VIRTUAL 2020 ESMO congress

IMpassion130: final OS analysis from the pivotal Phase III study of atezolizumab + *nab*-paclitaxel vs placebo + *nab*-paclitaxel in previously untreated locally advanced or metastatic triple-negative breast cancer

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Disclosures

- Dr Emens has the following to disclose:
  - Honoraria from AbbVie, Amgen, Celgene, Chugai, Gritstone, MedImmune, Peregrine, Shionogi and Syndax
  - Honoraria and travel support from AstraZeneca, Bayer, MacroGenics, Replimune and Vaccinex
  - Travel support from Bristol Myers Squibb, Genentech/Roche and Novartis
  - Potential future stock from MolecuVax
  - Institutional support from Aduro Biotech, AstraZeneca, Bolt Biotherapeutics, the Breast Cancer Research Foundation, Bristol Myers Squibb, Corvus, the US Department of Defense, EMD Serono, Genentech, MaxCyte, Merck, the National Cancer Institute, the NSABP Foundation, Roche, Silverback, the Translational Breast Cancer Research Consortium, Tempest and HeritX
  - Royalties from Aduro Biotech
  - Other (Roche): uncompensated IMpassion130 study steering committee co-chair and KATE2 study steering committee chair

IMpassion130 background

- mTNBC has a poor prognosis compared with other breast cancer subtypes[1,2]
- IMpassion130 (NCT02425891) is a global randomised, double-blind Phase III trial of atezolizumab + *nab*-paclitaxel (A + nP) compared with placebo + *nab*-paclitaxel nP (P + nP) in previously untreated inoperable locally advanced or mTNBC[3,4]
  - Co-primary endpoints were PFS (tested in ITT and PD-L1 immune cell [IC]+ patients[a]) and OS (in ITT, then if significant, the PD-L1 IC+ patients)
- The primary PFS analysis demonstrated statistically significant benefit with A + nP vs P + nP in the ITT and PD-L1 IC+ populations
  - In the first and second interim OS analyses, although not formally tested due to the pre-specified statistical analysis plan, meaningful improvement in OS was observed in the PD-L1 IC+ population
  - At both analyses, A + nP was tolerable, and its safety profile was consistent with that of each agent
- Based on findings from this pivotal study, international guidelines now recommend A + nP for the 1L treatment of patients with mTNBC whose tumours express PD-L1 on IC[5,6]

1L, first line; IC, tumour-infiltrating immune cells; ITT, intention-to-treat; mTNBC, metastatic triple-negative breast cancer; PFS, progression-free survival; OS, overall survival; PD-L1, programmed death ligand-1. [a] PD-L1-expressing IC covering ≥ 1% of tumour area (VENTANA SP142 IHC assay). References: 1. den Brok, *Breast Cancer Res Treat* 2017. 2. Bomotto, *Oncologist* 2014. 3. Schmid, *N Engl J Med* 2018. 4. Schmid, ASCO 2019. 5. NCCN Breast Cancer. V1.2020. 6. Thill, *Breast Care* 2019.

IMpassion130 study design[1]

Key eligibility criteria

- Histologically documented metastatic or inoperable, locally advanced TNBC
- No prior therapy for advanced TNBC[a]
  - Prior chemotherapy including taxanes allowed in curative setting if treatment-free interval ≥ 12 mo
- ECOG PS 0-1
- Eligible for taxane monotherapy
- Tumour tissue for PD-L1 testing

(N = 902)

R 1:1

Double-blind

Atezolizumab[b] + *nab*-paclitaxel[c]

Placebo + *nab*-paclitaxel[c]

Treatment until progression or unacceptable toxicity

Stratification factors

- Liver metastases (yes vs no)
- Prior taxanes (yes vs no)
- PD-L1 IC status (positive vs negative)[a]

Co-primary endpoints:

- PFS[d] and OS (hierarchically tested in ITT and PD-L1 IC+ populations)

[a] PD-L1 IC ≥ 1% vs < 1% per VENTANA SP142 assay. [b] 840 mg IV on days 1 and 15 (28-day cycle).
[c] 100 mg/m^2 IV on days 1, 8 and 15 (28-day cycle). [d] Per RECIST 1.1. Reference: 1. Schmid, *N Engl J Med* 2018.

