



Spring/Summer 2014

Harnessing the Immune System

Progress in the treatment of non-small cell lung cancer

Dr Peter Ellis

The immune system has been considered a therapeutic target in cancer for several decades now. There have been many studies of vaccine based treatments and other immune based therapies such as interferons and interleukins, but these have been mostly unsuccessful. However, stimulating a person's immune system to fight their cancer remains an appealing treatment strategy. Recent advances in immune-based therapy provide much hope and promise that these approaches to treatment will benefit patients with lung cancer.

New developments in vaccines

Older trials of vaccine based therapy for lung cancer did not improve the treatment for patients with lung cancer. However, a recent trial holds some promise. Tecemotide is a vaccine that targets the Mucin-1 antigen (MUC-1). A large international trial of tecemotide or placebo, in patients with stage III non small cell lung cancer (NSCLC) treated with chemoradiation, was recently published.¹ The trial did not show an improvement in overall survival for patients who received tecemotide after chemoradiation. However, a subgroup analysis of patients who received chemotherapy and radiation concurrently (rather than sequentially), suggested this group benefited from tecemotide. The side effects of tecemotide are generally mild. These results appear promising and in order to confirm these results, a further trial of tecemotide in patients receiving concurrent chemoradiation has been started.

Modulating the immune system

There is a lot of excitement about drugs that modulate the immune system (called checkpoint inhibition). Regulation of the immune system is complex. Certain white blood cells called T-cells are a central part of this regulation (Figure 1). There are signals that stimulate the immune system and signals that slow down (down regulate) the immune system. Proteins (ligands) such as CD80 and CD86, Cytotoxic T Lymphocyte Antigen 4 receptor (CTLA-4), Programmed cell death – 1 ligand (PD-L1) and its receptor (PD-1) are all important in down regulating the immune responses. This is one way in which cancers can hide from the immune system, by increasing expression (increasing the amount of) CTLA-4 or PD-L1.

Antibody treatments have been developed to block the effect of CTLA-4 or PD-L1 on the immune system. Removing these inhibitory signals (checkpoint inhibition), allows the body's immune system to recognize the cancer and more effectively attack the cancer cells.

Ipilimumab is a monoclonal antibody that blocks CTLA-4 and allows activation of cytotoxic T lymphocytes. Ipilimumab is already approved for the treatment of metastatic melanoma. In patients with metastatic NSCLC, it was tested in combination with chemotherapy. Giving ipilimumab after standard chemotherapy controlled the cancer for a longer time (improved progression free survival) than standard chemotherapy with carboplatin and paclitaxel.² Phase III trials are ongoing to determine if this strategy will help patients with NSCLC to live longer. A similar antibody, tremelimumab is also being tested in NSCLC as well as mesothelioma. Activating the immune system has the potential to attack healthy cells in the body (immune related toxicities). These include inflammation in the lungs (pneumonitis), liver (drug induced hepatitis) and endocrine glands such as the thyroid and pituitary, rash, diarrhea, although serious side effects are uncommon.

There are a number of monoclonal antibodies that attack either PD-1 receptor (nivolumab, MK-3475, Medi-4376), or the ligand PD-L1 (MPDL-3280A). As a result, cells in the immune system are

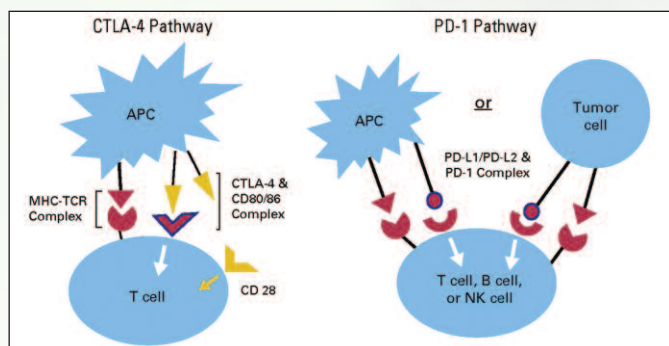


Fig. 1 The cytotoxic T-lymphocyte antigen-4 (CTLA-4) inhibitory checkpoint pathway is important in regulating early T-cell activation. Brahmier J Clin Oncol 31:1021-1028. Reused with permission. © 2014 American Society of Clinical Oncology. All rights reserved

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Patient Resources

A Patient's Guide to Lung Cancer is a Lung Cancer Canada publication designed to meet the educational needs of lung cancer patients and their families. Available in English and French.

