

## Polymorphisms associated with taxane-related sensory neuropathy

### Online Supplementary Material:

#### Supplementary Table 1: Published Studies of Putative Functional SNPs

##### Footnotes

Where a study has shown multiple SNPs with no association with TRSN not all SNPs have been shown in the table.

\*\*These haplotypes have not been included in the AML analysis, but some of the individual SNPs have been included.

§The two FZD3 SNPs are in tight LD and should be considered as a single marker. The FZD3 SNP could not be tested for replication in the African American population because of limited LD in this region.

††rs4141404 is located in LIMK2, but there is a large region of LD ( $r^2 > 0.7$ ) that covers several genes, from PLA2G3 to PISD.

‡†rs2425553 is in complete LD with rs2425556 and rs3092292.

§§rs6473187 in KIAA0146 is in complete LD with rs2632496 in KIAA0146, with rs4873774 in UBE2V2 and with rs8178108 in PRKD.

¶¶rs3829306 is in complete LD with rs4149013 and rs4149023, both in SLCO1B1.

#### Supplementary Table 2a: Drug Regimens and Doses of Taxanes by Study

#### Supplementary Table 2b: Comparison of Toxicity grades/rates by recruiting trial in PGSNPS included in Taxane Related Sensory Neuropathy Study

##### Footnotes

Chi-squared test for association of trial and case:control status (df=1); p-value=0.29

#### Supplementary Table 3: PGSNPS Taxane Treated Patient Characteristics

##### Footnotes

\*out of total cases; \*\*out of total control

#### Supplementary Table 4: All Putative Functional SNPs Replicated in the PGSNPS dataset (phenotype: cumulative dose to TRSN)

##### Footnotes

HR>1 indicates an increased risk of TRSN

HR<1 indicates a decreased risk of TRSN

Not all variants described in each study as having “no association with neuropathy” are reported in the table.

†Intergenic SNPs are denoted by the closest flanking annotated gene(s).

§The two FZD3 SNPs are in tight LD and should be considered as a single marker. The FZD3 SNP could not be tested for replication in the African American population because of limited LD in this region.

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§rs6473187 in KIAA0146 is in complete LD with rs2632496 in KIAA0146, with rs4873774 in UBE2V2 and with rs8178108 in PRKD.

¶rs3829306 is in complete LD with rs4149013 and rs4149023, both in SLCO1B1.

### Supplementary Table 5: All Putative Functional SNPs Replicated in the PGSNPS dataset (phenotype: maximum TRSN)

#### Footnotes

HR>1 indicates an increased risk of TRSN

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Not all variants described in each study as having “no association with neuropathy” are reported in the table.

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§The two FZD3 SNPs are in tight LD and should be considered as a single marker. The FZD3 SNP could not be tested for replication in the African American population because of limited LD in this region.

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¶rs3829306 is in complete LD with rs4149013 and rs4149023, both in SLCO1B1.

### Supplementary Figure 1: Percentage of Patients with TRSN $\geq$ grade 2 by genotype, for three statistically significant SNPs that were genotyped in PGSNPS (maximum TRSN)

Data is only shown for statistically significant genotyped SNPs (not for imputed SNPs).

### Supplementary Figures 2a-c: Kaplan-Meier curves

**Kaplan-Meier curves: Shows for each SNP, by genotype, the probability of TRSN grade 0-1 (i.e. the probability of not experiencing moderate/severe TRSN) as the cumulative dose increases.**

Data is only shown for statistically significant genotyped SNPs (not for imputed SNPs).

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Supplementary Table 1 – Published Studies of Putative Functional SNPs

GENE	SNP RS NUMBER	AMINO ACID CHANGE	SAMPLE SIZE	STUDY REFERENCE	PUBLISHED PUTATIVE FUNCTIONAL SNPs ASSOCIATED WITH NEUROPATHY :
CYP2C8	rs11572080	R139K; (K399R)	914	Marsh 2007 <sup>16</sup>	No association with neuropathy
CYP2C8	rs11572080	R139K; (K399R)	38	Green 2008 <sup>17</sup>	Increased motor neuropathy with heterozygote (p=0.034)
CYP2C8	rs11572080	R139K; (K399R)	118	Leskelä 2011 <sup>18</sup>	Association with increased neuropathy OR=1.72; 95%CI 1.05–2.82; p=0.032
CYP2C8	rs11572080	R139K; (K399R)	95	Rizzo 2010 <sup>19</sup>	No association with neuropathy
CYP2C8	rs11572080	R139K; (K399R)	36	Ofverholm 2010 <sup>20</sup>	No association with neuropathy
CYP2C8	rs11572080	R139K; (K399R)	411 (combined analysis)	Hertz 2013 <sup>21</sup>	Association with increased neuropathy OR=1.98; 95%CI 1.25–3.13; p=0.004 per allele risk
CYP2C8	rs1058930	I264M	914	Marsh 2007 <sup>16</sup>	No association with neuropathy
CYP2C8	rs1058930	I264M	95	Rizzo 2010 <sup>19</sup>	No association with neuropathy
CYP2C8	rs1058930	I264M	118	Leskelä 2011 <sup>18</sup>	No association with neuropathy
CYP2C8	rs1058930	I264M	119	Bergmann 2011(a) <sup>22</sup>	Exploratory analysis data not shown
CYP2C8	rs1058930	I264M	92	Bergmann 2011(b) <sup>23</sup>	No association with neuropathy
CYP2C8	rs1113129	-	118	Leskelä 2011 <sup>18</sup>	Association with decreased neuropathy OR=0.55 95%CI 0.34–0.89; p=0.014
CYP2C8	rs10509681	L329A	914	Marsh 2007 <sup>16</sup>	No information given
CYP2C8	rs10509681	L329A	119	Bergmann 2011(a) <sup>22</sup>	No association with neuropathy
CYP2C8	rs10509681	L329A	92	Bergmann 2011(b) <sup>23</sup>	No association with neuropathy
CYP2C8	rs10509681	L329A	209 (primary analysis) 411 (combined analysis)	Hertz 2013 <sup>21</sup>	Concordance of rs10509681 with rs11572080 result.
CYP2C8	rs7909236	-	38	Green 2008 <sup>17</sup>	No association with neuropathy
CYP2C8	rs7909236	-	118	Leskelä 2011 <sup>18</sup>	No association with neuropathy
CYP2C8	rs7909236	-	92	Bergmann 2011(b) <sup>23</sup>	No association with neuropathy
CYP2C8	rs11572103	-	95	Rizzo 2010 <sup>19</sup>	No variant allele observed in study population
CYP3A4	rs2740574	-	914	Marsh 2007 <sup>16</sup>	No association with neuropathy
CYP3A4	rs2740574	-	38	Green 2008 <sup>17</sup>	No association with neuropathy
CYP3A4	rs2740574	-	92	Bergmann 2011(b) <sup>23</sup>	No association with neuropathy
CYP3A4	rs2740574	-	36	Ofverholm 2010 <sup>20</sup>	No association with neuropathy
CYP3A4	rs2740574	-	118	Leskelä 2011 <sup>18</sup>	Association with increased neuropathy