Baseline characteristics (primary analysis)[1]

Characteristic	ITT population	
	Atezolizumab + *nab*-paclitaxel (n = 451)	Placebo + *nab*-paclitaxel (n = 451)
Median age (range), years	55 (20-82)	56 (26-86)
≥ 65 years, n (%)	104 (23)	115 (26)
Race, n (%)[a]		
White	308 (68)	301 (67)
Asian	85 (19)	76 (17)
Black/African American	26 (6)	33 (7)
ECOG PS 1, n/N (%)	193/450 (43)	179/450 (40)
PD-L1 IC+, n (%)[b]	185 (41)	184 (41)
Metastatic disease, n/N (%)	404/450 (90)	408/450 (91)
Liver metastases, n (%)	126 (28)	118 (26)
Prior taxane therapy, n (%)	231 (51)	230 (51)

[a] Per case-report form. [b] Per VENTANA SP142 assay. Reference: 1. Schmid, *N Engl J Med* 2018.

Disposition (final analysis)

	ITT population	
	Atezolizumab + *nab*-paclitaxel (n = 451)	Placebo + *nab*-paclitaxel (n = 451)
On study, n (%)		
Alive on treatment	27 (6)	8 (2)
Alive in survival follow-up	68 (15)	78 (17)
Discontinued study, n (%)		
Died	322 (71)	344 (76)
Lost to follow-up	34 (8)	21 (5)
Median duration of follow-up, months	19.7	18.0

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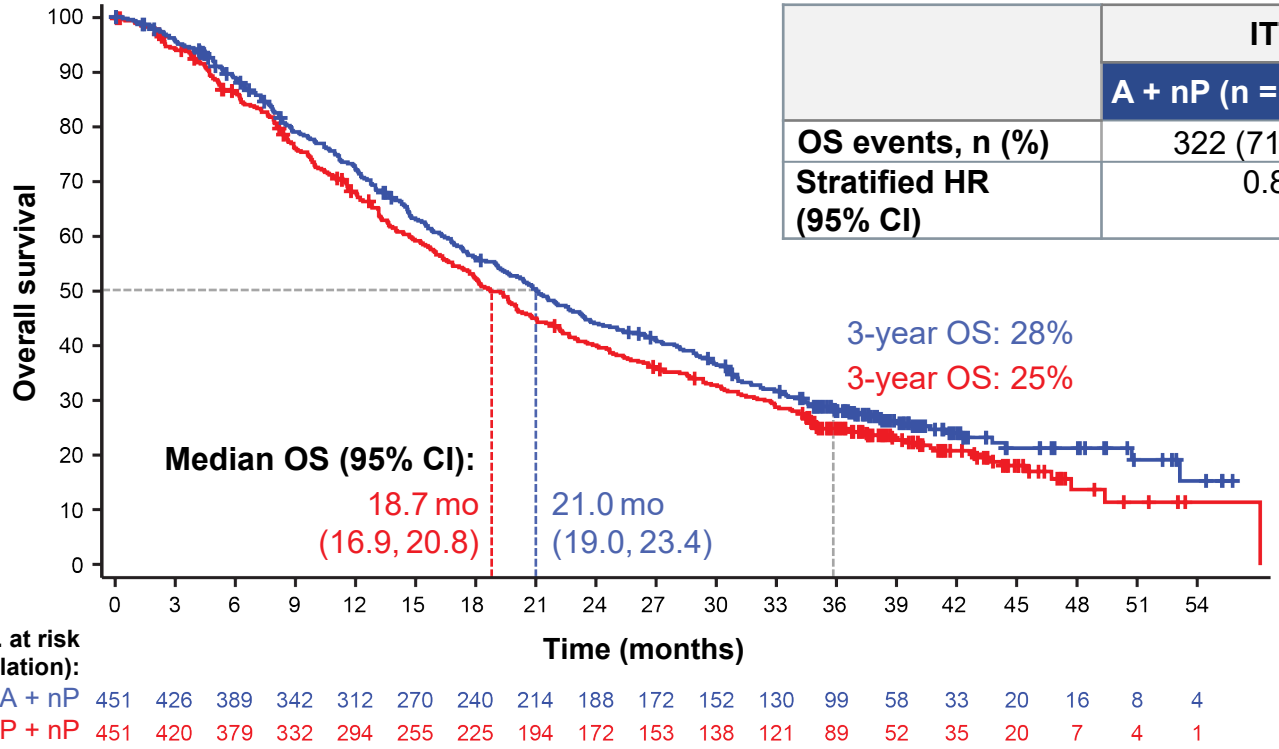
OS in the ITT population



