented and treated. Action is needed to reduce the morbidity and mortality of patients with cancer-associated thrombosis (CAT). There is a vital need to increase awareness of:

- the impact of CAT on cancer patients' morbidity and mortality, their quality of life and on health service costs
- the means of preventing and treating thrombosis more efficiently in cancer patients
- the need for early diagnosis of cancer-associated venous thromboembolism (VTE), which is the main form of CAT

The Expert Steering Group discussed and developed an action plan and endorsed the following goal:

"The goal of the action plan is to increase the provision of prevention, early diagnosis and appropriate treatment of VTE to all cancer patients, with the ultimate aim of reducing morbidity and mortality."

To achieve this goal, the group agreed that the lack of awareness, among all stakeholders, of the increasing risk and impact of thrombosis in cancer patients is the key barrier that needs to be overcome.

The action plan aims to raise the level of awareness of health care professionals, policy-makers, health authorities, patients and patient associations. This should be achieved at the national, European and international level by focusing on the following key areas:

- developing and increasing the medical scientific evidence base
- collecting and evaluating physicians' experience
- collecting more evidence of the current burden of cost for health services of CAT
- provision of expert advice and education to the medical profession
- dissemination of the medical scientific and economic facts to health care professionals, policy-makers, health authorities and patient associations
- monitoring of patients' experiences and their quality of life

This report sets out the findings of the meeting of the Expert Steering Group in detail and presents the call for action aimed at different target groups.

# About the Expert Steering Group

The Expert Steering Group met in Brussels on 11-12 December 2015, with the objective of setting the highlevel goal of reducing the negative impact of CAT on cancer patients and recommended actions required to achieve this goal. The group examined the current evidence of the impact of CAT, and the barriers to optimal treatment, early diagnosis and treatment. The Expert Steering Group was jointly chaired by Professor Manuel Monreal of the Universidad Autónoma, Barcelona and Evelyn Knight of the UK charity AntiCoagulation Europe; the members of the Group are listed in appendix on page 14.

# Overview of CAT: prevalence, prognosis, treatment, and costs

Although CAT is a significant health and economic burden, and a major cause of cancer death, its prevention and management is often being overlooked due to a major lack of awareness of its seriousness.

## Thrombosis is one of the leading causes of cancer death

Cancer is a leading cause of death, with 8.2 million cancerrelated deaths reported worldwide in 2012<sup>1</sup>. The European Commission has set a goal for reducing cancer-related deaths by 15% by 2020. Thrombosis is one of the leading causes of death in cancer<sup>2</sup>. Venous thromboembolism (VTE) is a common cause of CAT and often involves potentially-fatal blockage of a lung artery (pulmonary embolism) and of veins in the leg (deep vein thrombosis)<sup>2</sup>. Venous thromboembolism is registered as the cause of death in an estimated 4,000 patients per year in the UK<sup>3</sup>, although this is probably an under-estimate because VTE is often overlooked as a cause of death. The risk of death for cancer patients with VTE is more than 3-times greater than that for non-cancer patients with VTE<sup>4</sup>.

# Cancer patients have a high risk of suffering venous thromboembolism (VTE)

In both Europe and the USA, large population-based studies and surveys of large disease registries reveal that about 20% of patients with VTE have cancer<sup>4-7</sup>. However, this figure is likely to be revised upwards due to increased screening, in some countries, for non-symptomatic and often overlooked VTE<sup>8</sup>. The survey of the Spanish National Discharge Database<sup>7</sup> ffound that, of those patients who suffered secondary pulmonary embolism during hospitalisation for other reasons, the highest proportion were admitted because of cancer (21%), which was much more than the number admitted because of acute respiratory failure (11%), acute heart failure (6.4%), stroke (6.1%) or pneumonia (5.5%). A retrospective survey of 66,106 hospitalised cancer patients showed that, depending on the type of cancer, between 2.7% to 12.1% of these patients experienced VTE during their first hospitalisation<sup>9</sup>. Cancer patients are estimated to have a 2- to 20-fold higher risk of developing VTE than non-cancer patients<sup>10</sup>. The risk is highest during the first 3-6 months after cancer diagnosis<sup>10</sup>. Surgery, chemotherapy, radiotherapy,



hospitalisation and immobility increase the risk of cancer-associated VTE<sup>11</sup>. In several types of cancer, the risk of VTE is particularly high, such as in cancers of the brain, pancreas, ovary, stomach, lung, kidney and bone<sup>5</sup>.

