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Adherence of ticagrelOr in real world patients with aCute coronary syndrome: The AD-HOC study

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ABSTRACT

Background: Dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 receptor antagonist is the cornerstone of therapy in patients with acute coronary syndrome (ACS). Adherence to medical therapy is an important issue, as premature DAPT discontinuation increases the risk of new ischemic events. The aim of the present observational prospective multicenter study was to evaluate in the real-world incidence and discontinuation patterns of ticagrelor during the first 12 months after ACS.

Methods: We analyzed 431 ACS patients, discharged with ticagrelor, by 7 Italian centers. The primary end-point was the incidence of cessation of ticagrelor up to 12 months from the index event.

Results: Definitive ticagrelor cessations occurred in 52 patients (12.1%), of which 35 were discontinuations (clinically driven) and 17 disruptions (due to acute events). Temporary cessation occurred in 14 cases (3.3%). Age $\geq$ 80 years and anticoagulant therapy were independent predictors of premature discontinuation. Bleeding occurred in 74 patients, of which 25 suffered a BARC $\geq$ 2 bleeding event. Bleeding were more frequent in female sex (27.0% vs 17.2%, p-value 0.049) and in patients with a history of bleeding (8.1% vs 2.9%, p-value 0.035).

Conclusions: Our study found that the adherence to DAPT with ticagrelor after an ACS is still an important issue, premature discontinuation occurred mainly in fragile patients, like elderly, who suffered a previous bleeding or underwent previous percutaneous coronary intervention.

1. Introduction

Dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 receptor antagonist is the cornerstone of therapy in patients with acute coronary syndrome (ACS) to prevent stent-related and non-stent-related thrombotic events. Ideally, DAPT is generally recommended for 12 months, but a shorter duration should be considered in patients with a high bleeding risk [1,2].

In the PEGASUS-TIMI 54 trial [3], a prolonged DAPT with ticagrelor 60 mg bid over 12 months is associated with a significant reduction of

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ischemic events in patients at high or moderate thrombotic risk. However, thrombotic events sparing was partially counterbalanced by an increase of TIMI major and minor bleedings, without an increase of fatal or intracranial events.

Adherence to medical therapy is still an important issue. It has been demonstrated that premature DAPT discontinuation increases the risk of new ischemic events [4–7]. Several reasons of premature DAPT discontinuation have been reported, such as drug side effects, bleeding events, surgical interventions, patients' low-compliance [8,9]. In the pivotal trial PLATO, premature ticagrelor discontinuation occurred in 23.4% of patients and the overall rate of adherence to the study drug was 82.8%. Dyspnea was more common in the ticagrelor group than in the clopidogrel group (13.8% vs. 7.8%), even though only few patients discontinued the study drug because of dyspnea (0.9% in the ticagrelor group and 0.1% in the clopidogrel group) [10]. Dyspnea is probably triggered by adenosine, as ticagrelor inhibits its clearance, thus increasing its blood concentration. Adenosine receptors innervate C-fibers located in lung parenchyma, thereby inducing dyspnea. The rate of premature discontinuation of ticagrelor in the PEGASUS trial was as high as 28.7%.

In the DAPT trial, 9961 patients undergoing coronary drug eluting stent implantation, after 12 months of treatment with a thienopyridine (clopidogrel or prasugrel) plus aspirin have been randomly assigned to continue receiving thienopyridine treatment or to receive placebo for further 18 months and no significant difference in rates of discontinuation was found between the two groups (21.4% and 20.3%, respectively; $P = 0.18$) [11].

Notably, incidence, patterns, and causes of premature suspension of ticagrelor mainly derive from clinical trials, whereas data from real-world patients are lacking.

The aim of the present study was to evaluate in the real world incidence and discontinuation patterns of ticagrelor in the first 12 months after ACS and their potential association with adverse events.

2. Methods and study population

The AD-HOC (ADHerence of ticagrelOr in real-world patients with aCute coronary syndrome) is an observational, prospective, multicenter study of patients with ACS enrolled at 7 Italian Centers (Bergamo, Catania, Cuneo, Firenze, Genova, Grosseto, Pavia).