	ITT population	
	A + nP (n = 451)	P + nP (n = 451)
OS events, n (%)	322 (71)	344 (76)
Stratified HR (95% CI)	0.87 (0.75, 1.02) *P* = 0.077	

Data cutoff, 14 April 2020. Median survival follow-up, 18.8 months (all patients). HR, hazard ratio.

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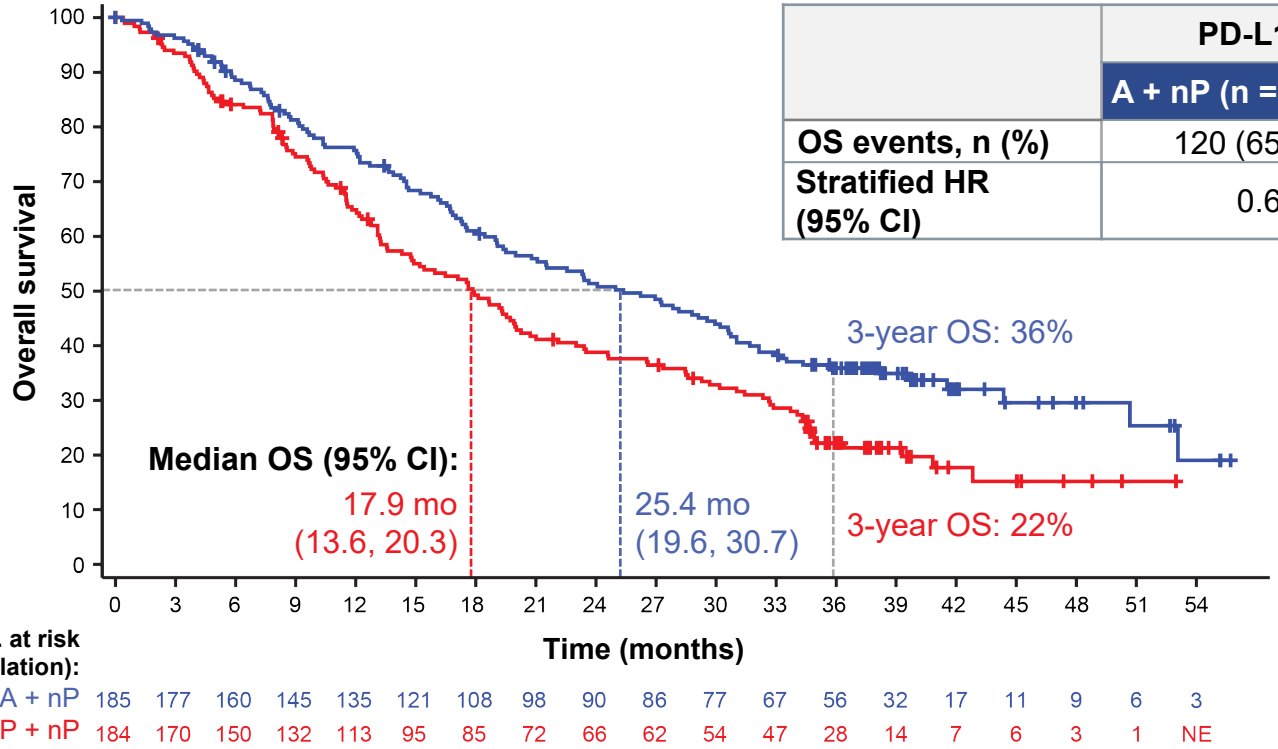
OS in the PD-L1 IC+ population



	PD-L1 IC+ population	
	A + nP (n = 185)	P + nP (n = 184)
OS events, n (%)	120 (65)	139 (76)
Stratified HR (95% CI)	0.67 (0.53, 0.86)[a]	

Data cutoff, 14 April 2020. NE, not estimable.