# The morbidity and mortality of VTE are much greater in cancer patients than in non-cancer patients

Separate population-based surveys of patients with VTE report that the rate of fatal pulmonary embolism is higher in patients with cancer<sup>4,7</sup>. Furthermore, the data from the RIETE registry<sup>4</sup> reveal a more than 2-fold greater risk of recurrent VTE and major bleeding in cancer patients with VTE than in non-cancer patients with VTE. Cancer patients with VTE were also found to have, in addition to increased risk of fatal pulmonary embolism, a greater risk of fatal bleeding. Renal dysfunction, metastatic disease and immobility (for  $\geq 4$  days) were each identified as independent factors contributing to this increased risk of morbidity and mortality. In one study, patients with cancer and VTE were approximately 4-times more likely to develop recurrent thromboembolic complications and twice as likely to develop major bleeding during anticoagulant treatment than non-cancer patients with VTE<sup>12</sup>.

Although the risk of VTE is reported to be greater with more advanced cancer, there is evidence that VTE may be more lethal in early-stage cancer<sup>13</sup>. Furthermore, early-stage cancer is generally associated with a better prognosis and such patients are likely to receive a greater survival benefit from anticoagulant treatment than late-stage cancer patients<sup>13</sup>.

The occurrence of VTE increases the risk of another vascular thromboembolic event; for example, during the first year after a pulmonary embolism, there is a three-fold increased risk of a cardiovascular event and a 2.5-fold risk of a cardiac arrest<sup>14</sup>. This increased risk is an important factor in cancer treatment, such as in the thrombosis-affected cancer patient who is under adjuvant anticancer therapy. Such patients are likely to survive long enough to experience a second thrombotic event<sup>13</sup>.

# Cancer patients with VTE have significantly increased treatment costs and a greatly reduced quality of life

Treatment of VTE in the cancer patient is needed long-term and this adversely affects the patient's quality of life<sup>15</sup>, such as by interfering with planned chemotherapy regimens<sup>16</sup>. It is also an extra financial burden. Data from the USA indicate that the average cost of VTE management ranges from 7,700 to 16,000 USD and, in cancer patients, VTE-associated costs can be as high as 20,000 USD<sup>17</sup>.

Hospitalisation, which is required in most patients with pulmonary embolism, is a major factor in increasing the economic burden of VTE in the cancer patient. Data from a 2-year nationwide survey in France<sup>18,19</sup> showed that, for cancers of the breast, lung, colon and prostate, hospitalisation due to VTE occurred in 2.0%, 2.2%, 9.6% and 6.0% of patients, respectively, while hospitalisation due to VTE recurrences occurred in 15.9%, 14.4%, 28.2% and 22.3% of patients, respectively. This survey revealed that the average cost per hospital stay ranged from 3,261 to 3,599 Euros, while the total cost per patient of at least one VTE recurrence ranged from 5,441 Euros in colonic cancer to 5,692 Euros in prostate cancer. The total cost of hospitalisation due to cancerassociated VTE was 1,98 million Euros for breast cancer, 1,43 million Euros for prostate cancer, 5,9 million Euros for lung

cancer and 3,99 million Euros for colon cancer, which is a grand total of 13,3 million Euros.

A number of studies indicate that the total cost of treating a cancer patient with VTE is considerably greater than the cost of treating a cancer patient without VTE<sup>10</sup>. A systematic review of data published between January 2000 and December 2012 revealed that mean total annual cost of treatment is almost 50% greater for the cancer patient with VTE<sup>10</sup>.

# There is an urgent need to increase use of thromboprophylaxis in cancer patients

Both cardiological<sup>20</sup> and oncological clinical guidelines<sup>11,21,22</sup> recommend anticoagulant prophylactic treatment in specific groups of cancer patients. Thromboprophylaxis is recommended for most hospitalized patients with cancer and only in those outpatients with cancer that have other VTE risk factors<sup>20-21</sup>. The most recent guidelines recommend low-molecular weight heparin (LMWH) over other anticoagulants<sup>21,22</sup>. They also state that, for patients undergoing major cancer surgery, thromboprophylaxis should start before surgery and continue for a minimum of 7-10 days and possibly up to 4 weeks in cases of major surgery. This guideline also states that cancer patients should be periodically assessed for VTE risk and oncologists should "educate" patients about the signs and symptoms of VTE. In patients with established VTE or pulmonary embolism, 5 to 10 days of treatment with LMWH is recommended, with long-term, secondary prophylaxis continuing for at least 6 months<sup>22</sup>.

