EUROPEAN LUNG CANCER CONFERENCE 2019

IMpower150: an exploratory analysis of efficacy outcomes in patients with *EGFR* mutations

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Disclosure Slide

- Dr. Reck reports honoraria for lectures and consultancy fees from
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NSCLC and Patients With *EGFR* Mutations

- After failure of first-line TKIs, patients with *EGFR* mutations have limited treatment options[1-3]
  - Continuation of TKI therapy with chemotherapy is generally associated with worse survival outcomes than treatment with later-generation TKIs[1,2]
  - Most patients who receive subsequent therapy will eventually receive chemotherapy[3]
- Patients with *EGFR* mutations treated with single-agent PD-L1 or PD-1 inhibitors after failure of TKI therapy have not shown significant survival benefit versus patients treated with chemotherapy in the second-line setting[4–7]
- Therefore, patients with NSCLC who have *EGFR* mutations need better therapies following TKI treatment
- IMpower150 is an all comer study that included patients with *EGFR* mutations who had experienced progression or intolerance to at least one approved TKI therapy

EGFR, epidermal growth factor receptor; PD-L1, programmed death-ligand 1; TKI, tyrosine kinase inhibitors.

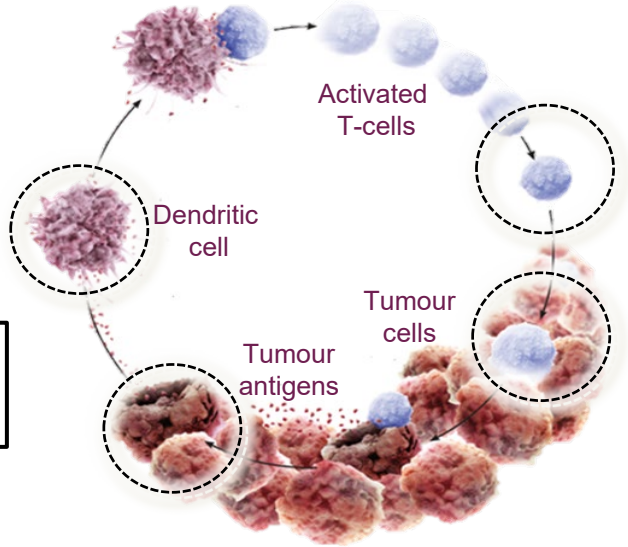
1. Soria J, et al. *Lancet Oncol*, 2015. 2. Mok TS, et al. *N Engl J Med*, 2017. 3. Soria J, et al. *N Engl J Med*, 2018.
4. Borghaei H, et al. *N Engl J Med*, 2015. 5. Herbst RS, et al. *Lancet*, 2016. 6. Rittmeyer A, et al. *Lancet,* 2017.
7. Lee CK, et al. *JAMA* 2017.

Rationale for the Combination of Atezolizumab + Bevacizumab + Chemotherapy

- In addition to its known anti-angiogenic effects[1], bevacizumab's inhibition of VEGF has immune modulatory effects[2]

Inhibition of VEGF can promote T-cell priming and activation via dendritic cell maturation[2-4]

Tumour cell killing by chemotherapy may expose the immune system to high levels of cancer cell antigens[9]



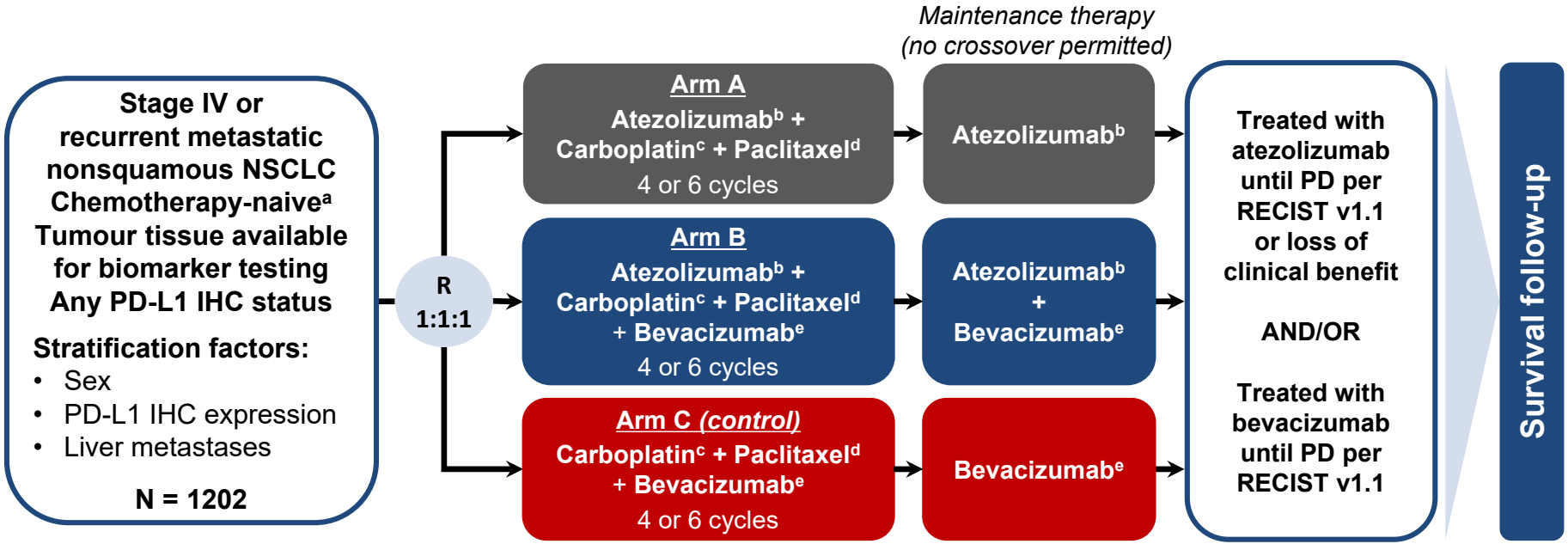
Normalization of the tumour vasculature through VEGF inhibition increases T-cell tumour infiltration[2,5-8]

