Supplemental Table 1. Two stereotyped CDR3 sequences found in our cohort

| Subset | IGHV     | IGHD     | IGHJ     | IGHV gene germline identity | HCDR3 length |
|--------|----------|----------|----------|-----------------------------|--------------|
| #220   | IGHV3-23 | IGHD1-26 | IGHJ5    | 93.30%                       | 7            |
| #235   | IGHV3-30-3 | IGHD6-13 | IGHJ5    | 92.79%                       | 11           |
Supplemental Table 2. The correlation of MYD88 L265P and IGHV segments in LPL/WM patients

| IGHV segments         | MYD88 L265P (n) | MYD88 wildtype (n) | p -Value |
|-----------------------|-----------------|-------------------|----------|
| IGHV3-23              |                 |                   | 0.176    |
| With                  | 18              | 0                 |          |
| Without               | 87              | 15                |          |
| IGHV3-74              |                 |                   | 0.454    |
| With                  | 10              | 0                 |          |
| Without               | 95              | 15                |          |
| IGHV3-23 and IGHV3-74 |                 |                   | 0.050    |
| With                  | 28              | 0                 |          |
| Without               | 77              | 15                |          |
| IGHV3-30              |                 |                   | 0.282    |
| With                  | 8               | 3                 |          |
| Without               | 97              | 12                |          |
| IGHV3-7               |                 |                   | 0.042    |
| With                  | 7               | 4                 |          |
| Without               | 98              | 11                |          |
| IGHV4-34              |                 |                   | 0.912    |
| With                  | 12              | 1                 |          |
| Without               | 93              | 14                |          |
| IGHV4-59              |                 |                   | 0.076    |
| With                  | 2               | 2                 |          |
| Without               | 103             | 13                |          |
| IGHV4-61              |                 |                   | 0.333    |
| With                  | 2               | 1                 |          |
| Without               | 103             | 14                |          |
| IGHV3                 |                 |                   | 0.887    |
| With                  | 65              | 9                 |          |
|          | With | Without |
|----------|------|---------|
| IGHV4    | 23   | 82      |
|          | 5    | 10      |
|          |      | 0.514   |
Supplemental Table 3. Distribution of clinical characteristics in LPL/WM patients according to IGHV genes

