

Supplementary material

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| Table S1. Number of newly diagnosed MM patients included in the four upfront trials conducted by the Spanish Myeloma Group GEM (GEM05mas65, GEM05menores65, GEM2010, GEM2012) | 2 |
| Table S2. Responses achieved after induction by different cytogenetic groups of patients included in the Spanish Myeloma trials (GEM05mas65, GEM05menores65, GEM2010, GEM2012) | 3 |
| Table S3: Comparison of basal characteristics of MM patients with and without t(4;14) included in the Spanish Myeloma trials (GEM05MAS65, GEM05MENOS65, GEM2010, GEM2012) | 4 |
| Table S4. Comparison of basal characteristics of MM patients with and without t(14;16) included in the Spanish Myeloma trials (GEM05MAS65, GEM05MENOS65, GEM2010, GEM2012) | 5 |
| Table S5. Comparison of basal characteristics of MM patients with and without del(17p) included in the Spanish Myeloma trials (GEM05MAS65, GEM05MENOS65, GEM2010, GEM2012). | 6 |
| Table S6. PFS and OS by different cut-off points based on the percentage of cells harboring del(17p) in the Spanish Myeloma trials (GEM05mas65, GEM05menores65, GEM2010, GEM2012). | 7 |

Table S1. Number of newly diagnosed MM patients included in the four upfront trials conducted by the Spanish Myeloma Group GEM (GEM05mas65, GEM05menores65, GEM2010, GEM2012)

| SPANISH MYELOMA TRIALS | Frequency | Percent (%) |
|------------------------|-----------|-------------|
| GEM05MAS65 | 257 | 19,7 |
| GEM2010 | 236 | 18,1 |
| GEM05MENOS65 | 354 | 27,1 |
| GEM2012 | 457 | 35,0 |
| Total | 1304 | 100,0 |

Table S2. Responses achieved after induction by different cytogenetic groups of patients included in the Spanish Myeloma trials (GEM05mas65, GEM05menores65, GEM2010, GEM2012)

| | | Response after induction | | |
|-----------------|-----------------|--------------------------|------------|---------|
| | | CR | <CR | p value |
| del(17p) | positive | 19 (22.9) | 64 (77.1) | NS |
| | negative | 321 (30.9) | 718 (69.1) | |
| t(4;14) | positive | 45 (32.6) | 93 (67.4) | NS |
| | negative | 293 (29.6) | 698 (70.4) | |
| t(14;16) | positive | 9 (29.0) | 22 (71.0) | NS |
| | negative | 326 (30.0) | 759 (70.0) | |
| gain(1q) | positive | 129 (34.8) | 242 (65.2) | 0.07 |
| | negative | 145 (29.0) | 355 (71.0) | |
| del(1p) | positive | 25 (35.7) | 45 (64.3) | NS |
| | negative | 246 (30.9) | 549 (69.1) | |

CR: complete response; <CR: less than complete response; NS: not statistically significant.

Table S3: Comparison of basal characteristics of MM patients with and without t(4;14) included in the Spanish Myeloma trials (GEM05MAS65, GEM05MENOS65, GEM2010, GEM2012)

