study. Age distribution at diagnosis resembled an 'M-shaped' pattern with peaks at 18 to 30 years (18%) and 50 to 70 years (17%) of age. The RLH (12.2%) and Castle Hill Hospital (6.2%) had highest recruitment. The most prevalent history of comorbidities before ITP were hypertension (16.7%), depression/anxiety (5.0%), diabetes (4.4%) osteoarthritis (4.1%) and arterial thromboembolism (4.0%). The cohort's median platelet count around diagnosis was 23.0 x10^9/L ([IQR 7-61 years]; 56.1% had platelet count <30 x10^9/L). Of those who received treatment within 3 months of ITP diagnosis, 96.9% had 1st line treatment [including prednisolone (86.1%) IVIg (34.3%), Anti-D (2.5%)], 19.8% had 2nd line treatment [including rituximab (6.3%); splenectomy (1.8%) and others (<1% to 4%)], and 11.9% had blood product transfusion [(platelet (8.8%), red blood cells (4.7%)]. Throughout the entire cohort history, common treatments were prednisolone (70.3%), IVIg (39.2%), splenectomy (12.8%), romiplostim (9.24%), Anti-D (6.5%) and eltrombopag (6.1%), whereas 19.5% had no treatment. For those with platelet counts <50 x10^9/L and bleed within 3 months of diagnosis, there was a significant association with use of both 1st and 2nd line treatment. A similar pattern of treatment was found for platelet counts ≥50 x10^9/L but to a lesser extent. Bleed from the respiratory system (*e.g.* haemoptysis), gastrointestinal system (exc. oral) and obstetric/gynaecological-related ones were associated with receiving transfusion (including platelet). The median time from ITP diagnosis to having a splenectomy was 1.4 (IQR 0.5-3.9) years; 77.1% were diagnosed below the age of 50. Fifteen individuals had this procedure within 3 months of diagnosis, of which 60% were before 2010. Over the last 2 decades there has been a decrease in the overall number of splenectomies carried out [and in relation to the year that the splenectomised patients were diagnosed (1990-99: 30.1%; 2000-09: 12.7%)], and for those diagnosed within the last five years, 4.4% had this procedure. The same time periods saw increased use of newer therapeutic agents (figure).

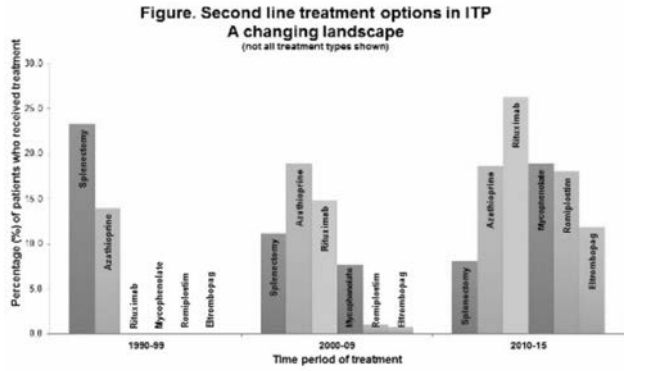

Figure 1.

Summary/Conclusions: Patients with low platelet and bleeding within the 1st three months of ITP diagnosis were likely to receive both 1st and 2nd line treatment options. Notable, is the decline of splenectomy as 2nd line treatment, while there are different drug options available. It would be important to increase the cohort size, including expanding internationally, to obtain more treatment data on higher number of patients who received 2nd line treatment options and long-term follow up data.

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EFFICACY AND SAFETY OF RIVAROXABAN FOR NON-VALVULAR ATRIAL FIBRILLATION IN PATIENTS WITH SEVERE RENAL IMPAIRMENT

