Supplementary Information

Supplementary Figure S1: Genes were selected through systematic search on PubMed database, looking for “name of drug”, “multiple myeloma or plasma cell leukemia”, and “pharmacogenetics or pharmacogenomics or polymorphisms”. GeneMANIA network analysis was performed on the global list of pharmacogenetic marker genes to reveal their potential associations, in terms of co-expression, co-localization, physical interactions, shared protein domains and pathways. Significant networks that were identified for all the listed genes (a) and for the ones specifically involved in the most representative pathways, DNA repair/response to DNA damage (b) and drug biotransformation (c), are reported.

Supplementary Table S1: Analysis of “The Pharmacogenomics Knowledgebase”, clinical information of germline genetic variation and efficacy/safety [1–45].

**Table S1.** Analysis of “The Pharmacogenomics Knowledgebase”, clinical information of germline genetic variation and efficacy/safety.

| Drug       | Gene | SNP       | Alleles | Amico Acid | Translation | Haplotypes | Annotation | Reference            |
|------------|------|-----------|---------|------------|-------------|------------|------------|----------------------|
| Cyclophosphamide     | ABCB1 | rs10276036 | C>T     |            | ABCB1*13    |            | Efficacy   | Caronia et al., 2011 [1] |
|                       |      | rs1128503  | A>G     |            | ABCB1*13    |            | Efficacy   | Caronia et al., 2011 [1] |
|                       |      | rs2032582  | A>T;    | Ser893 Ala; Ser893 Thr | ABCB1*13 | Efficacy   | Bray et al., 2010 [2] |
|                       |      | rs4148737  | T>C     |            |            |            |            | Caronia et al., 2011 [1] |
|                       | ABCC3 | rs4148416  | C>T     | Gly1013 Gly |            |            | Efficacy   | Caronia et al., 2011 [1] |
|                       | ABCC4 | rs9561778  | G>A;    |            |            |            | Toxicity/ADR | Low et al., 2009 [3] |
|                       |      | rs698      | T>C;    | Ile350 Val |            |            | Efficacy   | Khrunin et al., 2014 [4] |
|                       | ALDH1A | rs6151031  | -       |            |            |            | Toxicity/ADR | Ekhart et al., 2008 [5] |
|                       | CYP2B6 | rs12721655 | A>G     | Lys139Glu  | CYP2B6*8, CYP2B6*13, CYP2B6*13A, CYP2B6*13B | Efficacy | Bray et al., 2010 [2] |
| rs2279343 | A>G  | Lys262Arg | CYP2B6*4, CYP2B6*4A, CYP2B6*4B, CYP2B6*4C, CYP2B6*4D, CYP2B6*6, CYP2B6*6A, CYP2B6*6B, CYP2B6*6C, CYP2B6*7, CYP2B6*7A, CYP2B6*7B, CYP2B6*13, CYP2B6*13A, CYP2B6*13B, CYP2B6*16, CYP2B6*19, CYP2B6*20, CYP2B6*26, CYP2B6*34, CYP2B6*36, CYP2B6*37, CYP2B6*38 | Toxicity/ADR | Rocha et al., 2009 [7] |
| rs3211371 | C>T  | Arg487Cys | CYP2B6*5, CYP2B6*5A, CYP2B6*5B, CYP2B6*5C, CYP2B6*7, CYP2B6*7A, CYP2B6*7B | Toxicity/ADR | Bray et al., 2010 [2] |
| Gene      | SNP      | Chromosome | Effect | Reference            | Type                     | Reference                                      |
|-----------|----------|------------|--------|----------------------|--------------------------|------------------------------------------------|
| CYP2B6    | rs3745274|            | G>T    | Gln172His            | Toxicity/ADR; Dosage     | Bray et al., 2010 [2]; Rocha et al., 2009 [7] |
| CYP2B6    | rs8192709|            | C>T    | Arg22Cys             | Toxicity/ADR             | Rocha et al., 2009 [7]                         |
| CYP2C19   | rs4244285|            | G>A; C,G>C | Pro227Pro | Efficacy; Toxicity/ADR | Bray et al., 2010 [2]; Ngamjanyaporn et al., 2011 [8] |
| CYP2E1    | rs2070676|            | G>C    | -                    | Efficacy, Toxicity/ADR   | Khrunin et al., 2012 [9]                      |
|           | rs6413432|            | T>A    | -                    | Efficacy                 | Khrunin et al., 2012 [9]                      |
