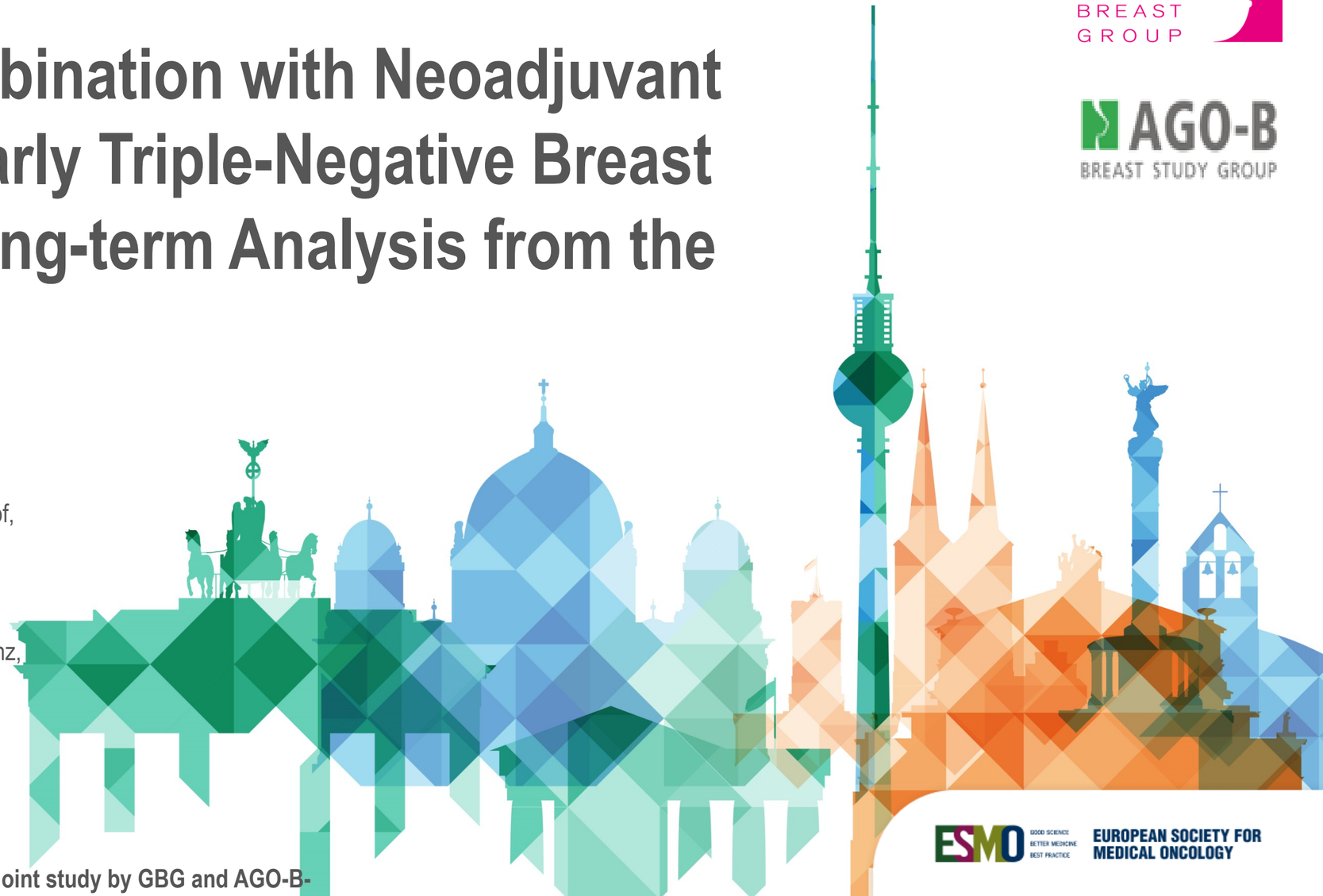
BERLIN 2025 ESMO congress

Durvalumab in Combination with Neoadjuvant Chemotherapy in Early Triple-Negative Breast Cancer (TNBC) – Long-term Analysis from the GeparNuevo Trial

Sibylle Loibl, Michael Untch, Jens Huober, Vanessa Schaser, Michael Braun, Carsten Denkert, Andreas Hartkopf, Jens-Uwe Blohmer, Claus Hanusch, Theresa Link, Mattea Reinisch, Dirk-Michael Zahm, Rudolf Weide, Vesna Bjelic-Radisic, Peter Staib, Hans Tesch, Kerstin Rhiem, Ralf Lorenz, Julia Rey, Andreas Schneeweiss

GBG Forschungs GmbH; Neu-Isenburg, Germany
Goethe University Frankfurt



-This is a joint study by GBG and AGO-B-

GeparNuevo

GBG GERMAN BREAST GROUP

AGO-B BREAST STUDY GROUP

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DECLARATION OF INTERESTS

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Grants and/or honorarium for adboards and/or contracts from the following entities / all paid to institution: AZ, Abbvie, Agendia, Amgen, BionTech, Celgene/BMS, Cellcuity, DSI, Exact Science, Gilead, GSK, Incyte, Lilly, Medscape, Molecular Health, MSD, Novartis, Pierre Fabre, Pfizer, Relay, Roche, Sanofi, Seagen, Stemline/Menarini, Olema, Bayer, Bicycle, JAZZ Pharma

