IMpower-132

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(PD1/PDL1-未)

Co-Primary Endpoint: OS(ITT), PFS(investigator)

Secondary Endpoint: ORR, DOR, POR and safety

Non-Sq NSCLC

化学療法未治療の非小細胞肺癌患者（1次治療）

・EGFR/ALK negative

・PD-L1発現 Any

R

Arm:APP

n=292

Induction Therapy: Atezolizumb(1200mg q3w) + CBDCA(AUC=6)or CDDP Pemetrexed(100mg/m2)

Up to 4-6 cycles

Maintenance: Atezolizumb

Arm:PP

n=286

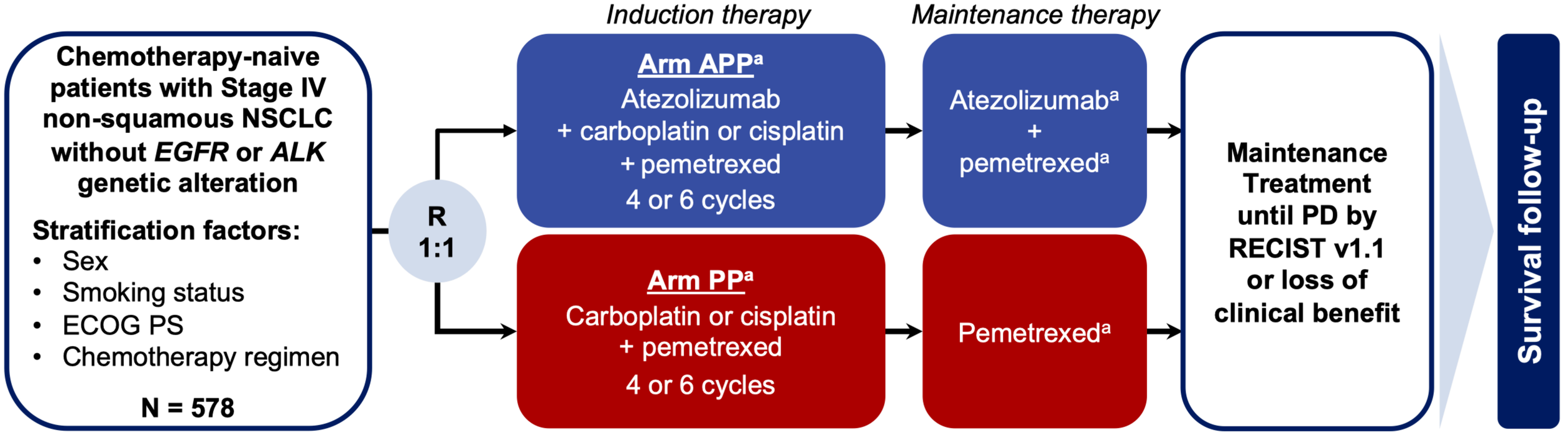
Induction Therapy: CBDCA(AUC=6)or CDDP Pemetrexed(100mg/m2)

Up to 4-6 cycles

Maintenance: Pemetrexed

Primary		Subgroups		
investigator PFS	Interim OS	mPFS PD-L1 High TC3 or IC3	mPFS PD-L1 Low TC1/2 or IC1/2	mPFS PD-L1 Negative TC0 or IC0
7.6ヵ月	18.1ヵ月	10.8ヵ月	6.2ヵ月	8.5ヵ月
HR=0.60 p<0.0001	HR=0.81 p=0.0797	HR=0.46	HR=0.80	HR=0.45
5.2ヵ月	13.6ヵ月	6.5ヵ月	5.7ヵ月	4.9ヵ月

IMpower132 Study Design



- Co-primary endpoints: INV-assessed PFS and OS
- Secondary endpoints: INV-assessed ORR and DOR, PRO and safety measures
- Exploratory analyses: clinical and biomarker subgroup analyses
  - Biomarker-evaluable tissue not mandatory for enrolment (was available from 60% of patients)