| CYP3A4    | rs2740574|            | C>T    | -                    | Toxicity/ADR             | Su et al., 2010 [10]                          |
| EPHX1     | rs1051740|            | T>C    | Tyr113His            | Toxicity/ADR             | Khrunin et al., 2014 [4]                      |
| ERCC1     | rs11615  |            | A>G    | Asn118Asn            | Toxicity/ADR             | Khrunin et al., 2010 [11]; Khrunin et al., 2012 [9] |
| ERCC2     | rs1799793|            | C>T    | Asp288Asn            | Efficacy, Toxicity/ADR   | Khrunin et al., 2010 [11]; Khrunin et al., 2012 [9] |
| Gene     | SNP ID/Allele | Effect | Outcome | Reference                          |
|----------|---------------|--------|---------|------------------------------------|
| GATA3    | rs3824662     | C>A    | Efficacy| Perez-Andreu et al., 2013 [12]     |
| GSTA1,   | rs3957357     | A>G    | Toxicity/ADR| Khrunin et al., 2010 [11]; Khrunin et al., 2012 [9] |
| GSTA6P   |               |        |         |                                    |
| GSTM3    | rs1799735     | C>CCT, C>   | Toxicity/ADR | Khrunin et al., 2010 [11]; Khrunin et al., 2012 [9] |
| GSTP1    | rs1695        | A>G    | Ile105Val | Efficacy | Khrunin et al., 2010 [11]; Khrunin et al., 2012 [9] |
| GSTP1    | rs1695        | A>G    | Ile105Val | Toxicity/ADR | Oliveira et al., 2010 [13]; Zhang et al., 2011 [14] |
| LIG3     | rs1052536     | C>T    | Toxicity/ADR | Khrunin et al., 2014 [4] |
| MTHFR    | rs1801133     | G>A    | Ala140Val| Toxicity/ADR | Henríquez-Hernández et al., 2010 [15]; Robien et al., 2004 [16]; Patiño-García et al., 2009 [17] |
| MTR      | rs1805087     | A>G    | Asp919Gly | Toxicity/ADR | Cui et al., 2011 [18]; Patiño-García et al., 2009 [17] |
| MUTYH    | rs3219484     | C>T    | Val22Met | Toxicity/ADR | Khrunin et al., 2014 [4] |
| Genes | Gene Identifier | SNP | Allele Changes | Protein Changes | Study Details |
|-------|----------------|-----|---------------|----------------|---------------|
| **NAT2** | rs1801280 | T>C | Ile114Thr | Toxicity/ADR | Khrunin et al., 2014 [4] |
| **NOS3** | rs1799983 | T>G | Asp298Glu | Efficacy | Choi et al., 2009 [19] |
| | rs2070744 | C>T | - | - | Efficacy | Choi et al., 2009 [19] |
| **NQO1** | rs1800566 | G>A | Pro149Ser | Efficacy | Fagerholm et al., 2008 [20]; Jamieson et al., 2011 [21]; Khrunin et al., 2014 [4]; Kolesar et al., 2002 [22]; Kolesar et al., 2011 [23]; Siegel et al., 1999 [24]; Siegel et al., 2001 [25]; Smith et al., 2001 [26] |
| **NQO2** | rs1143684 | C>T | Leu47Phe | Efficacy | Jamieson et al., 2011 [21] |
| **RAD52** | rs11226 | G>A | - | - | Toxicity/ADR | Khrunin et al., 2014 [4] |
| **SLC22A16** | rs12210538 | A>G | Met409Thr | Toxicity/ADR | Bray et al., 2010 [2] |
| | rs6907567 | A>G | Asn104Asn | Efficacy | Bray et al., 2010 [2] |
| | rs723685 | A>G | Val252Ala | - | Dosage | Bray et al., 2010 [2] |
| **SOD2** | rs4880 | A>G | Val116Ala | Efficacy | Glynn et al., 2009 [27] |
| Gene      | rs Number  | Allele  | Protein Change | Refseq Alleles          | Effect        | Sources                                                                 |
|-----------|------------|---------|----------------|-------------------------|---------------|-------------------------------------------------------------------------|
| TP53      | rs1042522  | G>C     | Pro33Arg       | -                       | Efficacy,    | Henríquez-Hernández et al., 2010 [15]; Huang et al., 2008 [28];     |
|           |            |         |                |                         | Toxicity/ADR  | Khrunin et al., 2010 [11]; Khrunin et al., 2012 [9]; Kim et al., 2009 [29] |
| TPMT      | rs1142345  | T>C     | Tyr240Cys      | TPMT*3A, TPMT*3C,       | Efficacy      | Khrunin et al., 2014 [4]                                               |
|           |            |         |                | TPMT*3D, TPMT*3E        |               |                                                                         |
| VEGFA     | rs2010963  | C>G     | -              | -                       | Efficacy      | Orlandi et al., 2013 [30]                                              |
