**MALAT1** long non-coding RNA is overexpressed in multiple myeloma and may serve as a marker to predict disease progression

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**Abstract**

**Background:** The pathogenesis of multiple myeloma involves complex genetic and epigenetic events. This study aimed to investigate the role and clinical relevance of the long non-coding RNA (lncRNA), metastasis-associated lung adenocarcinoma transcript 1 (**MALAT1**) in multiple myeloma.

**Methods:** Bone marrow mononuclear cells were collected for analysis. The samples of multiple myeloma were taken from 45 patients at diagnosis, 61 post-treatment, and 18 who relapsed or had progression. Control samples were collected from 20 healthy individuals. Real-time quantitative reverse transcription polymerase chain reactions were performed to evaluate the expression of **MALAT1**. The clinical relevance of **MALAT1** expression was also explored.

**Results:** **MALAT1** was overexpressed in the newly diagnosed patients compared with post-treatment patients (mean ΔC_T: -5.54 ± 0.16 vs. -3.84 ± 0.09, 3.25-fold change; p < 0.001) and healthy individuals (mean ΔC_T: -5.54 ± 0.16 vs. -3.95 ± 0.21, 3.01-fold change; p < 0.001). The expression of **MALAT1** strongly correlated with disease status, and the magnitude of change in **MALAT1** post-treatment had prognostic relevance. The patients with early progression had a significantly smaller change in **MALAT1** after treatment (mean ΔC_T change: 1.26 ± 1.06 vs. 2.09 ± 0.79, p = 0.011). A cut-off value of the change in **MALAT1** (ΔC_T change: 1.5) was obtained, and the patients with a greater decrease in **MALAT1** (difference in ΔC_T >1.5) had significantly longer progression-free survival compared with the patients with a smaller **MALAT1** change (24 months vs. 11 months; p = 0.001). For the post-treatment patients, the risk of early progression could be predicted using this cut-off value.

**Conclusions:** **MALAT1** was overexpressed in patients with myeloma and may play a role in its pathogenesis. In addition, **MALAT1** may serve as a molecular predictor of early progression.

**Keywords:** Multiple myeloma, Long non-coding RNA, Metastasis-associated lung adenocarcinoma transcript 1 (**MALAT1**)
The human genome project revealed that at least 90% of the human genome is actively transcribed to RNA, but less than 2% of RNA encodes proteins [11,12]. Non-coding RNAs (ncRNAs) are a class of RNA with little or no capacity for protein synthesis that includes small ncRNAs and long ncRNAs (lncRNAs), which have a length of more than 200 nucleotides. The lncRNAs have been highly conserved throughout mammalian evolution including in humans, and they have been shown to be aberrantly expressed in cancer tissue and to be involved in oncogenic or tumor suppressive processes [13].

Metastasis-associated lung adenocarcinoma transcript 1 (MALAT1) is one of the few biologically well-studied lncRNAs, and is located on chromosome 11 (11q13.1). This lncRNA is highly conserved in mammals and is more than 8000 nucleotides in length [14-16]. MALAT1 has been shown to be expressed in numerous tissues including the central nervous, endocrine, immune, reproductive and lymphoid systems [17,18]. With respect to its function, MALAT1 is localized to nuclear speckles and has been associated with regulation of gene expressions [19,20]. In addition, MALAT1 may play a role in the regulation of alternative splicing and cell cycle [21-23]. In terms of its association with cancer, MALAT1 has been shown to be oncogenic and to be overexpressed in several solid tumors including lung, colorectal, bladder and laryngeal cancers [24-27].

The association between lncRNAs and multiple myeloma remains undetermined, and related studies are lacking. It has been reported that deregulation of the cell cycle is an important event during carcinogenesis, and that this event is also associated with MALAT1 [23]. MALAT1 has also been reported to be expressed broadly in human tissues including lymphoid tissues, bone marrow and B lymphocytes [28,29]. Taken together, we hypothesized that MALAT1 may play a role in multiple myeloma. Therefore, the aim of the present study was to evaluate the expression of MALAT1 in bone marrow mononuclear cells from patients with multiple myeloma and with different disease status and healthy individuals.

