Lung Cancer Canada Give A Breath Research Award

https://lungcancercanada.ca/about-us/research-program/give-a-breath-research-award/

Deadline Date: January 31, 2025 at 11:59pm PST

Anticipated Notice of Decision: February 28, 2025

Earliest Funding Start Date: March 1, 2025

Application Form

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Project Title

Improving second-line anti-PD-1/PD-L1 therapy for oncogenic driver-positive metastatic non-small cell lung cancers progressing after targeted therapy

Project Description

Up to 60-80% of advanced/metastatic NSCLC cases worldwide are driven by oncogenic drivers – including EGFR mutations, ALK alterations, EGFR/HER2 exon 20 insertions, MET exon 14 skipping, ROS1/NTRK/NRG1 fusions, BRAF/KRAS mutations. The immunotherapy strategies currently available for NSCLC in clinic – both in the metastatic setting (i.e. first-line anti-PD-1 with or without chemotherapy, or second-line anti-PD-1/PD-L1 monotherapy) and unresectable stage III NSCLC (i.e. consolidative anti-PD-L1 after chemoradiation) – tend to yield greater benefits in the absence of oncogenic drivers and much smaller benefits in the presence of oncogenic drivers.

In Canada, we have funded targeted therapy options for a small subset of oncogene-addicted NSCLC (the ~30% that are EGFR-mutated or ALK/ROS1/RET-rearranged) and in the first-line setting only. In the second-line setting, there are very limited self-pay or compassionate-access or clinical trial options in terms of newer-generation targeted therapies.

Recently, phase III trials investigating the addition of dual pathway inhibition – co-targeting the PD-1/PD-L1 and the VEGF-A/VEGFR2 axes – to chemotherapy have shown promise in the second-line setting for oncogene-addicted NSCLC. Mechanistically, how these dual pathways synergize is not fully understood. The VEGF-A/VEGFR2 axis is a key angiogenic signaling pathway that regulates blood vessel endothelial cells. Our project seeks to identify endothelial cell subsets – those with inducible expression of immune checkpoint ligands (i.e., PD-L1 and beyond) – that may play a key role at the intersection of these dual pathways as gatekeepers of tumor-infiltrating lymphocytes entering the tumor microenvironment.

Specifically, the goal of this project is to develop a clinically translatable 2-color IHC-based assay to quantify immune checkpoint ligand expression on tumor blood vessels, which in turn will be tested for correlation with clinical responses to immunotherapies. Improved understanding of crosstalk between angiogenic and immune processes in the tumor microenvironment will enable further optimization and personalized delivery of these dual-pathway strategies after first-line treatment of oncogene-addicted NSCLC.

1. Letter of Intent

Dear Research Committee of Lung Cancer Canada,

We are pleased to submit an application to the Give A Breath Award competition with a research proposal that seeks to improve and broaden second- or subsequent-line immunotherapy options for patients with oncogene-addicted advanced/metastatic non-small cell lung cancers progressing (NSCLC) after first-line targeted therapy.

The knowledge to be gained through this proposed work will accelerate therapeutic innovations to impactfully reduce lung cancer burden, reduce mortality, and improve quality of life for this population.

We thank the adjudication panel for considering our application. We sincerely hope to have the opportunity to pursue the work outlined.

Dr. Cheryl Ho
Medical Oncologist, BC Cancer Vancouver
Clinical Associate Professor of Medicine, University of British Columbia

2a. Research Proposal

Background

Since 2014, Health Canada (HC) has approved five different antibody drugs against PD-1 (an immune checkpoint receptor expressed by activated T cells) or PD-L1 (ligand of PD-1) as treatment for non-small cell lung cancer (NSCLC)[1,2]: pembrolizumab, nivolumab, atezolizumab, and cemiplimab in the metastatic disease setting; consolidative durvalumab in the unresectable locally advanced setting; neoadjuvant nivolumab and adjuvant atezolizumab in the operable early-stage settings[1,2]. Despite these advances, **tumoral PD-L1 as defined by the 'tumor proportion score' (TPS) remains an imperfect biomarker for immune checkpoint inhibitors (ICIs)**[3,4]. Some TPS-high tumors do not respond to pembrolizumab – e.g., in KN024, overall response was only 44.8% in the TPS≥50% population[5]. Conversely, TPS-negative tumors often respond to pembrolizumab plus chemotherapy – e.g., in KN189, an overall survival (OS) benefit was seen in both TPS<1% and TPS>1% subgroups[6]. Moreover, pharmaceutical companies are now ending development of new ICIs against the TIGIT (another checkpoint receptor on T cells) after a series of negative Phase III trials combining anti-TIGIT and anti-PD-(L)1 agents for NSCLC[7,8]. Importantly, these trials stratified patients based on PD-L1 TPS only, without corresponding biomarkers for the TIGIT pathway.

