Duke Cardio-Oncology

news

A joint publication of the Duke Cancer Institute and the Duke Division of Cardiology

Issue 4 | February 2017

Welcome to the fourth edition of the Duke Cardio-Oncology newsletter

The cardio-oncology initiative at Duke continues to grow. We are planning the second cardio-oncology symposium in the fall of 2017.

The cardio-oncology field is moving at fast pace with many opportunities for collaboration, sharing knowledge. We hope this newsletter serves you to keep you abreast of the latest cardio-oncology news.

Global Cardio-Oncology Summit 2017

Royal College of Physicians, 11 St Andrews Place, Regent's Park, London, UK

The Global Cardio-Oncology Summit 2016

Co-hosted by the Canadian Cardiac Oncology Network and the International CardiOncology Society, the 2016 summit took place in Vancouver in late September and brought together experts in cardio-oncology from several countries. The summit has grown significantly, reaching 254 attendees. Sessions covered included contemporary breast cancer therapy, thrombotic and vascular considerations in cancer patients, imaging, prevention and long-term management in primary care. Below are some of the key messages conveyed during the summit:

- Anthracyclines still have a role in the treatment of breast cancer, especially in higher-risk disease. Even patients with small, node-negative breast cancer with aggressive histology benefit from anthracycline.
- Preventive therapy seems to help reduce the risk of heart failure in patients treated with anthracycline, but it is still unknown which patients will benefit most and how long the treatment should be continued.
- Novel therapies are changing clinical practice quickly. In addition to heart failure, conduction abnormalities, myocardial fibrosis, and endocrinopathies may become more important as the results of clinical trials are extrapolated to the general population.
- Thrombotic complications are frequent and blood clots kill people quickly. D-dimer seems to have low specificity in cancer patients. Direct oral anticoagulants have emerged as potential new strategies for prevention and treatment of thromboembolic complications, but data in cancer patients are lacking.
- Many questions remain unanswered in cardiac imaging. Assessing strain appears to be promising in the early detection of cardiac dysfunction, but what should we do when it is identified, and when should we intervene? CMR imagining allows for mapping of high T1 images that may distinguish etiology of damage, but when it should be done and in which patients?
- Outcomes of myeloma patients have significantly improved due to heavy treatment with different chemotherapy agents, but new concerns about heart failure and hypertension have emerged. Similarly, survival in renal cell carcinoma patients has doubled thanks to treatment with tyrosine kinase inhibitors, but those patients have also experienced blood pressure increases and an increased risk of flash pulmonary edema.

Several cardio-oncology studies are underway; we look forward to seeing the results!

The Global Cardio-Oncology Summit 2017 will be held in London September 20–21, 2017—SAVE the DATE!

Efficacy and Safety of Apixaban versus Warfarin in Patients with Atrial Fibrillation and Cancer: Insights from the ARISTOTLE trial

At the European Society of Cardiology meeting in Rome, Dr. Melloni presented recent findings from a sub-analysis performed using data from the ARISTOTLE trial.

In the ARISTOTLE study, 18,201 atrial fibrillation (AF) patients with increased risk of stroke were randomized to warfarin or apixaban. The purpose of this analysis was to describe AF patients with cancer, use of antithrombotic therapy and associated clinical outcomes in this population. Of the 1236 (7%) patients with a history of cancer at baseline, 157 (13%) had either active cancer or were treated within the last year and 1079 (87%) had remote cancer. Patients with history of cancer were older and with more comorbidities than patients without cancer. Overall the event rates/100 person years of stroke or systemic embolism (SE) were similar among patients with cancer (remote 1.2, active 1.9) and no cancer (1.4) (p-interaction=0.48) With similar event rates/100 person years, the effect of apixaban versus warfarin for the prevention of stroke or SE was consistent among patients with cancer (1.4 vs. 1.2; HR 1.09, 95%CI 0.53-2.26) and no cancer (1.3 vs. 1.6; HR 0.77, 95%CI 0.64-0.93) (p-int= 0.37). Overall, the safety and efficacy of apixaban versus warfarin were preserved among patients with and without active cancer with respect to each individual efficacy and safety outcome.