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Background: Patients with atrial fibrillation and severe renal impairment (CrCL <30ml/min) were excluded from the ROCKET-AF study and, indeed, most of the seminal phase 3 DOAC studies in atrial fibrillation. However, the summary of product characteristics states that rivaroxaban may be used at a reduced dose of 15mg OD for anti-coagulation management of atrial fibrillation in patients with severe renal impairment (CrCl 15-29 ml/min). This recommendation was solely based on pharmacokinetic analyses and has not been validated in a clinical study.
Aims: Assess safety and efficacy of rivaroxaban (15mg OD) in patients with atrial fibrillation and severe renal impairment (CrCl 15 – 29 ml/min). The primary safety point is occurrence of bleeding complications.
Methods: Retrospective cohort analysis of 30 patients with non-valvular atrial fibrillation and severe renal impairment who were commenced on rivaroxaban (15mg OD) in our anti-coagulation clinic between October 2012 and March 2015. Medical notes were reviewed and general practitioners were contacted by telephone or fax. Information collected included age, weight, CHA2DS2-Vasc and HAS-BLED scores, baseline blood investigations (CrCl, FBC, LFT and clotting screen) and where available blood investigations at the time of the bleeding event.
Results: A total of 30 patients were retrospectively followed up for a minimum of 10 months. The majority of patients were female (83.3%) with a median age and weight of 89.5 years and 54 kilograms respectively. Median CHA2DS2-Vasc score was 5, giving an estimated annual stroke risk of 6.7%, and approximately 76% of patients had a HAS-BLED score ≤2. Creatinine clearance was calculated using the Cockcroft-Gault formula, and the median CrCl was 26.39 ml/min. During the follow up period, 11 patients died (37%), one of whom died of massive gastrointestinal bleeding after being switched from rivaroxaban to warfarin due to worsening renal function. The cause of death for one patient could not be obtained, however there were no documented deaths due to rivaroxaban as a primary or contributing cause. A total of 6 rivaroxaban related bleeding events were identified with two events occurring in one patient. Bleeding sites included nasal (epistaxis), gastro-intestinal and genitourinary tracts but there were no incidents of intracranial haemorrhage or major bleeding as defined by the International Society on Thrombosis and Haemostasis. A patient who discontinued rivaroxaban due to haematuria later developed acute limb ischemia requiring embolectomy. Although compliance to treatment could not be assessed, a further patient developed an ischemic stroke whilst on rivaroxaban.
Summary/Conclusions: Clinically relevant bleeding events occurred in approximately 17% of our small cohort of very elderly patients with severe renal impairment receiving rivaroxaban (15mg) as anti-coagulant therapy for non-valvular atrial fibrillation. The event rate is almost identical to that in the Rocket-AF study (16.7%) and there were no major bleeding events. Our findings indicate that the use of rivaroxaban in this group of patients is feasible and relatively safe.

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ORAL DIRECT ANTICOAGULANTS IN THE TREATMENT OF NONVALVULAR ATRIAL FIBRILLATION. RESULTS OF THE DAILY CLINICAL PRACTICE

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Background: Atrial fibrillation (AF) is the most common arrhythmia. It leads to significant morbidity and mortality. The new oral anticoagulants (NOAC) represent an improvement compared with standard treatment (vitamin K antagonists (AVK)) in the prevention of thromboembolic complications in patients with non-valvular AF.
Aims: The aim of this study is to analyse the clinical characteristics of the patients (p) anticoagulated with NOAC and compared these with those taking AVK, as well as to assess their effectiveness and safety. The primary study outcome was the composite of stroke, systemic embolism, pulmonary embolism, myocardial infarction or death (MACE). The primary safety outcome was major haemorrhage.
Methods: We studied 688 p with a diagnosis of NVAF between November-2011 and November-2014. We made a prospective analysis, with a median follow-up of 14 months.
Results: A total of 688 p were included with a mean age of 73.4±7.9 in the AVK group *vs* 73.9±8.3 in the NOAC group (p=0.432). In the NOAC group,

hypertension was significantly more common (82.3% *vs* 92.2%, p<0.001), with more frequent history of heart failure (15.3% *vs* 30.4%, p<0.001), and more history of stroke or transient ischemic attack (10% *vs* 15.9%, p=0.022). Mean scores for thromboembolic and bleeding risk indices are shown in Table 1.

Table 1.

