

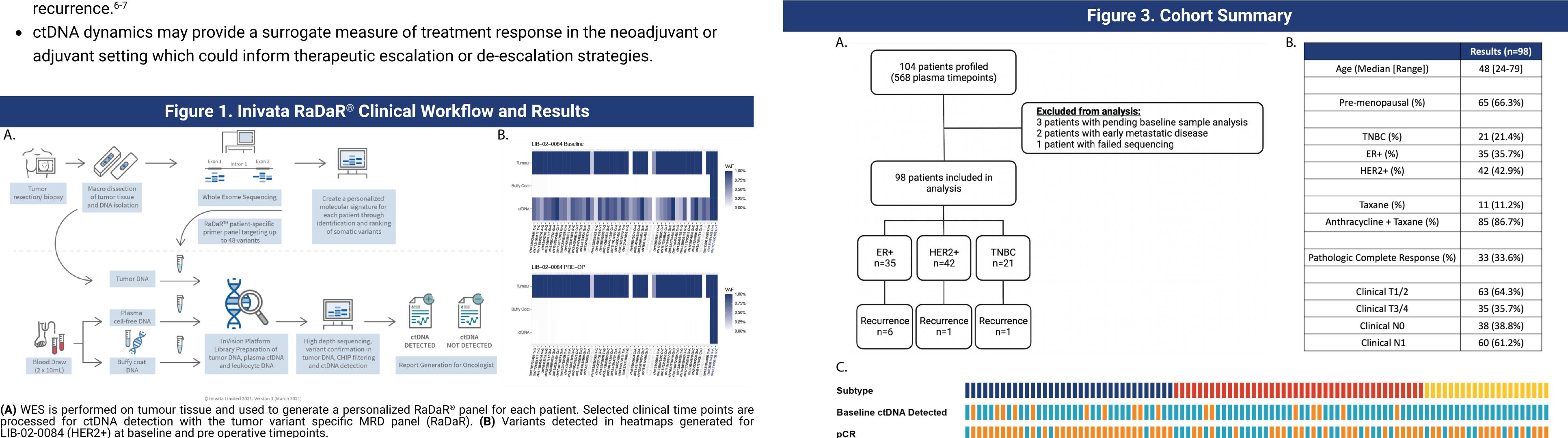
TORONTO

# Circulating Tumour DNA (ctDNA) Detection and Dynamics in Patients with Early Breast Cancer (EBC): Results of the Neoadjuvant TRACER cohort

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## INTRODUCTION

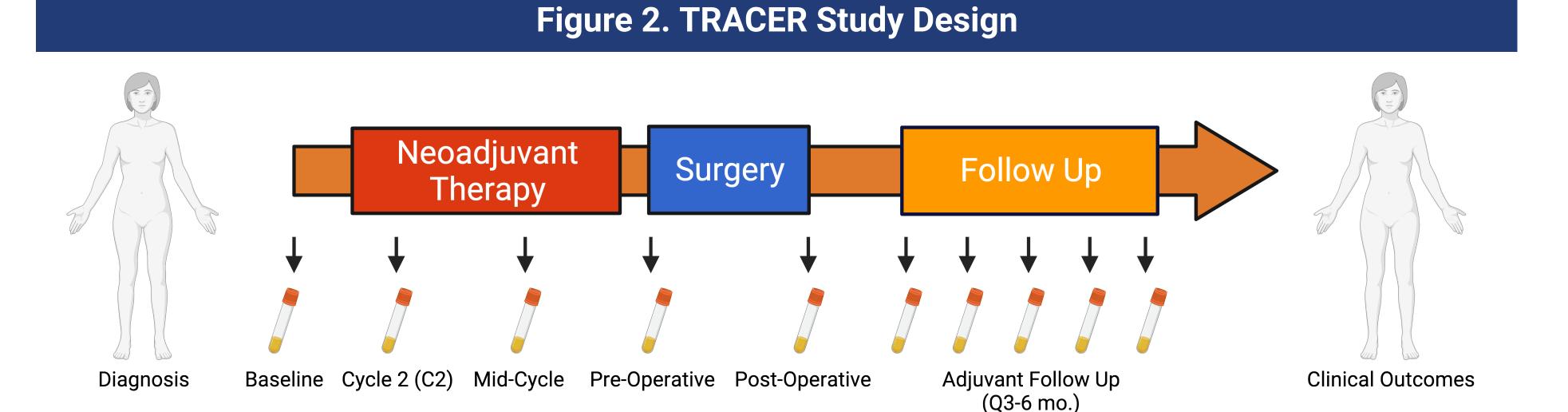
- Liquid biopsy permits the identification and characterization of tumor derived DNA fragments in the peripheral blood (circulating tumor DNA, ctDNA).<sup>1</sup>
- Changes in ctDNA levels (ctDNA dynamics) are associated with treatment response in many cancers.
- ctDNA detection following definitive treatment, "molecular residual disease" (MRD), is associated with disease recurrence in early breast cancer (EBC).<sup>1-5</sup>
- RaDaR<sup>®</sup> (Inivata Ltd.) is a personalized, tumor-informed assay capable of detecting ctDNA with high sensitivity and specificity via deep sequencing of up to 48 tumor-specific variants (Figure 1).<sup>6</sup>
- Post-operative ctDNA detection with RaDaR is associated with an elevated risk of disease recurrence.<sup>6-7</sup>
- adjuvant setting which could inform therapeutic escalation or de-escalation strategies.