The trial was registered at the ClinicalTrials.Gov PRS (ID NCT03129867). Adult patients (aged 18 years or older) discharged alive on DAPT with aspirin and ticagrelor 90 mg bid from January 2017 to August 2019 were eligible for enrolment.

The primary end-point was the incidence of cessation of ticagrelor up to 12 months from the index event. Secondary end-points were the identification of predictors and modalities of ticagrelor cessation and the relation of premature DAPT interruption with ischemic and hemorrhagic events.

Each local institutional review board approved the study protocol, and the investigation was conducted according to the ethical guidelines of the Declaration of Helsinki. All patients provided informed consent for data collection and analysis using the approved informed consent form.

2.1. Study endpoints and definitions

According to the PARIS study [12], prespecified modality of DAPT cessation included discontinuation, interruption, and disruption. Discontinuation was defined as recommended, physician-directed premature withdrawal of antiplatelet treatment for patients thought to no longer need DAPT. Interruption was defined as temporary cessation of antiplatelet treatment due to surgical procedures, with reinstitution of DAPT after surgery. Disruption included cessation of antiplatelet treatment due to bleeding or non-compliance. The modalities of DAPT cessation (discontinuation, interruption, or disruption) were not mutually exclusive, because patients could have more than one during the study.

Major adverse cardiac and cerebrovascular events (MACCE) were defined as the composite of death, definite or probable stent thrombosis (ST), spontaneous myocardial infarction (MI), stroke, transient ischemic attack. ST was defined according to the Academic Research Consortium (ARC) criteria [13]. MI was defined as the presence of clinical or electrocardiographic changes consistent with myocardial ischaemia in the setting of increased cardiac biomarkers above the upper limit of normal in accordance with the universal definition [14]. Bleeding events were classified according to the Bleeding Academic Research Consortium (BARC) criteria [15].

Baseline clinical characteristics, PEGASUS-like criteria [3] (such as age $\geq$ 65 years, diabetes mellitus requiring medication, a second prior spontaneous MI, multivessel coronary artery disease, or chronic renal dysfunction) and Giustino's criteria [16] were collected.

2.2. Follow-up

Follow-up was performed via telephone by trained research coordinators at each participating site at 3, 6, and 12 months using a standard questionnaire. Source documents were obtained for patients reporting any adverse event (ischaemic or bleeding) or any DAPT cessation. In case of ticagrelor cessation, all patients were also asked to provide information about the dates of stopping and restarting, and the reasons for drug cessation (physician-direction, need for surgery, bleeding, dyspnea, other). A questionnaire about adherence to ticagrelor was administered during follow-up. We asked how was the adherence to therapy, applying the Morisky scale [17], a score of 0–2 identifying non-adherent patients, a score of 3–4 identifying adherent patients. All data have been collected using an electronic Case Report Form (eCRF) specifically designed.

2.3. Statistical analysis

We summarized patient characteristics at baseline using descriptive statistics. We expressed continuous variables as medians and interquartile ranges (IQRs) and categorical ones as frequencies and percentages. Study population characteristics were stratified for premature definitive ticagrelor cessation (yes/no; regardless which kind of cessation, i.e. discontinuation or disruption). Study population characteristics were stratified also for MACCE (yes/no) and for bleeding (yes/no). Differences between groups were tested using the Mann-Whitney test for continuous variables and the chi-square test (or Fisher's exact test when appropriate) for categorical variables.

Notably, in the analyses, ticagrelor cessations at 12 months were captured considering 1 month of tolerance, i.e. at 12 ± 1 months.