VEGF blockade can establish an immune-permissive tumour microenvironment by decreasing myeloid-derived suppressor cell and regulatory T cell populations[2,8,10-13]

- Atezolizumab's T-cell mediated cancer cell killing may be enhanced through bevacizumab's reversal of VEGF-mediated immunosuppression

1. Ferrara N, et al. Nat Rev Drug Discov, 2004. 2. Hegde PS, et al. Semin Cancer Biol. 2017 . 3. Gabrilovich DI, et al. Nat Med, 1996. 4. Oyama T, et al. J Immunol, 1998. 5. Goel S, et al. Physiol Rev, 2011. 6. Motz GT, et al. Nat Med, 2014. 7. Hodi FS, et al. Cancer Immunol Res, 2014. 8. Wallin JJ, et al. Nat Commun, 2016. 9. Zitvogel L, et al. Immunity, 2013. 10. Gabrilovich DI, Nagaraj S. Nat Rev Immunol, 2009. 11. Roland CL, et al. PLoS One, 2009. 12. Facciabene A, et al. Nature, 2011. 13. Voron T, et al. J Exp Med, 2015.
Figure adapted from Chen DS, Mellman I. Immunity, 2013.

IMpower150 Study Design

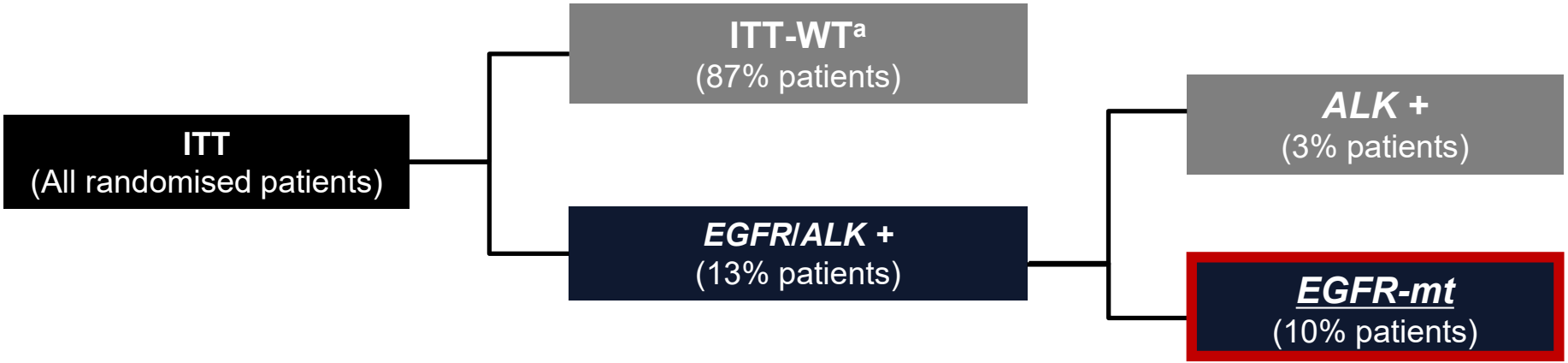


- In IMpower150, Arm B (ABCP) prolonged PFS and OS vs Arm C (BCP) in patients with first-line nonsquamous NSCLC, including patients with EGFR genomic alterations

[a] Patients with a sensitizing EGFR mutation or ALK translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies. [b] Atezolizumab: 1200 mg IV q3w. [c] Carboplatin: AUC 6 IV q3w. [d] Paclitaxel: 200 mg/m2 IV q3w. [e] Bevacizumab: 15 mg/kg IV q3w.

IMpower150 Subgroup Population and Objectives

- The efficacy and safety of atezolizumab and/or bevacizumab with chemotherapy is being further analysed in the subpopulation of patients with EGFR mutations



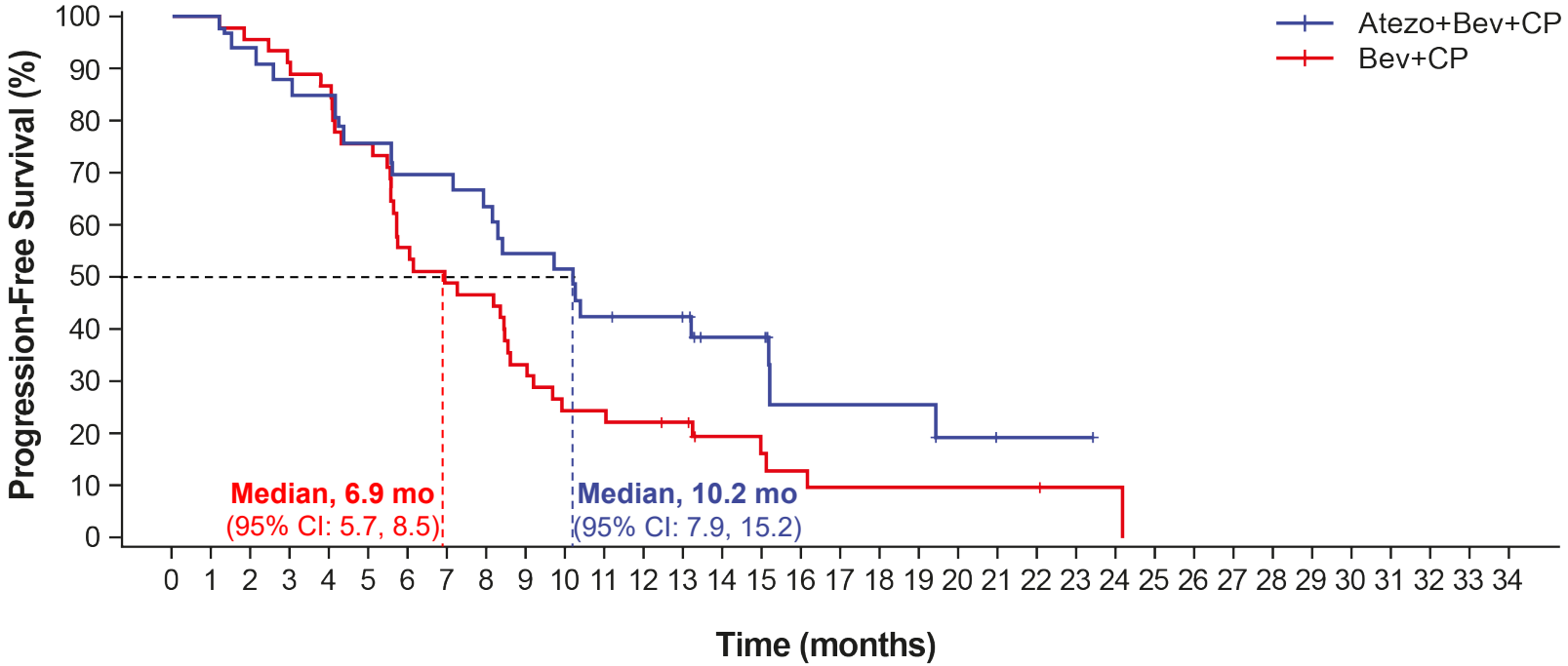
[a] WT refers to patients without EGFR or ALK genetic alterations.
ABCP, atezolizumab + bevacizumab + carboplatin + paclitaxel; BCP, bevacizumab + carboplatin + paclitaxel.