Methods

Multiple myeloma patients and samples

The study cohort included adult patients (aged 20 years and older) with multiple myeloma diagnosed at Kaohsiung Medical University Hospital from 2007 to 2012 who were free from other coexisting malignant diseases. The diagnosis of multiple myeloma was confirmed by bone marrow analysis which revealed a monoclonal plasma cell count over 10% by definition and related laboratory tests. The patients of extramedullary myeloma were not enrolled to this study. The diagnostic criteria, disease status and response to treatment were based on the criteria of the International Myeloma Working Group [17-19]. Forty-five samples were collected from newly diagnosed patients (29 males, 16 females; median age 62.3 years, range 49 to 79 years) with different subtypes (IgG: 21, IgA: 13, light chain: 11) and clinical stages (Durie-Salmon stage 1: 1, stage 2: 6, stage 3: 38 or international staging system stage 1: 7, stage 2: 17, stage 3: 21). In addition, 61 samples were collected from patients after myeloma treatment, and 18 samples from patients who had experienced disease progression or relapse. The disease status of the post-treatment patients was mainly a complete response (CR) and very good partial response (VGPR) based on the criteria of International Myeloma Working Group. In addition, the percentage of plasma cells in the patients achieving VGPR or CR after treatment was less than 5%.

We also enrolled 20 healthy and genetically unrelated Taiwanese volunteers (healthy individuals) as the control group. These healthy individuals had undergone bone marrow analysis to investigate cytopenia that had been noted in blood tests, but whose bone marrow examinations revealed no abnormalities. All patients and healthy individuals signed informed consent forms after the study had been thoroughly explained.

The research protocol was created in accordance with the Declaration of Helsinki, and it was reviewed, approved and registered by the Ethics Committee of Kaohsiung Medical University Hospital (KMUHIRB-2012-01-08(II)).

RNA extraction and reverse transcription

Bone marrow mononuclear cells were isolated for this study. First, the bone marrow samples were collected in tubes containing ethylenediaminetetraacetic acid (EDTA), preserved at 4°C and processed within 4 hours of collection. The bone marrow samples were then centrifuged at 12,000 × g for 15 minutes, after which ammonium chloride lysis buffer (10 mM NH4Cl, 10 mM KHCO3, 0.1 mM EDTA) was used to clear the red blood cells and effectively isolate the fraction of mononuclear cells.

The isolated bone marrow samples were stored at -80°C until RNA extraction. Isolation of RNA from 200 μL of cell suspension was carried out using the TRIzol protocol (Invitrogen). The extracted RNA was then treated with DNase (Promega) and the concentration was determined by spectrophotometric OD260 measurement. The integrity of the RNA was examined by 1.2% RNA denaturing agarose gel electrophoresis.

Reverse transcription was performed to generate complementary DNA in a final volume of 20 μL, containing 2 μg RNA, 25X dNTP mix (100 mM), 10X random primer (0.5 μM), RNase inhibitor, reverse transcriptase, reverse transcriptase buffer (10X) and diethylpyrocarbonate (DEPC)-treated water. The procedure was performed according to the manufacturer’s protocol (Applied Biosystems).
Real-time quantitative reverse transcription polymerase chain reaction (RT-PCR) analysis of MALAT1 expression

Real-time quantitative RT-PCR analysis was performed in a final volume of 10 μL containing 1 μL of RT product, 0.6 μL of primer (Roche), 1.2 μL of probe (Roche, cat. no. 04688945001), 2.2 μL of DEPC H2O and 5 μL of qPCR Master Mix (2X) (KAPA Biosystem, KK 4600). Analysis of the human glyceraldehyde-3-phosphate dehydrogenase (GAPDH) gene was used as the internal control.

The primer sequences of MALAT1 were as follows: forward, 5'-GACCCCTTACCCCTACC-3'; reverse, 5'-TTATGGATCATGCCCACAAG-3'; and the primer sequences of GAPDH were as follows: forward, 5'-AAAGTCCGCTATTTCGCAC-3'; and reverse, 5'-CCAAATCGTTAGCGCTCCTT-3'.

Real-time quantitative RT-PCR was performed in a LightCycler 480 Real-Time PCR System (Roche). The PCR cycling program consisted of incubation for enzyme activation at 95°C for 10 minutes, followed by melting at 95°C for 10 seconds, annealing at 60°C for 30 seconds, and then extension at 72°C for 1 second, for a total of 50 cycles.

The expression levels of MALAT1 were normalized to the internal control GAPDH reference to obtain the relative threshold cycle (ΔCT). The relative expression levels were calculated by the comparative C_T (ΔΔCT) method, and relative expression folds (2^ΔΔCT) were calculated.

