

# The Canadian Cardiac Chronicle

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## Adjudication of Clinical Endpoints—Why all the Fuss?

With the arrival of the fall, I find myself constantly “out on the road” participating in various national and international scientific sessions and meetings for ongoing and upcoming clinical trials. A frequent topic of conversation raised by busy study investigators and coordinators relates to the enormous amount of time and effort you are now exerting in studies in order to: identify all potential events, capture medical record information and related source documentation (that is often hard to obtain from other health care settings), provide narratives, and complete numerous forms while under the watchful eye of the trial operational leadership!

Indeed, the use of centralized committees to adjudicate clinical events (clinical endpoint or event committees; CECs) is common in large outcome trials, particularly for the assessment of nonfatal primary outcomes. Not surprisingly, site research staff are increasingly asking what is the rationale and value of this adjudication process (including the provision of source documentation) and why is it such a demanding task?

Earlier pivotal cardiovascular outcome trials (such as the ISIS-2 study, which established the role of ASA and fibrinolysis in the management of suspected acute myocardial infarction [MI]) did not, in fact, require central adjudication; however, these studies used all-cause mortality as the primary endpoint. Although no one is arguing for the need to adjudicate patient death itself, understanding the underlying cause (cardiovascular vs. non-cardiovascular) can be of added importance.

Since definitions for nonfatal events are generally heterogeneous and often times subjective, one reason for a central process of adjudication is to assist in assuring systematic application of the endpoint definitions used in the trial. This is particularly important when determination of nonfatal events, such as peri-procedural MI, can be challenging to sort out. For example, a patient presents with an ST-segment elevation MI and is randomized to receive a treatment aimed at preventing a second MI that can also potentially cause bleeding. If the patient then

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undergoes early stenting or coronary artery bypass surgery, how does one determine whether a recurrent MI has occurred when the troponin level continues to rise within the first 48 hours of the index event? Similarly, if the patient experiences some blood loss around the time of the procedure, how do we determine whether there was a clinically significant bleeding endpoint and can we attribute that adverse event to the randomized treatment or is it simply an expected complication for a patient undergoing revascularization? In addition, particularly in open-label trials, there is the possibility of systematic differential misclassification in determining the occurrence of events based on the patients’ or investigators’ belief that the experimental treatment is better or worse than the comparator. By assuring that the adjudication is done centrally, systematically, and blinded to treatment assignment, the CEC may provide protection against such differential misclassification. Regulatory authorities, including the U.S. FDA and Health Canada, derive confidence in the validity of trial results when central adjudication is performed and may therefore demand this approach before approving new treatments.

Investigators and coordinators have also noted a recent trend towards the use of “triggered” events whereby they receive a query regarding a possible endpoint even when they haven’t indicated any event has occurred. For example, even if an MI form hasn’t been completed by the local study team, the trial operational leadership may ask the site whether an MI might have happened. Indeed, a mild elevation of CK-MB following coronary stenting entered in the case report form as part of the systematic collection of all cardiac markers obtained during the patient’s admission, may trigger a series of questions, requests

## Co-Director's Message Continued...

for copies of all electrocardiograms and a discharge summary to be forwarded to the CEC. While this may not be considered "adjudication" in the true sense of the word, it can be an important chance to enhance the detection of true events that might otherwise be missed, thereby providing an opportunity to improve the eventual estimate of the treatment effect. In fact, there are several large-scale clinical trial examples where systematic ascertainment of events subsequently adjudicated centrally has changed what would have been a "neutral" result (based on investigator/coordinator-determined endpoints) to a "positive" finding (after incorporating the CEC's assessments).

So the next time a potential event occurs in one of your trial patients, put yourself in the shoes of a CEC member and walk

through the identification, documentation, and explanation process to ensure that those not directly caring for your patient can accurately ascertain whether such an endpoint meets the trial definition. Please know that we at the CVC are ready to assist you at any time in this process. Further, as a sign of how committed we are to the quality and importance of endpoint determination in clinical trials, several of our faculty and colleagues at the Universities of Toronto and British Columbia have recently embarked upon a formal collaboration with the Duke Clinical Research Institute (DCRI) to provide CEC membership and to become further engaged in the clinical trials operations process.

