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ABSTRACT

Introduction: Cancer-related pulmonary embolism (PE) is associated with poor prognosis. Some decision rules identifying patients eligible for home treatment categorize cancer patients at high risk of complications,

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precluding home treatment. We sought to assess the effectiveness and the safety of outpatient management of patients with low-risk cancer-associated PE.
Methods: In the HOME-PE trial, hemodynamically stable patients with symptomatic PE were randomized to either triaging with Hestia criteria or sPESI score. We analyzed 3 groups of low-risk PE patients: 47 with active cancer treated at home (group 1), 691 without active cancer treated at home (group 2), and 33 with active cancer as the only sPESI criterion qualifying them for hospitalization (group 3). The main outcome was the composite of recurrent venous thromboembolism, major bleeding, and all-cause death within 30 days after randomization.
Results: Patients treated at home had composite outcome rates of 4.3 % (2/47) for those with cancer vs. 1.0 % (7/691) for those without (odds ratio (OR) 4.98, 95%CI 1.15–21.49). Patients with cancer had rates of complications of 4.3 % when treated at home vs. 3.0 % (1/33) when hospitalized (OR 1.19, 95%CI 0.15–9.47). In multivariable analysis, active cancer was associated with an increased risk of complications for patients treated at home (OR 7.95; 95%CI 1.48–42.82). For patients with active cancer, home treatment was not associated with the primary outcome (OR 1.19, 95%CI 0.15–9.74).
Conclusions: Among patients treated at home, active cancer was a risk factor for complications, but among patients with active cancer, home treatment was not associated with adverse outcomes.

1. Introduction

Efficacy and safety of outpatient management of low-risk pulmonary embolism (PE) is now well-established. Guidelines recommend to consider for early discharge carefully selected patients at low risk of complications. The Hestia criteria [1], which are a pragmatic set of criteria identifying patients eligible or not for outpatient treatment, and the Pulmonary Embolism Severity Index (PESI) score (or its simplified version, the sPESI), assessing the risk of 30-day all-cause mortality, are well validated decision-making tools.

Venous thrombo-embolism (VTE) is associated with cancer in 20–30 % of cases [2,3], and represents the second leading cause of death after tumor progression in these patients [4]. The presence of cancer is a risk factor for short- and long-term mortality in patients with VTE [5,6], and appears to be independently associated with adverse events at 30 days [7]. For these reasons, some decision-making tools, such as the sPESI, categorize all cancer patients at high risk of complications. Consequently, a minority of patients with cancer-associated PE has been included in studies assessing the efficacy and safety of outpatient management, and data on their prognosis are lacking. Cancer-specific prognostic tools have been proposed to predict the risk of adverse events [8–12]. However, the lack of external validation, the poor reproducibility of their results, and the absence of direct comparison between these different scores limit their use for the selection of patients with cancer-associated PE at low-risk of complications who would be eligible for outpatient care in current clinical practice. Moreover, although hospitalization may benefit patients with acute PE by providing close monitoring and potentially early detection of adverse events, it may also expose them to a higher risk of iatrogenic complications, including infections, especially in the elderly. A propensity-matched cohort study suggested that hospitalized normotensive PE patients have a higher rate of recurrent VTE, major bleeding or deaths than patients managed as outpatients, regardless of their initial risk stratification [13]. Thus, avoiding hospital admission of patients with cancer could prevent the iatrogenic complications related to hospitalization and improve their quality of life (QoL), especially in the palliative care setting.

The aim of this post-hoc study was to evaluate safety of outpatient management of patients with low-risk PE and active cancer.

2. Materials and methods

The HOME-PE study was an international randomized open-label trial aiming to demonstrate that a triaging strategy based on the Hestia rule was non-inferior to a strategy based on the sPESI for home treatment of patients with objectively confirmed symptomatic PE [14].

For the purpose of this *post-hoc* analysis, patients included in the HOME-PE trial who met the following criteria were included and divided in three groups: patients with active cancer treated at home (group 1), patients without active cancer treated at home (group 2), and patients with active cancer as the only sPESI criterion qualifying them for hospitalization (group 3). This latter group included patients randomized to the sPESI arm and hospitalized because of a sPESI equal to 1 point due to the presence of cancer, and patients randomized to the Hestia group, without hospitalization criteria and with a retrospective calculation of the sPESI equal to 1 point due to cancer, but who were finally admitted to hospital following the decision of the physician-in-charge to overrule the Hestia rule as it was stated in the protocol. The retrospective calculation of the sPESI was a way to constitute a more homogeneous group.

All patients received therapeutic anticoagulation according to international guidelines [15].

