SHR-1316 vs placebo in combination with chemotherapy as perioperative treatment in patients with resectable stage II-III NSCLC: a randomized, double-blind, multicenter, phase 1b/3 trial

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Background

Background

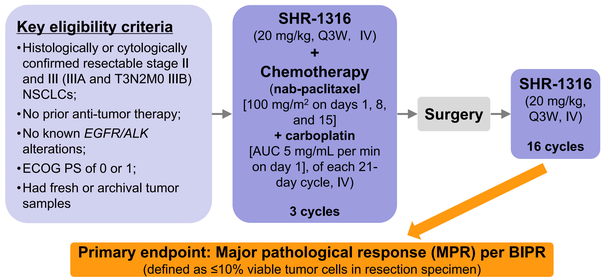
- The survival benefit of standard perioperative chemotherapy compared with surgery alone is modest in patients with resectable NSCLC.[1]
- Neoadjuvant immunotherapy is attractive because it can induce the dying tumor cells to release tumor-specific antigens and further stimulate the priming and expansion of tumor-specific T cells in tumors before surgical resection.[2]
- Immune checkpoint inhibitors in combination with chemotherapy have shown robust efficacy in metastatic NSCLC.[3, 4]
- SHR-1316 is a humanized IgG4 monoclonal PD-L1 antibody which has shown promising antitumor activity in solid tumors.[5]
- This phase 1b/3 trial evaluates the efficacy and safety of SHR-1316 plus chemotherapy vs placebo plus chemotherapy as perioperative treatment for resectable NSCLC.
- Here, we reported the results from the phase 1b part.

Methods

Patients and study design

- This is a randomized, multicenter, phase 1b/3 trial conducted in China (ClinicalTrials.gov NCT04316364; **Figure 1**).
- Eligible patients were resectable stage II and III (IIIA and T3N2M0 IIIB) NSCLCs without *EGFR/ALK* alterations.

Figure 1. Study design (Phase 1b part)



Results

Patients disposition and baseline characteristics

- From Jul 14, 2020 to May 12, 2021, 37 eligible patients were enrolled and received SHR-1316 plus chemotherapy neoadjuvant treatment (**Figure 2**).
- Baseline characteristics are presented in **Table 1**.
- 34 patients underwent surgery (**Table 2**).

Results

Table 1. Baseline characteristics

Characteristics	Total (n=37)	Characteristics	Total (n=37)
Age (years)		**Histology**	
Median (range)	63 (37-69)	Adenocarcinoma	5 (13.5)
Gender		Squamous	31 (83.8)
Male	35 (94.6)	Adeno-squamous	1 (2.7)
Female	2 (5.4)	**TNM stage: T**	
Smoking		T1c	2 (5.4)
Never	3 (8.1)	T2a	8 (21.6)
Former	32 (86.5)	T2b	6 (16.2)
Current	2 (5.4)	T3	12 (32.4)
ECOG PS		T4	9 (24.3)
0	18 (48.6)	**TNM stage: N**	
1	19 (51.4)	N0	8 (21.6)
PD-L1 TPS		N1	18 (48.6)
<1%	9 (24.3)	N2	11 (29.7)
≥1%	26 (70.3)	**Clinical disease stage**	
1%-50%	16 (43.2)	II	11 (29.7)
≥50%	10 (27.0)	IIIA	22 (59.5)
Unmeasurable	2 (5.4)	IIIB	4 (10.8)

Data are n (%) unless otherwise specified.

Figure 2. Trial profile

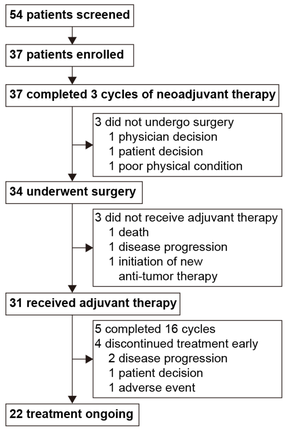


Table 2. Surgical outcomes

	Total (n=34)
Type of surgery	
Minimally invasive	21 (61.8)
Thoracotomy	9 (26.5)
Convert from minimally invasive to thoracotomy	4 (11.8)
Surgical resection	
Lobectomy	22 (64.7)
Bilobectomy	10 (29.4)
Pneumonectomy	2 (5.9)
R0 resection	32 (94.1)
Surgery delay*	4 (11.8)
Patient decision	2 (5.9)
Adverse event	1 (2.9)
COVID-19 pandemic	1 (2.9)
Duration from last dose to surgery, median (IQR), wks	5.1 (3.6-5.6)

Data are n (%) unless otherwise specified.
* >6 weeks after neoadjuvant therapy.