[a] *P* value not displayed since OS in the PD-L1+ population was not formally tested due to the hierarchical study design.

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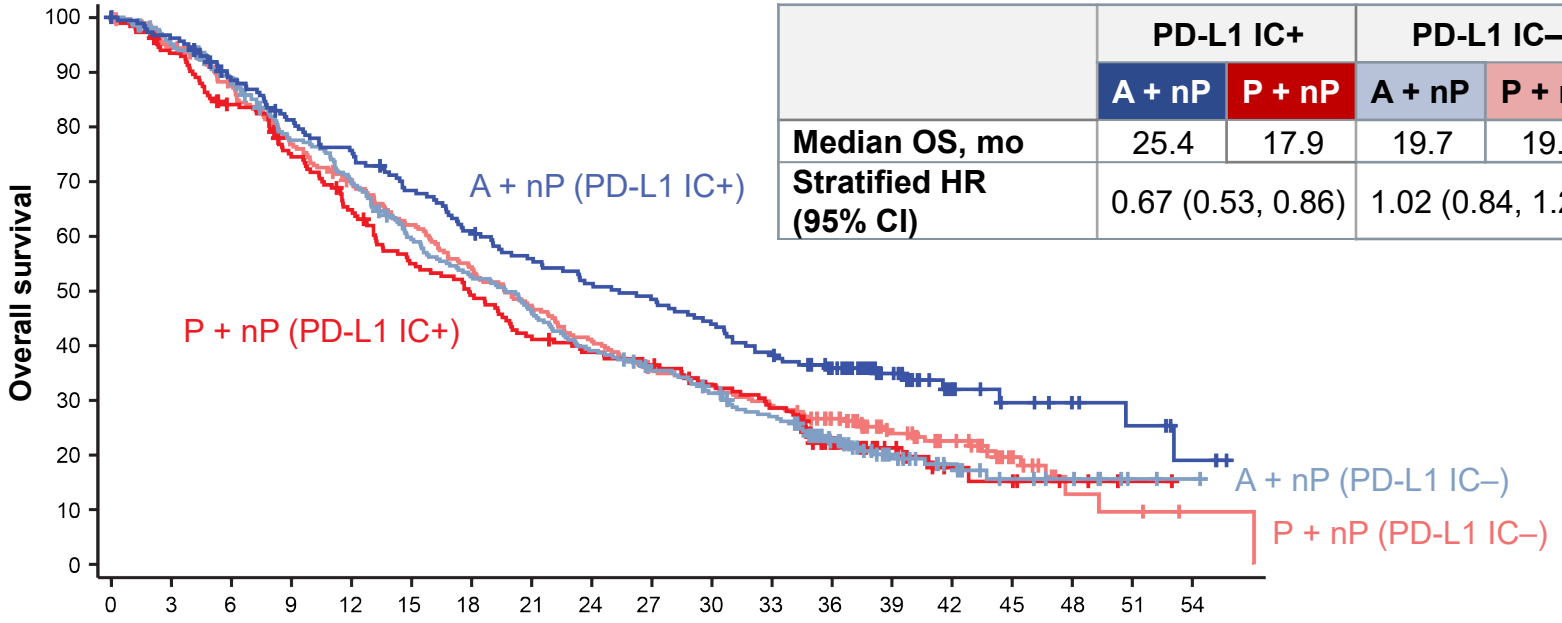
OS by PD-L1 IC status (PD-L1 IC+ vs PD-L1 IC–)

	PD-L1 IC+		PD-L1 IC–	
	A + nP	P + nP	A + nP	P + nP
Median OS, mo	25.4	17.9	19.7	19.7
Stratified HR (95% CI)	0.67 (0.53, 0.86)		1.02 (0.84, 1.24)	



No. at risk																			
A + nP (PD-L1 IC+)	185	177	160	145	135	121	108	98	90	86	77	67	56	32	17	11	9	6	3
A + nP (PD-L1 IC–)	266	249	229	197	177	149	132	116	98	86	75	63	43	26	16	9	7	2	1
P + nP (PD-L1 IC+)	184	170	150	132	113	95	85	72	66	62	54	47	28	14	7	6	3	1	NE
P + nP (PD-L1 IC–)	267	250	229	200	181	160	140	122	106	91	84	74	61	38	28	14	4	3	1

Data cutoff, 14 April 2020.