Due to inadequate compliance to guidelines on thromboprophylaxis, up to 10% of cancer outpatients and up to 20% of hospitalised cancer patients experience VTE during the course of their illness and, therefore, suffer the extra burden of the clinical effects of VTE on top of their cancer symptoms<sup>23</sup>.

Because acutely-hospitalised cancer patients suffer greater VTE-associated morbidity than non-cancer patients, including having a greater risk of developing pulmonary embolism, they should be considered for thromboprophylaxis<sup>7,24</sup>. Although, up to 78% of cancer patients who experience thrombosis, do so as outpatients<sup>25</sup>, United States and European guidelines do not recommend the routine widespread use of thromboprophylaxis for cancer outpatients.

Cancer patients have a significant risk of VTE, which can involve deep vein thrombosis and pulmonary embolism, and can be fatal. There is, therefore, a need for all healthcare professionals who are dealing with cancer patients to systematically assess the risk of VTE in regard to patient-, cancer-, and treatment-related factors.

# The barriers to treatment of cancer-associated VTE: evidence supporting the need to improve awareness of the risk of cancer-associated VTE

According to the European Society of Medical Oncology (ESMO), "most oncologists underestimate the prevalence of VTE and its negative impact on their patients"<sup>11</sup>. Clinical guidelines on treatment of cancer-associated VTE, specifically the recommended use of LMWH, are poorly followed or implemented by, amongst others, hospitals and pharmacies<sup>3,11</sup>. The American Society of Clinical Oncology (ASCO) guideline recommendations on prophylaxis and treatment of VTE in cancer are not being adequately followed either and this "underscores the need to further promote educational activities on VTE prophylaxis and treatment in cancer patients particularly among all physicians and nurses caring for cancer patients"<sup>23</sup>.

There is consistent evidence, derived from large multinational and national surveys of patients at risk of VTE, of the failure or reluctance to apply guidelines on the prophylaxis and treatment of VTE in cancer<sup>17</sup>. For example, in one French cohort, only 55% of cancer patients at risk of VTE received anticoagulant treatment<sup>26</sup>.

According to the UK Government's All-Party Parliamentary Thrombosis Group<sup>3</sup>, VTE is under-diagnosed to a large degree and only 54% of patients receiving chemotherapy are made aware of the associated risk of VTE. In the UK, only 41% of hospital trusts have a policy for managing cancer-associated VTE.

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# Cancer-associated VTE needs to be made a priority issue for health care professionals and policy-makers

Increasingly more cancer patients are being treated by nonspecialists, rather than by haematological oncologists or other specialists in VTE treatment<sup>23</sup>. This may partly explain the lack of compliance with current guidelines.

Most cancer patients are treated as outpatients and by general practitioners, gynaecologists, gastroenterologists, urologists, surgeons or other non-specialists, who may not be fully aware of current guidelines – these are generally published in specialist journals<sup>23</sup>. Therefore, there is a critical need to increase the awareness, among non-specialists but also specialists, of the unique significance of VTE in cancer patients as a major cause of increased morbidity and mortality, as well as of increased cost and reduced quality of life.

Furthermore, in order to reduce the morbidity and mortality of cancer patients caused by VTE, there must be increased provision, to all cancer patients, of prevention, early diagnosis and effective and safe treatment of VTE. In order that these aims are achieved, they must be prioritised by policy-makers and hospital heads, who must be, therefore, be made aware of the current low awareness of this important clinical issue, of the consequent high costs of treatment and the potential to considerably reduce healthcare costs. According to USA data, derived from a large study of cancer patients on chemotherapy<sup>27</sup>, healthcare costs were significantly higher in patients with VTE (110,719 USD) than in patients without VTE (76,804 USD). In France, pulmonary embolism and VTE were the most frequent diagnosis leading to hospital admission in patients with breast or prostate cancer. The mean cost per stay for the first thrombotic event was €3,611 and €3,302 for breast and prostate cancer patients, respectively<sup>18</sup>.



