2025 ESMO IMMUNO-ONCOLOGY
Annual Congress

ADVANTIG-302: PHASE 3 STUDY OF OCIPERLIMAB + TISLELIZUMAB VERSUS PEMBROLIZUMAB IN PROGRAMMED DEATH-LIGAND 1 HIGH, UNTREATED, LOCALLY ADVANCED, UNRESECTABLE, OR METASTATIC NON-SMALL CELL LUNG CANCER

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DISCLOSURES

MR: Payment or honoraria: Amgen, AstraZeneca, BeOne, Boehringer-Ingelheim, BMS, Daiichi-Sankyo, GSK, Lilly, Merck, MSD, Novartis, Pfizer, Regeneron, Roche, and Accord; consulting fees: Amgen, AstraZeneca, BeOne, Boehringer-Ingelheim, BMS, Daiichi-Sankyo, GSK, Lilly, Merck, MSD, Novartis, Pfizer, Regeneron, Roche, and Accord; speakers' bureaus: Amgen, AstraZeneca, BeOne, Boehringer-Ingelheim, BMS, Daiichi-Sankyo, GSK, Lilly, Merck, MSD, Novartis, Pfizer, Regeneron, Roche, and Accord; travel support: Amgen, AstraZeneca, BeOne, Boehringer-Ingelheim, BMS, Daiichi-Sankyo, GSK, Lilly, Merck, MSD, Novartis, Pfizer, Regeneron, Roche, and Accord; research funding (institution): BMS and Boehringer-Ingelheim.

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MN: Payment or honoraria: Ono Pharmaceuticals, Chugai Pharmaceutical Co., Ltd, Taiho Pharmaceutical, Bristol-Myers Squibb, Daiichi Sankyo Company, Limited, Eli Lilly Japan K.K, AstraZeneca Merck, Merck Sharp & Dohme, AbbVie, Takeda Pharmaceutical Company Limited, Pfizer Japan, Boehringer Ingelheim, Novartis Pharma K.K., Nippon Kayaku, Merck Biophama, and Janssen.

AIS: Grants or contracts: LAM Therapeutics, Roche, AstraZeneca, Boehringer Ingelheim, Astellas Pharma, MedImmune, Novartis, Incyte, AbbVie, Ignyta, Takeda, Macrogenics, CytomX Therapeutics, Astex Pharmaceuticals, Bristol Myers Squibb, Loxo, Gritstone, Plexxikon, Amgen, Daiichi Sankyo, ADCT, Janssen Oncology, Rubius, Synthekine, Mersana, Blueprint Medicines, Regeneron, Alkermes, Revolution Medicines, Medikine, Black Diamond Therapeutics, BluPrint Oncology, Nalo Therapeutics, Scorpion Therapeutics, ArriVent Biopharma, Prelude Therapeutics, and Lilly; consulting fees: Incyte, Amgen, Novartis, Mirati Therapeutics, Gritstone Oncology, Jazz Pharmaceuticals, Takeda, Janssen Research & Development, Mersana, Gritstone Bio, Daiichi Sankyo/AstraZeneca, Regeneron, Lilly, Black Diamond Therapeutics, Sanofi, ArriVent Biopharma, Synthekine, GSK, CRISPR Therapeutics, Revolution Medicines, AstraZeneca/MedImmune, Merck, Bristol Myers Squibb, and Blueprint Medicines; payment or honoraria: CytomX Therapeutics, AstraZeneca/MedImmune, Merck, Takeda, Amgen, Janssen Oncology, Novartis, Bristol Myers Squibb, Bayer, Prelude Therapeutics, AbbVie, and Astellas Pharma; leadership position: NEXT Oncology Virginia.

XY: Declares no potential conflicts of interest.

TM: Declares no potential conflicts of interest.

AZ: Declares no potential conflicts of interest.

AM-B: Payment or honoraria: AstraZeneca, GSK, and Seagen; participated on a data safety monitoring board or advisory board: Pfizer; travel support: AstraZeneca, GSK, MSD, and Roche.

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YZ: Employment: BeOne Medicines; Stock or other ownership: BeOne Medicines.

SC-D: Employment: BeOne Medicines; stock or other ownership; BeOne Medicines; employment (immediate family member): Blossom Hill Therapeutics; stock or other ownership (immediate family member): Blossom Hill Therapeutics.