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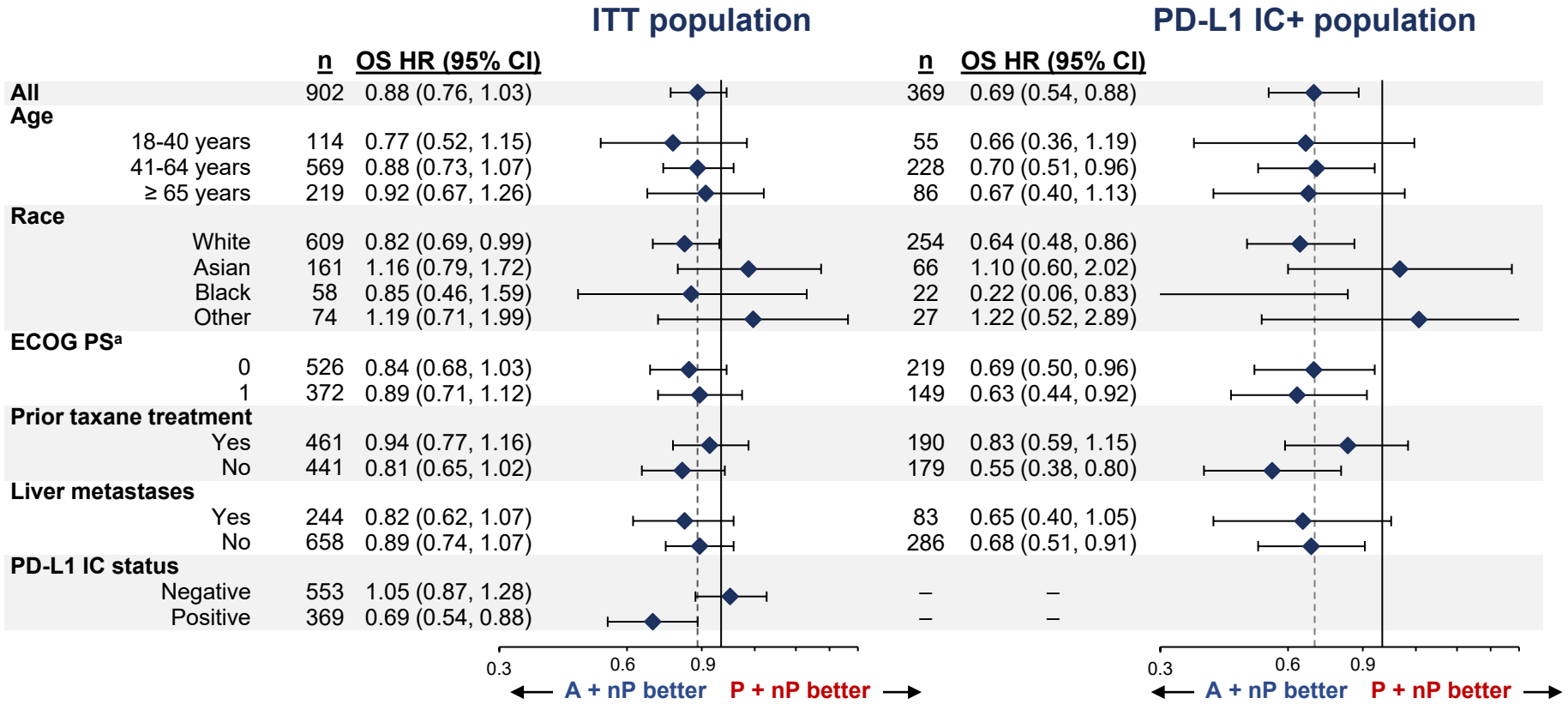
OS in clinical subgroups



Data cutoff, 14 April 2020.
Dashed line refers to all-patient or PD-L1 IC+ HR. [a] Patients with PS 2 or missing status (n = 2 each) not shown.