While the TPS only measures PD-L1 on tumor cells, it is noteworthy that PD-L1 and other immune checkpoint ligands can be expressed by endothelial cells (ECs)[9–11] **(Fig. 1A-C).** ECs can express PD-L1 when induced by inflammatory cytokines (including IFN-γ/α/β, TNF-α, IL-2) *in vitro* [13–15] (Fig. 2A) or *in vivo* (Fig. 2B). Our *in vitro* pilot experiments showed a much wider dynamic range of inducible PDL1 expression by ECs compared to tumor cells (Fig. 2A). Intriguingly, in the organ transplant literature, knockout of host endothelial PD-L1 accelerates the rejection of cardiac allografts in mice[12]. By extrapolation, PD-L1$^+$ ECs may play an unappreciated but key role in anti-tumor immunity. Mechanistically, circulating lymphocytes must extravasate to enter the tumor microenvironment and any PD-L1$^+$ ECs at this step may inhibit anti-tumor activity of the T cells (Fig. 1A & 2B). Similarly, ECs express PVR and nectin2 (the ligands for TIGIT) in response to IFNγ *in vitro*[13]. In fact, tumor ECs express PVR and nectin2 more prevalently and intensely *in vivo* compared to PD-L1 or PD-L2, based on our pilot single-cell sequencing data (Fig. 3A) and IHC staining (our pilot endothelial PD-L1 staining (Fig. 3B) versus published endothelial PVR/nectin2 staining[14]). **We thus hypothesize that the TPS as a predictive biomarker for ICIs can be improved upon by additionally accounting for endothelial PD-L1, PD-L2, PVR, and nectin2 expression.**

Preclinical evidence has implicated endothelial PD-L1 as a potential therapeutic target of ICIs. PD-L1$^+$ CD31$^+$ ECs were shown to contribute to immune evasion through inhibition of cytotoxic T cells in murine melanoma models [15]. Furthermore, upregulation of endothelial PD-L1 was observed in murine pancreatic and breast cancer models after antiangiogenic therapies against VEGFR2 (expressed on ECs) or VEGF (the ligand of VEGFR2), and this was implicated in the enhanced anti-tumor efficacy seen when further combined with ICIs[16,17]. These **preclinical studies suggest that endothelial PD-L1 – and by extension, PD-L2, PVR, nectin2 – warrant investigation as potential predictive biomarkers for combined antiangiogenic + ICI strategies**[18,19].

This would be particularly timely endeavour for oncogene-driven metastatic NSCLCs because of promising results coming in from phase III trials – ATTLAS (investigating second-line anti-PD-L1 + anti-VEGF + chemotherapy [20]) and HARMONI-A (investigating second-line bispecific antibody against VEGF and PD-1 plus chemotherapy [21]) – for EGFR-mutated or ALK-rearranged NSCLC progressing after first-line targeted therapy, as summarized in Fig. 4A. The mechanisms

underlying the additive or synergistic effects of combining anti-VEGF and anti-PD1/PD-L1 agents for oncogene-driven metastatic NSCLCs are not fully understood.

Hypotheses: PD-L1$^+$/PD-L2$^+$/PVR$^+$/nectin2$^+$ EC subsets contribute to the exhaustion of tumor-infiltrating CD8$^+$ T lymphocytes and play a key role in the additive/synergistic effects of combined ICI + antiangiogenic therapies. Modifying the TPS to incorporate endothelial scoring of immune checkpoint ligands will improve predictions of response to ICI-based therapies.

Study Objectives:

- **To develop clinically translatable IHC-based assays to measure endothelial expression of PD-L1, PD-L2, PVR, and nectin2** (2-color assays, with ERG as an EC marker, as in Fig. 3B).
- **To score PD-L1$^+$/ PD-L2$^+$/ PVR$^+$/ nectin2$^+$ ECs in oncogene-addicted NSCLC biopsies and correlate these with clinical outcomes after standard of care anti-PD-(L)1 therapy** (details below and illustrated in Fig. 4B).

Optimization + Aim #1. Prevalence in oncogene-addicted NSCLC Using our provincial cancer centre's pharmacy databases, we will identify: (i) patients who had surgical resection of early-stage EGFR-mutated NSCLC prior to adjuvant osimertinib (n=10); and (ii) patients who had core biopsies (≤18G) collected at initial diagnosis prior to receiving first-line targeted therapies (EGFR inhibitors n=6; ALK inhibitors n=6; ROS/RET/NTRK n=3). Archival FFPE blocks from these surgical resections and core biopsies will be retrieved and four whole-slide sections will be obtained from each block. These slides will be used for IHC assay optimization and a survey of baseline prevalence of PD-L1$^+$/ PD-L2$^+$/ PVR$^+$/ nectin2$^+$ ECs prior to targeted therapy. Small amendments will be required to existing REB approvals to our group (e.g., UBC BC Cancer H22-01017).

Aim #2. Prognostic or predictive value in advanced/metastatic oncogene-addicted NSCLC
Through our provincial cancer centre's pharmacy database, we will identify deceased patients who got a repeat core biopsy (≤18G) prior to later-line atezolizumab or nivolumab monotherapy for their oncogene-driven NSCLC progressing on prior targeted therapy and chemotherapy. Small amendments will be required to existing REB approvals to our group (e.g., UBC BC Cancer H22-01017). Whole-slides will be cut in a non-exhaustive manner from the FFPE blocks, scored for PD-L1$^+$/ PD-L2$^+$/ PVR$^+$/ nectin2$^+$ ECs, and correlated with progression-free survival (PFS) and OS.
If we are unable to attain sufficient sample sizes (n=5 EGFR mutated + n=5 ALK altered) from retrospective retrieval of FFPE blocks, there may be an opportunity to piggyback onto the prospective THRIVE study (on which Dr. Laskin is a study PI), which seeks to obtain repeat biopsies in this same setting for bulk whole-genome transcriptomic analysis. Amendments to the REB will be required to offer participants the option of additional core biopsies for IHC staining and analysis.

