haematologica
Journal of the Ferrata Storti Foundation

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Received: May 23, 2026.
Accepted: August 20, 2026.

Citation: Nicolas Gendron, Carla Rial, Christine Le Beller, Aurelie Sarthou, Armand Schmeltz, Shaya Sable, Laetitia Mauge, Aurelien Philippe, Lina Khider, Maude Laney, Roya Nili, Anne Godier, Jean Luc Diehl, Pascale Gaussem, Emmanuelle Florens, Olivier Sanchez, Richard Chocron, Dominique Helley, David M. Smadja and Agnes Lillo-Le Louet. Bleeding, thrombosis, and anti-Xa monitoring in danaparoid-treated patients with suspected heparin-induced thrombocytopenia: a retrospective single-center study.
Haematologica. 2026 Aug 27. doi: 10.3324/haematol.2026.301270 [Epub ahead of print]

Bleeding, thrombosis, and anti-Xa monitoring in danaparoid-treated patients with suspected heparin-induced thrombocytopenia: a retrospective single-center study

Short title: Danaparoid for HIT suspicion

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Acknowledgement

The authors acknowledge all nurses, technicians, and physicians involved in the departments of the George Pompidou European Hospital for their help in taking care of patients and including them in the study. Communication presented as a poster at the congress of the International Society on Thrombosis and Haemostasis, June 21, 2025, Washington D.C

Authorship

Contribution: C.R. N.G., S.S., M.L. and D.H. collected data, analyzed data, and wrote the manuscript; C.R., N.G., A.S., A.S., and M.L. contributed to data collection; C.R., N.G., S.S., C.L.B., L.M., A.P., L.K., R.N., A.G., J.-L.D., P.G., E.F., O.S., R.R., A.L.-L.L., D.M.S., and D.H. contributed to data analysis and manuscript revision; and all other authors provided clinical or biological data and reviewed the manuscript.

Conflict of interest

Conflict-of-interest disclosure: N.G. received consulting fees or travel awards from Stago and Werfen. A.G. received speaker fees from Aguettant, Bristol Myers Squibb–Pfizer, Sanofi, CSL Behring, LFB, Octapharma, Stago, and Viatris. D.M.S received a research grant from Viatris. The remaining authors declare no competing financial interests.

Data sharing statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: danaparoid, heparin-induced thrombocytopenia, bleeding, thrombosis, mortality

Heparin-induced thrombocytopenia (HIT) is an uncommon, life-threatening, immune-mediated prothrombotic disorder caused by IgG antibodies against platelet factor 4/heparin complexes, leading to platelet, monocyte, and neutrophil activation and a marked prothrombotic state[1]. Suspicion of HIT requires immediate discontinuation of heparin and initiation of a therapeutic-dose alternative anticoagulant,[2,3] most commonly danaparoid or argatroban. Danaparoid is a synthetic heparinoid with anti-Factor Xa (anti-Xa) activity and anti-thrombin activities. It is used in stable patients due to its long half-life (~25 hours) and is eliminated by the kidneys, limiting its use in renal failure[2,3]. Despite decades of use in France, real-world data on outcomes and anti-Xa monitoring during danaparoid treatment for suspected HIT remain limited.

We therefore retrospectively analyzed all patients with suspected HIT treated with danaparoid over a 6-year period at our institution, focusing on bleeding, thrombosis, and 30-day mortality. This single-center retrospective cohort included all consecutive patients with suspected HIT referred to the HIT Team of the European Georges Pompidou Hospital (Paris, France), previously described[4], from January 2017 to December 2022 and treated with danaparoid (IV or SC), excluding patients with prior HIT. HIT diagnosis was supported by clinical assessment, anti-PF4/heparin antibody testing (Zymutest HIA IgG HYPHEN BioMed), and a platelet functional assay (serotonin release assay, SRA). Danaparoid-specific anti-Xa activity were performed with STA®-Liquid Anti-Xa on STAR coagulometers (Diagnostica Stago). Each anti-Xa level measured was classified as below, within, or above target, based on two reference values: i) a locally defined initiation protocol and therapeutic target, adapted on a case-by-case basis by the HIT team, and ii) the target range specified in the summary of product characteristics (SmPC) of danaparoid. The local target was determined at the discretion of the HIT team and could differ from the SmPC, particularly in patients with a high bleeding risk (e.g., impaired renal function, history of major bleeding, recent surgery). Classification of anti-Xa levels relative to the specified target took into account the route of administration, as dosing