DOR, duration of response; INV, investigator; R, randomization; ORR, objective response rate; OS, overall survival; PD, progressive disease, PFS, progression-free survival; PRO, patient-reported outcomes. [a] Atezolizumab: 1200 mg IV q3w; Carboplatin: AUC 6 mg/mL/min IV q3w; Cisplatin: 75 mg/m^2 IV q3w; Pemetrexed: 500 mg/m^2 IV q3w. NCT02657434. Data cutoff: May 22, 2018

Baseline Characteristics

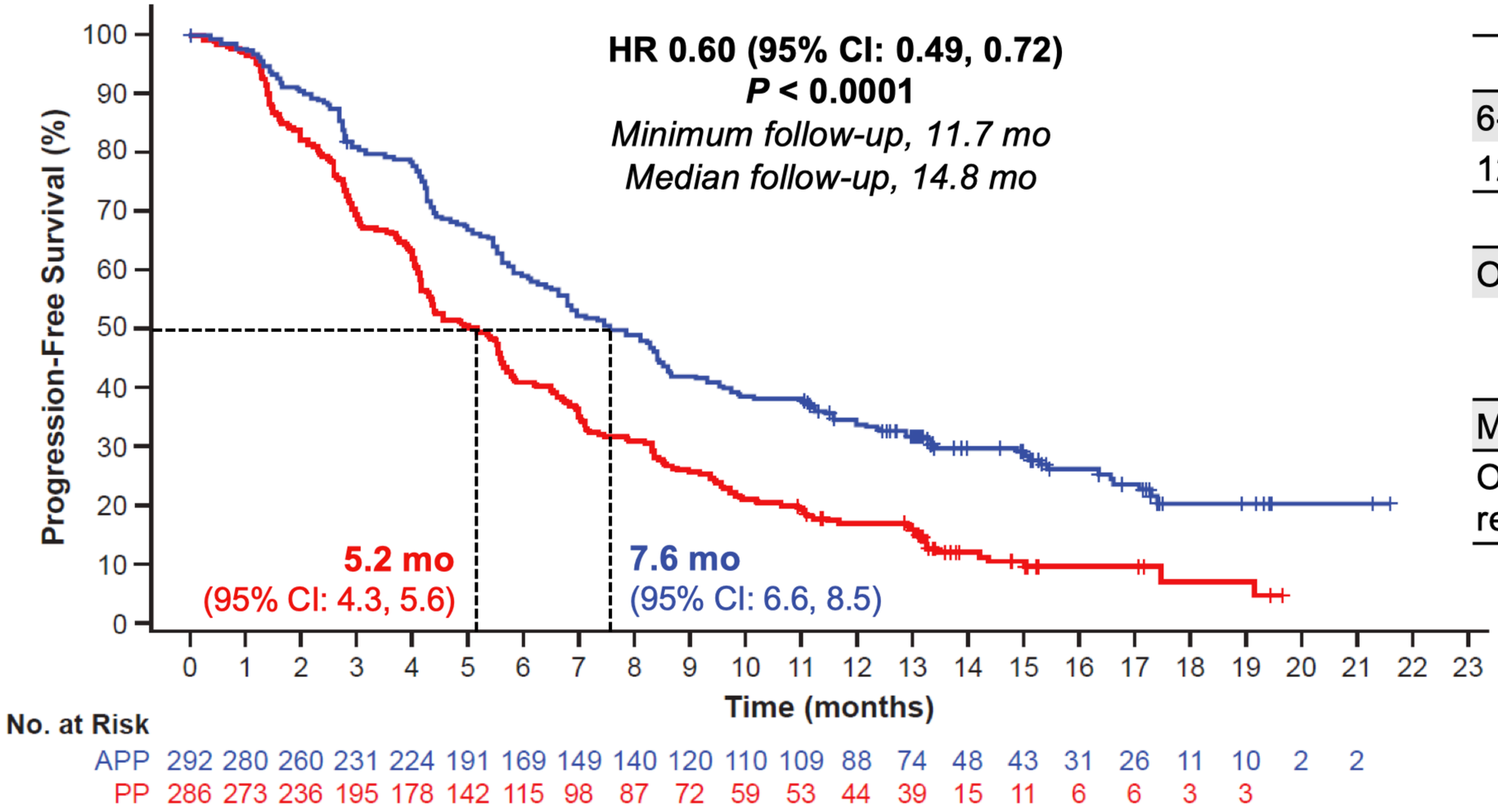
Characteristic	APP (n = 292)	PP (n = 286)
Median age (range), years	64.0 (31-85)	63.0 (33-83)
< 65 years, n (%)	153 (52.4%)	167 (58.4%)
Sex, male, n (%)	192 (65.8%)	192 (67.1%)
Race, n (%)[a]		
White	193 (66.1%)	203 (71.0%)
Asian	71 (24.3%)	65 (22.7%)
ECOG PS 0, n (%)[b]	126 (43.2%)	114 (40.1%)
Carboplatin, n (%)	177 (60.6%)	175 (61.1%)
Intended 4 cycles, n (%)	197 (67.5%)	190 (66.4%)

