The prognostic value of whole-blood PSMB5, CXCR4, POMP and RPL5 mRNA expression in patients with multiple myeloma treated with bortezomib

**Suplemental Data**

Table S1. mRNA expression in MM patients with complete remission (CR) to bortezomib-based chemotherapy and those without. The higher ΔCt value represents lower expression of the gene at mRNA level.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| mRNA | ΔCt <CR  mean ± SD | ΔCt CR  mean ± SD | FC | p-value | FWER |
| ABCB1 | 7.54 ± 1.00 | 7.56 ± 1.00 | 1.01 | 0.9462 | 1.0000 |
| CXCR4 | 3.79 ± 0.81 | 3.92 ± 0.86 | 1.10 | 0.5222 | 1.0000 |
| MAF | 7.65 ± 1.12 | 7.97 ± 0.98 | 1.25 | 0.2206 | 1.0000 |
| MARCKS | 5.95 ± 0.73 | 6.09 ± 1.01 | 1.10 | 0.5506 | 1.0000 |
| POMP | 5.10 ± 0.59 | 5.31 ± 0.79 | 1.16 | 0.2610 | 1.0000 |
| PSMB5 | 6.97 ± 0.74 | 6.92 ± 0.88 | 0.97 | 0.8123 | 1.0000 |
| RPL5 | 2.80 ± 0.76 | 2.60 ± 0.92 | 0.87 | 0.3593 | 1.0000 |
| TXN | 3.36 ± 0.75 | 3.57 ± 0.70 | 1.16 | 0.2532 | 1.0000 |
| XBP1 | 3.20 ± 0.92 | 3.39 ± 0.91 | 1.14 | 0.4154 | 1.0000 |

Table S2. mRNA expression in MM patients with at least very good partial response (≥VGPR) and with partial response, stable disease or disease progression (<VGPR) after bortezomib-based treatment. Higher ΔCt values represent lower expression of the gene at the mRNA level.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| mRNA | ΔCt <VGPR  mean ± SD | ΔCt ≥VGPR  mean ± SD | FC | p-value | FWER |
| ABCB1 | 7.56 ± 1.04 | 7.54 ± 0.97 | 0.99 | 0.9510 | 1.0000 |
| CXCR4 | 3.70 ± 0.79 | 3.95 ± 0.84 | 1.19 | 0.2035 | 1.0000 |
| MAF | 7.63 ± 1.14 | 7.86 ± 1.02 | 1.17 | 0.3754 | 1.0000 |
| MARCKS | 5.91 ± 0.71 | 6.06 ± 0.93 | 1.11 | 0.4558 | 1.0000 |
| POMP | 5.10 ± 0.51 | 5.23 ± 0.77 | 1.09 | 0.4085 | 1.0000 |
| PSMB5 | 7.01 ± 0.72 | 6.91 ± 0.84 | 0.93 | 0.6020 | 1.0000 |
| RPL5 | 2.74 ± 0.78 | 2.73 ± 0.85 | 0.99 | 0.9552 | 1.0000 |
| TXN | 3.33 ± 0.62 | 3.52 ± 0.82 | 1.14 | 0.2645 | 1.0000 |
| XBP1 | 3.30 ± 0.91 | 3.23 ± 0.93 | 0.95 | 0.7327 | 1.0000 |

**Table S3.** mRNA expression in MM patients treatment-naive and previously treated. The higher ΔCt value represents the lower expression of gene at mRNA level.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| mRNA | **Δ Ct** Previously treated | | **Δ Ct** Newly diagnosed | | *p* |
| Mean | SD | Mean | SD |
| CXCR4 | 3.75 | 0.77 | 3.81 | 0.85 | 0.81 |
| POMP | 5.04 | 0.70 | 5.18 | 0.67 | 0.52 |
| PSMb5 | 6.96 | 0.67 | 6.94 | 0.81 | 0.93 |
| RPL5 | 2.84 | 0.69 | 2.73 | 0.84 | 0.64 |
| ABCB1 | 6.95 | 1.17 | 7.62 | 1.02 | 0.08 |
| MAF | 7.48 | 1.52 | 7.80 | 0.99 | 0.51 |
| MARCKS | 6.15 | 0.73 | 5.94 | 0.87 | 0.40 |
| TXN | 3.53 | 0.53 | 3.38 | 0.79 | 0.42 |
| XBP1 | 3.12 | 1.02 | 3.30 | 0.89 | 0.58 |

