GARFIELD-VTE is exploring acute and long-term management and outcomes in patients with symptomatic DVTs and PEs treated in a real-world setting with standard therapy and new oral anticoagulants (OACs).

VTE-Prevention – An Essential Task for Every Health Care System

About VTE

Deep-vein thrombosis (DVT) and pulmonary embolism (PE), either as the primary event or as a complication of DVT, are known collectively as venous thromboembolism (VTE).

Thrombosis can affect virtually any venous circulation. PE occurs when part of a clot formed in a deep vein, for example in the leg, is carried to the lung, via the heart, preventing the uptake of oxygen.

VTE is associated with reduced survival and substantial healthcare costs, and recurs frequently.

VTE is the third most common cardiovascular illness[i], after acute coronary syndrome and stroke, and is responsible for approximately 780,000 deaths in Europe and the United States each year.

In patients with PE, up to 25% die within three months of the acute event. In around 90% of fatal cases, the embolism is undetected or untreatable prior to death, making VTE-prevention an essential task for every healthcare system.[ii]

Complications following DVT are also common. Up to 50% of patients develop post-thrombotic syndrome (PTS), which is severe in 10-15% of cases, leading to symptoms of pain, swelling, varicose veins and skin discolouration. 3-4% of patients develop venous ulcers, which are chronic wounds that require dressing and compression. Both PTS and venous ulcers have a significant impact on a patient's quality of life and are associated with significant direct and indirect costs.

Chronic thromboembolic pulmonary hypertension (CTEPH) can develop in people who have experienced an acute PE. In fact, as many as 1 out of every 25 people who had a PE (even those who were treated with at least 3 months of anticoagulants [blood thinners]), could develop CTEPH'.[iii]

The total cost of VTE treatment and management is estimated to be £640 million per year in the United Kingdom.[ii]

GARFIELD-VTE Registry Status

Observing treatment and outcomes in patients with treated acute Venous Thromboembolic Events in the real world.

- Goals:
  - To describe the acute, sub-acute and extended duration of anticoagulation management;
  - To describe the clinical and economic outcomes in patients with treated acute VTE (DVT and PE) in the real-world setting.
- 10,879 newly diagnosed VTE patients at 415 sites, in 28 countries comprising 2 sequential cohorts of 5,000 patients
- Key milestones:
  - Study start date: July 2014;
  - Recruitment target met: September 2016;
  - Study end date: April 2020

New oral anticoagulants (OACs) have been developed to serve as a single-drug solution approved for the treatment and subsequent prevention of VTE, providing simplified patient management without the need for injections or routine coagulation monitoring.

Emerging Registry Insights

The first results from the Global Anticoagulant Registry in the Field - Venous Thromboembolism (GARFIELD-VTE) will be presented at the International Society of Thrombosis and Haemostasis (ISTH) Congress 2017.

The key findings were as follows:

- There is a wide heterogeneity among VTE patients, necessitating an individualised approach to therapy;[iv]
- In keeping with guidelines, the majority of VTE patients with cancer are treated with low molecular weight heparin (LMWH) monotherapy, while direct oral anticoagulants (DOACs) are prescribed in almost 25% of patients;[v]
- Anticoagulant treatment patterns for VTE vary by patient population, geographic region and site of DVT;[vi]
- Death was the most frequent major adverse outcome reported in patients over 6 months after VTE; half of these deaths were cancer-related.[vii]

Further details are provided below.

Results from the GARFIELD-VTE Registry

Clinical characteristics and management of 10,329 patients with a confirmed diagnosis of venous thromboembolism: the GARFIELD-VTE Registry[iviii]

Interim data on patient demographics, risk factors, and diagnostic and treatment strategies were collected at 415 sites in 28 countries, to describe the baseline characteristics of patients enrolled from 2014 to 2016.