Statistical analysis

The independent two samples t-test was used to compare the expression levels of MALAT1 in the different subgroups. The frequency between each categorical variable was compared by the chi-square test (χ² test), with Yates correction or Fisher’s exact test. Analysis of correlation was performed using Pearson correlations or Spearman correlation coefficients. Receiver operating characteristic (ROC) analysis was used to evaluate the cut-off value. Survival curves were plotted using the Kaplan–Meier method and compared using the log-rank test. Relative risk analysis was performed by calculating the odds ratio (OR) and 95% confidence interval (CI) by Cox regression analysis.

All statistical analyses were based on two-sided hypothesis tests with a significance level of p < 0.05. The analyses were performed using SPSS version 17.0 (SPSS, Chicago, IL, USA).

Results

Correlation of MALAT1 expression with disease status in multiple myeloma

The expression of MALAT1 was significantly higher in the patients at diagnosis compared with the patients post-treatment (mean ΔC_T: -5.54 ± 0.16 vs. -3.84 ± 0.09, 3.25-fold change; p < 0.001) or the healthy individuals (mean ΔC_T: -5.54 ± 0.16 vs. -3.95 ± 0.21, 3.01-fold change; p < 0.001) (Table 1). This suggests that MALAT1 may be deregulated and overexpressed in patients with multiple myeloma.

The association of MALAT1 expression pattern with disease status was further analyzed. The expression of MALAT1 was found to be significantly decreased in the post-treatment patients to a level that was similar to that of the healthy individuals (mean ΔC_T: -3.84 ± 0.09 vs. -3.95 ± 0.21, p = 0.614). In addition, in the patients in whom the disease had progressed or relapsed, the expression of MALAT1 was significantly increased compared with the post-treatment patients (mean ΔC_T: -4.92 ± 0.23 vs. -3.84 ± 0.09, 1.89-fold change; p < 0.001) (Table 1). For the patients who underwent multiple bone marrow examinations during treatment and follow-up, the expression of MALAT1 changed dynamically and was correlated with disease status (Figure 1).

Association between MALAT1 expression and clinical outcome

The clinical relevance of MALAT1 was analyzed. The expressions of MALAT1 in the 45 newly diagnosed patients with different clinical characteristics were listed in Additional file 1: Table S1. We noticed that the expression of MALAT1 was not associated with the percentage of plasma cells in the bone marrow (r = -0.037, p = 0.808) (Additional file 2: Table S2). With regards to the association between MALAT1 expression and prognosis,

Table 1 Expression of MALAT1 in patients with multiple myeloma and healthy individuals

| Population          | No. | Expression of MALAT1 (Mean ΔC_T) |
|---------------------|-----|---------------------------------|
| Newly diagnosed     | 45  | -5.54 ± 0.16                    |
| Post-treatment      | 61  | -3.84 ± 0.09                    |
| Relapse or progression | 18  | -4.92 ± 0.23                    |
| Healthy individuals | 20  | -3.95 ± 0.21                    |
|                     |     | ΔΔC_T | Fold change | P value |
| Newly diagnosed vs. Post-treatment | -1.70 | 3.25 | <0.001 |
| Newly diagnosed vs. Healthy individuals | -1.59 | 3.01 | <0.001 |
| Relapse or progression vs. Post-treatment | -0.92 | 1.89 | <0.001 |
| Post-treatment vs. Healthy individuals | 0.11 | 1.08 | 0.614 |

The 61 post-treatment samples were composed of 58 samples collected in disease status of VGPR or CR from 42 patients. The percentages of plasma cells were all less than 5%.

The 3 samples collected at a disease status of partial response came from 3 patients.

Note:

ΔC_T = C_T (MALAT1 - GAPDH).

Increased expression (fold change) was calculated as 2^ΔΔCT.
the results showed that the initial higher MALAT1 expression level (Cut-off value: $\Delta C_T = -5.30$) determined by ROC analysis was not associated with inferior prognosis including progression-free survival (PFS) (median PFS: $21.0 \pm 9.9$ vs. $15.0 \pm 6.0$ months, $p = 0.390$) or overall survival (OS) (median OS: Not reached; mean OS: $31.9 \pm 4.3$ vs. $37.8 \pm 3.6$ months, $p = 0.172$) (Additional file 3: Figure S1). However, we hypothesized the magnitude of the change (decrease) after myeloma-related therapy may have been related to the degree of treatment response and prognosis, because the expression of MALAT1 changed after treatment.