| Clinical Characteristic | Patients with IGHV4 genes | Patients with non-IGHV4 genes | p-Value | Patients with IGHV3 genes | Patients with non-IGHV3 genes | p-Value |
|------------------------|----------------------------|-------------------------------|---------|---------------------------|-----------------------------|---------|
| Age                    |                            |                               |         |                           |                             |         |
| ≤65                    | 26 of 33                   | 67 of 103                     | 0.140   | 55 of 82                  | 38 of 54                    | 0.686   |
| >65                    | 7 of 33                    | 36 of 103                     |         | 27 of 82                  | 16 of 54                    |         |
| Sex                    |                            |                               | 0.473   |                           |                             | 0.843   |
| Male                   | 24 of 33                   | 68 of 103                     |         | 56 of 82                  | 36 of 54                    |         |
| Female                 | 9 of 33                    | 35 of 103                     |         | 26 of 82                  | 18 of 54                    |         |
| IPSS stage             |                            |                               | 0.223   |                           |                             | 0.278   |
| Low risk               | 9 of 33                    | 15 of 98                      |         | 11 of 78                  | 13 of 53                    |         |
| Intermediate risk      | 13 of 33                   | 37 of 98                      |         | 30 of 78                  | 20 of 53                    |         |
| High risk              | 11 of 33                   | 46 of 98                      |         | 37 of 78                  | 20 of 53                    |         |
| WBC                    |                            |                               | 0.068   |                           |                             | 0.088   |
| ≤10×10^9/L             | 30 of 33                   | 77 of 101                     |         | 60 of 80                  | 47 of 54                    |         |
| >10×10^9/L             | 3 of 33                    | 24 of 101                     |         | 20 of 80                  | 7 of 54                     |         |
| PLT                    |                            |                               | 0.486   |                           |                             | 0.728   |
| <100×10^9/L            | 17 of 33                   | 45 of 101                     |         | 38 of 80                  | 24 of 54                    |         |
| ≥100×10^9/L            | 16 of 33                   | 56 of 101                     |         | 42 of 80                  | 30 of 54                    |         |
| HBG                    |                            |                               | 0.370   |                           |                             | 0.039   |
| ≤90g/L                 | 16 of 33                   | 58 of 101                     |         | 50 of 80                  | 24 of 54                    |         |
| >90g/L                 | 17 of 33                   | 43 of 101                     |         | 30 of 80                  | 30 of 54                    |         |
| ALB level              |                            |                               | 0.056   |                           |                             | 0.007   |
| ≤35 g/L                | 14 of 33                   | 62 of 101                     |         | 53 of 80                  | 23 of 54                    |         |
| >35 g/L                | 19 of 33                   | 39 of 101                     |         | 27 of 80                  | 31 of 54                    |         |
| LDH level              |                            |                               | 0.050   |                           |                             | 0.164   |
| ≤247 U/L               | 24 of 33                   | 88 of 99                      |         | 69 of 78                  | 43 of 54                    |         |
| >247 U/L               | 9 of 33                    | 11 of 99                      |         | 9 of 78                   | 11 of 54                    |         |
|                          | IgM level |           |           |
|--------------------------|-----------|-----------|-----------|
|                          | 0.968     | 0.367     |
| ≤3 g/L                   | 5 of 33   | 13 of 101 | 9 of 80   |
| >3 g/L                   | 28 of 33  | 88 of 101 | 71 of 80  |
| Serum β2-MG level        |           | 0.173     | 0.326     |
| ≤3 g/L                   | 10 of 32  | 18 of 92  | 14 of 72  |
| >3 g/L                   | 22 of 32  | 74 of 92  | 58 of 72  |
| Karyotype                |           | 0.763     | 0.781     |
| Normal karyotype         | 20 of 28  | 58 of 78  | 45 of 62  |
| Abnormal aryotype        | 8 of 28   | 20 of 78  | 17 of 62  |
| TP53 deletion            |           | 1.000     | 0.631     |
| With                     | 1 of 29   | 4 of 95   | 4 of 74   |
| Without                  | 28 of 29  | 91 of 95  | 70 of 74  |
| ATM deletion              |           | 0.447     | 1.000     |
| With                     | 1 of 25   | 1 of 73   | 1 of 57   |
| Without                  | 24 of 25  | 72 of 73  | 56 of 57  |
| RB-1                     |           | 0.654     | 0.640     |
| With                     | 2 of 23   | 3 of 82   | 2 of 63   |
| Without                  | 21 of 23  | 79 of 82  | 61 of 63  |
| MYD88 L265P mutation     |           | 0.514     | 0.887     |
| With                     | 23 of 28  | 82 of 92  | 65 of 74  |
| Without                  | 5 of 28   | 10 of 92  | 9 of 74   |
| Treatment regimen        |           | 0.651     | 1.000     |
| BTK inhibitor based therapy | 3 of 31   | 12 of 93  | 9 of 72   |
| Bortezomib-based therapy | 9 of 31   | 18 of 93  | 16 of 72  |
| Rituximab-based therapy  | 14 of 31  | 50 of 93  | 37 of 72  |
| Other                    | 5 of 31   | 13 of 93  | 10 of 72  |
| Lines of therapy          |     |     |     |
|---------------------------|-----|-----|-----|
|                           | 0.051 |     | 0.342 |
| First-line therapy        | 30 of 31 | 72 of 93 | 57 of 72 | 45 of 52 |
| Second-line therapy       | 1 of 31 | 18 of 93 | 12 of 72 | 7 of 52 |
| Other                     | 0 of 31 | 3 of 93 | 3 of 72 | 0 of 52 |

WBC, white blood cell, PLT, platelets, HGB, hemoglobin, ALB, albumin, LDH, lactate dehydrogenase, IgM, immunoglobulin M, serum β2-MG, serum β2-microglobulin
### Supplemental Table 4. IGH repertoire for LPL/WM in different series

| Study                          | Country | n   | IGHV Mutated(%) | IGHV3-23 | IGHV3-34 | IGHV3-7 | IGHV3-74 | MYD88 L265P | IGHV SHM rate with MYD88L265P | Correlation between IGHV segments and MYD88 mutation status |
|-------------------------------|---------|-----|-----------------|----------|----------|---------|---------|-------------|-------------------------------|-------------------------------------------------------------|
| Loizos Petrikkos, et al, 2014[16] | Greece  | 36  | 91%             | 74.3%    | unavailable | 25.70%  | 8.57%   | unavailable | 65.50%                        | IGHV3-23 and IGHV3-74 were more frequently detected in MYD88-mutated patients. |
| N Gachard, et al, 2013[15]     | France  | 31  | 100%            | 77%      | unavailable | 27%    | unavailable | 22%         | unavailable                        | IGHV3-7 usage is represented more in MYD88-mutated patients with no statistical significance. |
| Marzia Varettoni, et al, 2013[25] | Italy   | 55  | 95% (WM and IgM-MGUS) | 87%   | 2%        | 25%    | 2%      | unavailable | unavailable                        | unavailable |
| Jun Wang, et al               | China   | 136 | 97%             | 60.3%    | 24.3%    | 15.4%  | 10.3%  | 8.1%        | 87.5%                        | IGHV3-23 and IGHV3-74 segments were more frequently detected in MYD88-mutated patients. IGHV3-7 presented more frequently in MYD88 wild-type patients. |
Supplemental Figure 1. Survival analysis of patients with IGHV3-7 gene. Progression-free survival (PFS) (A) and overall survival (OS) (B) estimates for patients with LPL/WM according to IGHV3-7 gene usage.