Support for attending meetings and/or travel: DSI, ESMO, SGBCC, ASCO, AGO Kommission Mamma

Patents planned, issued or pending: EP14153692.0 / EP21152186.9 / EP15702464.7

Royalties to institution: VM Scope

Background

- Neoadjuvant therapy in patients with early triple negative breast cancer (TNBC) is standard.[1]
- Tumor-infiltrating lymphocytes (TILs) and PD-L1 expression correlate with pCR rates after NACT+/- CPI.[2-5]
- In contrast to metastatic breast cancer, PD-L1 expression does not predict response to CPI.[6]
- In metastatic TNBC, the PD-L1 inhibitor durvalumab as single agent has shown efficacy.[7]
- The addition of PD-(L)1 inhibitors to NACT has shown to improve pCR rates and improve long-term outcomes in patients with early TNBC.[8-10]
- EFS and OS were in general improved but less pronounced with PD-L1 than PD-1 inhibitors.[6,8-12]
- The GeparNuevo trial investigated whether adding PD-L1 inhibitor durvalumab to NACT in patients with early TNBC and cT1b-cT4a-d tumors would improve pCR rates and patient survival.

[1]Holanek M, et al. Cancers 2021; [2]Denkert C, et al. Lancet Oncol 2018; [3]Loibl S, et al. Ann Oncol 2019; [4]Karn T, et al. Ann Oncol 2020; [5]Loi S, et al. npj Breast Cancer 2022; [6]Loibl S, et al. Ann Oncol 2022; [7]Bachelot T, et al. Nat Med 2021; [8]Schmid P, et al. N Engl J Med 2020; [9]Schmid P, et al. N Engl J Med 2024; [10]Mittendorf EA, et al. Lancet 2020; [11]Mittendorf EA, et al. Nat Med 2025; [12]Geyer C,et al. Clin Cancer Res 2025.

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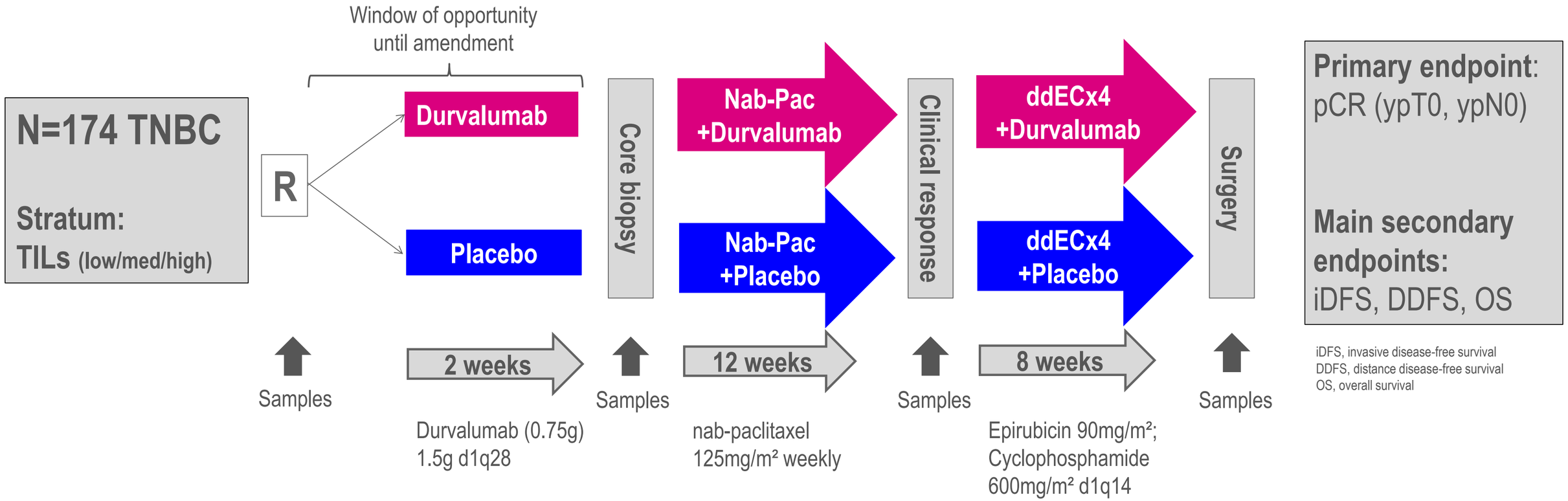
Study Design



Primary endpoint:
pCR (ypT0, ypN0)

Main secondary endpoints:
iDFS, DDFS, OS

iDFS, invasive disease-free survival
DDFS, distance disease-free survival
OS, overall survival