regimens and biological monitoring may vary between IV and SC use. Study outcomes were major bleeding or non-major clinically relevant bleeding (CRNMB), new thrombosis during danaparoid treatment, and death within 30 days of danaparoid initiation, regardless of HIT confirmation. All suspected outcome events were adjudicated in a blinded manner, blinded to the final diagnosis of HIT and anticoagulant type. Clinical and biological characteristics at danaparoid initiation were analyzed as potential predictors of thrombotic and bleeding outcomes. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local medical ethics committee (CERAPHP.5, #00011928, RESTI-HOP study). The HIT suspicion and diagnosis strategy, data collection and further details are described elsewhere[4]. Continuous variables were presented as median values with their interquartile range, and categorical variables were detailed as counts and percentages. Associations between categorical groups were ascertained using Pearson's Chi-squared test, with Fisher's exact test being employed when Chi-squared test assumptions were unmet. Continuous variables were analyzed using the Wilcoxon rank sum test based on data distribution and sample size. Statistical analyses were conducted using R version 4.1.1 on R Studio Software.

Between 2017 and 2022, 425 patients with suspected HIT were evaluated, of whom 68 (17%) were treated with danaparoid; HIT was confirmed in 42 (62%). The baseline characteristics of the patients are shown in **Supplemental Table 1**. Median age was 65 years (IQR 53–71), and 65% were men, with no difference between confirmed and non-confirmed HIT. Only BMI was significantly higher in confirmed HIT patients. Most patients were hospitalized in intensive care (53%) or cardiac surgery (18%). Unfractionated heparin had been used more frequently in confirmed HIT patients than in non-HIT patients (88% vs 65%, p=0.024). Median platelet count at HIT suspicion was 90×10^9/L (IQR 54–131), and median anti-PF4/heparin antibody level was higher in confirmed HIT ($p<0.001$, **Supplemental Table 2**). SRA was positive in all confirmed

HIT patients and negative in 88% of non-HIT patients. Among the danaparoid-treated patients, 65 (96%) received danaparoid as initial treatment, while 2 (3%) received argatroban and 1 (2%) received apixaban prior to switching to danaparoid.

During danaparoid treatment, according to the locally defined anti-Xa target, median times spent in, above or under the target range were 6 days (IQR 2–14), 1 day (IQR 0–2) and 1 day (IQR 0–4), respectively, with no significant differences observed between HIT and non-HIT patients (**Table 1**). Furthermore, according to the SmPC anti-Xa target, median times spent in, above and under the target range were 2 days (IQR 1–10), 0 day (IQR 0–1) and 2 days (IQR 1–10), respectively, again with no significant differences between HIT and non-HIT patients. After HIT suspicion, while on danaparoid, new thrombotic events occurred in 8 patients (12%): 4 (50%) had VTE, 2 (25%) had arterial thrombosis; and 2 (25%) developed thrombotic material in dialysis filters. Thrombotic events occurred at a similar rate (12%) in HIT and non-HIT patients. Median time between thrombotic event and danaparoid initiation was 11 days (IQR 5–15) with no significant difference between HIT and non-HIT patients. Danaparoid duration was longer in patients with thrombosis (33 IQR 14–54 vs 7 days IQR 3–15, p=0.01), and first anti-Xa activity was lower (0.3 IQR 0.3–0.5 vs 0.5 U/mL IQR 0.4–0.7, p=0.028, **Table 2**). Patients with thrombosis spent more time below both the local (p<0.001) and SmPC targets (p=0.003).