WD: Employment: BeOne Medicines.

JZ: Employment: BeOne Medicines.

SL: Grants or contracts: AstraZeneca, Hutchison MediPharma, BMS, Hengrui Therapeutics, BeiGene, Roche, Hansoh, and Lilly Suzhou Pharmaceutical Co Ltd; speakers' bureaus: AstraZeneca, Roche, Hansoh Pharma, and Hengrui Therapeutics; consulting fees (institution) consulting fees from AstraZeneca, Pfizer, Boehringer Ingelheim, Hutchison MediPharma, Simcere Pharmaceutical Group, Zai Lab, GenomiCare, Yuhan, Prime Oncology, and Roche.

50 YEARS ESMO

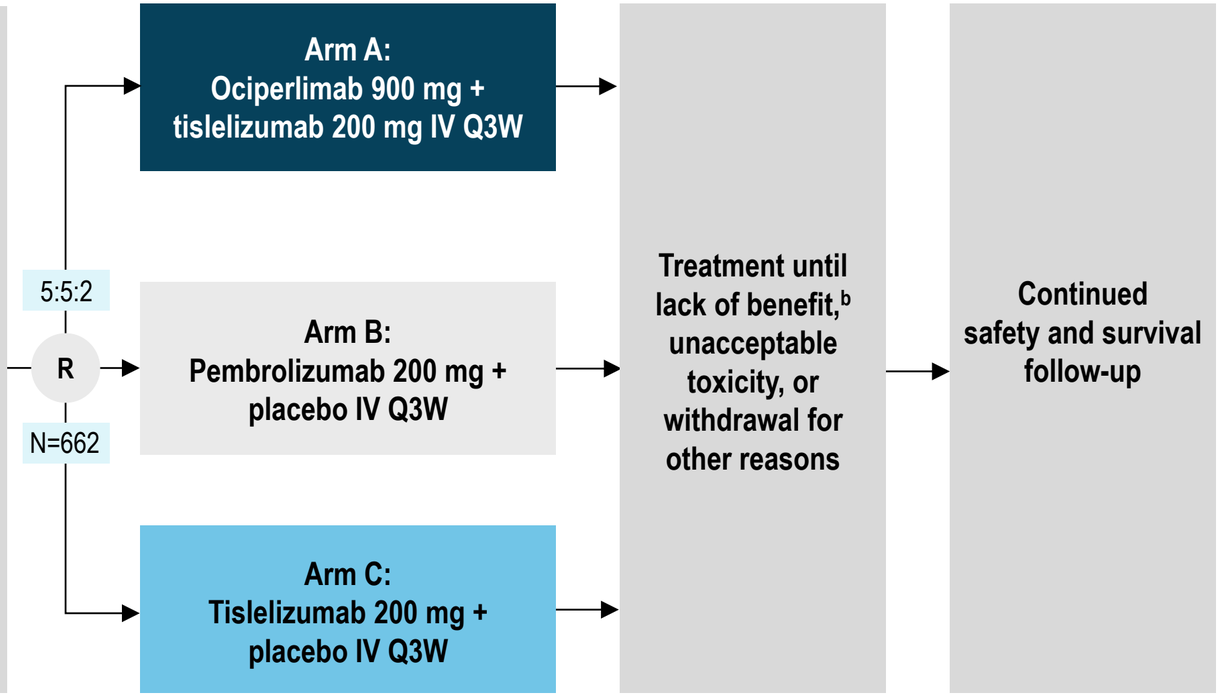
INTRODUCTION AND METHODS

- **Here we present results from an interim analysis of AdvanTIG-302, a phase 3 trial in untreated PD-L1 high (PD-L1 TC ≥50%), locally advanced/recurrent or metastatic NSCLC**
  - Ociperlimab is a humanized Fc intact IgG1 mAb designed to target TIGIT with high specificity and affinity[1]
  - Tislelizumab is an anti-PD-1 mAb that blocks the PD-1/PD-L1 immune checkpoint, resulting in T-cell activation
    - Preclinical studies suggest that blockade of TIGIT and PD-1 enhances the activity of anti-PD-1 therapy[2]