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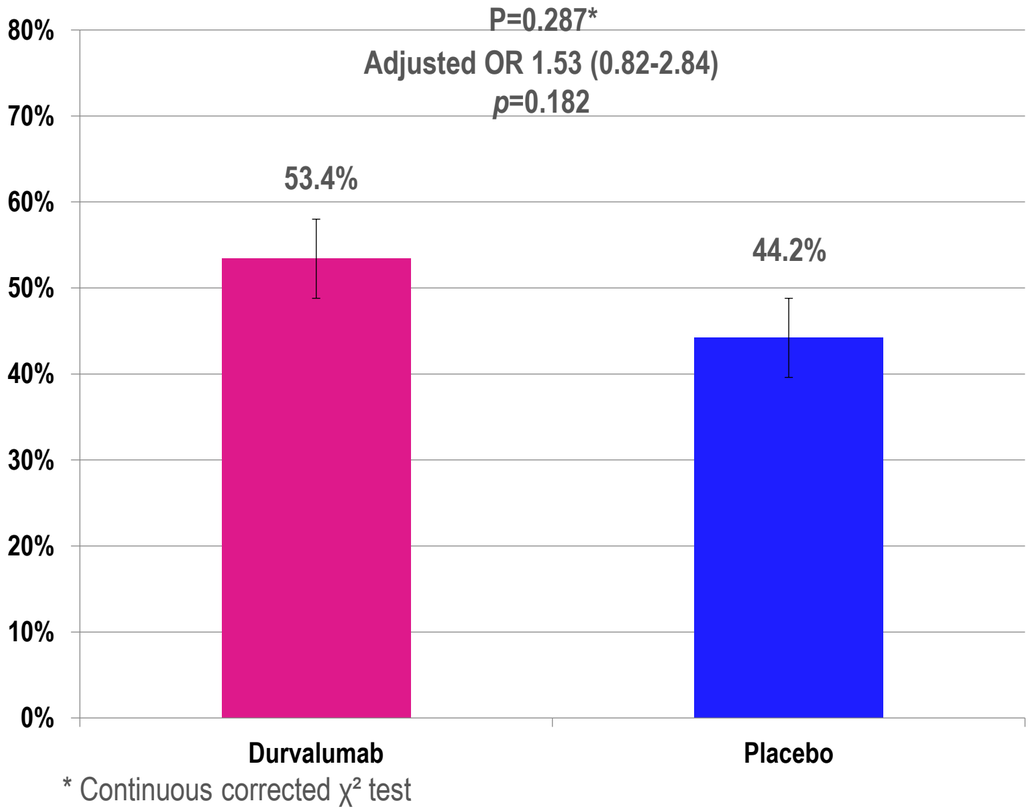
Patient and Tumor Characteristics

	Durvalumab N=88 N(%)	Placebo N=86 N(%)
Age (yrs), median (range)	49.5 (25.0, 74.0)	49.5 (23.0, 76.0)
cT3/4	7 (8.0)	3 (3.5)
cN+	27 (30.7)	27 (31.4)
Stage IIA and higher	56 (63.6)	57 (66.3)
G3	74 (84.1)	71 (82.6)
TILs		
low (0-10%)	34 (38.6)	32 (37.2)
intermediate (11-59%)	42 (47.7)	41 (47.7)
high (≥60%)	12 (13.6)	13 (15.1)
Durvalumab/placebo alone (window)	59 (67.0)	58 (67.4)

Loibl S, et al. Ann Oncol 2019

Primary Efficacy Endpoints

Primary endpoint: pCR – ypT0, ypN0



* Continuous corrected χ^2 test

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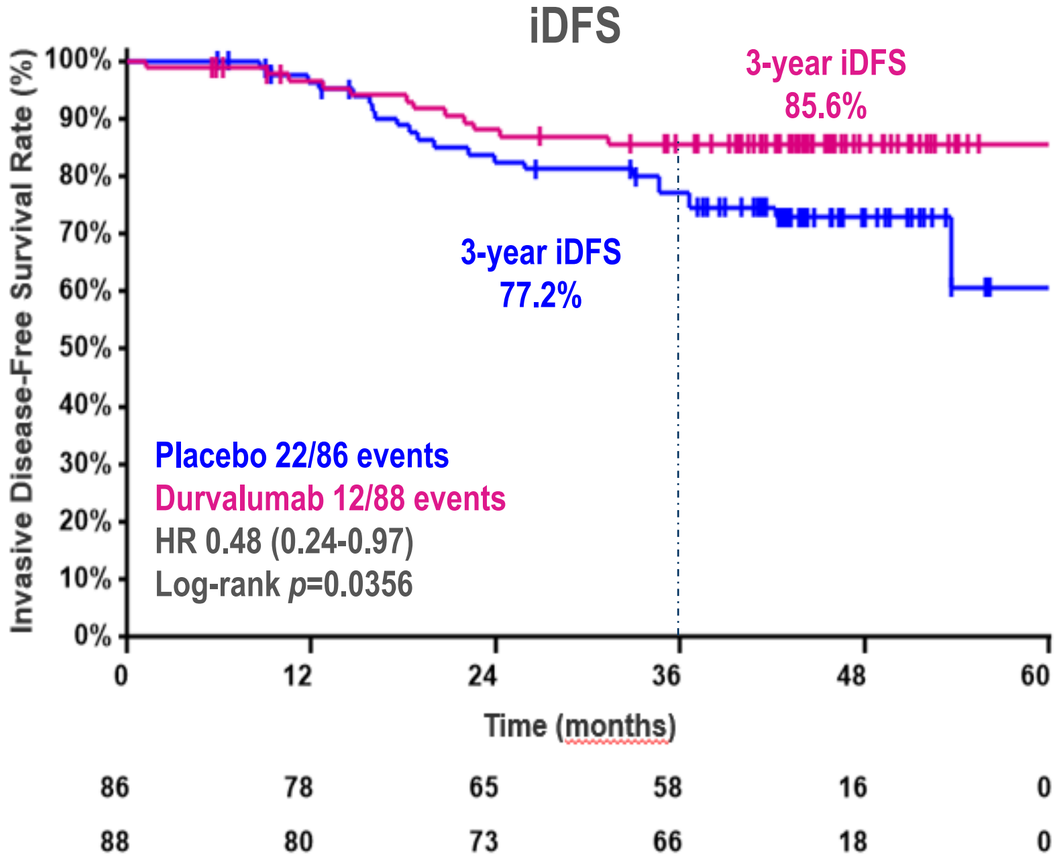
Median follow-up 43.7 (range 4.9-56.1) months