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					OR=2.13 95% CI=(0.98–4.66) p=0.057
CYP3A4	rs55785340	-	119	Bergmann 2011(a) <sup>22</sup>	Exploratory analysis data not shown
CYP3A5	rs776746	splice variant	914	Marsh 2007 <sup>16</sup>	No association with neuropathy
CYP3A5	rs776746	splice variant	118	Leskelä 2011 <sup>18</sup>	Association with decreased neuropathy OR=0.51; 95%CI 0.30–0.86; p=0.012
CYP3A5	rs776746	splice variant	119	Bergmann 2011(a) <sup>22</sup>	Exploratory analysis data not shown
CYP3A5	rs776746	splice variant	92	Bergmann 2011(b) <sup>23</sup>	No association with neuropathy
ABCB1	rs2032582	A893S	22	Sissung 2006 <sup>24</sup>	No information given
ABCB1	rs2032582	A893S	914	Marsh 2007 <sup>16</sup>	No association with neuropathy
ABCB1	rs2032582	A893S	38	Green 2008 <sup>17</sup>	Reduced sensory neuropathy with heterozygote and homozygote (p=0.186)
ABCB1	rs2032582	A893S	73	Sissung 2008 <sup>25</sup>	No association with neuropathy for patients on Docetaxel (p=0.68), but association with increased neuropathy for patients on Docetaxel and thalidomide (p=0.007)
ABCB1	rs2032582	A893S	121	Chang 2009 <sup>26</sup>	No association with neuropathy
ABCB1	rs2032582	A893S	36	Ofverholm 2010 <sup>20</sup>	No association with neuropathy
ABCB1	rs2032582	A893S	95	Rizzo 2010 <sup>19</sup>	No association with neuropathy
ABCB1	rs2032582	A893S	118	Leskelä 2011 <sup>18</sup>	No association with neuropathy
ABCB1	rs2032582	A893S	119	Bergmann 2011(a) <sup>22</sup>	No association with neuropathy
ABCB1	rs2032582	A893S	92	Bergmann 2011(b) <sup>23</sup>	No association with neuropathy
ABCB1	rs1128503	G412G	22	Sissung 2006 <sup>24</sup>	No information given
ABCB1	rs1128503	G412G	38	Green 2008 <sup>17</sup>	No association with neuropathy
ABCB1	rs1128503	G412G	73	Sissung 2008 <sup>25</sup>	No association with neuropathy
ABCB1	rs1128503	G412G	914	Marsh 2007 <sup>16</sup>	No association with neuropathy
ABCB1	rs1128503	G412G	95	Rizzo 2010 <sup>19</sup>	No association with neuropathy
ABCB1	rs1128503	G412G	119	Bergmann 2011(a) <sup>22</sup>	No association with neuropathy
ABCB1	rs1128503	G412G	92	Bergmann 2011(b) <sup>23</sup>	No association with neuropathy
ABCB1	rs1128503	G412G	118	Leskelä 2011 <sup>18</sup>	No association with neuropathy
ABCB1	rs1045642	I1145I	22	Sissung 2006 <sup>24</sup>	Trend for reduced neuropathy in homozygote (rare) p=0.09
ABCB1	rs1045642	I1145I	914	Marsh 2007 <sup>16</sup>	No association with neuropathy
ABCB1	rs1045642	I1145I	38	Green 2008 <sup>17</sup>	Association with decreased neuropathy no p-value
ABCB1	rs1045642	I1145I	73	Sissung 2008 <sup>25</sup>	No association with neuropathy
ABCB1	rs1045642	I1145I	121	Chang 2009 <sup>26</sup>	No association with neuropathy
ABCB1	rs1045642	I1145I	36	Ofverholm 2010 <sup>20</sup>	No association with neuropathy
ABCB1	rs1045642	I1145I	95	Rizzo 2010 <sup>19</sup>	No association with neuropathy
ABCB1	rs1045642	I1145I	118	Leskelä 2011 <sup>18</sup>	Association with decreased neuropathy OR=0.71; 95%CI 0.47–1.06; p=0.093
ABCB1	rs1045642	I1145I	119	Bergmann 2011(a) <sup>22</sup>	No association with neuropathy
ABCB1	rs9282564	Asn21Asp	118	Leskelä 2011 <sup>18</sup>	Association with decreased neuropathy

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		(N21D)			OR=0.43 95%CI 0.17-1.04; p=0.061
<i>ABCB1</i>	rs9282564	Asn21Asp (N21D)	92	Bergmann 2011(b) <sup>23</sup>	No association with neuropathy
<i>ABCC1</i>	rs2230671	S1334S	914	Marsh 2007 <sup>16</sup>	No association with neuropathy
<i>ABCC2</i>	rs717620	-	914	Marsh 2007 <sup>16</sup>	No association with neuropathy
<i>ABCC2</i>	rs2273697	V417I	914	Marsh 2007 <sup>16</sup>	No association with neuropathy
<i>ABCC2</i>	rs2273697	V417I	119	Bergmann 2011(a) <sup>22</sup>	Exploratory analysis data not shown
<i>ABCC2</i>	rs8187710	Cys1515Tyr	119	Bergmann 2011(a) <sup>22</sup>	Exploratory analysis data not shown
<i>ABCC2</i>	rs8187710	Cys1515Tyr	92	Bergmann 2011(b) <sup>23</sup>	No association with neuropathy
<i>ABCC2</i>	rs17222723	Val1188Glu	119	Bergmann 2011(a) <sup>22</sup>	Exploratory analysis data not shown
<i>ABCC2</i>	rs17222723	Val1188Glu	92	Bergmann 2011(b) <sup>23</sup>	No association with neuropathy
<i>ABCG2</i>	rs2231142	Gln141Lys (Q141K)	914	Marsh 2007 <sup>16</sup>	No association with neuropathy
<i>ABCG2</i>	rs2231142	Gln141Lys (Q141K)	119	Bergmann 2011(a) <sup>22</sup>	Exploratory analysis data not shown
<i>CYP1B1</i>	rs1056836	L432V	914	Marsh 2007 <sup>16</sup>	No association with neuropathy
<i>CYP1B1</i>	rs1056836	L432V	95	Rizzo 2010 <sup>19</sup>	No association with neuropathy
<i>CYP1B1</i>	rs1056836	L432V	92	Bergmann 2011(b) <sup>23</sup>	No association with neuropathy
<i>TP53</i>	rs1042522	Pro72Arg (R72P)	914	Marsh 2007 <sup>16</sup>	No association with neuropathy
<i>GSTP1</i>	rs947894 has merged into rs1695	I105V	914	Marsh 2007 <sup>16</sup>	No association with neuropathy
<i>GSTP1</i>	rs947894 has merged into rs1695	I105V	58	Mir 2009 <sup>27</sup>	Increased association with sensory neuropathy OR=6.11; 95%CI 1.17-31.94; p=0.03 multivariable p=0.01
<i>GSTP1</i>	rs1138272	A114V	914	Marsh 2007 <sup>16</sup>	No association with neuropathy
<i>SLCO1B1</i>	rs4149056	V174A	118	Leskelä 2011 <sup>18</sup>	No association with neuropathy
<i>SLCO1B3</i>	rs4149117	S112A	118	Leskelä 2011 <sup>18</sup>	No association with neuropathy
<i>SLCO1B3</i>	rs4149117	S112A	119	Bergmann 2011(a) <sup>22</sup>	Exploratory analysis data not shown
<i>SLCO1B3</i>	rs7311358	M233I	118	Leskelä 2011 <sup>18</sup>	No association with neuropathy
<i>SLCO1B3</i>	rs7311358	M233I	119	Bergmann 2011(a) <sup>22</sup>	Exploratory analysis data not shown
<i>SLCO1B3</i>	rs7311358	M233I	92	Bergmann 2011(b) <sup>23</sup>	No association with neuropathy
<i>FANCD2</i>	rs7648104	-	888	Sucheston 2011 <sup>28</sup>	Association with increased neuropathy OR=1.86; 95%CI 1.30-2.65; p<0.001
<i>FANCD2</i>	rs7637888	-	888	Sucheston 2011 <sup>28</sup>	Association with increased neuropathy OR=1.87; 95%CI 1.30-2.67; p<0.001
<i>FANCD2</i>	rs6786638	-	888	Sucheston 2011 <sup>28</sup>	Association with increased neuropathy OR=1.90; 95%CI 1.32-2.72; p<0.001
<i>FANCD2</i>	rs6442150	-	888	Sucheston 2011 <sup>28</sup>	Association with increased neuropathy OR=1.89; 95%CI 1.32-2.72; p<0.001
<i>FANCD2</i>	**rs7648104- rs7637888	-	888	Sucheston 2011 <sup>28</sup>	Association with increased neuropathy OR=2.84; 95%CI 1.2-6.9; p=0.03