Among the 45 patients, 36 (including 21 men) with a mean age of 61.3 years received bone marrow examinations at least twice including at diagnosis and after treatment, and hence the expression of MALAT1 was available for further analysis. The median PFS of these 36 patients was 18 months (95% CI 8.95-25.35), and we used this median PFS as a cut-off value to divide the patients into two groups of early (PFS $\leq 18$ months) or late (PFS $> 18$ months) progression, with 18 patients in each group. We found that the only parameter which showed a significant difference between these two groups was the magnitude of MALAT1 change after treatment. The patients with early progression had a significantly smaller magnitude of MALAT1 change after treatment compared with the patients with late progression (mean difference of $\Delta C_T$: $1.26 \pm 1.06$ vs. $2.09 \pm 0.79$; $p = 0.011$) (Table 2).

**Role of MALAT1 in predicting early progression**

The previous results showed that the magnitude of MALAT1 change (as quantified by the difference in $\Delta C_T$) was the only parameter associated with PFS. We then used ROC analysis and obtained a cut-off expression change value of 1.5 (post-treatment $\Delta C_T$ – pre-treatment $\Delta C_T$; approximately a 2.8-fold change) with an estimated area under the ROC curve of 0.79 ($p = 0.003$). The proportion of patients with a lower MALAT1 change (difference in $\Delta C_T \leq 1.5$) was significantly higher in those who displayed early progression ($n = 13, 72.2\%$) compared with those who displayed late progression ($n = 4, 22.2\%; p = 0.007$).

In terms of an association between clinical characteristics and magnitude of MALAT1 change, the patients with greater changes (difference in $\Delta C_T > 1.5$) may have had a better treatment response (Additional file 4: Table S3). The PFS and OS rates were also analyzed using the cut-off value from ROC analysis. With a minimum follow-up period of 12 months (range: 12 to 48 months), the patients with a greater MALAT1 decrease (difference in $\Delta C_T > 1.5$) had a significantly prolonged median PFS (24 months, range 11-48 months) compared with the patients with a smaller MALAT1 change (11 months, range: 6-21 months; $p = 0.001$). There was no significant difference in OS between the two groups (median OS: Not reached; mean OS: $39.2 \pm 3.6$ months, range: 12-48 months vs. $32.8 \pm 4.2$ months, range: 12-48 months; $p = 0.313$) (Figure 2).

Cox regression analysis was used to identify the relative risk of early progression, which revealed that autologous hematopoietic stem cell transplantation (Auto-HSCT) and the magnitude of MALAT1 change were significantly associated with the prognosis. For all post-treatment patients ($n = 36$), those with a smaller MALAT1 change (difference in $\Delta C_T \leq 1.5$) had a significantly higher risk of early progression of disease (OR 4.89, 95% CI 1.73-13.86; $p = 0.003$), while auto-HSCT reduced the risk of early progression (OR 0.22, 95% CI 0.05-0.97; $p = 0.046$). For the post-treatment patients with a VGPR or CR ($n = 33$), a smaller MALAT1 change (difference in $\Delta C_T \leq 1.5$) remained the single factor predictive of early progression of multiple myeloma (OR 4.38, 95% CI 1.48-12.99; $p = 0.008$) (Table 3). Using the cut-off value to predict the patients who would show early progression (PFS $\leq 18$ months), the estimated accuracy was 75% with a sensitivity of 72.2%, a specificity of 77.8%, a positive predictive value of 76.5%, and a negative predictive value of 73.7%.

**Discussion**

In the current study, we demonstrated that MALAT1 was overexpressed in the patients with newly diagnosed
multiple myeloma. This finding indicates that \textit{MALAT1} may play a role in multiple myeloma.

The results of the present study are in contrast with the study by Isin et al., in which the expression of \textit{MALAT1} was found to be significantly lower in patients with multiple myeloma [30]. A possible explanation for this discrepancy may be due to different sample sources. Our study analyzed the expression of \textit{MALAT1} in bone marrow mononuclear cells rather than plasma samples, because the pathogenesis of myeloma is closely related to bone marrow. Another possible explanation for the higher expression of \textit{MALAT1} in the current study may be associated with the bone marrow microenvironment which supports the proliferation of myeloma cells. In addition, our analysis revealed that expression of \textit{MALAT1} in newly diagnosed myeloma patients is not associated with the total percentage of plasma cells in the bone marrow. This finding indicated that the expression of \textit{MALAT1} may be associated with interactions between myeloma cells and the bone marrow microenvironment. The detailed mechanism needs further studies to elucidate.