SCORE	ACENOCOUMAROL	NOAC	p
CHADS2	1.9±1.0	2.3±1.1	P<0.001
CHA2DS2VASc	3.5±1.3	3.9±1.5	P<0.001
HASBLED	1.3±0.7	1.4±0.7	P=0.086

The primary outcome occurred in 12 p receiving AVK (2.9%) and 11 p receiving NOAC (4.1%) (p=0.413) (HR acenocoumarol *vs* NOAC 1.737; IC 95%: 0.760-3.969, p=0.190). MACE were more common in patients with poor INR control (58.3% *vs* 41.8%, p=0.037). In the univariate analysis, the factor associated with MACE in the AVK group was the poor INR control (4.009 (1.266-12.696), p=0.018), showing the sex female category a strong trend to be a protective factor (0.228 (0.050-1.043), p=0.057). In the NOAC group, valvulopathy ≥moderate (3.840 (1.166-12.652), p=0.027) and renal insufficiency (7.197 (1.743-29-772), p=0.006) were significantly associated with MACE. The rate of major bleeding was 3.51% with AVK, as compared with 0.6% per year in the group that received NOAC (17 events -4.1% >vs. 2 events, 0.7%, p=0.009) (figure 1; HR acenocoumarol *vs* NOAC 0.252; IC 95%: 0.058-1.101, p=0.067). In the univariate analysis, the factors associated with bleeding in the AVK group were age ≥75 years (3.187 (1.028-9.882), p=0.045) and HASBLED score (2.106 (1.072-4.136), p=0.031). The rate of intracranial bleeding was 1.02% with AVK compared with 0.34% per year in NOAC group (5 events – 1.2% *vs* 1 event – 0.4%, p=0.248). There were no significantly differences in the rates of gastrointestinal bleeding (1.02% with AVK *vs* 0.94% per year, p=0.902) neither minor bleeding (4.88% with AVK *vs* 3.51% per year, p=0.309). There was a significantly higher rate of discontinuation with AVK (17.14% *vs* 6.68% per year, p<0.001).

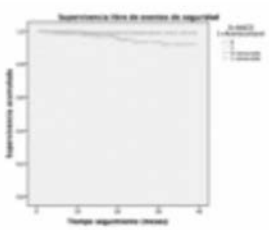

Figure 1.

Summary/Conclusions: Patients with NVAF anticoagulated with NOAC have higher embolic risk than those that receive acenocoumarol. No differences were found in efficiency. Patients anticoagulated with NOAC show a trend to lower bleeding risk. In the multivariate analysis, the predictors of events in the acenocoumarol group were the male category, poor INR control, ≥75 years, anemia and HASBLED score. The predictors of events in the NOAC group were valvulopathy≥moderate, renal insufficiency and anaemia.

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SWITCH FROM VKA, LMWH OR FONDAPARINUX TO DOACS IN THE CLINICAL PRACTICE

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Background: New oral anti-coagulant drugs (NOACs) are largely used both in AF (Atrial Fibrillation) and in VTE (Venous Thromboembolism) and, due to their important advantages over older drugs, many patients have been switched from VKA (Vitamin K antagonists), LMWH (Low Molecular Weight Heparin) or Fondaparinux to NOACs. Current recommendations by scientific society suggest switching from VKAs to NOACs according to the INR test result. Regarding how to switch from Fondaparinux or LMWH to NOACs the suggested wash out period is 24 hours.
Aims: Evaluate safety and efficacy of switching anticoagulant therapy from old to new anticoagulant drugs without monitoring the INR. Safety outcomes were major and minor bleeding rate. Effectiveness outcomes were VTE events. We also evaluate the tolerability of the new treatment.
Methods: We switched patients, affected by AF or DVT, from VKAs or LMWH or Fondaparinux to NOACs regardless from the INR. We follow current recommendations for switching from LMWH and Fondaparinux; we applied to the VKAs-DOACs switch the same schedule prescribed by current guidelines for bridging therapy from VKAs to LMWH. Therefore, we began the NOACs treatment after 24 hours since the last previous anticoagulant intake, if the patient has been switched from LMWH, Fondaparinux or Acenocumarol. We began the NOACs treatment after 48 hours if Warfarin was the patient's therapy. We checked the platelet count and the Creatinine Clearance collecting these laboratory measurements within 30 days before the end of VKA treatment. We collected outcomes measures until 30 days from the switch. Data are presented as mean±standard deviation (SD).
Results: We enrolled in the present study 603 patients: 458 have been switched to NOACs from VKAs, 101 from LMWH and 44 patients from Fondaparinux. 179 patients were affected by AF and 424 by VTE. Thirty days after the switching 99% of the patients were still on NOACs. Three patients complained about nausea, dyspepsia and abdominal pain. Two of them came back to VKAs and one patient change Rivaroxaban with Apixaban, without further side effects. Two patients reported minor bleedings: gingival hemorrhage and hematuria. One of them remained on NOACs treatment and another switch to acetylsalicylic acid. There were no VTE recurrence and no bleedings in the whole cohort.