Among this population of patients with atrial fibrillation, no significant associations between cancer and the risk of stroke or systemic embolism were observed. The superior safety and efficacy of apixaban versus warfarin was consistent among patients with and without active cancer. These data are exploratory, but they suggest that apixaban may be at least as good as warfarin among patients with active cancer. Further evaluation of apixaban is warranted in other populations of patients with cancer.

EXTEND trial

Safety and Efficacy of EXercise Training in Men Receiving ENzalutamide in Combination with Conventional Androgen Deprivation Therapy for Hormone Naïve Prostate Cancer

Principal Investigator:
Michael Harrison, MD
Sponsor: Medivation/Astellas

The androgen receptor (AR) is a well-known target in prostate cancer, as prostate cancer growth is dependent on androgens. Depleting or blocking androgen action has been a mainstay of treatment for over six decades in the setting of metastatic disease or when prostate cancer recurs following resection and/or radiation. However, androgen deprivation therapy (ADT) does not completely suppress androgen signaling in prostate cancer and the novel anti-androgen enzalutamide provides more potent inhibition of the androgen receptor than prior anti-androgens. Furthermore, ADT has been prospectively demonstrated to cause decreased lean muscle mass, increased fat mass, weight gain, increased cholesterol and triglycerides, insulin resistance, and loss of bone mineral density. In population-based analyses it has been associated with an increased incidence of diabetes and cardiovascular disease. Combining enzalutamide with ADT appears to be highly effective approach, but may nevertheless exacerbate the well-described adverse toxicities associated with androgen suppression.

There is strong evidence that patients tolerate relatively short-term supervised exercise training (aerobic alone, resistance alone, or the combination) and have significant improvements in a broad range of physiological and subject-reported outcomes in men either initiating or currently receiving androgen suppression therapy. No study to date has examined the efficacy, tolerability, and safety of exercise training to

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EXTEND trial

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prevent and/or mitigate common adverse toxicities in men receiving ADT + enzalutamide for hormone-naïve prostate cancer.

The primary objective of the EXTEND trial is to study the effect of supervised exercise training on cardiopulmonary function in men receiving the combination of enzalutamide (ENZ) and androgen deprivation therapy (ADT) for treatment of hormone-naïve prostate cancer.

This is a two-arm, non-blinded randomized (1:1) phase II trial to determine the efficacy on aerobic capacity of the combination of enzalutamide (ENZ) with androgen deprivation therapy (ADT) compared to the same regimen plus supervised exercise training (ENZ-ADT plus exercise training) in men with hormone-naïve prostate cancer (N=56). This study will be conducted at 2 centers: Duke Cancer Institute (DCI) and Memorial Sloan-Kettering Cancer Center (MSKCC). Subjects will be treated with enzalutamide plus ADT for 32 weeks. If randomized to the exercise arm, subjects will undergo supervised exercise training for 16 weeks, which includes a four-week lead-in of exercise training alone prior to receiving ENZ-ADT. The primary endpoint of the study is change in VO2peak from baseline to 16 weeks and the trial is powered to show a difference between the two arms.

For more information: https://clinicaltrials.gov/ct2/show/NCT02256111

2016 European Society of Cardiology (ESC) position paper on cancer treatments and cardiotoxicity. European Heart Journal (2017) 19, 9–42

In September 2016, the first ESC position paper on cancer treatments and cardiovascular toxicity was published. This document summarizes all available evidence on major cardiovascular complications and their underlying pathophysiologic mechanism and provides general recommendations on risk assessment and ways to prevent or treat cardiovascular complications.

We encourage you to consult this document as a reference guide while treating oncology patients at risk of or with cardiovascular complications.

From the Cardio-Oncology working group:

James L. Abbruzzese, MD is the Chief of the Duke Division of Medical Oncology and serves as the Associate Director for Clinical Research and Training for the Duke Cancer Institute (DCI). Dr. Abbruzzese is a leading expert in the clinical study and treatment of pancreatic cancer, and his management experience and vision for clinical research and the Division substantially supports cancer care and research at Duke.

He earned his medical degree with honors from the University Of Chicago Pritzker School Of Medicine and completed his residency in Internal Medicine at Johns Hopkins Hospital. He also completed clinical fellowships in Infectious Diseases at the Johns Hopkins and in Medical Oncology and Medical Oncology Research Laboratory of Neoplastic Disease Mechanisms at the Dana-Farber Cancer Institute of Harvard Medical School.

