Circulating tumor DNA (ctDNA) dynamics in patients with hormone receptor positive (HR+)/HER2 negative (HER2-) advanced breast cancer (aBC) treated in first line with ribociclib and letrozole in the BioItaLEE trial

Giampaolo Bianchini
Department of Medical Oncology, Ospedale San Raffaele, Milano, Italy
VAF clearance – Dynamic patterns

Four dynamic patterns were identified for VAF clearance

• **Pattern 1: Sustained clearance**
  
  VAF clearance at D15 and C2D1

C, cycle; D, day; VAF, variant allele frequency.
VAF clearance – Dynamic patterns

Four dynamic patterns were identified for VAF clearance

- **Pattern 1: Sustained clearance**
  
  VAF clearance at D15 and C2D1

- **Pattern 2: Rebound after clearance**
  
  VAF clearance at D15, no clearance at C2D1

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VAF clearance – Dynamic patterns

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- **Pattern 1: Sustained clearance**
  
  VAF clearance at D15 and C2D1

- **Pattern 2: Rebound after clearance**
  
  VAF clearance at D15, no clearance at C2D1

- **Pattern 3: Delayed clearance**
  
  No VAF clearance at D15, clearance at C2D1

C, cycle; D, day; VAF, variant allele frequency.
VAF clearance – Dynamic patterns

Four dynamic patterns were identified for VAF clearance:

- **Pattern 1: Sustained clearance**
  - VAF clearance at D15 and C2D1

- **Pattern 2: Rebound after clearance**
  - VAF clearance at D15, no clearance at C2D1

- **Pattern 3: Delayed clearance**
  - No VAF clearance at D15, clearance at C2D1

- **Pattern 4: NO clearance**
  - No VAF clearance at D15 or C2D1

C, cycle; D, day; VAF, variant allele frequency.
### Frequency of ctDNA dynamic patterns

<table>
<thead>
<tr>
<th>Pattern 1 (SUSTAINED)</th>
<th>Pattern 2 (REBOUND)</th>
<th>Pattern 3 (DELAYED)</th>
<th>Pattern 4 (NO CLEARANCE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>D15</strong></td>
<td><strong>C2D1</strong></td>
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- **Pattern 1 (SUSTAINED)**: Clearance in D15 and Clearance in C2D1 (n=39, 38.4%)
- **Pattern 2 (REBOUND)**: Clearance in D15 and NO clearance in C2D1 (n=38, 38.4%)
- **Pattern 3 (DELAYED)**: NO clearance in D15 and Clearance in C2D1 (n=9, 9.1%)
- **Pattern 4 (NO CLEARANCE)**: NO clearance in D15 and NO clearance in C2D1 (n=13, 13.1%)

C, cycle; ctDNA, circulating tumor DNA; D, day.

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Predictive value of pharmacodynamic change of ctDNA at D15 and C2D1

Patients with SUSTAINED clearance (Pattern 1) had the lowest risk of progression compared to the NO CLEARANCE group (Pattern 4) (HR, 0.40 [95% CI: 0.20,0.79; P=0.084])

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</tr>
<tr>
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</tbody>
</table>

Patients at risk:

- Pattern 1: 39 32 26 26 24 20 15 3 2 1
- Pattern 2: 13 10 9 6 6 5 5 3 2 1
- Pattern 3: 9 8 6 5 4 3 3 3 2 0
- Pattern 4: 38 28 23 21 16 12 11 5 1 1

Kaplan-Meier Curve of Progression-Free Survival (months)

C, cycle; CI, confidence interval; ctDNA, circulating tumor DNA; D, day; HR, hazard ratio; VAF, variant allele frequency.