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<i>FANCD2</i>	**rs3846177–rs9849434	-	888	Sucheston 2011 <sup>28</sup>	Association with increased neuropathy OR=1.8; 95%CI 1.3-2.5; p=0.005
<i>FANCD2</i>	**rs1552244–rs12152512	-	888	Sucheston 2011 <sup>28</sup>	Association with increased neuropathy OR=1.7; 95%CI 1.2-2.4; p=0.007
<i>EPHA5</i>	rs7349683	Gly965Gly	855 (discovery cohort) 271 (validation cohort)	Baldwin 2012 <sup>2</sup>	Cumulative dose to event analysis: Discovery set: HR=1.63; 95%CI 1.34–1.98; p=9.6x10 <sup>-7</sup> Caucasian Replication set: HR=0.96; 95%CI 0.57–1.60; p=0.43 African-American Replication set: HR=1.16; 95%CI 0.55–2.42; p= 0.35
<i>XKR4</i>	rs4737264	-	855 (discovery cohort) 271 (validation cohort)	Baldwin 2012 <sup>2</sup>	Cumulative dose to event analysis: Discovery set: HR=1.68; 95%CI 1.36–2.09; p=1.9x10 <sup>-6</sup> Caucasian Replication set: HR=1.84; 95%CI 1.02–3.33; p=0.021 African-American Replication set: HR=1.23; 95%CI 0.69–2.21; p= 0.24
<i>FGD4</i>	rs10771973	-	855 (discovery cohort) 271 (validation cohort)	Baldwin 2012 <sup>2</sup>	Cumulative dose to event analysis: Discovery set: HR=1.57; 95%CI 1.30–1.91; p=2.6x10 <sup>-6</sup> Caucasian Replication set: HR=1.72; 95%CI 1.06–2.80; p=0.013 African-American Replication set: HR=1.93; 95%CI 1.13-3.28; p= 0.0067
<i>PITPNA</i>	rs16948748	-	855 (discovery cohort) 271 (validation cohort)	Baldwin 2012 <sup>2</sup>	Cumulative dose to event analysis: Discovery set: HR=2.37; 95%CI 1.63–3.44; p=2.7x10 <sup>-6</sup> Caucasian Replication set: HR=2.65; 95%CI 0.63–11.1; p=0.083 African-American Replication set: HR=1.07; 95%CI 0.41–2.77; p= 0.45
<i>CACNB2</i>	rs16916932	-	855 (discovery cohort) 271 (validation cohort)	Baldwin 2012 <sup>2</sup>	Cumulative dose to event analysis: Discovery set: HR=2.08; 95%CI 1.51–2.87; p=4.3x10 <sup>-6</sup> Caucasian Replication set: HR=0.38; 95%CI 0.09–1.58; p=0.082 African-American Replication set: HR=1.13; 95%CI 0.47–2.74; p=0.39
<i>GRIP1/CAND1</i>	rs17781082	-	855 (discovery cohort) 271 (validation cohort)	Baldwin 2012 <sup>2</sup>	Cumulative dose to event analysis: Discovery set: HR=1.60; 95%CI 1.31–1.96; p=4.3x10 <sup>-6</sup> Caucasian Replication set: HR=1.22; 95%CI 0.74–1.99; p=0.22 African-American Replication set: HR=1.32; 95%CI 0.76–2.30; p= 0.16
<i>BCL6</i>	rs1903216	-	855 (discovery cohort) 271 (validation cohort)	Baldwin 2012 <sup>2</sup>	Cumulative dose to event analysis: Discovery set: HR=1.59; 95%CI 1.30–1.95; p=5.6x10 <sup>-6</sup> Caucasian Replication set: HR=2.08; 95%CI 0.99–4.37; p=0.024 African-American Replication set: HR=3.02; 95%CI 1.04–8.73; p= 0.016
<i>NDRG1</i>	rs2233335	-	855 (discovery cohort) 271 (validation cohort)	Baldwin 2012 <sup>2</sup>	Cumulative dose to event analysis: Discovery set: HR=0.65; 95%CI 0.52–0.80; p=5.2x10 <sup>-5</sup> Caucasian Replication set: HR=0.94; 95%CI 0.58–1.53; p=0.41 African-American Replication set: HR=1.40; 95%CI 0.75–2.60; p= 0.14
<sup>§</sup> <i>FZD3</i>	rs7001034 (proxy SNP: rs7833751)	-	855 (discovery cohort) 271 (validation cohort)	Baldwin 2012 <sup>2</sup>	Ordinal analysis: Discovery: association with decreased neuropathy OR=0.57; 95%CI 0.48–0.69; p=3.1x10 <sup>-9</sup> Did not replicate in either population
<sup>§</sup> <i>FZD3</i>	rs7833751	-	855 (discovery cohort) 271 (validation cohort)	Baldwin 2012 <sup>2</sup>	Ordinal analysis: Discovery: association with decreased neuropathy OR=0.58 95%CI 0.49–0.70; p=7.5x10 <sup>-9</sup> Caucasian Replication set: borderline increased association with neuropathy

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					OR=1.67; 95%CI 0.88–3.19; p=0.058 Did not replicate in African-American population
<i>SHROOM</i>	rs5934683	-	855 (discovery cohort) 271 (validation cohort)	Baldwin 2012 <sup>2</sup>	Ordinal analysis: Discovery: increased association with neuropathy OR=1.61; 95%CI 1.33–1.93; p=6.0x10 <sup>-7</sup> Caucasian Replication set: no association with neuropathy OR=0.99; 95%CI 0.54–1.82; p=0.49 African-American set: no association with neuropathy OR=1.96; 95%CI 0.49–7.89; p=0.17
<i>ZFPM2</i>	rs2941627	-	855 (discovery cohort) 271 (validation cohort)	Baldwin 2012 <sup>2</sup>	Ordinal analysis: Discovery: increased association with neuropathy OR=1.91; 95%CI 1.40–2.51; p=3.5x10 <sup>-6</sup> Caucasian Replication set: borderline increased association with neuropathy OR=1.37; 95%CI 0.68–2.73; p=0.058 African-American set: decreased association with neuropathy OR=0.49; 95%CI 0.24–0.97; p=0.021
<i>BCAT1</i>	rs7973533	-	855 (discovery cohort) 271 (validation cohort)	Baldwin 2012 <sup>2</sup>	Ordinal analysis: Discovery: decreased association with neuropathy OR=0.66 95%CI 0.55–0.79; p=8.4x10 <sup>-6</sup> Caucasian Replication set: no association with neuropathy OR=0.75 95%CI 0.68–2.73; p=0.19 African-American set: no association with neuropathy OR=1.13 95%CI 0.65–1.94; p=0.33
<i>TUBB2A</i>	rs909965	-	214	Leandro-Garcia 2012 <sup>29</sup>	Decreased association with neuropathy i.e. decreased risk for -101C/-112G variant. HR=0.6 95%CI 0.41–0.90; p=0.012
<i>TUBB2A</i>	rs909964	-	214	Leandro-Garcia 2012 <sup>29</sup>	Decreased association with neuropathy i.e. decreased risk for -101C/-112G variant. HR=0.6 95%CI 0.41–0.90; p=0.012
<i>TUBB2A</i>	rs9501929	-	214	Leandro-Garcia 2012 <sup>29</sup>	No association with neuropathy
<i>EPHA4</i>	rs17348202	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=4.85; 95%CI 2.57–9.13; p=1.02x10 <sup>-6</sup>
<i>LIMK2</i> ( <i>PLA2G3- PISD</i> )††	rs4141404	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=2.41; 95%CI 1.66–3.48; p=3.22x10 <sup>-6</sup>
<i>PAPD7</i>	rs275456	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=2.26; 95%CI 1.60–3.18; p=3.31x10 <sup>-6</sup>
<i>RP11-466L17.1</i>	rs1165472	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=2.36; 95%CI 1.64–3.40; p=3.65x10 <sup>-6</sup>
<i>CD9</i>	rs3181157	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=3.22; 95%CI 1.96–5.29; p=4.05x10 <sup>-6</sup>
<i>PSD3/NAT2</i>	rs10090117	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=2.38; 95%CI 1.64–3.44; p=4.23x10 <sup>-6</sup>
<i>TRIO</i>	rs10065203	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=2.51; 95%CI 1.69–3.71; p=4.25x10 <sup>-6</sup>