| XRCC1     | rs25487    | T>C     | Glu399Arg      | -                       | Efficacy,    | Khrunin et al., 2010 [11]; Khrunin et al., 2012 [9]                   |
|           |            |         |                |                         | Toxicity/ADR  |                                                                         |
| Dexamethasone GATA3 | rs3824662 | C>A     | -              | -                       | Efficacy      | Perez-Andreu et al., 2013 [12]                                         |
| ABCB1     | rs10276036 | C>T     | -              | ABCB1*13                | Efficacy      | Caronia et al., 2011 [1]                                               |
|           | rs1045642  | A>T; A>G| Ile1145Ile     | ABCB1*13                | Efficacy      | Cizmarikova et al., 2010 [31]; Giovannetti et al., 2011 [32]; Greén et al., 2012 [33]; Kafka et al., 2003 [34]; Lal et al., 2008 [35] |
|           | rs1128503  | A>G     | Gly412Gly      | ABCB1*13                | Efficacy      | Caronia et al., 2011 [1]                                               |
|           | rs2032582  | A>T; A>C| Ser893Ala; Ser893Thr | ABCB1*13 | Efficacy; Pharmacocynetic | Bray et al., 2010 [2]; Lal et al., 2008 [35] |
|           | rs4148737  | T>C     | -              | -                       | Efficacy      | Caronia et al., 2011 [1]                                               |
| ABCC1     | rs45511401 | G>T     | Gly671Val      | -                       | Toxicity/ADR  | Wojnowski et al., 2005 [36]                                            |
| ABCC2     | rs17222723 | T>A     | Val1188Glu     | -                       | Toxicity/ADR  | Wojnowski et al., 2005 [36]                                            |
|           | rs187710   | G>A     | Cys1515Tyr     | -                       | Toxicity/ADR  | Wojnowski et al., 2005 [36]                                            |
| ABCC3     | rs4148416  | C>T     | Gly1013Gly     | -                       | Efficacy      | Caronia et al., 2011 [1]                                               |
| ABCC4     | rs9561778  | G>A; G>T| -              | -                       | Toxicity/ADR  | Low et al., 2009 [3]                                                   |
| CBR1      | rs20572    | C>T     | Ala209Ala      | -                       | Dosage        | Lal et al., 2008 [37]                                                  |
| CBR3      | rs8133052  | G>A     | Cys4Tyr        | -                       | Efficacy,    | Fan et al., 2008 [39]                                                  |
|           |            |         |                |                         | Toxicity/ADR  | Wojnowski et al., 2005 [36]                                            |
| CYBA      | rs4673     | A>G     | Tyr72His       | -                       | Toxicity/ADR  | Wojnowski et al., 2005 [36]                                            |
| SNP        | rsID       | Allele | Gene Symbol | rsID | Allele | Gene Symbol | Function       | Ref.                       |
|------------|------------|--------|-------------|------|--------|-------------|----------------|----------------------------|
| CYP2B6     | rs12721655 | A>G    | Lys139Glu   |      |        |             | Efficacy       | Bray *2010 [2]             |
|            | rs3211371  | C>T    | Arg487Cys   |      |        |             | Toxicity/ADR   | Bray *2010 [2]             |
|            | rs3745274  | G>T    | Gln172His   |      |        |             | Dosage         | Bray *2010 [2]             |
| CYP2C19    | rs4244285  | G>A; C>G | Pro227Pro   |      |        |             | Efficacy       | Bray *2010 [2]             |
| GATA3      | rs3824662  | C>A    | -           |      |        |             | Efficacy       | Perez-Andreu *2013 [12]    |
| GST1       | rs3957357  | A>G    | -           |      |        |             | Efficacy       | Gelderblom *2014 [40]      |
