**Part I: PROphet® Results**

**NEGATIVE**

The PROphet® Score is a clinically validated metric reflecting the patient’s likelihood of clinical benefit (defined as progression-free survival of at least 12 months) when treated with PD-1/PD-L1 inhibitors as a single agent or in combination with chemotherapy.

The PROphet® Score ranges between 0 (lowest clinical benefit probability) to 10 (highest clinical benefit probability) and when combined with the patient’s PD-L1 level, may be used to compare overall survival (OS) outcomes on different treatment modalities.

For further information and definitions, see Part V: Methods.

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**Part II: Treatment Considerations**

Treatment considerations are based on NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and on the PROPHETIC clinical trial (NCT04056247) – see Part III: Clinical Evidence.

### RESULTS

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<th>PD-L1 &gt;50%* and PROphet® NEGATIVE</th>
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This patient is not a good candidate for PD-1/PD-L1 inhibitors as a single agent.
Consider using PD-1/PD-L1 inhibitors in combination with chemotherapy, as recommended by NCCN Guidelines®.

| RESULTS |
| PD-L1 1-49%* and PROphet® NEGATIVE |
| TREATMENT CONSIDERATIONS |

This patient is expected to obtain low to moderate benefit from PD-1/PD-L1 inhibitors in combination with chemotherapy.
Consider other approved therapies, as recommended by NCCN Guidelines®.

| RESULTS |
| PD-L1 <1%* and PROphet® NEGATIVE |
| TREATMENT CONSIDERATIONS |

This patient is not a good candidate for PD-1/PD-L1 inhibitors with or without chemotherapy.
Consider other approved therapies, or a first-line clinical trial, as recommended by NCCN Guidelines®.

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*PD-L1 results are not provided by OncoHost.
Part III: Clinical Evidence

The PROphet® model was developed on blood samples and clinical data collected from a cohort of 500 patients treated with PD-1/PD-L1 inhibitors taking part in OncoHost’s ongoing, international, multicenter PROPHETIC clinical trial (NCT04056247). As a comparator for PD-L1 <1% and PD-L1 1-49%, PROphet® predictions were compared to a retrospective cohort of 85 patients treated with chemotherapy.

Based on the developed model, the overall survival (OS) of each sub-group was examined. See below:

**PD-L1 ≥50%**

**PROphet® NEGATIVE**

- Median overall survival (OS) for patients with PD-L1 ≥50% and a PROphet® NEGATIVE result was greater than 30.0 months on PD-1/PD-L1 inhibitors in combination with chemotherapy (n=38) vs. 11.1 months on PD-1/PD-L1 inhibitors as a single agent (n=67).

- HR = 0.23, CI: 0.10-0.51, p=0.003.

**PD-L1 1-49%**

**PROphet® NEGATIVE**

- Median overall survival (OS) for patients with PD-L1 1-49% and a PROphet® NEGATIVE result was 12.1 months on PD-1/PD-L1 inhibitors combined with chemotherapy (n=52) vs. 9.2 months on PD-1/PD-L1 inhibitors as a single agent (n=23), vs. 6.7 months on chemotherapy as a single agent (n=42).

- HR (ICI + chemotherapy: ICi = 0.61, CI: 0.35-1.04, p=0.069.
- HR (ICI + chemotherapy: Chemo = 0.51, CI: 0.32-0.81, p=0.004.

**PD-L1 <1%**

**PROphet® NEGATIVE**

- Median overall survival (OS) for patients with PD-L1 <1% and a PROphet® NEGATIVE result was 7.5 months on PD-1/PD-L1 inhibitors in combination with chemotherapy (n=53) vs. 6.7 months on chemotherapy as a single agent (n=42).

- HR = 0.66, CI: 0.42-1.04, p=0.073.

The survival analyses were performed separately for each PD-L1 classification group (≥50%, 1-49%, <1%) based on the NCCN Guidelines. National Comprehensive Cancer Network® (NCCN®) categories of evidence and categories of preference are denoted per treatment:

- For PD-L1 ≥50%, the compared treatments are PD-1/PD-L1 inhibitors as a single agent (Category 1, Preferred) and PD-1/PD-L1 inhibitors in combination with chemotherapy (Category 1, Preferred).
- For PD-L1 1-49%, the compared treatments are PD-1/PD-L1 inhibitors in combination with chemotherapy (Category 1, Preferred), PD-1/PD-L1 inhibitors as a single agent (Category 2B, Useful in Certain Circumstances) and chemotherapy as a single agent (Control arm).
- For PD-L1 <1%, the compared treatments are PD-1/PD-L1 inhibitors in combination with chemotherapy (Category 1, Preferred for Performance Status 0-1), and chemotherapy as a single agent (Category 2A, Preferred for Performance Status 2, Category 1, Useful in Certain Circumstances for Performance Status 0-1). Note that PD-1/PD-L1 inhibitors as a single agent are not recommended by the NCCN Guidelines for this population.

