

Phase 2 study of pembrolizumab (Pemb) plus plinabulin (Plin) and docetaxel (Doc) for patients with metastatic NSCLC after failure on first-line immune checkpoint inhibitor alone or combination therapy: updated efficacy and safety results on immune re-sensitization

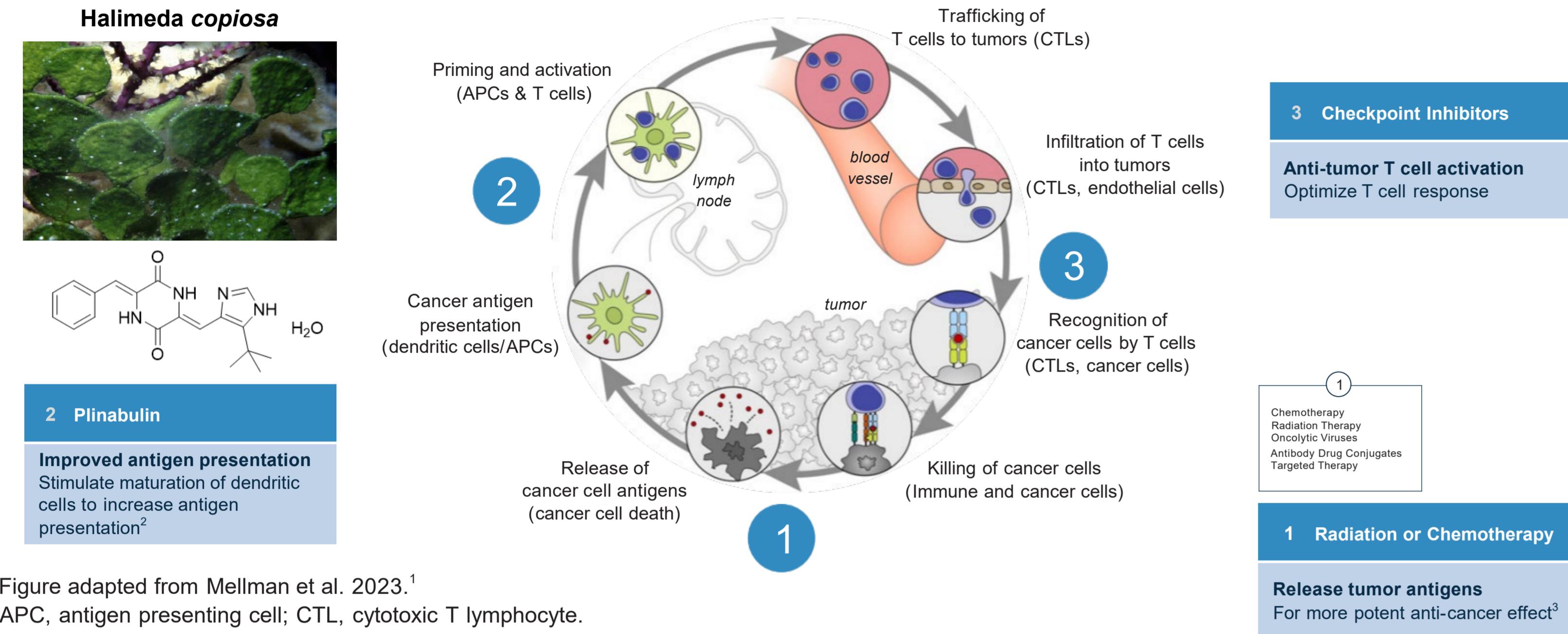
Yan Xu¹, Xiaoxing Gao¹, Minjiang Chen¹, Xiaoyan Liu¹, Wei Zhong¹, Jing Zhao¹, RuiLi Pan¹, Mengzhao Wang¹

Department of Respiratory and Critical Care Medicine, Peking Union Medical College Hospital, Peking Union Medical College & Chinese Academy of Medical Science, Beijing, China

