Predicting sensitivity to Lantern Pharma’s pipeline drug candidate LP-184 using the Response Algorithm for Drug positioning and Rescue (RADR™)

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Abstract

LP-184 is a potent inhibitor of PTGSR1, a novel G protein-coupled receptor identified as a potential therapeutic target for the treatment of cancer. PTGSR1 drives tumor initiation, progression, proliferation, and chemoresistance in a variety of cancers, including prostate, lung, ovarian, breast, and colorectal cancers. By targeting PTGSR1, LP-184 has the potential to achieve clinical benefits in multiple tumor types, including prostate cancer, without the risk of resistance. Our aim is to improve the gaps in screening and treatment of cancer patients by developing predictive biomarker signatures that can predict response and lead to personalized treatment strategies.

Challenges

Despite recent developments in diagnostic and therapeutic strategies, patients with solid tumors, there are a number of critical knowledge gaps in relation to their screening and treatment.

- Insufficient knowledge of patient characteristics including genetic profiles for optimal stratification of patients into response groups at the time of diagnosis.
- Lack of understanding of the risk factors in developing or dying from cancer and lack of effective implementation of real-world evidence into clinical practice.
- Suboptimal predictive value of biomarkers in decision making around which patients have the best outcomes with specific treatments.

Our aim is to represent the gaps in screening and treatment of cancer patients by developing predictive biomarker signatures that can predict response and lead to personalized treatment strategies.

Objectives

- Develop generic feature selection methodologies that can be gene change in the development of Comparison Diagnostics (CDx) for oncological management.
- Derive a robust, validated and biologically meaningful gene signature to predict the potential for a patient to respond to a specific cancer treatment.
- Strатify patients prospectively using RADR™-derived genomic and biomarker analyses for greater success, and lower cost in clinical trials.

RADR™ Technology Overview

- Radrac™ Process Architecture
- Radrac™ Modules
- Radrac™ Technology Overview

Radrac™-derived analysis of LP-184-specific biomarkers

Figure 2. Radrac™ validation for LP-184 sensitivity in preclinical experiments.

RADR™ was used to analyze Lantern’s proprietary preclinical dataset on LP-184 sensitivity to and baseline gene expression profiles of 57 cell lines from the NCI 60 panel. Figure 2A highlights the comparison of LP-184 sensitivity prediction accuracy across a range of biomarker groups. Figure 2B shows the scatterplot of LP-184 sensitivity with gene expression profiles derived from 39 cell lines in NCI 60 dataset.

Figure 3. Relative importance of LP-184 signature genes

In this relative variable importance plot, gene significance analysis was performed using C成绩的 Blood Test (CPT) to derive the LP-184 signature in solid tumors. PTGSR1 (Prostaglandin F2α receptor 1) stands out as the gene with the highest relative importance.

LP-184 Overview

- Enhanced efficacy and potency with anticancer activity.
- Ablation of drug resistant cancer cells during therapy.
- Superior clinical activity with minimal toxicity.

Figure 4. Clinical mapping of PTGSR1 expression profile in a dataset of 150 patients with prostate cancer.

Analysis of Lantern Pharma’s asset LP-184 using the Radrac™ platform yielded a 10-genic pan-cancer signature of biomarkers associated with LP-184 sensitivity.

Reference


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Drug candidate

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<th>Potential cancer indications</th>
<th>RADR™ derived LP-184 sensitivity (Tumor biopsy samples)</th>
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Based on preclinical data analysis, RADR™ derived a 10-genic signature of candidate biomarkers predictive of response to LP-184.

- Genes from this set have been shown to be functionally involved in the postulated mechanism of action of LP-184.
- The goal is to determine the molecular profiles of patient tumors that predict drug responses and to derive a diagnostic assay for stratifying patients.
- Precision biomarker approach increases the likelihood that a treatment will be found to be effective in a relatively small phase II cohort by eliminating the most likely non-responders and selecting the most likely responders.

Figure 1. Process architecture and modules of RADR™

Figure 4. Effect of RADR™ on drug activity in preclinical studies.