Supplementary Material to:

Renal and extra-renal phenotypes in patients with *HNF1B* variants and chromosome 17q12 micro deletions

Buffin-Meyer and Richard et al.,

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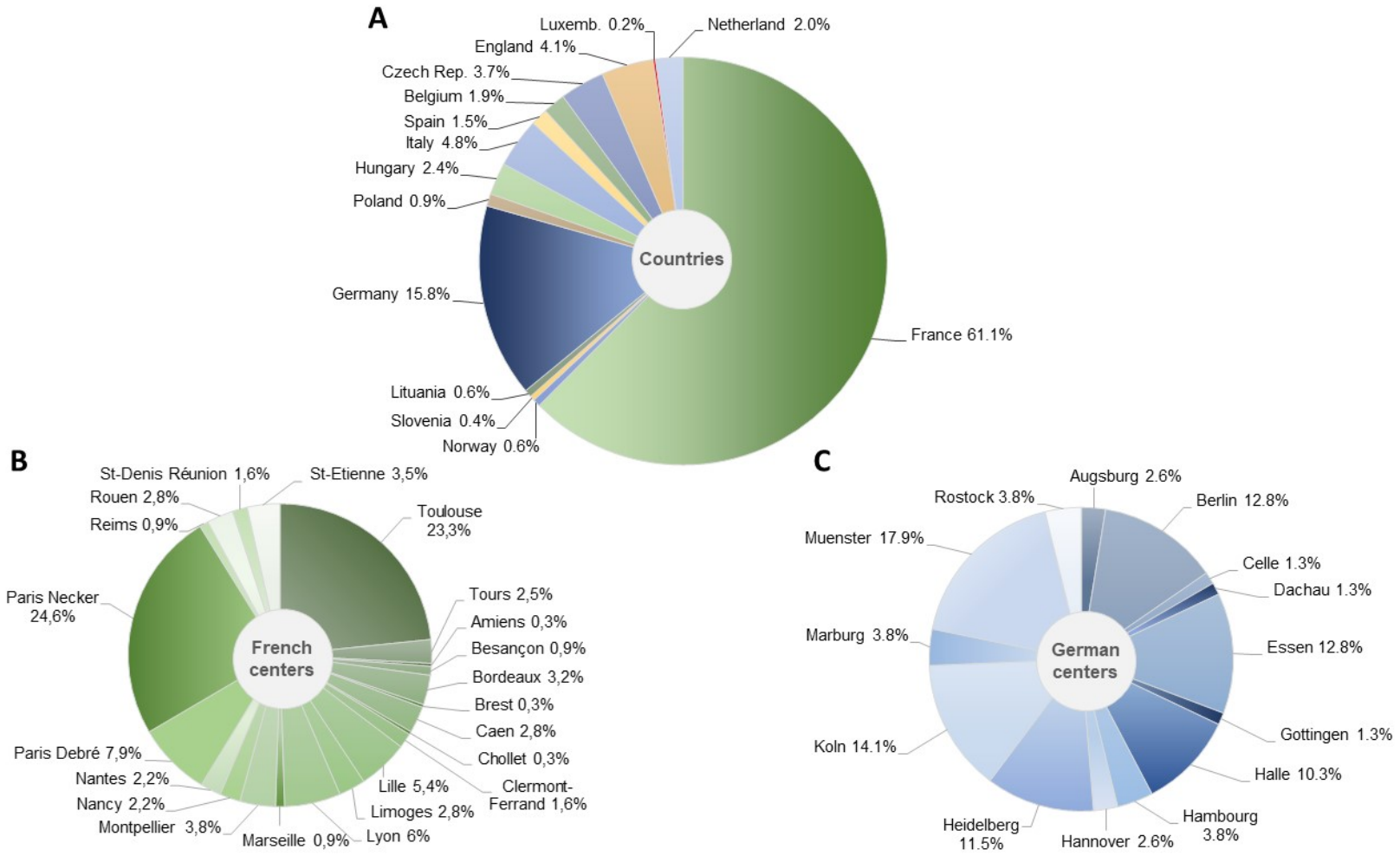
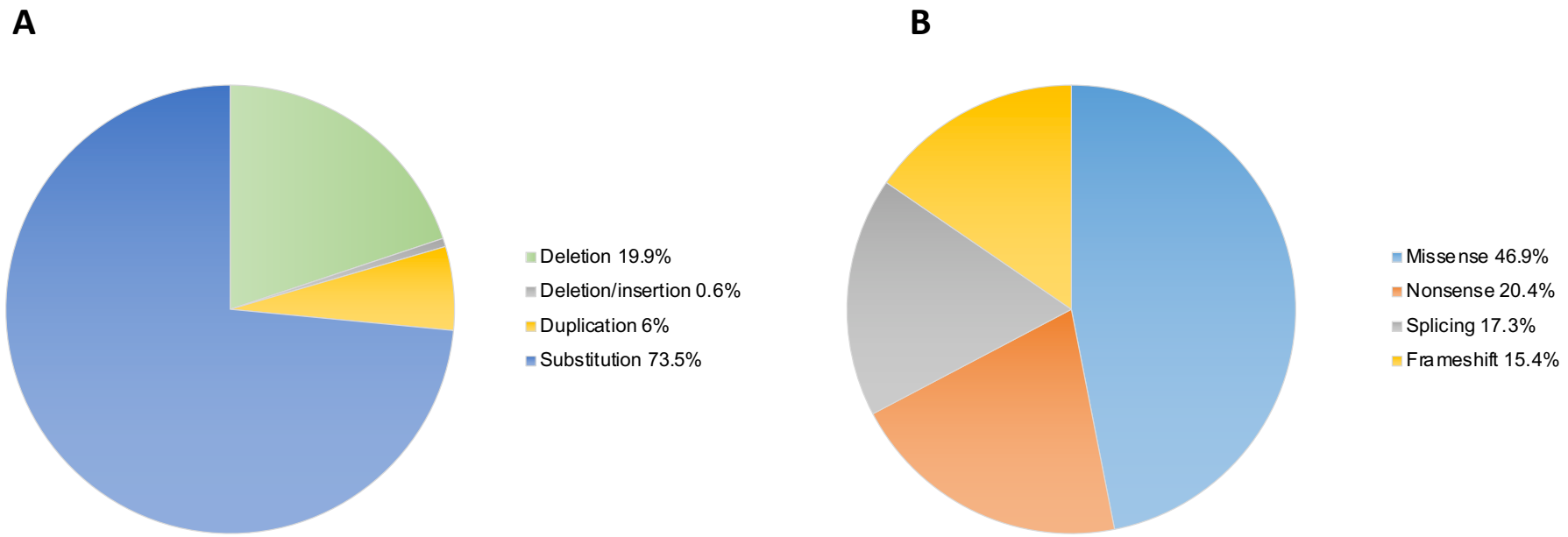
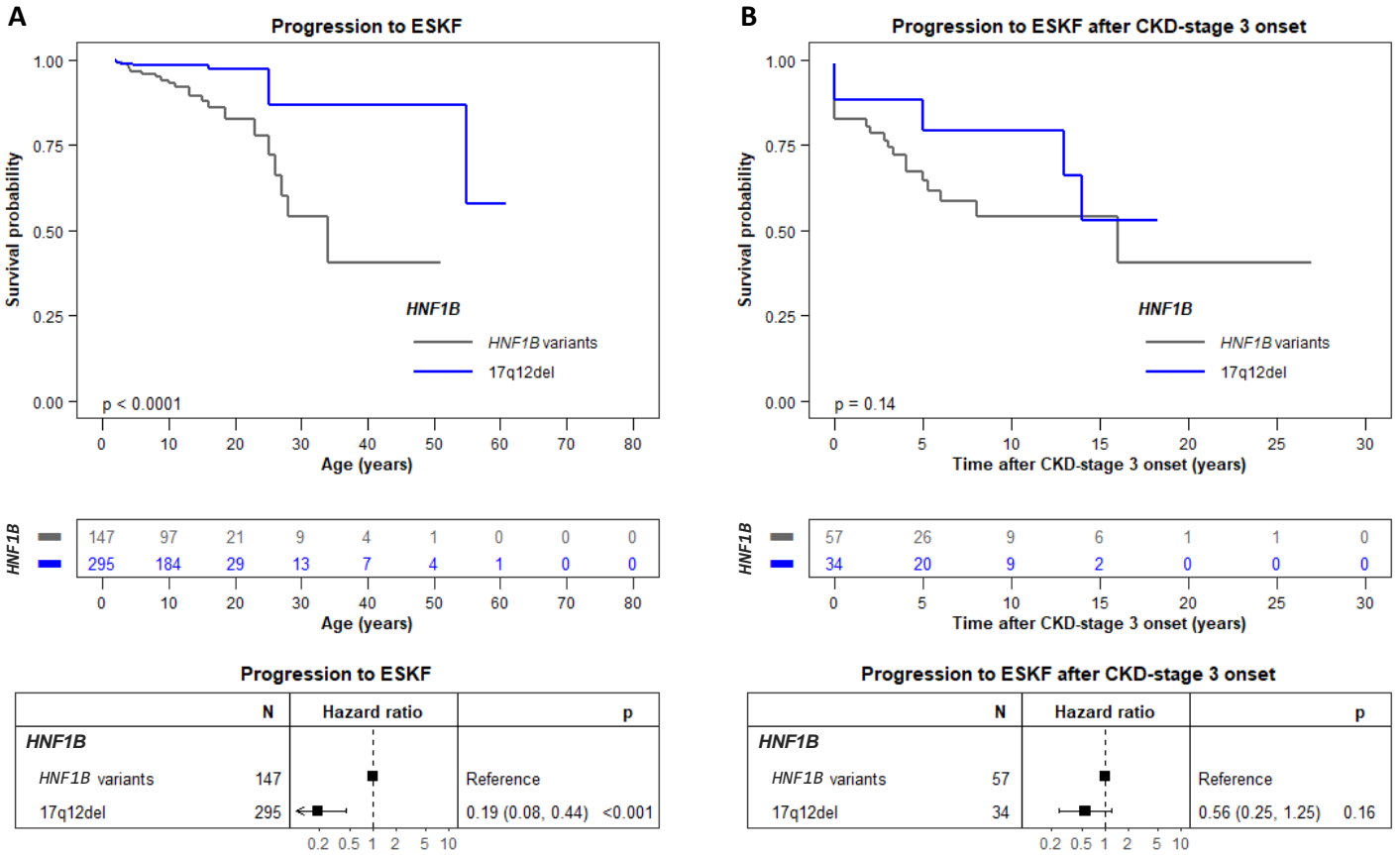
2. Supplementary figures