Aim #3. Prognostic or predictive value in unresectable stage III oncogene-addicted NSCLC
For a subset of oncogene-driven unresectable stage III NSCLCs – especially those who would not have funded targeted therapies in the metastatic setting if they were to experience a recurrence/progression after curative-intent chemoradiation – oncologists and patients may opt to undergo consolidative durvalumab. Ten such patients with core biopsies done at the time of initial diagnosis will be identified with REB approval (with small amendments to UBC BC Cancer H22-01017) through our provincial cancer centre's pharmacy database. Whole slides will be obtained in a non-exhaustive manner from their archival FFPE blocks, scored for of PD-L1$^+$/ PD-L2$^+$/ PVR$^+$/ nectin2$^+$ ECs, and correlated with PFS and OS.

2b. References

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2c. Appendix

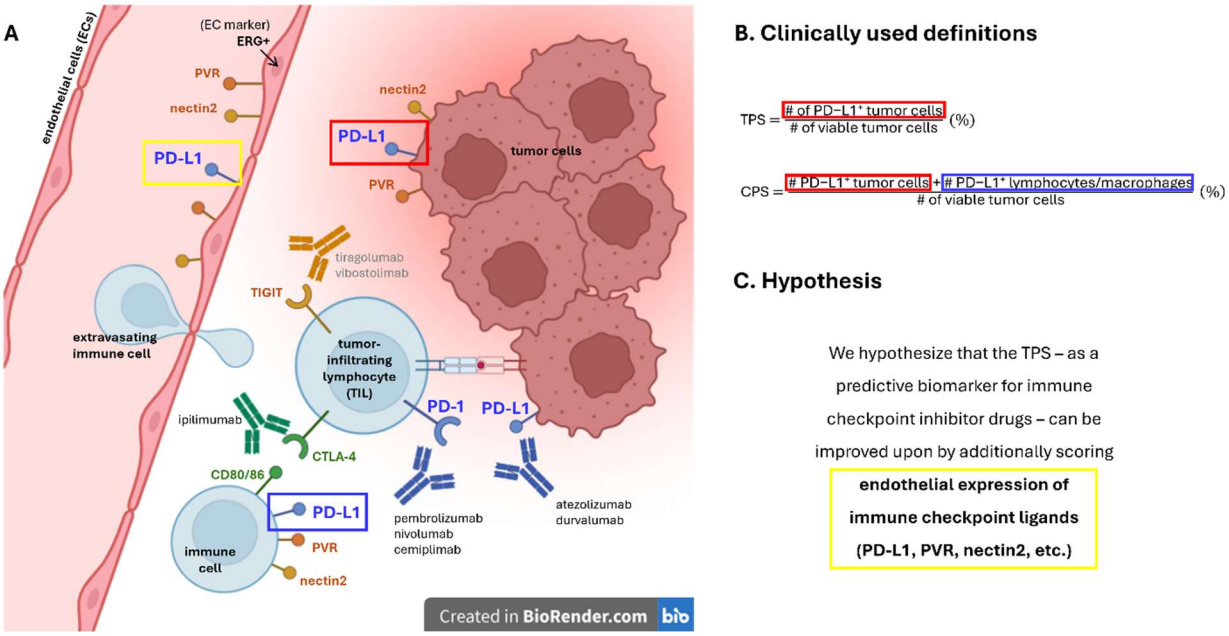


FIGURE 1. PROJECT RATIONALE

A. BACKGROUND: The presumed cellular targets of PD-1/PD-L1 pathway inhibitor drugs used in clinic are PD-1$^+$ T cells and PD-L1$^+$ tumor/immune cells. However, stromal cells including endothelial cells (ECs), are also capable of induced expression of immune checkpoint ligands – including PD-L1 and PD-L2 (ligands of PD-1), as well as PVR and nectin2 (ligands of TIGIT). Of note, ERG is a nuclear EC marker commonly used by clinical pathologists in IHC-based assays.

B. CLINICAL GAP: Current companion IHC assays for immune checkpoint inhibitors (ICIs) only quantify cell-surface or membranous PD-L1 staining on tumor cells (i.e., the tumor proportion score 'TPS' as used in lung cancers) or tumor cells plus immune cells (i.e., the combined positive score 'CPS' as used in head & neck, cervical, gastroesophageal, and breast cancers). The TPS and CPS are imperfect predictive biomarkers for ICI therapy.

C. HYPOTHESIS: Endothelial cell (EC) subsets that express immune checkpoint ligands may play a role in polarizing the types of tumor-infiltrating lymphocytes (TILs) that get into the tumor microenvironment (TME) and thereby affect tumor response to ICI therapy. **OBJECTIVES:** To develop clinically translatable IHC-based assays to measure endothelial expression of immune checkpoint ligands (e.g., PD-L1, PD-L2, PVR and nectin2) and test for potential prognostic and predictive correlations with clinical outcomes.