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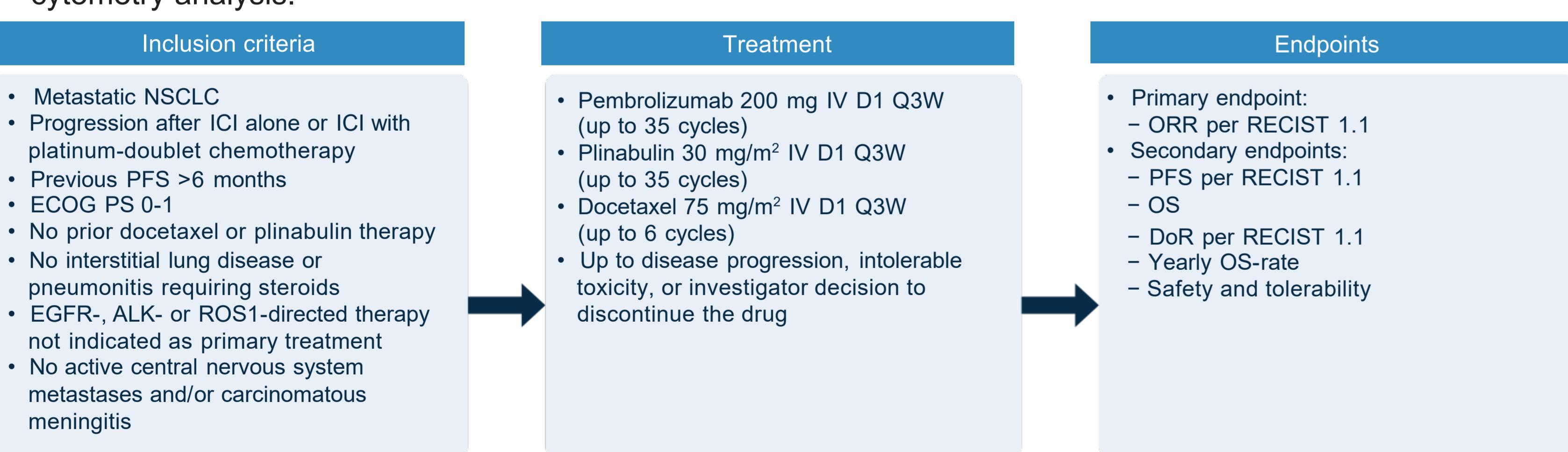
Background and Aim



- Immune checkpoint inhibitor (ICI)-based regimens have become the standard of care for first-line treatment of NSCLC. Once progressed, it is not recommended to continue using ICI monotherapy, and the effect of chemotherapy is limited (ORR ~10% with doc), so there is a high unmet need. [2]
- 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.^[3-5]
- This phase 2 study was aimed to evaluate the efficacy and safety of pemb plus plin and doc in pts with metastatic NSCLC who had progressed after ICI.

Methods and Materials

- This single-arm phase 2 303 study (NCT05599789) enrolled 47 pts (30 non-squamous [NSQ], 17 squamous [SQ]) who had progressed on ICI (n=6) or in combination with platinum doublets (n=41). Only patients with secondary resistance (prior ICI ≥6 months PFS) were enrolled.
- Participants received Pembro 200 mg, Plin 30 mg/m², and Doc 75 mg/m² intravenously on Day 1 in 21-day cycles.
- The primary endpoint was investigator-based ORR per RECIST 1.1. The secondary endpoints included PFS/OS/DoR and safety. For phenotyping of peripheral blood T-lymphocytes, whole blood was collected prior to drug administration on Cycle 1 Day 0 (C1D0) and Cycle 3 Day 0 (C3D0) and subjected to a five-color flow cytometry analysis.



ALK, anaplastic lymphoma kinase; D, day; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EGFR, epidermal growth factor receptor; ICI, immune checkpoint inhibitor; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumours; ROS1, proto-oncogene tyrosine-protein kinase.

Contact

Yan XU, E-mail: maraxu@163.com
Mengzhao WANG, E-mail: mengzhawang@sina.com

Disclosures

The presenting author has no relevant disclosures.

Results

- Median follow-up was 16.9 months at the data cut-off date of Sep 31, 2025. 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. Please refer to Tables 1-3 and Figure 1.
- In 42 patients who completed blood sampling on C1D0 and C3D0 (Figure 2), the proportions of CD4+ and CD8+ T cells remained stable ($p>0.05$) while Ki67+CD8+ T cells were significantly increased ($p=0.004$). The frequencies of CD38+HLA-DR+CD4+T cells and CD38+HLA-DR+CD8+T cells were dramatically elevated ($p<0.0001$).