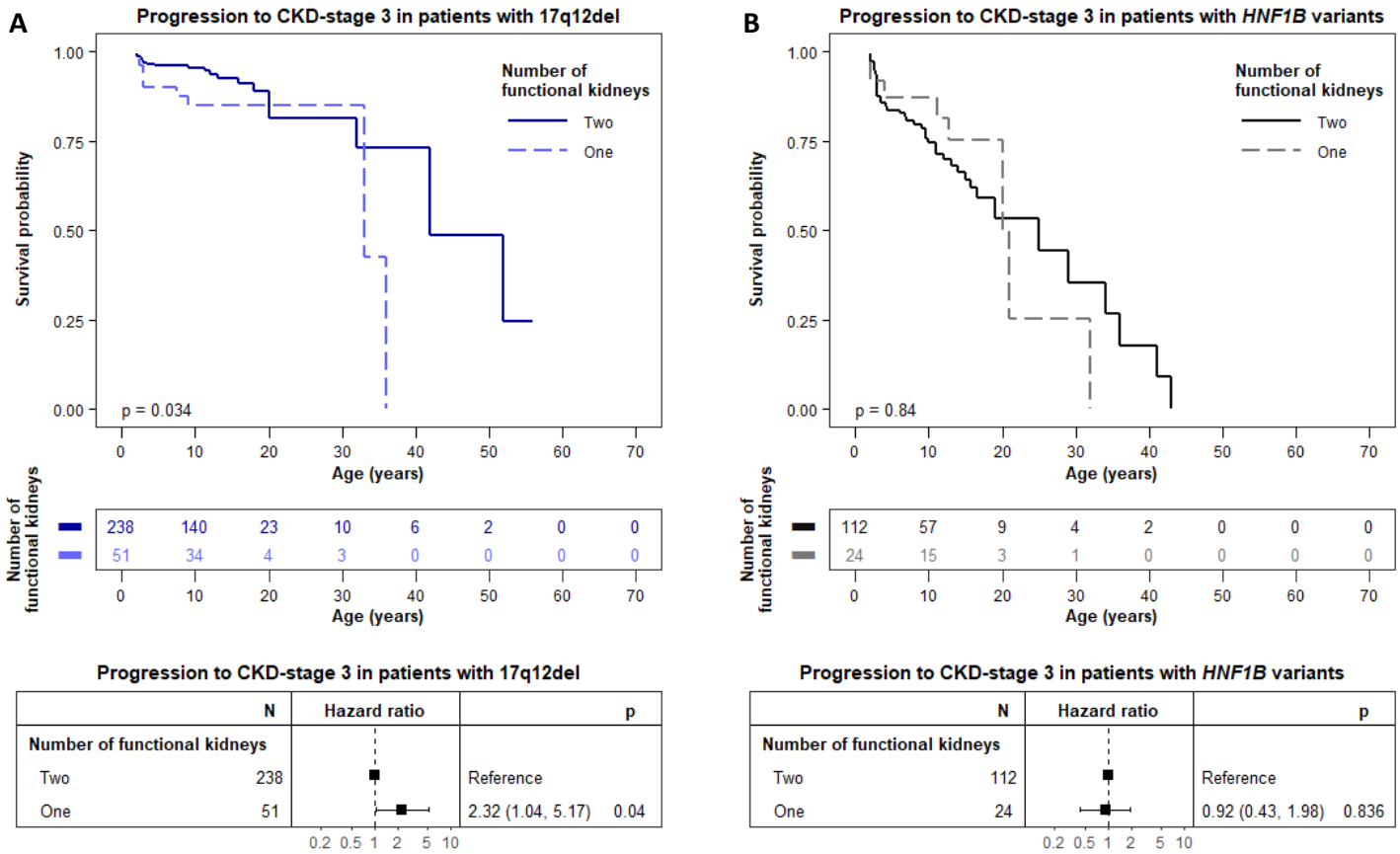
Supplementary Figure S1: An international multicenter study. A) 14 European countries participated in the study. A total of **B)** 22 centers from France and **C)** 14 centers from Germany, the two major participating countries, were involved.