## Upcoming Trials

The Canadian VIGOUR Centre is partnering with the Duke Clinical Research Institute (DCRI), Stanford Center for Clinical Research and a global pharmaceutical company on an exciting Phase III study in patients with chronic heart failure. Importantly, this program is expected to enroll a broad range of patients with both reduced and preserved ejection fraction and hence be very inclusive.

Please stay tuned for more information coming your way in the New Year.



## LEVO-CTS



Canadian National Leadership - Dr. S. van Diepen, Dr. S. Fremes, Dr. S. Goodman

We are very pleased to have all of our Canadian sites now active and look forward to having our newly activated sites finding their first patient in the coming weeks. Over 250 patients have been randomized into LEVO-CTS with 18 of those from Canada.

Amendment 2 version 4 was sent to the sites in September. Training on this amendment was provided via a webex in October. All sites have submitted this amendment to their REB, and nearly all sites have received ethics approval, and completed their training. By December, sites should receive the hard copies of the study materials for the new amendment.

The next DSMB Meeting is planned for January 2016, where the data on the first 200 patients will be reviewed. Thanks to all

enrolling sites for keeping the data as current and clean (i.e., query free) as possible for the data cut that was in November.

Important reminders for the trial:

- Ensure training on the amendment is documented for ALL study staff listed on your site delegation log, and send a copy of all training logs (or attestations) to CVC.
- LEVO-CTS Study website contains great information and resources (e.g., for training purposes). Please refer to Issue #4 of the Newsletter for more information.

Dr. Bozinovski's site has taken the title of "fastest site to randomize a patient" (at 5 days following site activation). And they are currently the top enrolling site for Canada! Congratulations to the team at Victoria Heart Institute!

If you have any questions about this trial, please contact Clinical Trial Project Lead, Jodi Parrotta at 1-800-707-9098, ext. 3 or by email at [jodi.parrotta@ualberta.ca](mailto:jodi.parrotta@ualberta.ca).

Sponsored by Tenax Therapeutics, Inc., LEVO-CTS is a Double Blind, Randomized, Placebo-Controlled Study of Levosimendan in Patients with Left Ventricular Systolic Dysfunction Undergoing Cardiac Surgery Requiring Cardiopulmonary Bypass.

levosimendan in cardio thoracic surgery

**ClinicalTrials.gov Identifier: NCT02025621**

## EXSCEL

Thank you to everyone for a terrific turnout at the 2015 North American Rejuvenation Meeting held October 15-16, 2015 in Alexandria, VA! Patient retention and keeping patients on study drug was a key topic and will be a key area for sites to stay focused on for the remainder of the study. The meeting was a great opportunity to share some strategies related to this. We appreciate all your efforts to keep your patients engaged in the trial.

The TrialNetworks Tool went live at the end of October and your hard work in moving your patients through the tool is greatly appreciated. This platform is helping us better manage patient retention activities and will hopefully assist in preventing permanent drug discontinuations and lost to follow up patients. If you did not receive your welcome and registration email, please contact your Clinical Trial Project Lead.

Thank you to all Study Coordinators for resolving queries and

updating your data in preparation for the recent DSMB meeting. As a reminder, data entry is required within 2 business days of the follow-up visit and sites are expected to maintain data at a 90% "clean and entered" status at all times. Please do not hesitate to contact your Clinical Trial Project Lead for assistance with data entry or query resolution.

If you have any questions about this trial, please contact Clinical Trial Project Lead, Karin Kushniruk at 1-800-707-9098, ext. 1 or by email at [kushniru@ualberta.ca](mailto:kushniru@ualberta.ca).