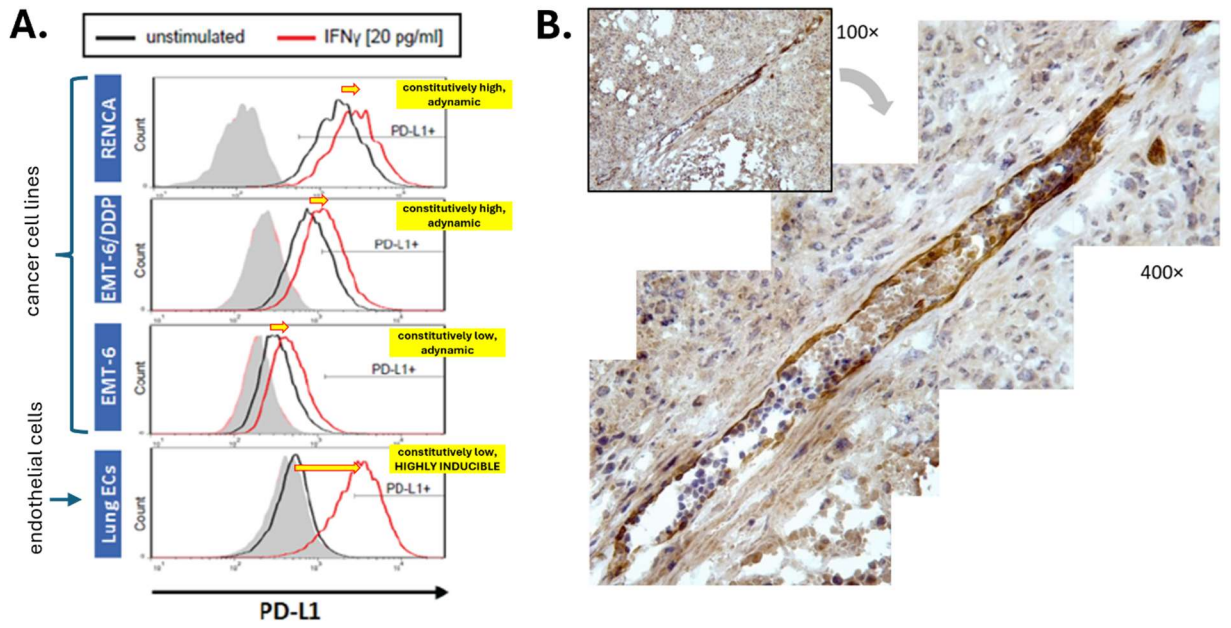


FIGURE 2. PILOT DATA: murine endothelial cells express PD-L1 *in vitro* and *in vivo* (unpublished data, FTH Wu & RS Kerbel).

A. Flow cytometry detection of *in vitro* PD-L1 expression: Solid lines represent mouse PD-L1 staining (PE rat IgG2b,κ, clone 10F.9G2, Biolegend #124308). Shaded histograms represent isotype controls (eBioscience #12-4032-82). ◆ Murine kidney cancer (RENCA) and murine breast cancer (cisplatin-resistant EMT-6/CDDP) cell lines constitutively express PD-L1. ◆ In contrast, VeraVec™ murine lung microvascular endothelial cells (Lung ECs) express negligible PD-L1 at baseline, but show highly inducible PD-L1 expression upon IFNγ (20pg/mL) stimulation.

B. IHC staining of *in vivo* endothelial PD-L1 expression: Frozen sections of orthotopically grown primary EMT6/CDDP murine breast tumors were stained for PD-L1 (clone GEN130-47-4 from Genentech).