The expert group considered the clinical and economic impact of CAT and the existing challenges and opportunities for providing optimal management of CAT, and agreed on the following goal:

The goal of the action plan is to increase the provision of prevention, early diagnosis and appropriate treatment of VTE to all cancer patients, with the ultimate aim of reducing morbidity and mortality.

To achieve this goal, the group agreed that the lack of awareness, among all stakeholders, of the increasing risk and impact of thrombosis in cancer patients is the key barrier that needs to be overcome.





early diagnosis and appropriate treatment

reduce morbidity and mortality

# Action is needed to inform key groups about appropriate prevention, early diagnosis and effective and safe treatment of VTE

Relevant data on the prevention, early diagnosis and effective and safe treatment of VTE need to be collected and assessed in order to be able to further substantiate the clinical and economic burden of CAT. Expert oncology groups need to be contacted to initiate efforts to harmonise Clinical Guidelines on prevention, early diagnosis and treatment of cancerassociated VTE and for the publication of such guidelines in as many journals as required in order to reach non-specialists and specialists in VTE prevention and management in cancer patients.

In order to achieve effective deployment of patient-centred and multidisciplinary care for the complex condition of CAT, all relevant stakeholders need to be targeted. These include the following groups:

- Patients, families and care-providers
- Medical practitioners oncologists, general practitioners, local authorities and social services, public health, other medical specialties, intensive care staff, surgeons, radiologists, radiographers, chemotherapists, emergency personnel, palliative care personnel, psychologists – ancillary personnel and supportive services
- Nurses (including specialist nurses and nurse practitioners)
- Policy-makers (including national and regional authorities)
- Hospital leaders (including payers, administrators, safety personnel)
- Pharmacists
- Patient associations
- Press / media / internet (including celebrity role models)
- Professional medical associations.

The Expert Steering Group decided to prioritise target groups for specific, limited actions that focused on selected issues (one or two per group) that are relevant to the specific group.

The table in section 9 lists how the target groups are to be prioritised and the respective actions.

# Summary of goal and recommendations for action

**The goal of the action plan** is to increase the provision of prevention, early diagnosis and appropriate treatment of VTE to all cancer patients, with the ultimate aim of reducing morbidity and mortality