Baseline Characteristics in *EGFR*-mt patients

Baseline characteristics of *EGFR*-mutant patients	Arm A: atezo + CP (n = 45)	Arm B: atezo + bev + CP (n = 34)	Arm C (control): bev + CP (n = 45)
Median age (range), years	63 (38-82)	64 (37-76)	61 (31-81)
Sex, male, n (%)	17 (38%)	18 (53%)	21 (47%)
ECOG PS, 0, n (%)	20 (44%)	18 (53%)	27 (60%)
Tobacco use history, n (%)			
Current/previous smoker	16 (36%)	14 (41%)	25 (56%)
Never smoker	29 (64%)	20 (59%)	20 (44%)
Liver metastases, yes, n (%)	9 (20%)	4 (12%)	7 (16%)

These data represent ≥ 20-mo follow-up (data cutoff: 22 Jan 2018). 124 patients were EGFR-mt, including 91 with a sensitising mutation. Baseline characteristics of patients with EGFR-mt across the treatment arms were generally comparable to the ITT population.
Data cutoff 22 Jan 2018.

PFS in *EGFR*-mt patients (Arm B vs Arm C)



No. at Risk																							
Atezo+Bev+CP	34	33	31	29	28	25	23	23	21	18	17	14	13	12	8	8	4	4	4	4	2	1	1	1
Bev+CP	45	45	43	41	39	34	25	22	21	15	11	11	10	9	6	5	4	3	2	2	2	2	1	1

Data cutoff 22 Jan 2018.

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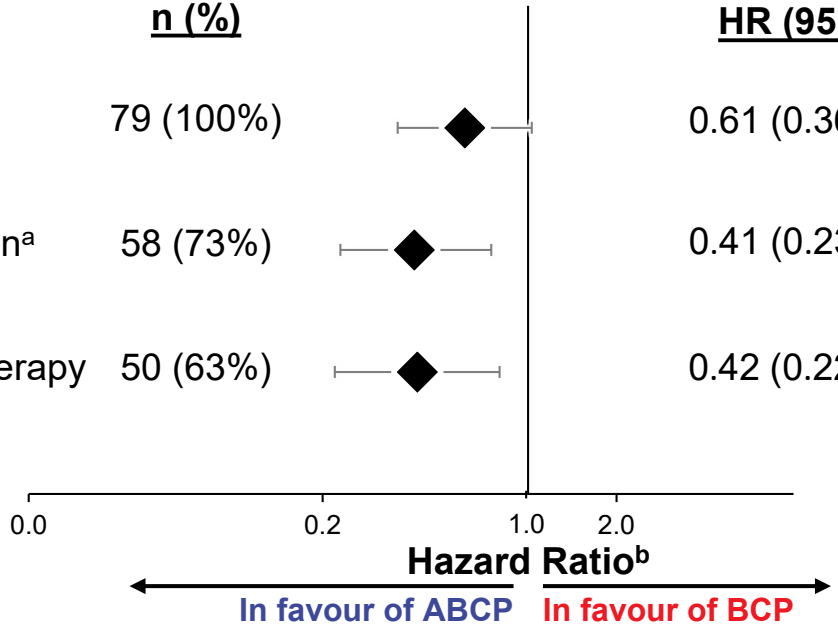
PFS in *EGFR*-mt patients (Arm B vs Arm C)