Safety summary

Safety-evaluable population[a]	Atezolizumab + *nab*-paclitaxel (n = 460)		Placebo + *nab*-paclitaxel (n = 430)	
	Atezolizumab	*nab*-paclitaxel	Placebo	*nab*-paclitaxel
Treatment exposure, n (%)				
Up to 24 months	60 (13)	35 (8)	19 (4)	14 (3)
≥ 24 months	38 (8)	22 (5)	3 (1)	6 (1)
Deaths	322 (70)		337 (78)	
All-Grade AEs[b]	457 (99)		421 (98)	
Grade 3-4	233 (51)		183 (43)	
Treatment-related Grade 3/4 AEs	191 (42)		129 (30)	
Grade 5 AEs	6 (1)		3 (1)	
Treatment-related Grade 5 AEs[c]	2 (< 1)		1 (< 1)	
Serious AEs	110 (24)		80 (19)	
Treatment-related serious AEs	58 (13)		31 (7)	
AE leading to any treatment withdrawal[d]	88 (19)		36 (8)	
AE leading to atezolizumab/placebo withdrawal	37 (8)		4 (1)	
AE leading to *nab*-paclitaxel withdrawal	85 (19)		36 (8)	
AESI[e]	270 (59)		179 (42)	
Grade 3-4 AESI	39 (9)		20 (5)	

AE, adverse event; AESI, AE of special interest. [a] Patients who received any amount of any study drug. [b] No confirmed or suspected COVID-19 AEs were reported. [c] Grade 5 AEs: autoimmune hepatitis (A), septic shock, (A + nP) hepatic failure (P + nP). [d] Most commonly due to neuropathy. [e] Sponsor defined based on immune-mediated risks of atezolizumab and other in-class agents.

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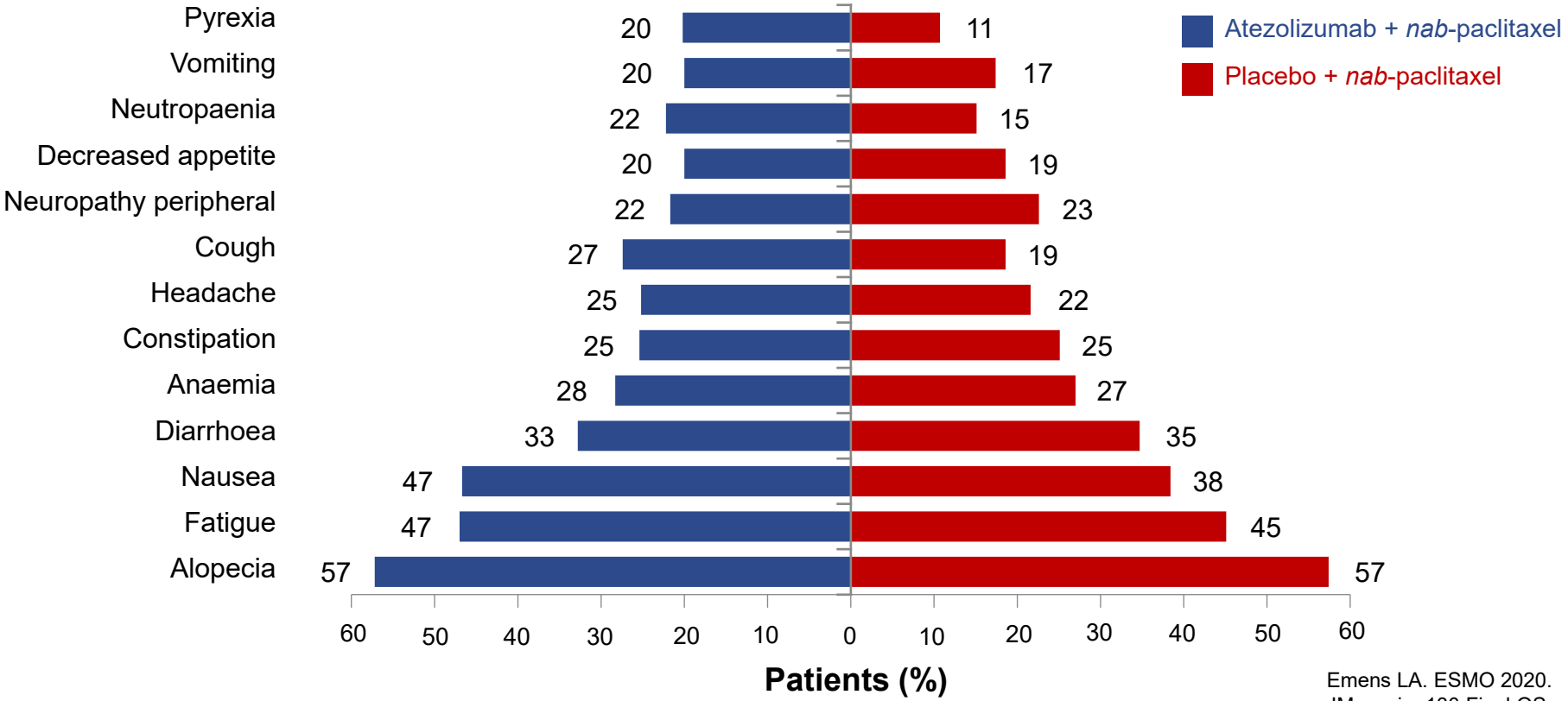
AEs with ≥ 20% incidence