Among his many accomplishments, Dr. Abbruzzese is a Fellow of the American College of Physicians and Fellow of the American Society of Clinical Oncology. He has co-authored more than 400 research publications and is the immediate past Chair of the Clinical Trials and Translational Research Advisory Committee of the National Cancer Institute. He currently serves as the Chair of the NCI Pancreatic Ductal Adenocarcinoma Progress Working Group.

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James L. Abbruzzese, MD, FACP, FASCO, DSc (hon)
DCI Distinguished Professor of Medical Oncology,
Chief of Medical Oncology, Department of Medicine,
Associate Director for Clinical Research and Training,
Duke Cancer Institute

From the Cardio-Oncology working group:

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Kathryn Pollak, PhD is a social psychologist and Professor in Community and Family Medicine. She also is the Co-Leader of Cancer Control and Population Sciences. She has been developing behavioral interventions for 19 years, mostly to promote smoking cessation, increase exercise, and improve nutrition with many populations, including cancer survivors. She has studied clinician-patient communication for the past 13 years and serves as a Communication Coach in which she teaches clinicians directly for the past 5 years. She has been on the Cardio-oncology working group since its inception in 2015. Her role is to link the behavioral aspects that cause both cardiovascular disease and cancer and develop interventions for cancer survivors to reduce their cardiovascular risk. These include helping patients increase their physical activity and another to help patients quit smoking. With her expertise in clinician-patient communication, she also serves as a bridge in showing both oncologists and cardiologists how they can help their patients (i.e., cardiologists whose patients are cancer survivors, oncologists whose patients have heart disease).

Kathryn Pollak, PhD

Recent publications

2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines: European Journal of Heart Failure (2017) 19, 9–42.

Husam Abdel-Qadir, MD; Peter C. Austin, PhD; Douglas S. Lee, MD, PhD; Eitan Amir, MB, ChB, PhD; Jack V. Tu, MD, PhD; Paaladinesh Thavendiranathan, MD, MSc; Kinwah Fung, MSc; GeoffreyM. Anderson, MD, PhD. A Population-Based Study of Cardiovascular Mortality Following Early-Stage Breast Cancer JAMA Cardiol. doi:10.1001/jamacardio.2016.3841 Published online October 12, 2016.

Javid J. Moslehi, M.D. Cardiovascular Toxic Effects of Targeted Cancer Therapies. N Engl J Med 2016;375:1457–67.

Armenian SH, Lacchetti C, Barac A, Carver J, Constine LS, Denduluri N, Dent S, Douglas PS, Durand JB, Ewer M, Fabian C, Hudson M, Jessup M, Jones LW, Ky B, Mayer EL, Moslehi J, Oeffinger K, Ray K, Ruddy K, Lenihan D. Prevention and Monitoring of Cardiac Dysfunction in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol. 2016 Dec. [Epub ahead of print].

Nabati M1, Janbabai G, Baghyari S, Esmaili M, Yazdani J. Cardioprotective Effects of Carvedilol in Inhibiting Doxorubicin-induced Cardiotoxicity. J Cardiovasc Pharmacol. 2017 Jan 30. [Epub ahead of print].

Yu AF, Jones LW. Breast cancer treatment-associated cardiovascular toxicity and effects of exercise countermeasures. Cardiooncology. 2016;2. pii: 1. doi: 10.1186/s40959-016-0011-5.

Narayan HK1, Wei W2, Feng Z2, Lenihan D3, Plappert T4, Englefield V4, Fisch M5, Ky B6.Cardiac mechanics and dysfunction with anthracyclines in the community: results from the PREDICT study. Open Heart. 2017 Jan 16;4(1):e000524. eCollection 2017.

Menna P, Salvatorelli E. Primary Prevention Strategies for Anthracycline Cardiotoxicity: A Brief Overview. Chemotherapy. 2017 Jan 26;62(3):159–168.

Craig LA, Ekert PG, Conyers R, Elliott DA Genetic determinants of anthracycline cardiotoxicity - ready for the clinic? . Br J Clin Pharmacol. 2017 Jan 24. [Epub ahead of print].