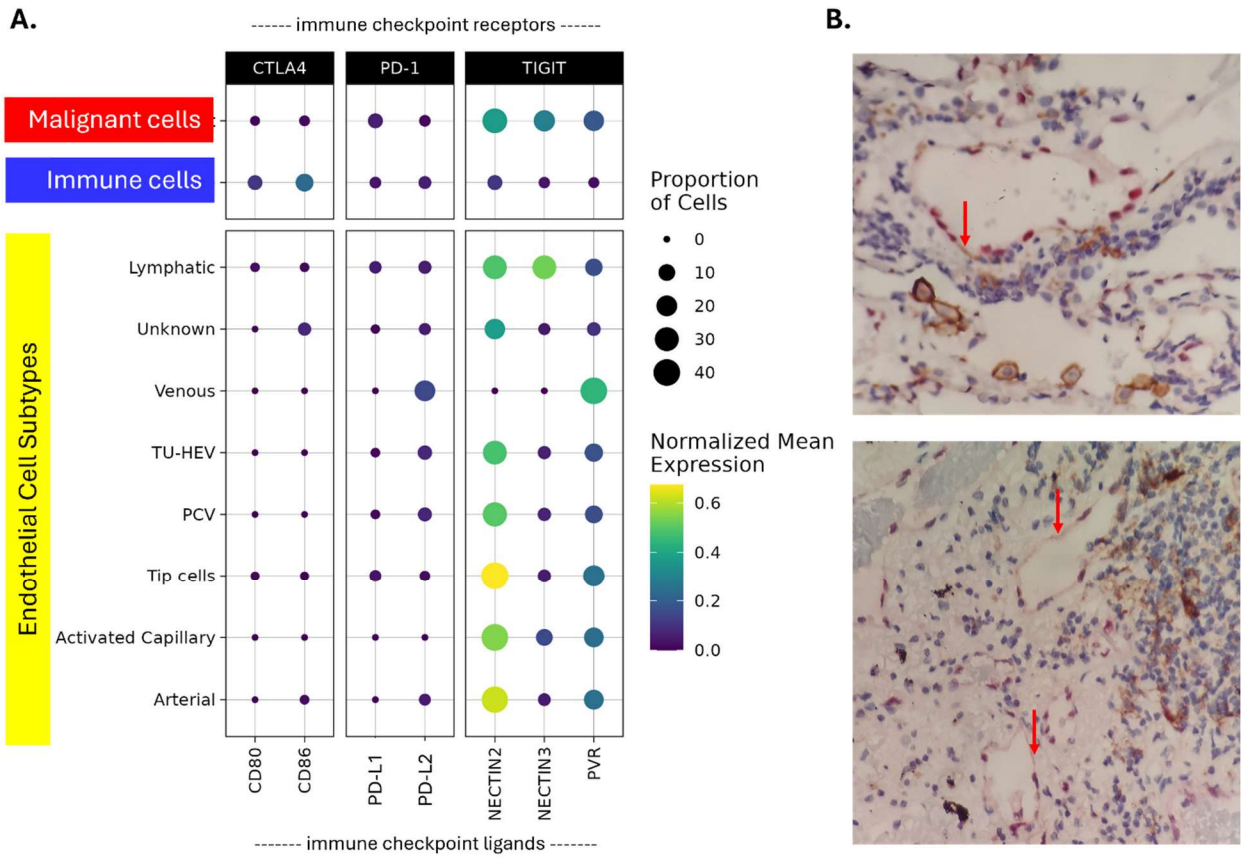


FIGURE 3. PILOT DATA: endothelial PD-L1 expression in human NSCLC specimens by snRNA-seq (unpublished data, C Yan & MA Marra) and IHC (unpublished data, J Naso & C Ho).

A. Single nucleus RNA sequencing (snRNA-seq) was performed on 13 non-small cell lung cancer (NSCLC) specimens – biopsies of lung primaries/metastases or lymph node metastases – using the 10X Chromium Multiome kit. Cell types were classified and annotated by orthogonal methods (SingleR & Seurat) [22,23]. Endothelial cells (ECs) were further sub-clustered into subtypes (e.g. arterial, capillary, tip-like, post-capillary vein (PCV), tumor-associated high-endothelial venule (TU-HEV), venous, lymphatic) based on published reference datasets [24,25]. ◆ PD-1 ligands were expressed by ECs at low prevalence and low intensity (PD-L2 slightly higher than PD-L1 and possibly enriched in certain EC subtypes). ◆ In contrast, TIGIT ligands (especially nectin2 and PVR) were broadly expressed by ECs. These findings are pending confirmation on a larger cohort of NSCLC specimens (n~30).

B. Pilot run of a 2-color IHC assay on whole slides of resected early-stage NSCLC (n=10) confirmed low-prevalence and low-intensity expression of PD-L1 by endothelial cells. Cell-surface PD-L1 is detected using a rabbit anti-human PD-L1 (clone 73-10) primary antibody and DAB (brown) stained. Nuclear ERG (an EC marker) is detected by a mouse anti-human ERG (clonse EPR3864) primary antibody and stained by Warp Red.