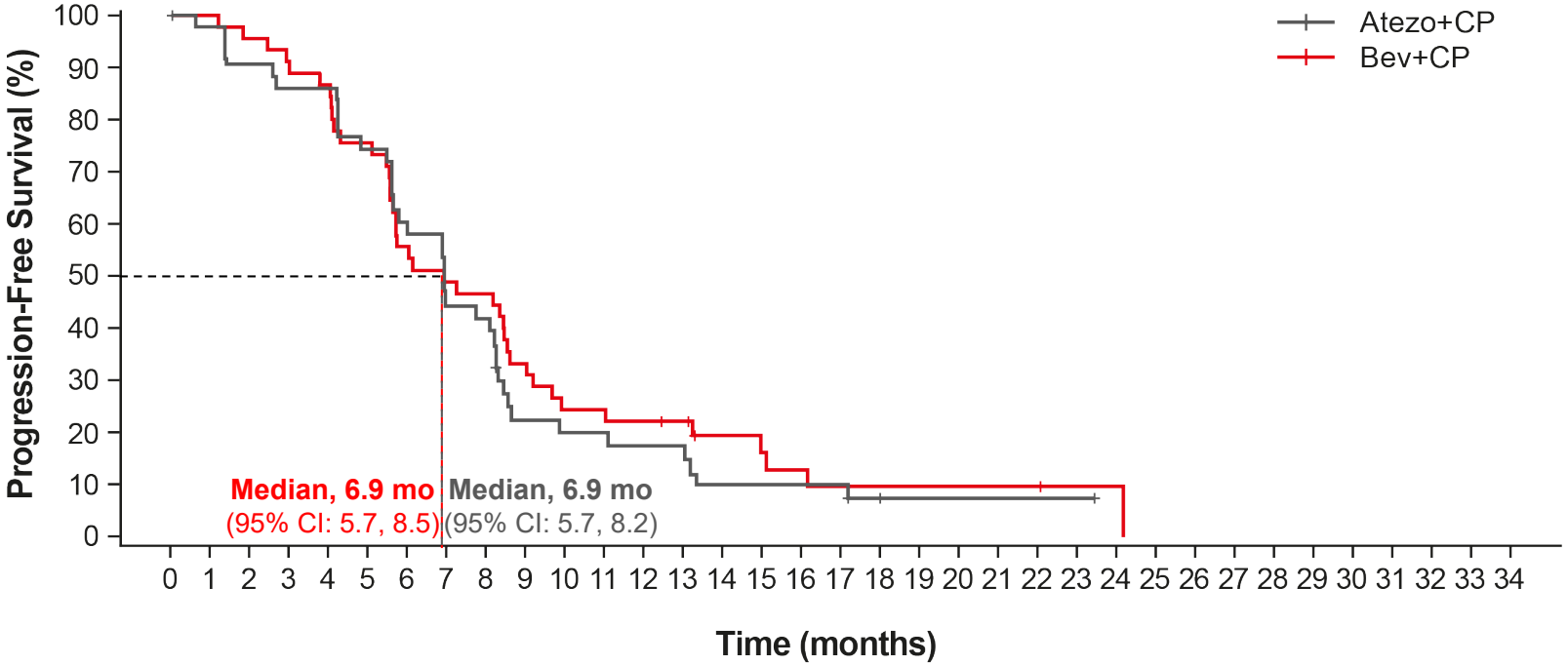
Subgroup	n (%)	HR (95% CI)	Median PFS, mo ABCP	Median PFS, mo BCP
EGFR Mutation	79 (100%)	0.61 (0.36–1.03)	10.2	6.9
Sensitising *EGFR* Mutation[a]	58 (73%)	0.41 (0.23–0.75)	10.3	6.1
Received Prior TKI Therapy	50 (63%)	0.42 (0.22–0.80)	9.7	6.1



- The addition of atezolizumab to bevacizumab and chemotherapy increased PFS benefit across all *EGFR*-mut patient subgroups, especially those who have received prior TKI

[a] Defined as exon 19 deletions or L858R mutations. [b] Unstratified HR.
Data cutoff 22 Jan 2018.

PFS in *EGFR*-mt patients (Arm A vs Arm C)



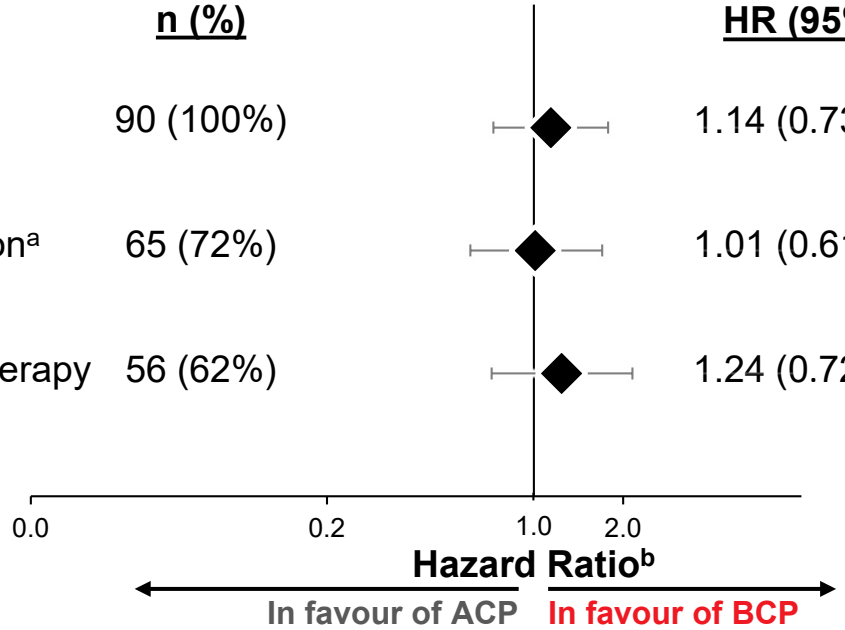
No. at Risk

Atezo+CP	45	42	39	37	37	32	26	19	18	9	8	8	7	7	4	4	4	4	2	1	1	1	1	1
Bev+CP	45	45	43	41	39	34	25	22	21	15	11	11	10	9	6	5	4	3	2	2	2	2	1	1

Data cutoff 22 Jan 2018.