We calculated time to cessation of ticagrelor as the time (months) between hospitalization and the permanent drug cessation and we censored the time for patients that continue the drug at the last date of follow-up. The distribution of cessations over time was plotted by Kaplan-Meier curves. Time to MACCE was calculated as the time (months) between hospitalization and the first occurrence of the event. The effect of potential predictors on premature definitive cessation and on MACCE was estimated by Cox proportional hazards models and expressed as hazard ratios (HRs) and corresponding 95% confidence intervals (CIs). The multivariable models included terms for demographic characteristics and covariates that resulted significantly different between strata of patients in the univariate analysis at a p-value level of 0.05, or covariates clinically relevant.

For all tested hypotheses, two-sided p-values of 0.05 or less were considered significant. Statistical analysis was performed using STATA software, release 16.1 (StataCorp LP, College Station TX, USA) and was carried out at the biostatistical laboratory of the FROM Research Foundation of Papa Giovanni XXIII Hospital in Bergamo.

3. Results

Overall, 487 patients were enrolled in the study. Fifty-six patients were lost to follow-up. Thus, 431 cases were included in the present analysis, with a median follow-up of 12.1 months (IQR 11.9–12.2).

Table 1 reports baseline clinical characteristics. Median age was 64 years, with 40 patients (9.3%) aged ≥ 80 year. Male gender was prevalent (81%). Among the 16 cases (3.8%) with a previous bleeding, 9 had BARC type ≥ 2. At the time of ACS, 86 (21.0%) patients were on single antiplatelet therapy, of which 77 (90%) on aspirin. Notably, 25 patients (7.7%) were on DAPT, with ticagrelor in 75% of them. The diagnosis of hospital admission was ST elevation MI (STEMI) in 220 patients (51.0%), non-STEMI (NSTEMI) in 160 (37.1%), and unstable angina (UA) in 51 (11.9%). The vast majority of patients underwent coronary angiography and in 401 cases (93.0%) a PCI was performed, with at least 3 lesions treated in 14.9% of cases, bifurcation with 2 stents in 11.9% and a total stent length ≥ 60 mm in 16.7%.

Premature definitive ticagrelor cessations (within 12 months) occurred in 52 patients (12.1%) (Table 2), for discontinuations in 35 cases and for disruption in the remaining 17. Two hundred and sixty-three (61.0%) patients suspended definitely ticagrelor at 12 ± 1 months. Notably, 111 (25.8%) patients were still on ticagrelor after 13 months of follow-up. Fig. 1 shows the distribution of the total 315 definitive ticagrelor cessations. Temporary disruptions and interruptions occurred in 6 (1.4%) and 8 (1.9%) patients, respectively (Table S1).

At univariate analysis, patients who definitely withdrew ticagrelor within 12 months were older (68 vs. 64 years, p-value 0.018) and females in almost 1 out of 3 patients (28.8% vs 17.8%, p-value 0.058) (Table S2). Furthermore, among the 40 patients aged ≥ 80 years, 7 experienced discontinuation, and 6 disruption. Age ≥ 80 years, and anticoagulant therapy were independent predictors of premature discontinuation at multivariate analysis (Table 3). During 12 months follow-up 21 MACCE occurred, and details are reported in the supplementary material (Table S4).

Concerning mortality, five (0.7%) non-cardiovascular deaths occurred over the study period.

Twelve patients experienced a MACCE within 12 months of follow-up, among the cohort of premature temporary or definitive suspension. Four MACCEs happened after the suspension of ticagrelor, while drug suspension occurred after the event in 8 cases. In 4 cases (two transient ischemic attack, 1 S and 1 NSTEMI) ticagrelor discontinuation occurred the same day, probably to avoid hemorrhagic evolution of neurological ischemic attack, and for a switch to a different P2Y12 inhibitor in NSTEMI. Nine were the MACCE in the group adherent to ticagrelor (2.4%). Univariate analysis (Table S3) shows that MACCE were more frequent in women (38.1% vs 18%, p-value 0.022), in patients with previous PCI (38.1% vs 17.4%, p-value 0.017) and in those with previous bleeding (14.3% vs 3.3%, p-value 0.04). Female sex, previous PCI and previous bleeding resulted independently related to MACCE (Table 3).