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<i>ATPBD4/RP11-702M1.1</i>	rs2947253	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=3.38; 95%CI 2.01–5.68; p=4.36x10 <sup>-6</sup>
<i>ACTL7B</i>	rs10512385	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=2.58; 95%CI 1.71–3.89; p=5.70x10 <sup>-6</sup>
<i>AGMOI DGKB</i>	rs12699683	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=3.66; 95%CI 2.08–6.45; p=6.65x10 <sup>-6</sup>
<i>GLIS3</i>	rs501461	-	144	Leandro-Garcia 2012 <sup>11</sup>	Decreased association with neuropathy HR=0.43; 95%CI 0.29–0.63; p=1.24x10 <sup>-5</sup>
<i>PALLD</i>	rs6846708	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=3.64; 95%CI 2.03–6.53; p=1.50x10 <sup>-5</sup>
<i>PTPRT</i>	rs2425553 [in complete LD with rs2425556 and rs3092292]††	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=2.33; 95%CI 1.58–3.44; p=1.94x10 <sup>-5</sup>
<i>SGCG</i>	rs1753097	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=2.18; 95%CI 1.52–3.11; p=1.96x10 <sup>-5</sup>
<i>KIAA0146-PRKD§§</i>	rs6473187	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=3.37; 95%CI 1.92–5.91; p=2.17x10 <sup>-5</sup>
<i>PAPD7</i>	rs13163920	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=2.41; 95%CI 1.60–3.61; p=2.23x10 <sup>-5</sup>
<i>ERBB4</i>	rs10932374	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=2.25; 95%CI 1.54–3.28; p=2.58x10 <sup>-5</sup>
<i>SLCO1B1¶¶</i>	rs3829306	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=3.10; 95%CI 1.82–5.26; p=2.84x10 <sup>-5</sup>
<i>C19orf21</i>	rs8110536	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=2.24; 95%CI 1.53–3.27; p=2.98x10 <sup>-5</sup>
<i>LPP</i>	rs189372	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=2.27; 95%CI 1.55–3.35; p=2.98x10 <sup>-5</sup>
<i>HAND2</i>	rs7655560	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=2.97; 95%CI 1.78–4.95; p=3.37x10 <sup>-5</sup>
<i>PARK2</i>	rs9365397	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=4.33; 95%CI 2.16–8.65; p=3.42x10 <sup>-5</sup>
<i>EPHA6</i>	rs301927	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=2.35; 95%CI 1.57–3.53; p=3.42x10 <sup>-5</sup>
<i>LIMK2</i>	rs2413045	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=2.36; 95%CI 1.57–3.56; p=3.67x10 <sup>-5</sup>
<i>TYW3ILHX8</i>	rs12743802	-	144	Leandro-Garcia 2012 <sup>11</sup>	Increased association with neuropathy HR=4.06; 95%CI 2.08–7.91; p=3.85x10 <sup>-5</sup>



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**Supplementary Table 2a: Comparison of Drugs and Dosages across PGSNPS Taxane Related Sensory Neuropathy Study**

<b>DRUG</b>	<b>PGSNPS Dose mg/m<sup>2</sup></b>	<b>Dosing Schedule</b>
EPIRUBICIN	90	3 weekly
CYCLOPHOSPHAMIDE	600	3 weekly
PACLITAXEL (as part of tAnGo Trial – PGSNPS)	175	3 weekly
PACLITAXEL (as part of Neo-tAnGo Trial – PGSNPS)	175	2 weekly
GEMCITABINE (as part of tAnGo Trial – PGSNPS)	1250	Day1 and Day 8
GEMCITABINE (as part of Neo-tAnGo Trial – PGSNPS)	2000	2 weekly

**Supplementary Table 2b: Comparison of toxicity grades/rates in cases across the trials in PGSNPS included in Taxane Related Sensory Neuropathy Study**

<b>TRSN Grade</b>	<b>Neotango patients in PGSNPS %  (n=431 received paclitaxel)</b>	<b>Tango patients in PGSNPS %  (n=872 received paclitaxel)</b>
Grade 0	25.8% (111)	18.8% (164)
Grade 1	48.5% (209)	52.6% (459)
Grade 2	21.4% (92)	24.1% (210)
Grade 3	4.3% (19)	4.5% (39)
Grade 4	0 % (0)	0 % (0)
Overall toxicity rate for ≥grade 2	25.8%	28.6%

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Supplementary Table 3: PGSNPS Taxane Treated Patient Characteristics

	Cases (n=360)		Controls (n=943)	
	N	%*	N	%**
<b>Age</b>				
<40	49	13.6	140	14.9
40-49	115	31.9	348	36.9
50-59	127	35.3	322	34.2
60-69	64	17.8	121	12.8
≥70	5	1.4	12	1.3
<b>ER Status</b>				
negative	113	31.4	333	35.3
positive	247	68.6	610	64.7
<b>Her2 Status</b>				
negative	228	63.3	597	63.3
positive	58	16.1	160	17.0
missing data	74	20.6	186	19.7
<b>Nodal Status</b>				
negative	124	34.5	302	32.0
1-3 positive	94	26.1	273	29.0
4+ positive	94	26.1	215	22.8
clinically positive, neoadjuvant	48	13.3	153	16.2
<b>ECOG performance status</b>				
0	220	61.1	583	61.8
1	29	8.1	40	4.2
missing data	111	30.8	320	33.9
<b>Tumour Size</b>				
0-20mm	131	36.4	270	28.6
21-50mm	199	55.3	532	56.4
>50mm	19	5.3	90	9.4
missing data	11	3.0	51	5.4
<b>Tumour Grade</b>				
1	10	2.8	27	2.9
2	127	35.3	291	30.9
3	189	52.5	515	54.6
missing data	34	9.4	110	11.7
<b>Menopausal Status</b>				
pre	154	42.8	453	48.0
peri	22	6.1	64	6.8
post	134	37.2	317	33.6
bilateral salpingo-oophorectomy	25	6.9	46	4.9
hysterectomy	2	0.6	9	1.0
missing data	23	6.4	54	5.7
<b>BMI</b>				
underweight	7	1.9	31	3.3
healthy weight	113	31.4	406	43.0
overweight	130	36.1	326	34.6
obese	110	30.6	180	19.1