**Table S4.** Univariate Cox regression analyses for progression-free survival with missing data (n=7) replaced by overall survival.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | | | | |
| **Coefficient** | **p-value** | **HR** | **95% CI** | |
| **lower** | **upper** |
| ABCB1 expression (high vs. low) | -0.253 | 0.2240 | 0.603 | 0.267 | 1.362 |
| CXCR4 expression (high vs. low) | 0.524 | 0.0290 | 2.851 | 1.113 | 7.299 |
| MAF expression (high vs. low) | 0.156 | 0.3242 | 1.365 | 0.735 | 2.533 |
| PSMB5 expression (high vs. low) | 0.416 | 0.0102 | 2.296 | 1.218 | 4.329 |
| RPL5 expression (high vs. low) | -0.089 | 0.5688 | 0.836 | 0.453 | 1.546 |
| MARCKS expression (high vs. low) | 0.464 | 0.0053 | 2.532 | 1.317 | 4.867 |
| POMP expression (high vs. low) | 0.378 | 0.0249 | 2.132 | 1.100 | 4.129 |
| TXN expression (high vs. low) | 0.360 | 0.0323 | 2.056 | 1.063 | 3.978 |
| XBP1 expression (high vs. low) | 0.393 | 0.0161 | 2.193 | 1.157 | 4.159 |

Table S5. Univariate Cox regression analyses for progression-free survival and overall survival.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Variables** | **PFS** | | | | **OS** | | | |
| **p-value** | **HR** | **95% CI** | | **p-value** | **HR** | **95% CI** | |
| **lower** | **upper** | **lower** | **upper** |
| ABCB1 expression | 0.7519 | 0.947 | 0.674 | 1.330 | 0.5221 | 0.868 | 0.562 | 1.340 |
| CXCR4 expression | 0.2101 | 1.217 | 0.895 | 1.656 | 0.4274 | 1.211 | 0.755 | 1.938 |
| MAF expression | 0.1661 | 1.284 | 0.902 | 1.828 | 0.8496 | 1.045 | 0.662 | 1.650 |
| MARCKS expression | **0.0099** | 1.715 | 1.139 | 2.591 | 0.783 | 0.938 | 0.595 | 1.479 |
| POMP expression | **0.0027** | 2.660 | 1.404 | 5.025 | **0.0239** | 2.262 | 1.114 | 4.587 |
| PSMB5 expression | 0.0827 | 1.435 | 0.954 | 2.155 | 0.298 | 1.332 | 0.776 | 2.283 |
| RPL5 expression | 0.7674 | 1.060 | 0.720 | 1.560 | **0.0386** | 1.592 | 1.025 | 2.475 |
| TXN expression | **0.033** | 1.653 | 1.042 | 2.625 | 0.1491 | 1.517 | 0.861 | 2.674 |
| XBP1 expression | **0.0353** | 1.499 | 1.029 | 2.183 | 0.3182 | 1.287 | 0.784 | 2.114 |

**Table S6.** Comparison of final Cox regression of multivariate models based on dichotomized variables (model 1) and continuous variables (model 2).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Model | Variables | p-value | HR | 95% CI | | AIC |
| **lower** | **upper** |
| Model 1 | PSMB5 expression (high vs. low) | 0.0451 | 2.164 | 1.017 | 4.603 | 189.486 |
| CXCR expression (high vs. low) | 0.0073 | 4.465 | 1.496 | 13.32 |
| ASCT |  |  |  |  |
| No |  | Reference |  |  |
| Yes | 0.0024 | 0.294 | 0.133 | 0.649 |
| Model 2 | MARCKS expression | 0.0051 | 0.565 | 0.378 | 0.842 | 194.737 |
| ASCT |  |  |  |  |
| No |  | Reference |  |  |
| Yes | 0.0022 | 3.333 | 1.543 | 7.194 |

Table S7: Normalized ΔCt of mRNA expression for all samples and with class assignments (0- control, 1 –sensitive, 2 – refractory; J13,  *fx* -3,61166666666667)