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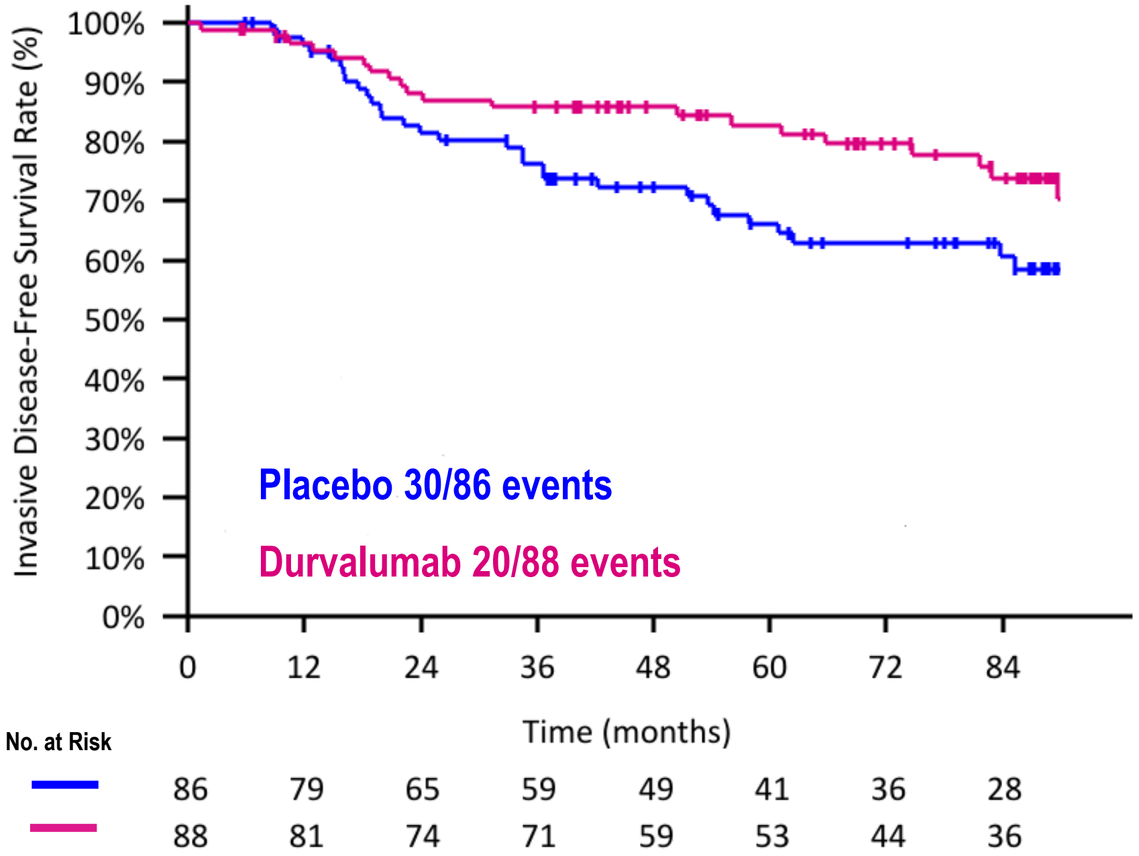
Statistical Considerations

- Primary efficacy endpoint was pCR (ypT0 ypN0) as reported previously
- The time-to-event analysis was changed from an initially planned event-driven analysis at 43 events (to detect HR=0.773 with 13.5% power) to a time-driven analysis after 3.5 years median follow-up with the respective results also reported previously
- All analyses are stratified by stromal TILs (sTILs)
- This analysis presented thereafter represents an update of the time-to event analysis with a longer follow-up
  - FU completeness was ~80%
  - Reported iDFS events: Placebo 30/86 events; Durvalumab 20/88 events

Updated Results: iDFS



Median follow-up 86.4 (range 4.9-103) months

	Placebo	Durvalumab
6-year iDFS (95% CI)	62.8% (50.7%, 72.8%)	79.6% (68.7%, 87.1%)
7-year iDFS (95% CI)	60.7% (48.2%, 71.0%)	73.7% (61.4%, 82.6%)
HR 0.56 (0.32-0.99) Log-rank *p*=0.043		