Bleeding (major or CRNMB) occurred in 7 (10%) patients, with no fatal events. No difference in bleeding occurrence was noticed according to HIT confirmation or not (**Table 3**). Baseline predictors of bleeding included male sex (100% vs 61%, p=0.046) and higher leukocyte count (16 IQR 13–20 vs 10 $\times 10^9$/L IQR 8–13, p=0.009). Additionally, longer danaparoid duration (33 IQR 29–49 vs 7 days IQR 3–14, p<0.001) and delayed platelet count normalization (12 IQR 9–18 vs 7 days IQR 4–9, p=0.03) were retrospectively associated with bleeding events. The first anti-Xa measurement did not differ between patients with and without bleeding. Patients with

bleeding spent more time below, within, and above the locally defined target compared to those without bleeding (all $p<0.05$), reflecting longer overall treatment duration. According to the SmPC target, patients with bleeding spent more time below target ($p=0.003$), with no difference above or within target. Death at 30 days occurred for 8 (12%) patients, 3 (38%) patients with confirmed HIT and 5 (62%) non-HIT patients, with no significant difference between groups ($p=0.2$). Kaplan-Meier survival curves depicting outcomes free of thrombosis, bleeding and death at 30 days are represented in **Supplemental figure 1**. The median time of outcome free survival was 15.0 days (IQR 12.0–31.0) for non-HIT patients and 20.5 days (IQR 16.0–33.0) for HIT patients, with no difference between the two groups.

In this retrospective study, thrombotic and bleeding events occurred in 12% and 10% of danaparoid-treated patients with suspected HIT, respectively, with no difference according to final HIT confirmation. This mirrors recent findings[5] who reported similar outcomes in 1,393 patients regardless of anti-PF4/heparin antibody status (only two patients received danaparoid), and confirms that patients with suspected HIT remain at risk while awaiting diagnosis, supporting prompt initiation of alternative anticoagulation regardless of platelet functional assay turnaround time.

Danaparoid has been used since 1993 [6] with the only prospective trial demonstrating superiority over dextran 70 in 42 HIT-suspected patients with thrombosis.[7] A retrospective comparison found similar outcomes between danaparoid and lepirudin at therapeutic dose, though prophylactic-dose danaparoid in patients without thrombosis was associated with a higher cumulative risk than lepirudin, while major bleeding was more frequent with lepirudin (10.4% vs 2.5%)[8]. Our findings are consistent with those of Lubenow et al., [9] who reported a strikingly similar thrombosis rate of 12.9% in 62 danaparoid-treated HIT patients, supporting the reproducibility of danaparoid outcomes despite a 20-year interval between these two studies.

Subsequent meta-analyses[10–12] reported thrombosis rates of 7–10% and major bleeding of 5–8% with danaparoid, consistent with our findings, generally without one anticoagulant emerging as clearly superior. In our cohort, longer danaparoid treatment duration was a risk factor for thrombosis, independent of HIT confirmation.

Bleeding risk factors included male sex, longer treatment duration, delayed platelet count normalization, and higher leukocyte count; the relationship between leukocytosis and bleeding under danaparoid warrants further study. The prognostic value of anti-Xa monitoring remains debated even for heparins, and is even less established for danaparoid. In our study, low first anti-Xa activity was associated with thrombosis, supporting the importance of avoiding under-dosing at HIT suspicion. Patients with thrombosis also spent more time below target. Conversely, anti-Xa levels did not predict bleeding risk, though the SmPC target appeared more discriminant than locally adapted targets, suggesting the latter had been adjusted for bleeding risk in these fragile patients. These findings echo prior reports of inconsistent correlation between anti-Xa levels and clinical outcomes[13,14] and support combining clinical judgment with anti-Xa monitoring, particularly in patients with renal impairment or high body weight[15].

Strengths of our study include systematic HIT diagnosis assessment using gold standard assays, danaparoid-specific anti-Xa monitoring, and ISTH-classified bleeding events across 6 years of consecutive real-life practice. To our knowledge, this is the largest cohort of danaparoid-treated confirmed HIT patients with available biological data. Limitations include its single-center retrospective design and non-standardized anti-Xa sampling, which led us to focus on time in therapeutic range rather than individual values. HIT remains a prothrombotic disorder with substantial morbidity despite anticoagulation. Our findings support danaparoid use in acute HIT and underscore the need for therapeutic dosing until diagnosis is confirmed, along with anti-Xa monitoring to mitigate thrombotic risk.