| TARGET GROUPS   | ACTIONS   |  |   |  |  |  |  |
|---|---|--|---|--|--|--|--|
| Patients, families<br>and carers  | Provide better information<br>for patients at their 1st<br>appointment (diagnosis &<br>repeat at 2nd appointment) -<br>CAT Patient Charter  | Provide information on<br>signs of VTE as another<br>complication but without<br>causing anxiety. Important<br>role in improving treatment<br>compliance | Increase awareness<br>of psychological /<br>emotional impact<br>and psychosocial<br>consequences                |  |  |  |  |
| Oncologists and all<br>medical specialists,<br>including family<br>physicians, who see<br>and treat cancer<br>patients. | Increase awareness of:<br>1. impact of VTE on QoL<br>2. patients at risk<br>3. importance of prophylaxis<br>4. significance of immobility<br>5. need to refer high-risk<br>patients | Publish formal paper<br>on overall survival with<br>cancer-associated VTE in<br>oncology / haematology<br>journal  | Raise awareness<br>of importance of<br>supportive care  | Manage of incidental<br>PEs / duration of<br>treatment   | Use brief simple<br>messages with<br>data  |  |  |
| Hospital leaders <sup>1</sup>   | Demonstrate cost burden on<br>society   | Issue "invest-to-save"<br>message; potential to save<br>lives & money  | Emphasize<br>importance of<br>adequate prophylaxis  | Emphasize value<br>of accreditation as<br>a multidisciplinary<br>cancer centre – the<br>best market strategy |  |  |  |
| Professional medical associations   | Provide evidence required for them to update guidelines   | Organise meeting of key<br>national guideline authors<br>& promote harmonised<br>guidelines – before WTD<br>2016   | Develop prevention /<br>diagnosis / treatment<br>algorithms for<br>policymakers                                 |  |  |  |  |
| Health partners<br>and medical<br>professionals <sup>2</sup>  | Raise awareness of the<br>importance of supportive care   | Map patient journey &<br>indicate stages at which<br>each health partner group<br>can have an influenced and<br>provide benefit improved<br>by each      | Develop harmonised<br>education package<br>that can be adapted<br>for each health partner<br>group's guidelines | Provide specialised<br>information on<br>signs & symptoms<br>for radiologists and<br>radiographers           | Devise risk<br>assessment<br>model (RAM)   |  |  |
| Nurses <sup>3</sup>   | Raise awareness of importance<br>of supportive care and exercise<br>(walking)   | Provide tools to enable<br>them to support patients<br>pre- and post-cancer-<br>associated VTE   | Inform of the need to<br>improve monitoring<br>and recognition of VTE<br>symptoms                               | Improve injection<br>techniques  | Emphasize need<br>more specialist<br>cancer-associated<br>VTE nurses in<br>urban centres |  |  |
| Policymakers <sup>4</sup>   | Demonstrate cost burden<br>on society; invest-to-save<br>message; potential to save lives<br>and money  | Demonstrate the meaning<br>of their own data compared<br>to that in other areas /<br>countries   | Promote use of<br>quality control / audit<br>/ accreditation with<br>potential penalties                        |  |  |  |  |
| Pharmacists   | Inform on safety issues<br>regarding VTE treatment and<br>some cancer drugs   | Provide tools to enable<br>them to support patients<br>pre- & post-cancer-<br>associated VTE   | Raise awareness<br>of importance of<br>supportive care  | Ensure secure<br>means of<br>communication with<br>drugs experts   | Invest to save<br>message;<br>potential to save<br>lives and money                       |  |  |
| Press / media /<br>internet <sup>5</sup>  | Use to promote key messages:<br>WTD; VTE & cancer;<br>harmonising international<br>clinical guidelines  | Promote simple, accessible<br>messages on self-care<br>actions that will help<br>prevent VTE / improve QoL   | Provide numbers of<br>preventable deaths<br>& disability / money<br>saving potential                            | Make use of WTD<br>event / celebrity<br>with cancer / VTE as<br>role model                                   | Provide patient<br>stories / use<br>social media   |  |  |
| Patient associations<br>and charities   | Provide information on signs<br>& symptoms to raise patient<br>awareness without anxiety  | Encourage them to put<br>constant pressure on<br>policymakers & hospital<br>leaders  | Encourage them to<br>give information on<br>cancer-associated<br>VTE in newsletters,<br>leaflets, hotline etc   |  |  |  |  |

SHADING CODE

NEXT-TO-TOP PRIORITY

1. including payers, administrators, safety personnel

- 2. including GPs, local authorities and social services, public health, other medical specialties, intensive care staff, surgeons, radiologists, radiographers,
- chemotherapists, emergency personnel, palliative care personnel, psychologists
- 3. including specialist nurses and nurse practitioners

4. including government departments

5. including celebrity role models

# Action plan

The experts identified the following actions as of highest priority. Those actions (marked in blue in the table) are presented below:

# (i) Improve information about VTE and cancer-associated VTE to patients, families, carers and patient associations

At the first appointment, when their diagnosis is established, (and repeated at their second appointment) cancer patients need to be made fully aware that VTE is another possible complication of their disease and be told, without causing alarm and increasing anxiety, how to recognise signs of VTE. Provision of this information to the patient is vital and clinicians need to be made aware of their role in this. This requirement of clinicians and the information that they need to provide to the patient need to be contained in the relevant clinical guidelines. The information for the patients must be standardised across the guidelines and made simple and presented in a way that the patient is made aware that VTE could be another potential complication of cancer or its treatment, as is the case with nausea and vomiting.

The CAT Patient Charter will provide information and guidance, and set out key questions for patients to ask their healthcare professionals about how their risk of CAT will be managed. The aim is to ensure effective and evidence-based care for all cancer patients at risk of thrombosis. The objective of the patient charter is to empower patients to feel comfortable discussing how to prevent or manage CAT. CAT is a real concern for patients and may be life-threatening. It is important that further action is taken to assess patients for risk of CAT and then strive to prevent CAT and strive to make patients feel comfortable discussing CAT with their doctor or nurse, to ensure optimum quality of life.

# **CAT Patient Charter**

## AIM:

to ensure effective and evidencebased care for all cancer patients at risk of thrombosis

## **OBJECTIVE:**

to empower patients to feel comfortable discussing how to prevent or manage CAT

## (ii) Increase awareness of all aspects of VTE and cancerassociated VTE among oncologists and relevant nonspecialists

Because of the current low awareness of CAT, there is an urgent need to increase awareness, among all clinicians who are treating cancer patients, of the following:

- i. the impact of VTE on patient quality-of-life,
- ii. which patients are at risk of VTE,
- iii. the importance of prophylaxis,
- iv. the significance of immobility in increasing VTE risk,
- v. the need to refer high-risk patients.