Key eligibility criteria
- Metastatic squamous/non-squamous NSCLC, or locally advanced/recurrent NSCLC ineligible for curative therapies
- PD-LI expression TC ≥50%[a]
- No known *EGFR*, *ALK*, BRAFV600E or *ROSI* mutations
- No prior systemic treatment/ICIs for metastatic NSCLC

Stratification:
- Region (Asia versus non-Asia)
- Histology (squamous versus non-squamous)

Analysis and statistical methods
- A total of 660 patients were planned, of which approximately 572 patients were to be enrolled into Arms A and B to provide 93% power at a 1-sided type I error rate of 0.025 to detect the superiority of Arm A over Arm B, corresponding to an assumed HR of 0.70
- Arm C was not powered for any comparisons



Endpoints
- Primary
  - OS (Arm A versus Arm B)
- Secondary
  - PFS (Arm A versus Arm B)
  - ORR and DoR (Arm A versus Arm B)
  - Safety

Data cutoff date: May 30, 2025
Median (range) study follow up time: 22.8 (0.2-44.2) months for Arm A, 22.3 (0.3-45.0) months for Arm B, and 21.3 (0.1-42.9) months for Arm C

Safety was assessed by the type, frequency, and severity (as graded by NCI-CTCAE v5.0) of AEs. Efficacy was assessed by the investigator per RECIST v1.1.
[a]Assessed centrally (or locally in the US and Japan) using the VENTANA® PD-L1 (SP263) CDx assay (Roche Diagnostics, Basel, Switzerland). [b]The time point at which the investigator considers that the patient is no longer benefiting from study treatment.
1. Chen X, et al. *Front Immunol*. 2022:13:828319; 2. Chu X, et al. *Mol Cancer*. 2023;22:101.

RESULTS: BASELINE CHARACTERISTICS

- Baseline characteristics were generally balanced across the three arms

	Arm A: Ociperlimab + Tislelizumab (N=287)	Arm B: Pembrolizumab (N=287)	Arm C: Tislelizumab (N=88)
Median (range) age, years	66.0 (33.0-83.0)	66.0 (29.0-91.0)	66.0 (38.0-86.0)
Sex, n (%)			
Male	230 (80.1)	235 (81.9)	67 (76.1)
Female	57 (19.9)	52 (18.1)	21 (23.9)
Race, n (%)			
Asian	150 (52.3)	151 (52.6)	45 (51.1)
Black or African	2 (0.7)	0 (0.0)	0 (0.0)
White	133 (46.3)	133 (46.3)	43 (48.9)
Unknown/ not reported	1 (0.3)	2 (0.7)	0 (0.0)
Other	1 (0.3)	1 (0.3)	0 (0.0)
Geographic region, n (%)			
Non-Asia	137 (47.7)	136 (47.4)	45 (51.1)
Asia	150 (52.3)	151 (52.6)	43 (48.9)

	Arm A: Ociperlimab + Tislelizumab (N=287)	Arm B: Pembrolizumab (N=287)	Arm C: Tislelizumab (N=88)
Tobacco use status, n (%)			
Never	34 (11.8)	34 (11.8)	14 (15.9)
Former	205 (71.4)	190 (66.2)	62 (70.5)
Current	48 (16.7)	63 (22.0)	12 (13.6)
ECOG PS, n (%)			
0	74 (25.8)	81 (28.2)	24 (27.3)
1	213 (74.2)	206 (71.8)	64 (72.7)
Histology, n (%)			
Squamous	115 (40.1)	115 (40.1)	33 (37.5)
Non-squamous	172 (59.9)	172 (59.9)	55 (62.5)
PD-L1 expression by central testing, n (%)			
≥50%	281 (97.9)	282 (98.3)	84 (95.5)
<50%[a]	4 (1.4)	4 (1.4)	4 (4.5)
Unknown[a]	2 (0.7)	1 (0.3)	0 (0.0)

