# Phase 2 Study of Pembrolizumab (pemb) Plus Plinabulin (plin) and Docetaxel (doc) for Patients (pts) with Metastatic NSCLC after Failure on First-line Immune Checkpoint Inhibitor Alone or Combination Therapy: Updated Efficacy and Safety Results on Immune Re-sensitization

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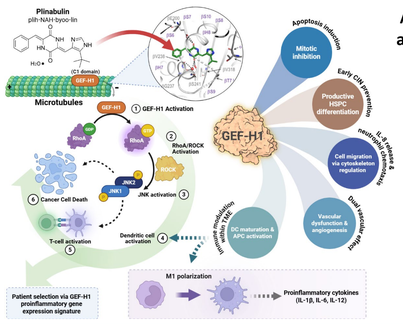
## Background

- Immune checkpoint inhibitors (ICI) ± chemotherapy has become first-line treatment for advanced/ metastatic non-small cell lung cancer (a/mNSCLC). Once progressed, patients (pts) with EGFR wild-type a/mNSCLC are frequently treated with docetaxel as a key second- or third-line therapy despite its limited efficacy and high incidence of severe neutropenia.[1-3]
- As a **differentiated fast-off tubulin binder**, plinabulin (Plin, BPI-2358) **activates GEF-H1, a C1 domain-associated highly spatio-temporally regulated RhoA activator**.[4-6] When administered after docetaxel (Doc), Plin has the potential to **overcome ICI resistance by strengthening the cancer-immunity cycle**.[7]
- This investigator-initiated phase 2 study (NCT05599789) was aimed to evaluate the efficacy and safety of Doc/Plin plus pembrolizumab (Pemb) in pts with a/mNSCLC who had progressed after ICI.




**As a GEF-H1 agonist, Plin has the following anti-cancer mechanism:**

a) Activates the RhoA/ROCK signaling that leads to **DC maturation/M1 polarization and T-cell activation**, which has been validated in preclinical/clinical studies.[8-10]

b) Promotes **HSPC proliferation** biasing towards the GMP lineage during GEF-H1-dependent productive hematopoiesis, contributing to **CIN prevention benefit**.[11-12]

c) **Modulates tumor vasculature**, likely due to GEF-H1's association with tight junction and pericyte phenotype switching.[13-14]

## Methods

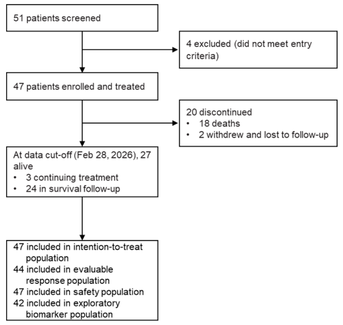
Between Feb 1, 2023 and Jan 21, 2025, 47 pts (30 non-squamous [NSQ], 17 squamous[SQ]) who had progressed on ICI (n=6) or ICI plus platinum doublets (n=41) were enrolled. All pts had secondary resistance (prior ICI ≥6months PFS). Participants received Pemb 200mg, Plin 30mg/m2, and Doc 75mg/m2 intravenously on Day 1 in 21-day cycles. The primary endpoint was investigator-based ORR per RECIST1.1. The secondary endpoints included PFS/OS/DoR and safety. For immunophenotyping, whole blood was collected prior to drug administration on Cycle1 Day0 (C1D0) and Cycle3 Day0 (C3D0) and subjected to a five-color flow cytometry analysis.

## Results/Graphs/Data

**Table 1.** Clinical characteristics

| Clinical Characteristics | Pemb + Plin + Doc (N=47); n (%) |
|---|---|
| Previously received anti-tumor immunotherapy | |
| Yes | 47(100) |
| Age | |
| Median age | 67 (44-83) |
| Gender | |
| Female | 9 (19.1) |
| Male | 38 (80.9) |
| Smoking status | |
| Non-Smoker | 13 (27.7) |
| Smoker | 34 (72.3) |
| Histology | |
| Squamous | 17 (36.2) |
| Non-squamous | 30 (63.8) |

**Figure 1.** Trial profile




**Plinabulin (BPI-2358) is a selective immunomodulating microtubule-binding agent which promotes dendritic cell maturation and enhances anti-tumor T cell response, and have the potential to overcome immunotherapy resistance and provide a more durable response.**

## Results/Graphs/Data

At the data cut off date of February 28, 2026, the median follow-up time was 28.8 months, and 3 patients were still undergoing treatment, and 24 patients remained alive in the survival follow-up period. Out of 47 enrolled patients, median age was 67 (44-83) with 80.9% male and 19.1% female. 72.3% were current or former smokers. Histology included 63.8% with non-squamous cell carcinoma, 36.2% with squamous cell carcinoma.

