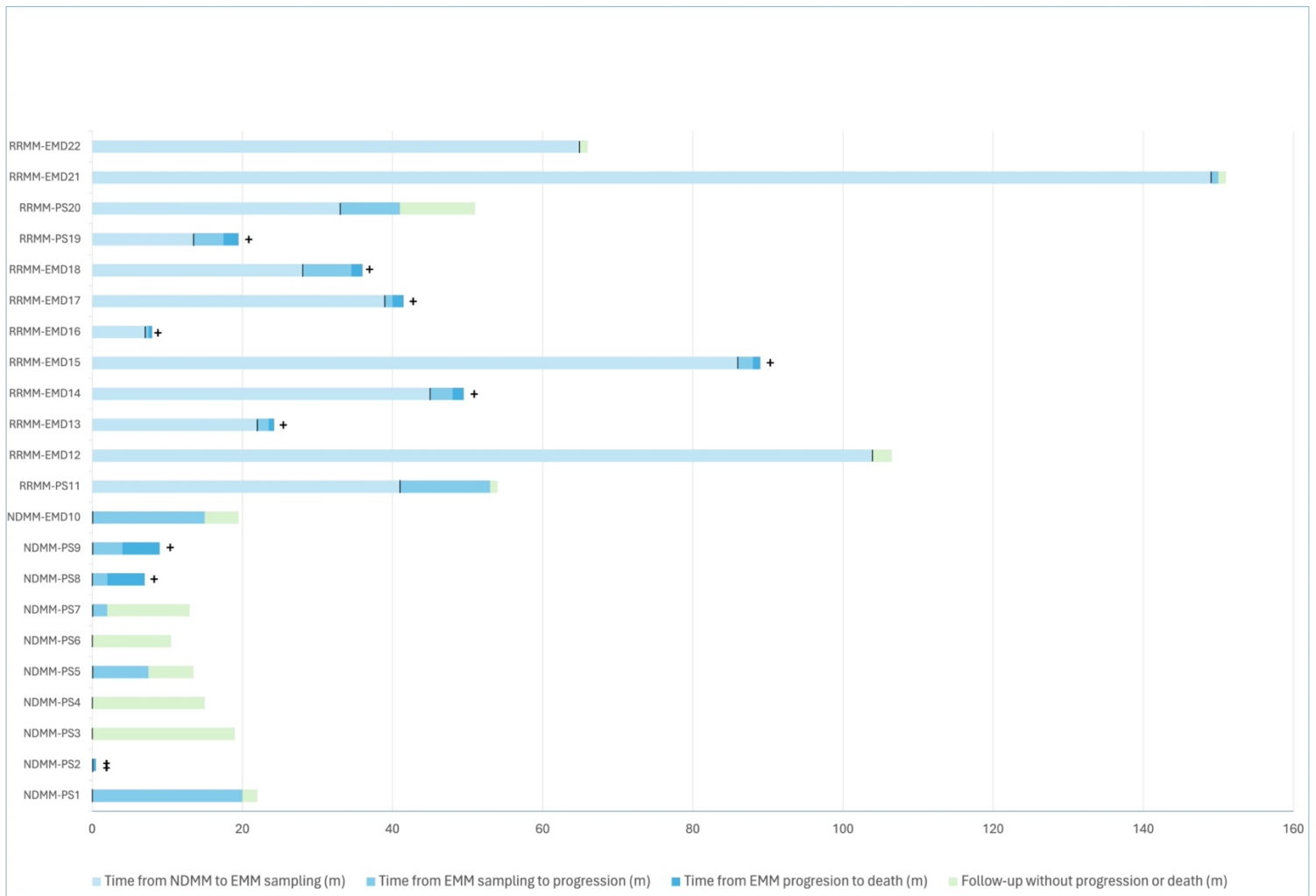


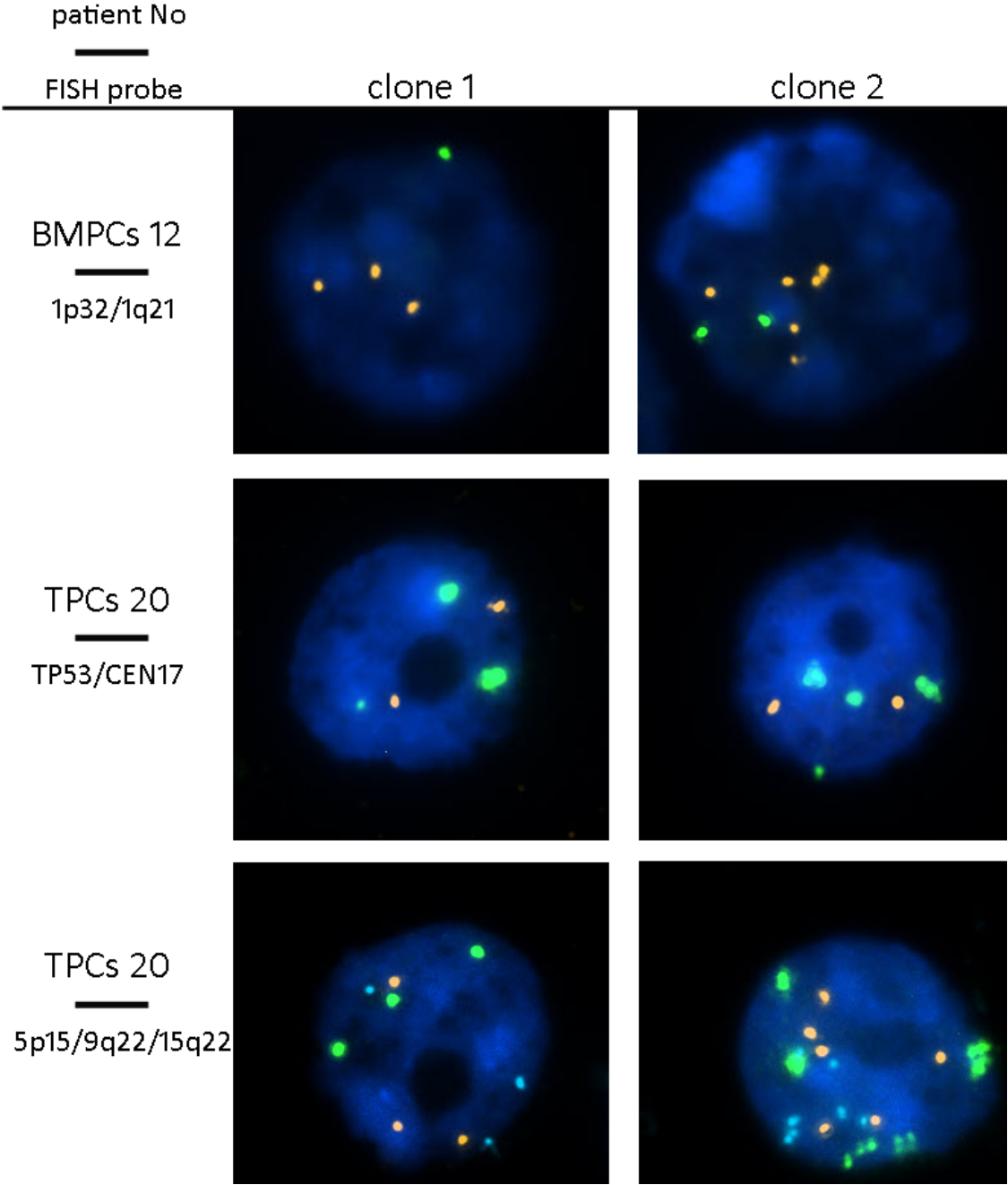
**Supplementary Tables and