Official Title: ATIVO Study – Anticoagulation Therapy In The Very Old

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Pen Bay Healthcare
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ATIVO STUDY
ANTICOAGULATION THERAPY IN THE VERY OLD

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List of Abbreviations

ACS – Penobscot Bay Medical Center Anticoagulation Services
PBMC – Penobscot Bay Medical Center
TTR – Time in Therapeutic Range

1 Introduction:

Atrial fibrillation increases the risk of stroke by allowing the formation of clot within the left atrium and left atrial appendage. This clot is then able to embolise to the cerebral circulation producing vascular occlusion and stroke often with severe disabling deficit or death. Anticoagulation has been shown to substantially decrease the risk of stroke in patients with atrial fibrillation. Unfortunately anticoagulation increases the risk of major hemorrhage. Almost 15% of patients with atrial fibrillation followed by the Pen Bay Anticoagulation Service are over 90 years old. There is presently no clear guidance for anticoagulation in the very old. Our preliminary data suggest that in this very old group there is an increased risk of both thrombotic and hemorrhagic complications but that stroke prevention can be safely achieved.

2 Study Objectives

This study is designed to evaluate the efficacy and safety of warfarin anticoagulation in the very old and attempt to identify risk factors which may impede safe and effective anticoagulation.

3 Study Design

This is a prospective registry study with data being collected continuously for 24 months.

4 Subject Selection and Withdrawal

4.1 Inclusion Criteria

1. Subject must be 70 years of age or older
2. Subject must have electrocardiographically confirmed atrial fibrillation
3. Anticipated regular follow with patient by PBMC Anticoagulation Services
4. Subject (or legally authorized representative) must be willing to provide informed consent

4.2 Exclusion Criteria

1. Patients not being followed by the PBMC Anticoagulation Services will be excluded from the study.

4.3 Subject Recruitment and Screening

Subjects will be recruited from the PBMC Anticoagulation Services (ACS) department. The medical records used by the ACS will be searched using age $\geq$ 70 and diagnosis of atrial fibrillation as search criteria. All patients aged 90 years or older who fit the criteria will be approached about participation in the study.
An equal number of patients from the ACS who are aged 80-89 years and, an equal number of patients from the ACS will be enrolled who are aged 70-79 years will be enrolled.

4.4 Early Withdrawal of Subjects

Subjects may withdraw from study participation at any time without any effect on their care at the ACS. Additionally; subjects will be withdrawn early from the study if the investigators are unable to communicate with them or obtain medical records.

5 Study Procedures

5.1 Enrollment

At the enrollment visit, after obtaining written informed consent, information will be obtained from the subject and/or caregiver, as well as from the medical record.

All evaluations will be performed by a trained clinician. See attached Baseline Data Collection Form for all the information that will be obtained at this visit.

5.2 Follow Up

Every 6 months (+/- 4 weeks), subjects will be contacted and follow up information will be obtained. When possible, these visits will be conducted when the subject has an appointment at the ACS and will be done in person. If the subject is no longer being seen by the ACS, information will be obtained by phone or by searching the subject's medical record. If needed, family or friends as designated by the subject at study enrollment, will be contacted in order to obtain information about the subject outcomes.

If the subject was enrolled utilizing an LAR, the study will be re-explained and assent will be obtained and documented in the source document prior to any study procedures.

Follow up Mini-Cog™ evaluations will only be done if the visit is done in person. See attached Follow-Up Data Collection Form for details regarding what information will be obtained at these visits.

5.3 Final Visit

The final visit will be done 24 months (+/- 4 weeks) after the enrollment visit. It will not differ from the other follow up visits in any way.

5.4 Assessments

Mini-Cog™ (used by permission) is a validated screening tool used to detect dementia. [5]

CHA_2DS_2-VASc score is a validated tool for stroke risk stratification. [3]

HAS-BLED score is a validated schema for risk stratification for bleeding events among anticoagulated patients. [1]

Dalhousie University Clinical Frailty Scale is a simplified scale to assess frailty.[4]

Mobility score is a simple noting of patient mobility at each visit– ambulating without assist, ambulating with cane, ambulating with walker, or arrived in wheelchair.

Time in Therapeutic Range (TTR) will be calculated utilizing the Rosendaal method of percentage days in therapeutic range in the past 6 months.

6 Analysis Plan

Compare by decade:

Sex
Living arrangement

Alcohol use
CHA2DS2-VASc score
HAS-BLED score
Dalhousie University Clinical Frailty Scale
Mobility score
TTR for 2 years and best and worse 6 months
Death secondary to anticoagulation
Death secondary to cardiovascular causes
Number of hospitalizations
Major bleeding defined as any bleeding meeting at least one of the following criteria:

- Fatal bleeding
- Symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intraarticular or pericardial or intramuscular with compartment syndrome, and/or
- Bleeding causing a fall in hemoglobin level of 2 g/dl or more, or leading to transfusion of two or more units of whole blood or red cells. [2]

CNS Bleeds with death, disability, or no disability
Embolic ischemic stroke
Non embolic ischemic stroke
Mechanism unknown ischemic stroke
Hemorrhagic stroke non traumatic
Traumatic intracerebral hemorrhage
Traumatic subdural hemorrhage
Cardiovascular events (non stroke type)

7 Confidentiality

Subject information will be kept in the PBMC Clinical Research office which is locked when unattended. Information entered into a database will be housed on a PBMC shared drive which is password protected Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

- Protected health information (PHI) which will be collected from subjects in this study include, demographics, medical history, medication list, information related to adverse events, symptoms related to atrial fibrillation and the use of anticoagulants.
- The investigator and his designees will have access to this information.
- The subject has the right to revoke their authorization for use of their PHI at any time. In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization.

8 Study Finances

8.1 Funding Source

At this time, there is no funding for this research study. It will be conducted using existing resources.

8.2 Conflict of Interest

Neither the investigator, nor any of his designees have any conflicts of interest related to this study.

8.3 Subject Stipends or Payments

Subjects will not be compensated for their participation in this study.

9 References

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2. Schulman, S. and Kearon, C. (2005). Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. *Journal of Thrombosis and Haemostasis, 3;* 692-694.

3. Lip, G.Y.H., et al (2010). Refining Clinical Risk Stratification for Predicting Stroke and Thromboembolism in Atrial Fibrillation Using a Novel Risk Factor-Based Approach. *Chest, 137/2.* 263-272

4. Fisher, C., et al (2015). Predicting intensive care and hospital outcome with the Dalhousie Clinical Frailty Scale: a pilot assessment. *Anaesth Intensive Care 43:3* 361-368.

5. Borson, S, Scanlan, J.M., Chen, P., Ganquli, M. (2003). The Mini-Cog as a screen for dementia: validation in a population-based sample. *J Am Geriatr Soc 51(10).* 1451-1454.