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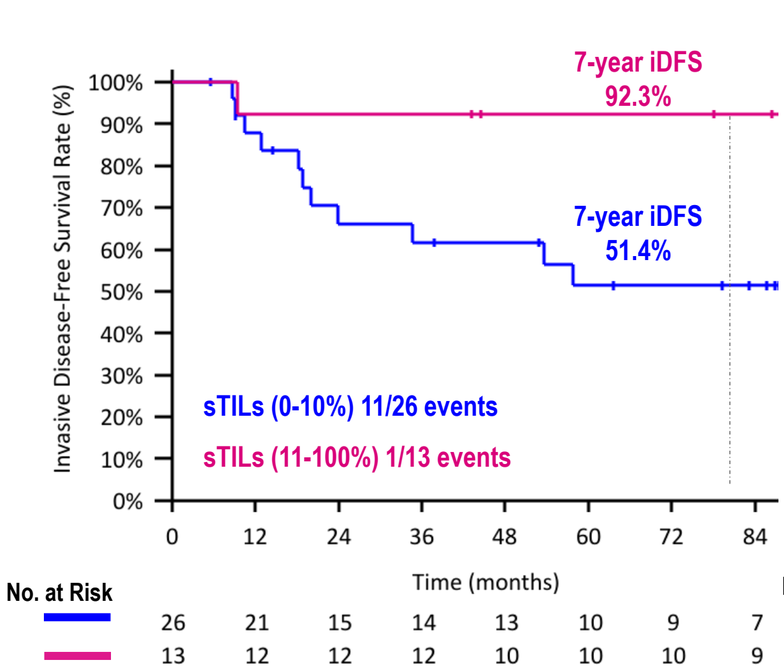
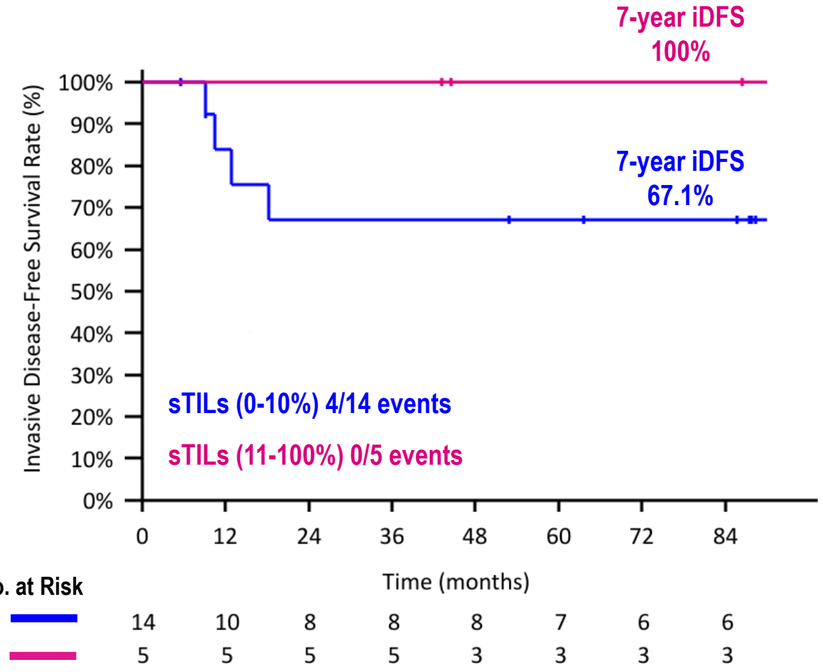
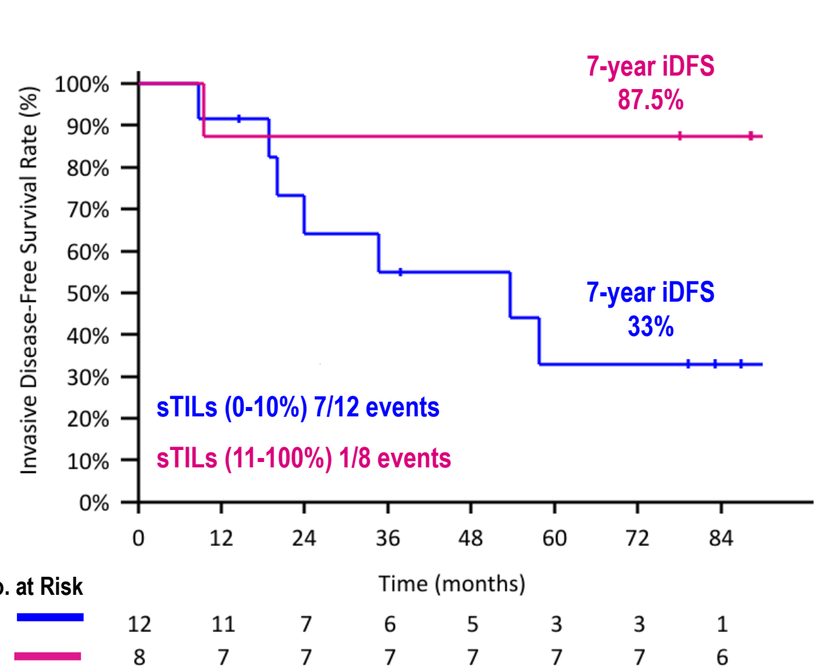
iDFS by sTILs in Residual Tumor