Clinicians need to be made aware or be convinced that VTE is a serious risk in at least some cancer patients and that it is considerably under-diagnosed. They should consider CAT as being as clinical significant as cancer-associated neutropenia, for which there is a high level of awareness among clinicians. It is well established that anticoagulants are effective in preventing and treating VTE. However, clinicians need to be made aware how to diagnose VTE. They need to know that not all cancer patients are at a similar risk of VTE and that more data are needed in order that the individual cancer patient's risk of VTE can be better defined. More needs to be known about (i) how the risk of VTE varies between the type and stage of cancer and (ii) the effect of VTE and its treatment on the patient's quality of life.

Data on the increased risk of VTE in cancer patients need to be shared among oncologists and non-specialist clinicians in order for them to be comfortable informing patients of this risk; a "champion" key opinion leader is needed. There is substantial evidence from current practice that many cancer specialists do not consider any cancer patients as being at risk of VTE. They need convincing that assessing VTE risk should be an integral part of a multidisciplinary team approach to cancer management that begins at diagnosis.

Clinicians need to be provided with methods to determine which cancer patients are at risk of VTE.

(iii) Demonstrate to policy-makers the clinical and economic burden to society of cancer-associated VTE and how investment in the provision of disease information and of measures for its prevention, early diagnosis and treatment is a way to save lives and costs

Policy-makers need to receive information on the clinical and financial burden on society of cancer-associated VTE. The "invest-to-save" message for potentially saving lives and costs needs to be communicated to them, particularly in the context of current pressure on health services to reduce costs. For example, in the UK, data on the national clinical burden and cost of VTE in cancer patients is being shared with UK National Health Service Clinical Commissioning Groups (NHSCCGs), who could be shown the potential savings achieved through investment in simple education. This process was instigated by a parliamentary group of MPs and could be replicated within the EU, at national and European level. In general it would be of merit to provide more data to politicians about the burden of disease in their constituencies.

#### (iv) Clinical guidelines on the prevention, early diagnosis and treatment of VTE need to be harmonised and properly implemented so that cancer patients benefit from clinicians receiving consistent information

The organisations responsible for producing the relevant guidelines need to be contacted and provided with the required evidence for harmonising current guidelines and for updating them, so they contain consistent and relevant information. The current barriers to the proper implementation of guidelines on cancer-related VTE need to be identified. This would benefit patients by ensuring that they get the recommended and, therefore, safest treatment. It could for example be facilitated by organising meetings of key guideline authors in order to promote these aims – ideally before World Thrombosis Day (WTD) 2016.

# (v) Raise awareness among pharmacists about safety issues associated with VTE treatment and cancer drugs

Pharmacists need to be educated on (i) which anti-cancer drugs are associated with a risk of VTE and (ii) potential safety issues associated with VTE treatment. This should be facilitated by providing tools to enable them to support cancer patients, in an effort to prevent as well as treat VTE.

## (vi) Leverage media to promote key messages about CAT

The key messages need to be formulated and promoted through the media. The current low awareness of CAT has to be highlighted along with the key needs of providing information on the disease and its prevention, early diagnosis, and effective and safe treatment. The media should be engaged on World Thrombosis Day and at the publication of harmonised international clinical guidelines. Conclusions

Cancer-associated thrombosis has not received enough attention as a major cause of morbidity and mortality in patients with cancer.

This is despite the availability of treatments and international guidelines for prevention and management of cancerassociated VTE. The major clinical burden and health costs of CAT demand that action be taken to increase the awareness of all stakeholders of (i) the impact of cancer-associated VTE and (ii) the need to improve the deployment of available treatments and guidelines for diagnosis, prevention and treatment of cancer-associated VTE.

The Expert Steering Group proposes an action plan with the goal of ensuring an increased awareness of and education on the issues that need to be addressed in order to improve the provision of appropriate prevention, early diagnosis and effective and safe treatment of VTE to all cancer patients, and ultimately to reduce morbidity and mortality.