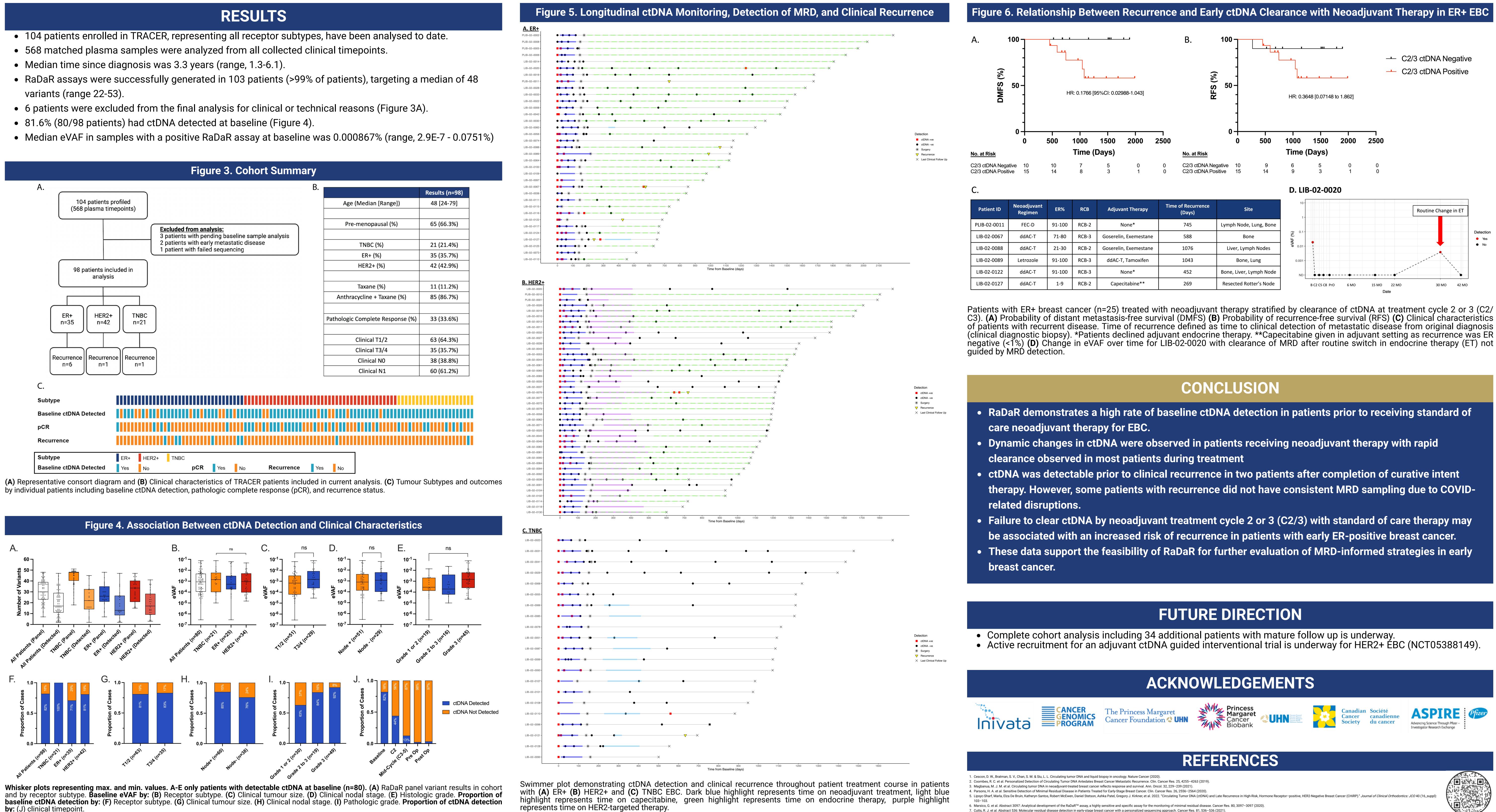
LIB-02-0084 (HER2+) at baseline and pre operative timepoints