Figures:**

**Supplementary Figure 1 - Survival in patients with paired samples.**



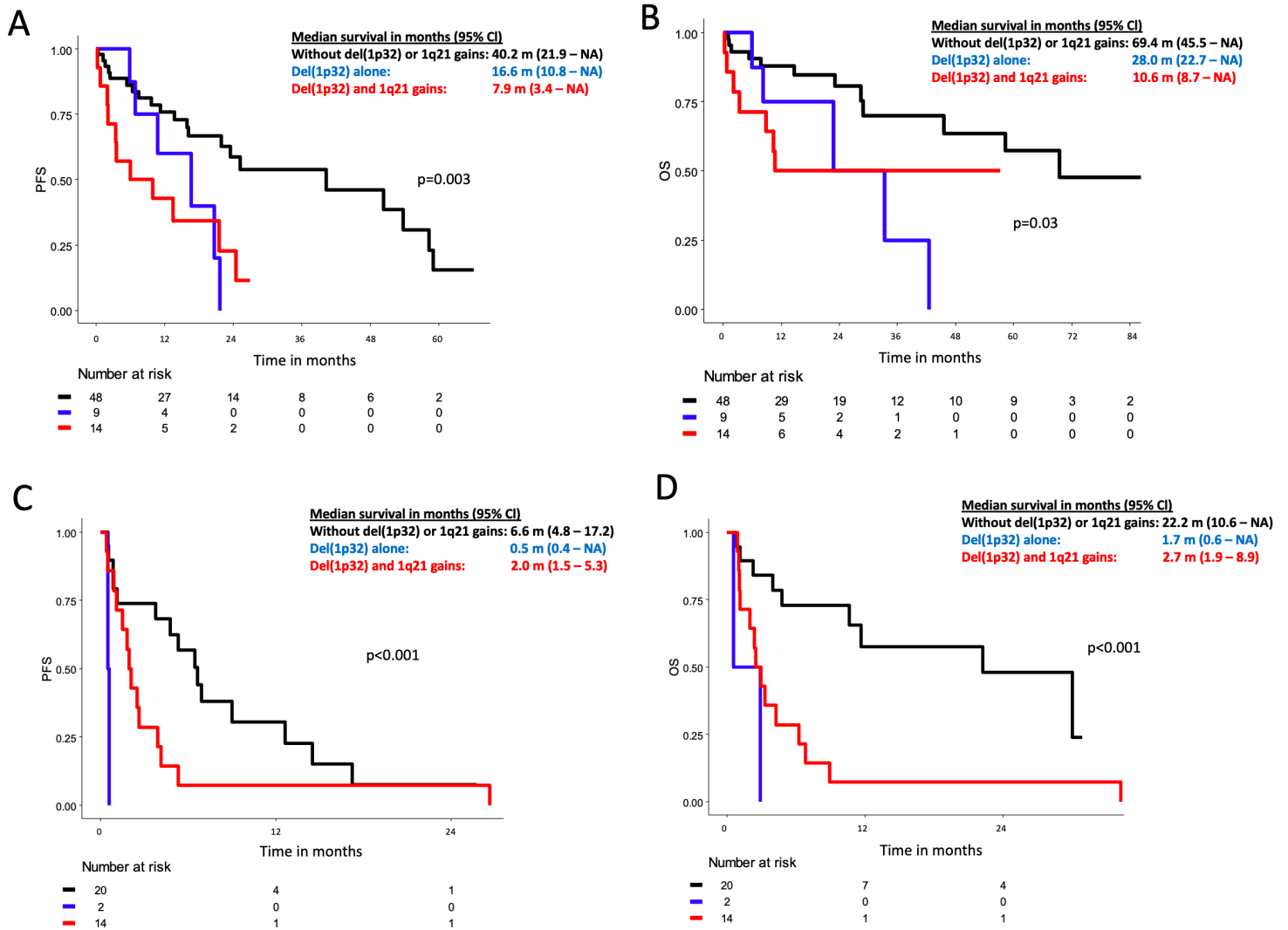
| - EMM sampling; + - death on disease progression; ‡ - death without disease progression

