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Durvalumab in combination with neoadjuvant chemotherapy in early triple-negative breast cancer (TNBC): Long-term analysis from the GeparNuevo trial

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Background

The phase II GeparNuevo trial evaluated adding anti-PD-L1 checkpoint inhibitor (CPI) durvalumab (D) to neoadjuvant chemotherapy (NACT) in patients (pts) with early TNBC. While D overall did not significantly increase pCR rates (primary endpoint), it improved secondary endpoints invasive disease-free survival (iDFS), distant disease-free survival (DDFS) and overall survival (OS) compared to placebo (P). Here, we present updated long-term survival data.

Methods

GeparNuevo randomized pts with centrally confirmed TNBC and cT1b-cT4a-d tumors 1:1 to intravenous D or P q4w concurrently with weekly nab-paclitaxel followed by dose-dense EC. Pts were stratified by stromal tumor-infiltrating lymphocytes (sTILs).

Results

A total of 174 pts were enrolled between 06/2016 and 09/2017. After a median follow-up of 86.4 months (51.2, 91.4), 50 iDFS events occurred. 6 and 7-year survival rates are summarized in table. A sustained significant improvement in iDFS for D vs P as well as significant improvements in DDFS and OS were observed. Among pts with pCR, 7-year OS rate was 100% in the D arm vs 82.5% in the P arm (log-rank $p=0.0053$). sTILs in the residual disease (RD) could be assessed in 39 out of 71 pts with no pCR. Post hoc analyses by sTILs high (>10%) and sTILs low (<10%) in the RD showed estimated 7-year iDFS rates of (95% CI) 92.3% (56.6%, 98.9%) and 51.4% (29.2%, 69.7%) respectively. Exploratory subgroup analysis revealed greater iDFS benefit from D in pts with initially affected nodes [HR 0.33, CI 0.144-0.771, $p=0.01$; interaction $p=0.045$]. Table: 292MO

6 and 7-year survival rates

	Durvalumab	Placebo	HR (95% CI)	P value (log-rank)
iDFS				
6-year rates (%)	79.6	62.8	0.56 (0.32-0.99)	0.0431
7-year rates (%)	73.7	60.7		
DDFS				
6-year rates (%)	83.6	66.7	0.41 (0.21-0.80)	0.0069
7-year rates (%)	81.6	62.9		
OS				
6-year rates (%)	93.6	74.7	0.33 (0.14, 0.79)	0.0085
7-year rates (%)	91.6	74.7		

Conclusions

Durvalumab added to dose-dense NACT alone as part of the neoadjuvant therapy without additional adjuvant continuation significantly improved all long-term outcomes, especially in pts with a pCR. These findings underscore the need to investigate the value of additional adjuvant CPI and its impact on long-term survival in early TNBC.

Clinical trial identification

NCT02685059.

Legal entity responsible for the study

GBG Forschungs GmbH.

Funding

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Disclosure

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