Overall



Durvalumab



Placebo

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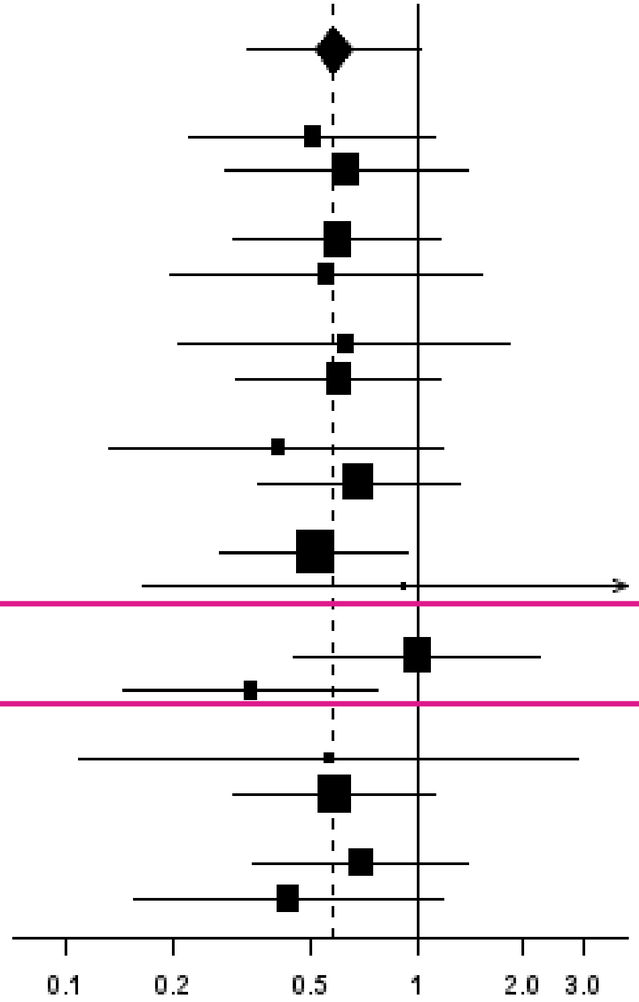
iDFS Subgroup Analysis

Subgroup	N patients	Hazard Ratio (95% CI)	p-Value	Test for Interaction
Overall	174	.579 (.329, 1.02)	0.058	
sTILs				0.674
low (0-10%)	66	.499 (.224, 1.11)	0.089	
intermediate/high (11-100%)	108	.625 (.281, 1.39)	0.250	
Window				0.925
window	117	.590 (.298, 1.17)	0.130	
no window	57	.549 (.199, 1.51)	0.246	
Breast Cancer Stage				0.908
Stage 0 or I	61	.618 (.207, 1.84)	0.388	
Stage IIA and higher	113	.595 (.306, 1.16)	0.126	
Age				0.376
<40	47	.398 (.133, 1.19)	0.099	
>=40	127	.677 (.349, 1.31)	0.248	
cT				0.552
cT1-2	164	.508 (.275, .940)	0.031	
cT3-4	10	.915 (.164, 5.12)	0.920	
cN				0.045
cN0	118	.993 (.446, 2.21)	0.986	
cN+	54	.333 (.144, .771)	0.010	
PD-L1				0.975
negative	20	.558 (.109, 2.86)	0.484	
positive	138	.580 (.300, 1.12)	0.104	
pCR (ypT0 ypN0)				0.490
no	88	.688 (.342, 1.38)	0.294	
yes	85	.429 (.156, 1.18)	0.102	



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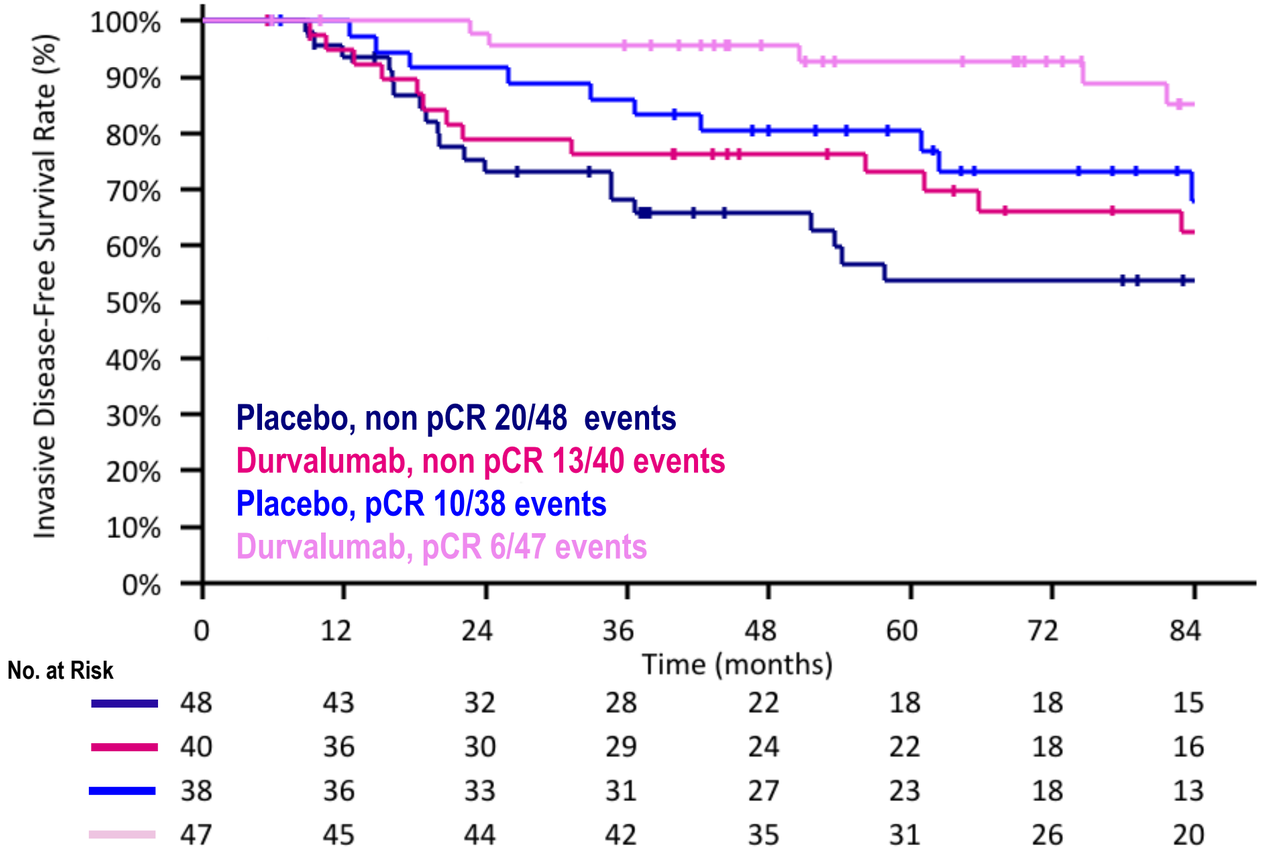
7-years iDFS by pCR and Treatment Arm