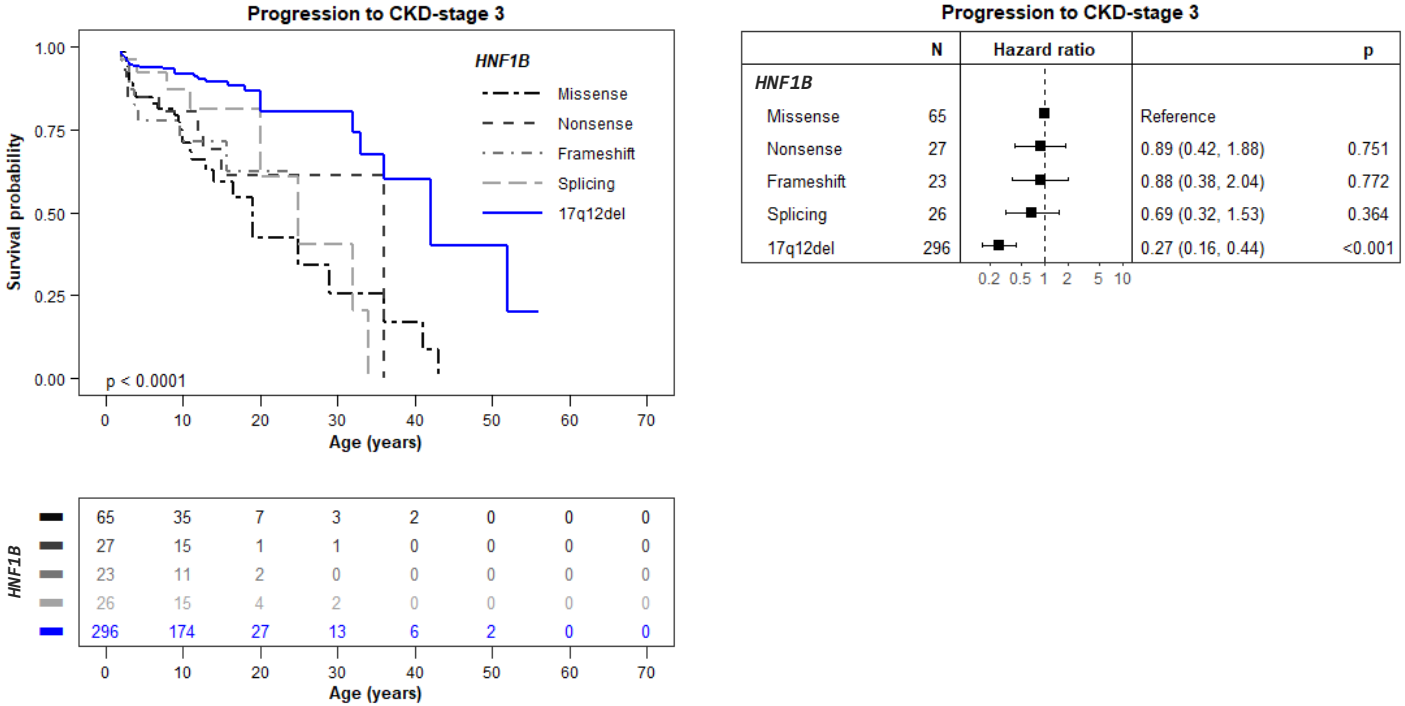
Supplementary Figure S2: Distribution of *HNF1B* variants other than the 17q12del. A) Nature of variants and **B)** Resulting variants.



Supplementary Figure S3: Progression to ESKF of patients with *HNF1B* disease. A) Progression to ESKF is significantly delayed in patients with the 17q12del compared to patients with *HNF1B* variants. **B)** Progression to ESKF after developing CKD is not different between the 62 patients with *HNF1B* variants and 33 patients with the 17q12del. The survival curves were generated using data from children ≥ 2 years of age to dismiss changes in eGFR evolution in early life. The point in time of progression to ESKF was entered as the chronological age of each patient. We considered that patients entered the study (baseline) at birth given the fact the *HNF1B* disease is a congenital nephropathy. In **A)** The log rank test for difference in survival yielded a p-value of p<0.0001 indicating that the patients with 17q12del and *HNF1B* variants differed significantly in progression towards ESKF.



Supplementary Figure S4: Impact of one or two functional kidneys in patients with *HNF1B* disease on progression to CKD-stage 3. A) Kidney survival of patients with the 17q12del is worse in patients with one functional kidney. **B)** Kidney survival of patients with *HNF1B* variants is similar irrespective of the number of functional kidneys. The survival curves were generated using data from children ≥ 2 years of age to dismiss changes in eGFR in early life. The point in time of progression to CKD-stage 3 (eGFR < 60 mL/min/1.73m^2) was entered as the chronological age of each patient. We considered that patients entered the study (baseline) at birth given the fact the *HNF1B* disease is a congenital nephropathy. In **A)** The log rank test for difference in survival yielded a p-value of p = 0.034 indicating that the patients with 17q12del with one functional kidney differed significantly in progression towards CKD-stage 3.



Supplementary Figure S5: Impact of the nature of the change at the HNF1B **protein level on progression to CKD-stage 3.** Kidney survival of patients is not different between missense, nonsense, splicing or frameshift *HNF1B* variants. The survival curves were generated using data from children >2 years of age to dismiss changes in eGFR in early life. The point in time of progression to CKD-stage 3 (eGFR < 60 mL/min/1.73m^2) was entered as the chronological age of each patient. We considered that patients entered the study (baseline) at birth given the fact the *HNF1B* disease is a congenital nephropathy.

3. Supplementary tables

Supplementary Table S1: Characteristics of *HNF1B* gene variants.

Supplementary Table S2: Follow-up data of patients with *HNF1B* disease.