Cheraghi Z, Ayubi E, Doosti-Irani A. Obesity As a Risk Factor for Anthracyclines and Trastuzumab Cardiotoxicity in Breast Cancer: Methodologic Issues to Avoid Misinterpretation in the Meta-Analysis. J Clin Oncol. 2017 Jan 23. [Epub ahead of print].

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Recent publications (from page 8)

Narayan HK, Finkelman BS, French B, Plappert T, Hyman D, Smith AM, Margulies KB, Ky B. Detailed Echocardiographic Phenotyping in Breast Cancer Patients: Associations with Ejection Fraction Decline, Recovery, and Heart Failure Symptoms over 3 Years of Followup. Circulation. 2017 Jan 19. pii: CIRCULATIONAHA. 116.023463. doi: 10.1161/CIRCULATIONAHA. 116.023463.

Cardinale D, Biasillo G, Salvatici M, Sandri MT, Cipolla CM. Using biomarkers to predict and to prevent cardiotoxicity of cancer therapy. Expert Rev Mol Diagn. 2017 Jan 29:1–12.

Pearson EJ, Nair A, Daoud Y, Blum JL. The incidence of cardiomyopathy in BRCA1 and BRCA2 mutation carriers after anthracycline-based adjuvant chemotherapy. Breast Cancer Res Treat. 2017 Jan 9. Epub ahead of print.

Mohty D, Magne J, Aboyans V. Global longitudinal strain: mature for early detection of anthracyclines-induced cardiotoxicity? Eur Heart J Cardiovasc Imaging. 2017 Jan 8. [Epub ahead of print].

Charbonnel C, Convers-Domart R, Rigaudeau S, Taksin AL, Baron N, Lambert J, Ghez S, Georges JL, Farhat H, Lambert J, Rousselot P, Livarek B. Assessment of global longitudinal strain at low-dose anthracycline-based chemotherapy, for the prediction of subsequent cardiotoxicity. Eur Heart J Cardiovasc Imaging. 2017 Jan 6.

Tsai HT, Pfeiffer RM, Philips GK, Barac A, Fu AZ, Penson DF, Zhou Y, Potosky AL. Risks of Serious Toxicities from Intermittent versus Continuous Androgen Deprivation Therapy for Advanced Prostate Cancer Patients: A Population-based Study. J Urol. 2016 Dec 16. [Epub ahead of print].

Haque R, Shi J, Schottinger JE, Chung J, Avila C, Amundsen B, Xu X, Barac A, Chlebowski RT. Cardiovascular Disease After Aromatase Inhibitor Use. JAMA Oncol. 2016 Dec 1;2(12):1590–1597.

Barac A, Swain SM. Cardiac Protection in HER2-Targeted Treatment: How Should We Measure New Strategies? JAMA Oncol. 2016 Aug 1;2(8):1037–9.

Campia U, Barac A. Exercise and Aerobic Fitness to Reduce Cancer-Related Cardiovascular Toxicity. Curr Treat Options Cardiovasc Med. 2016 Jul;18(7):44. Review.

Upcoming meetings

American College of Cardiology (ACC) Scientific Session 2017

MARCH 17–19, 2017 WASHINGTON, DC, USA

March 18, 2017, 10:45–12:15 PM, Room 140 B
Imaging of Cancer Treatment Associated CV Toxicity: Applying Guidelines to Clinical Practice

March 18, 2017, 12:30–1:45 PM Room 209 C
Vasculo-Oncology: What You Need to Know About Vascular and Thrombotic Complications of Cancer and Cancer Therapeutics

March 19, 2017, 10:45–12:15 PM, Room 144 A
Heart Failure and Cancer Care

American Society of Clinical Oncology (ASCO) Annual Meeting

JUNE 2–6, 2017, CHICAGO, ILLINOIS, USA

Global Cardio-Oncology Summit 2017

SEPTEMBER 20–21, 2017, LONDON, UK

Useful links

cardiooncologyjournal.biomedcentral.com, a new open access cardio-oncology journal

https://www.acc.org/clinical-topics/cardio-oncology

icosna.org, International Cardioncology Society, North America

cardiaconcology.ca, Canadian Cardiac Oncology Network (CCON)

MD Anderson cancer lecture series on the practice of onco-cardiology discussing important topics relevant to cancer patients with heart disease and cardiotoxicity

Contact us

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