The current study also investigated the clinical relevance of \textit{MALAT1} in patients with multiple myeloma. We found that the expression of \textit{MALAT1} changed dynamically when stratified by disease status. In addition, the major clinical significance was the magnitude of change in expression after treatment rather than the initial expression. This finding is different from previous studies of solid tumors which have reported that a higher expression

| Table 2 The clinical characteristics of patients with early (PFS \(\leq 18\) months) or late (PFS >18 months) progression |
|-----------------------------------------------|-----------------|-----------------|-----------------|-----------------|
| All patients \((N = 36)\) | PFS \(\leq 18\) months \((N = 18)\) | PFS >18 months \((N = 18)\) | \(P\) value |
| Age (years, mean(SD)) | 61.3(8.3) | 61.9 ± 7.8 | 60.6 ± 8.7 | 0.633 |
| Male, n (%) | 21(58.3%) | 10(55.6%) | 11(61.1%) | 1.000 |
| M protein | | | | 0.210 |
| IgG, n (%) | 19(52.8%) | 7(38.9%) | 12(66.6%) | |
| IgA, n (%) | 10(27.8%) | 7(38.9%) | 3(16.7%) | |
| Light chain, n (%) | 7(19.4%) | 4(22.2%) | 3(16.7%) | |
| International staging system | | | | 0.881 |
| Stage 1, n (%) | 5(13.9%) | 2(11.1%) | 3(16.7%) | |
| Stage 2, n (%) | 12(33.3%) | 6(33.3%) | 6(33.3%) | |
| Stage 3, n (%) | 19(52.8%) | 10(55.6%) | 9(50%) | |
| Durie-Salmon stage | | | | 1.000 |
| Stage 1, n (%) | 0 | 0 | 0 | |
| Stage 2, n (%) | 5(13.9%) | 2(11.1%) | 3(16.7%) | |
| Stage 3, n (%) | 31(86.1%) | 16(88.9%) | 15(83.3%) | |
| Percentage of plasma cell in bone marrow (\%, mean (SD)) | 50.8 ± 25.3 | 54.3 ± 26.8 | 47.3 ± 23.8 | 0.740 |
| Anemia, n (%) | 27(75%) | 14(77.8%) | 13(72.2%) | 1.000 |
| Renal insufficiency, n (%) | 9(25%) | 5(27.8%) | 4(22.2%) | 1.000 |
| Hypercalcemia, n (%) | 14(38.9%) | 8(44.4%) | 6(33.3%) | 0.733 |
| Bone disease, n (%) | 25(69.4%) | 14(77.8%) | 11(61.1%) | 0.471 |
| Cytogenetic abnormality, n (%) | 7(19.4%) | 3(16.7%) | 4(22.2%) | 1.000 |
| Auto-HSCT containing induction Tx, n (%) | 11(30.6%) | 4(22.2%) | 7(38.9%) | 0.471 |
| Auto-HSCT in 1st fine Tx, n (%) | 9(25%) | 2(11.1%) | 7(38.9%) | 0.121 |
| Treatment response: | | | | |
| CR, n (%) | 7(19.4%) | 1(5.6%) | 6(33.3%) | 0.088 |
| VGPR, n (%) | 26(72.2%) | 14(77.8%) | 12(66.7%) | 0.711 |
| PR, n (%) | 3(8.3%) | 3(16.7%) | 0 | 0.229 |
| Expression of \textit{MALAT1} at diagnosis (Mean Δ\textit{Ct} ± SD) | -5.52 ± 1.15 | -5.77 ± 0.89 | -5.77 ± 0.89 | 0.353 |
| Magnitude of \textit{MALAT1} change after treatment (Difference in Δ\textit{Ct}) | 1.26 ± 1.06 | 2.09 ± 0.79 | 0.011 |

\(\Delta\text{Ct}\) = \(\Delta\text{Ct}\) (Post-treatment - newly diagnosed).

Auto-HSCT, autologous hematopoietic stem cell transplantation; CR, complete response; VGPR, very good partial response; PFS, progression-free survival; Tx, treatment.
is related to poorer prognosis. We observed that the patients with a greater decrease in MALAT1 after initial treatment had a significantly prolonged PFS, which is consistent with the current consensus that therapeutic intervention to achieve a maximal response is beneficial for patients with multiple myeloma [31,32]. In terms of OS, we did not find a significant benefit in the post-treatment patients with a greater decrease in MALAT1. A possible explanation may be the incorporation of potent and effective salvage treatment in the patients who experienced a relapse or progression of disease, as well as the fact that some patients received auto-HSCT after salvage treatment.