Results

Anti-tumor activity

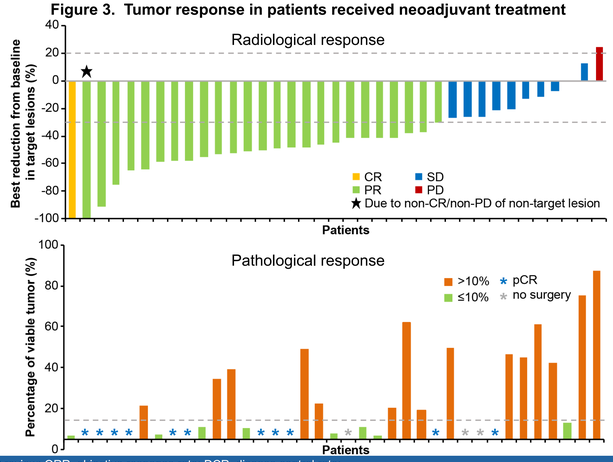
- As of data cutoff on Nov 26, 2021, among the 34 patients underwent surgery, 19 (55.9%, 95% CI 39.5-71.1) patients achieved MPR per BIPR; 11 (32.4%, 95% CI 19.1-49.2) patients achieved pathologic complete response (pCR).
- Subgroup analyses of MPR in patients received neoadjuvant treatment are listed in **Table 3**.
- Among the 37 patients received neoadjuvant treatment, ORR per RECIST v1.1 was 70.3% (95% CI 54.2-82.5; 26/37) and DCR was 97.3% (36/37) (**Figure 3**).
- Among 34 patients underwent surgery, 19 (73.1%) of 26 patients with positive lymph node at baseline had nodal downstaging after neoadjuvant treatment.

Table 3. Subgroup analyses of MPR in patients received neoadjuvant treatment

Subgroups	N	MPR	Subgroups	N	MPR
Smoking			**PD-L1 TPS**		
Former/Current	34	18 (52.9)	<1%*	11	4 (36.4)
Never	3	1 (33.3)	≥1%	26	15 (57.7)
Histology			1%-50%	16	8 (50.0)
Adenocarcinoma	5	2 (40.0)	≥50%	10	7 (70.0)
Squamous	31	16 (51.6)	**Objective response**		
Adeno-squamous	1	1 (100)	CR/PR	26	17 (65.4)
Clinical disease stage			SD/PD	11	2 (18.2)
II	11	6 (54.5)			
III	26	13 (50.0)			

Data are n (%). *Patients with unmeasurable PD-L1 expression were classified as <1%.

Figure 3. Tumor response in patients received neoadjuvant treatment

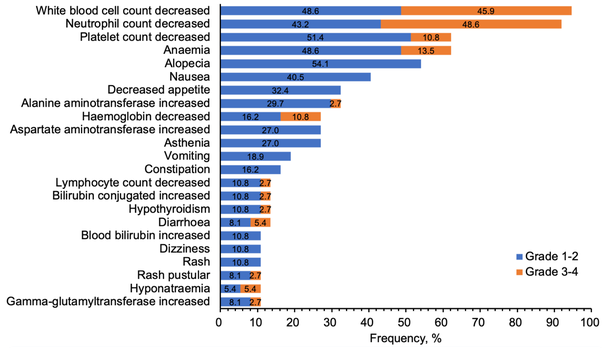


Results

Safety

- Treatment-related adverse events (AEs) were reported in all the 37 (100%) patients (**Figure 4**).
- 29 (78.4%) patients had grade ≥3 treatment-related AEs.
- No treatment-related deaths occurred.
- Among the 34 patients underwent surgery, 27 (79.4%) or 28 (82.4%) had surgery-related adverse events within 30 or 90 days after surgery; the most common of which was incision site pain (41.2%, 14/34).
- Grade ≥3 surgery-related AEs within 30 or 90 days after surgery were both reported in 6 (17.6%) patients.

Figure 4. Treatment-related AEs



Conclusion

- SHR-1316 in combination with nab-paclitaxel and carboplatin as neoadjuvant therapy showed promising anti-tumor activities in resectable NSCLC.
  - ORR 70.3% (26/37), DCR 97.3% (36/37)
  - MPR 55.9% (19/34), pCR 32.4% (11/34)
  - 73.1% (19/26) of patients had nodal downstaging
- The safety profile was well tolerated.
  - All 37 patients completed neoadjuvant treatment
  - No obvious surgery delay (median duration from last dose to surgery: 5.1 wks [IQR 3.6-5.6])
  - 61.8% (21/34) of patients underwent minimally invasive
  - No new safety signal were identified
- Based on the phase 1b results, the phase 3 trial was initiated and ongoing.

Conflicts of Interest

- Yi-Long Wu reports honoraria from AstraZeneca, Lilly, Roche, Pfizer, BI, MSD, BMS, and Hengrui, consulting or advisory fees from AstraZeneca, Roche, BI, Takeda, and research fundings from BI, Roche, Pfizer, and BMS.

Acknowledgements

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Abbreviations: BIPR, blinded independent pathologist review; ORR, objective response rate; DCR, disease control rate; CR, complete response; PR, partial response; SD, stable disease; PD, progression disease.

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