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Tables:

Table 1. Outcomes during danaparoid treatment in patients with HIT suspicion and time spent within the target range

IQR: interquartile range; HIT: heparin induced thrombocytopenia; DVT: deep vein thrombosis; PE: pulmonary embolism; CRNMB: critical non major bleeding; NA for non-availed; SmPC: summary of product characteristics

Bleeding events we classified during the period of treatment by danaparoid, according to the ISTH classification. For the purpose of group comparison, each patient was evaluated based on the first occurrence of their most severe bleeding, categorizing the data into two primary groups: "no bleeding or minor bleeding" and "major or clinically relevant non-major bleeding (CRNMB)". For categorical attributes like the severity of complications, the maximum severity noted for any event was considered for each patient.

*One patient had a stroke, and one had both an infrarenal aortic thrombosis and a stroke.

**Patients may have had multiple bleeding sites.

	Total patients with HIT suspicion N=68	Non-HIT patients n=26	HIT patients n=42	p-value
Thrombotic event – n (%)	**8 (12)**	**3 (12)**	**5 (12)**	1.0
Thrombosis localization – n (%)				
Venous thrombosis	**4 (6)**	**3 (12)**	**1 (2)**	
PE	1 (2)	1 (4)	0 (0)	
DVT	2 (6)	1 (12)	1 (2)	
Extension of previous VTE	1 (2)	0 (0)	1 (2)	
Arterial thrombosis*	**2 (3)**	**0 (0)**	**2 (5)**	
Dialysis filter thrombosis	**2 (3)**	**0 (0)**	**2 (5)**	
Time between thrombosis and danaparoid initiation (d) – median [IQR]	11 [5–15]	14 [11–17]	5 [5–15]	0.5
Bleeding event – n (%)	**7 (10)**	**1 (4)**	**6 (14)**	0.2
Bleeding severity – n (%)				
Major	5 (71)	1 (100)	4 (6)	
CRNMB	2 (29)	0 (0)	2 (33)	
Minor	0 (0)	0 (0)	0 (0)	
Death at 30 days since danaparoid initiation – n (%)	8 (12)	5 (19)	3 (7)	0.2
During hospitalization, number of days with anti-Xa – median [IQR]:				
Target locally defined				
Above target	1 [0–2]	1 [0–2]	1 [0–2]	0.5
In target	6 [2–14]	3 [2–10]	7 [2–18]	0.4
Under target	1 [0–4]	1 [0–4]	1 [0–3]	0.3
Target according to the SmPC				
Above target	0 [0–1]	0 [0–0]	0 [0–1]	0.8
In target	2 [1–10]	2 [1–7]	4 [1–10]	0.5
Under target	2 [1–10]	2 [1–7]	4 [1–10]	0.5

Table 2. Characteristics of patients with thrombosis or no thrombosis during danaparoid treatment

IQR for interquartile range; HIT for heparin induced thrombocytopenia; SmPC: summary of product characteristics

	Total patients with HIT suspicion, N=68	**No thrombosis n=60**	**Thrombosis n=8**	**p-value**
Age – median [IQR]	65 [53–71]	65 [53–74]	59 [53–67]	0.3
Male sex – n (%)	44 (65)	37 (62)	7 (88)	0.2
HIT confirmed – n (%)	42 (62)	37 (62)	5 (62)	1.0
Duration of danaparoid treatment (d)	7 [3–20]	7 [3–15]	33 [14–54]	**0.01**
Time to normalize platelets (d)	7 [4–10]	7 [4–9]	10 [3–16]	0.5
Dialysis at the time of HIT diagnosis – n (%)	15 (22)	11 (18)	4 (50)	0.07
Chronic kidney disease– n (%)	7 (10)	5 (8.3)	2 (25)	0.2
Biology at the time of danaparoid initiation				
Leukocyte count ($x10^9$/L)	11 [8–13]	11 [8–13]	12 [9–14]	0.6
Hemoglobin (g/L)	94 [84–107]	94 [84–107]	93 [77–108]	0.6
Platelets ($x10^9$/L)	79 [47–114]	82 [47–116]	70 [58–92]	0.9
Creatinine clearance (mL/min)	78 [60–99]	78 [61–99]	77[29–90]	0.5
First anti-Xa (UI/mL)	0.5 [0.4–0.7]	0.5 [0.4–0.7]	0.3 [0.3–0.5]	**0.028**
During hospitalization, number of days with anti-Xa – median [IQR]:				
Target locally defined				
Above target	1 [0–2]	1 [0–2]	2 [1–2]	0.1
In target	6 [2–14]	4 [2–10]	23 [16–36]	**0.01**
Under target	1 [0–4]	1 [0–2]	6 [5–12]	**<0.001**
Target according to the SmPC				
Above target	0 [0–1]	0 [0–1]	0 [0–0]	0.8
In target	2 [1–10]	2 [1–7]	13 [6–16]	0.056
Under target	1 [0–9]	1 [0–6]	16 [9–24]	**0.003**