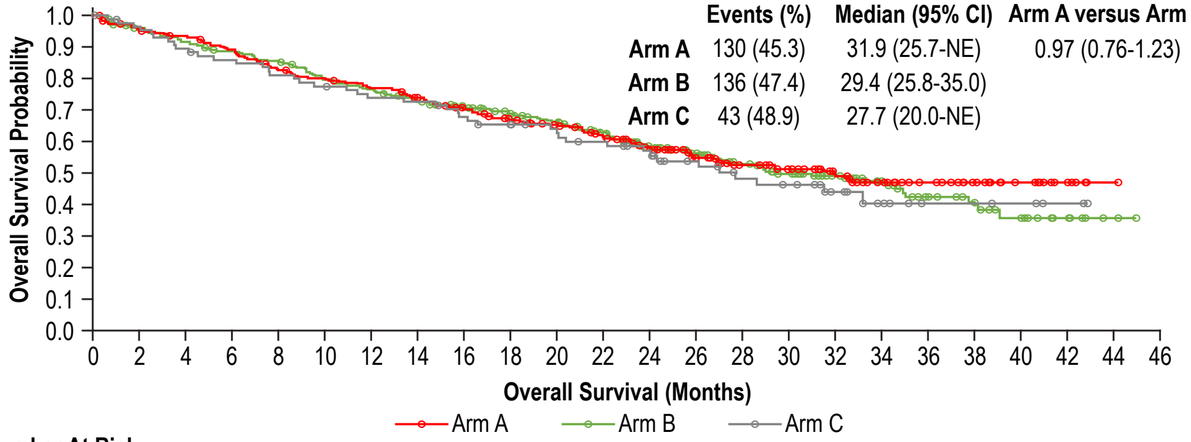
[a]Patients with unknown or <50% PD-L1 expression by central testing had ≥50% PD-L1 expression by local testing.

ITT analysis set.

RESULTS: EFFICACY

- Ociperlimab plus tislelizumab showed no improvement in OS compared with pembrolizumab; median OS was comparable across the 3 arms
- Ociperlimab plus tislelizumab and tislelizumab had numerical improvements in PFS and ORR compared with pembrolizumab

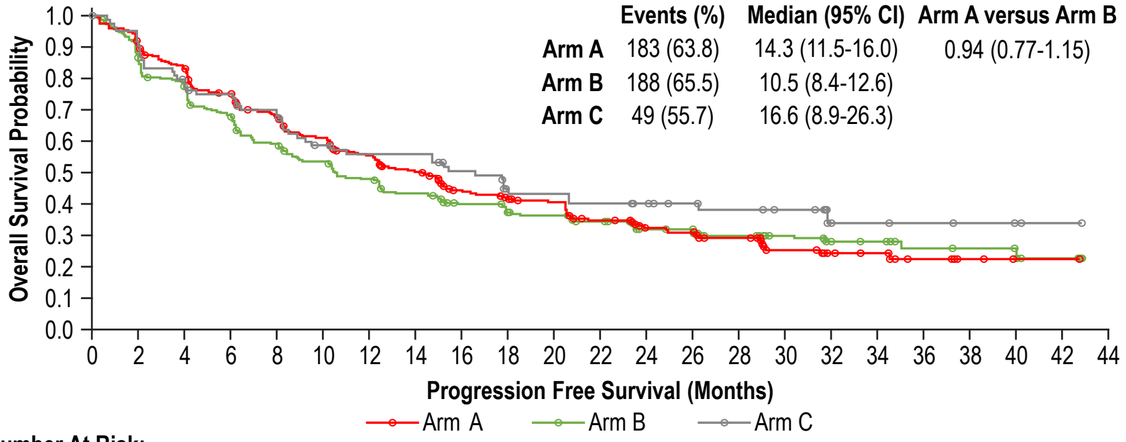
OS (ITT Analysis Set)



Number At Risk:

Arm A	287	270	262	249	230	221	211	199	187	170	160	148	128	106	82	75	59	42	30	20	13	6	1	0
Arm B	287	271	258	248	239	221	212	198	187	172	161	145	122	105	90	79	64	43	26	20	13	7	2	0
Arm C	88	82	76	72	68	65	61	60	55	50	47	43	38	30	25	23	14	9	5	5	4	2	0	0

PFS (ITT Analysis Set)



Number At Risk:

Arm A	287	254	229	205	180	161	142	123	99	90	84	67	51	49	38	24	16	14	9	4	1	1	0
Arm B	287	245	217	188	161	143	127	113	95	85	80	70	55	54	43	34	23	21	12	9	8	3	0
Arm C	88	77	65	61	55	45	42	42	36	29	28	26	24	21	19	16	6	5	4	3	2	1	0

Efficacy Summary (ITT Analysis Set)