2.1. Definition of active cancer and data of interest related to the oncologic history

Active cancer was defined as an ongoing cancer treatment in the year prior to inclusion in HOME-PE, or a cancer diagnosed in the year before or at the time of PE diagnosis. These criteria were checked for all patients included in the first and third group. Patients who didn't meet these criteria were reclassified as having a history of cancer and were not included in group 1 or 3.

Lastly, the following complementary data related to the cancer history and treatment were retrospectively collected from patients' medical records by an investigator:

- interval between cancer diagnosis and PE diagnosis; for patients who had multiple primary cancers, the diagnostic date used for the analyses was the one corresponding to the tumor diagnosed at the date closest to inclusion in HOME-PE,
- the anatomical site of the primary tumor,
- the stage of the cancer at inclusion or the stage available closest to inclusion, according to the TNM classification, divided into localized (TNM 1–2), locally advanced (TNM 3), metastatic (TNM 4), or not applicable when the TNM classification did not apply
- ongoing cancer therapies (chemotherapy, immunotherapy, anti-angiogenic therapy, hormonotherapy, radiotherapy, surgery, or palliative care) at the time of inclusion in HOME-PE, as well as the previously received antitumor treatments.

2.2. Outcomes

2.2.1. Primary outcome

The primary composite outcome was the rate of recurrent venous thrombo-embolism (VTE) event, major bleeding or all-cause death within 30 days of randomization. Recurrent VTE was defined as symptomatic, objectively confirmed deep venous thrombosis (DVT), non-fatal or fatal PE. Major bleeding was defined according to the criteria

proposed by the International Society on Thrombosis and Hemostasis [16]. All clinical events were adjudicated by an independent event adjudication committee.

2.2.2. Secondary outcomes

The composite rate of adverse events (recurrent VTE, major bleeding or all-cause death within 30 days after randomization) within 3 months after randomization was collected and compared between the first group and the two other groups.

An analysis of risk factors for the primary outcome was conducted among patients with active cancer (groups 1 and 3) and among patients treated as outpatients (groups 1 and 2).

Lastly, data related to patient quality of life and satisfaction were analyzed. Quality of life was evaluated with the 40-item *Pulmonary Embolism Quality of Life Questionnaire* (*PEmb-QoL*) [17], to quantify health-related quality of life in patients having experienced PE. Patient satisfaction with care was assessed using the *Anti-Clot Treatment Scale* (*ACTS*), which consists of two global questions and 15 items divided into two subscales: the *ACTS* Burdens scale (12 items) and the *ACTS* Benefits scale (3 items). Each item is rated from "not at all" to "extremely" using a five-point Likert scale. The items are coded so that higher scores indicate greater satisfaction.

2.3. Statistical analysis

We compared the rate of the primary outcome between the first and the second group (i.e., patients treated at home with and without active cancer respectively) and between the first and the third group (i.e., patients with active cancer or in remission for less than one year, treated at home or in hospital respectively). Comparisons between the different groups were conducted using the following tests: for quantitative variables, Student's *t*-test or Wilcoxon-Mann-Whitney test were used as appropriate. For comparisons of proportions of qualitative variables, the Chi-squared test or Fisher's exact test were performed. The level of statistical significance was set at a level of *p-value* <0.05. For quantitative variables, the results are presented as means $\pm$ standard deviation (SD) or medians and interquartile range [Q1; Q3] according to the variable distribution. For qualitative parameters, the results are presented as ratios (proportions in %) reported to available data. Missing data, if they exceeded 5 % in one of the three groups, were included in the total number of patients to which the proportions are reported.

For the identification of factors associated with the primary endpoint, a pre-selection was performed using the univariable association tests described above, and a bivariate logistic regression model. Variables with a *p*-value of 0.2 or less were retained. The independent risk factors were then obtained by construction and optimization of a multivariable logistic regression model, with a stepwise variable selection and minimization of the Akaike criterion (AIC).

The results are presented as odds ratios (OR) and corresponding 95 % confidence interval (CI). The association between a variable and the primary outcome was statistically significant in bivariate and multivariable analysis when the OR confidence interval did not include the value 1.

All statistical analyses and figures were performed with R software.

2.4. Ethics

This study was registered in the Commission Nationale Informatique et Liberté (CNIL) register of the CHU of Angers (n° ar21-0121v0) or approved by local ethics committee according to local regulation. All alive patients, for whom additional information not included in the initial database of the HOME-PE study were collected retrospectively, received an information letter. Only data from patients who did not express opposition were analyzed.

3. Results

3.1. Patients

A total of 1970 patients were randomized in the HOME-PE study and included in the intention to treat population. Among them, 249 patients were considered to have an active cancer or in remission for <1 year. However, 3 did not fulfill the criteria of active cancer after retrospective analysis of cancer related data and were reclassified as "history of cancer", leaving 246 patients with active cancer. Among them, 48 patients were discharged home but one patient was excluded because he could not be located to grant access to his medical chart, leaving 47 patients in group 1. In this group, 31 patients were randomized to the Hestia arm and 16 to the sPESI arm. Among these latter 16 patients with a sPESI$\geq$1, 7 refused to be hospitalized and 9 were discharged within 24 h after their randomization.