Table 3. Characteristics of patients with major bleeding or CRNMB bleeding compared to no bleeding or minor bleeding during danaparoid treatment

IQR: interquartile range; HIT: heparin induced thrombocytopenia; SmPC: summary of product characteristics

	Total population N=68	**No bleeding n=61**	**Bleeding n=7**	**p-value**
Age – median [IQR]	65 [53–71]	65 [53–71]	60 [52–72]	0.7
Male sex – n (%)	44 (65)	37 (61)	7 (100)	**0.046**
HIT – n (%)	42 (62)	36 (59)	6 (86)	0.2
Danaparoid duration (d)	7 [3–20]	7 [3–14]	33 [29–49]	**<0.001**
Time to normalize platelets (d)	7 [4–10]	7 [4–9]	12 [9–18]	**0.03**
Dialysis at the time of HIT diagnosis – n (%)	15 (22)	13 (21)	2 (29)	0.6
Chronic kidney disease– n (%)	7 (10)	7 (11)	0 (0)	1.0
Biology at the time of danaparoid initiation				
First anti-Xa (UI/mL)	0.5 [0.4–0.7]	0.5 [0.4–0.7]	0.4 [0.3–0.6]	0.2
Leukocyte count ($x10^9$/L)	11 [8–13]	10 [8–13]	16 [13–20]	**0.009**
Hemoglobin (g/L)	94 [84–107]	94 [84–108]	93 [83–103]	0.7
Platelets ($x10^9$/L)	79 [47–114]	83 [48–114]	48 [35–88]	0.2
Plasma creatinine level (µmol/L)	93 [64–116]	85 [63–111]	109 [106–178]	**0.026**
Creatinine clearance (mL/min)	78 (60, 99)	78 (61, 99)	74 (43, 95)	0.6
During hospitalization, number of days with anti-Xa – median [IQR]:				
Target locally defined				
Above target	1 [0–2]	1 [0–2]	2 [2–3]	**0.002**
In target	6 [2–14]	4 [1–10]	26 [19–35]	**<0.001**
Under target	1 [0–4]	1 [0–2]	4 [2–6]	**0.025**
Target according to the SmPC				
Above target	0 [0–1]	0 [0–1]	0 [0–0]	1.0
In target	2 [1–10]	2 [1–8]	9 [3–14]	0.3
Under target	1 [0–9]	1 [0–5]	26 [12–38]	**0.003**

Supplemental data for "Bleeding, thrombosis, and anti-Xa monitoring in danaparoid-treated patients with suspected heparin-induced thrombocytopenia: a retrospective single-center study"

Supplemental Table 1. Characteristics of HIT-suspected patients treated by danaparoid during hospitalization.

IQR: interquartile range; HIT: heparin induced thrombocytopenia; BMI: body mass index; VKA: vitamin K antagonist; LMWH: low molecular weight heparin; UFH: unfractionated heparin; CABG: coronary artery bypass graft surgery; ECMO: extracorporeal membrane oxygenation; d: day.

*Patients may have received both UFH and LMWH at different time points during hospitalization (not concurrently).