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| . | ABCB1 | CXCR4 | MAF | MARCKS | POMP | PSMB5 | RPL5 | TXN | XBP1 |
| 1 | 8,181667 | 3,841667 | 7,331667 | 6,681667 | 5,266667 | 7,141667 | 2,501667 | 3,651667 | 2,991667 |
| 2 | 8,051667 | 3,416667 | 7,856667 | 6,856667 | 4,961667 | 7,296667 | 2,896667 | 3,666667 | 3,801667 |
| 2 | 9,858333 | 4,818333 | 9,998333 | 6,218333 | 5,558333 | 7,543333 | 2,883333 | 3,538333 | 4,258333 |
| 2 | 7,218333 | 3,993333 | 6,818333 | 6,423333 | 5,028333 | 6,818333 | 1,723333 | 3,913333 | 2,858333 |
| 2 | 8,698333 | 3,783333 | 8,178333 | 5,563333 | 4,593333 | 6,403333 | 2,683333 | 3,003333 | 3,938333 |
| 2 | 9,908333 | 2,108333 | 8,933333 | 6,438333 | 5,188333 | 8,418333 | 3,348333 | 2,388333 | 4,558333 |
| 1 | 6,203333 | 3,223333 | 6,118333 | 6,128333 | 4,628333 | 6,168333 | 2,073333 | 4,818333 | 2,228333 |
| 1 | 8,086667 | 4,026667 | 8,676667 | 6,676667 | 5,101667 | 7,831667 | 3,316667 | 2,676667 | 4,276667 |
| 1 | 9,303333 | 5,628333 | 10,10333 | 7,768333 | 6,978333 | 9,203333 | 4,578333 | 4,123333 | 5,653333 |
| 1 | 6,591667 | 4,646667 | 7,661667 | 6,716667 | 5,616667 | 7,076667 | 2,336667 | 4,521667 | 3,821667 |
| 1 | 9,54 | 5,22 | 8,725 | 7,1 | 5,445 | 7,49 | 2,95 | 2,73 | 4,445 |
| 2 | 7,626667 | 3,351667 | 8,416667 | 6,496667 | 5,141667 | 7,491667 | 2,541667 | 3,941667 | 3,611667 |
| 1 | 8,823333 | 5,108333 | 9,498333 | 6,943333 | 6,628333 | 7,903333 | 3,808333 | 5,183333 | 5,293333 |
| 1 | 7,365 | 4,225 | 8,885 | 5,865 | 5,285 | 7,675 | 3,76 | 2,87 | 4,09 |
| 1 | 5,893333 | 3,353333 | 8,953333 | 6,188333 | 5,533333 | 7,378333 | 2,003333 | 3,638333 | 3,233333 |
| 1 | 7,001667 | 3,576667 | 7,566667 | 5,981667 | 5,481667 | 5,766667 | 1,736667 | 4,101667 | 3,566667 |
| 2 | 5,753333 | 3,178333 | 6,763333 | 5,153333 | 3,848333 | 5,568333 | 1,848333 | 2,283333 | 2,793333 |
| 1 | 7,658333 | 0,793333 | 7,843333 | 6,133333 | 5,188333 | 7,223333 | 2,578333 | 2,283333 | 3,593333 |
| 1 | 7,726667 | 4,641667 | 8,396667 | 7,166667 | 5,681667 | 7,821667 | 3,706667 | 3,546667 | 5,011667 |
| 1 | 6,658333 | 3,368333 | 6,838333 | 5,883333 | 4,993333 | 7,578333 | 2,943333 | 3,248333 | 3,808333 |
| 1 | 7,053333 | 3,513333 | 6,723333 | 5,263333 | 4,733333 | 6,178333 | 2,268333 | 3,468333 | 2,613333 |
| 2 | 6,186667 | 4,181667 | 7,111667 | 6,466667 | 4,791667 | 6,586667 | 2,346667 | 3,181667 | 3,371667 |
| 1 | 6,526667 | 3,631667 | 7,151667 | 5,856667 | 5,156667 | 6,546667 | 2,576667 | 3,241667 | 3,601667 |
| 2 | 8,67 | 3,685 | 9,335 | 5,505 | 5,995 | 7,93 | 3,74 | 3,02 | 3,2 |
| 2 | 6,785 | 3,24 | 7,195 | 4,415 | 4,62 | 6,19 | 2,54 | 2,67 | 2,635 |
| 1 | 8,905 | 4,43 | 8,665 | 7,375 | 6,165 | 7,65 | 2,5 | 3,69 | 4,395 |
| 1 | 6,383333 | 3,983333 | 6,523333 | 6,458333 | 4,653333 | 5,823333 | 1,928333 | 3,368333 | 2,098333 |