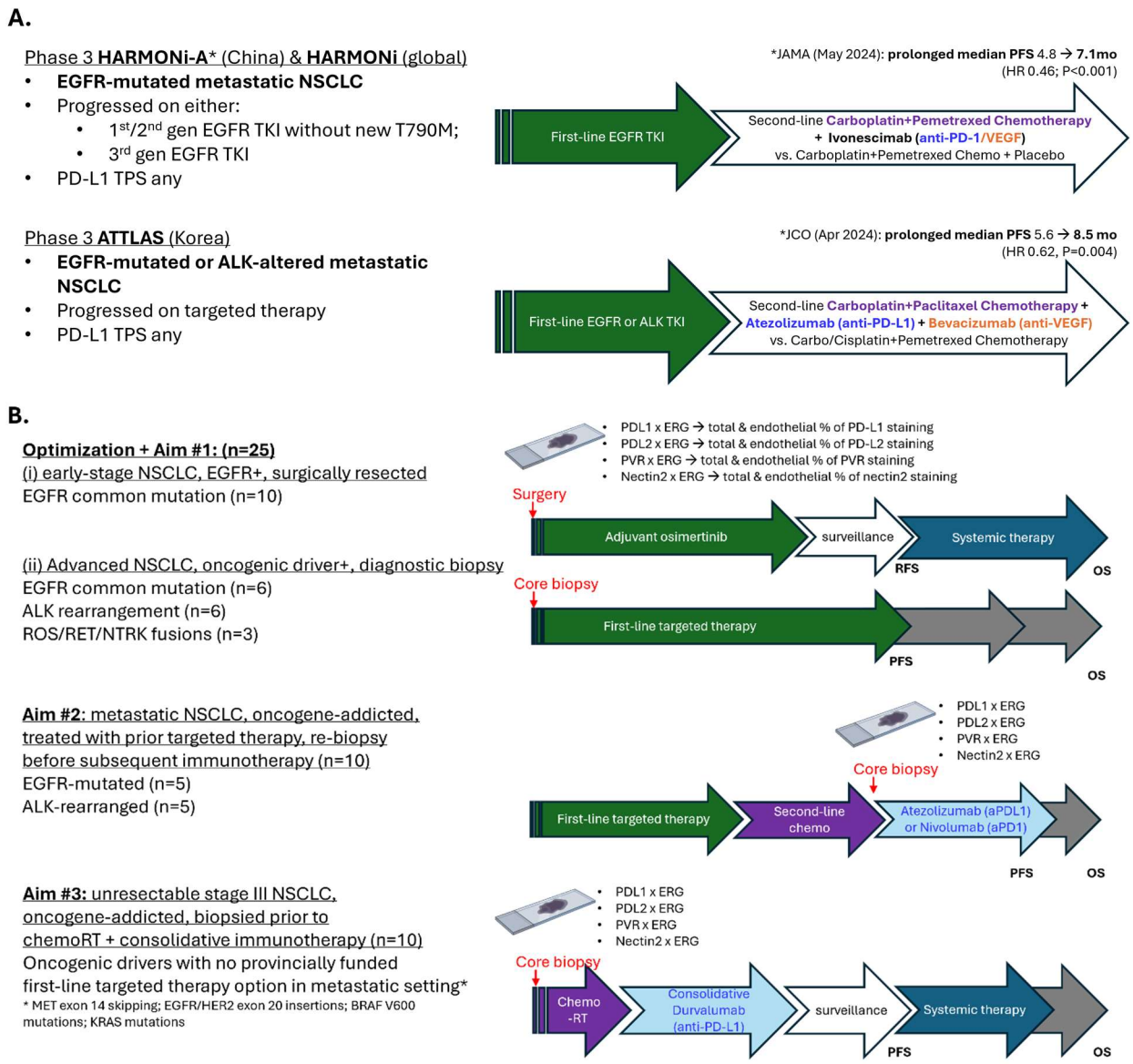


FIGURE 4. BASIS & DESIGN OF AIM #1-3 COHORTS.

A. Phase III clinical trials (e.g., HARMONi-A[21] and ATTLAS[20]) showed survival prolongations when anti-PD-1/PD-L1 therapy with concurrent VEGF blockade is added to second-line chemotherapy for oncogene-addicted NSCLC progressing after first-line targeted therapy. The mechanisms of how concurrent VEGF inhibition adds to or synergizes with PD-1/PD-L1 inhibition in this setting are not fully understood. It is well established that VEGF blockers inhibit vascular processes (e.g., vascular permeability and angiogenesis) by reducing activation of VEGFR2 signaling in ECs. Preclinical studies have reported an upregulation of endothelial PD-L1 after anti-VEGF/VEGFR2 therapies[16,17,26], as a potential mechanism by which VEGF blockade potentiates anti-PD-1/PD-L1 therapies.

B. While our cancer centre participated in the HARMONi study (the global replication of HARMONi-A), re-biopsies at the time of trial enrollment and targeted therapy resistance was not mandated. In

lieu of that ideal cohort of NSCLC biopsies, we propose three real-world cohorts as depicted, where endothelial PD-L1 / PD-L2 / PVR / nectin2 expression at the protein level will be assayed by 2-color IHC (similar setup as Figure 2B). With **Aim #1**, the baseline prevalence and intensity of PD-L1 / PD-L2 / PVR / nectin2 expression on ECs will be assessed in surgical resections (i) and core biopsies (ii) of targeted therapy-naïve oncogene-addicted NSCLC. With **Aims #2-3**, endothelial PD-L1 / PD-L2 / PVR / nectin2 will be scored and correlated with clinical outcomes after anti-PD-1/PD-L1 therapy in the stage IV (Aim#2) and stage III (Aim#3) setting of oncogene-addicted NSCLC. RFS = recurrence-free survival. PFS = progression-free survival. OS = overall survival.

3. Impact Statement

According to the Canadian Cancer Society, 20,700 Canadians died from lung and bronchus cancers, making up 23% of cancer deaths, in 2024. About 85% of those would have been **non-small cell lung cancers**, 55% of which would be adenocarcinomas, and in turn 60-80% of which would be **oncogene-driven** (i.e. **5,806 to 7,742 Canadian deaths per year**). **This research proposal is seeking to reduce these numbers, by broadening and improving the effectiveness of second-line therapy options for this specific population.**

There are already very effective first-line targeted therapies for perhaps 30% of oncogene-driven NSCLCs, in the form of small-molecule tyrosine kinase inhibitor against EGFR, ALK, ROS1, RET. In contrast, immunotherapies – particularly in the form of anti-PD-1/PD-L1 monotherapy – are much less effective for oncogene-driven NSCLCs than non-oncogene-driven NSCLCs in the stage IV refractory setting or stage III consolidative setting.