The remaining 198 patients were hospitalized. Among them, 33 were admitted only because of their active cancer and were included in group 3: 32 patients were randomized to the sPESI arm and were hospitalized because of a sPESI equal to 1 point for cancer. One of the Hestia patients was finally hospitalized, with a retrospectively calculated sPESI score of 1 point for cancer. Lastly, among the 1724 patients without active cancer, 691 were treated at home and were included in the group 2 (Fig. 1).

The baseline characteristics of the three groups are presented in Table 1. In patients with active cancer, the main anticoagulant treatment received during the 30 days following inclusion was low molecular weight heparin (LMWH). Most patients without active cancer (90.3 %) received direct oral anticoagulants (DOACs).

Data related to cancer history are shown in *Supplementary data*. The distribution of primary tumor sites was similar between the group 1 and 3; the main cancers affected the genito-urinary or gastro-intestinal tracts and breast; 67.5 % of all cancers had been diagnosed >6 months prior to the acute PE presentation. Cancer was diagnosed at the time of PE in 7.8 % of patients. In group 1, 21.3 % of cancers were localized, 10.6 % locally advanced, and 44.7 % metastatic. In group 3, 21.2 %, 15.2 % and 30.3 % were localized, locally advanced and metastatic, respectively.

At the time of inclusion in the study, 34 (72.3 %) patients in group 1 and 21 (63.6 %) in group 3 received at least one anticancer treatment. Only one patient (group 1) was in palliative care (*Fig. 3 Supplementary data*).

3.2. Study outcomes and clinical events

At day-30, the primary composite outcome occurred in 4.3 % (2/47) in group 1, 1.0 % (7/691) in group 2 and 3.0 % (1/33) in group 3. The rate of the composite outcome was significantly higher in patients with active cancer treated at home compared with those without (OR 4.98, 95 % CI 1.15–21.49) but was not different between patients with an active cancer treated at home or hospitalized (OR 1.19, 95%CI 0.15–9.47) (Table 2).

At day-90, the frequency of the composite outcome was higher in group 1 (6.5 %, 3/47) and in group 3 (15.2 %, 5/33) than in group 2 (1.9 %, 13/691) but the difference between group 1 and group 2 did not reach statistical significance (OR 3.58, 95%CI 0.8–11.64), nor between group 1 and group 3 (OR 0.39, 95%CI 0.08–1.72).

The majority of the complications occurred beyond the first 10 days of follow-up. Only 3 adverse events were observed before D10: one patient had a major bleeding and died 24 h later in group 1, and one VTE recurrence occurred in group 2 (Fig. 2 and Table 3).

3.3. Risk factors of adverse events at day-30

The results of the bivariate and multivariable analysis among patients treated at home are presented in *Supplementary data (e-Table 1)*. In the multivariable analysis, bed rest $\geq$72 h in the last 3 months, current