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Atezolizumab AESIs

AE (medical concept), n (%)[a]	Atezolizumab + *nab*-paclitaxel (n = 460)		Placebo + *nab*-paclitaxel (n = 430)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
Hepatitis (diagnosis)[b]	11 (2)	7 (2)	7 (2)	1 (< 1)
Hypothyroidism	84 (18)	0	19 (4)	0
Hyperthyroidism	22 (5)	1 (< 1)	5 (1)	0
Adrenal insufficiency	5 (1)	1 (< 1)	0	0
Pneumonitis	18 (4)	2 (< 1)	1 (< 1)	0
Colitis	7 (2)	2 (< 1)	3 (1)	1 (< 1)
Pancreatitis[c]	2 (< 1)	1 (< 1)	0	0
Diabetes mellitus	1 (< 1)	1 (< 1)	3 (1)	2 (< 1)
Hypophysitis	1 (< 1)	1 (< 1)	0	0
Myositis	3 (1)	1 (< 1)	1 (< 1)	1 (< 1)
Rash	165 (36)	5 (1)	112 (26)	2 (1)
Severe cutaneous reactions	4 (1)	1 (< 1)	3 (1)	0

[a] Grouped MedDRA preferred terms. [b] Sponsor-defined group of terms representing events suggestive of hepatitis.
[c] Enzyme elevations only.

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IMpassion130: summary

- Here we report mature OS data from the prespecified final OS analysis
  - The OS boundary for statistical significance was not crossed in the ITT population, precluding further formal testing
  - Clinical meaningful OS was observed in the PD-L1 IC+ population
    - Final OS HR, 0.67 (95% CI: 0.53, 0.86) and a +7.5-mo median OS improvement with A + nP vs P + nP
  - OS results in the PD-L1 IC+ population were consistent with the first and second interim analyses
    - OS HR, 0.62 (95% CI: 0.45, 0.86) in the first interim analysis and 0.71 (95% CI: 0.54, 0.93) in the second interim analysis
- With additional follow-up, A + nP remained safe and tolerable
  - The safety profile was consistent with those of the individual treatment components
  - No new safety signals were identified
- These results support a positive benefit-risk profile for A + nP as first-line therapy in patients with PD-L1 IC+ mTNBC

Acknowledgements

- The patients and their families
- The investigators and clinical study sites
- This study is sponsored by F. Hoffmann-La Roche, Ltd
- Medical writing assistance for this oral presentation was provided by Madhubrata Ghosh, PhD, of Health Interactions and funded by F. Hoffmann-La Roche, Ltd