Bleeding was documented in 74 patients (Table S5), of which 25 suffered a BARC ≥ 2 bleeding event. Bleeding occurred predominantly in female sex (27.0% vs 17.2%, p-value 0.049) and in patients with a history of bleeding (8.1% vs 2.9%, p-value 0.035).

Table 4 shows that, out of 24 disruptions occurred over the entire studied period, 23 were premature. Of these, 14 (60.9%) were due to bleeding, 6 to dyspnea and 3 to other reasons.

Non-adherence to ticagrelor according with Morisky scale resulted < 10% across the 12 months of observation, varying from 5.1% to 8.6% (supplementary material, Table S7).

4. Discussion

The present prospective Italian multicenter registry addressed adherence, causes, and modalities of ticagrelor withdrawal in patients

Table 1
Baseline characteristics of the 431 patients.

	N - Non missing	Total (N = 431)
Demography		
Age, *median (IQR)*	431	64.0 (56.0–72.0)
≥80, *n (%)*		40 (9.3)
Male, *n (%)*		349 (81.0)
Clinical history		
Hypertension, *n (%)*	418	272 (65.1)
Smoking, *n (%)*	418	
Yes		143 (34.2)
Previous		102 (24.4)
Dyslipidemia, *n (%)*	418	219 (52.4)
Diabetes, *n (%)*	418	76 (18.2)
Insulin-dependent		19 (4.5)
Chronic kidney disease, *n (%)*	418	22 (5.3)
Stroke, *n (%)*	418	5 (1.2)
TIA, *n (%)*	418	10 (2.4)
Peripheral arterial vasculopaty, *n (%)*	418	29 (6.9)
Prior MI, *n (%)*	418	66 (15.8)
Prior revascularizations, *n (%)*	418	77 (18.4)
Prior bleeding episodes, *n (%)*	418	16 (3.8)
ACS hospitalization		
Single AntiPlatelet Therapy, *n (%)*	409	86 (21.0)
ASA		77 (90)
Ticagrelor		2 (2)
Clopidogrel		6 (7)
Other		1 (1)
Dual AntiPlatelet Therapy, *n (%)*	323	25 (7.7)
ACS characteristics, *n (%)*	409	
STEMI		220 (51.0)
NSTEMI		160 (37.1)
Unstable angina		51 (11.9)
Angiographic charachteristics		
Coronary angiography, *n (%)*	431	428 (99.3)
Normal coronaries, *n (%)*		19 (4.4)
CAD with non-critical ateromasia, *n (%)*		8 (1.9)
CAD with critical stenosis, *n (%)*		401 (93.7)
CAD multivessel, *n (%)*	406	257 (63.3)
Procedural data		
PCI, *n (%)*	406	401 (98.8)
At least 3 vessels treated, *n (%)*	402	28 (7.0)
At least 3 stents, *n (%)*	402	75 (18.7)
At least 3 lesions treated, *n (%)*	402	60 (14.9)
Bifurcation with 2 stents, *n (%)*	402	48 (11.9)
Total lenght stents ≥ 60 mm, *n (%)*	402	67 (16.7)
Chronic occlusion treated, *n (%)*	402	29 (7.2)
Ticagrelor therapy		
P2Y12 Switch (in hospital), *n (%)*	417	
From Clopidogrel		17 (4.1)
From Prasugrel		2 (0.5)
Discharge		
Therapy at discharge, *n (%)*		
Beta-blockers	431	329 (76.3)
Diuretics	431	109 (25.3)
ACE-I/ARBs	431	301 (69.8)
Statins	431	403 (93.5)
Anticoagulants	431	4 (0.9)
Recommended ticagrelor duration, *n (%)*	417	
Non specified		34 (8.2)
6 months		2 (0.5)
12 months		366 (87.8)
>12 months		15 (3.6)

TIA: transient ischemic attack; MI: myocardial infarction; ACS: acute coronary syndrome; STEMI: ST elevation MI; NSTEMI: non ST elevation MI; CAD: coronary artery disease; PCI: percutaneous coronary intervention; ACEI angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker.