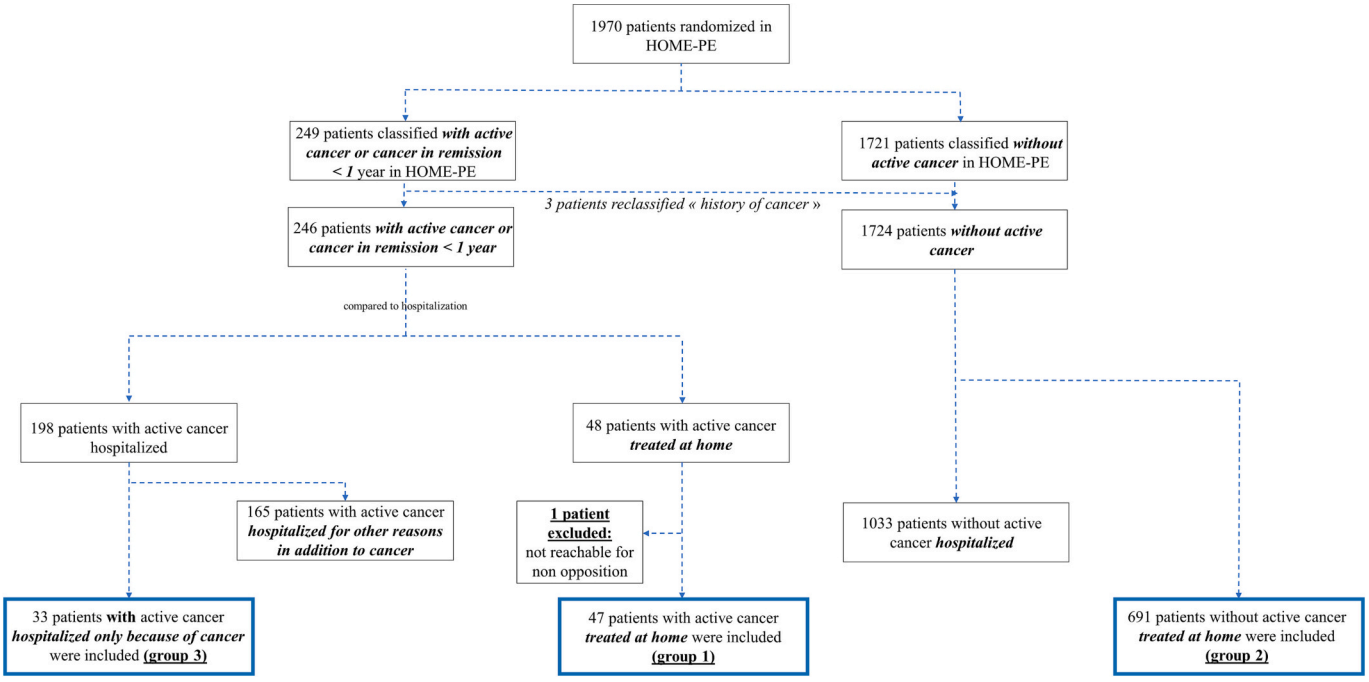

Fig. 1. Flow chart.

oestrogen therapy, and the presence of active cancer were independently associated with the primary composite outcome at 30 days. After adjustment for the presence or absence of active cancer, only the association with recent bed rest remained significant (OR 6.02, 95 CI% 1.59–22.79).

Among patients with an active cancer or in remission for less than one year, the results of the bivariate and multivariable analysis are presented in *Supplementary data (e-Table 2)*. Bed rest ≥72 h within past 3 months was independently associated with the primary outcome at 30-day. Home treatment was not associated with adverse event at 30-day (OR 1.19, IC 95 % 0.15–9.74).

3.4. Quality of life and satisfaction assessment

The results of the *PEmb-QoL* and *ACTS* questionnaires are presented in *Supplementary data eTable 3*. The results of the *PEmb-Qol* answers were comparable between the two groups of patients treated at home The *ACTS* score indicated that patients without active cancer and treated at home reported higher satisfaction. This group experienced a lower negative impact of oral anticoagulants compared to patients with active cancer, who were mostly treated with subcutaneous heparin injections.

No difference was noted in the *PEmb-Qol* and *ACTS* results between the two groups of patients with active cancer, whether they were treated at home or hospitalized.

4. Discussions

This *post-hoc* analysis of the HOME-PE study showed that active cancer was a risk factor of the composite of recurrent VTE, major bleeding and all-cause mortality among patients with symptomatic low-risk PE treated at home. However, the rate of complications was similar for patients with active cancer and low risk PE, irrespective of whether they were hospitalized or discharged to home directly. These data suggest that outpatient management of patients with low-risk PE and active cancer does not worsen their prognosis compared to hospitalization.

Only a minority of patients (<10 %) with cancer have been included in published studies assessing the efficacy and safety of PE home treatment [1,18,19], and this subgroup was not specifically analyzed. To our knowledge, only four studies evaluating home treatment of patients with cancer-associated VTE events have been published [10,20–22]. All these studies were observational, monocentric, with small sample size, often including both PE and DVT, with the latter being known to be at a lower risk of complications [20,21]. The outcomes were heterogeneous across the studies, with different timings and endpoints, making their comparison difficult. Beyond these limitations, these studies suggest that home treatment of cancer-related VTE might be feasible without worsening PE prognosis.

Our study population has been carefully defined. After reviewing the data from each patient's oncological history, only those with active cancer or in remission for less than one year were included. Unlike both the OTPE randomized trial [18] and another study [23], we excluded patients without active cancer but who only have a history of cancer, as they are at lower risk of complications. The distribution of primary tumor sites was comparable to other studies [10,20–22]. Almost 70 % of our patients with active cancer were undergoing either chemotherapy or hormonotherapy at the time of PE, both known to be risk factor for thrombosis [4,24]. The percentage of patients with metastatic cancer was 38.8 %, a somewhat lower figure than in other studies assessing home treatment of cancer-associated thrombosis [10,20]. Our population is therefore representative of patients with cancer-associated PE and can be considered at risk of complications based on their oncologic history. Nevertheless, the rate of complications was lower than reported in other studies [20]. This difference may be due to the eligibility criteria of a randomized trial such as the HOME-PE study, that may lead to the inclusion of patients with fewer comorbidities and better prognosis than non-eligible patients [25].