Lung Cancer Canada Info Sheets

Available in English and French.

- Questions to Ask Your Oncologist When You've Been Diagnosed with Lung Cancer
- Lung Cancer and the Use of Oxygen Therapy
- How to Prepare for Lung Cancer Surgery When You Smoke
- Nutrition and Lung Cancer
- For Patients and Caregivers: Coping and Emotional Support
- Thoracic Surgery for Symptom Control
- Managing Daily Activities: Energy Conservation and Work Efficiency

Managing Shortness of Breath

Produced by Lorraine Martelli, MN, RN(EC),
Nurse Practitioner Lung DST,
Juravinski Cancer Program

The CD consists of a five part series:

1. Introduction/Learning Abdominal Breathing
2. Managing an Acute Episode of Shortness of Breath
3. Sitting to Standing
4. Climbing Stairs
5. Respiratory Muscle Exercises
6. Relaxation Techniques

Check out the video series link on our homepage.

Call or email Lung Cancer Canada to order material.

Materials and resources are free for individual patients and caregivers.

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Connect with us    from our home page:

www.lungcancercanada.ca

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Lung Cancer Canada wishes to acknowledge our community partners:





Dr Paul Wheatley-Price – Medical Advisory Board Chair

Since September 2009, Dr Wheatley-Price has been on faculty at The Ottawa Hospital Cancer Centre / University of Ottawa as an Assistant Professor in Medical Oncology. Clinically, he treats lung cancer and breast cancer.

Dr Paul Wheatley-Price attended medical school in the UK, at the University of St. Andrews and the University of Manchester, subsequently training in internal medicine in Manchester and London. He then received specialist medical oncology training in Wellington, New Zealand and in London at the Royal Free Hospital, Guy's and St. Thomas' Hospitals and St. George's Hospital, and subsequently a Fellow in Lung Cancer Research at Princess Margaret Hospital, Toronto, under the supervision of Dr. Frances Shepherd.

His research interests are in thoracic oncology (with a sub-interest in mesothelioma and thymic malignancies), and in



developing prognostic tools in understudied clinical scenarios (e.g. in-patients, octogenarians, non-surgical stage 2 NSCLC, 3rd line SCLC).

He is also actively involved in teaching and mentoring at the University of Ottawa Medical School, and supervises multiple resident and fellow research projects in lung cancer topics, the elderly and poor performance status cancer patients. He also collaborates closely with the palliative care physicians in research projects, training programs and development of education

programs in the area of advance decision-making.

Lung Cancer Canada is honoured to have Dr Wheatley-Price accept the position and look forward to working with him and the rest of the Medical Advisory Committee to further our goals of awareness, support and education. 🌿

Harnessing the Immune System ...Continued.

switched on and more able to recognize and fight the cancer. A phase I clinical trial of nivolumab in patients with a variety of cancers, who had all received other therapies, showed that nearly one in five patients had significant response to nivolumab.³ At the 2013 World Congress in Lung Cancer data were presented from early phase clinical trials summarising the activity of nivolumab, MK-3475 and MPDL-3280A. All of these trials included patients with NSCLC who had received two or more previous therapies. Approximately 20% of patients responded to therapy with one of these agents. Many of these patients who responded to treatment remained well a year or more later. Some groups of patients (those with tumors that had higher levels of the PD-L1) had an even higher chance of responding to one of these therapies. This observation requires more research though. Side effects of these drugs were mostly mild or moderate in severity.