Table 2
Time distribution of ticagrelor premature definitive cessation (discontinuation or disruption).

	N (%)
<11 month	52 (12.1)
11–13 months	263 (61.0)
Death	5 (1.2)
No cessation	111 (25.8)

with ACS.

The main finding of the AD-HOC study has been that a premature permanent ticagrelor cessation is not uncommon within the first 12 months after ACS in real-world patients and more frequent in elderly patients, and in women. Second, age ≥ 80 year, and anticoagulant therapy were independent predictors of discontinuation.

The crucial role of DAPT in improving clinical outcomes in ACS, and in patients submitted to PCI, emerged from the beginning of the stent era.

Studies published in the first decade of the XXI century dealing with adherence to DAPT, revealed that a non-negligible number of patients prematurely discontinue DAPT (2–4,6,7).

The main causes of premature discontinuation emerged in these studies were bleeding events, planned major surgery, oral anticoagulant treatment, and drug intolerance. Antiplatelet discontinuation occurred more frequently in older patients and in presence of chronic kidney disease (CKD). In the PREMIER registry [18], social characteristics, like low education, single living, and low economic income, were associated to premature antiplatelet withdrawal.

The last decade has been characterized by a significant improvement in ACS treatment with the new P2Y12 inhibitors (prasugrel and ticagrelor), more effective in terms of thrombotic event reduction compared to clopidogrel, and new generation drug eluting stents (DES) with thinner struts and more biocompatible polymers. These innovations, along with the implementation of intravascular imaging in daily practice, blunted the incidence of ST [19–21], that nevertheless still represents a dramatic event. However, recent studies highlighted how adherence to new P2Y12 inhibitors, like ticagrelor, is still a concern, because an increase of thrombotic events is evident in patients who

Table 3
Hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) for premature definitive cessation and for major adverse cardiac and cerebrovascular event (MACCE) according to selected characteristics. Multivariate analysis.

	HR (95% CI)	p-value
Premature definitive cessations		
Age (year)		
<80	1 (ref)	0.000
≥80	3.33 (1.76–6.31)	
Sex		
Men	1 (ref)	0.114
Women	1.63 (0.89–3.00)	
Anticoagulants		
No	1 (ref)	0.000
Yes	10.9 (3.34–35.66)	
MACCE		
Sex		
Men	1 (ref)	0.036
Women	2.68 (1.07–6.74)	
Prior revascularization		
No	1 (ref)	0.013
Yes	3.13 (1.28–7.68)	
Prior bleeding events		
No	1 (ref)	0.052
Yes	3.51 (0.99–12.47)	
Premature definitive cessation		
No	1 (ref)	0.680
Yes	1.30 (0.37–4.51)	

Table 4
Causes of premature, temporary and permanent, disruption (within 11 months).

		Premature disruption (within 11 months)	
	Total N = 23	**Temporary N = 6**	**Permanent N = 17**
Bleeding	14 (60.9)	4 (66.7)	10 (58.8)
Mild dyspnea	1 (4.2)	0	1 (5.9)
Moderate dyspnea	2 (8.3)	1 (16.7)	1 (5,9)
Severe dyspnea	3 (12.5)	0	3 (17.7)
Other	3 (12.5)	1 (16.7)	2 (11.8)