Characteristic	APP (n = 292)	PP (n = 286)
Smoking status, n (%)		
Current or former	255 (87.3%)	256 (89.5%)
Never	37 (12.7%)	30 (10.5%)
Liver metastases, n (%)	37 (12.7%)	36 (12.6%)
PD-L1 expression, n (%)[c]	n = 176	n = 168
Negative	88 (50.0%)	75 (44.6%)
Positive	88 (50.0%)	93 (55.4%)
PD-L1–low	63 (35.8%)	73 (43.5%)
PD-L1–high	25 (14.2%)	20 (11.9%)

ECOG, eastern cooperative oncology group; PS, performance status.

[a] American Indian or Alaska Native race (n = 2), Black or African American (n = 6) and Unknown race (n = 38) not included in table. [b] 2 patients had missing baseline ECOG PS. [c] PD-L1 status available in 60% of patients. PD-L1–high (TC3/IC3): patients with PD-L1 expression in ≥50% of tumor cells or ≥10% of tumor-infiltrating immune cells; PD-L1–low (TC12/IC12): patients with PD-L1 expression in ≥1% and <50% of tumor cells or ≥1% and <10% of tumor-infiltrating immune cells; and PD-L1–negative (TC0/IC0): patients with PD-L1 expression in <1% of tumor cells and <1% of tumor-infiltrating immune cells.

Final Investigator-Assessed PFS, ORR and DOR



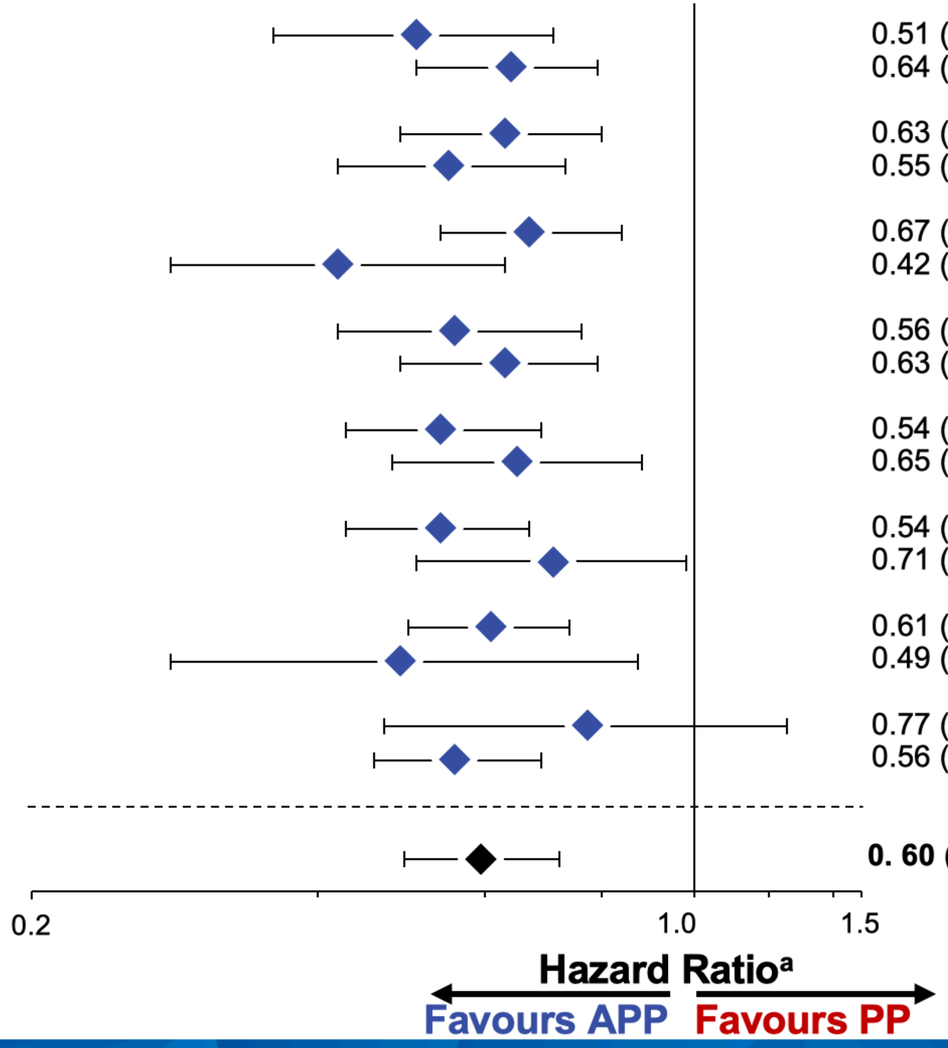
	APP	PP
6-mo PFS	59.1%	40.9%
12-mo PFS	33.7%	17.0%