Among independent risk factors of complications during home treatment, ongoing oestrogen therapy was significantly associated with the composite outcome. This was mainly explained by major bleeding, particularly gynaecological, observed exclusively in group 2. Bleeding probably followed oral contraceptive discontinuation upon PE diagnosis. However, this association between bleeding and oestrogen therapy did not persist after adjusting for the presence of active cancer. Bed rest within the previous 3 months was also strongly correlated with adverse outcomes during home treatment. Recent immobilization for a medical reason has been identified as a strong predictor of short-term

Table 1
Demographics and clinical characteristics of patients at baseline.

	Patients with active cancer treated at home (group 1) n = 47	Patients without active cancer treated at home (group 2) n = 691	Patients with active cancer hospitalized (group 3) n = 33	p-Value (Group 1 VS group 2)	p-Value (Group 1 VS group 3)
Characteristics					
Age, years, *median [Q1;Q3]*	65 [55.5; 73]	59 [45; 69]	70 [63; 75]	0.005	0.10
>80 years, *n (%)*	5 (10.6 %)	30 (4.3 %)	0 (0 %)	0.049	0.07
Female sex, *n (%)*	22 (46.8 %)	318 (46.0 %)	16 (48.5 %)	0.92	0.88
ED presentation to randomization, *h, median [Q1; Q3]*	0.36 [0.16; 0.75]	0.5 [0.23;0.86]	0.46 [0.26;0.93]	0.19	0.33
Duration of hospitalization at day-30, *days, median [Q1;Q3]*	1 [0;2]	1 [0;1]	5 [3;8]	0.23	<0.001
Medical history, *n (%)*					
Previous venous thrombo-embolism	10 (21.3 %)	179 (26.4 %)	6 (18.2 %)	0.44	0.73
Current oestrogen therapy	0 (0 %)	64 (9.4 %)	3 (9.1 %)	0.02	0.07
Bed rest >72 h within past 3 months	6 (12.8 %)	50 (7.4 %)	2 (6.1 %)	0.18	0.46
Surgery within past 3 months	10 (21.3 %)	57 (8.4 %)	5 (15.2 %)	0.003	0.49
Chronic heart failure	1 (2.1 %)	7 (1.0 %)	0 (0 %)	0.42	1.00
Chronic lung disease	1 (2.1 %)	37 (5.4 %)	0 (0 %)	0.50	1.00
PE diagnosed during anticoagulation	4 (8.5 %)	33 (4.9 %)	3 (9.1 %)	0.29	1.00
Signs and symptoms, *n (%)*					
Syncope	0 (0 %)	18 (2.6 %)	2 (6.1 %)	0.62	0.17
Systolic blood pressure <100 mmHg	1 (2.1 %)	2 (0.3 %)	0 (0 %)	0.18	1.00
Heart rate ≥ 110 b.p.m.	5 (10.6 %)	61 (9.0 %)	0 (0 %)	0.70	0.07
Oxygen saturation <90 %	1 (2.2 %)	2 (0.3 %)	0 (0 %)	0.18	1.00
Right ventricular dilatation[a]	1 (2.1 %)	89 (12.9 %)	7 (21.2 %)	0.02	0.006
High level of troponin[b]	6 (12.8 %)	84 (12.2 %)	12 (36.4 %)	0.23	0.22
High level of BNP or NT-proBNP[c]	2 (4.3 %)	28 (4.1 %)	6 (18.2 %)	NA	NA
Anticoagulant treatment[d], *n (%)*					
Direct oral anticoagulant	12 (25.5 %)	624 (90.3 %)	7 (21.2 %)	<0.001	0.48
Low molecular weight or unfractionated heparin	33 (70.2 %)	27 (3.9 %)	22 (66.7 %)		
Vitamin K antagonist	0 (0 %)	19 (2.7 %)	2 (6.1 %)		
Miscellaneous	2 (4.3 %)	21 (3.0 %)	2 (6.1 %)		
Biological parameters, *median [Q1;Q3]*					
Hemoglobin (g/dL)	12.4 [11.2; 13.4]	13.8 [12.8; 14.9]	12.1 [10.7; 13.6]	<0.001	0.53
Platelet count (G/L)	204 [148; 250]	240 [196; 282]	215 [133; 277]	0.001	0.81
Creatinine level (μmol/L)	76 [60; 86]	76 [64; 88]	82 [64; 94]	0.42	0.24