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<b>Epirubicin received</b>					
	yes	359	99.7	941	99.8
	no	1	0.3	2	0.2
<b>Cyclophosphamide received</b>					
	yes	359	99.7	941	99.8
	no	1	0.3	2	0.2
<b>Paclitaxel received</b>					
	yes	360	100	943	100
<b>Gemcitabine received</b>					
	yes	187	51.9	456	48.4
	no	173	48.1	487	51.6

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**SupplementaryTable 4 - All Putative Functional SNPs Replicated in the PGSNPS dataset (phenotype: cumulative dose to TRSN)**

GENE	VARIANT	SNP RS NUMBER AND NUCLEOTIDE CHANGE	CHROMOSOME	POSITION DBSNP BUILD 37	TYPE of SNP		Imputation R <sup>2</sup>	HAZARD RATIO (HR)	95% CONFIDENCE INTERVALS (95%CI)	P-VALUE	INCLUDED IN AML	
					Genotyped (G)	Imputed (I)					YES (Y)	NO(N)
CYP2C8	*3	rs11572080	10	96827030	I		1	1.13	0.91□1.40	0.27		Y
<b>CYP2C8</b>	<b>*4</b>	<b>rs1058930</b>	<b>10</b>	<b>96818119</b>	<b>G</b>			<b>1.38</b>	<b>1.03□1.86</b>	<b>0.04</b>		<b>Y</b>
CYP2C8	*HapC	rs1113129	10	96811045	I		1	1.04	0.87□1.23	0.68		Y
CYP2C8	*3	**rs10509681	10	96798749	G			1.13	0.92□1.41	0.26		N (high correlation with other SNP(s))
†CYP2C8	*2	rs11572103	10	96818106	<b>MAF&lt;0.001</b>		0.86	NA	NA	NA		N (rare SNP)
CYP2C8	*1B	rs7909236	10	96829430	G			0.97	0.82□1.15	0.73		Y
CYP3A4	*1B/V	rs2740574	7	99382096	I		0.94	1.35	0.95□1.92	0.10		Y
†CYP3A4	*2	rs55785340	7	99365983	<b>MAF&lt;0.001</b>		0.55	NA	NA	NA		N (rare SNP)
†CYP3A4	*16	rs12721627	7	99366093	<b>MISSING</b>			NA	NA	NA		N (missing data)
CYP3A5	*3C	rs776746	7	99270539	G			0.97	0.74□1.29	0.86		Y
<b>ABCB1</b>	-	<b>rs2032582</b>	<b>7</b>	<b>87160618</b>	<b>I</b>		<b>0.99</b>	<b>1.19</b>	<b>1.04□1.36</b>	<b>0.02</b>		<b>Y</b>
ABCB1	-	**rs1128503	7	87179601	I		1			0.11		N (high

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							1.12	0.98-1.30		correlation with other SNP(s)
<b>ABCB1</b>	-	<b>**rs1045642</b>	<b>7</b>	<b>87138645</b>	<b>G</b>		<b>0.83</b>	<b>0.72-0.95</b>	<b>0.009</b>	<b>N (high correlation with other SNP(s))</b>
ABCB1	-	rs9282564	7	87229440	G		1.19	0.96-1.49	0.13	Y
<b>ABCB1</b>	-	<b>rs3213619</b>	<b>7</b>	<b>87230193</b>	<b>I</b>	<b>0.99</b>	<b>0.51</b>	<b>0.31-0.85</b>	<b>0.004</b>	<b>Y</b>
ABCC1	-	rs2230671	16	16228242	I	0.91	1.02	0.86-1.21	0.79	Y
ABCC2	-	rs717620	10	101542578	G		0.92	0.82-1.16	0.74	Y
ABCC2	-	rs2273697	10	101563815	G		1.07	0.90-1.27	0.44	Y
<b>ABCC2</b>	-	<b>rs8187710</b>	<b>10</b>	<b>101611294</b>	<b>I</b>	<b>1</b>	<b>0.71</b>	<b>0.50-1.02</b>	<b>0.05</b>	<b>Y</b>
ABCC2	-	<b>**rs17222723</b>	<b>10</b>	<b>101595996</b>	<b>I</b>	<b>1</b>	<b>0.72</b>	<b>0.50-1.04</b>	<b>0.06</b>	<b>N (high correlation with other SNP(s))</b>
ABCG2	-	rs2231142	4	89052323	I	1	0.87	0.68-1.10	0.23	Y
<b>CYP1B1</b>	<b>*3</b>	<b>rs1056836</b>	<b>2</b>	<b>38298203</b>	<b>G</b>		<b>0.83</b>	<b>0.72-0.96</b>	<b>0.01</b>	<b>Y</b>
TP53	-	rs1042522	17	7579472	I	0.97	0.93	0.79-1.10	0.39	Y
GSTP1	-	rs947894 has merged into rs1695	11	67352689	I	0.93	1.07	0.92-1.26	0.38	Y
†GSTP1	-	rs1138272	11	67353579	I	0.88	1.19	0.90-1.58	0.24	Y
SLCO1B1	-	rs4149056		21331549	G		0.95	0.77-1.17	0.60	Y

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			12							
<i>SLCO1B3</i>	-	**rs4149117	12	21011480	I	1	0.98	0.80□1.21	0.87	N (high correlation with other SNP(s))
<i>SLCO1B3</i>	-	rs7311358	12	21015760	I	1	0.99	0.80□1.22	0.90	Y
<i>FANCD2</i>	-	**rs7648104	3	10073311	I	1	0.93	0.77□1.13	0.46	N (high correlation with other SNP(s))
<i>FANCD2</i>	-	**rs7637888	3	10080722	I	1	0.93	0.77□1.13	0.46	N (high correlation with other SNP(s))
<i>FANCD2</i>	-	rs6786638	3	10118075	I	1	0.93	0.77□1.13	0.46	Y
<i>FANCD2</i>	-	**rs6442150	3	10122575	I	1	0.93	0.77□1.13	0.46	N (high correlation with other SNP(s))
<i>EPHA5</i>	-	rs7349683	4	66197804	I	1	0.94	0.81□1.10	0.44	Y
<i>XKR4</i>	-	rs4737264	8	56111322	I	0.99	0.90	0.76□1.07	0.24	Y
<i>FGD4</i>	-	rs10771973	12	32792974	I	0.99	0.97	0.83□1.14	0.72	Y
<i>PITPNA</i>	-	rs16948748	17	1457839	I	0.96	1.23	0.88-1.71	0.24	Y
<i>CACNB2</i>	-	rs16916932	10	18476276	G		0.86	0.62□1.20	0.37	Y
<i>GRIP1/CAND1</i>	-	rs17781082	12	67476327	G		0.93	0.80□1.07	0.30	Y
<i>BCL6</i>	-	rs1903216	3	187629503	G		0.97	0.84□1.12	0.64	Y