Supplementary Table S1: Characteristics of *HNF1B* variants

Patient	cVariant	Position	pVariant	Allele frequency[1]	Mutation	Mutation consequence	Pathogenicity_ClinVar[2]	Pathogenicity_LOVD[3]	Pathogenicity_Leipzig_University[4]	Mutation pathogenicity
1	Exon 1-2 deletion	Exon 1			Deletion		NA	NA	NA	VUS
2	c.3G>A	Exon 1	p.Met1Ile		Substitution	Missense (non-start)	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
3	c.3G>A	Exon 1	p.Met1Ile		Substitution	Missense (non-start)	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
4	c.143del	Exon 1	p.Leu48fs		Deletion	Frameshift	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
5	c.143del	Exon 1	p.Leu48fs		Deletion	Frameshift	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
6	c.156del	Exon 1	p.Ser52fs		Deletion	Frameshift	NA	Pathogenic	NA	Pathogenic
7	c.212_218del	Exon 1	p.Lys71fs		Deletion	Frameshift	NA	Pathogenic	NA	Pathogenic
8	c.232G>T	Exon 1	p.Glu78Ter	6.85e-7	Substitution	Nonsense	Pathogenic	Pathogenic	Pathogenic	Pathogenic
9	c.301G>A	Exon 1	p.Glu101Lys		Substitution	Missense	NA	NA	NA	VUS
10	c.313G>A	Exon 1	p.Glu105Lys	6.35e-5	Substitution	Missense	Likely benign/VUS	Effect unknown/Likely pathogenic	VUS	VUS
11		Exon 1	p.Glu109fs		Deletion	Frameshift	NA	Pathogenic	Likely pathogenic	Pathogenic
12	c.341T>C	Exon 1	p.Leu114Pro		Substitution	Missense	NA	NA	NA	VUS
13	c.344G>A	Exon 1	p.Ser115Asn		Substitution	Missense	VUS/Likely pathogenic	Likely pathogenic	NA	VUS
14	c.344+2	Intron 1				Splicing	NA	NA	NA	VUS
15	c.345-1G>A	Intron 1			Substitution	Splicing	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
16	c.345-1G>A	Intron 1			Substitution	Splicing	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
17	c.372G>T	Exon 2	p.Met124Ile		Substitution	Missense	Likely pathogenic	Likely pathogenic	NA	Pathogenic
18	c.374T>C	Exon 2	p.Ile125Thr		Substitution	Missense	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
19	c.406C>G	Exon 2	p.Gln136Glu		Substitution	Missense	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
20	c.412G>A	Exon 2	p.Glu138Lys		Substitution	Missense	NA	Likely pathogenic	Likely pathogenic	Pathogenic
21	c.412G>A	Exon 2	p.Glu138Lys		Substitution	Missense	NA	Likely pathogenic	Likely pathogenic	Pathogenic
22	c.412G>A	Exon 2	p.Glu138Lys		Substitution	Missense	NA	Likely pathogenic	Likely pathogenic	Pathogenic
23	c.443C>T	Exon 2	p.Ser148Leu		Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
24	c.443C>T	Exon 2	p.Ser148Leu		Substitution	Missense	NA	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
25	c.443C>T	Exon 2	p.Ser148Leu		Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
26	c.443C>G	Exon 2	p.Ser148Trp		Substitution	Missense	Pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
27	c.443C>G	Exon 2	p.Ser148Trp		Substitution	Missense	Pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
28	c.443C>T	Exon 2	p.Ser148Leu		Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
29		Exon 2	p.Ser148Leu		Substitution	Missense	NA	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
30	c.451T>C	Exon 2	p.Ser151Pro		Substitution	Missense	Likely pathogenic	Likely pathogenic	Likely pathogenic	Pathogenic
31	c.452C>G	Exon 2	p.Ser151Cys		Substitution	Missense	Likely pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
32	c.460C>T	Exon 2	p.Leu154Phe		Substitution	Missense	Likely pathogenic	Likely pathogenic	NA	Pathogenic
33	c.476del	Exon 2	p.Pro159fs		Deletion	Frameshift	NA	NA	NA	VUS
34	c.479T>G	Exon 2	p.Met160Arg		Substitution	Missense	VUS	NA	NA	VUS
35	c.487del	Exon 2	p.Gln163fs		Deletion	Frameshift	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
36		Exon 2	p.Arg165His		Substitution	Missense	NA	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
37	c.494G>C	Exon 2	p.Arg165Pro		Substitution	Missense	Likely pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
38	c.494G>A	Exon 2	p.Arg165His		Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
39	c.494G>A	Exon 2	p.Arg165His		Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
40		Exon 2	p.Arg165His		Substitution	Missense	NA	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
41	c.494G>A	Exon 2	p.Arg165His		Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
42	c.494G>A	Exon 2	p.Arg165His		Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
43	c.494G>A	Exon 2	p.Arg165His		Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
44	c.511T>C	Exon 2	p.Trp171Arg		Substitution	Missense	Likely pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
45	c.512G>A	Exon 2	p.Trp171Ter		Substitution	Nonsense	NA	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
46	c.512G>A	Exon 2	p.Trp171Ter		Substitution	Nonsense	NA	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
47	c.513G>A	Exon 2	p.Trp171Ter		Substitution	Nonsense	Pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
48	c.513G>A	Exon 2	p.Trp171Ter		Substitution	Nonsense	Pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
49		Exon 2	p.Tyr172Ter		Substitution	Nonsense	NA	NA	NA	Pathogenic
50		Exon 2	p.Gln174Glu		Substitution	Missense	NA	NA	NA	VUS
51		Exon 2	p.Lys175Ter		Substitution	Nonsense	NA	NA	Likely pathogenic	VUS
52	c.526C>T	Exon 2	p.Gln176Ter		Substitution	Nonsense	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic	Pathogenic
53	c.529C>T	Exon 2	p.Arg177Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Pathogenic	Pathogenic
54	c.529C>T	Exon 2	p.Arg177Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Pathogenic	Pathogenic
55	c.529C>T	Exon 2	p.Arg177Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Pathogenic	Pathogenic
56	c.541C>T	Exon 2	p.Arg181Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Pathogenic	Pathogenic
57	c.541C>T	Exon 2	p.Arg181Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Pathogenic	Pathogenic
58	c.541C>T	Exon 2	p.Arg181Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Pathogenic	Pathogenic
59	c.544C>T	Exon 2	p.Gln182Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Pathogenic	Pathogenic
60	c.544C>T	Exon 2	p.Gln182Ter		Substitution	Nonsense	NA	Pathogenic	Pathogenic	Pathogenic