[a] Right ventricle/left ventricle >1 on computed tomography pulmonary angiography or on transthoracic echocardiography; assessed in 40 (85.1 %) patients in the group 1, 575 (83.2 %) patients in the group 2 and 27 (81.8 %) patients in the group 3.
[b] Troponin level > 99th percentile according to local technique; assessed in 20 (42.6 %) patients in the group 1, 439 (63.5 %) patients in the group 2 and 25 (75.8 %) patients in the group 3.
[c] BNP (B-type natriuretic peptide) >100 ng/L or NT-proBNP (N-terminal proBNP) >600 ng/L; assessed in 2 (4.3 %) patients in the group 1, 28 (4.1 %) patients in the group 2, and 6 (18.2 %) patients in the group 3.
[d] Main anticoagulant treatment, i.e. drug prescribed ≥90 % of the time, within 30 days following inclusion.

mortality during acute PE [26]. Immobilization is a marker of severe comorbidities, and a more impaired general condition. In our study, all patients with active cancer treated at home who met the composite endpoint had a recent immobilization. Bed rest is a factor included in other prognostic model, such as the RIETE score [9]. Whether bed rest is due to the adverse effects of cancer treatments, an acute event or the cancer itself, it remains a poor prognostic factor, reflective of an increased underlying fragility.

During home treatment, active cancer was significantly associated with the primary outcome at day-30, after adjustment for potential confounders (OR 7.95, CI 95 % 1.48–42.82). Even if these patients were categorized at low risk regarding their PE, active cancer exposed them to a worse outcome than the population without cancer. Nevertheless, among patients with active cancer, home treatment was not independently associated with an increased risk of complications. While the presence of underlying cancer is one of the main reasons for hospital admission for low-risk PE [27], our results suggest that active cancer alone may not justify hospitalization. Notably, we found that a minority (11.5 %) of 3-month complications occurred within the first 10 days of follow-up, as reported previously [18]. These results provide further evidence that the benefits of routine hospitalization of low-risk PE patients with cancer are questionable, as they have an increased risk of complications. However, home treatment may require a close follow up. In the HOME-PE trial, a thrombosis team conducted patients' follow-up at 3 days, 14 days, 1 month and 3 months and provided a support and a telephone service in case of complication.

Table 2
Clinical outcomes at day-30 and day-90.

	Patients with active cancer treated at home (group 1) n = 47	Patients without active cancer treated at home (group 2) n = 691	Patients with active cancer hospitalized (group 3) n = 33	OR (Group 1 VS group 2) [95 % CI]	OR (Group 1 VS group 3) [95 % CI]
Main outcome (at day-30), n (%)	**2 (4.3 %)**	**7 (1.0 %)**	**1 (3.0 %)**	**4.98 [1.15–21.49]**	**1.19 [0.15–9.47]**
All-cause death	1 (2.1 %)	1 (0.1 %)	0		
Recurrent VTE	0	2 (0.3 %)	0		
Major bleeding	2 (4.3 %)	4 (0.6 %)	1 (3.0 %)		
Missing data	0	5	0		
Clinical events at day-90, n (%)	**3 (6.5 %)**	**13 (1.9 %)**	**5 (15.2 %)**	**3.58 [0.8–11.64]**	**0.39 [0.08–1.72]**
All-cause death	1 (2.2 %)	2 (0.3 %)	5 (15.2 %)		
Recurrent VTE	2 (4.3 %)	4 (0.6 %)	0		
Major bleeding	2 (4.3 %)	9 (1.3 %)	1 (3.0 %)		
Missing data	1	10	0		