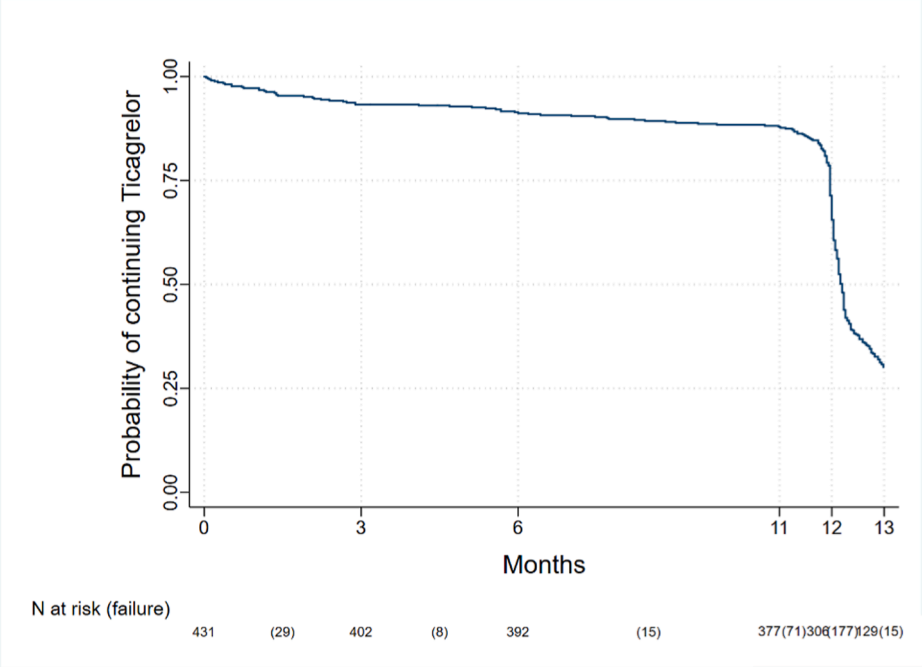

Fig. 1. Kaplan-Meier curve for premature definitive cessation from ticagrelor.

prematurely discontinue ticagrelor [22].

The overall rate of adherence to ticagrelor observed in the large phase III trial PLATO [10] (82.8%) is consistent with the one observed in the present real-world registry (84.7%). In our study we quantified the adherence to ticagrelor with the Morisky scale. Over 90% of patients declared to assume regularly ticagrelor, during follow-up.

Premature discontinuation of ticagrelor occurred in 23.4% of the group of patients randomized to ticagrelor in the PLATO trial, whilst in the AD-HOC registry we observed a lower rate of temporary or permanent withdrawal, within 12 months (15.3%). This apparent discrepancy can be explained considering that in PLATO, 10.1% of patients randomized to ticagrelor discontinued for unwillingness to continue the study. Moreover, in PLATO the rate of major bleeding according to study criteria (11.6%) or to TIMI definition (7.9%), are higher than in AD-HOC, where 5.8% of BARC $\geq$ 2 bleeding has been observed. This lower rate of bleeding can be the consequence of a broader use of radial access in a recent trial - according to modern guidelines, the lack of patients treated with coronary artery bypass grafting (CABG) in our cohort (10% of patients underwent CABG in PLATO) and probably a relatively high rate of GPIIb/IIIa inhibitors used in PLATO in patients blindly treated with ticagrelor (26.4%). The lower rate of bleeding in AD-HOC study can contribute to explain the lower rate of premature cessation.

In a metanalysis [23] of 4 randomized controlled trials evaluating ticagrelor in different clinical settings, with various comparators (clopidogrel in PLATO and EUCLID, aspirin in SOCRATES and placebo in PEGASUS-TIMI 54), in a total of 68,870 patients followed for a median of 18 months, discontinuation was 25% higher for patients receiving ticagrelor, and the discontinuation related to any adverse events was 59% higher. Dyspnea, bleedings and bradyarrhythmia were the most common causes of therapy withdraw.

Data from observational experiences report a rate of ticagrelor cessation within 12 months varying between 20 and 25%. In a Dutch registry based on 354 patients treated with ticagrelor over a period of 330 days, the rate of cessation was 24.3%, due principally to dyspnea (11.6%), bleeding (3.7%), and planned surgery (2.7%) [24].

In a retrospective German study of 614 patients (REAL-TICA registry) [25], among those patients surviving 12 months after discharge, 20.2% discontinued ticagrelor prematurely and age > 75 years, atrial fibrillation and prior stroke were identified as predictors of early discontinuation. In 2.8% of the total population, premature discontinuation of ticagrelor was due to side effects, mainly dyspnea (1.8%).