61	c.544C>T	Exon 2	p.Gln182Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Pathogenic	Pathogenic
62	c.544C>T	Exon 2	p.Gln182Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Pathogenic	Pathogenic
63	c.544C>T	Exon 2	p.Gln182Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Pathogenic	Pathogenic
64	c.544C>T	Exon 2	p.Gln182Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Pathogenic	Pathogenic
65	c.544C>T	Exon 2	p.Gln182Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Pathogenic	Pathogenic
66	c.IVS2+1_4del	Intron 2			Deletion	Splicing	NA	NA	NA	VUS
67	c.544+1G>C	Intron 2			Substitution	Splicing	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
68	c.544+1G>A	Intron 2			Substitution	Splicing	Pathogenic	Pathogenic	Pathogenic	Pathogenic
69	c.544+1G>T	Intron 2			Substitution	Splicing	Pathogenic	Pathogenic	Pathogenic	Pathogenic
70	c.544+1G>T	Intron 2			Substitution	Splicing	Pathogenic	Pathogenic	Pathogenic	Pathogenic
71	c.544+1G>C	Intron 2			Substitution	Splicing	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
72	c.544+2	Intron 2				Splicing	NA	NA	NA	VUS
73	c.544+2dup	Intron 2			Duplication	Splicing	Pathogenic	Pathogenic	Pathogenic	Pathogenic
74	c.544+3_544+6del	Intron 2			Deletion	Splicing	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
75	c.544+3_544+11delins	Intron 2			Deletion/insertion	Splicing	NA	NA	NA	VUS
76	c.544+3_544+6del	Intron 2			Deletion	Splicing	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
77	c.544+3_544+6del	Intron 2			Deletion	Splicing	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
78	c.544+3_544+6del	Intron 2			Deletion	Splicing	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
79	c.544+3_544+6del	Intron 2			Deletion	Splicing	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
80	c.544+3_544+6del	Intron 2			Deletion	Splicing	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
81	c.544+3_544+6del	Intron 2			Deletion	Splicing	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
82	c.544+3_544+6del	Intron 2			Deletion	Splicing	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
83	c.544+3_544+6del	Intron 2			Deletion	Splicing	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
84	Exon 3-8 duplication	Exon 3			Duplication		NA	NA	NA	VUS
85	Exon 3-8 duplication	Exon 3			Duplication		NA	NA	NA	VUS
86	c.605del	Exon 3	p.Leu202fs		Deletion	Frameshift	NA	Pathogenic	NA	Pathogenic
87	c.628del	Exon 3	p.Ser210fs		Deletion	Frameshift	Pathogenic	Pathogenic	NA	Pathogenic
88	c.694C>T	Exon 3	p.Arg232Cys	1.37e-6	Substitution	Missense	NA	NA	VUS	VUS
89	c.704G>A	Exon 3	p.Arg235Gln	3.18e-6	Substitution	Missense	VUS/Likely pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	VUS
90	c.708C>G	Exon 3	p.Phe236Leu		Substitution	Missense	NA	Likely pathogenic	NA	VUS
91	c.708C>G	Exon 3	p.Phe236Leu		Substitution	Missense	NA	Likely pathogenic	NA	VUS
92	c.713G>T	Exon 3	p.Trp238Leu		Substitution	Missense	NA	NA	VUS	VUS
93	c.717del	Exon 3	p.Ala241fs		Deletion	Frameshift	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
94	c.719_720dup	Exon 3	p.Ala241fs		Duplication	Frameshift	Likely pathogenic/Pathogenic	Pathogenic	NA	Pathogenic
95	c.721G>A	Exon 3	p.Ala241Thr	7.43e-6	Substitution	Missense	VUS	VUS	VUS	VUS
96	c.721G>A	Exon 3	p.Ala241Thr	7.43e-6	Substitution	Missense	VUS	VUS	VUS	VUS
97	c.727C>T	Exon 3	p.Gln243Ter		Substitution	Nonsense	NA	NA	NA	VUS
98	c.738G>T	Exon 3	p.Leu246Phe		Substitution	Missense	VUS	Likely pathogenic	NA	VUS
99	c.738G>T	Exon 3	p.Leu246Phe		Substitution	Missense	VUS	Likely pathogenic	NA	VUS
100		Exon 3	p.Gln253Pro		Substitution	Missense	NA	Likely pathogenic	VUS	VUS
101	c.781A>G	Exon 3	p.Arg261Gly		Substitution	Missense	VUS/Likely pathogenic	Likely pathogenic	VUS	VUS
102	c.809G>A	Exon 3	p.Arg270Lys		Substitution	Missense	NA	NA	NA	VUS
103	c.809G>C	Exon 3	p.Arg270Thr		Substitution	Missense	NA	NA	NA	VUS
104	c.809+1G>A	Intron 3			Substitution	Splicing	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
105	c.809+1G>A	Intron 3			Substitution	Splicing	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
106	Exon 4 deletion	Exon 4			Deletion		NA	NA	NA	VUS
107	Exon 4 deletion	Exon 4			Deletion	Frameshift	NA	NA	NA	VUS
108	c.826C>T	Exon 4	p.Arg276Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Pathogenic	Pathogenic
109	c.826C>T	Exon 4	p.Arg276Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Pathogenic	Pathogenic
110		Exon 4	p.Arg276Ter		Substitution	Nonsense	NA	Pathogenic	Pathogenic	Pathogenic
111	c.827G>A	Exon 4	p.Arg276Gln		Substitution	Missense	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic	Pathogenic
112	c.827G>A	Exon 4	p.Arg276Gln		Substitution	Missense	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic	Pathogenic
113	c.827G>A	Exon 4	p.Arg276Gln		Substitution	Missense	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic	Pathogenic
114	c.850del	Exon 4	p.His284fs		Deletion	Frameshift	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
115	c.850del	Exon 4	p.His284fs		Deletion	Frameshift	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
116	c.854G>A	Exon 4	p.Gly285Asp		Substitution	Missense	Pathogenic	Likely pathogenic/Pathogenic	Likely pathogenic	Pathogenic
117	c.856C>G	Exon 4	p.Leu286Val		Substitution	Missense	Likely pathogenic	Likely pathogenic	NA	Pathogenic
118	c.883C>T	Exon 4	p.Arg295Cys	1.20e-6	Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
119	c.883C>T	Exon 4	p.Arg295Cys	1.20e-6	Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
120	c.883C>T	Exon 4	p.Arg295Cys	1.20e-6	Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic

121	c.883C>T	Exon 4	p.Arg295Cys	1.20e-6	Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
122	c.883C>T	Exon 4	p.Arg295Cys	1.20e-6	Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
123	c.883C>T	Exon 4	p.Arg295Cys	1.20e-6	Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
124	c.883C>T	Exon 4	p.Arg295Cys	1.20e-6	Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
125	c.883C>T	Exon 4	p.Arg295Cys	1.20e-6	Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
126	c.883C>T	Exon 4	p.Arg295Cys	1.20e-6	Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
127	c.883C>T	Exon 4	p.Arg295Cys	1.20e-6	Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
128	c.883C>T	Exon 4	p.Arg295Cys	1.20e-6	Substitution	Missense	Likely pathogenic/Pathogenic	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic
129	c.895T>G	Exon 4	p.Trp299Gly		Substitution	Missense	Likely pathogenic	Likely pathogenic	VUS	Pathogenic
130	c.904A>G	Exon 4	p.Asn302Asp		Substitution	Missense	Likely pathogenic	Likely pathogenic	NA	Pathogenic
131	c.906C>A	Exon 4	p.Asn302Lys		Substitution	Missense	Likely pathogenic	Likely pathogenic	VUS	Pathogenic
132	c.907G>T	Exon 4	p.Arg303Cys		Substitution	Missense	NA	Likely pathogenic	NA	VUS
133	c.929G>A	Exon 4	p.Arg310Gln	3.42e-6	Substitution	Missense	NA	VUS	NA	VUS
134	c.949del	Exon 4	p.Ala317fs		Deletion	Frameshift	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
135	c.953dup	Exon 4	p.Tyr318Ter		Duplication	Nonsense	Pathogenic	Pathogenic	NA	Pathogenic
136	c.964del	Exon 4	p.Gln322fs		Deletion	Frameshift	NA	NA	NA	VUS
137	c.964del	Exon 4	p.Gln322fs		Deletion	Frameshift	NA	NA	NA	VUS
138	c.1006dup	Exon 4	p.His336fs		Duplication	Frameshift	Likely pathogenic/Pathogenic	Pathogenic	Pathogenic	Pathogenic
139	c.1037A>G	Exon 4	p.Lys346Arg		Substitution	Missense	NA	NA	NA	VUS
140	c.1037A>G	Exon 4	p.Lys346Arg		Substitution	Missense	NA	NA	NA	VUS
141	c.1046-2A>C	Intron 4			Substitution	Splicing	NA	NA	NA	VUS
142	c.1046-2A>G	Intron 4			Substitution	Splicing	Pathogenic	Likely pathogenic/Pathogenic	VUS	VUS
143	Exon 5 duplication	Exon 5			Duplication		NA	NA	NA	VUS
144	Exon 5 duplication	Exon 5			Duplication		NA	NA	NA	VUS
145	c.1099A>G	Exon 5	p.Ser367Gly	1.86e-5	Substitution	Missense	NA	NA	VUS	VUS
146	c.1136C>A	Exon 5	p.Ser379Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
147	c.1207-1G>T	Intron 5			Substitution	Splicing	NA	NA	NA	VUS
148	Exon 6 deletion	Exon 6			Deletion	Frameshift	NA	NA	NA	VUS
149	c.1211_1212del	Exon 6	p.Ser404fs		Deletion	Frameshift	NA	NA	Likely pathogenic	VUS
150	c.1253A>T	Exon 6	p.Asn418Ile		Substitution	Missense	Likely pathogenic	Likely pathogenic	NA	Pathogenic
151	c.1310C>T	Exon 6	p.Pro437Leu		Substitution	Missense	Likely pathogenic	Likely pathogenic	NA	Pathogenic