Table 1. Clinical characteristics

Clinical Characteristics	Pemb + Plin + Doc (N=47); n (%)
Previously received anti-tumour immunotherapy	47 (100)
Age	
Median age, years	67.0 (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)

Table 2. Efficacy endpoints

Endpoint	ITT (N=47)	Non-Squamous (N=30)	Squamous (N=17)
Primary endpoint			
Confirmed ORR (RECIST 1.1)	18.2%	13.8%	33.3%
Secondary endpoints			
Median PFS (RECIST 1.1)	7.0 months	7.0 months	7.0 months
Median OS	Not reached	NE	NE
Median DoR (RECIST 1.1)	7.2 months	NE	6.8 months
Disease Control Rate (DCR)	85.1%	86.7%	82.4%
6 month PFS rate	56.2%	60.0%	50.0%
12 month PFS rate	23.8%	25.1%	15.6%
6 months OS rate	91.4%	90.0%	94.1%
12 months OS rate	79.3%	82.9%	72.8%
24 months OS rate	65.9%	73.7%	55.5%

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

PT	Pemb + Plin + Doc (N=47) n (%)	PT	Pemb + Plin + Doc (N=47) n (%)
All TRAE, CTCAE ≥ grade 3	25 (53.2)	All TRAE, CTCAE ≥ grade 3	25 (53.2)
Neutrophil decrease	8 (17.0)	Elevated blood glucose	1 (2.1)
Hypertension	8 (17.0)	Febrile neutropenia	1 (2.1)
Diarrhea	4 (8.5)	Infectious pneumonia	1 (2.1)
Decreased white blood cell count	3 (6.4)	Sepsis	1 (2.1)
Ileus	2 (4.3)	Acidosis	1 (2.1)
Respiratory Failure	2 (4.3)	Acute kidney injury	1 (2.1)
Abdominal distension	1 (2.1)	Atrial fibrillation	1 (2.1)

CTCAE, Common Terminology Criteria for Adverse Events; TRAE, Treatment-Related Adverse Event.

Results

Figure 1. Waterfall plot of PFS and best response (%) (Response Evaluable Population)