**Supplementary Figure 2** - Examples of individual clones on microscope images.



In sample BMPCs 12, clone 1 presents with deletion of 1p32 (green signal) and gain of 1q21 (orange signals), in clone 2 the aberrant pattern is duplicated. In sample TPCs 20, clone 1 has trisomy of chromosome 17 (green centromeric signals) with deletion of one copy of TP53 gene (orange signals), clone 2 has tetrasomy of chromosome 17 and deletion of two copies of TP53 gene. In the same sample, there is one hyperdiploid clone with trisomies of chromosomes 5 (green signals), 9 (blue signals) and 15 (orange signals), and a second clone where these aberrations are duplicated.

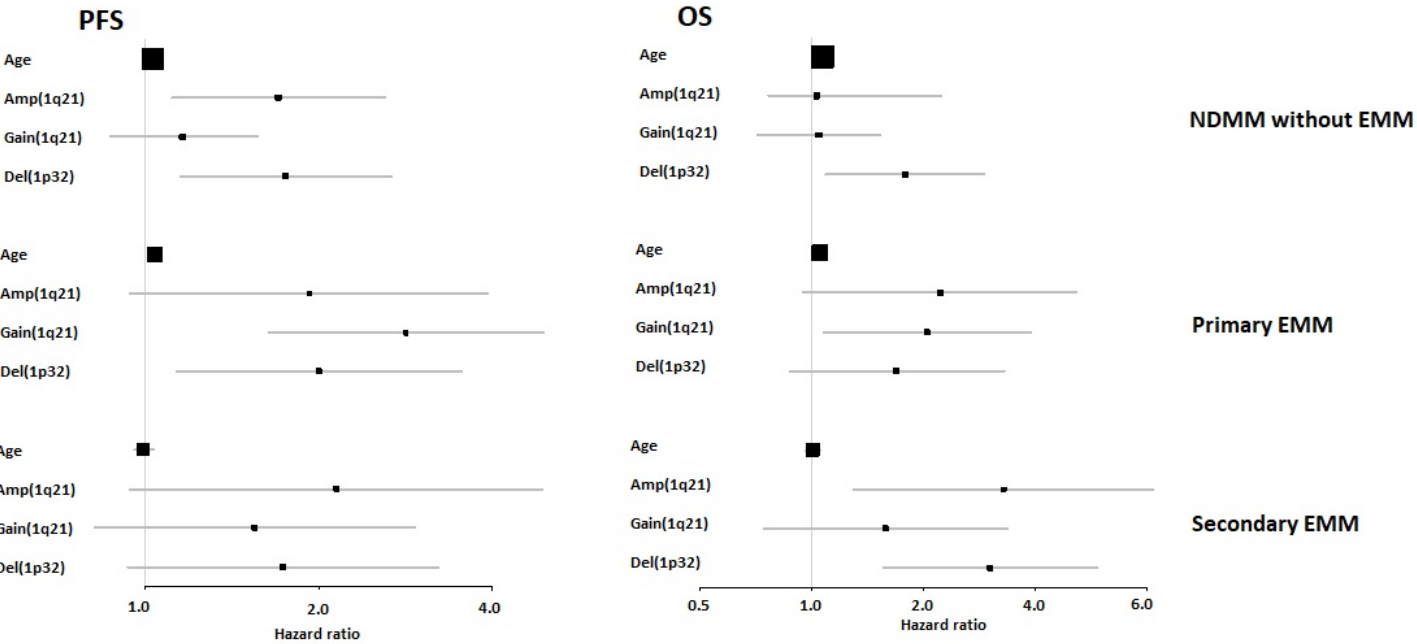
**Supplementary Figure 3** - Kaplan-Meier curves illustrating survival intervals according to the presence of del(1p32) and 1q21 gains.