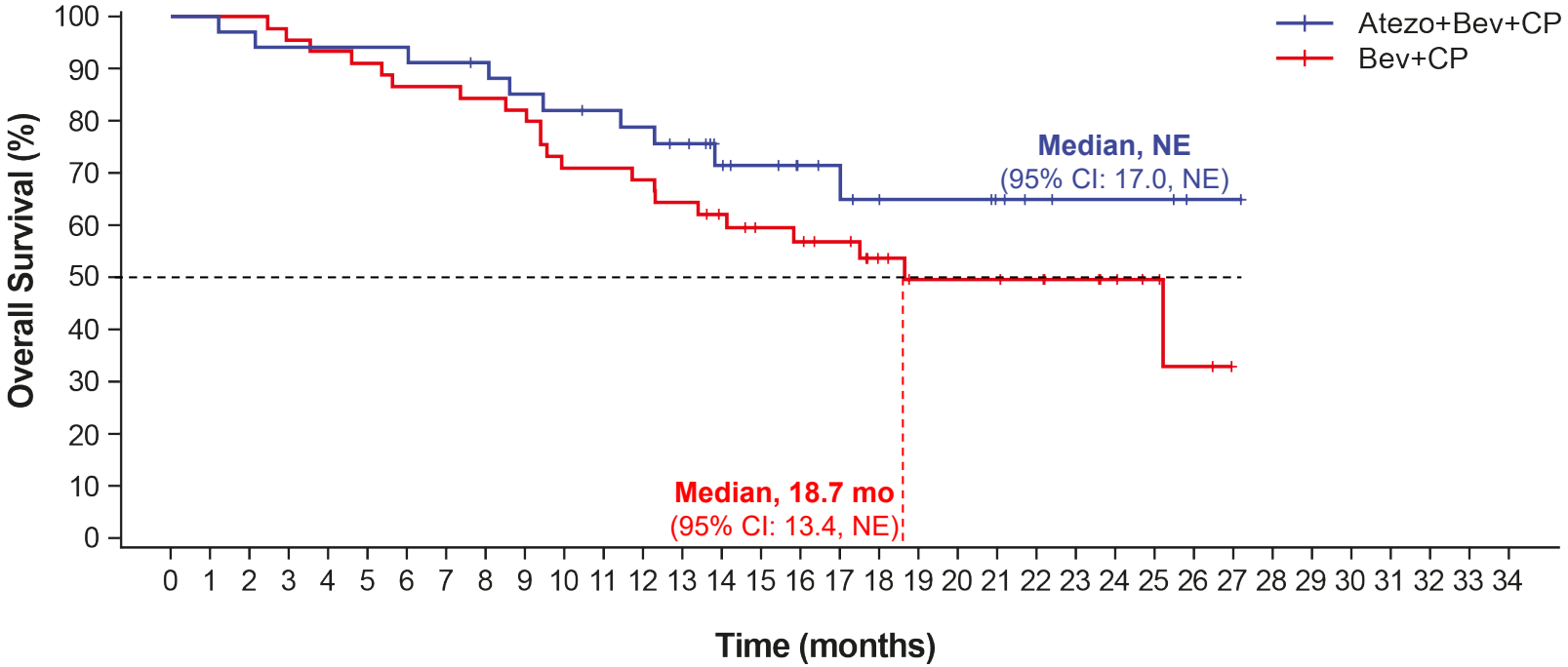
PFS in *EGFR*-mt patients (Arm A vs Arm C)

Subgroup	n (%)	HR (95% CI)	Median PFS, mo ACP	Median PFS, mo BCP
EGFR Mutation	90 (100%)	1.14 (0.73–1.78)	6.9	6.9
Sensitising *EGFR* Mutation[a]	65 (72%)	1.01 (0.61–1.70)	6.0	6.1
Received Prior TKI Therapy	56 (62%)	1.24 (0.72–2.15)	5.7	6.1



[a] Defined as exon 19 deletions or L858R mutations. [b] Unstratified HR
Data cutoff 22 Jan 2018.

OS in *EGFR*-mt patients (Arm B vs Arm C)

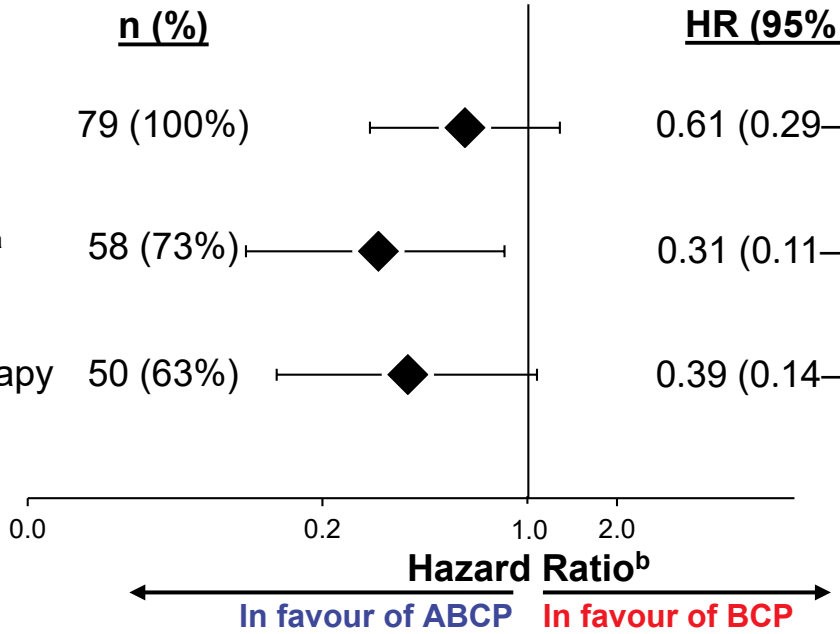


No. at Risk																										
Atezo+Bev+CP	34	34	33	32	32	32	32	31	30	28	27	26	25	23	17	15	12	11	9	8	8	6	4	3	3	3	1	1
Bev+CP	45	45	45	43	42	41	39	39	38	37	32	32	31	29	25	22	21	19	14	11	11	11	10	8	6	4	2	

Data cutoff 22 Jan 2018.