Exenatide Study of Cardiovascular Event Lowering

Exenatide Study of Cardiovascular Event Lowering

Sponsored by AstraZeneca, this trial is a pragmatic, long term, placebo- controlled, double-blinded trial which seeks to characterize the effects of exenatide once weekly on cardiovascular(CV)-related outcomes in patients with type 2 diabetes when added to the current usual care for glycemic control in a standard care setting.

**ClinicalTrials.gov Identifier: NCT01144338**

## PROACT

After approximately 2 years of recruiting patients into the PROACT-4 study and thanks to the hard work and dedication from the Edmonton EMS teams and patients who volunteered to participate, CVC Co-director, Dr. Justin Ezekowitz was pleased to share the results during the late breaking clinical trial session at the American Heart Association meetings in Orlando, Florida on Tuesday, November 10, 2015.

The primary objective of the PROACT-4 study was to look at patients with chest pain who presented via ambulance and determine if measuring Point of Care (POC)-Troponin in the ambulance facilitated a shorter time from first medical contact to final patient disposition in the emergency department (ED). A total of 601 patients giving verbal assent were randomized to either the POC-Troponin arm in the ambulance or usual care. Patients randomized to the POC-Troponin had their troponin measured in the ambulance during transport to the local ED.

The results showed that after the 911 call, patients randomized to usual care had a median time of 139 min to the first troponin being available compared to the POC-Troponin which had a median of 38 min. The primary endpoint was shorter in patients randomized to POC-Troponin (median 8.75 hours [6.2-10.77] compared to usual care (median 9.14 hours [6.69-11.17], p=0.05). Recognizing there were limitations, the trial concluded that while modest, the POC-Troponin in the ambulance did accelerate the time to final disposition.

The AHA Late Breaking Clinical Trial Presentation along with the abstract are available at the following link: [http://my.americanheart.org/professional/Sessions/ScientificSessions/ScienceNews/SS15-Late-Breaking-Clinical-Trials-Science-News\\_UCM\\_478839\\_Article.jsp#lbct03](http://my.americanheart.org/professional/Sessions/ScientificSessions/ScienceNews/SS15-Late-Breaking-Clinical-Trials-Science-News_UCM_478839_Article.jsp#lbct03). We are also pleased to share that the manuscript was accepted and will be available online in the Journal of the American Heart Association.



This was a collaborative effort and could not have been accomplished without the hard work and dedication of the Edmonton Emergency Medical Services staff, emergency physicians and nurses, medical records departments and of course the patients. A special thank-you to all of you for your efforts throughout this study.

We would also like to acknowledge our supporters of the PROACT-4 study; the Heart and Stroke Foundation, Mazankowski Alberta Heart Institute, University Hospital Foundation, Alberta Health Services and Alere Inc., Canada for their in-kind support.

If you have any questions related to this project please don't hesitate to contact Paula Priest @ [paula.priest@ualberta.ca](mailto:paula.priest@ualberta.ca) or by phone at 1-800-707-9098.

Providing Rapid Out of Hospital Acute Cardiovascular Treatment

An Edmonton-region local initiative sponsored by the University Hospital Foundation and the Mazankowski Alberta Heart Institute. Additional support for point of care meters provided by Alere Inc.

**ClinicalTrials.gov Identifier: NCT01634425**

## AEGIS-I



Global enrollment in both the Main Study and PK/PD Substudy has now concluded, with the target number of patients being met well ahead of study projections.

Canada contributed 25 patients from 8 sites. With the rapid recruitment around the world and the slower start in Canada we were disappointed to miss the opportunity to contribute more patients. We want to applaud the efforts of our sites for diligently screening and randomizing the appropriate patients! We have not seen any patient withdrawals or study discontinuations as of yet in Canada and we want to work hard at maintaining this status. Our focus will now be on following our

patients throughout the follow-up period and entering and cleaning the data quickly and efficiently.

Thank you to each of our sites for ensuring that all of the data was entered and clean well ahead of the recent deadline. As a reminder, please ensure that all regulatory documents and REB submissions and approvals pertaining to Protocol Amendment #3 have been sent to CVC.

