HUDSON: Open-Label, Multidrug Umbrella Phase II Study in Patients With Advanced NSCLC After Progression on PD-1/PD-L1 Inhibitor Therapy

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HUDSON: Background

- Several mechanisms contribute to resistance to PD-1 and PD-L1 targeted therapy in NSCLC[1,2]
- No current standard of care for patients whose disease has progressed despite treatment with platinum-doublet chemotherapy and immune checkpoint inhibition[3]
- HUDSON is ongoing, modular phase II trial evaluating several treatment options for patients with biomarker matched or nonmatched locally advanced/metastatic NSCLC after receipt of a platinum doublet and failure of anti–PD-1/PD-L1 immunotherapy[4,5]
- Current analysis reports results from cohorts of durvalumab in combination with either ceralasertib (ATR inhibitor), danvatirsen (STAT3 inhibitor), olaparib (PARP inhibitor), or oleclumab (anti-CD73 mAb)[5]

HUDSON: Study Design

Locally advanced or metastatic NSCLC; previous platinum-doublet chemotherapy and PD-1/PD-L1 targeted therapy; no *EGFR, ALK, ROS1, BRAF, MET,* or *RET* targetable mutations (N = 225)

Group A: Biomarker Matched (n = 86)

- HRRm: durvalumab + olaparib (n = 21)
- LKB1: durvalumab + olaparib (n = 21)
- ATM: durvalumab + ceralasertib* (n = 21)
- ATM: ceralasertib*
- CD73h: durvalumab + oleclumab (n = 23)
- HER2e/m: durvalumab + trastuzumab deruxtecan†

Group B: Biomarker Nonmatched (n = 169)

Primary Resistance (PD‡ ≤24 Wk)

- Durvalumab + olaparib (n = 22)
- Durvalumab + danvatirsen (n = 23)
- Durvalumab + ceralasertib (n = 20)
- Durvalumab + oleclumab (n = 9)

Acquired Resistance (PD‡ >24 Wk)

- Durvalumab + olaparib (n = 23)
- Durvalumab + danvatirsen (n = 22)
- Durvalumab + ceralasertib (n = 25)
- Durvalumab + oleclumab (n = 25)
- Durvalumab + cediranib†

*Ongoing †data not yet mature.
‡PD on anti-PD-1/PD-L1 immunotherapy.

- Multidrug, nonrandomized umbrella phase II study (data cutoff April 14, 2021)
- **Primary endpoint:** ORR
- **Secondary endpoints:** DCR, PFS, OS, safety

Besse. WCLC 2022. Abstr OA15.05.

HUDSON: Baseline Characteristics by Tx (Groups A + B)

Characteristic	D + Ceralasertib (n = 66)	D + Olaparib (n = 87)	D + Danvatirsen (n = 45)	D + Oleclumab (n = 57)
Median age, yr (range)	64.0 (45-80)	63.0 (35-85)	65.0 (39-80)	64.0 (37-79)
Male, n (%)	43 (65.2)	50 (57.5)	23 (51.1)	30 (52.6)
Current/former smoker, n (%)	58 (87.9)	69 (79.3)	40 (88.9)	52 (91.2)
Histology, n (%)				
▪ Adenocarcinoma	44 (66.7)	62 (71.3)	31 (68.9)	38 (66.7)
▪ Squamous	17 (25.8)	18 (20.7)	12 (26.7)	13 (22.8)
▪ Other	5 (7.5)	7 (8.0)	2 (4.4)	6 (10.5)
Sites of metastases, n (%)				
▪ 0	2 (3.0)	1 (1.1)	2 (4.4)	3 (5.3)
▪ 1-2	28 (42.4)	40 (46.0)	37 (82.2)	31 (54.4)
▪ ≥3	36 (54.5)	46 (52.9)	6 (13.3)	23 (40.4)
PD-L1 status, n (%)				
▪ Positive (TC ≥1%)	26 (39.4)	22 (25.3)	21 (46.7)	31 (54.4)
▪ Negative	22 (33.3)	27 (31.0)	11 (24.4)	13 (22.8)
▪ Unknown	18 (27.3)	38 (43.7)	13 (28.9)	13 (22.8)
Prior tx regimens, n (%)				
▪ 1-2	33 (50.0)	51 (58.6)	25 (55.6)	32 (56.1)
▪ ≥3	33 (50.0)	36 (41.4)	20 (44.4)	25 (43.9)

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HUDSON: Efficacy by Treatment (Groups A + B)

Efficacy Parameter	Durvalumab + Ceralasertib (n = 66)	Durvalumab + Olaparib (n = 87)	Durvalumab + Danvatirsen (n = 45)	Durvalumab + Oleclumab (n = 57)
ORR (primary endpoint), %	16.7	4.6	0	1.8
Median tx duration, mo				
▪ Durvalumab	7.3	3.7	2.8	2.9
▪ Other tx agent	6.3	3.2	2.8	2.9
12-wk disease control rate, %	60.6	36.8	26.7	29.8
24-wk disease control rate, %	42.4	17.2	13.3	15.8

- Due to low activity (ORR <5%) seen in durvalumab + olaparib, durvalumab + danvatirsen, and durvalumab + oleclumab groups, these 3 regimens were pooled as an internal control

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HUDSON: PFS by Treatment (Groups A + B)

PFS Parameter	Durvalumab + Ceralasertib (n = 66)	Other Regimens* (n = 189)	Durvalumab + Olaparib (n = 87)	Durvalumab + Danvatirsen (n = 45)	Durvalumab + Oleclumab (n = 57)
Median PFS, mo (80% CI)	6.0 (4.6-7.5)	2.7 (1.8-2.8)	2.7 (1.6-3.0)	2.9 (1.7-3.1)	1.8 (1.6-2.7)
6-mo PFS, % (80% CI)	46.3 (37.9-54.2)	18.0 (14.5-21.9)	18.7 (13.5-24.5)	18.8 (11.5-27.6)	16.6 (10.8-23.6)

*Pooled internal control of durvalumab + olaparib, durvalumab + danvatirsen, and durvalumab + oleclumab.