7-year IDFS (95% CI)	Placebo	Durvalumab
pCR	68.1% (47.6%, 81.9%)	85.1% (66.9%, 93.7%)
non-pCR	53.8% (37.1%, 67.9%)	62.3% (43.5%, 76.5%)
HR (pCR vs non-pCR) =0.41 (0.23-0.75) log-rank p=0.003		

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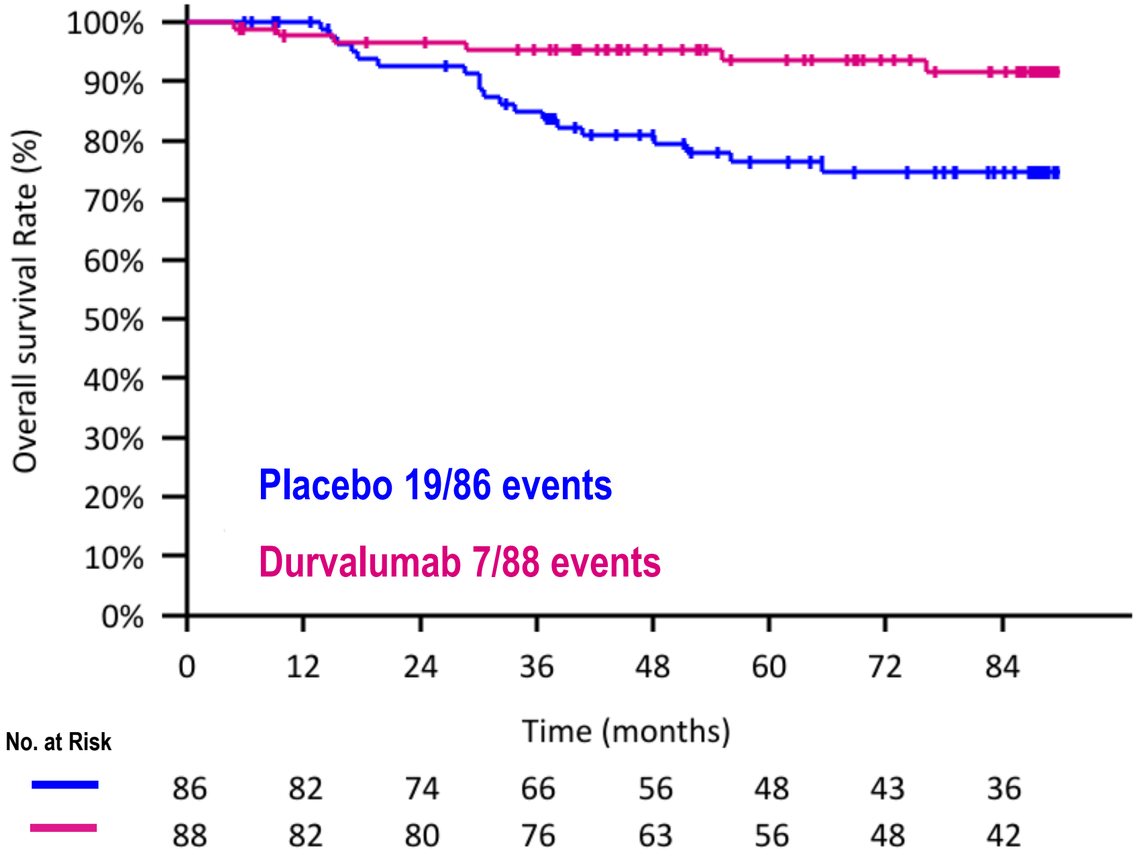
7-year Overall Survival



Median follow-up 86.4 (range 4.9-103) months

	Placebo	Durvalumab
6-year IDFS (95% CI)	74.7% (63.0%, 83.1%)	93.6% (85.2%, 97.3%)
7-year IDFS (95% CI)	74.7% (63.0%, 83.1%)	91.6% (81.8%, 96.2%)
HR 0.33 (0.14-0.79) Log-rank *p*=0.009		