	APP	PP
ORR, %	47%	32%
CR	2%	1%
PR	45%	32%
Median DOR, mo	10.1	7.2
Ongoing response, %	42%	30%

CR, complete response; DOR, duration of response; HR, hazard ratio; IRF, independent review facility; ORR, objective response rate; PR, partial response.
IRF-assessed median PFS was 7.2 mo with APP and 6.6 mo with PP (stratified HR: 0.758 [95% CI: 0.623, 0.923] *P* = 0.055)
Data cutoff: May 22, 2018.

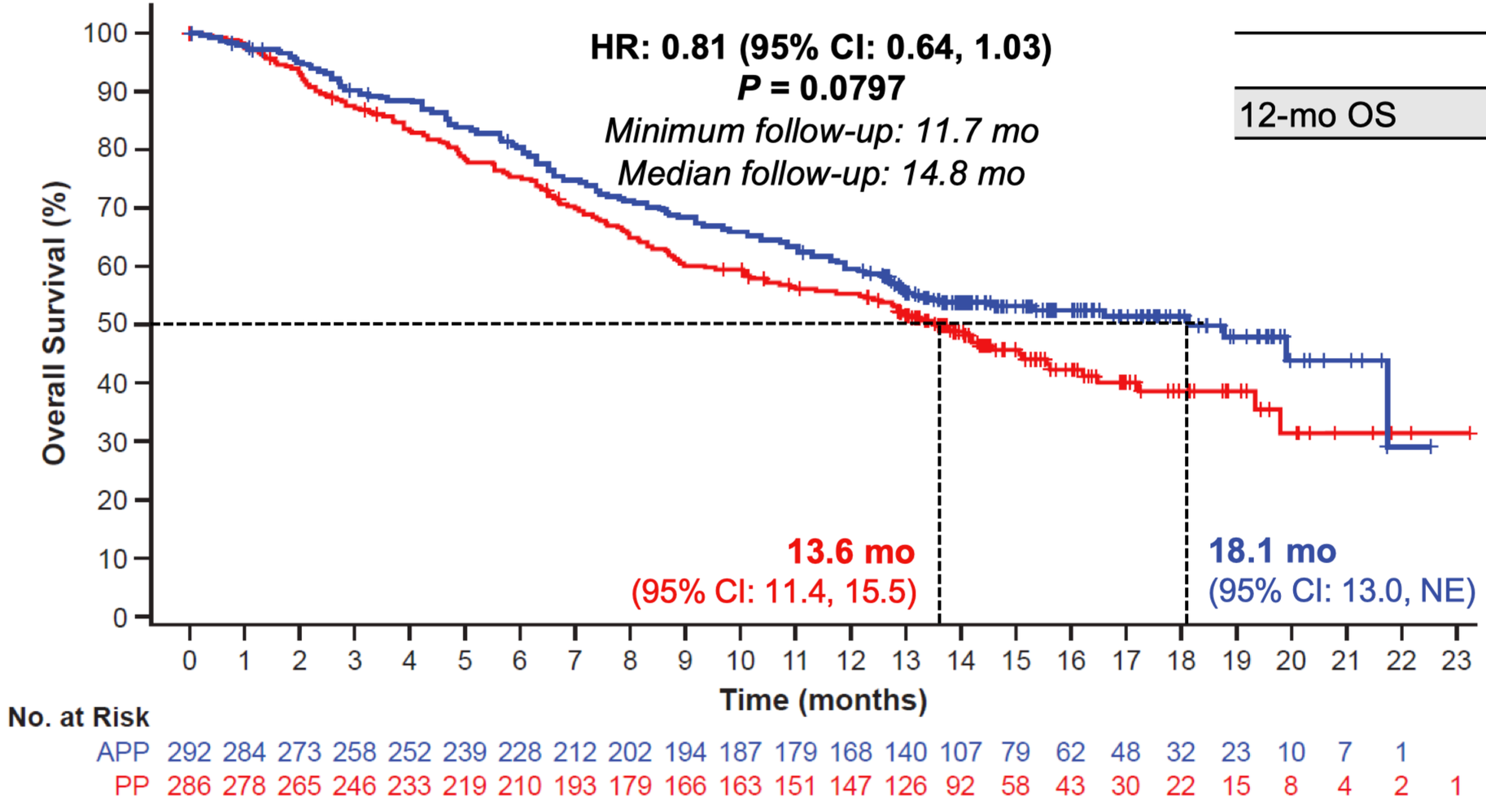
PFS in Key Patient Subgroups

Subgroup	n (%)	HR (95% CI)[a]	Median PFS, mo	
			APP	PP
Female	194 (34)	0.51 (0.36–0.71)	8.3	5.3
Male	384 (66)	0.64 (0.51–0.79)	7.5	4.9
< 65 y	320 (55)	0.63 (0.49–0.80)	6.9	4.4
≥ 65 y	258 (45)	0.55 (0.42–0.73)	8.4	5.6
White[b]	396 (69)	0.67 (0.54–0.84)	6.9	4.9
Asian	136 (24)	0.42 (0.28–0.63)	10.2	5.3
ECOG PS 0[b]	240 (42)	0.56 (0.42–0.76)	8.6	5.8
ECOG PS 1	336 (58)	0.63 (0.49–0.79)	6.8	4.4
Received carboplatin	352 (61)	0.54 (0.43–0.69)	8.1	5.5
Received cisplatin	226 (39)	0.65 (0.48–0.88)	7.1	4.4
Intended 4 cycles	387 (67)	0.54 (0.43–0.67)	7.8	4.5
Intended 6 cycles	191 (33)	0.71 (0.51–0.98)	7.6	5.6
Current or former smoker	511 (88)	0.61 (0.50–0.74)	7.5	5.1
Never smoker	67 (12)	0.49 (0.28–0.87)	8.6	5.5
Liver metastases	73 (13)	0.77 (0.47–1.25)	4.4	4.0
No liver metastases	505 (87)	0.56 (0.46–0.69)	8.4	5.5
ITT population	**578 (100)**	**0. 60 (0.49–0.72)**	**7.6**	**5.2**



[a] Stratified HR for ITT; unstratified for all other subgroups.
[b] Patients with other/unknown race (n = 46) and unknown baseline ECOG PS (n = 2) not included.
Data cutoff: May 22, 2018.