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HUDSON: OS by Treatment (Groups A + B)

OS Parameter	Durvalumab + Ceralasertib (n = 66)	Other Regimens* (n = 189)	Durvalumab + Olaparib (n = 87)	Durvalumab + Danvatirsen (n = 45)	Durvalumab + Oleclumab (n = 57)
Median OS, mo (80% CI)	15.9 (14.1-20.3)	9.4 (7.5-10.6)	9.4 (6.9-10.8)	7.9 (6.0-10.6)	11.0 (7.6-13.5)
12-mo OS, % (80% CI)	61.6 (53.4-68.8)	39.7 (35.1-44.3)	40.8 (34.0-47.5)	28.8 (20.2-38.0)	46.2 (37.5-54.5)

*Pooled internal control of durvalumab + olaparib, durvalumab + danvatirsen, and durvalumab + oleclumab.

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HUDSON: Efficacy by Cohort (Durvalumab + Ceralasertib)

Efficacy Parameter	Biomarker Matched (ATM) (n = 21)	Biomarker Nonmatched	
		Primary Resistance (n = 20)	Acquired Resistance (n = 25)
ORR, % ▪ PR	28.6 28.6	15.0 15.0	8.0 8.0
SD ≥40 days, % ▪ Unconfirmed PR	47.6 9.5	45.0 0	64.0 0
Progression, % ▪ RECIST disease progression ▪ Death	19.0 19.0 0	35.0 30.0 5.0	24.0 16.0 8.0
12-wk disease control rate, %	71.4	55.0	56.0
24-wk disease control rate, %	57.1	40.0	32.0
Median PFS, mo (80% CI) ▪ 6-mo PFS, %	8.4 (6.0-9.7) 64.3	4.9 (1.9-6.8) 41.5	4.6 (3.6-6.0) 35.2
Median OS, mo (80% CI) ▪ 12-mo PFS, %	22.8* (12.6-29.9) 70.2	11.8 (6.6-18.8) 45.0	19.1 (14.1-20.3) 68.0

*Data still accruing.

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HUDSON: Safety by Treatment (Groups A + B)

Safety Parameter, n (%)	Durvalumab + Ceralasertib (n = 66)	Durvalumab + Olaparib (n = 87)	Durvalumab + Danvatirsen (n = 45)	Durvalumab + Oleclumab (n = 57)
Any TEAE	64 (97.0)	80 (92.0)	43 (95.6)	48 (84.2)
▪ Related to any tx	52 (78.8)	67 (77.0)	33 (73.3)	34 (59.6)
Any grade ≥3 TEAE	33 (50.0)	47 (54.0)	28 (62.2)	23 (40.4)
▪ Related to any tx	15 (22.7)	30 (34.5)	17 (37.8)	9 (15.8)
▪ Resulted in death	2 (3.0)	1 (1.1)	3 (6.7)	1 (1.8)
Any SAE	28 (42.4)	33 (37.9)	20 (44.4)	16 (28.1)
▪ Related to any tx	8 (12.1)	9 (10.3)	3 (6.7)	4 (7.0)
Any TEAE resulting in discontinuation	8 (12.1)	9 (10.3)	10 (22.2)	7 (12.3)
▪ Related to any tx	5 (7.6)	8 (9.2)	7 (15.6)	3 (5.3)
Most common TRAEs (≥15%*)				
▪ Nausea	34 (51.5)	37 (42.5)	1 (2.2)	4 (7.0)
▪ Vomiting	19 (28.8)	18 (20.7)	2 (4.4)	1 (1.8)
▪ Decreased appetite	15 (22.7)	8 (9.2)	2 (4.4)	4 (7.0)
▪ Anemia	14 (21.2)	22 (25.3)	4 (8.9)	2 (3.5)
▪ Fatigue	11 (16.7)	18 (20.7)	6 (13.3)	8 (14.0)
▪ Diarrhea	10 (15.2)	11 (12.6)	5 (11.1)	7 (12.3)

*In the durvalumab + ceralasertib treatment group.

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HUDSON: Conclusions

- In this umbrella phase II study, durvalumab + ceralasertib showed promising activity in both biomarker matched (ATM) and nonmatched patients with advanced NSCLC who failed previous PD-1/PD-L1 therapy and platinum-based chemotherapy with an ORR of 16.7% compared with 0% to 4.8% in other evaluated regimens
- Median OS was notable for biomarker matched (22.8 mo), primary resistance (11.8 mo), and acquired resistance (19.1 mo) cohorts for durvalumab + ceralasertib
- All 4 reported regimens seem to have tolerable safety profiles according to investigators
- HUDSON remains ongoing, with patients continuing to enroll in ceralasertib-based treatment regimens in both biomarker matched and nonmatched cohorts

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THANK YOU