OS in *EGFR*-mt patients (Arm B vs Arm C)

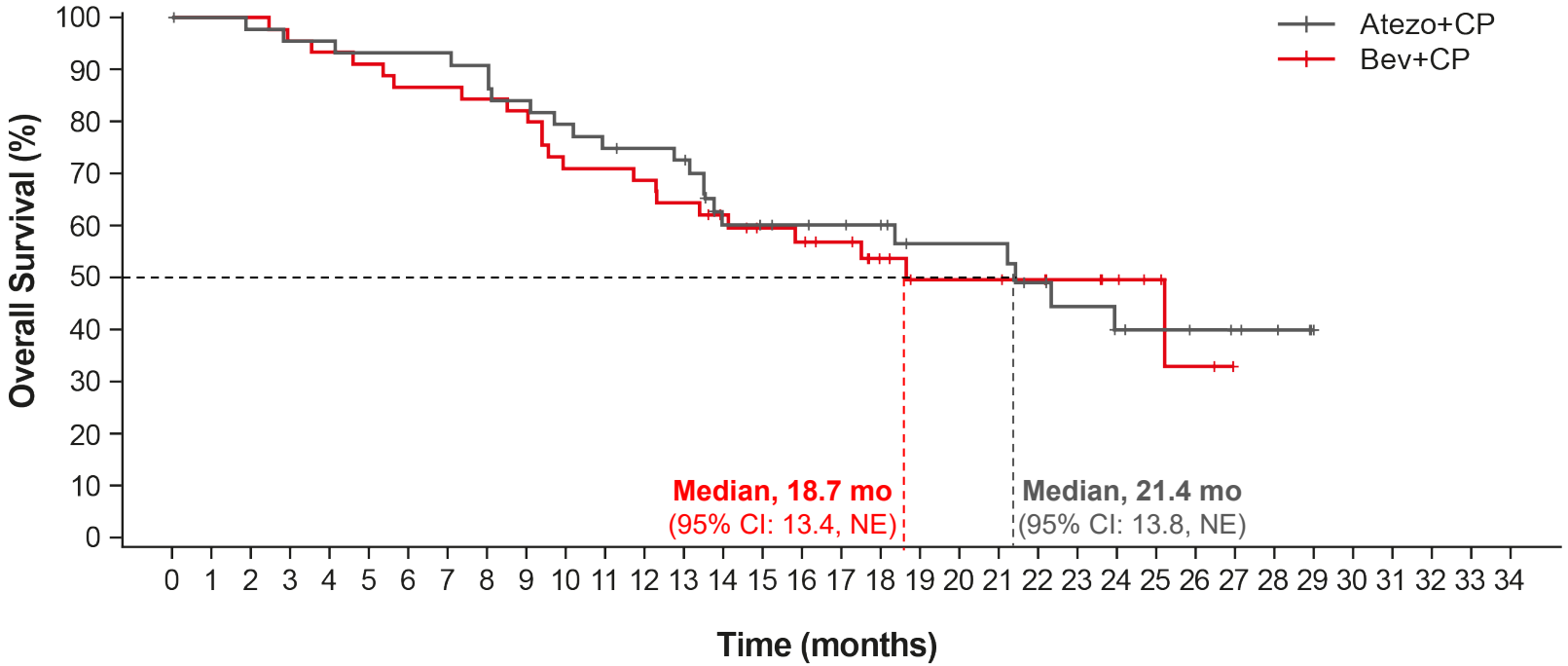
Subgroup	n (%)	HR (95% CI)	Median OS, mo ABCP	Median OS, mo BCP
EGFR Mutation	79 (100%)	0.61 (0.29–1.28)	NE	18.7
Sensitising *EGFR* Mutation[a]	58 (73%)	0.31 (0.11–0.83)	NE	17.5
Received Prior TKI Therapy	50 (63%)	0.39 (0.14–1.07)	NE	17.5



- The addition of atezolizumab to bevacizumab and chemotherapy increased OS benefit across all *EGFR* patient subgroups

NE, not estimable.
[a] Defined as exon 19 deletions or L858R mutations. [b] Unstratified HR.
Data cutoff 22 Jan 2018.

OS in *EGFR*-mt patients (Arm A vs Arm C)



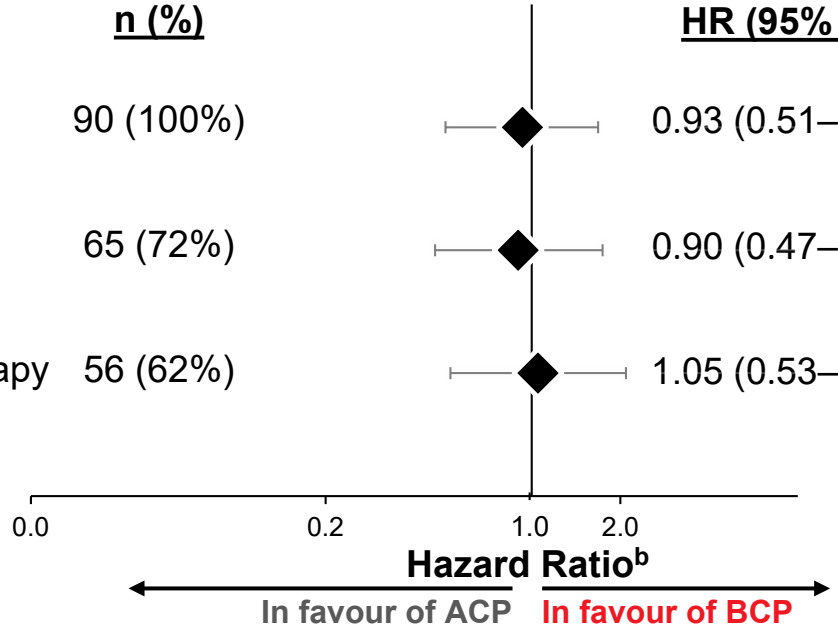
No. at Risk

Atezo+CP	45	44	43	42	42	41	41	41	40	37	35	33	32	31	23	22	21	20	19	15	15	15	12	10	8	7	6	5	4	1
Bev+CP	45	45	45	43	42	41	39	39	38	37	32	32	31	29	25	22	21	19	14	11	11	11	10	8	6	4	2			

Data cutoff 22 Jan 2018.