Interim OS Analysis

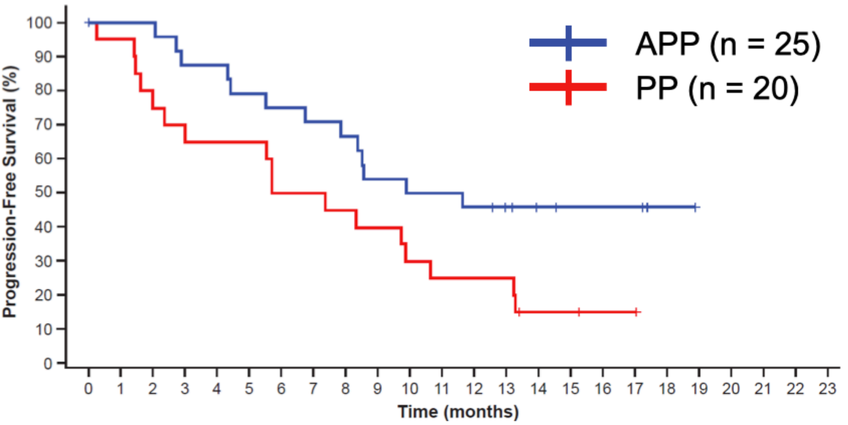


	APP	PP
12-mo OS	59.6%	55.4%

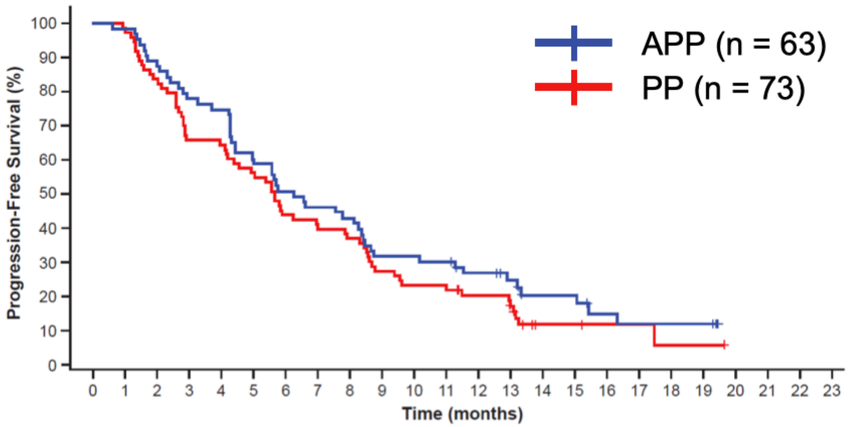
Data cutoff: May 22, 2018. Frequency of OS events: 44% and 49% in arms APP and PP respectively.

Exploratory Analysis: PFS by PD-L1 Status in Biomarker-Evaluable Patients[a]

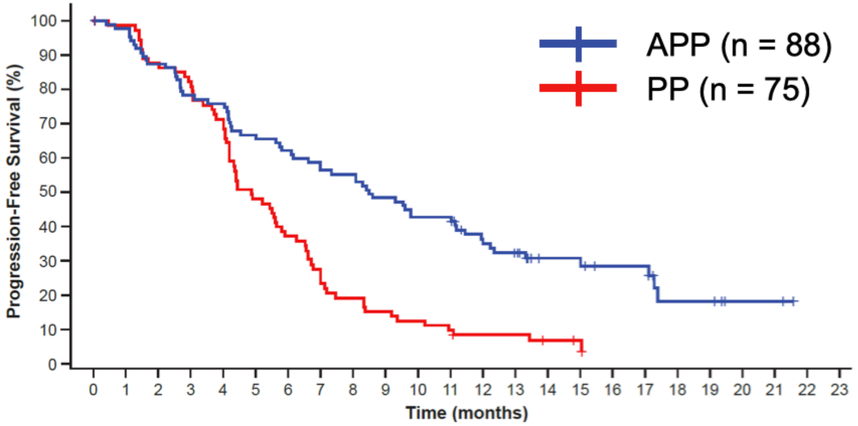
PD-L1 High
TC3 or IC3



PD-L1 Low
TC1/2 or IC1/2



PD-L1 Negative
TC0 and IC0



	APP	PP	APP	PP	APP	PP
ORR, %	72%	55%	38%	38%	44%	27%
CR | PR, %	0 | 72%	5% | 50%	2% | 37%	0 | 38%	2% | 42%	0 | 27%
Median DOR, mo	NE	7.2	7.2	7.2	10.1	4.2
12-month PFS	46%	25%	27%	20%	35%	8%
Median PFS, mo	10.8	6.5	6.2	5.7	8.5	4.9
HR[b] (95% CI)	0.46 (0.22, 0.96)		0.80 (0.56, 1.16)		0.45 (0.31, 0.64)	

[a] Overall HR 0.57 (0.45, 0.73) in biomarker-evaluable patients (60% of ITT). [b] Unstratified HR. Data cutoff: May 22, 2018.