For further information, contact Clinical Trial Project Lead, Lyndsey Garritty at 800-707-9098, ext 8 or via email at [lyndsey.garritty@ualberta.ca](mailto:lyndsey.garritty@ualberta.ca) or Unblinded Project Lead, Tracy Temple at 1-800-707-9098 Option 5 or via email at [tracy.temple@ualberta.ca](mailto:tracy.temple@ualberta.ca).

Sponsored by CSL Behring LLC, this study is a Phase 2b, multi-center, randomized, placebo-controlled, dose-ranging study to investigate the safety and tolerability of multiple dose administration of CSL112 in subjects with acute myocardial infarction.  
**ClinicalTrials.gov Identifier: NCT02108262**



## SODIUM-HF

The SODIUM-HF trial now has over 155 subjects randomized at 15 active sites. A number of new sites have expressed interest in participating in this exciting trial and we look forward to activating several additional sites in Canada and internationally in the coming months. Thank you to all sites for a strong month of enrollment in October (16 subjects enrolled) – we appreciate all your hard work and look forward to seeing this continue in the coming months.

Congratulations to the following sites on recently enrolling 2 subjects / month:

- Vancouver General Hospital: Dr. Virani, Elan Wang, Naomi Uchida
- Curans Heart Centre (Thunder Bay): Dr. Lai, Lisa Stein
- IMSS (Mexico City): Dr. Escobedo, Luvia Velazquez

Two important memos were distributed recently to all sites:

- clarification on Protocol Inclusion Criteria #4 (re: optimal medical therapy)
- increases to the study budget.

These revisions are intended to facilitate screening and enrollment at each site. Please contact your Clinical Trials Project Lead with any questions on these memos.

Thank you to all site personnel who joined the recent Dietitian Working Group (DWG) Teleconference on November 19. If you were not able to join, please review the November newsletter for trial updates as well as the DWG minutes on the last page of the newsletter.

Reminders:

- 3-days food records should be submitted within 3 business day of the study visit to [sodium-corelab@ualberta.ca](mailto:sodium-corelab@ualberta.ca)
- Please be sure to complete all fields in the Dietary Randomization form and update the form status to “complete” when randomizing a subject. Leaving even one field incomplete can cause issues in REDCap.

If you are interested in further information about SODIUM-HF, please contact Clinical Trial Project Lead, Melisa Spaling at 780-492-8476 or via email at [mbspaling@ualberta.ca](mailto:mbspaling@ualberta.ca).

Funded by the Canadian Institute of Health Research (CIHR), SODIUM-HF is a multicenter, randomized, open-label Study of Dietary Intervention Under 100 μMOL in Heart Failure.



**ClinicalTrials.gov Identifier: NCT02012179**

## GUIDE-IT

GUIDE-IT currently has over 700 subjects randomized with approximately 100 of those from Canada. Thank you to all Investigators and Study Coordinators who attended the recent meeting in September. This was a great opportunity to share updates and discuss best practices for the care of patients in this study.

Congratulations to Dr. McKelvie and Barbara Miller, at Hamilton Health Sciences, on being recognized as a top performing site in terms of adherence. Congratulations to Kim Ronak, from our Calgary site for being awarded the “Above and Beyond” certificate at the meeting for her excellent contributions as a Study Coordinator

To recap, adherence is pertinent to the success of the trial and remains an area of key focus for GUIDE-IT. A number of initiatives have been developed, based on site suggestions / requests, to optimize adherence. Please be sure to implement as many of these strategies as you can at your site and provide feedback, as applicable.

As a reminder, the NIH Conflicts of Interest Policy has changed

– please take a few minutes to confirm if your institution has a PHS (Public Health Services) Policy in place as this will impact requirements for annual collection of COI forms at your site.

Please note the next DSMB meeting is scheduled for January. Thank you to all Study Coordinators for your hard work in preparing for the December data cut – Canada continues to have great performance in various data metrics! As a reminder, please continue to prioritize CEC queries and ensure the requested documentation is submitted to DCRI in a timely manner.