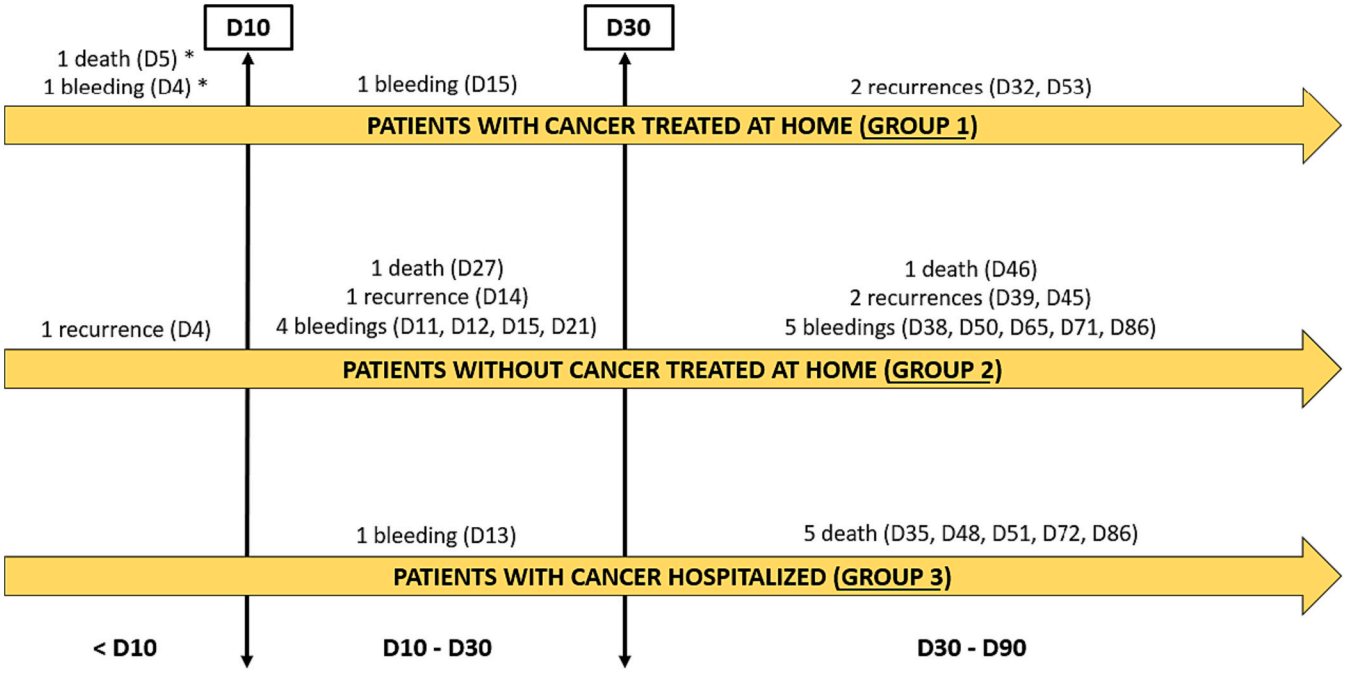

Fig. 2. Timing of onset of adverse events during follow-up. *: in group 1, both complications occurred in the same patient. *D = Day.*

Identifying the best candidates for home treatment among patients with cancer-related PE remains challenging. The sPESI score is a widespread decision-making tool in routine practice but it categorizes all patients with a history of cancer at risk of 30-day all-cause death, excluding them from home treatment. It's worth noting that the PESI and sPESI score were initially developed to classify PE patients into categories of increasing risk of 30-day all-cause mortality, and not as a tool to select candidates for home treatment. Interestingly, Yamashita et al. reported in patients with active cancer a lower overall mortality rate at 30-day among patients with an sPESI score = 1 (with no item other than cancer) compared to those with a score ≥ 2 (5.8 % and 14.5 % respectively, $p = 0.02$), in the subgroup of out-of-hospital PE [28]. The more pragmatic Hestia criteria could allow a better selection. In the HOME-PE trial, all data were prospectively collected in the electronic case report form (eCRF) for possible retrospective calculation of sPESI or Hestia for all patients. Among the 32 patients randomized in the sPESI arm and qualified for hospitalization solely on the item "cancer", 20 had no Hestia criteria and would have been therefore eligible for home treatment.

Home treatment is important for retaining of patients' autonomy and may improve their perception of health and quality of life. The psychosocial advantages and QoL considerations of home treatment are particularly relevant for cancer patients. Studies in patients with advanced cancer showed significant decline in QoL during hospitalization [29]. The quality of life and satisfaction scores used in the HOME-PE study did not show any significant difference between cancer patients treated in hospital and those treated at home. While home management seems well accepted and appreciated, it is generally difficult to obtain a significant difference in scores between outpatients and hospitalized patients. The timing of the assessment, i.e., at 30 days, may have been too delayed, and may have attenuated the differences between groups. Notably, among patients without cancer treated at home, the negative impact of anticoagulant was lower than for patients with an active cancer who were mainly treated with injections of LMWH. Considering the recent results of trials supporting the non-inferiority of DOAC compared of low-molecular weight heparin during cancer-associated VTE [30], quality of life and satisfaction in home-treated cancer patients may be similar to those of non-cancer patients.

4.1. *Strengths and limitations of the study*

This study compared for the first time PE patients with active cancer

Table 3
Summary of characteristics of patients who met the primary outcome.

