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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.

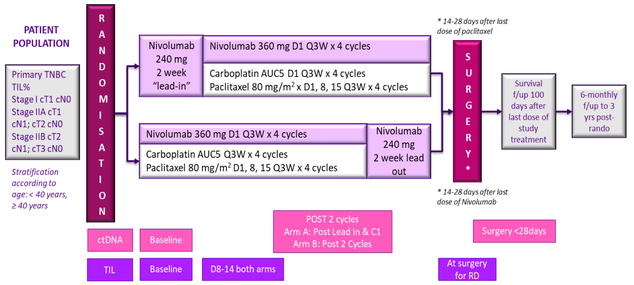
## Methods

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 |

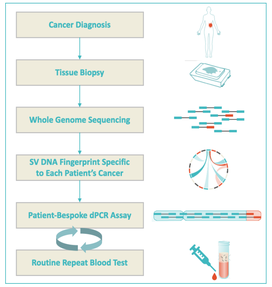
## Results: 3yr EFS/OS

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.

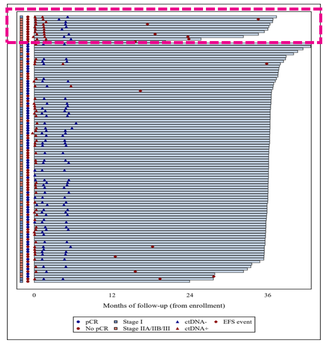
| Change in ctDNA status: baseline to on treatment | EFS events | OS events | Total pts |
|---|---|---|---|
| Neg/Neg | 0 | 0 | 5 (8%) |
| Pos/Neg | 4 | 2 | 46 (74%) |
| Pos/Pos | 6 | 5 | 11 (18%) |
| Unknown | 3 | 1 | 46 |

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

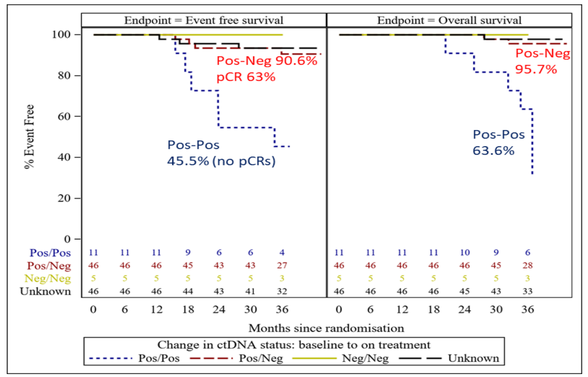
Of these 76/86 (88%) had sufficient material and successful assay design

These results are with first 64 patients

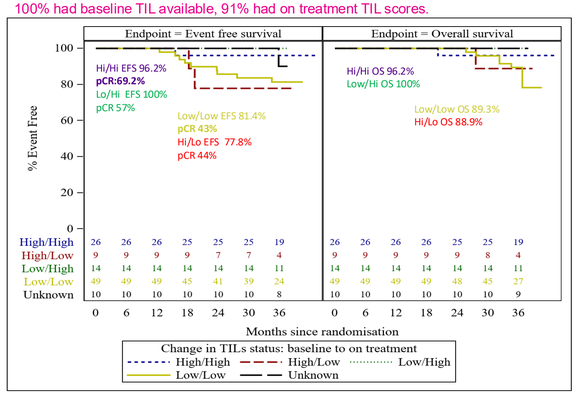
- 91% (58/64) had (+) ctDNA at baseline
- 18% (11/62) remained positive at T1
- 3% (2/55) positive at landmark at T2




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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