| GSTM1      | GSTM1 null |        | -           |      |        |             | Efficacy, Toxicity/ADR | Altés *2013 [41]           |
| Gene | rsID | SNP | Allele | Effect | Reference |
|------|------|-----|--------|--------|-----------|
| MTR  | rs1805087 | A>G | Asp919Gly | - | Toxicity/ADR |
|      | rs1883112 | G>A | - | - | Toxicity/ADR |
|      | rs1799983 | T>G | Asp298Glu | - | Efficacy |
|      | rs2070744 | C>T | - | - | Efficacy |
| NCF4 | rs1800566 | G>A | Pro149Ser | - | Efficacy |
| NOS3 | rs1143684 | C>T | Leu47Phe | - | Efficacy |
| NQO1 | rs13058338 | T>A | - | - | Toxicity/ADR |
|      | rs12210538 | A>G | Met497Thr | - | Toxicity/ADR |
|      | rs9607567 | A>G | Asn104Asn | - | Efficacy |
|      | rs714368 | T>C | His49Arg | - | Other |
|      | rs723685 | A>G | Val252Ala | - | Dosage |
| NQO2 | rs12238472 | C>T | Arg1268Gln | - | Toxicity |
|      | rs2227291 | G>C | Val767Leu | - | toxicity |
|      | rs12418 | G>A | - | - | efficacy |
|      | rs1871450 | G>A | - | - | toxicity/toxicity |
|      | rs4148943 | C>T | - | - | efficacy |
|      | rs4148945 | C>T | - | - | efficacy/toxicity |
|      | rs4148947 | T>C | - | - | efficacy |
|      | rs148950 | G>A | - | - | efficacy/toxicity |
|      | rs730720 | C>T | - | - | efficacy |
| CYP4B1 | rs4646487 | C>T | Arg173Trp | CYP4B1*3, CYP4B1*6 | toxicity |
| polymorphism | rsID | SNP | AA change | effect | reference |
|--------------|------|-----|-----------|--------|-----------|
| **NAT2**     |      |     |           |        |           |
| rs1799931    |      | G>A | Gly286Glu | toxicity | Deeken et al., 2010 [43] |
| **PPARD**    |      |     |           |        |           |
| rs1883322    |      | C>T | -         | efficacy | Deeken et al., 2010 [43] |
| rs2016520    |      | C>T | -         | efficacy | Deeken et al., 2010 [43] |
| rs3734254    |      | C>T | -         | efficacy | Deeken et al., 2010 [43] |
| rs6922548    |      | A>G | -         | efficacy | Deeken et al., 2010 [43] |
| rs7769719    |      | G>A | -         | efficacy | Deeken et al., 2010 [43] |
| **SLC10A2**  |      |     |           |        |           |
| rs2301159    |      | G>A | -         | toxicity | Deeken et al., 2010 [43] |
| **SPG7**     |      |     |           |        |           |
| rs12960      |      | G>A | Arg688Gln | toxicity | Deeken et al., 2010 [43] |
| rs2292954    |      | A>G | Thr503Ala | toxicity | Deeken et al., 2010 [43] |
| **SULT1C4**  |      |     |           |        |           |
| rs1402467    |      | C>G | Asp5Glu   | -       | efficacy | Deeken et al., 2010 [43] |
| **ABCB1**    |      |     |           |        |           |
| rs10276036   |      | C>T | -         | ABCB1*13 | Caronia et al., 2011 [1] |
| rs1045642    |      | A>G | Ile1145Ile | ABCB1*13 | Ceppi et al., 2014 [44] |
| rs1128503    |      | A>G | Gly412Gly | ABCB1*13 | Caronia et al., 2011 [1] |
| rs4148737    |      | T>C | -         | Efficacy | Caronia et al., 2011 [1] |
| rs4728709    |      | G>A | -         | Toxicity/ADR | Ceppi et al., 2014 [44] |
| **ABCC3**    |      |     |           |        |           |
| rs4148416    |      | C>T | Gly1013Gly | - | Efficacy | Caronia et al., 2011 [1] |
| **ACTG1**    |      |     |           |        |           |
| rs1135989    |      | G>A | Ala403Ala | - | Toxicity/ADR | Ceppi et al., 2014 [44] |
| **CAPG**     |      |     |           |        |           |
| rs3770102    |      | G>T | -         | - | Toxicity/ADR | Ceppi et al., 2014 [44] |
| **CEPT2**    |      | C>T | -         | - | Toxicity/ADR | Diouf et al., 2015 [45] |
| **GATA3**    |      | C>A | -         | Efficacy | Perez-Andreu et al., 2013 [12] |
| **MTR**      |      | A>G | Asp919Gly | - | Toxicity/ADR | Patiño-García et al., 2009 [17]; Cui et al., 2011 [18] |

ADR—adverse drug reaction.
Figure S1. Gene networks of pharmacogenetic markers performed with GeneMANIA. (a) All listed genes; (b) genes involved in DNA repair/response to DNA damage; (c) genes involved in drug biotransformation.
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