Progression Free Survival (PFS). Overall Survival (OS).

Panels show: A) PFS in primary EMM patients, B) OS in primary EMM patients, C) PFS in secondary EMM patients, and D) OS in secondary EMM patients. Cox univariate models were used for time-to-event response variables.

**Supplementary Figure 4** - Hazard ratio of PFS/OS in separate chromosome 1 aberrations showed in forest plot model.



Cox univariate models (in case of time-event type of response variables)

**Supplementary Table 1** – Characteristics of patients with paired samples

| Patient no.<br>(inc.EMM<br>type) | Site of EMM      | Age at<br>EMM<br>sampling<br>(y) | gender | Monoclonal<br>Ig type | ISS | Number of<br>previous<br>treatment<br>lines before<br>EMM<br>sampling | Refractory status<br>before EMM<br>sampling |
|----------------------------------|------------------|----------------------------------|--------|-----------------------|-----|-----------------------------------------------------------------------|---------------------------------------------|
| NDMM-PS1                         | skul             | 62                               | M      | FLC only              | 1   | 0                                                                     | NA                                          |
| NDMM-PS2                         | rib              | 73                               | M      | IgG kappa             | 3   | 0                                                                     | NA                                          |
| NDMM-PS3                         | sternum          | 71                               | M      | FLC only              | 1   | 0                                                                     | NA                                          |
| NDMM-PS4                         | spine            | 61                               | F      | IgG kappa             | 1   | 0                                                                     | NA                                          |
| NDMM-PS5                         | spine            | 73                               | M      | IgA lambda            | 2   | 0                                                                     | NA                                          |
| NDMM-PS6                         | spine            | 79                               | F      | IgG kappa             | 2   | 0                                                                     | NA                                          |
| NDMM-PS7                         | spine            | 63                               | M      | IgG kappa             | 3   | 0                                                                     | NA                                          |
| NDMM-PS8                         | skull            | 64                               | F      | FLC only              | 3   | 0                                                                     | NA                                          |
| NDMM-PS9                         | spine            | 57                               | M      | FLC only              | 2   | 0                                                                     | NA                                          |
| NDMM-EMD10                       | liver            | 77                               | F      | IgA kappa             | 3   | 0                                                                     | NA                                          |
| RRMM-PS11                        | orbital cavity   | 76                               | F      | IgA kappa             | 1   | 2                                                                     | double                                      |
| RRMM-EMD12                       | peripheral nerve | 68                               | F      | FLC only              | 3   | 2                                                                     | double                                      |
| RRMM-EMD13                       | skin             | 76                               | F      | FLC only              | 3   | 1                                                                     | len                                         |
| RRMM-EMD14                       | skin             | 68                               | F      | FLC only              | 3   | 5                                                                     | penta                                       |
| RRMM-EMD15                       | skin             | 69                               | F      | IgG kappa             | 2   | 7                                                                     | penta                                       |
| RRMM-EMD16                       | skin             | 70                               | M      | IgG lambda            | 3   | 4                                                                     | triple                                      |
| RRMM-EMD17                       | skin             | 61                               | M      | IgG lambda            | 1   | 8                                                                     | penta                                       |
| RRMM-EMD18                       | effusion         | 69                               | F      | IgA lambda            | 3   | 3                                                                     | triple                                      |
| RRMM-PS19                        | maxila           | 79                               | F      | IgG kappa             | 3   | 3                                                                     | triple                                      |
| RRMM-PS20                        | skull            | 78                               | F      | IgG kappa             | 3   | 2                                                                     | triple                                      |
| RRMM-EMD21                       | chest wall       | 66                               | M      | IgG kappa             | 1   | 9                                                                     | penta                                       |
| RRMM-EMD22                       | skin             | 74                               | M      | IgG kappa             | 3   | 4                                                                     | penta                                       |