**Table 2.** Efficacy endpoints

| | |
|---|---|
| **Primary Endpoint** | |
| Confirmed ORR（RECIST 1.1) | 18.2% |
| **Secondary Endpoint** | |
| Median PFS（RECIST 1.1) | 7.0 months |
| Median OS | Not reached |
| Median DoR（RECIST 1.1) | 9.3 months |
| Disease Control Rate (DCR) (PR + SD > 4 months) | 79.5% |
| 6-month PFS rate | 56.2% |
| 12-month PFS rate | 78.1% |
| 6-month OS rate | 91.4% |
| 12-month OS rate | 78.1% |
| 24-month OS rate | 58.0% |

**Figure 2.** PFS (A) and OS (B) in ITT population

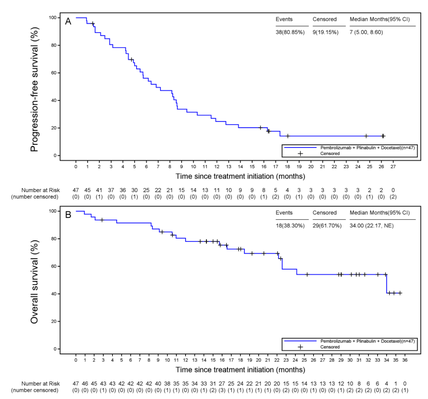



**Table 3.** Treatment-related adverse events (CTCAE ≥ Grade 3)

| Preferred Terms | Pemb + Plin + Doc (N=47); n (%) |
|---|---|
| **All TRAE, CTCAE >= grade 3** | **25 (53.2)** |
| **Vascular disorders** | **8 (17.0)** |
| Hypertension | 8 (17.0) |
| **Gastrointestinal disorders** | **7 (14.9)** |
| Diarrhea | 4 (8.5) |
| Ileus | 2 (4.3) |
| Abdominal distension | 1 (2.1) |
| **Blood system disorders** | **8 (17.0)** |
| Neutrophil decrease | 8 (17.0) |
| Decreased white blood cell count | 3 (6.4) |
| Febrile neutropenia | 1 (2.1) |
| **Infections and infestations** | **2 (4.3)** |
| pneumonia | 1 (2.1) |
| Sepsis | 1 (2.1) |

| Preferred Terms | Pemb + Plin + Doc (N=47); n (%) |
|---|---|
| **All TRAE, CTCAE >= grade 3** | **25 (53.2)** |
| **Respiratory,thoracic and mediastinal disorders** | **2 (4.3)** |
| Respiratory Failure | 2 (4.3) |
| **Metabolism disorders** | **1 (2.1)** |
| Acidosis （Related to diabetes） | 1 (2.1) |
| Elevated blood glucose | 1 (2.1) |
| **Renal and urinary disorders** | **1 (2.1)** |
| Acute kidney injury | 1 (2.1) |
| **Cardiac disorders** | **1 (2.1)** |
| Atrial fibrillation | 1 (2.1) |

## Results/Graphs/Data

**Figure 3.** Swimmers Plot summarizing patient outcomes during the study (ITT population)

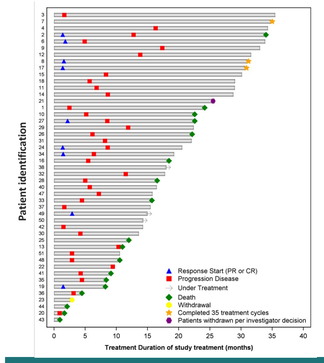



**Figure 4** Target legion best response in the evaluable response population

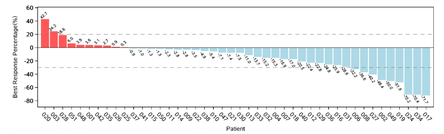
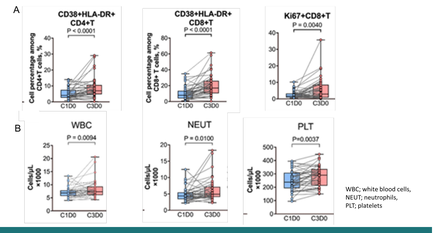



**Figure 5.** Phenotyping (A) and standard hematology (B)




## Future Directions for Research

Plinabulin/docetaxel/pembrolizumab triplet in metastatic NSCLC with secondary resistance to ICI continues to show clinically efficacy with manageable side effects. The activity outcome surpassed the historical data of docetaxel in similar patient populations (TROPION-Lung01 or EVOKE-01: mPFS 3.7 or 3.9 months, mOS 11.8 or 9.8 months, respectively). In addition to increased frequencies of activated CD4+/CD8+T-cells post-treatment, hematology test showed significantly higher levels of WBCs, neutrophils and platelets. A future randomized control trial is warranted in post-ICI settings.

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**References**

1. Leal and Socinski. *Expert Rev Anticancer Ther*. 2023; **23**(8):817–33.
2. Memon D, et al. *Cancer Cell*. 2024; **42**(2):209–24 e9.
3. Hendriks LEL, et al. *Annals of Oncology*. 2025; **36**(10):1223–7.
4. La Sala G, et al. *Chem*. 2019; **5**:1–18.
5. Kashyap AS, et al. *Cell Rep*. 2019; **28**(13):3367–80 e8.
6. Choi SR, et al. *Cell*. 2026; **189**(2):461–77.e16.
7. Mellman I, et al. *Immunity*. 2023; **56**(10):2188–205.
8. Lin SH, et al. *Med*. 2025; **6**(10):100752.
9. Lin SH et al. *J. ImmunoTher. Cancer*. 2025; **13**(Suppl 2):A766.
10. Xu Y, et al., *J. ImmunoTher. Cancer*. 2025; **13**(Suppl 3):A1571.
11. Tonra JR, et al., *Cancer Chemother. Pharmacol*. 2020; **85**(2):461-468.
12. Blayney D, et al. *JAMA Network*. 2022; **5**(1):e2145446.
13. Mita MM, et al., *Clin. Cancer Res*. 2010; **16**(23):5892-9.
14. He B, et al. *EMBO Mol Med*. 2025; **17**(5):1071-1100.