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LBA15

Primary results from IMpassion131, a double-blind placebo-controlled randomised phase III trial of first-line paclitaxel (PAC) ± atezolizumab (atezo) for unresectable locally advanced/metastatic triple-negative breast cancer (mTNBC)

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Background

In the phase 3 IMpassion130 trial, combining atezo with first-line nab-paclitaxel for mTNBC showed significantly improved progression-free survival (PFS) and clinically meaningful overall survival (OS) benefit in patients with PD-L1+ mTNBC [Schmid NEJM 2018]. IMpassion131 (NCT03125902) evaluated atezo + PAC as first-line treatment for mTNBC.

Methods

Eligible patients (no prior systemic therapy or ≥12 months since [neo]adjuvant chemotherapy) were randomised 2:1 to atezo 840 mg or placebo (d 1 & 15 q28d), both with PAC 90 mg/m^2 (d 1, 8 & 15 q28d) until disease progression or unacceptable toxicity. Stratification factors were tumour PD-L1 status (immune cell [IC] expression <1% vs ≥1% by VENTANA SP142 assay), prior taxane, liver metastases and geographic region. The primary endpoint was investigator-assessed PFS, tested hierarchically first in the PD-L1+ (IC ≥1%) population, then in the intent-to-treat (ITT) population. OS and overall response rate (ORR) were secondary endpoints.

Results

Of 651 randomised patients, 45% had PD-L1+ mTNBC, 48% were taxane pretreated, 31% had de novo mTNBC and 27% liver metastases. Adding atezo to PAC did not improve PFS or OS in either the PD-L1+ or ITT populations (Table). PFS results in subgroups were consistent with primary results. PAC exposure was not compromised by the addition of atezo. Grade 5 (2% placebo vs 2% atezo) and grade 3/4 AEs (43% vs 49%) were balanced between arms and the safety profile was consistent with known risks of each study drug.Table: LBA15

	PD-L1+		ITT	
	Placebo + PAC (n=101)	Atezo + PAC (n=191)	Placebo + PAC (n=220)	Atezo + PAC (n=431)
Data cut-off: 15 Nov 2019				
PFS events, n (%)	64 (63)	115 (60)	155 (70)	283 (66)
Median PFS, months (95% CI)	5.7 (5.4–7.2)	6.0 (5.6–7.4)	5.6 (5.4–6.5)	5.7 (5.4–7.2)
PFS HR (95% CI)	0.82 (0.60–1.12)	0.86 (0.70–1.05)		
Stratified log-rank p-value	0.20	Not formally tested		
Best ORR, % (95% CI)[a]	55 (45–65)	63 (56–70)	47 (41–54)	54 (49–58)
Data cut-off: 19 Aug 2020				
Deaths, n (%)	38 (38)	82 (43)	97 (44)	207 (48)
Median OS, months (95% CI)	28.3 (19.1–NE)	22.1 (19.2–30.5)	22.8 (17.1–28.3)	19.2 (16.8–22.5)
OS HR (95% CI)	1.12 (0.76–1.65)	1.11 (0.87–1.42)		
2-year OS rate, % (95% CI)	51 (38–65)	49 (40–58)	45 (36–54)	42 (36–48)

[a]Unconfirmed

Conclusions

Atezo + PAC did not improve PFS or OS vs placebo + PAC. No new safety signals were seen. Potential reasons for the contrast with the benefit seen in IMpassion130 (atezo + nab-paclitaxel) need further exploration.

Clinical trial identification

NCT03125902.

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