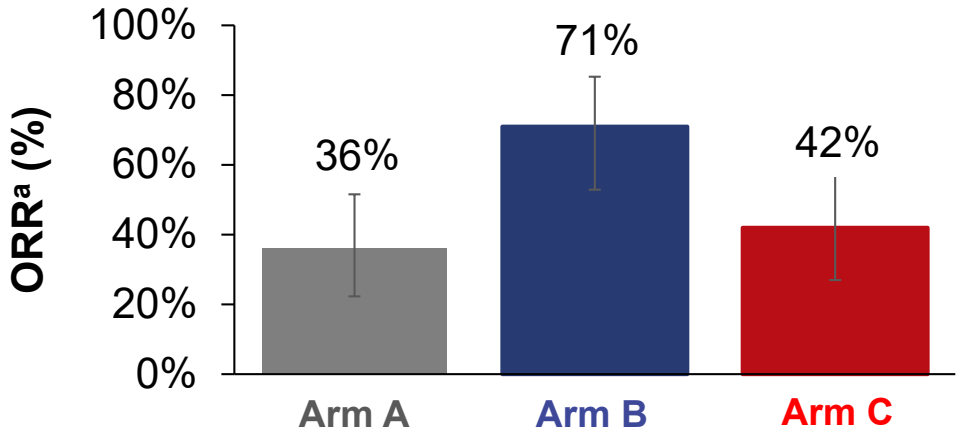
OS in *EGFR*-mt patients (Arm A vs Arm C)

Subgroup	n (%)	HR (95% CI)	Median OS, mo ACP	Median OS, mo BCP
EGFR Mutation	90 (100%)	0.93 (0.51–1.68)	21.4	18.7
Sensitising *EGFR* Mutation[a]	65 (72%)	0.90 (0.47–1.74)	21.2	17.5
Received Prior TKI Therapy	56 (62%)	1.05 (0.53–2.09)	14.0	17.5



[a] Defined as exon 19 deletions or L858R mutations. [b] Unstratified HR
Data cutoff 22 Jan 2018.

ORR and DOR in *EGFR*-mt patients

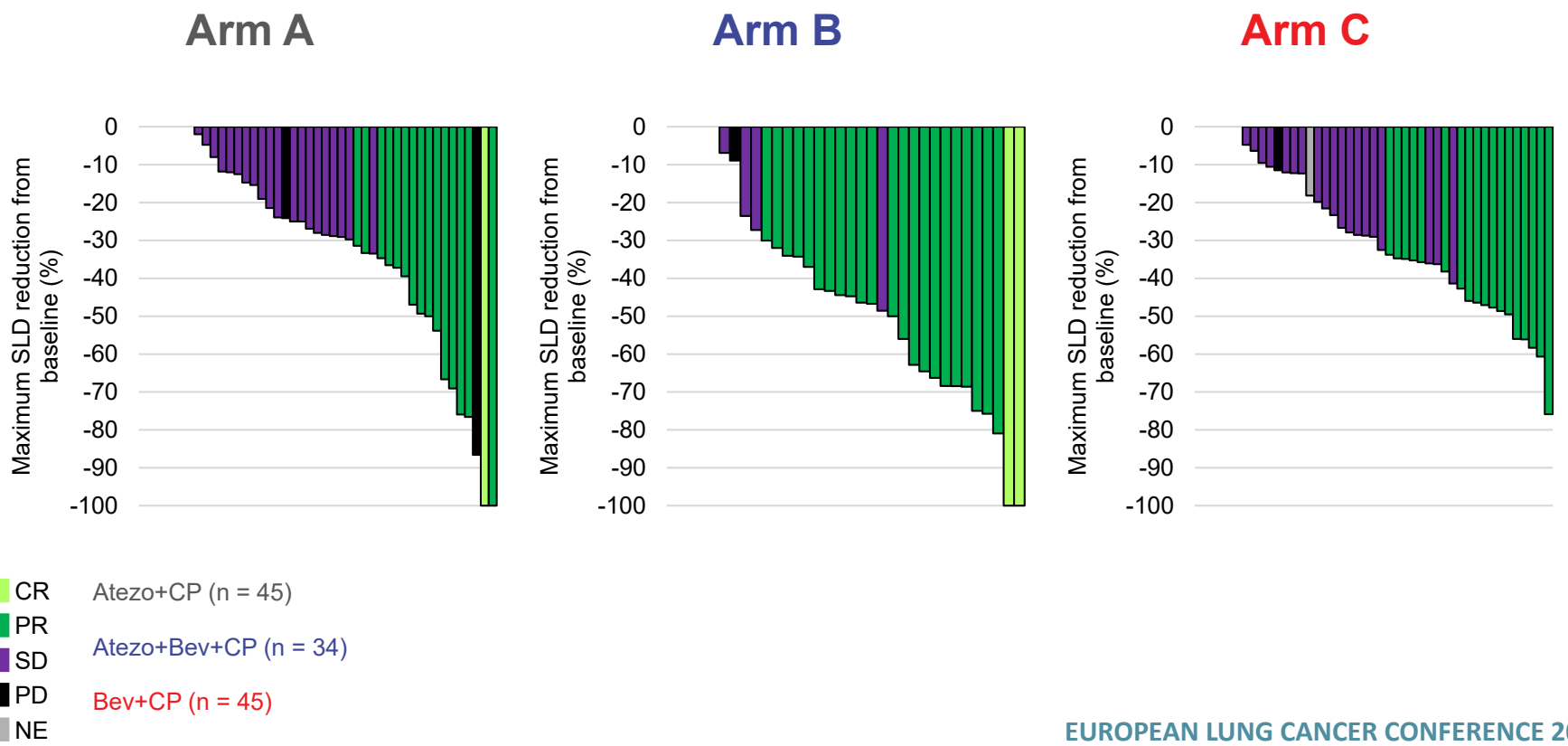


	Atezo + CP	Atezo + bev + CP	Bev + CP
Median DOR (range), mo	5.6 (2.6–15.2)	11.1 (2.8–18.0)	4.7 (2.6–13.5)

- The addition of bevacizumab to atezolizumab and chemotherapy almost doubled the overall response rate and duration of response in *EGFR*-mt patients

[a] Responses are confirmed. Includes patients with measurable disease.
Data cutoff 22 Jan 2018.