| Basal Characteristics | t(4;14) (n=142) | Non t(4;14) (n=1023) | P value |
|----------------------------------|----------------------------|---------------------------------|----------------|
| Gender | | | |
| Male, No. (%) | 69 (48.6) | 542 (53.0) | NS |
| Female, No. (%) | 73 (51.4) | 481 (47.0) | |
| Light chain MM, No. (%): | 11 (7.7) | 141 (13.9) | 0.04 |
| Ig G, IG A or Ig D MM, No. (%) | 131 (92.3) | 873 (86.1) | |
| Light chain subtype: | | | |
| kappa, No. (%) | 92 (64.8) | 630 (62.1) | NS |
| lambda, No. (%) | 50 (35.2) | 384 (37.9) | |
| Serum M-protein: | | | |
| < 1g/dL, No. (%) | 13 (9.2) | 177 (17.5) | 0.01 |
| ≥ 1 g/dL, No. (%) | 129 (90.8) | 835 (82.5) | |
| Serum M-protein: | | | |
| ≥ 3 g/dL, No. (%) | 95 (66.9) | 552 (54.7) | 0.006 |
| < 3 g/dL, No. (%) | 47 (33.1) | 457 (45.3) | |
| BM PC by morphology: | | | |
| ≥ 60% | 32 (23.0) | 209 (21.7) | NS |
| 10-59% | 107 (77.0) | 756 (78.3) | |
| Hypercalcemia (>11g/dL), No. (%) | 14 (9.9) | 84 (8.3) | NS |
| Creatinine: | | | |
| ≥ 1.5 g/dL, No. (%) | 10 (7.0) | 109 (10.7) | NS |
| < 1.5 g/dL, No. (%) | 132 (93.0) | 909 (89.3) | |
| Hemoglobin: | | | |
| ≤ 10 g/dL, No. (%) | 67 (47.2) | 369 (36.2) | 0.01 |
| > 10 g/dL, No. (%) | 75 (52.8) | 650 (63.8) | |
| ISS stage, No. (%): | | | |
| I | 35 (24.8) | 346 (34.2) | NS |
| II | 68 (48.2) | 418 (41.3) | |
| III | 38 (27.0) | 248 (24.5) | |
| High LDH, No. (%) | 25 (17.7) | 151 (14.8) | NS |

Table S4. Comparison of basal characteristics of MM patients with and without t(14;16) included in the Spanish Myeloma trials (GEM05MAS65, GEM05MENOS65, GEM2010, GEM2012)

| Basal Characteristics | t (14;16) (n=31) | Absence of t (14;16) (n=1119) | P value |
|---|------------------------------------|--|----------------|
| Male/ female, No. (%) | 11 (35.5) / 20 (64.5) | 592 (52.9) / 527 (47.1) | 0.06 |
| Light chain MM, No. (%): Ig G, IG A or Ig D MM, No. (%) | 4 (12.9) 27 (87.1) | 144 (13.0) 967 (87.0) | NS |
| Light chain subtype: kappa, No. (%) lambda, No. (%) | 17 (54.8) 14 (45.2) | 696 (62.6) 415 (37.4) | NS |
| Serum M-protein: < 1g/dL, No. (%) ≥ 1 g/dL, No. (%) | 6 (20.0) 24 (80.0) | 179 (16.1) 930 (83.9) | NS |
| BM PC by morphology: ≥ 60% 10-59% | 9 (30.0) 21 (70.0) | 230 (21.7) 829 (78.3) | NS |
| Hypercalcemia (11g/dL), No. (%) | 1 (3.3) | 96 (8.6) | NS |
| Creatinine: < 1.5 g/dL, No. (%) ≥ 1.5 g/dL, No. (%) | 26 (86.7) 4 (13.3) | 1002 (89.9) 113 (10.1) | NS |
| Hemoglobin: ≤ 10 g/dL, No. (%) > 10 g/dL, No. (%) | 12 (40.0) 18 (60.0) | 419 (37.5) 697 (62.5) | NS |
| ISS stage, No. (%): I II III | 7 (23.3) 10 (33.3) 13 (43.3) | 369 (33.3) 472 (42.6) 267 (24.1) | 0.05 |
| High LDH, No. (%) | 4 (12.9) | 171 (15.4) | NS |

MM: multiple myeloma; yrs: years-old; No.: number of patients; BM PC: bone marrow plasma cells; ISS: International Staging System; LDH: lactate dehydrogenase

Table S5. Comparison of basal characteristics of MM patients with and without del(17p) included in the Spanish Myeloma trials (GEM05MAS65, GEM05MENOS65, GEM2010, GEM2012).