Of the 10,329 patients eligible for analysis, 61.7% had DVT and 38.3% had PE. The mean age was 58.4 years, and 49.7% were female. Provoking factors included: surgery (12.3%), hospitalisation (11.8%), trauma (7.7%), acute illness (5.6%), known thrombophilia (2.8%) and in women, oral contraceptives (10.0%), pregnancy (3.6%) and hormone replacement therapy (2.8%). A total of 2,057 patients had either a history of cancer (10.8%) or active cancer (9.1%), and 3.7% had renal insufficiency. DVT was diagnosed using compression ultrasonography in 95.4% and PE by CT scan in 91.5%. DVT commonly involved the lower limb (89.9%), on the left side (53.6%) and 6.6% were bilateral. Upper limb involvement occurred in 8.4%. The most

proximal artery involvement in PE patients was: main (29.5%), lobar (29.5%), segmental (31.3%) or subsegmental (9.7%). Anticoagulant (AC) treatment within ±2 weeks of diagnosis included: parenteral AC only (17.6%), parenteral AC followed by vitamin K antagonists (VKA) (28.3%), VKA only (3.7%), and DOACs (50.5%). In addition, 4.4% received thrombolytic therapy; 2.1% underwent surgical/ mechanical interventions; and 34.8% of patients received graduated compression stockings.

The data indicate that there is wide heterogeneity among VTE patients necessitating an individualised approach to therapy.

GARFIELD-VTE Registry

As many as one in four VTEs occur in patients with a previous VTE. The estimated increasing risk of recurrence in unprovoked VTE is 10% at one year and 30% at 10 years. Both morbidity and mortality are increased with recurrent VTE.

The traditional standard of care for acute VTE treatment and long-term prevention of recurrence is a dual-drug approach of daily injections of a low molecular weight heparin (LMWH) followed by a transition to long-term oral anticoagulant therapy with a vitamin K antagonist (VKA), such as warfarin.

Clinical characteristics and treatment of patients with cancer-associated venous thromboembolism: results from the GARFIELD-VTE Registry[viv]

Patients with active cancer are susceptible to VTE. Although guidelines recommend low molecular weight heparin (LMWH) for cancer-associated thrombosis (CAT), direct oral anticoagulants (DOACs) and other agents also are prescribed.

Baseline data in 701 patients with active cancer were compared with those in 7,307 patients without active cancer who received initial anticoagulant treatment between 2014 and 2016.

Patients with active cancer tended to be older than those without active cancer (65.7 years and 59.4 years, respectively), and more were of Asian ethnicity (31.7% and 14.6%, respectively). Common sites of underlying cancers in men, women and overall are shown in the Table below. The proportion of patients with DVT was similar in patients with and without cancer (59.3% and 61.3%, respectively) as was the proportion with pulmonary embolism ± DVT (40.7% and 38.7%); a slightly higher proportion of cancer patients had upper limb DVT (12.2% and 8.1%, respectively). Patients with active cancer were more likely to receive LMWH monotherapy or another parenteral anticoagulant as initial therapy than those without cancer (64.0% and 13.1%, respectively), and were less likely to receive a DOAC with or without a heparin lead-in (22.8% and 53.2%, respectively).

These data show that in keeping with guidelines, the majority of cancer patients are treated with LMWH monotherapy. However, DOACs are prescribed for almost 25% of patients.

Men (n=219)		Women (n=232)		Overall (n=451)	
Lung	21.9%	Gynecological	22.0%	Lung	17.3%
Colorectal	15.5%	Breast	18.1%	Colorectal	12.4%
Prostate	11.4%	Lung	12.9%	Gynecological	11.3%
Urological	9.1%	Colorectal	9.5%	Breast	9.3%
Lymphoma	8.2%	Lymphoma	7.8%	Lymphoma	8.0%

[Table: The most common sites of cancer in VTE patients]

Anticoagulation treatment patterns of venous thromboembolism in GARFIELD-VTE patients[v][iv]

Parenteral anticoagulation overlapping with vitamin K antagonists (VKA) has been the cornerstone of venous thromboembolism (VTE) treatment. With the recent introduction of four direct oral anticoagulants (DOACs), physicians now have broader treatment choices.

Interim data was collected on the initial anticoagulation (AC) treatment of VTE patients prospectively enrolled at 361 sites in 28 countries from July 2014 to September 2016. Patients with documented initial AC therapy within ±2 weeks of diagnosis (n=8,017) were stratified into four treatment groups: 1. parenteral AC alone, 2. parenteral AC followed by a VKA, 3. VKA alone, and 4. DOAC with or without a heparin lead in.