Len – lenalidomide; double refractory – PI and IMiD; triple class refractory – PI, IMiD, anti-CD38 antibody; penta-refractory – 2 PIs, 2 IMiDs and anti-CD38 antibody

**Supplementary table 2** - Cytogenetic data of patients` groups.

| Category                                   | NDMM without plasmacytoma (N=243) | Primary EMM (N=111) | Secondary EMM (N=56) | p-value*         |
|--------------------------------------------|-----------------------------------|---------------------|----------------------|------------------|
| <b>Gender (male)</b>                       | 47.7% (116/243)                   | 59.4% (66/111)      | 58.9% (33/56)        | 0,071            |
| <b>Age (median; min-max)</b>               | 71 (40–92)                        | 66 (42–83)          | 65 (44–82)           | <b>0.002</b>     |
| <b>ECOG (%)</b>                            |                                   |                     |                      | 0.190            |
| Stage 0-1                                  | 73.7% (179/243)                   | 71.2% (79/111)      | 64.3% (36/56)        |                  |
| Stage 2                                    | 17.3% (42/243)                    | 18.0% (20/111)      | 30.6% (17/56)        |                  |
| Stage 3-4                                  | 9.0% (22/243)                     | 10.8% (12/111)      | 5.3% (3/56)          |                  |
| <b>ISS (%)</b>                             |                                   |                     |                      | <b>0.031</b>     |
| Stage 1                                    | 25.9% (63/243)                    | 32.4% (36/111)      | 25.0% (14/56)        |                  |
| Stage 2                                    | 29.6% (72/243)                    | 38.7% (43/111)      | 32.1% (18/56)        |                  |
| Stage 3                                    | 44.4% (108/243)                   | 26.1% (29/111)      | 42.9% (24/56)        |                  |
| <b>R-ISS (%)</b>                           |                                   |                     |                      | 0.078            |
| Stage 1                                    | 18.9% (46/243)                    | 20.7% (23/111)      | 5.4% (3/56)          |                  |
| Stage 2                                    | 55.1% (134/243)                   | 59.4% (66/111)      | 66.1% (37/56)        |                  |
| Stage 3                                    | 25.9% (63/243)                    | 19.8% (22/111)      | 28.6% (16/56)        |                  |
| <b>Number of osteolytic lesions (%)</b>    |                                   |                     |                      | <b>&lt;0.001</b> |
| no lesions                                 | 21.4% (52/243)                    | 0%                  | 5.4% (3/56)          |                  |
| 1 lesion                                   | 10.7% (26/243)                    | 5.4% (6/111)        | 0%                   |                  |
| 2 lesions                                  | 7.4% (18/243)                     | 7.2% (8/111)        | 8.9% (5/56)          |                  |
| >2 lesions                                 | 60.5% (147/243)                   | 87.4% (97/111)      | 85.7% (48/56)        |                  |
| <b>Plasmacytoma type</b>                   |                                   |                     |                      | <b>0.007</b>     |
| PS                                         | NA                                | 89.2% (99/111)      | 71.4% (40/56)        |                  |
| EMD                                        | NA                                | 10.8% (12/111)      | 28.6% (16/56)        |                  |
| <b>1<sup>st</sup> line treatment (%)</b>   |                                   |                     |                      | <b>0.003</b>     |
| PI+IMiD based                              | 39.9% (97/243)                    | 57.7% (64/111)      | 37.5% (21/56)        |                  |
| PI based                                   | 55.6% (135/243)                   | 39.6% (44/111)      | 60.7% (34/56)        |                  |
| IMiD based                                 | 0%                                | 0.9% (1/111)        | 1.8% (1/56)          |                  |
| other                                      | 4.5% (11/243)                     | 1.8% (2/111)        | 0%                   |                  |
| <b>1<sup>st</sup> line ASCT (%)</b>        | 23.0% (56/243)                    | 33.3% (37/111)      | 48.2% (27/56)        | <b>&lt;0.001</b> |
| <b>Follow up (months, median; min-max)</b> | 27.9 (0.1–104.3)                  | 17.7 (0.1–95.1)     | 43.2 (0.4–108.9)     | <b>&lt;0.001</b> |