The experts decided on a plan of high priority actions aimed at increasing awareness of VTE in cancer. These planned actions target patients, families, carers and patient associations, who should become aware that VTE is a possible complication of cancer and its treatment. Oncologists and relevant nonspecialists are also targeted in order to increase their awareness of all aspects of VTE and cancer-associated VTE. Policy-makers will be approached with information on the clinical and economic burden to society of cancer-associated VTE and how provision of prevention, early diagnosis and effective and safe treatment of VTE can save lives and costs. Efforts will be made to improve relevant clinical guidelines and their implementation. All possible and relevant media forms and events will be used to promote the fact that VTE risk in cancer patients is a neglected issue that needs to be urgently addressed.

## High priority action plan targets:

PATIENTS FAMILIES CARERS PATIENT ASSOCIATIONS



## **POLICY-MAKERS**

## Appendix – List of Steering Group Members

## Steering Group Co-Chairs:

- Prof. Manuel Monreal, Clinical Professor of Internal Medicine at the Faculty of Medicine, Universidad Autónoma in Barcelona, and Head of Internal Medicine at the Hospital Universitari Germans Trias i Pujol in Barcelona, Spain
- Evelyn Knight, Co-Founder and Chief Executive, AntiCoagulation Europe

## Members:

- Prof. Dr. Miguel Ángel Calleja Hernández, Associate Professor, Pharmacology Department at Granada University, Spain
- Prof. Jacob C. Easaw, Associate Professor in the Division of Medical Oncology at the Tom Baker Cancer Center, Calgary, Alberta
- Prof. Ismaïl Elalamy, Professor of Haematology and Head of the Haematology Department at Tenon University Hospital, Paris, and current President of the French Society of Angiology

## Participating by telephone (Lync) link:

• Prof. Annie Young, Professor of Nursing at the University of Warwick, UK

#### Other participants:

- Her Excellency Louise Bang Jespersen, Ambassador of Denmark to Belgium
- Vibe Balthazar-Christensen, LEO Pharma, Denmark
- Germán Domecq, LEO Pharma, Denmark
- Jaime Manzanera, LEO Pharma, Spain
- Michael Bachmann Copentown Healthcare Consultants, Denmark
- Dr. Vivienne Kendall Copentown Healthcare Consultants, UK

# Invited participants who were unable to attend, but who have contributed to this report through their active involvement before and after the meeting:

- Dr. Isabelle Borget, Institut Gustave Roussy, Health Economy Service, Paris, France
- Prof. Dr. med. Axel Matzdorff, Head of Department of Hematology/Oncology, Hemostasis, Gastroenterology, Nephrology, Asklepios Clinic Uckermark, Schwedt, Germany