Best confirmed overall response in *EGFR*-mt patients



Data cutoff 22 Jan 2018.

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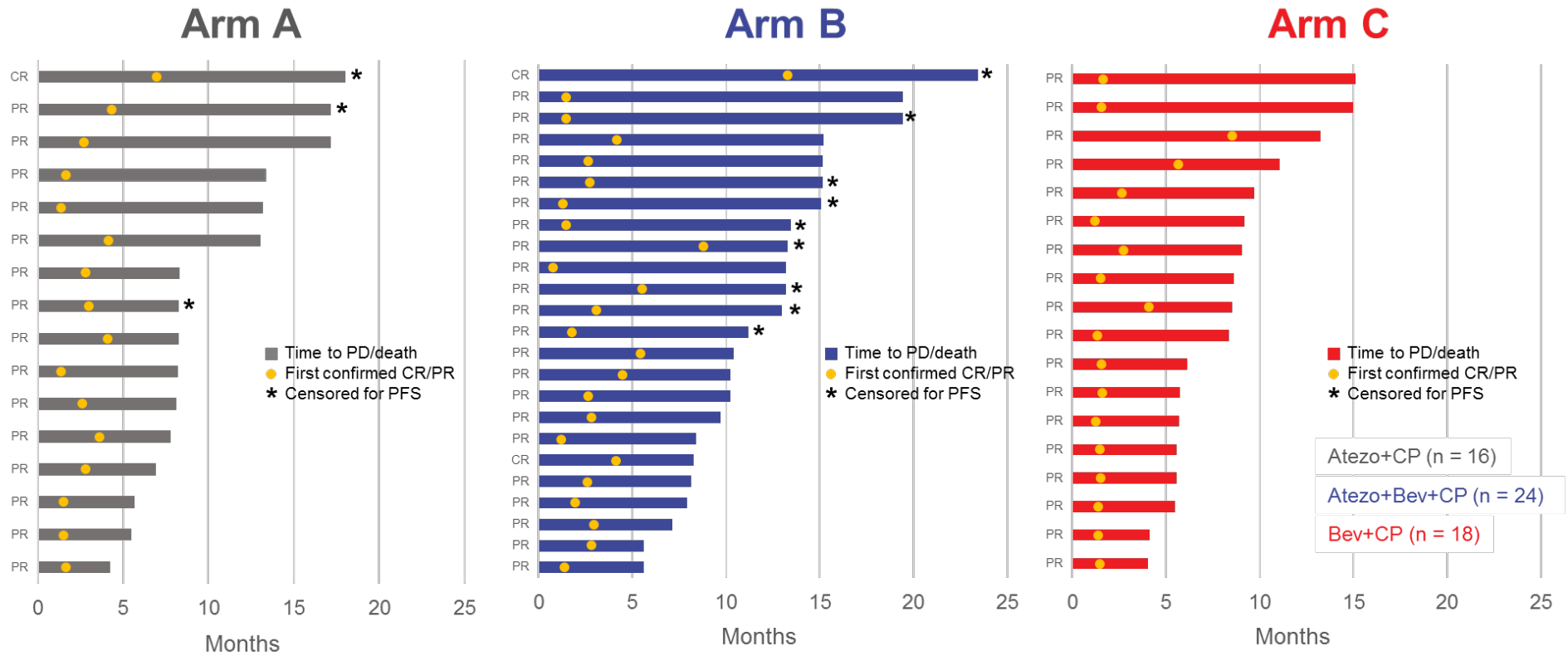
Time to PD/death in *EGFR*-mt patients



Data cutoff 22 Jan 2018.

Safety *EGFR*-mt patients

Incidence	Arm A: atezo + CP (n = 44)	Arm B: atezo + bev + CP (n = 33)	Arm C (control): bev + CP (n = 44)
Median number of doses received (range)			
Atezolizumab	10 (1-43)	14 (1-38)	NA
Bevacizumab	NA	12 (1-38)	8.5 (1-38)
Treatment-related AE[a]	39 (89%)	33 (100%)	42 (96%)
Grade 3-4	25 (57%)	21 (64%)	25 (57%)
Grade 5[b]	0 (0%)	0 (0%)	1 (2%)
Serious AE	15 (34%)	12 (36%)	9 (21%)
AE leading to withdrawal from any treatment	6 (14%)	11 (33%)	7 (16%)
Immune-related AEs[c] in > 5 patients in any arm			
Rash	16 (36%)	10 (30%)	5 (11%)
Hypothyroidism	1 (2%)	6 (18%)	1 (2%)

[a] Related to any study treatment. [b] Pulmonary haemorrhage. [c] Immune-related AEs were defined using MedDRA Preferred Terms that included both diagnosed immune conditions and signs and symptoms potentially representative of immune-related events, regardless of investigator-assessed causality. Data cutoff 22 Jan 2018.

Summary

- IMpower150 met its co-primary PFS and OS endpoints and demonstrated a statistically significant and clinically meaningful benefit with atezolizumab + bevacizumab + chemotherapy vs bevacizumab + chemotherapy in 1L nonsquamous NSCLC[1]
- Adding atezolizumab to standard-of-care bevacizumab and chemotherapy increased OS and PFS benefit across the examined *EGFR* patient subgroups
- Therefore, this combination treatment may represent a potential new option in *EGFR*-mutant patients for whom TKIs have failed

1. Socinski, MA, et al. *N Engl J Med*, 2018.

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