In our study, premature temporary and definitive ticagrelor cessation affects approximately 1 out of 6,5 patients (15.3%). In 35 cases (53%) the decision to interrupt within 12 months was due to medical advice (discontinuation). Twenty-three patients experienced a disruption for a sudden event (bleeding in 60.9%, dyspnea in 26.1% and bradyarrhythmia in 13,0%). In four cases of bleeding and in one patient with dyspnea ticagrelor was only temporarily suspended.

Dyspnea is considered one of the most common side effects of ticagrelor. Notably, both in the PLATO trial and in the AD-HOC registry, the rate of disruption due to dyspnea is extremely low (0.9% and 1.4%, respectively).

The relatively low rate of premature withdraw and the few MACCE occurred after ticagrelor cessation in AD-HOC probably explain why, although MACCE resulted more frequent after suspension [4/65 (6.2%) vs 9/379 (2.4%)], the multivariate analysis was not able to identify premature interruption as an independent predictor of MACCE. In the present prospective Italian registry, female sex, prior revascularization and a history of bleeding are the independent predictors of MACCE in patients treated with ticagrelor<12 months.

The relation between age and DAPT cessation emerged in the present study, has been also observed in other recent publications, like a sub analysis of the PARIS study [26], where patients $\geq$ 75 years had the highest DAPT cessation rates. Clearly, comorbidities and, consequently risk of bleeding increase with age. Moreover, older patients have higher probability to undergo surgery, and lower compliance to therapy, mainly due to polypharmacy. Our data, in the subgroup of 40 octogenarians, account 7 (17,5%) clinically driven discontinuations and 6 (15%) disruptions.

Clinical characteristics of the population of the AD-HOC registry, identified 191 (44.3%) "PEGASUS like" patients, that could have been treated with ticagrelor 60 mg bid up to three years. Although a recommended ticagrelor duration > 12 months have been declared in 15 cases in the eCRF, in only 3 cases prolonged DAPT with ticagrelor 60 mg bid was prescribed. The low rate of long DAPT with ticagrelor prescription can be explained in different ways. DAPT with clopidogrel and aspirin could have been preferred at least in some cases [11]. Moreover, at the time of our study, in guidelines long DAPT had a IIb level of recommendation, subsequently upgraded to IIa [1,2]. Another reason can be a relative skepticism about the benefit-risk ratio of this practice, with a more selective choice of very high-risk patients deserving prolonged DAPT. Nevertheless, at the end of our follow-up, 111 patients (25.8%) were still assuming ticagrelor 90 mg bid, and we cannot exclude that some of them could have been treated afterwards with prolonged DAPT.

In our opinion, when we prescribe DAPT therapy it is important to carefully evaluate the clinical, mental and social conditions of the patient. Enough time should be spent to explain how important is to regularly assume the drug, and which could be the negative events in case of premature interruption.

It is also conceivable that patients included in an observational prospective study like the AD-HOC are closely followed-up and so are more motivated to assume the prescribed medications, as evidenced by the high grade of adherence to the therapy declared by our patients. It is very likely that, for patients not included in a follow-up program, the adherence to ticagrelor can be lower than that reported in literature.

Our study has some limitations, mainly the relatively small sample size, and the low number of premature suspensions of ticagrelor, which does not allow to highlight their relationship with MACCE, for instance. A further limitation is the lack of the baseline precise-DAPT score of the enrolled patients. On the other hand, the peculiarity, in our opinion, is the deep analysis of the modalities of premature DAPT cessation, that allows to discriminate between clinical decision and adverse events, temporary and definitive events. Moreover, the introduction in eCFR of PEGASUS and Giustino's criteria for prolonged DAPT, gives us the real word prescription of prolonged DAPT with ticagrelor, that seems lower than expected among patients with clinical indication.

In conclusion, this prospective Italian registry highlights how in daily practice, adherence to DAPT with ticagrelor after an ACS, is still an important issue, mainly in fragile patients like elderly, who suffered a previous bleeding or underwent previous PCI.

Declaration of Competing Interest

The authors 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 material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2022.101092.

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