	Total patients with HIT suspicion N=68	**Non-HIT Patients n=26**	**HIT Patients n=42**	**p-value**
Male sex – n (%)	44 (65)	17 (65)	27 (64)	0.9
Age, years – median [IQR]	65 [53–71]	66 [58–74]	64 [50–71]	0.4
BMI, kg/m2– median [IQR]	25.7 [23.2–29.6]	24.4 [20.7–25.4]	28.1 [23.7–30.6]	**0.003**
Medical history – n (%)				
Coronary syndrome	5 (7)	2 (8)	3 (7)	1.0
Atrial fibrillation	9 (13)	4 (15)	5 (12)	0.7
Heart failure	6 (9)	2 (8)	4 (10)	1.0
Valvular disease	18 (26)	8 (31)	10 (24)	0.5
Stroke	3 (4)	1 (4)	2 (5)	1.0
Deep vein thrombosis	6 (9)	4 (15)	2 (5)	0.2
Pulmonary embolism	4 (6)	2 (8)	2 (5)	0.6
Active cancer	15 (22)	7 (27)	8 (19)	0.4
Chronic kidney disease	7 (10)	3 (12)	4 (10)	1.0
Antithrombotic at admission – n (%)				
Rivaroxaban	3 (4)	2 (8)	1 (2)	0.5
Apixaban	6 (9)	2 (8)	4 (10)	0.5
Dabigatran	1 (2)	1 (4)	0 (0)	0.4
VKA	3 (4)	2 (8)	1 (2)	0.5
LMWH	5 (7)	4 (15)	1 (2)	0.1
Aspirin	15 (22)	7 (27)	8 (19)	0.4
None	50 (74)	15 (58)	35 (83)	**0.006**
Hospitalization at the time of HIT suspicion – n (%)				
Medicine	14 (21)	6 (23)	8 (19)	0.7
Intensive care unit	36 (53)	12 (46)	24 (57)	0.4
Cardiac surgery	12 (18)	5 (19)	7 (17)	1.0
Vascular surgery	2 (3)	1 (4)	1 (2)	1.0
Other surgery	4 (6)	2 (8)	2 (5)	0.6

Length of stay (d) – median [IQR]	32 [16–52]	26 [16–36]	36 [16–54]	0.4
Events during hospitalization				
CABG	27 (40)	11 (42)	16 (38)	0.7
ECMO	6 (9)	2 (8)	4 (10)	1.0
Dialysis	15 (22)	8 (31)	7 (17)	0.2
Citrate dialysis	8 (53)	5 (62)	3 (43)	0.6
Heparin dialysis	7 (47)	3 (38)	4 (57)	0.6
COVID-19– n (%)	5 (7)	1 (4)	4 (10)	0.6
Heparin during hospitalization – n (%)				
LMWH*	43 (63)	17 (65)	26 (62)	0.7
UFH*	54 (79)	17 (65)	37 (88)	**0.024**
Anticoagulant medication at the time of HIT suspicion – n (%)				
LMWH	27 (40)	12 (46)	15 (36)	0.4
UFH	41 (60)	14 (54)	27 (64)	0.4
Therapeutic dose	41 (60)	13 (50)	28 (68)	0.2
Prophylactic dose	13 (19)	6 (23)	7 (17)	0.5
Unknown	14 (21)	7 (27)	7 (17)	0.4
Time between HIT suspicion and heparin initiation – median [IQR]	9 [7–12]	9 [6–12]	8 [7–11]	0.7

Supplemental Table 2. HIT biology and diagnosis in HIT-suspected patients treated with danaparoid

IQR for interquartile range; HIT for heparin induced thrombocytopenia; PT for prothrombin time; LP for low probability; IP for intermediate probability; HP for high probability; anti-PF4/H for anti-PF4/heparin antibodies; SRA for serotonin release assay

4Ts score was calculated for each patient. An intermediate or high probability for HIT (4Ts score ≥4) led to IgG anti-PF4/H antibodies testing by enzyme-linked immunosorbent assay. This assay was performed according to the manufacturer's instructions, and an optical density (OD) ≥0.50 was considered positive; weakly positive when $0.30 \leq OD < 0.50$; or negative if $OD < 0.30$. As only a subset of anti-PF4/H antibodies is able to activate platelets and cause clinical HIT, a functional platelet assay was performed to confirm HIT diagnosis when antibody testing was positive using the "gold standard" 14C-SRA. This test investigates the capability of the antibodies to activate platelets in the presence of heparin. Washed platelets of three selected healthy donors free from aspirin and non-steroidal anti-inflammatory drugs for at least 10 days and known to react well in the SRA were used for the assays. Patient plasma and increasing concentrations of UFH were added to healthy donor platelets previously incubated with radioactive 14C-serotonin. The percent of 14C-serotonin released by activated platelets in response to the presence of anti-PF4/H antibodies was measured. A positive SRA test was defined by significant serotonin release (>30%) from donor platelets when mixed with patient plasma and low heparin doses (0.1 U/ml and 0.5 U/mL) associated with the inhibition of platelet activation by at least 50% from maximal activation values when high dose heparin (100 U/mL) was added. If the release was over 30% in the presence of high-dose heparin, the result was considered indeterminate. The result was considered negative if serotonin release was <20% and indeterminate if it was between 20% and 30% using low UFH doses with at least three healthy platelet donors. Positive and negative control plasma were tested in parallel in each series