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<i>NDRG1</i>	-	rs2233335	8	134261065	I	0.99	0.96	0.82-1.11	0.55	Y
<sup>§</sup> <i>FZD3</i>	-	rs7001034	8	28363378	I	0.99	1.03	0.89-1.19	0.70	N (high correlation with other SNP(s))
<sup>§</sup> <i>FZD3</i>	-	rs7833751	8	28362792	G		1.05	0.91-1.22	0.49	Y
<i>SHROOM</i>	-	rs5934683	X	9751474	I	1	0.94	0.80-1.10	0.44	Y
<i>ZFPM2</i>	-	rs2941627	8	106283030	I	0.97	1.16	0.92-1.46	0.21	Y
<i>BCAT1</i>	-	rs7973533	12	24917962	I	0.85	0.89	0.76-1.04	0.15	Y
<i>TUBB2A</i>	-	rs909965	6	3157809	I	0.66	1.06	0.87-1.28	0.58	N (high correlation with other SNP(s))
<b>**<i>TUBB2A</i></b>	-	rs909964	6	3157798	I	0.66	1.05	0.86-1.27	0.63	Y
<b><i>TUBB2A</i></b>	-	<b>rs9501929</b>	<b>6</b>	<b>3157854</b>	<b>I</b>	<b>0.96</b>	<b>1.60</b>	<b>1.18-2.18</b>	<b>0.005</b>	<b>Y</b>
<i>EPHA4</i>	-	rs17348202	2	222072178	I	0.93	1.07	0.77-1.49	0.68	Y
<i>LIMK2</i> ( <i>PLA2G3- PISD</i> )††	-	rs4141404	22	31675185	I	1	1.07	0.91-1.25	0.41	Y
<i>PAPD7</i>	-	rs275456	5	6813937	I	0.99	1.04	0.88-1.23	0.63	Y
<i>RP11- 466L17.1</i>	-	rs1165472	1	56108604	I	1	0.95	0.81-1.12	0.56	Y
<i>CD9</i>	-	rs3181157	12	6308523	I	0.89	1.08	0.85-1.39	0.53	Y
<i>PSD3/NAT2</i>	-	rs10090117	8	18381235	I	1	1.07	0.90-1.29	0.45	Y
<i>TRIO</i>	-	rs10065203	5	14393621	I	0.85	1.08	0.91-1.27	0.40	Y
<i>ATPBD4/RP11- 702M1.1</i>	-	rs2947253	15	36049492	I	0.87	1.19	0.94-1.51	0.15	Y
<i>ACTL7B</i>	-	rs10512385	9	111455575	G	1	1.24	1.00-1.55	0.06	Y

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<i>AGMOI DGKB</i>	-	rs12699683	7	15133127	G	1	0.96	0.74-1.25	0.75	Y
<i>GLIS3</i>	-	rs501461	9	4039727	I	0.99	0.93	0.80-1.08	0.32	Y
<i>PALLD</i>	-	rs6846708	4	169586731	I	0.98	0.97	0.75-1.26	0.84	Y
<i>PTPRT</i>	-	rs2425553 [in complete LD with rs2425556 and rs3092292]††	20	41670237	G	1	1.11	0.93-1.33	0.25	Y
<i>SGCG</i>	-	rs1753097	13	23878686	I	1	0.98	0.81-1.18	0.82	Y
<i>KIAA0146-PRKD§§</i>	-	rs6473187	8	48483958	I	0.91	1.30	0.96-1.76	0.10	Y
<i>PAPD7</i>	-	rs13163920	5	6759714	I	0.95	0.97	0.83-1.15	0.76	Y
<i>ERBB4</i>	-	rs10932374	2	212244403	G	1	1.05	0.89-1.24	0.56	Y
<b><i>SLCO1B1¶¶</i></b>	-	<b>rs3829306</b>	<b>12</b>	<b>21292280</b>	<b>I</b>	<b>0.99</b>	<b>0.67</b>	<b>0.46-0.97</b>	<b>0.02</b>	<b>Y</b>
<b><i>C19orf21</i></b>	-	<b>rs8110536</b>	<b>19</b>	<b>756985</b>	<b>I</b>	<b>0.37</b>	<b>1.37</b>	<b>1.01-1.87</b>	<b>0.05</b>	<b>Y</b>
<i>LPP</i>	-	rs189372	3	187839070	G	1	1.03	0.88-1.20	0.71	Y
<i>HAND2</i>	-	rs7655560	4	174438897	I	0.81	1.12	0.79-1.61	0.53	Y
<i>PARK2</i>	-	rs9365397	6	162702534	I	0.99	1.12	0.75-1.68	0.58	Y
<b><i>EPHA6</i></b>	-	<b>rs301927</b>	<b>3</b>	<b>97346618</b>	<b>I</b>	<b>0.99</b>	<b>1.29</b>	<b>1.07-1.55</b>	<b>0.008</b>	<b>Y</b>
<i>LIMK2</i>	-	rs2413045	22	31665862	I	0.95	1.12	0.94-1.34	0.22	Y
<i>TYW3ILHX8</i>	-	rs12743802	1	75458806	I	0.76	0.90	0.56-1.46	0.67	Y



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**Supplementary Table 5: All Putative Functional SNPs Replicated in the PGSNPS dataset (phenotype: maximum TRSN)**

GENE	VARIANT	SNP RS NUMBER	CHROMOSOME	POSITION DBSNP BUILD 37	MAJOR/MINOR ALLELE	TYPE of SNP		IMPUTATION R <sup>2</sup>	ODDS RATIO (OR) <sup>◇</sup>	95% CONFIDENCE INTERVALS (95%CI) <sup>◇</sup>	P-VALUE	INCLUDED IN AML
						Genotyped (G)	Imputed (I)					YES (Y)
<i>CYP2C8</i>	*3	rs11572080	10	96827030	C/T	I		1	1.22	0.93□1.59	0.14	Y
<b><i>CYP2C8</i></b>	<b>*4</b>	<b>rs1058930</b>	<b>10</b>	<b>96818119</b>	<b>G/C</b>	<b>G</b>			<b>1.48</b>	<b>1.02□2.15</b>	<b>0.04</b>	<b>Y</b>
<i>CYP2C8</i>	*HapC	rs1113129	10	96811045	G/C	I		1	1.04	0.85□1.28	0.68	Y
<i>CYP2C8</i>	*3	**rs10509681	10	96798749	T/C	G			1.20	0.92□1.56	0.18	N (high correlation with other SNP(s))
† <i>CYP2C8</i>	*2	rs11572103	10	96818106	<b>T/A</b>		<b>MAF=0.0005</b>	0.86	NA	NA	NA	N (rare SNP)
<i>CYP2C8</i>	*1B	rs7909236	10	96829430	G/T	G			0.95	0.78□1.17	0.66	Y
<i>CYP3A4</i>	*1B/V	rs2740574	7	99382096	T/C	I		0.94	1.32	0.84□2.07	0.22	Y
† <i>CYP3A4</i>	*2	rs55785340	7	99365983	<b>A/G</b>		<b>MAF=0.0007</b>	0.55	NA	NA	NA	N (rare SNP)
† <i>CYP3A4</i>	*16	rs12721627	7	99366093			<b>MISSING</b>		NA	NA	NA	N (missing data)
<i>CYP3A5</i>	*3C	rs776746	7	99270539	C/T	G			0.97	0.69□1.36	0.86	Y
<b><i>ABCB1</i></b>	-	<b>rs2032582</b>	<b>7</b>	<b>87160618</b>	<b>C/A</b>	<b>I</b>		<b>0.99</b>	<b>1.22</b>	<b>1.03□1.45</b>	<b>0.02</b>	<b>Y</b>
<i>ABCB1</i>	-	**rs1128503	7	87179601	G/A	I		1	1.13	0.95□1.34	0.16	N (high correlation with other