\*Fisher exact test

**Supplementary table 3A** - Progression Free Survival (PFS) in groups of EMM patients according to chromosome 1 aberrations.

|                  |                      |            | PFS              |             |              |                  |             |
|------------------|----------------------|------------|------------------|-------------|--------------|------------------|-------------|
|                  |                      |            | median in months | 95 %CI      |              | p-value          | No. of pts. |
| <b>+ 1q21</b>    | <b>Primary EMM</b>   | Amp(1q21)  | 15,74            | 7,77        | NA           | 0.073            | 14          |
|                  |                      | Gain(1q21) | <b>14,33</b>     | <b>5,54</b> | <b>21,41</b> | <b>&lt;0.001</b> | <b>40</b>   |
|                  |                      | negative   | 23,44            | 16,59       | 58,10        | -                | 57          |
|                  | <b>Secondary EMM</b> | Amp(1q21)  | 1,61             | 0,56        | NA           | 0.071            | 9           |
|                  |                      | Gain(1q21) | 2,30             | 1,80        | 4,13         | 0.190            | 25          |
|                  |                      | negative   | 6,43             | 1,11        | 14,46        | -                | 22          |
| <b>Del(1p32)</b> | <b>Primary EMM</b>   | negative   | 21,51            | 15,80       | 32,33        | -                | 88          |
|                  |                      | Del(1p32)  | <b>10,75</b>     | <b>5,93</b> | <b>24,43</b> | <b>0.017</b>     | <b>23</b>   |
|                  | <b>Secondary EMM</b> | negative   | 3,77             | 2,00        | 6,59         | -                | 40          |
|                  |                      | Del(1p32)  | 1,87             | 0,89        | 4,10         | 0.083            | 16          |

Survival in months. **Bold values** show significant difference in survival when compared to reference group without aberration (Wald test).

**Supplementary table 3B** - Overall Survival (OS) in groups of EMM patients according to chromosome 1 aberrations.

|                  |                      |            | OS               |              |             |              |             |
|------------------|----------------------|------------|------------------|--------------|-------------|--------------|-------------|
|                  |                      |            | median in months | 95 %CI       |             | p-value      | No. of pts. |
| <b>+ 1q21</b>    | <b>Primary EMM</b>   | Amp(1q21)  | 22,39            | 9,21         | NA          | 0.065        | 14          |
|                  |                      | Gain(1q21) | <b>32,69</b>     | <b>23,05</b> | <b>NA</b>   | <b>0.029</b> | <b>40</b>   |
|                  |                      | negative   | 58,10            | 33,28        | NA          | -            | 57          |
|                  | <b>Secondary EMM</b> | Amp(1q21)  | <b>2,69</b>      | <b>1,08</b>  | <b>NA</b>   | <b>0.012</b> | <b>9</b>    |
|                  |                      | Gain(1q21) | 4,59             | 3,34         | NA          | 0.230        | 25          |
|                  |                      | negative   | 22,16            | 4,75         | NA          | -            | 22          |
| <b>Del(1p32)</b> | <b>Primary EMM</b>   | negative   | 35,64            | 28,79        | NA          | -            | 88          |
|                  |                      | Del(1p32)  | 33,28            | 10,30        | NA          | 0.120        | 23          |
|                  | <b>Secondary EMM</b> | negative   | 10,59            | 4,59         | NA          | -            | 40          |
|                  |                      | Del(1p32)  | <b>2,69</b>      | <b>1,08</b>  | <b>6,79</b> | <b>0.001</b> | <b>16</b>   |

Survival in months. **Bold values** show significant difference in survival when compared to reference group without aberration (Wald test).