For further information, please contact Clinical Trial Project Lead Melisa Spaling at [mbspaling@ualberta.ca](mailto:mbspaling@ualberta.ca) or 1-780-492-8476.

In collaboration with DCRI (Duke Clinical Research Institute) and Roche, GUIDE-IT is a prospective, randomized 1:1, multi-centre clinical trial **GUIDing Evidence Based Therapy Using Biomarker Intensified Treatment** in Heart Failure.



**ClinicalTrials.gov Identifier: NCT01685840**

## ODYSSEY

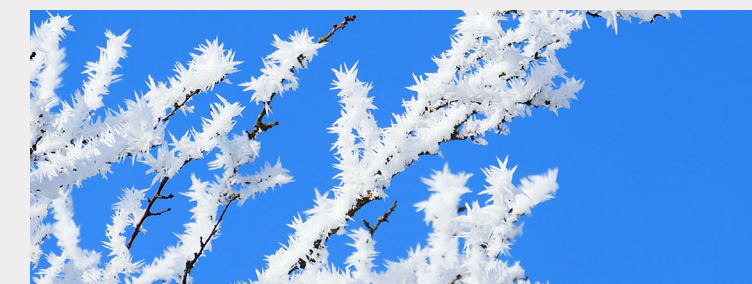
Randomization officially closed for the ODYSSEY Outcomes trial on November 11th, 2015, with over 18,000 patients randomized worldwide. Thanks to the fantastic effort of our Canadian ODYSSEY Outcomes sites, Canada was able to contribute over 360 patients!

As we transition into the patient retention phase of the trial, we ask that you continue to communicate to us any patients that may come off study drug, or may potentially be lost to follow up. With your on-going efforts, we are certain that we will be able to keep the numbers of these patient groups to a minimum.

Data will continue to be one of our main focus points as we move into the new year. We appreciate all of your efforts up to this point in completing data and resolving queries in a timely fashion. Thanks to your hard work, we have seen a dramatic decrease in the number of missing pages and open queries for Canada! We will continue to send updates on your site’s data status and would ask that you work through any outstanding data issues as soon as possible.

There are a number of patient and site materials that will be making their way to you over the next few months. Please remember that all patient materials require REB approval prior to distribution to your patients. We will be updating the “Patient Materials Checklist” for each of you so please keep us up-to-date with your REB approvals and/or acknowledgements of these new materials.

As was communicated to all of you via email with the release of protocol amendment 8 and the updated investigator brochure



(version 8, am. 2), please ensure that all of the required training is completed, signature pages are completed and returned, and that your REB submission is underway. Remember to have your updated ICF approved by CVC prior to submitting it to your REB. If you have any questions or need any assistance, please reach out to your Clinical Trial Project Lead.

Once again, thank you all for your outstanding work to-date on this important trial! For further information regarding this trial, please contact Clinical Trials Project Lead, Amanda Carapellucci at 1-800-707-9098 (ext. 2) or by email at [amanda.carapellucci@ualberta.ca](mailto:amanda.carapellucci@ualberta.ca) or Paula Priest (ext. 9) or [paula.priest@ualberta.ca](mailto:paula.priest@ualberta.ca).

Sponsored by Sanofi-aventis Recherche & Développement this is a randomized, double-blind, placebo-controlled, parallel-group study to evaluate the effect of Alirocumab on the occurrence of cardiovascular events in patients who have recently experienced an Acute Coronary Syndrome.



**ClinicalTrials.gov Identifier: NCT01663402**

## BLAST-AHF

The BLAST-AHF trial currently has over 500 subjects randomized with 70 active sites and we are rapidly approaching the completion of enrollment in early 2016!

Non-recruiting Canadian sites should anticipate a close out visit in early 2016, likely in January. CVC will continue to keep you updated on study timelines and plans for close out over the coming weeks.

