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Efficacy of adjuvant anti-PD-L1 avelumab by tumor infiltrating lymphocytes (TILs) for high-risk triple-negative breast cancer in the phase III A-BRAVE trial

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Background

We investigated the efficacy of adjuvant avelumab according to TILs in pts with TNBC at high risk of relapse in the A-BRAVE trial.

Methods

The phase III A-BRAVE trial randomized 466 pts with high risk early TNBC to 1 year avelumab vs observation after surgery and neoadjuvant/adjuvant chemotherapy. High risk definition: high disease burden in case of primary surgery (n=83 Stratum A) or invasive residual disease after NACT (n=383 Stratum B). TILs were centrally scored: baseline (BSL) TILs on treatment-naive tumor samples, RD-TILs on post-NACT surgical samples (Stratum B). Here, we report DDFS by BSL-TILs and by combined BSL-TILs and RD-TILs in Stratum B, exploring interactions with treatment. When specified, cox models were adjusted for: age, stage at diagnosis, carboplatin (ITT); age, residual cancer burden, carboplatin, adjuvant capecitabine (Stratum B).

Results

BSL-TILs were associated with DDFS: adj HR 0.93, 95%CI 0.88-0.98, p=0.011 for each 5% increase; 3-yr DDFS rate 71.2% for BSL-TILs<30% and 82.2% for BSL-TILs>30%, p=0.017. RD-TILs further stratified DDFS in Stratum B: 3-yr DDFS 77.5% for BSL-TILs>30% & any RD-TILs, 82.5% for BSL-TILs<30% & RD-TILs>10%, 60.1% for BSL-TILs<30% & RD-TILs<10%, p<0.001. Pts with BSL-TILs>30% derived a significant benefit from avelumab, which was absent in pts with BSL-TILs<30%, with significant test for interaction in Stratum B. In Stratum B pts with BSL-TILs<30%, there was a significant interaction between treatment and RD-TILs: avelumab improved DDFS in RD-TILs<10%, while being associated with numerically worse outcome in RD-TILs>10% (only 22 total events in this group).Table: 323MO

Population	Groups	N pts	3-yr DDFS, % Avelumab	3-yr DDFS, % Control	HR (95%CI)	interaction p	adj interaction p
ITT	BSL-TILs>30% BSL-TILs<30%	92 295	93.5 70.9	69.8 71.5	0.31 (0.11-0.87) 0.89 (0.60-1.33)	0.055	0.065
Stratum B	BSL-TILs>30% BSL-TILs<30%	69 251	92.0 70.1	58.7 70.4	0.20 (0.07-0.64) 0.92 (0.60-1.40)	0.013	0.009
Stratum B, BSL-TILs<30%	RD-TILs>10% RD-TILs<10%	110 121	75.7 64.4	90.2 55.5	1.96 (0.80-4.81) 0.71 (0.41-1.20)	0.050	0.045

Conclusions

Efficacy of adjuvant avelumab for high risk TNBC differed according to the level of BSL-TILs. In pts with residual disease after NACT, RD-TILs further informed both prognosis and prediction of avelumab efficacy. Pending validation, these results support TILs as a biomarker to guide immunotherapy in TNBC.

Clinical trial identification

NCT02926196.

Legal entity responsible for the study

University of Padova.

Funding

Merck KGaA.

Disclosure

M.V. Dieci: Financial Interests, Personal, Advisory Board: Novartis, Eli Lilly, Seagen, Exact Science, Daiichi Sankyo, Gilead, AstraZeneca, MSD; Financial Interests, Personal, Other, Consultancy: Pfizer; Financial Interests, Personal, Invited Speaker: Exact sciences, Daiichi Sankyo, Novartis, Eli Lilly, AstraZeneca, Roche; Financial Interests, Personal, Other, Consultancy on educational project: Roche; Financial Interests, Personal, Other, training: MSD, Daiichi Sankyo; Financial Interests, Personal, Other, consultancy: AstraZeneca; Financial Interests, Personal, Other, travel/accomodation: Eli Lilly Japan, Roche, Roche, Gilead; Financial Interests, Personal, Advisory Board, listed as co-inventor in patent applications for HER2DX: Reveal Genomics; Financial Interests, Institutional, Research Grant: Roche. P. 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