Table 1.

Population	n	Age (y)	ClCr (ml/min)	CHA2DS2-VASc	HAS-BLED	Major Bleeding	Minor Bleeding	TEV recurrences
AF (from VKA)	179	75.3±7.4	69±29	4.5	3	0	0	0
VTE	424	62.5±15.3	84.4±31.3	/	/	0	2(0.0047%)	0
p value		<0.00001	<0.00001				0.85	
from VKA	279	62.7±15.1	83.8±31	/	/	0	0	0
from LMWH	101	63.1±14.2	86.2 ± 32	/	/	0	1(0.001%)	0
from Fondaparinux	44	58.8 ±18.3	83.3 ± 26.6	/	/	0	1(0.022%)	0
p value		0.25	0.81	/	/		0.37	

Summary/Conclusions: Safety and efficacy of switching anticoagulant therapy in our center are really satisfying compared to the studies that closely monitored INR to adjust anticoagulant therapy switching, suggesting that monitoring INR may not be routinely needed for the switch. Further studies are needed to confirm these findings.

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HIGH HEMOGLOBIN CONCENTRATIONS AND RISK OF THROMBOSIS: CAUSALITY OR CONFOUNDING?

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Background: Patients with polycythemia vera are known to have an increased risk for thrombotic events. This effect has also been observed among those with high as well as low concentrations of hemoglobin (Hgb) in the general population. However many of the earlier studies lack sufficient clinical data to account for underlying disease or causes of high Hgb.
Aims: To assess whether high concentrations of Hgb is an independent risk factor for thrombotic events.
Methods: Hgb measurements and baseline characteristics were obtained from participants in the Reykjavik-AGES study at enrollment in 2002. The Reykjavik-AGES study, a nationwide screening study of 5755 elderly individuals, includes thorough medical history, physical examination, and blood measurements. Lifetime incidents of thrombotic events were recorded up to 2015 in the Icelandic National Health Service and linked to the participants of the study through the National Registry. Primary outcomes of arterial and venous thrombosis were considered separately 10 years before and after enrollment. Hgb measurements at enrollment were used to determine exposure, both as a continuous variable in steps of 10g/L and stratified into five strata (<130, 130-144,145-159,160-175 and >175g/L for men and <120, 120-134,135-149,150-159, >160g/L for women). Men with Hgb concentrations of 120-144g/L and women with Hgb concentration of 120-134g/L were used as reference. Cox proportional hazard regression was used for the statistical analyses and adjusted for confounders (gender, age, body mass index (BMI), diabetes mellitus, smoking, hypertension, and statin use) in three different models.
Results: Analysis of Hgb concentration as a continuous variable in steps of 10 g/L revealed increased risk of arterial and venous thrombosis with increasing Hgb concentration (hazard ratio (HR) 1.06 95% confidence interval (CI) [1.04-1.09] p<0.001 and HR 1.08 95% CI [1.05-1.106] p<0.001). Adjustment for confounders revealed a reverse effect (HR 0.92 95% CI [0.89-0.94] p<0.001 and HR 0.89 95% CI [0.87-0.92] p<0.001). After excluding anemic patients (Hgb <130g/L for men and <120g/L for women) there was however, no association (Table 1). Crude analysis, using stratified Hgb levels, revealed increased risk of arterial and venous thrombosis associated with high Hgb (Hgb: 160-175g/L for men and 150-159g/L for women. HR 1.10 95% CI [1.02-1.20] p=0.02 and HR 1.17 95% CI [1.07-1.29] p<0.001). After adjusting for gender, age, and BMI, this association was no longer evident. There was however marginally increased risk of venous thrombosis in those with slightly higher Hgb concentrations than the reference group (Hgb: 145-