Differences in therapeutic approach were observed by geographical region, patient population and site of DVT (Table). As recommended by current guidelines, patients with active cancer and pregnant women were more likely to be treated with a parenteral AC alone. AC treatment was similar in patients with DVT and pulmonary embolism, but parenteral anticoagulant alone was more frequently used for upper than lower limb DVT. Furthermore, analyses of AC treatment patterns by geographical regions found that VKA alone was more frequently prescribed in countries outside Asia, Europe and North America (Table).

GARFIELD-VTE provides a global perspective on AC treatment patterns for VTE, which not only varies by patient population, but also by geographic region and site of DVT.

		Parenteral alone	Parenteral+ VKA	VKA alone	DOACs ± Parenteral
Overall		17.6%	28.3%	3.7%	50.5%
Regions	Europe (n=4981)	17.3%	27.6%	2.7%	52.4%
	Asia (n=1116)	28.2%	23.0%	4.2%	44.5%
	North America (n=757)	16.4%	30.5%	2.2%	50.9%
	Other (n=1163)	9.2%	34.6%	8.3%	48.0%
Patient Populations	Active (n=710) / History (n=829) of cancer	64.2% / 36.1%	11.5% / 20.3%	1.4% / 2.8%	22.8% / 40.9%
	Pregnancy (n=115)	49.6%	23.5%	8.7%	18.3%
	Renal impairment (n=279)	21.1%	42.3%	7.2%	29.4%
Site of DVT	Upper (n=512) / Lower (n= 5500) limb	25.2% / 16.6%	22.5% / 28.9%	3.5% / 3.8%	48.8% / 51.6%

[Table. Treatment approach by geographic region, patient populations and site of DVT]

6-months outcomes of patients: results from GARFIELD-VTE[vii][vi]

Interim data on 8,842 patients with a confirmed diagnosis of VTE and 6-month follow-up data were analysed from 396 sites in 28 countries from 2014 to 2016.

Patients were recruited from Europe (59.3%), Asia (15.0%), North America (9.9%) and the rest of the world (15.7%). The median age was 60.1 years.

Over 6-months follow-up, the rates of all-cause mortality and first occurrence of major bleeding and VTE recurrence were: 11.1, 2.8, and 3.6 per 100 person years, respectively. The rates of all three major outcome events were higher in the first month of follow-up (Table) than in the subsequent 5 months. Overall, 17% of bleeds were major, requiring transfusion in 16.2% of cases. Fatal bleeding occurred in 2.2% of patients with any bleeding event (n=502). The most common cause of death at 6 months was cancer in 50.9% of cases (of these, 14.6% were due to lung cancer; 9.3% to colorectal; 8.6% to pancreatic; and 8.6% to lymphoma). A further 5.1% of deaths were due to pulmonary embolism and 1.3% due to other VTE complications

Death was the most frequent major adverse outcome in patients diagnosed with VTE, although half were cancer-related. The highest event rates for death and major bleeding occurred during the first month of follow-up.

	Event rate per 100 person-years(95% CI)	
Follow-up	1-month	6-months
All-cause mortality	15.0 (12.3 to 18.2)	11.1 (10.0 to 12.3)
Major bleeds	5.8 (4.3 to 8.0)	2.8 (2.3 to 3.4)
Recurrent VTE	3.9 (2.7 to 5.7)	3.6 (3.0 to 4.3)

[Table. Event rates during the first and 6 months of follow-up]

Visit http://www.garfieldregistries.org/ for more information.

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About the TRI

The Thrombosis Research Institute (TRI) is dedicated to bringing new solutions to patients for the detection, prevention and treatment of blood clots. The TRI's goal is to advance the science of real-world enquiry so that the value of real-world data is realised and becomes a critical link in the chain of evidence. Their pioneering research programme, across medical disciplines and across the world, continues to provide breakthrough solutions in thrombosis.

The TRI is a member of University College London Partners' Academic Health Science Network. For more information, visit http://www.tri-london.ac.uk/.

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