| Basal Characteristics | del(17p) (No=89) | Absence of del(17p) (No=1059) | P value |
|---------------------------------|-----------------------------|--|----------------|
| Male/ female, No. (%) | 40 (44.9) / 49 (55.1) | 568 (53.2) / 500 (46.8) | NS |
| Ig G, IG A or Ig D MM, no. (%) | 69 (77.5) | 927 (87.5) | 0.01 |
| Light chain MM, no. (%): | 20 (22.5) | 132 (12.5) | |
| Light chain subtype: | | | NS |
| Kappa, No. (%) | 58 (65.2) | 656 (61.9) | |
| Lambda, No. (%) | 31 (34.8) | 403 (38.1) | |
| Serum M-protein: | | | 0.02 |
| < 1g/dL, No. (%) | 23 (25.8) | 168 (15.9) | |
| ≥ 1 g/dL, No. (%) | 66 (74.2) | 889 (84.1) | |
| BM PC by morphology: | | | 0.04 |
| ≥ 60% | 25 (30.5) | 211 (20.8) | |
| 10-59% | 57 (69.5) | 804 (79.2) | |
| Hypercalcemia (11g/dL), No. (%) | 12 (13.5) | 86 (8.1) | 0.08 |
| Creatinine: | | | NS |
| < 1.5 g/dL, No. (%) | 77 (86.5) | 958 (90.1) | |
| ≥ 1.5 g/dL, No. (%) | 12 (13.5) | 105 (9.9) | |
| Hemoglobin: | | | NS |
| ≤ 10 g/dL, No. (%) | 38 (42.7) | 392 (36.8) | |
| > 10 g/dL, No. (%) | 51 (57.3) | 672 (63.2) | |
| ISS stage, No. (%): | | | 0.03 |
| I | 19 (22.1) | 365 (34.5) | |
| II | 38 (44.2) | 442 (41.7) | |
| III | 29 (33.7) | 252 (23.8) | |
| High LDH, No. (%) | 27 (30.3) | 146 (13.7) | <0.001 |

MM: multiple myeloma; yrs: years-old; No.: number of patients; BM PC: bone marrow plasma cells; ISS: International Staging System; LDH: lactate dehydrogenase

Table S6. PFS and OS by different cut-off points based on the percentage of cells harboring del(17p) in the Spanish Myeloma trials (GEM05mas65, GEM05menores65, GEM2010, GEM2012).

| Cut off for percentage of cells with del17p | | No. of patients with the chr abnormality | % of patients studied with the chr abnormality | Median PFS (months) | HR for PFS (CI 95%)* | Median OS (months) | HR for OS (CI 95%) |
|---|------------------|--|--|---------------------|----------------------|--------------------|--------------------|
| ≥20% | Negative (0-19%) | 1043 | 92.3 | 46.0 | 1.9 (1.5-2.4) | NR | 2.5 (1.9-3.3) |
| | ≥20% | 89 | 7.7 | 23.9 | | 37.0 | |
| ≥30% | Negative (0-29%) | 1062 | 93.8 | 45.4 | 1.9 (1.4-2.5) | NR | 2.4 (1.8-3.3) |
| | ≥30% | 70 | 6.2 | 22.0 | | 38.1 | |
| ≥40% | Negative (0-39%) | 1072 | 94.7 | 45.4 | 2.0 (1.5-2.7) | NR | 2.6 (1.9-3.6) |
| | ≥40% | 60 | 5.3 | 21.0 | | 32.5 | |
| ≥50% | Negative (0-49%) | 1078 | 95.2 | 45.3 | 2.0 (1.5-2.7) | NR | 2.6 (1.8-3.6) |
| | ≥50% | 54 | 4.8 | 20.2 | | 32.5 | |
| ≥60% | Negative (0-59%) | 1091 | 96.4 | 45.0 | 2.0 (1.4-2.9) | NR | 2.3 (1.5-3.4) |
| | ≥60% | 41 | 3.6 | 21.0 | | 38.1 | |
| ≥70% | Negative (0-69%) | 1098 | 97 | 44.7 | 2.0 (1.4-2.9) | NR | 2.3 (1.5-3.5) |
| | ≥70% | 34 | 3.0 | 18.8 | | 38.1 | |
| ≥80% | Negative (0-79%) | 1110 | 98.1 | 44.3 | 2.3 (1.5-3.7) | NR | 2.2 (1.3-3.7) |
| | ≥80% | 22 | 1.9 | 13.8 | | 45.6 | |
| ≥90% | Negative (0-89%) | 1119 | 98.9 | 44.3 | 3.6 (2.1-6.4) | NR | 2.8 (1.5-5.4) |
| | ≥90% | 13 | 1.1 | 8.4 | | 31.2 | |

*All differences are statistically significant (p-value < 0.05). Comparison are made between patients with presence of del(17p) and negative patients.
NR: Not reached.