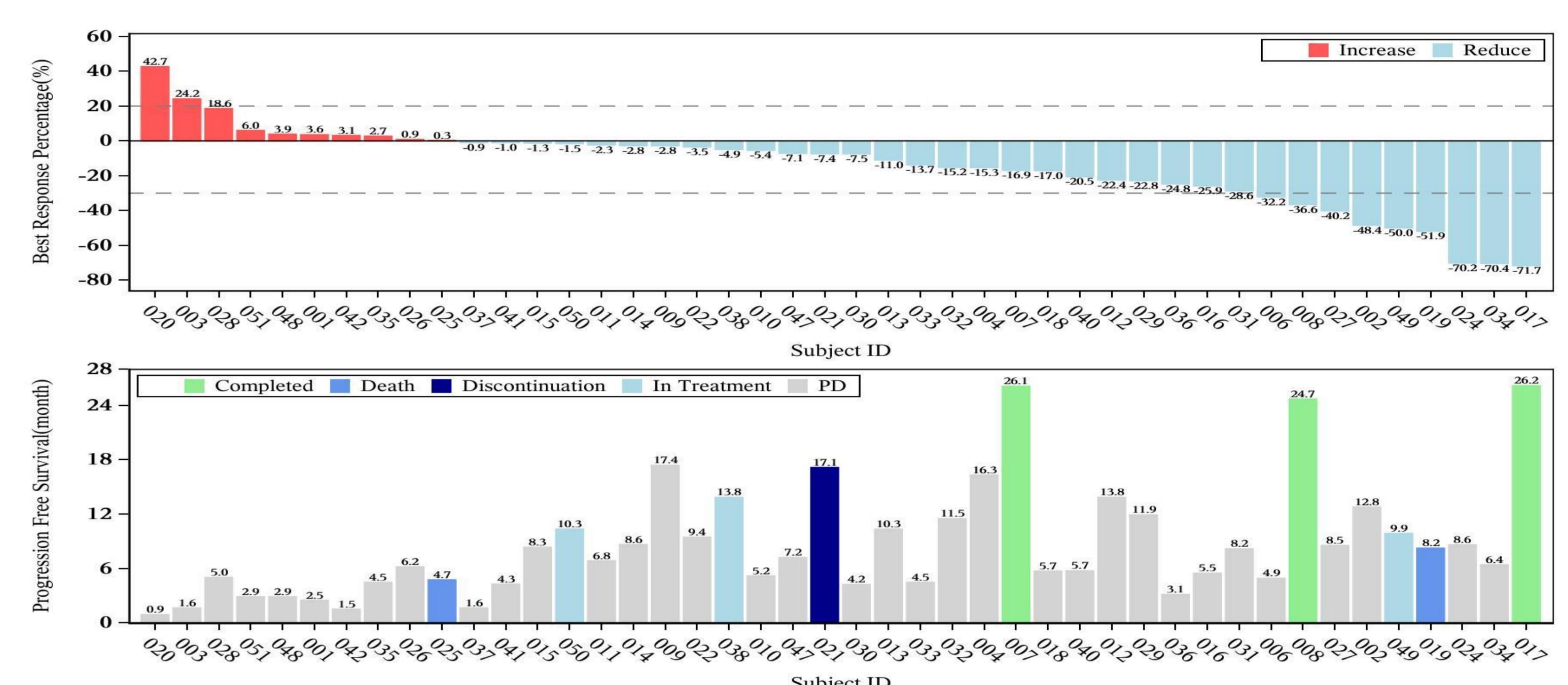
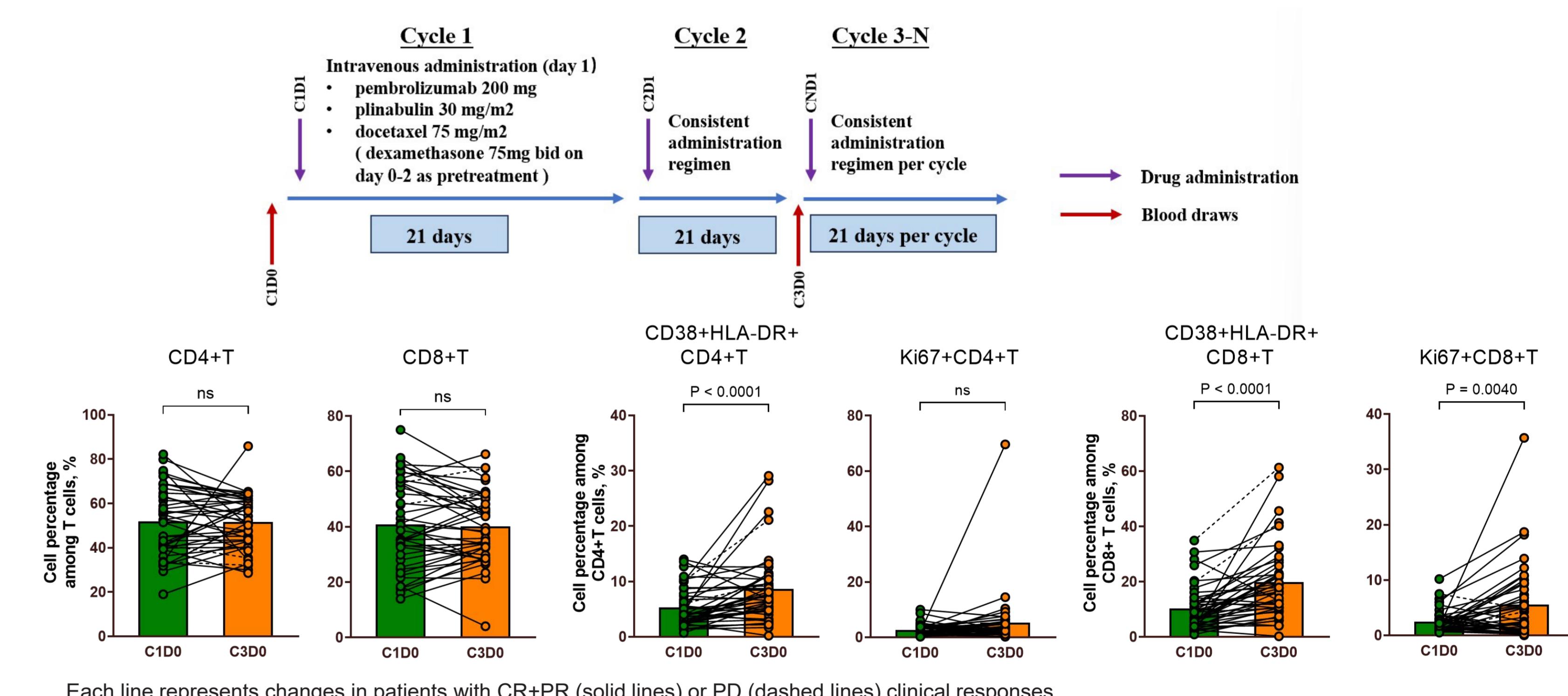


Figure 2. Immunophenotyping of peripheral blood T-lymphocytes



Conclusions

Plinabulin/docetaxel/pembrolizumab triplet in metastatic NSCLC with secondary resistance to ICI shows clinically meaningful efficacy with manageable side effects. Compared to historical data of SOC docetaxel in similar population (TROPION-Lung01: ~10% ORR and mPFS 3.7 months [6]), this combination almost doubled ORR and PFS. Whole blood analysis indicated higher proportions of activated CD4+/CD8+ T-cells post treatment.

Use the QR code to find more information about the KeyPemls-004 study protocol



Contact

Yan XU, E-mail: maraxu@163.com
Mengzhao WANG, E-mail: mengzhawang@sina.com

Disclosures

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