Please note the Sponsor clarified Inclusion Criteria #3 (re: medications), which might assist in screening at your site over the remaining weeks. Please bear in mind a few study reminders:

- Use the Protocol Deviation Log V 2.0 to record all deviations identified at your site – as a reminder, Protocol Deviation Log V 1.0 should no longer be used as of 12-Nov-2015.
- Please remember to enter study data within 5 days of the visit.

- Lab kits and supplies are not auto-resupplied. Please be sure to check the expiry dates as the various kits expire at different times. Log in to PPD INSITE to re-order any supplies you may need (note: please allow 2 weeks for delivery).

- As applicable, please check the expiry dates on your BNP kits and ensure adequate supplies are re-ordered well in advance.

For any questions related to BLAST-AHF, please contact Clinical Trial Project Lead, Melisa Spaling at 780-492-8476 or via email at [mbspaling@ualberta.ca](mailto:mbspaling@ualberta.ca)

Sponsored by Trevena Inc., BLAST-AHF is A Randomized, Double-Blind, Placebo-Controlled, Dose Ranging Study to Explore the Efficacy of TRV027 in Patients Hospitalized for Acute Decompensated Heart Failure.

ClinicalTrials.gov Identifier: **NCT01966601**

**BLAST-AHF**



## GALILEO

GALILEO is a new study comparing a Rivaroxaban-based anti-thrombotic strategy to an antiplatelet-based strategy after a successful transcatheter aortic valve replacement (TAVR).

This is a global study with approximately 90 centres planned in Europe, 34 centres in the US, and 10 centres in Canada. We look forward to the first patient in the trial soon. The study has received approval from Health Canada, and we are looking forward to completing site selection and working to activate Canadian sites in the new year.

In Canada, the study will be led by Dr. Robert Welsh from the University of Alberta Hospital as the National Leader and a member of the Executive Committee.

Plans are currently well underway for our Investigator Meeting in January.

If you are interested in hearing more about this trial, please contact Clinical Trial Project Lead, Jodi Parrotta at 1-800-707-9098, ext. 3 or by email at [jodi.parrotta@ualberta.ca](mailto:jodi.parrotta@ualberta.ca).

Sponsored by Bayer Healthcare AG, GALILEO is a Global multicenter, open-label, randomized, event-driven, active-controlled study comparing a rivaroxaban-based antithrombotic strategy to an antiplatelet-based strategy after transcatheter aortic valve replacement (TAVR) to Optimize clinical outcomes.

ClinicalTrials.gov Identifier: **NCT02556203**

**GALILEO**

## 2016 CVC Colloquium

Planning is currently underway for the 3rd annual CVC Clinical Trials Colloquium which will be held in collaboration with the ACC Rockies meeting in Banff, Alberta in March 2016. We look forward to bringing together a broad selection of our sites from across Canada who are interested in continuing to enhance and seek out efficient ways to conduct clinical research in Canada. Recognizing we are only able to include a small number of our sites in the colloquium, we will continue to share key tips and output from the meeting throughout 2016 in our Chronicle.



## Monitoring Tips

We would like to take this opportunity to thank all of our investigators and study coordinators who take time out of their schedules throughout the year to accommodate and work with our monitors while on site. We understand that your time is valuable and our team aims to make the best use of your time and theirs while on site. We appreciate that it can be difficult to have someone review your work and point out items requiring correction. We hope you know our monitors are there to work with you and want to ensure you are always audit ready. Just as you have a responsibility to adhere to the protocol, regulations, and good clinical practice in conducting all clinical research studies at your site, we want to remind you that our monitors also have obligations with respect to ensuring appropriate adherence to these documents, regulations and GCP when they are monitoring.

Monitors have a number of things that require review in the short time while they are on site with you including, ensuring that the source documentation you are providing supports what has been documented in the Case Report Form (CRF), that the drug is appropriately stored and temperature monitored according to the protocol, that drug accountability is complete and accurate, and that you have on file all documentation required to support your involvement in the clinical trial including training records, regulatory documenta-

tion, screening logs, delegation logs, master subject logs, ethics approvals, submission of SAE's, etc.