*Three patients had both venous and arterial thrombosis **One patient had both venous thrombosis and a cutaneous manifestation ***One patient had both arterial thrombosis and a cutaneous manifestation

	Total patients with HIT suspicions (N=68)	Non-HIT Patients (n=26)	HIT Patients (n=42)	p-value
Biology at admission – median [IQR]				
Leukocytes (x10^9/L)	9.7 [6.1–14.0]	9.1 [6.1–13.8]	9.8 [6.2–14.4]	0.8
Hemoglobin (g/L)	127 [108–145]	12.1 [101–142]	131 [109–147]	0.1
Platelet count (x10^9/L)	228 [182–286]	238 [190–318]	219 [178–271]	0.5
Biology at the time of HIT suspicion – median IQR				
Leukocytes (x10^9/L)	11.3 [8.9–14.1]	10.1 [7.6–13.5]	11.8 [9.4–14.7]	0.1
Hemoglobin (g/L)	93 [81–108]	94 [88–112]	91 [80–105]	0.2
Platelet count (x10^9/L)	90 [54–131]	90 [75–127]	90 [52–138]	0.6
Fibrinogen (g/L)	5.5 [4.5–6.5]	5.5 [5.0–6.2]	5.6 [4.3–6.8]	0.8
D-dimer (ng/mL)	4,832 [3,045–8,055]	4,073 [2,174–7,932]	5,513 [3,219–7,697]	0.4
Creatinine clearance (mL/min)	78 [57–105]	69 [43–83]	83 [61–114]	0.1
Hemoglobin nadir (g/L)	84 [75–93]	87 [77–94]	83 [73–93]	0.5
Platelets nadir (x10^9/L)	55 [33–87]	57 [33–86]	48 [34–86]	0.5
HIT characteristics				
4Ts score				
Low (1–3) – n (%)	6 (9)	5 (19)	1 (2.4)	**0.027**
Intermediate (4–5) – n (%)	47 (69)	19 (73)	28 (67)	0.6
High (6–8) – n (%)	15 (22)	2 (8)	13 (31)	**0.025**
Time to normalize platelets level (d) – median [IQR]	7 [4–10]	8 [6–11]	7 [4–9]	0.3
Venous thrombosis [*,**] – n (%)	11 (16)	3 (12)	8 (19)	0.5
Arterial thrombosis [*,***] – n (%)	9 (13)	3 (12)	6 (14)	1.0
Cutaneous effect [**,***] – n (%)	6 (8.8)	1 (3.8)	5 (12)	0.4
Anti-PF4/H level OD – median [IQR]	1.7 [0.9–2.3]	0.7 [0.2–1.5]	2.0 [1.6–2.6]	**<0.001**
SRA results among tested patients				
Positive – n (%)	42 (71)	0 (0)	42 (100)	**<0.001**
Indeterminate – n (%)	2 (3)	2 (12)	0 (0)	0.08
Negative – n (%)	15 (26)	15 (88)	0 (0)	**<0.001**

Supplemental Figure 1. Kaplan Meyer of thrombosis or major bleeding or CRNMB or death at 30 days in patients treated by danaparoid for heparin-induced thrombocytopenia and according to confirmation of diagnosis.

Median time of outcome free survival was 15.0 days (IQR 12.0–31.0) for non-HIT patients and 20.5 days (IQR 16.0–33.0) for HIT patients, with no difference between the two groups (p=0.5).

HIT: heparin-induced thrombocytopenia

Censured on death