Many of these drugs are now being tested in randomized trials

compared to second-line chemotherapy drugs such as docetaxel. Other trials of PD-1 and PD-L1 inhibitors are combining them with first-line chemotherapy. Combinations with other immune based therapies such as ipilimumab or tremelimumab are also being tested. These combinations though have seen more side effects though.

Conclusions

A lot of progress has been made in recent years in the field of immune-based therapies. The immune modulating drugs in particular, appear active in NSCLC. However, they remain investigational agents at this time and are only available as part of clinical trials. Trials are ongoing comparing many of these agents with standard treatment options to determine where they might fit in the treatment algorithms for NSCLC. They do appear to offer significant promise in the future for patients with lung cancer. 🌿

1. Butts C, Socinski MA, Mitchell PL, et al. Tecemotide (L-BLP25) versus placebo after chemoradiotherapy for stage III non-small-cell lung cancer (START): a randomised, double-blind, phase 3 trial. *The lancet oncology* 2014;15:59-68.

2. Lynch TJ, Bondarenko I, Luft A, et al. Ipilimumab in combination with paclitaxel and carboplatin as first-line treatment in stage IIIB/IV non-small-cell lung cancer: results from a randomized, double-blind, multicenter phase II study. *J Clin Oncol* 2012;30:2046-54.

3. Topalian SL, Hodi FS, Brahmer JR, et al. Safety, Activity, and Immune Correlates of Anti-PD-1 Antibody in Cancer. *N Engl J Med* 2012;366:2443-54.



In Memory of Philip Clarke

Louise Bowles

My friend and colleague, Philip Clarke, a seemingly healthy and vibrant individual, was diagnosed with stage IV lung cancer on November 12, 2012; 14 months later, at the age of 48, Philip lost his battle. The initial diagnosis was a shock that quickly turned to a devastating reality as the prognosis was understood.

Once diagnosed, Philip was determined to learn all he could about lung cancer. He focused his time and energy supporting Lung Cancer Canada who work on behalf of the one in 12 Canadians who will be diagnosed with lung cancer in their lifetime. I recall his incredible frustration when he discovered that survival rates for lung cancer patients have not really changed over the past 20 years, that no screening program exists and that new drug approvals to treat lung cancer patients trail far behind.



From left to right: Jennifer Downey, Dr Garth Nicholas, Philip Clarke, Louise Bowles, Dr Farid Shamji and Dr Natasha Leigh

Philip was fiercely committed to raising funds and awareness for lung cancer. It was from his unwavering commitment, and the strong desire of everyone who loved Philip and felt helpless in their efforts to support him in his steadfast resolve to beat this disease, that the inaugural Evening of Hope fundraiser was held in Ottawa on November 21, 2013.

A few weeks before he died, Philip made me promise to continue fundraising efforts. He did not want anyone else to endure what he and his family had endured during his 14-month battle. The promise will not be broken and we will continue in earnest to raise funds and awareness. The second Annual Evening of Hope will be held in Ottawa on Thursday, November 20, 2014 at the Ottawa Convention Center in memory of Philip.

Louise Bowles is a friend and former colleague of Philip. To connect or help with the Ottawa Evening of Hope, please contact info@lungcancerCanada.ca. 🌿

In Memory of Phil Kornblum

Jaye Kornblum-Rea Daughter and Lung Cancer Survivor



When we lost my father to cancer last year, we knew that he would want us to honour his memory by doing something to help others. My family decided to donate my father's memorial fund to Lung Cancer Canada (LCC). My father had passed away from prostate cancer so you might ask why we have chosen to support lung cancer rather than the cancer he was diagnosed with.