While our monitors are happy to work with and support you as is our in-house team, the expectation is that your data is up to date, your documents are appropriately filed and readily available, and that your drug accountability is complete when they come on site. This will not only facilitate completion of their work quickly and efficiently but will limit the number of requests to you throughout the day.

Quality assurance is part of doing clinical research and it is the responsibility of everyone involved to ensure each clinical trial is conducted according to the protocol, the agreement you sign and the regulations we are bound by. Our monitors have a lot of experience and have been through many audits so we would encourage you to take the opportunity and utilize them as a resource while on site.

Happy Holidays!

For questions or concerns related to monitoring please contact Halina Nawrocki, Lead CRA at [halina.nawrocki@rogers.com](mailto:halina.nawrocki@rogers.com) or Tracy Temple, Assistant Director, Clinical Trials at [tracy.temple@ualberta.ca](mailto:tracy.temple@ualberta.ca) or 1-800-707-9098 Option 5.

## CVC News



travelling and horticulture.

Francine Nole joins CVC as a monitor for our Eastern Canadian sites and brings an extensive research background. As a registered nurse, she has over 17 years of relevant experience in national/international clinical research in many different therapeutic areas as well as experience with in-hospital clinical trials. In her spare time she enjoys running, cycling, yoga as well as

## CVC Holiday Closure

**December 25, 2015 to January 1, 2016**

**Should any urgent issues arise, we ask that you call the designated Helpline for the study.**

**CVC's main voicemail will be checked daily throughout the closure to address any important study-related issues and staff email will be checked intermittently. Any urgent requests can be sent to [tracy.temple@ualberta.ca](mailto:tracy.temple@ualberta.ca)**

## Publications

Clemmensen P, Roe MT, Hochman JS, Cyr DD, Neely ML, McGuire DK, Cornel JH, Huber K, Zamoryakhin D, White HD, Armstrong PW, Fox KA, Prabhakaran D, Ohman EM; TRILOGY ACS Investigators. Long-term outcomes for women versus men with unstable angina/non-ST-segment elevation myocardial infarction managed medically without revascularization: Insights from the Targeted platelet Inhibition to Clarify the Optimal strategy to medically manage Acute Coronary Syndromes trial. 2015 Oct <http://www.ncbi.nlm.nih.gov/pubmed/26386793>

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activity, and clinical outcomes in patients with acute coronary syndromes treated with prasugrel versus clopidogrel and managed without revascularization: Insights from the Targeted Platelet Inhibition to Clarify the Optimal Strategy to Medically Manage Acute Coronary Syndromes trial. 2015 Oct 17 <http://www.ncbi.nlm.nih.gov/pubmed/26386792>

Ambrosy AP, Hernandez AF, Armstrong PW, Butler J, Dunning A, Ezekowitz JA, Felker GM, Greene SJ, Kaul P, McMurray JJ, Metra M, O'Connor CM, Reed SD, Schulte PJ, Starling RC, Wilson Tang WH, Voors AA, Mentz RJ. The clinical course of health status and association with outcomes in patients hospitalized for heart failure: insights from ASCEND-HF. 2015 Oct 14 <http://www.ncbi.nlm.nih.gov/pubmed/26467269>

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Reid R, Ezekowitz JA, Brown PM, McAlister FA, Rowe BH, Braam B. The Prognostic Importance of Changes in Renal Function during Treatment for Acute Heart Failure Depends on Admission Renal Function. 2015 Sep 18 <http://www.ncbi.nlm.nih.gov/pubmed/26380982>

Simpson J, Castagno D, Doughty RN, Poppe KK, Earle N, Squire I, Richards M, Andersson B, Ezekowitz JA, Komajda M, Petrie MC, McAlister FA, Gamble GD, Whalley GA, McMurray JJ; Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC). Is heart rate a risk marker in patients with chronic heart failure and concomitant atrial fibrillation? Results from the MAGGIC meta-analysis. 2015 Sep 11 <http://www.ncbi.nlm.nih.gov/pubmed/26358762>

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