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<b>ABCB1</b>	-	<b>**rs1045642</b>	<b>7</b>	<b>87138645</b>	<b>A/G</b>	<b>G</b>		<b>0.83</b>	<b>0.70□0.98</b>	<b>0.03</b>	<b>N (high correlation with other SNP(s))</b>
ABCB1	-	rs9282564	7	87229440	T/C	G		1.15	0.87□1.51	0.33	Y
<b>ABCB1</b>	-	<b>rs3213619</b>	<b>7</b>	<b>87230193</b>	<b>A/G</b>	<b>I</b>	<b>0.99</b>	<b>0.47</b>	<b>0.28□0.79</b>	<b>0.004</b>	<b>Y</b>
ABCC1	-	rs2230671	16	16228242	G/A	I	0.91	1.02	0.83-1.25	0.86	Y
ABCC2	-	rs717620	10	101542578	C/T	G		1.00	0.81□1.23	0.97	Y
ABCC2	-	rs2273697	10	101563815	G/A	G		1.03	0.84□1.27	0.75	Y
<b>ABCC2</b>	-	<b>rs8187710</b>	<b>10</b>	<b>101611294</b>	<b>G/A</b>	<b>I</b>	<b>1</b>	<b>0.63</b>	<b>0.42□0.93</b>	<b>0.02</b>	<b>Y</b>
<b>ABCC2</b>	-	<b>**rs17222723</b>	<b>10</b>	<b>101595996</b>	<b>T/A</b>	<b>I</b>	<b>1</b>	<b>0.66</b>	<b>0.44□1.01</b>	<b>0.05</b>	<b>N (high correlation with other SNP(s))</b>
ABCG2	-	rs2231142	4	89052323	G/T	I	1	0.86	0.65□1.13	0.27	Y
<b>CYP1B1</b>	<b>*3</b>	<b>rs1056836</b>	<b>2</b>	<b>38298203</b>	<b>G/C</b>	<b>G</b>		<b>0.81</b>	<b>0.68□0.96</b>	<b>0.02</b>	<b>Y</b>
TP53	-	rs1042522	17	7579472	C/G	I	0.97	0.89	0.73□1.09	0.25	Y
GSTP1	-	rs947894 has merged into rs1695	11	67352689	A/G	I	0.93	1.10	0.91□1.34	0.32	Y
†GSTP1	-	rs1138272	11	67353579	C/T	I	0.88	1.29	0.91-1.83	0.16	Y
SLCO1B1	-	rs4149056	12	21331549	T/C	G		0.95	0.74□1.22	0.71	Y

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<i>SLCO1B3</i>	-	**rs4149117	12	21011480	G/T	I	1	0.98	0.76□1.26	0.85	N (high correlation with other SNP(s))
<i>SLCO1B3</i>	-	rs7311358	12	21015760	A/G	I	1	0.96	0.75□1.23	0.75	Y
<i>FANCD2</i>	-	**rs7648104	3	10073311	C/A	I	1	0.94	0.74□1.18	0.58	N (high correlation with other SNP(s))
<i>FANCD2</i>	-	**rs7637888	3	10080722	T/C	I	1	0.94	0.74□1.18	0.58	N (high correlation with other SNP(s))
<i>FANCD2</i>	-	rs6786638	3	10118075	G/C	I	1	0.94	0.75□1.18	0.59	Y
<i>FANCD2</i>	-	**rs6442150	3	10122575	T/C	I	1	0.94	0.74□1.18	0.58	N (high correlation with other SNP(s))
<i>EPHA5</i>	-	rs7349683	4	66197804	C/T	I	1	0.90	0.74□1.08	0.25	Y
<i>XKR4</i>	-	rs4737264	8	56111322	A/C	I	0.99	0.94	0.77□1.16	0.58	Y
<i>FGD4</i>	-	rs10771973	12	32792974	G/A	I	0.99	0.99	0.82□1.20	0.92	Y
<i>PITPNA</i>	-	rs16948748	17	1457839	T/G	I	0.96	1.33	0.87-2.03	0.19	Y
<i>CACNB2</i>	-	rs16916932	10	18476276	C/T	G		0.86	0.58□1.26	0.44	Y
<i>GRIP1/CAND1</i>	-	rs17781082	12	67476327	C/T	G		0.95	0.79□1.13	0.53	Y
<i>BCL6</i>	-	rs1903216	3	187629503	G/A	G		0.95	0.80□1.13	0.56	Y

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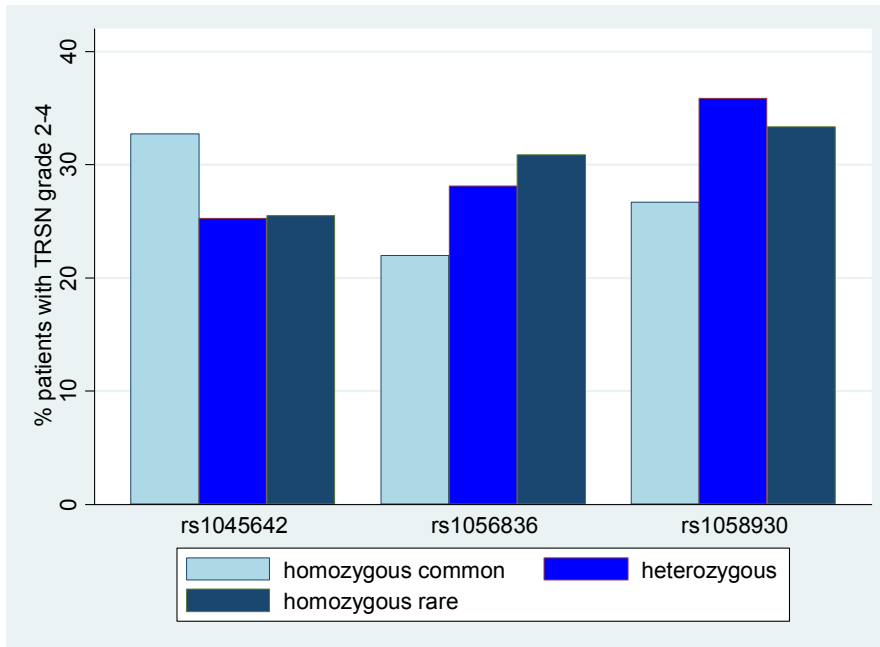
<i>NDRG1</i>	-	rs2233335	8	134261065	T/G	I	0.99	0.94	0.79□1.13	0.52	Y
<sup>§</sup> <i>FZD3</i>	-	rs7001034	8	28363378	G/A	I	0.99	1.04	0.88□1.24	0.63	N (high correlation with other SNP(s))
<sup>§</sup> <i>FZD3</i>	-	rs7833751	8	28362792	G/T	G		1.08	0.91□1.29	0.38	Y
<i>SHROOM</i>	-	rs5934683	X	9751474	C/T	I	1	0.95	0.78□1.14	0.56	Y
<i>ZFPM2</i>	-	rs2941627	8	106283030	A/G	I	0.97	1.16	0.87□1.53	0.31	Y
<i>BCAT1</i>	-	rs7973533	12	24917962	T/G	I	0.85	0.85	0.71□1.03	0.10	Y
<i>TUBB2A</i>	-	rs909965	6	3157809	T/C	I	0.66	1.09	0.87□1.38	0.45	N (high correlation with other SNP(s))
<b>**<i>TUBB2A</i></b>	-	rs909964	6	3157798	A/G	I	0.66	1.11	0.88□1.41	0.37	Y
<b><i>TUBB2A</i></b>	-	<b>rs9501929</b>	<b>6</b>	<b>3157854</b>	<b>T/C</b>	<b>I</b>	<b>0.96</b>	<b>1.80</b>	<b>1.20□2.72</b>	<b>0.005</b>	<b>Y</b>
<i>EPHA4</i>	-	rs17348202	2	222072178	T/C	I	0.93	1.11	0.74-1.67	0.62	Y
<i>LIMK2 (PLA2G3-PISD)**</i>	-	rs4141404	22	31675185	C/A	I	1	1.05	0.87-1.27	0.63	Y
<i>PAPD7</i>	-	rs275456	5	6813937	G/T	I	0.99	1.03	0.84-1.26	0.79	Y
<i>RP11-466L17.1</i>	-	rs1165472	1	56108604	A/G	I	1	0.95	0.78-1.15	0.58	Y
<i>CD9</i>	-	rs3181157	12	6308523	C/T	I	0.89	1.08	0.80-1.46	0.63	Y
<i>PSD3/NAT2</i>	-	rs10090117	8	18381235	T/C	I	1	1.11	0.89-1.38	0.34	Y
<i>TRIO</i>	-	rs10065203	5	14393621	C/T	I	0.85	1.10	0.89-1.34	0.38	Y
<i>ATPBD4/RP11-702M1.1</i>	-	rs2947253	15	36049492	A/G	I	0.87	1.12	0.84-1.50	0.44	Y

