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ABOUND.2L+: *nab*-paclitaxel (*nab*-P) +/- CC-486 or durvalumab in previously treated patients with advanced non-small cell lung cancer (NSCLC)

Background: Therapy selection for previously treated patients with advanced NSCLC is complex. ABOUND.2L+ evaluated safety and efficacy of *nab*-P monotherapy, *nab*-P + the epigenetic modifying agent, CC-486, or *nab*-P + the PD-L1 inhibitor, durvalumab.

Methods: Patients with advanced nonsquamous NSCLC and ≤ 1 prior chemotherapy were randomized to *nab*-P 100 mg/m² on days 8, 15 + CC-486 200 mg QD on days 1-14 or *nab*-P alone 100 mg/m² on days 1, 8, both administered q3w. The protocol was amended to include a *nab*-P + durvalumab arm (*nab*-P 100 mg/m² on days 1, 8 + durvalumab 1125 mg on day 15, q3w) which began enrolling after the other arms had completed enrollment, allowing patients with squamous histology or prior immunotherapy treatment. For all patients, treatment continued until unacceptable toxicity or tumor progression.

Results: A total of 240 patients were enrolled. For the *nab*-P + CC-486 and *nab*-P arms, the median number of cycles was 4 and median cumulative dose of *nab*-P was 600 and 800 mg/m², respectively. Grade 3 or 4 (G3/4) treatment-emergent adverse events (AEs) were 59.5% and 54.4%, respectively. The most frequent hematologic G3/4 AEs were neutropenia (16.5% vs 10.1%) and anemia (1.3% vs 7.6%). G3/4 peripheral neuropathy occurred in 2.5% vs 7.6% of patients (*nab*-P + CC-486 vs *nab*-P). Adding CC-486 to *nab*-P did not result in improvements in PFS, OS, ORR, or DCR (Table). Preliminary data for 79 patients in the *nab*-P + durvalumab arm showed a median PFS of 4.4 months, median OS not estimable, a 20% ORR, and a 71% DCR. No new safety signals were identified.

Conclusions: Single agent *nab*-P is promising in previously treated nonsquamous NSCLC; addition of CC-486 did not appear to benefit patients clinically. Updated data for the ongoing durvalumab combination arm of the study will be presented. NCT02250326

	<i>nab</i> -P + CC-486 n = 81	<i>nab</i> -P n = 80
Efficacy		
Primary endpoint		
Median PFS, months	3.2	4.2
HR (95% CI)	1.3 (0.9 - 2.0)	
Secondary endpoints		
Median OS, months	8.4	12.7
HR (95% CI)	1.4 (0.88 - 2.31)	
ORR, n (%) ^a	11 (13.6)	11 (13.8)
Response rate ratio (95% CI)	0.99 (0.45 - 2.15)	
Complete Response	0	0
Partial Response	11 (13.6)	11 (13.8)
Stable Disease	41 (50.6)	43 (53.8)
Progressive Disease	22 (27.2)	19 (23.8)
DCR (≥ SD)	52 (64.2)	54 (67.5)

DCR, disease control rate; HR, hazard ratio; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; ^a Response rate was based on the intent-to-treat population; however, 14 patients did not have a response assessment.