Recent phase III clinical trial evidence showed promising survival benefits when dual pathway inhibition of the PD-1/PD-L1 and VEGF/VEFR2 axes (e.g. with the bispecific agent, ivonescimab) is added to chemotherapy in the second-line setting of EGFR-mutated or ALK-rearranged NSCLCs. Our research proposal seeks to understand the molecular and cellular underpinnings of this type of combination therapy. Specifically, we hypothesize that a subset of endothelial cells capable of induced expression of immune checkpoint ligands (PD-L1, PD-L2, PVR, nectin2) may be upregulated by VEGF/VEFR2 blockade, which then potentiates the effectiveness of PD-1/PD-L1 inhibitors. Our project seeks to test this hypothesis using real-world archived clinical specimens. The **tangible deliverables of our proposed project are four simple 2-color IHC assays for measuring the endothelial contributions to total PD-L1/PD-L2/PVR/nectin2 staining in NSCLC biopsies**, which would be easily and immediately translatable for clinical application if our hypothesis is confirmed.

Dual inhibition of the PD-1/PD-L1 and VEGF/VEFR2 axes likely will have applications beyond oncogene-driven NSCLC. As an example, ivonescimab has shown significant promise in the first-line setting as monotherapy for non-oncogene-driven metastatic NSCLC with PD-L1 TPS >1% (Phase III HaRMONi-2), in the peri-operative space of non-oncogene-driven NSCLC (Phase II NCT05247684), as well as in the colorectal / breast / head & neck cancer space (Phase II trials). Thus, **in the longer term**, our four 2-color IHC assays for measuring endothelial PD-L1/PD-L2/PVR/nectin2 **may have broader applications beyond oncogene-driven NSCLC and beyond thoracic oncology as well**.

4. Public, non-scientific summary

85% of lung cancers are non-small cell lung cancers (NSCLCs). These can be broadly divided into two categories – those that are oncogene-driven (i.e. fueled by typically one dominant signaling pathway, e.g., EGFR or ALK) versus those that are not. For a small subset of oncogene-driven NSCLC, there are targeted therapies (e.g., "EGFR inhibitors" and "ALK inhibitors") that work very well by shutting down these dominant signaling pathways. In contrast, immunotherapies – specifically antibody drugs against PD-1 or PD-L1, which re-invigorate the body's immune system to eliminate cancer cells – tend to work less well for NSCLCs that are oncogene-driven, compared to those that are not oncogene-driven. This is a big clinical gap since oncogene-driven NSCLCs account for about 5,806 to 7,742 Canadian deaths per year. Our project seeks to lower these mortality rates by increasing and improving second-line treatment options for oncogene-driven NSCLCs when targeted therapies stop working.

Recent phase III clinical trials have shown a possible way around the ineffectiveness of immunotherapies for NSCLCs with an oncogenic driver – by combining immunotherapies ("PD-1 or PD-L1 inhibitors") with blood vessel-targeting agents ("VEGF inhibitors"). We hypothesize that this combination works because the endothelial cells that make up blood vessels can sometimes express immune checkpoint proteins (like PD-L1) when stimulated, which may then amplify the effectiveness of immunotherapies aimed at the PD-1/PD-L1 pathway. Our goal is to develop pathology assays to measure this phenomenon in archived NSCLC biopsy specimens. We will test whether the amount of immune checkpoint proteins expressed by endothelial cells correlate with the effectiveness of immunotherapies. This work might help us identify the patients most likely to respond to these novel combination strategies, when they become available in the clinic, while avoiding immunotherapy-related side effects like autoimmunity for patients unlikely to respond.

5. Budget

Purchasing IHC antibodies = $4,024

EC marker

- Anti-**ERG** [EPR3864] Mouse IgG2b, chimeric (ab214341) = CAD **$642** / 100uL

Immune checkpoint ligands (ICL):

- Anti-**PD-L1** [73-10] Rabbit IgG (ab228415) = CAD **$1,430** / 100uL
- Anti-**PD-L2** [EPR25200-50] Rabbit IgG (ab288298) = CAD **$882** / 100uL
- Anti-**PVR** (D3G7H) Rabbit IgG (CellSignaling #13544) = CAD **$440** / 100uL
- Anti-**Nectin-2** (D8D3F) Rabbit IgG (CellSignaling #95333) = CAD **$480** / 100uL

Shipping (2) = **$150**

IHC optimization = $2,585

- Single stains: ($40 per slide) x (6 slides per Ab) x (5 antibodies above) = **$1,200**
- 2-plex stains: ($100 per slide) x (3 slides per 2-plex) x (4 ERG x ICL pair) = **$1,200**
- Tissue sectioning: ($5 per slide) x (37 test slides) = **$185**

Aim 1 = $4,875

- Retrieval from archives: ($25 per FFPE block) x (15 FFPE blocks) = **$375**
- Tissue sectioning: ($5 per slide) x (4 slides per block) x (15 FFPE blocks) = **$300**
- 2-plex staining: ($70 per slide) x (60 slides) = **$4,200**

Aim 2 = $3,250

- Retrieval from archives: ($25 per FFPE block) x (10 FFPE blocks) = **$250**
- Tissue sectioning: ($5 per slide) x (4 slides per block) x (10 FFPE blocks) = **$200**
- 2-plex staining: ($70 per slide) x (40 slides) = **$2,800**

Aim 3 = $9,750

- Retrieval from archives: ($25 per FFPE block) x (30 FFPE blocks) = **$750**
- Tissue sectioning: ($5 per slide) x (4 slides per block) x (30 FFPE blocks) = **$600**
- 2-plex staining: ($70 per slide) x (120 slides) = **$8,400**