## References

- 1. WHO 2015. http://www.who.int/mediacentre/factsheets/fs297/en/.
- 2. Khorana AA. Cancer-associated thrombosis: updates and controversies. Hematology Am Soc Hematol Educ Program. 2012;2012:626-30.
- 3. APPTG, Venous Thromboembolism in Cancer: cancer chemotherapy and clots., A.-P.P.T. Group, Editor. 2015: London.
- 4. Monreal M, Falga C, Valdes M, Suarez C, Gabriel F, Tolosa C et al. Fatal pulmonary embolism and fatal bleeding in cancer patients with venous thromboembolism: findings from the RIETE registry. J Thromb Haemost. 2006;4(9):1950-6.
- 5. Heit JA, Spencer FA, White RH. The epidemiology of venous thromboembolism. J Thromb Thrombolysis. 2016;41(1):3-14.
- 6. Imberti D, Agnelli G, Ageno W, Moia M, Palareti G, Pistelli R et al. Clinical characteristics and management of cancer-associated acute venous thromboembolism: findings from the MASTER Registry. Haematologica. 2008;93(2):273-8.
- 7. Guijarro R, de Miguel-Diez J, Jimenez D, Trujillo-Santos J, Otero R, Barba R et al. Pulmonary embolism, acute coronary syndrome and ischemic stroke in the Spanish National Discharge Database. Eur J Intern Med. 2016;28:65-9.
- 8. Wun T, White RH. Epidemiology of cancer-related venous thromboembolism. Best Pract Res Clin Haematol. 2009;22(1):9-23.
- 9. Khorana AA, Francis CW, Culakova E, Fisher RI, Kuderer NM, Lyman GH. Thromboembolism in hospitalized neutropenic cancer patients. J Clin Oncol. 2006;24(3):484-90.
- 10. Kourlaba G, Relakis J, Mylonas C, Kapaki V, Kontodimas S, Holm MV et al. The humanistic and economic burden of venous thromboembolism in cancer patients: a systematic review. Blood Coagul Fibrinolysis. 2015;26(1):13-31.
- 11. Mandala M, Falanga A, Roila F. Management of venous thromboembolism (VTE) in cancer patients: ESMO Clinical Practice Guidelines. Ann Oncol. 2011;22 Suppl 6:vi85-92.
- 12. Prandoni P, Lensing AW, Piccioli A, Bernardi E, Simioni P, Girolami B et al. Recurrent venous thromboembolism and bleeding complications during anticoagulant treatment in patients with cancer and venous thrombosis. Blood. 2002;100(10):3484-8.
- 13. Maraveyas A, Johnson M. Does clinical method mask significant VTE-related mortality and morbidity in malignant disease? Br J Cancer. 2009;100(12):1837-41.
- 14. Sorensen HT, Horvath-Puho E, Pedersen L, Baron JA, Prandoni P. Venous thromboembolism and subsequent hospitalisation due to acute arterial cardiovascular events: a 20-year cohort study. Lancet. 2007;370(9601):1773-9.
- 15. Noble S, Prout H, Nelson A. Patients' Experiences of Llving with CANcer-associated thrombosis: the PELICAN study. Patient Prefer Adherence. 2015;9:337-45.
- 16. Lee AY. Cancer and venous thromboembolism: prevention, treatment and survival. J Thromb Thrombolysis. 2008;25(1):33-6.
- 17. Elting LS, Escalante CP, Cooksley C, Avritscher EB, Kurtin D, Hamblin L, et al. Outcomes and cost of deep venous thrombosis among patients with cancer. Arch Intern Med. 2004;164(15):1653–61.
- 18. Scotte F, Martelli N, Vainchtock A, Borget I. The cost of thromboembolic events in hospitalized patients with breast or prostate cancer in France. Adv Ther. 2015;32(2):138-47.
- 19. Borget I, Meyer G, Scotté F, Martelli N, Vainchtock A, Elalamy I. The Cost of Hospitalization for Thromboembolic Events in Patients with Colon or Lung Cancer Blood. 2014;124:3515.
- 20. Kahn SR, Lim W, Dunn AS, Cushman M, Dentali F, Akl EA et al. Prevention of VTE in Nonsurgical Patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2, Supplement):e195S-e226S.
- NCCN. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>™</sup>) https://www.nccn.org/ professionals/physician\_gls/f\_guidelines.asp: Cancer-associated venous thromboembolic disease Version 1 2015. 2015.
- 22. Lyman GH, Bohlke K, Khorana AA, Kuderer NM, Lee AY, Arcelus JI et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: american society of clinical oncology clinical practice guideline update 2014. J Clin Oncol. 2015;33(6):654-6.
- 23. Matzdorff A, Schwindel U, Müller M, Hutt HJ. Variable support towards ASCO recommendations for prophylaxis and treatment of cancer-associated venous thromboembolism (VTE). Phlebologie. 2015;44(6):320-3.
- 24. Lyman GH, Eckert L, Wang Y, Wang H, Cohen A. Venous thromboembolism risk in patients with cancer receiving chemotherapy: a real-world analysis. Oncologist. 2013;18(12):1321-9.
- 25. Streiff MB. Association between cancer types, cancer treatments, and venous thromboembolism in medical oncology patients. Clin Adv Hematol Oncol. 2013;11(6):349-57.
- 26. Bergmann JF, Cohen AT, Tapson VF, Goldhaber SZ, Kakkar AK, Deslandes B et al. Venous thromboembolism risk and prophylaxis in hospitalised medically ill patients. The ENDORSE Global Survey. Thromb Haemost. 2010;103(4):736-48.
- 27. Lyman GH, Khorana AA, Falanga A. Thrombosis and cancer: emerging data for the practicing oncologist. Am Soc Clin Oncol Educ Book. 2013.

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## **About LEO Pharma**

LEO Pharma is a research-based pharmaceutical company that has devoted many years to the development of a holistic approach to patients who have suffered, or are at risk of, venous thromboembolism (VTE), a major form of thrombosis.

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