| 2 | 6,873333 | 3,763333 | 6,613333 | 5,843333 | 4,138333 | 5,898333 | 1,433333 | 2,733333 | 1,523333 |
| 2 | 7,686667 | 3,911667 | 7,251667 | 5,016667 | 4,646667 | 6,441667 | 3,371667 | 3,271667 | 2,976667 |
| 1 | 7,605 | 4,67 | 7,85 | 7,495 | 6,065 | 7,755 | 2,765 | 3,12 | 3,425 |
| 2 | 6,798333 | 4,913333 | 7,268333 | 6,263333 | 4,543333 | 6,158333 | 2,998333 | 3,303333 | 1,928333 |
| 2 | 6,001667 | 2,851667 | 3,846667 | 6,426667 | 5,086667 | 6,206667 | 2,476667 | 3,916667 | 1,921667 |
| 2 | 7,745 | 4,66 | 9,235 | 6,72 | 6,125 | 7,765 | 3,445 | 4,43 | 3,88 |
| 1 | 7,996667 | 4,101667 | 6,731667 | 6,341667 | 4,421667 | 6,271667 | 1,661667 | 2,341667 | 1,851667 |
| 1 | 7,658333 | 3,473333 | 7,408333 | 5,968333 | 5,288333 | 5,903333 | 2,468333 | 3,398333 | 3,518333 |
| 2 | 6,665 | 4,54 | 8,16 | 6,28 | 4,675 | 6,725 | 2,355 | 3,31 | 4,03 |
| 1 | 6,873333 | 3,348333 | 6,703333 | 4,573333 | 5,663333 | 5,913333 | 2,133333 | 3,288333 | 2,223333 |
| 2 | 3,951667 | 2,351667 |  | 6,491667 | 5,771667 |  | 3,081667 | 2,896667 | 3,436667 |
| 2 | 8,273333 | 4,518333 | 7,758333 | 6,443333 | 5,148333 | 6,608333 | 2,733333 | 3,903333 | 4,253333 |
| 1 | 5,99 | 4,415 | 6,565 | 6,035 | 4,57 | 6,065 | 2,43 | 3,735 | 2,265 |
| 2 | 7,258333 | 4,238333 | 8,163333 | 5,518333 | 5,913333 | 7,203333 | 2,898333 | 4,618333 | 3,933333 |
| 1 | 7,65 | 2,42 | 8,33 | 4,855 | 5,845 | 6,975 | 3,76 | 2,65 | 3,895 |
| 1 | 7,361667 | 3,571667 | 7,666667 | 5,031667 | 5,226667 | 6,421667 | 3,141667 | 2,976667 | 2,021667 |
| 1 | 8,47 | 4,27 | 8,445 | 6,005 | 6,255 | 8,185 | 3,6 | 3,44 | 4,09 |
| 2 | 7,356667 | 2,771667 | 7,416667 | 5,831667 | 4,861667 | 7,256667 | 3,051667 | 2,071667 | 3,006667 |
| 2 | 7,363333 | 2,908333 | 7,283333 | 4,473333 | 4,863333 | 7,393333 | 3,513333 | 2,433333 | 3,773333 |
| 2 | 7,19 | 3,805 | 9,16 | 4,78 | 5,41 | 7,885 | 4,135 | 3,76 | 3,14 |
| 1 | 8,673333 | 5,678333 | 8,968333 | 8,093333 | 7,158333 | 8,578333 | 3,898333 | 5,638333 | 2,748333 |
| 2 | 7,98 | 4,36 | 8,485 | 6,22 | 5,88 | 7,735 | 4,32 | 4,53 | 3,715 |
| 2 | 7,293333 | 2,773333 | 7,623333 | 5,363333 | 4,483333 | 6,623333 | 2,123333 | 2,788333 | 3,053333 |
| 2 | 7,063333 | 4,513333 | 7,023333 | 5,313333 | 4,378333 | 6,548333 | 2,878333 | 3,533333 | 2,833333 |
| 2 | 8,696667 | 3,841667 | 9,306667 | 5,616667 | 5,071667 | 7,501667 | 3,741667 | 2,816667 | 3,786667 |
| 2 | 6,613333 | 4,123333 | 7,133333 | 6,968333 | 5,113333 | 6,763333 | 2,098333 | 3,448333 | 3,398333 |
| 2 | 6,846667 | 3,826667 | 6,496667 | 6,291667 | 5,111667 | 7,036667 | 3,126667 | 4,111667 | 1,481667 |
| 2 | 7,338333 | 3,228333 | 7,958333 | 5,178333 | 5,208333 | 5,878333 | 0,298333 | 3,303333 | 1,963333 |
| 2 | 8,965 | 3,85 | 7,94 | 5,585 | 4,565 | 6,975 | 1,48 | 2,535 | 3,65 |