Subsequent Cancer Therapies

	APP (n = 292)	PP (n = 286)
Total no. of patients with ≥ 1 treatment, n (%)	94 (32.2%)	148 (51.7%)
No. of patients with ≥ 1 immunotherapy treatment, n (%)	8 (2.7%)	106 (37.1%)
No. of treatments by immunotherapy agent, n	10	117
Nivolumab, n (%)	4 (1.4%)	64 (22.4%)
Pembrolizumab, n (%)	0	27 (9.4%)
Atezolizumab, n (%)	2 (0.7%)	10 (3.5%)
Durvalumab, n (%)	0	3 (1.0%)
Daratumumab, n (%)	0	2 (0.7%)
Other immunotherapy agents, n (%)[a]	4 (1.4%)	7 (2.6%)
No. of patients with ≥ 1 chemotherapy, n (%)	86 (29.5%)	71 (24.8%)
No. of patients with ≥ 1 targeted therapy, n (%)	36 (12.3%)	36 (12.6%)
No. of treatments with anti-angiogenic agents, n (%)[b]	33 (11.3%)	29 (10.1%)

[a] n = 1 for each treatment. [b] Anti-angiogenic agents used: bevacizumab, nintedanib, ramucirumab.
Data cutoff: May 22, 2018.

Safety Summary

	APP (n = 291)	PP (n = 274)
All-cause AEs, n (%)	286 (98%)	266 (97%)
Grade 3-4	181 (62%)	147 (54%)
Grade 5	21 (7%)	14 (5%)
TRAEs, n (%)	267 (92%)	239 (87%)
Grade 3-4	156 (54%)	107 (39%)
Grade 5	11 (4%)	7 (3%)
SAEs, n (%)	134 (46%)	84 (31%)
Tx-related SAEs	96 (33%)	43 (16%)
AEs leading to withdrawal, n (%)		
Of any treatment	69 (24%)	48 (18%)
Of atezolizumab	44 (15%)	0
AESI, n (%)	141 (49%)	104 (38%)

	APP (n = 291)		PP (n = 274)	
AEs of Special Interest, n (%)	All Grade	Grade 3-4	All Grade	Grade 3-4
Rash	71 (24%)	9 (3%)	58 (21%)	5 (2%)
Hypothyroidism	23 (8%)	1 (<1%)	6 (2%)	0
Pneumonitis	16 (6%)	6 (2%)[a]	6 (2%)	3 (1%)[a]
Hepatitis (Diagnosis)	13 (5%)	7 (2%)[a]	2 (1%)	0
Infusion-Related Reactions	8 (3%)	1 (<1%)	2 (1%)	1 (<1%)
Hyperthyroidism	6 (2%)	1 (<1%)	3 (1%)	0
Severe Cutaneous Adverse Reaction	4 (1%)	2 (1%)	2 (1%)	0
Pancreatitis	4 (1%)	1 (<1%)	2 (1%)	2 (1%)
Colitis	5 (2%)	2 (1%)	0	0

- PRO data also support the positive benefit-risk profile demonstrated by these clinical data

AE, adverse event; AESI, adverse event of special interest; SAE, serious adverse event; TRAE, treatment-related adverse event.[a] Grade 5 event observed.
Data cutoff: May 22, 2018.

Conclusions

- IMpower132 met its co-primary endpoint of investigator-assessed PFS in the ITT
- The addition of atezolizumab to carboplatin/cisplatin + pemetrexed improved median PFS in the ITT population (7.6 mo vs 5.2 mo, HR 0.60) and across key clinical subgroups
- Atezolizumab + pemetrexed + carboplatin or cisplatin has a manageable safety profile consistent with known safety risks of the individual therapies; no new safety signals were identified
- Interim OS data showed numerical improvement; next OS analysis is anticipated in 1H 2019