TOTAL ($24,484)

6. PI, co-PI, and co-Investigators

Principal Investigator: Cheryl Ho**,** MD, MSc, FRCP(C) CCV attached separately
Medical Oncologist, BC Cancer Vancouver
Clinical Associate Professor, Department of Medicine, UBC

Co-Investigator: Florence T.H. Wu, MD/PhD, FRCP(C)
PGY6, UBC Clinician Investigator Program, Vancouver, BC
Thoracic Medical Oncology Fellow, Princess Margaret - UHN, Toronto, ON

Co-Investigator: Julia Naso, MD/PhD, FRCP(C)
Anatomic Pathologist, Vancouver General Hospital
Clinical Assistant Professor, Department of Pathology and Laboratory Medicine, UBC

Co-Investigator: Spencer D. Martin, MD, PhD, FRCP(C)
PGY5, Anatomic Pathology, UBC

Co-Investigator: Anna L. McGuire, MD, MSc, FRCP(C)
Thoracic Surgeon, Clinician Scientist, Vancouver General Hospital & VGH Research Institute
Clinical Associate Professor, Department of Surgery, UBC

Co-Investigator: Janessa J. Laskin**,** MD, MSc, FRCP(C)
Medical Oncologist, BC Cancer Vancouver
Clinical Associate Professor, Department of Medicine, UBC

Co-Investigator: Marco A. Marra, PhD, FRS(C), FCAHS, O.B.C., O.C.
Distinguished Scientist, Canada's Michael Smith Genome Sciences Centre, BC Cancer Research Institute
UBC Killam Professor, Department of Medical Genetics
Tier 1 Canada Research Chair, Genome Science

Co-Investigator: Cathy Yan
PhD Student, Department of Medical Genetics, UBC
Canada's Michael Smith Genome Sciences Centre, BC Cancer Research Institute

Co-Investigator: Calum MacAulay, PhD
Distinguished Scientist & Head, Integrative Oncology, BC Cancer Research Centre
Clinical Associate Professor, Department of Pathology and Laboratory Medicine, UBC

Co-Investigator: Katey S.S. Enfield, PhD
Scientist, Integrative Oncology, BC Cancer Research Centre
Assistant Professor, Department of Pathology and Laboratory Medicine, UBC

Co-Investigator: Martial Guillaud, PhD
Senior Scientist, Integrative Oncology, BC Cancer Research Centre
Assistant Professor, Department of Pathology and Laboratory Medicine, UBC
Adjunct Professor, Department of Statistics, UBC

Co-Investigator: John English, MD, FRCP(C)
Anatomic Pathologist, Vancouver General Hospital & VGH Research Institute
Clinical Professor, Department of Pathology and Laboratory Medicine, UBC

Co-Investigator: Robert S. Kerbel, PhD
Senior Scientist, Biological Sciences, Odette Cancer Research Program, Sunnybrook Research Institute
Professor, Medical Biophysics, University of Toronto
Tier 1 Canada Research Chair (2001-2015), Tumor Biology, Angiogenesis & Antiangiogenic Therapy

7. Statement of support from applicant's institution

Dr. Stephen K. Chia, MD, FRCPC
Medical Oncologist, BC Cancer Vancouver
Professor of Medicine, University of British Columbia (UBC)
Head, Division of Medical Oncology, UBC
Co-chair, Breast Disease Site, Canadian Cancer Trials Group

Provincial Health Services Authority

Lung Cancer Canada
133 Richmond St. W., Suite 208
Toronto, ON M5H 2L3

January 28, 2025

Re: Lung Cancer Canada Give a Breath Research Grant

Dear Lung Cancer Canada,

As Department Head, Clinical Research, I am providing this letter of institutional support to confirm the feasibility of this outstanding research proposal put forward by Dr. Cheryl Ho as supervising Principal Investigator.

The proposed project is highly innovative and translational – with the potential to reshape the use of immune checkpoint inhibitors within thoracic oncology and beyond.

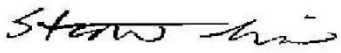
The team assembled here includes world-class senior scientists and oncologists crossing multiple disciplines with all the necessary expertise. There is no better team than the one proposed here to carry this project through.

Collectively, the team has laboratory infrastructure and personnel support from the BC Cancer Vancouver Centre (BCC-VC), the BC Cancer Research Institute (BCCRI), the Vancouver Coastal Health Research Institute (VCHRI), as well as the UBC Department of Pathology & Laboratory Medicine.

UBC and BC Cancer have efficient REB review and approval processes, and this team is well experienced with applying for and accessing archival clinical specimens as proposed. They have put together a sound budget based on cost estimates from our Molecular and Advanced Pathology Core Facility (MAPcore).

I hereby strongly recommend Dr. Ho and her team to be considered for the Lung Cancer Canada Give a Breath Research Grant, as we eagerly await the outcome of their planned studies.

Sincerely,



Dr. Stephen K. Chia, MD, FRCPC
Medical Oncologist, BC Cancer Vancouver
Head, Department of Clinical Research, BC Cancer
Professor of Medicine, University of British Columbia (UBC)
Head, Division of Medical Oncology, UBC
Co-chair, Breast Disease Site, Canadian Cancer Trials Group