Patient's group	Time to onset of the event	Type of adverse event	Baseline characteristics	Thromboembolic risk factors	Symptoms and signs at baseline	Anticoagulant treatment within 30 days following inclusion	Data related to cancer
Group 1	Day-4	Major bleeding	Male, 62 years old	Bed rest, surgery <3 months	HR ≥110 b.p.m.	miscellaneous	Diagnosis<6 months before inclusion Metastatic hepato-bilio-pancreatic cancer Receiving chemotherapy
	Day-5	Death					
Group 1	Day-15	Major bleeding	Male, 71 years old	Bed rest	High level of cardiac biomarkers	LMWH	Diagnosis >6 months before inclusion Metastatic genitourinary cancer Receiving hormonotherapy
Group 2	Day-14	Recurrence	Male, 51 years old		Right ventricular dilatation, high level of troponin	DOAC	NA
Group 2	Day-27	Death	Female, 63 years old	Previous venous thrombo-embolism, oestrogen therapy, bed rest	High level of troponin	DOAC	NA
Group 2	Day-12	Major bleeding	Female, 50 years old	Surgery <3 months	Right ventricular dilatation	DOAC	NA
Group 2	Day-15	Major bleeding	Female, 36 years old	Oestrogen therapy		DOAC	NA
Group 2	Day-11	Major bleeding	Female, 54 years old	Oestrogen therapy	High level of BNP or NT-pro-BNP	DOAC	NA
Group 2	Day-4	Recurrence	Female, 44 years old	Oestrogen therapy	Right ventricular dilatation	DOAC	NA
Group 2	Day-21	Major bleeding	Female, 48 years old			DOAC	NA
Group 3	Day-13	Major bleeding	Male, 75 years old	Bed rest	High level of troponin	Miscellaneous	Diagnosis >6 months before inclusion Hepato-bilio-pancreatic cancer

treated at home to cancer patients hospitalized solely due to the presence of cancer and to PE patients without active cancer treated at home. Our work differs in this from most available studies [10,20,21]. Indeed, cancer-associated VTE studies often included both PE and DVT patients. In our study, we focused on the prognosis of PE. Therefore, the low rates of complications observed in our study correspond to the most severe presentation of VTE. In addition, studies evaluating outpatient management or early discharge include highly variable in-hospital lengths of stay, ranging from <12 h to >3 days, complicating the reproducibility and generalization of their results [31]. In our study, patients treated at home were discharged within 24 h after randomization, the closest to a real home management strategy. Secondly, all clinical events were adjudicated by an independent event adjudication committee. There were very few lost of follow up, and the data collection was exhaustive and closely monitored.

The most important limitation is the small sample size which lowers the precision of outcome estimates and the determination of risk factor of worse outcome. Lastly, data related to cancer history were collected retrospectively, which resulted in missing data, especially regarding the tumor stage at the time of the study.

5. Conclusion

In our study, among patients with PE treated at home, the presence of an active cancer was an independent risk factor for recurrent VTE, major bleeding and all-cause mortality. However, the rates of adverse events were low, and not significantly different between cancer patients treated at home and those hospitalized solely because of the cancer. Larger prospective randomized dedicated studies are needed to establish the safety of home treatment compared to hospitalization in patients with low-risk cancer associated PE.

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CRediT authorship contribution statement

Sérine Chaibi: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Pierre-Marie Roy:** Writing – review & editing. **Armelle Arnoux Guénégou:** Formal analysis. **Yohann Tran:** Formal analysis. **Olivier Hugli:** Writing – review & editing, Data curation. **Andréa Penaloza:** Writing – review & editing. **Francis Couturaud:** Writing – review & editing. **Cécile Tromeur:** Writing – review & editing. **Tali-Anne Szwebel:** Writing – review & editing. **Gilles Pernod:** Writing – review & editing. **Antoine Elias:** Writing – review & editing. **Alexandre Ghuysen:** Writing – review & editing. **Ygal Benhamou:** Writing – review & editing. **Nicolas Falvo:** Writing – review & editing. **Henry Juchet:** Writing – review & editing. **Mathilde Nijkeuter:** Writing – review & editing. **Ronne Mairuhu:** Writing – review & editing. **Laura M. Faber:** Writing – review & editing. **Isabelle Mahé:** Writing – review & editing. **Karine Montaclair:** Writing – review & editing. **Benjamin Planquette:** Writing – review & editing. **David Jimenez:** Writing – review & editing. **Menno V. Huisman:** Writing – review & editing. **Federikus A. Klok:** Writing – review & editing. **Olivier Sanchez:** Writing – review & editing, Validation, Supervision, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Olivier SANCHEZ reports a relationship with Bayer AG that includes: board membership, consulting or advisory, and speaking and lecture fees. Olivier SANCHEZ reports a relationship with Bristol Myers Squibb Co that includes: board membership, consulting or advisory, funding grants, and speaking and lecture fees. Olivier SANCHEZ reports a relationship with Pfizer France that includes: board membership, funding grants, and speaking and lecture fees. Olivier SANCHEZ reports a relationship with Sanofi Aventis France that includes: board membership, consulting or advisory, and speaking and lecture fees. Olivier SANCHEZ reports a relationship with Boston Scientific Corp that includes: board membership. Olivier SANCHEZ reports a relationship with Inari Medical Inc that includes: board membership, funding grants, and speaking and lecture fees. Olivier SANCHEZ reports a relationship with Boehringer Ingelheim Pharmaceuticals Inc that includes: board membership and funding grants. Olivier SANCHEZ reports a relationship with LEO Pharma France that includes: speaking and lecture fees. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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