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Neo-N: three-year event-free survival (EFS) and overall survival (OS) and ultrasensitive ctDNA and tumor infiltrating lymphocyte (TIL) dynamics in early triple-negative breast cancer (tnbc) treated with neoadjuvant carboplatin/paclitaxel and nivolumab

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Background

The Neo-N trial previously showed a pathological complete response (pCR) rate of 53% with 12 weeks of carboplatin/paclitaxel plus nivolumab: *Zdenkowski et al, 2025*

Here, we report 3-year EFS/OS and associations of an ultrasensitive tumor-informed structural-variant (SV)–based circulating tumor DNA (ctDNA) assay as well as TIL on (H&E) dynamics with EFS/OS.

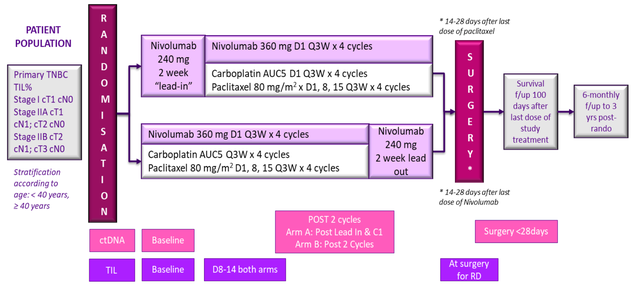
Methods

Neo-N is an investigator-initiated, non-comparative, open-label, randomized phase 2 trial across 14 sites. Adults with operable stage I–II TNBC received carboplatin AUC5 q3w + weekly paclitaxel for 12 weeks with nivolumab per assigned schedule- A: lead in monotherapy or B: concurrent Nivolumab, followed by surgery and adjuvant therapy per investigator.

We conducted tumor-informed ctDNA SV testing using an assay derived from whole genome sequencing. Plasma was collected at: T0 (baseline) and T1 (5+/-1 weeks) and T2 <28 days post-surgery.

Primary objectives of this report are reporting of long-term survival as well as
- association of ctDNA status and dynamics with EFS/OS
- tumor infiltrating lymphocyte (sTIL) changes on H&E with EFS/OS

Study Schema



Conclusions

- A 12-week anthracycline-free regimen of carbo/paclitaxel/nivolumab in stage I/II TNBC gives 3yr-EFS 87.5%; OS 93.4%
- ctDNA: An early on treatment ctDNA timepoint can stratify patients: ctDNA positive have NO pCRs; 45% 3yr-EFS; vs. those who clear ctDNA have a pCR rate 60%; 90% 3yr-EFS
- TILs: early on treatment high TIL≥30% were also associated with better outcomes
- Combining both these markers may help us personalize treatment for patients with early-stage Stage I/II TNBC

Baseline Tumor Characteristics

	Treatment cohort				Evaluable participants	
	A (Nivo lead-in)		B (Nivo concurrent)			
	N	%	N	%	N	%
Evaluable participants	53	100.0	55	100.0	108	100.0
<40 years	14	26.4	9	16.4	23	21.3
41-50 years	14	26.4	24	43.6	38	35.2
51-60 years	13	24.5	11	20.0	24	22.2
61-70 years	9	17.0	8	14.5	17	15.7
>70 years	3	5.7	3	5.5	6	5.6
T2	32	60.4	29	52.7	61	56.5
N0	47	88.7	43	78.2	90	83.3
High TILs (≥30%)	20	37.7	18	32.7	38	35.2
PD-L1 Positive (SP142 ≥1%)	23	43.4	28	50.9	51	47.2

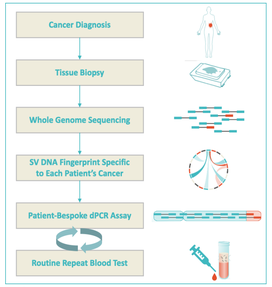
Results: 3yr EFS/OS

The planned data cutoff median follow-up was 36 months (range 20-43mo).

Among all randomized participants (n=108),
36mo EFS rate was **87.6%**
Cohort A 92.4% (90% CI 83.5-96.6%); Cohort B **83.1%** (90% CI: 72.4% to 89.9%).
36-month OS was 93.4% overall (Cohort A 98%; Cohort B 89%).

No new safety signals were observed; immune-related adverse events were consistent with prior reporting.

Results – ultrasensitive SV ctDNA &TIL



Workflow of "Pathlight" assay

Swimmers plot: ctDNA positivity at all timepoints and EFS events sorted by ctDNA status on treatment and duration of survival.

Boxed is the Pos-Pos group who all recurred distantly, no pCRs.

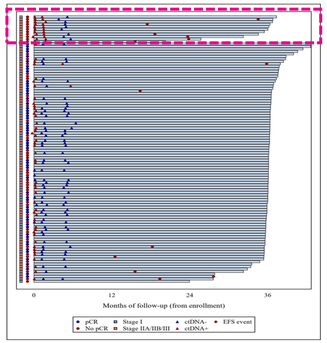
Change in ctDNA status: baseline to on treatment	EFS events	OS events	Total pts
Neg/Neg	0	0	5 (8%)
Pos/Neg	4	2	46 (74%)
Pos/Pos	6	5	11 (18%)
Unknown	3	1	46

Of 108 patients, 86 had available tumor/plasma for ctDNA analysis

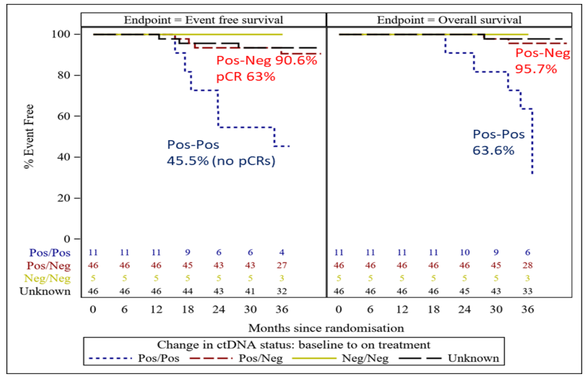
Of these 76/86 (88%) had sufficient material and successful assay design

These results are with first 64 patients

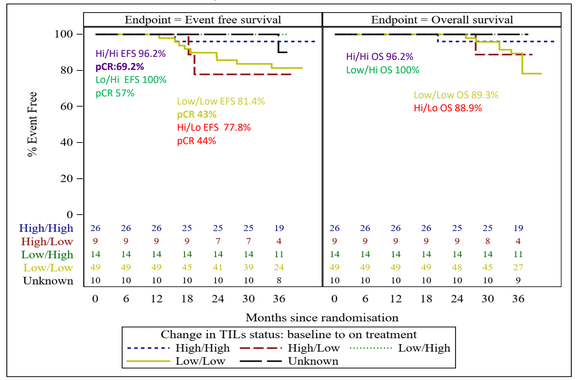
- 91% (58/64) had (+) ctDNA at baseline
- 18% (11/62) remained positive at T1
- 3% (2/55) positive at landmark at T2



ctDNA dynamics are strongly prognostic: baseline to T1 (negative= undetectable)



sTIL on H&E dynamics associated with outcomes: baseline to T1 (positive ≥30%)
100% had baseline TIL available, 91% had on treatment TIL scores.



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