## METHODS

- Patients with EBC of all receptor subtypes receiving standard of care neoadjuvant therapy at the Princess Margaret Cancer Centre were enrolled in a prospective cohort between Oct. 2016 - Feb. 2021 (NCT03702309).
- Plasma samples (3x streck tubes) were collected at baseline, during treatment, perioperatively, and during follow-up (Figure 2).
- Somatic variants were identified through whole exome sequencing of available archival formalinfixed, paraffin embedded tissue from a diagnostic biopsy.
- Additional deep sequencing is performed on the patient's cfDNA and leukocyte DNA. The buffy coat fraction is sequenced to determine confounding signals derived from clonal hematopoiesis of indeterminate potential.
- Plasma ctDNA profiling of all available clinical timepoints using personalized RaDaR assays was performed by Inivata.
- Clinical and pathologic characteristics, treatment, and recurrence outcomes were collected.



- variants (range 22-53).



# Princess Margaret Cancer Centr

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|   | Neoadjuvant<br>Regimen | ER%    | RCB   | Adjuvant Therapy      | Time of Recurrence<br>(Days) | Site                    | 10.           |                |      |   |       |       |         |            |             |             |             |
|---|------------------------|--------|-------|-----------------------|------------------------------|-------------------------|---------------|----------------|------|---|-------|-------|---------|------------|-------------|-------------|-------------|
| 1 | FEC-D                  | 91-100 | RCB-2 | None*                 | 745                          | Lymph Node, Lung, Bone  |               |                |      |   |       |       |         |            |             |             |             |
| 7 | ddAC-T                 | 71-80  | RCB-3 | Goserelin, Exemestane | 588                          | Bone                    | 0.1<br>(%) 4F |                |      |   |       |       |         |            |             |             |             |
| 3 | ddAC-T                 | 21-30  | RCB-2 | Goserelin, Exemestane | 1076                         | Liver, Lymph Nodes      | <b>6/AF</b>   |                |      |   |       |       |         |            |             |             |             |
| ) | Letrozole              | 91-100 | RCB-3 | ddAC-T, Tamoxifen     | 1043                         | Bone, Lung              | 0.001         |                |      |   |       |       |         |            |             |             |             |
| 2 | ddAC-T                 | 91-100 | RCB-3 | None*                 | 452                          | Bone, Liver, Lymph Node | ND            |                |      | _ |       | •     |         |            | •-··        |             | •           |
| 7 | ddAC-T                 | 1-9    | RCB-2 | Capecitabine**        | 269                          | Resected Rotter's Node  |               | B C2 C5 C8 PrO | 6 MO |   | 15 MC | 15 MO | 15 MO 2 | 15 MO 22 N | 15 MO 22 MC | 15 MO 22 MO | 15 MO 22 MO |
|   |                        |        |       | •                     |                              |                         | I             |                |      |   |       | Da    | Date    | Date       | Date        | Date        | Date        |

- 7. Cutts, R. J. et al. Abstract 536: Molecular residual disease detection in early-stage breast cancer with a personalized sequencing approach. Cancer Res. 81, 536-536 (2021)