| 2 | 6,598333 | 4,348333 | 6,788333 | 6,213333 | 3,573333 | 6,058333 | 1,808333 | 2,983333 | 1,748333 |
| 2 | 7,495 | 3,725 | 7,3 | 6,335 | 5,455 | 6,63 | 1,39 | 4,095 | 2,775 |
| 2 | 8,203333 | 4,363333 | 8,183333 | 5,963333 | 5,433333 | 7,368333 | 2,888333 | 3,903333 | 4,058333 |
| 1 | 7,166667 | 2,881667 | 8,306667 | 4,496667 | 5,116667 | 7,266667 | 2,566667 | 3,671667 | 3,446667 |
| 2 | 6,906667 | 3,176667 | 6,511667 | 5,346667 | 4,441667 | 6,531667 | 2,261667 | 3,761667 | 1,946667 |
| 2 | 9,646667 | 4,596667 | 9,566667 | 5,031667 | 3,801667 | 7,911667 | 3,801667 | 2,391667 | 3,786667 |
| 1 | 8,248333 | 4,098333 | 8,783333 | 5,648333 | 5,648333 | 7,823333 | 3,218333 | 3,518333 | 3,638333 |
| 2 | 7,113333 | 3,173333 | 7,898333 | 4,573333 | 5,118333 | 6,598333 | 2,263333 | 2,768333 | 2,363333 |
| 1 | 6,663333 | 3,918333 | 6,823333 | 5,803333 | 5,493333 | 6,948333 | 2,163333 | 3,593333 | 4,278333 |
| 2 | 6,08 | 5,02 | 6,26 | 6,115 | 5,285 | 5,315 | 4,215 | 5,275 | 2,515 |
| 2 | 9,191667 | 3,656667 | 8,566667 | 6,446667 | 5,336667 | 6,421667 | 2,146667 | 2,931667 | 3,056667 |
| 2 | 7,946667 | 3,461667 | 8,376667 | 6,216667 | 4,946667 | 7,016667 | 1,711667 | 3,246667 | 3,871667 |
| 1 | 6,813333 | 4,343333 | 6,403333 | 7,673333 | 5,118333 | 7,153333 | 2,008333 | 3,918333 | 3,298333 |
| 2 | 7,921667 | 2,286667 | 7,221667 | 5,186667 | 4,521667 | 6,406667 | 2,671667 | 2,486667 | 2,361667 |
| 2 | 7,701667 | 3,671667 | 6,741667 | 4,391667 | 4,551667 | 6,201667 | 3,841667 | 3,681667 | 2,311667 |
| 2 | 8,255 | 3,185 |  | 4,34 | 4,13 | 6,19 | 3,965 | 1,835 | 3,715 |
| 2 | 7,31 | 3,05 | 7,755 | 5,765 | 5,03 | 6,985 | 2,465 | 3,315 | 2,19 |
| 0 | 8,39 | 3,68 | 8,685 | 5,515 | 4,76 | 6,84 | 1,98 | 3,15 | 4,47 |
| 0 | 7,103333 | 3,808333 | 6,743333 | 5,868333 | 5,178333 | 7,078333 | 1,493333 | 3,813333 | 3,248333 |
| 0 | 7,06 | 3,765 | 7,255 | 6,59 | 5,07 | 7,505 | 1,325 | 3,645 | 3,17 |
| 0 | 5,641667 | 3,671667 | 5,721667 | 5,926667 | 4,706667 | 5,351667 | 1,556667 | 4,031667 | 2,076667 |
| 0 | 7,213333 | 3,353333 | 7,143333 | 5,578333 | 5,448333 | 7,143333 | 2,603333 | 3,273333 | 3,868333 |
| 0 | 7,093333 | 3,193333 | 7,053333 | 5,788333 | 5,313333 | 6,808333 | 2,123333 | 3,778333 | 3,218333 |
| 0 | 7,426667 | 3,391667 | 7,671667 | 4,701667 | 4,826667 | 7,076667 | 1,981667 | 2,546667 | 3,631667 |
| 0 | 6,576667 | 3,406667 | 5,926667 | 4,531667 | 4,656667 | 6,341667 | 1,701667 | 3,561667 | 2,686667 |
| 0 | 7,913333 | 3,778333 | 7,683333 | 5,278333 | 5,453333 | 7,073333 | 2,588333 | 3,973333 | 2,618333 |
| 0 | 7,466667 | 3,666667 | 7,851667 | 7,571667 | 5,906667 | 7,191667 | 2,326667 | 5,216667 | 3,471667 |
| 0 | 6,445 | 3,4 | 7,515 | 4,595 | 5,025 | 6,35 | 2,525 | 3,63 | 2,805 |
|  |  |  |  |  |  |  |  |  |  |