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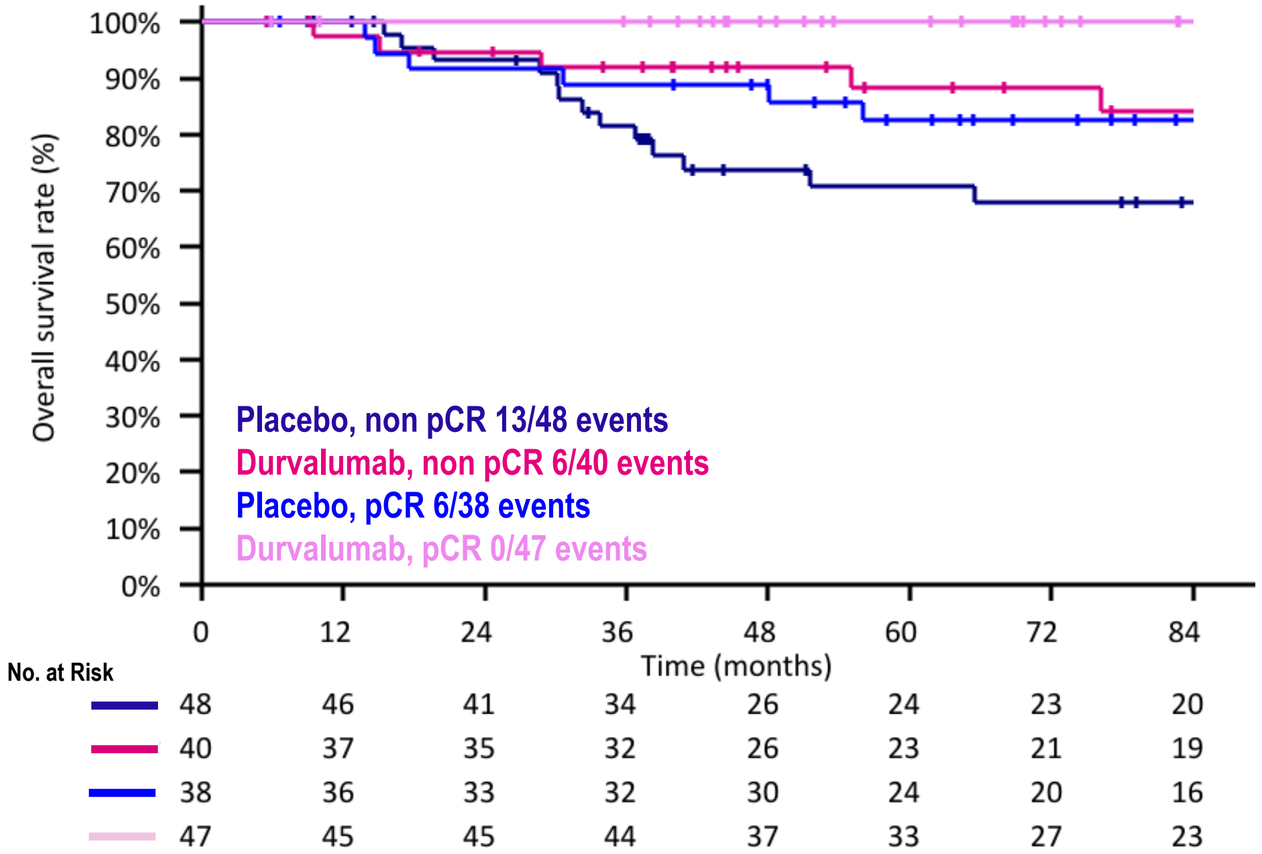
7-year OS by pCR and Treatment Arm



7-year OS (95% CI)	Placebo	Durvalumab
pCR	82.5% (65.0%, 91.8%)	100% (100%, 100%)
non-pCR	67.9% (50.9%, 80.1%)	84.1% (65.2%, 93.2%)
HR (pCR vs non-pCR)=0.29 (0.12-0.74) log-rank p=0.006		

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Conclusions

- The addition of the checkpoint inhibitor (CPI) durvalumab to carboplatinum-free, but dose-dense NACT in patients with early TNBC resulted in statistically significant improvement of iDFS, DDFS, and OS despite no administration of adjuvant CPI.
- 7-year follow-up data confirm earlier results:
  - Survival benefit observed irrespective of pCR
  - Patients with TILs in the residual tumor have an excellent outcome.
- As in the NSABP-B58/GeparDouze study – there is a significant interaction with the nodal status.
- GeparNuevo raises two questions:
  - Shall patients with cN0 receive a CPI?
  - Do patients need to continue after surgery with the CPI?
- GeparNuevo is the only trial to prove survival benefit in the presence of dose-dense NACT without carboplatinum and the only trial to report survival benefit for a PD-L1 inhibitor.

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Acknowledgements

All patients and their families and all participating sites

Cooperating partners

Philipps Universität Marburg

CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN

AstraZeneca

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Members of the Subboard GBG and AGO-B
GBG Team

Medical Team: Dr. Johannes Holtschmidt
Dr. Nader Hirmas
Statistics: Dr. Valentina Nekljudova

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