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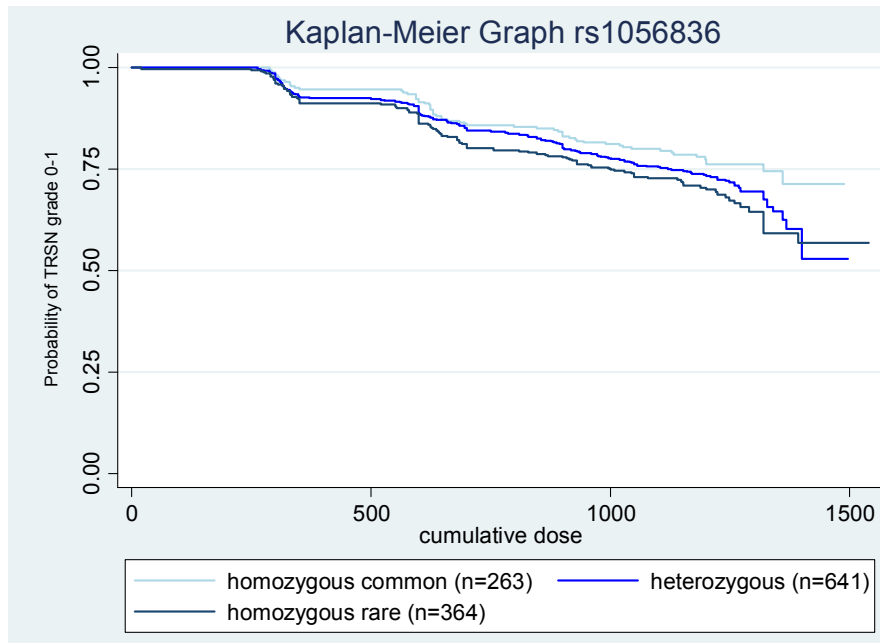
<i>ACTL7B</i>	-	rs10512385	9	111455575	A/G	G	1	1.27	0.97-1.68	0.09	Y
<i>AGMO1 DGKB</i>	-	rs12699683	7	15133127	G/T	G	1	0.95	0.69-1.30	0.73	Y
<i>GLIS3</i>	-	rs501461	9	4039727	T/G	I	0.99	0.90	0.75-1.07	0.24	Y
<i>PALLD</i>	-	rs6846708	4	169586731	A/G	I	0.98	0.95	0.70-1.30	0.75	Y
<i>PTPRT</i>	-	rs2425553 [in complete LD with rs2425556 and rs3092292]††	20	41670237	C/T	G	1	1.12	0.90-1.39	0.32	Y
<i>SGCG</i>	-	rs1753097	13	23878686	A/G	I	1	0.97	0.77-1.21	0.78	Y
<b><i>KIAA0146-PRKD§§</i></b>	-	<b>rs6473187</b>	<b>8</b>	<b>48483958</b>	<b>A/G</b>	<b>I</b>	<b>0.91</b>	<b>1.48</b>	<b>1.01-2.17</b>	<b>0.04</b>	<b>Y</b>
<i>PAPD7</i>	-	rs13163920	5	6759714	C/T	I	0.95	0.96	0.78-1.17	0.65	Y
<i>ERBB4</i>	-	rs10932374	2	212244403	G/A	G	1	1.02	0.83-1.24	0.87	Y
<b><i>SLCO1B1¶¶</i></b>	-	<b>rs3829306</b>	<b>12</b>	<b>21292280</b>	<b>C/T</b>	<b>I</b>	<b>0.99</b>	<b>0.66</b>	<b>0.44-1.01</b>	<b>0.05</b>	<b>Y</b>
<i>C19orf21</i>	-	rs8110536	19	756985	T/G	I	0.37	1.45	0.98-2.14	0.06	Y
<i>LPP</i>	-	rs189372	3	187839070	C/T	G	1	1.02	0.85-1.23	0.81	Y
<i>HAND2</i>	-	rs7655560	4	174438897	G/A	I	0.81	1.13	0.73-1.75	0.58	Y
<i>PARK2</i>	-	rs9365397	6	162702534	T/C	I	0.99	1.15	0.70-1.88	0.59	Y
<b><i>EPHA6</i></b>	-	<b>rs301927</b>	<b>3</b>	<b>97346618</b>	<b>A/G</b>	<b>I</b>	<b>0.99</b>	<b>1.35</b>	<b>1.07-1.70</b>	<b>0.01</b>	<b>Y</b>
<i>LIMK2</i>	-	rs2413045	22	31665862	G/A	I	0.95	1.15	0.92-1.42	0.22	N (high correlation with other SNP(s))
<i>TYW3ILHX8</i>	-	rs12743802	1	75458806	G/A	I	0.76	0.97	0.55-1.69	0.91	Y

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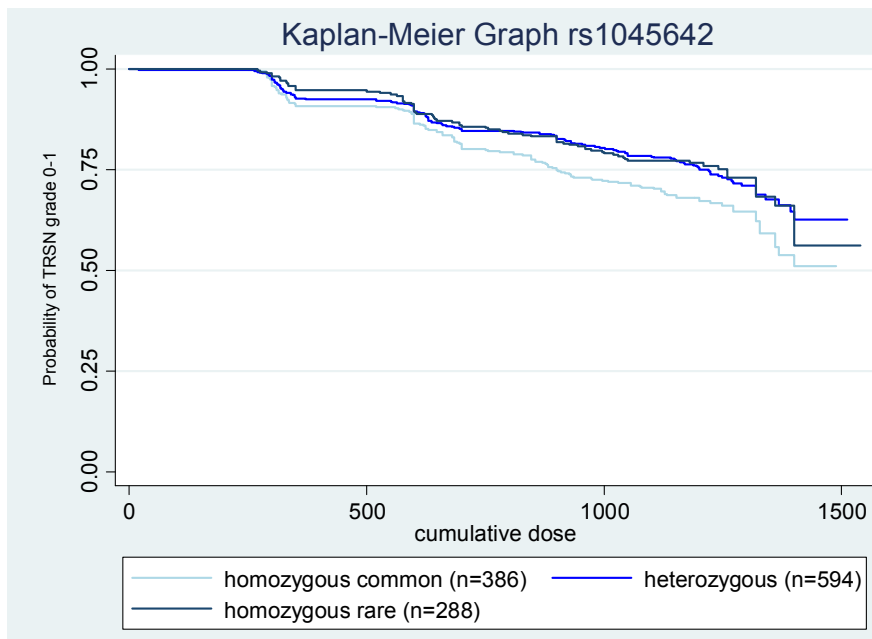
**Supplementary Figure 1: Percentage of Patients with TRSN  $\geq$  grade 2 by genotype, for each of the three statistically significant SNPs that were genotyped in PGSNPS (maximum TRSN)**



Supplementary Figure 2a: Kaplan-Meier curves for rs1056836



Supplementary Figure 2b: Kaplan-Meier curves for rs1045642



**Supplementary Figure 2c: Kaplan-Meier curves for rs1058930**