I am a 56 year old lung cancer survivor and believe strongly in the work that Lung Cancer Canada is doing. When I was first diagnosed in 2005 with Bronchioloalveolar cancer (BAC), a non-small cell lung cancer, my father was devastated. No parent wants to think about the possibility of losing a child, or that a beloved grandson might grow up without his mother. Since diagnosis, I have been privileged to have an excellent medical team and two successful operations.

As a family, we hope this donation will add momentum to Lung Cancer Canada's mission of increasing awareness, supporting patients living with lung cancer and their caregivers, and providing educational resources. On a very personal level, I have experienced the lung cancer stigma. Lung Cancer Canada is working hard to change the face of lung cancer. It also works with the media to provide balanced reporting on lung cancer, often through the stories of survivors like me. Social attitudes, though, are resilient and change will take patience.

My father was a wonderful man, loved by all that knew him. He lived life to the fullest when his health allowed him to. He was a special man who cared deeply for his family and the people in his life. He would be proud to have the Phil Kornblum Memorial Fund support Lung Cancer Canada. He always encouraged me to be strong and we know that he would be happy with our decision to support this important patient focused organization. 🌿

We wanted to acknowledge the help and support of a few special people that have really helped to shape Lung Cancer Canada, our goals, programs and support.

Dominique Au-Yeung and Ruth MacNeur made significant contributions to Lung Cancer Canada. Although they lost their fight with lung cancer, their spirit and contribution will continue. Philip Clarke and Phil Kornblum are two others whose memory will continue to be honoured.



Frequently Asked Questions

Detecting and Testing for Radon

Janet Whitehead

The Fall/Winter 2013 Lung Cancer Connection featured an article on the relationship between radon gas and lung cancer. Many readers asked questions about testing for radon gas. This issue of Lung Cancer Connection answers your questions.

Detecting radon levels

Since you cannot taste, smell or see radon gas, radon detection technology has been developed to test and monitor radon levels in homes and workplaces. There are two basic ways to test for radon: short term and long term. Short term testing takes two to seven days. Long-term testing takes one month to a year.

What's the difference between short-term and long-term testing?

Radon gas levels in a home are not the same every day. Weather changes, how often windows and doors are opened and closed,

the type of air conditioning/heating systems, and lifestyle all contribute to the level of radon gas in your home each day.

A short-term test may show unusually high or low levels due to the weather and activity in your home. A long-term test will average your exposure to radon levels over a period of time, and experts agree that this gives a more conclusive test result.

How do I test for radon?

There are a number of ways to measure radon. One method involves alpha track technology. The detector is placed in your home from one month to one year, sent for analysis and a report is returned to you.

You can also continuously test for radon using an electronic radon gas detector. They have the advantage of a numeric display and audible alarm for high radon levels. 🌿

LCC at the 2014 Scotiabank Toronto Waterfront Marathon



COME JOIN OUR TEAM – OCTOBER 19, 2014!

Lung Cancer Canada has once again been chosen as one of the official charities for this year's Scotiabank Toronto Waterfront Marathon. Enter as a team or individual. www.torontowaterfrontmarathon.com

For more information on putting together a team and our fundraising goal, contact Lung Cancer Canada at info@lungcancercanada.ca

So come on down! Join the fun! Raise money for a great cause! We hope to hear from you soon!

Lung Cancer Donation Charity

This past summer a couple of young girls ran lemonade stands to raise a bit of money. They started out raising the money for themselves but then decided that maybe they could raise the



Members of LCDC are (Back Row L to R) Emily Hallen, Dakota Lipka, Lexie Gulka, Katie Hobman Gultzan, Helper: Meegan McDonald, (Front row L to R) Juneau Hayter, Hope Dennis, Burklyn Tuleta, Carlee Hayter Binkley. Macey McDonald also came out to help the girls.

money for something special. They decided to donate the money to cancer. After a bit of research it was decided to donate it to Lung Cancer. During their research they learned that Lung Cancer was the most untreated and less donated to cancer.