*Patients treated with chemotherapy were not stratified by PD-L1 expression level.

HR – Hazard Ratio | CI – Confidence Interval | OS – Overall Survival | ICI – Immune Checkpoint Inhibitor

Part IV: Available Treatment Options

Available treatment options, including approved therapies and clinical trials, can be found by scanning the QR code or accessing the OncoHost website link below:

**OR VISIT**

[https://www.oncohost.com/NSCLC/treatments](https://www.oncohost.com/NSCLC/treatments)
Part V: Methods

The PROphet® test was developed based on clinical, demographic, and proteomic data of 625 patients within the framework of an ongoing clinical study conducted by OncoHost (PROPHETIC, NCT04056247). Plasma was isolated from the blood and profiled via the SomaScan® Assay v4.1[3], and the resulting proteomic profiles were analyzed in conjunction with patient clinical data. The clinical benefit prediction algorithm was developed to identify patients who are more likely to benefit from PD-1/PD-L1 inhibitor treatment[4]. Patient clinical benefit probability is predicted and linearly transformed to a PROphet® Score between 0 to 10.

For more details regarding the methods used, you can access: https://www.oncohost.com/product-nscle - resources

About PROphet®

The PROphet® platform combines bioinformatics, system biology, proteomic pattern recognition and machine learning in a cancer patient’s blood plasma to predict clinical benefit (probability for at least 12 months progression-free survival) in response to PD-1/PD-L1 inhibitors - as a single agent or in combination with chemotherapy.

The PROphet® NSCLC Test is a novel and robust predictive computational model that uses SomaScan® Assay V4.1 to analyze and identify proteomic profiles in pre-treatment blood plasma to predict the probability of clinical benefit when treated with PD-1/PD-L1 inhibitors. The analytical validity of the PROphet® test is described in detail in Yellin et. al[3].

The PROphet® NSCLC Score is a clinically validated metric reflecting the patient’s likelihood of clinical benefit (defined as a progression-free survival of at least 12 months) and prolonged overall survival when treated with PD-1/PD-L1 inhibitors as a single agent or in combination with chemotherapy. The PROphet® Score ranges between 0 (lowest clinical benefit probability) to 10 (highest clinical benefit probability) and is based on identification of differentially expressed proteins using a novel and robust predictive computational model that analyzes proteomic patterns in pre-treatment plasma.

Intellectual Property

PROphet® is protected by trademarks and patent applications.

Intended Use

The PROphet® NSCLC Test is intended for use as a treatment decision tool in the management of newly diagnosed stage IV non-small cell lung cancer (NSCLC) patients being considered for treatment with PD-1/PD-L1 inhibitors as a single agent or in combination with chemotherapy in the first-line setting. The test is intended for patients aged 18 and above, with ECOG performance status of 0-2, normal hematologic, renal, and liver functions. The test is not intended for patients with any concurrent and/or other active malignancies that have required systemic treatment within two years of the first dose of therapy.

OncoHost Disclaimer

All content herein related to the PROphet® result, PROphet® Score, treatment options and clinical evidence is provided for informational purposes only. The patient’s physician is responsible for considering all available information and options before making patients-specific management or treatment decisions. OncoHost is not liable for medical judgment regarding diagnosis, prognosis, or treatment. PROphet® Test results and information contained within this report are current as of the date provided and will not be updated by OncoHost, even if subsequent changes would have led to additional or conflicting results. PROphet® uses an internal data set with data gathered from various sources. The analyses may be subjected to certain biases that restrict the generalizability or applicability to individual patients. The data that comprise the PROphet® dataset may not represent patient populations as a whole, nor be relevant to this specific patient. Testing is performed by OncoHost’s CLIA-certified and COLA-accredited laboratory located in the USA. The test was developed, and its performance characteristics were determined by OncoHost Ltd. The test has not been cleared or approved by the FDA.

References