We also found that MALAT1 may serve as a marker to predict early progression. Because the duration of response decreases with an increasing number of salvage regimens after progression, identification of patients at risk of early progression after first-line treatment is an important issue. More intensive treatment may improve the prognosis in this subgroup. We also found that patients with a smaller MALAT1 change after treatment had a significantly higher risk for early progression, even in those with a VGPR, CR and normal percentage of plasma cells in bone marrow. This finding suggests that the expression of MALAT1 can be used to identify the patients at risk of early progression. Accordingly, the therapeutic strategy may be adjusted to be initially more aggressive, as more potent treatment may reduce the risk of early progression and prolong PFS.

Our findings may provide a new insight into the pathogenesis of multiple myeloma. However, there are some limitations to this study. First, the cytogenetic examinations were done by conventional G-band metaphase chromosome analysis, and the percentage of cytogenetic abnormalities was relative low. Therefore, the association between MALAT1 and specific cytogenetic abnormalities remains to be determined. Further analysis by fluorescent in-situ hybridization with larger cohort may provide more impactful insight on the clinical relevance of MALAT1 expression in multiple myeloma. Second, we didn’t evaluate the expression of MALAT1 in patients resistant to myeloma therapy due to no available samples. Third, the number of cases to evaluate the clinical relevance of MALAT1 was limited, which was likely due to the stringency of the enrollment criteria.

**Conclusions**

In conclusion, this study revealed that MALAT1 was overexpressed in patients with multiple myeloma, and

![Figure 2](https://example.com/figure2.png)

**Figure 2** Kaplan-Meier estimates of the probability of progression-free survival (PFS, A) and overall survival (OS, B) are shown according to the magnitude in the change of MALAT1 expression after treatment. The patients were divided into two groups by a cut-off value (difference in ΔC T: 1.5).

| Table 3 Multivariate Cox regression analysis for all post-treatment patients and post-treatment patients with a treatment response of VGPR/CR |
|---------------------------------------------------------------|
| **PFS ≤18 months (N = 18)** | **PFS >18 months (N = 18)** | **Cox regression analysis** |
| Auto-HSCT in 1st line treatment, n | 9 | 2(11.1%) | 7(38.9%) | 0.22 0.05-0.97 0.046 |
| Difference in ΔC T ≤1.5, n | 17 | 13(72.2%) | 4(22.2%) | 4.89 1.73-13.86 0.003 |
| PFS ≤18 months (N = 15) | PFS >18 months (N = 18) |
| Patients with VGPR/CR (N = 33) | Auto-HSCT in 1st line treatment, n | 9 | 2(13.3%) | 7(38.9%) | 0.24 0.05-1.09 0.066 |
| Difference in ΔC T ≤1.5, n | 14 | 10(66.7%) | 4(22.2%) | 4.38 1.48-12.99 0.008 |

OR, Odds ratio; CI, confidential interval; Auto-HSCT, autologous hematopoietic stem-cell transplantation; CR, complete response; VGPR, very good partial response; PFS, progression-free survival.
this lncRNA may play a role in the pathogenesis of the disease. In addition, the change in MALAT1 expression after treatment was clinically significant and may serve as a molecular predictor of the patients at risk of early progression of multiple myeloma.

### Additional files

**Additional file 1: Table S1.** The clinical characteristics and expression of MALAT1 in 45 newly diagnosed patients with myeloma.

**Additional file 2: Table S2.** Expression of MALAT1 and plasma cell percentage in the bone marrow in 45 newly diagnosed patients.

**Additional file 3: Figure S1.** Kaplan-Meier estimates of the probability of progression-free survival (PFS, 1A) and overall survival (OS, 1B) are based on the initial level of MALAT1 expression. The patients were divided into two groups by a cut-off value (△CT: -5.30).

**Additional file 4: Table S3.**

### Competing interests
The authors declare that they have no competing interest.

### Authors' contributions
SFC, JGC and TCL designed the study. SFC, YCC, CSC, SFL, YCL, HHH, TCL contributed to collection and review of clinical data. SFC and YCC performed statistical analysis. S-FC and CSC performed molecular examination. S-FC and YCC performed cytogenetic analysis. SFC, JGC and TCL designed the study. SFC, YCC, CSC, SFL, YCL, HHH, TCL

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14. JGC and TCL designed the study. SFC, YCC, CSC, SFL, YCL, HH, TCL contributed to collection and review of clinical data. YCC performed molecular examination. S-FC and CSC performed statistical analysis. SFC wrote the manuscript. SFC, TCL, JGC critically reviewed the manuscript. TCL and JGC approved the final version of the manuscript. All authors read and approved the final manuscript.

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