Minimal residual disease assessment in transplanteligible patients with multiple myeloma: real-world applications of multiparametric flow cytometry-**DURAClone (CAREMM-2104)**

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Supplementary Tables

Supplementary Table 1. Response status trajectory in patients with very good partial response (VGPR) and minimal residual disease (MRD) status at 3 months after autologous stem cell transplantation.

| No. | Response at 3m | MRD at 3m | CR achievement | Time to achievement of CR ¹⁾ | Achievement of sustained MRD ²⁾ | Event of PFS | Follow-up time ³⁾ |
|-----|----------------|--------------|-------------------|---|--|--------------|------------------------------|
| 4 | VGPR | (-) | Yes | 28 | Yes | No | 34.3 |
| 12 | VGPR | (-) | Yes | 31 | Yes | No | 26.8 |
| 23 | VGPR | (-) | Yes | 189 | Yes | No | 17.3 |
| 29 | VGPR | (-) | Yes | 428 | Yes | No | 29.0 |
| 48 | VGPR | (-) | Yes | 7 | Yes | No | 22.9 |
| 61 | VGPR | (-) | Yes | 201 | No | Yes | 14.4 |
| 137 | VGPR | (-) | Yes | 35 | No | No | 34.6 |
| 140 | VGPR | (-) | Yes | 85 | No | Yes | 23.7 |
| 162 | VGPR | (-) | Yes | 84 | No | Yes | 33.5 |

Abbreviations: 3m, 3 months post-ASCT; MRD, minimal residual disease; CR, complete response; PFS, progression-free survival

Days from 1st MRD assessment; ²⁾ Evaluated after 1 year from 1st MRD assessment; ³⁾ Months

Supplementary Table 2. Univariate analysis to identify factors associated with survival outcomes

| Variables | Number | Progression-free survival rate | | | Cumulative incidences of progression | | |
|--|----------|--------------------------------|-----------|-----------------|--------------------------------------|-----------|-----------------|
| | Nullibei | % at 24 months | 95% CI | <i>p</i> -value | % at 24 months | 95% CI | <i>p</i> -value |
| MRD status at 3 months | | | | < 0.001 | | | 0.001 |
| MRD+ | 52 | 50.1 | 34.6-63.8 | | 47.3 | 31.8-61.2 | |
| MRD- | 114 | 72.4 | 61.4-80.8 | | 26.7 | 17.6-36.6 | |
| Response status at 3 months | | | | 0.038 | | | 0.028 |
| CR | 138 | 69.2 | 59.3-77.1 | | 29.0 | 20.6-38.0 | |
| VGPR | 28 | 48.3 | 27.6-66.3 | | 51.7 | 29.8-69.8 | |
| Age at transplant, years | | | | 0.771 | | | 0.998 |
| ≥ 60 | 75 | 62.9 | 48.6-74.3 | | 37.1 | 20.0-41.1 | |
| < 60 | 91 | 67.1 | 55.0-76.7 | | 30.2 | 24.2-49.9 | |
| Sex | | | | 0.266 | | | 0.429 |
| Male | 86 | 60.6 | 47.7-71.3 | | 36.5 | 24.9-48.1 | |
| Female | 80 | 70.8 | 57.9-80.4 | | 29.2 | 18.5-40.7 | |
| Type of multiple myeloma | | | | < 0.001 | | | 0.001 |
| IgD type | 8 | 33.3 | 5.6-65.8 | | 66.7 | 20.5-35.9 | |
| Other type | 158 | 68.2 | 59.1-75.7 | | 30.2 | 22.3-38.5 | |
| Light chain type (unclassified, n=1) | | | | 0.209 | | | 0.364 |
| Kappa | 86 | 72.1 | 59.7-81.3 | | 25.9 | 16.1-36.6 | |
| Lambda | 79 | 57.5 | 43.9-68.9 | | 34.7 | 23.3-46.3 | |
| Presence of plasmacytoma at diagnosis (missing n=1) | | | | 0.093 | | | 0.134 |
| None | 119 | 68.2 | 57.5-76.7 | | 30.9 | 21.7-40.7 | |
| Present | 46 | 60.7 | 43.1-74.3 | | 36.1 | 21.1-51.3 | |
| International staging system (missing n=3) | | | | 0.034 | | | 0.01 |
| Ι | 54 | 77.3 | 61.3-87.3 | | 18.4 | 8.3-31.6 | |
| II | 59 | 67.5 | 51.1-79.5 | | 32.5 | 18.8-46.9 | |
| III | 50 | 50.0 | 34.5-63.7 | | 50.0 | 34.2-63.9 | |
| Cytogenetic risk (missing n=34) | | | | 0.015 | | | 0.009 |
| Standard | 77 | 80.0 | 68.3-87.8 | | 18.7 | 10.4-28.8 | |
| High | 55 | 52.7 | 37.0-66.2 | | 47.3 | 31.7-61.3 | |
| Time to ASCT from diagnosis, months | | | | 0.874 | | | 0.894 |
| < median (6.8 months) | 81 | 61.6 | 44.6-74.7 | | 30.2 | 18.6-42.6 | |
| ≥ median (6.8 months) | 85 | 66.2 | 54.6-75.5 | | 29.8 | 20.1-40.0 | |
| Induction treatment | | | | 0.671 | | | 0.766 |
| Bortezomib-thalidomide-dexamethasone | 140 | 64.5 | 54.8-72.7 | | 33.8 | 25.0-42.7 | |
| Others ¹⁾ | 26 | 70.8 | 44.8-86.2 | | 26 | 10.8-50.7 | |
| Lactate dehydrogenase at diagnosis, (missing n=1) | 20 | 70.0 | 00.2 | 0.106 | 20 | 10.0 20.7 | 0.078 |
| Normal | 140 | 69.2 | 59.6-77.0 | 0.100 | 29.0 | 20.8-37.7 | 0.070 |
| High | 25 | 43.9 | 21.5-64.3 | | 56.1 | 30.1-75.8 | |
| Infused CD34+ cell, x10 ⁶ /kg | 23 | 13.7 | 21.5 01.5 | 0.374 | 20.1 | 30.1 73.0 | 0.381 |
| $\geq \text{median } (5.55)$ | 81 | 62.3 | 48.4-73.5 | 0.577 | 35.8 | 23.5-48.2 | 0.501 |
| < median (5.55) | 84 | 68.1 | 56.0-77.6 | | 30.7 | 20.3-41.6 | |
| Further treatment following ASCT | 0- | 00.1 | 30.0-77.0 | 0.401 | 50.7 | 20.5-41.0 | 0.372 |
| No | 66 | 66.1 | 50.8-77.7 | 0.401 | 25.7 | 15.0-37.7 | 0.372 |
| Yes | 100 | 65.1 | 53.5-74.4 | | 32.2 | 22.3-42.5 | |
| Abbreviations: CI. confidence interval: MRD. minimal | | | | 1 | | | 11 |

Abbreviations: CI, confidence interval; MRD, minimal residual disease; CR, complete response; VGPR, very good partial response; ASCT, autologous stem cell transplantation

¹⁾ Others include 14 of bortezomib-lenalidomide-dexamethasone, eight of daratumumab-bortezomib-thalidomide-dexamethasone, and four of bortezomib-melphalan-prednisolone

Supplementary Figures

Supplementary Figure 1. Workflow for (A) DURAClone RE PC and (B) EuroFlow method