As word spread to what they were doing more of their friends joined the group and now they had to come up with a name. It was decided that they would be known as LCDC which stood for Lung Cancer Donation Charity.

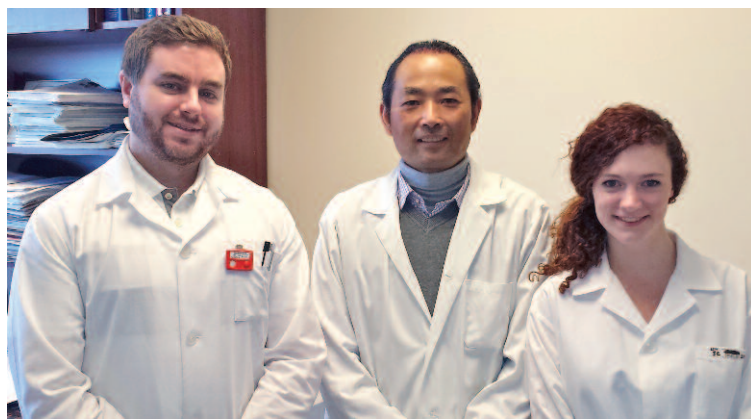
Their lemonade stand netted just under \$200, but the girls were not done raising money. They decided a bake sale would be a good way to raise some more money, so they contacted Mrs Pilon at the Post-Review to see if they could have their bake sale there during Moonlight Madness.

And raise money they did, thanks to the parents and grandma's who helped with the baking they were able to raise \$559.10 from the sale. Now that this is done they are looking for ideas as to who to raise money for next. 🌿



Lung Cancer Canada Research Awards

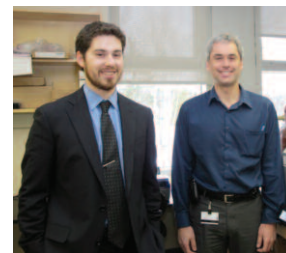
Lung Cancer Canada, the Convoy of Hope – Atlantic and the Beatrice Hunter Cancer Institute have partnered with two provincial associations, the New Brunswick Health Research Foundation and Dalhousie Cancer Awareness Research Society, to provide lung cancer focused research opportunities to students in eastern Canada. Two studentships will be funded in 2014. In New Brunswick, second year medical student Ethan Tournishey is the recipient of the award and undergraduate Shonara Gibson is the award recipient in Nova Scotia.



Left to right:
Postdoctoral Fellow Dr Adam J MacNeil; Dr Tong-Jun Lin; Shonara Gibson


Ethan became involved in cancer research through an early elective program at Dalhousie Medicine. The supervisor of Ethan's current project is Dr Tony Reiman of Dalhousie Medicine New Brunswick. Dr Reiman was also the physician who treated his

father. The experience Ethan's family had was testament to the impact of research advances on cancer treatment and motivated Ethan to become a part of the research team. Ethan and Dr Reiman hope to increase our understanding of targeted therapies by investigating a potentially new specific molecular target for lung cancer.



Left to right: Ethan Tournishey,
Dr Tony Reiman

Shonara is working with Dr Tong-Jun Lin in the department of Microbiology and Immunology at Dalhousie University in Halifax. The title of her project is: Contribution of Copy Number Loss to Reduced MKK3 Expression in Lung Cancer Patients. As a student working in a pathology lab, she noticed that lung cancer samples appeared very often. This experience and the memory of a close family friend who had lost her life to lung cancer inspired Shonara to seek out opportunities to participate in lung cancer research.

Both Ethan and Shonara encourage students to get involved in research and to believe that they make meaningful contributions. "There are many fantastic mentors out there and you should make the effort to become comfortable with as many parts of the discovery process as possible while you are still a student," says Ethan. Shonara adds, "Work hard and put passion into what you're doing; it will show. Accept that you have a lot left to learn, and that you may be the one adding answers to some of life's yet unsolved mysteries." 

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