	Arm A: Ociperlimab + Tislelizumab (N=287)	Arm B: Pembrolizumab (N=287)	Arm C: Tislelizumab (N=88)
ORR, n (%)	175 (61.0)	140 (48.8)	49 (55.7)
95% CI, %[a]	55.1-66.7	42.9-54.7	44.7-66.3
OR Arm A versus Arm B (95% CI)[b]	1.65 (1.18-2.30); 2-sided *P*=.0032[c]	-	-
Median DoR, months (95% CI)	18.6 (16.5-24.2)	28.3 (16.3-NE)	NR (16.0-NE)

[a]The 95% CI was estimated using the Clopper–Pearson method. [b]Mantel–Haenszel common OR was estimated along with its 95% CI constructed by a normal approximation of log odds ratio and the Robins, Breslow, and Greenland variance estimate stratified by regions of enrolment (Asia versus non-Asia) and histology (squamous versus non-squamous) with Arm B as the reference group. [c]The *P*-value of Arm A versus Arm B was obtained using the Cochran–Mantel–Haenszel method stratified by regions of enrolment (Asia versus non-Asia) and histology (squamous versus non-squamous). *P*-value is displayed for descriptive purposes only.

RESULTS: SAFETY AND TOLERABILITY

- Ociperlimab plus tislelizumab, pembrolizumab, and tislelizumab were generally well tolerated

Overall Safety Summary (Safety Analysis Set)

	Arm A: Ociperlimab + Tislelizumab (N=286)	Arm B: Pembrolizumab (N=287)	Arm C: Tislelizumab (N=87)
Patients with any treatment-related TEAE, n (%)	241 (84.3)	228 (79.4)	69 (79.3)
Grade ≥3	99 (34.6)	58 (20.2)	24 (27.6)
Serious	76 (26.6)	43 (15.0)	14 (16.1)
Leading to death[a]	7 (2.4)	3 (1.0)	1 (1.1)
Leading to treatment discontinuation	53 (18.5)	30 (10.5)	13 (14.9)
Patients with any imAE, n (%)	173 (60.5)	125 (43.6)	48 (55.2)
Patients with IRRs, n (%)	48 (16.8)	19 (6.6)	7 (8.0)

AEs were classified based on MedDRA v27.0 and graded for severity using NCI-CTCAE v5.0. A TEAE is defined as an AE that had an onset date or a worsening in severity from baseline (pretreatment) on or after the first dose of study drug(s) up to 30 days following last dose of study drug(s) or initiation of a new anticancer therapy, whichever occurs first. Treatment-related TEAEs include those events considered by the investigator to be related or with missing assessment of the causal relationship.
[a]The summary of TEAE leading to death only includes TEAEs leading to death excluding deaths due to disease under study.

Treatment-related TEAEs in ≥10% of Patients in Arms A, B, or C (Safety Analysis Set)

	Arm A: Ociperlimab + Tislelizumab (N=286)	Arm B: Pembrolizumab (N=287)	Arm C: Tislelizumab (N=87)
Pruritus	72 (25.2)	33 (11.5)	18 (20.7)
Hypothyroidism	43 (15.0)	43 (15.0)	18 (20.7)
Pyrexia	37 (12.9)	27 (9.4)	7 (8.0)
AST increased	36 (12.6)	23 (8.0)	9 (10.3)
Rash	35 (12.2)	19 (6.6)	8 (9.2)
ALT increased	34 (11.9)	30 (10.5)	7 (8.0)
Anaemia	34 (11.9)	27 (9.4)	7 (8.0)
Rash maculo-papular	31 (10.8)	9 (3.1)	6 (6.9)

Events were sorted by decreasing frequency of preferred term in Arm A. AEs were classified based on MedDRA v27.0 and graded for severity using NCI-CTCAE v5.0.

TEAE, treatment-emergent adverse event.

CONCLUSIONS

- Ociperlimab plus tislelizumab showed no improvement in OS compared with pembrolizumab
  - Median OS was comparable across all three arms
- Ociperlimab plus tislelizumab and tislelizumab had numerical improvements in PFS and ORR compared with pembrolizumab; however, data should be interpreted cautiously given the descriptive nature of this comparison
- No new or unexpected safety signals were observed across all treatment arms and overall treatment regimens were generally well tolerated

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