152	c.1310C>T	Exon 6	p.Pro437Leu		Substitution	Missense	Likely pathogenic	Likely pathogenic	NA	Pathogenic
153	c.1326G>A	Exon 6	p.Met442Ile	1.59e-6	Substitution	Missense	NA	NA	NA	VUS
154	c.1340-1G>A	Intron 6			Substitution	Splicing	NA	NA	Likely pathogenic	VUS
155	c.1340-1G>A	Intron 6			Substitution	Splicing	NA	NA	Likely pathogenic	VUS
156	c.1360_1361del	Exon 7	p.Gln454fs		Deletion	Frameshift	Pathogenic	Pathogenic	NA	Pathogenic
157		Exon 7	p.Gln454Ter		Substitution	Nonsense	NA	Pathogenic	Likely pathogenic	Pathogenic
158	c.1363_1364del	Exon 7	p.Ser455fs		Deletion	Frameshift	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
159	c.1363_1364del	Exon 7	p.Ser455fs		Deletion	Frameshift	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
160	c.1398_1405dup	Exon 7	p.Leu469fs		Duplication	Frameshift	NA	NA	NA	VUS
161	c.1399_1414dup	Exon 7	p.Val472fs		Duplication	Frameshift	NA	Pathogenic	NA	Pathogenic
162	c.1408C>T	Exon 7	p.Gln470Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
163	c.1408C>T	Exon 7	p.Gln470Ter		Substitution	Nonsense	Pathogenic	Pathogenic	Likely pathogenic	Pathogenic
164	c.1489C>T	Exon 7	p.Gln497Ter		Substitution	Nonsense	NA	Pathogenic	NA	Pathogenic
165	c.1492C>T	Exon 7	p.Gln498Ter		Substitution	Nonsense	NA	NA	Pathogenic	Pathogenic
166	c.1538A>G	Exon 8	p.Tyr513Cys	1.20e-6	Substitution	Missense	Likely pathogenic	Likely pathogenic	NA	Pathogenic
167	c.1561C>T	Exon 8	p.Gln521Ter		Substitution	Nonsense	Likely pathogenic/Pathogenic	Pathogenic	NA	Pathogenic
168	c.1610C>A	Exon 8	p.Thr537Asn		Substitution	Missense	VUS	VUS	NA	VUS
169	c.182T>G	Exon 1	p.Val61Gly	3.48e-4	Substitution	Missense	Benign/Likely benign/VUS	Likely benign/VUS	Likely benign	Benign
170	c.182T>G	Exon 1	p.Val61Gly	3.48e-4	Substitution	Missense	Benign/Likely benign/VUS	Likely benign/VUS	Likely benign	Benign
171	c.182T>G	Exon 1	p.Val61Gly	3.48e-4	Substitution	Missense	Benign/Likely benign/VUS	Likely benign/VUS	Likely benign	Benign
172		Exon 1	p.Val61Gly		Substitution	Missense	NA	Likely benign/VUS	Likely benign	Benign
173		Exon 1	p.Gly76Cys		Substitution	Missense	Benign/Likely benign/VUS	Benign/Likely benign/VUS	VUS	Benign
174		Exon 1	p.Gly76Cys		Substitution	Missense	Benign/Likely benign/VUS	Benign/Likely benign/VUS	VUS	Benign
175	c.226G>T	Exon 1	p.Gly76Cys	3.99e-4	Substitution	Missense	Likely benign/VUS	Benign/Likely benign/VUS	VUS	Benign
176	c.226G>T	Exon 1	p.Gly76Cys	3.99e-4	Substitution	Missense	Likely benign/VUS	Benign/Likely benign/VUS	VUS	Benign
177		Exon 1	p.Gly76Cys		Substitution	Missense	Benign/Likely benign/VUS	Benign/Likely benign/VUS	VUS	Benign
178	c.244G>A	Exon 1	p.Asp82Asn	9.36e-4	Substitution	Missense	Benign/Likely benign/VUS	Likely benign/VUS	VUS	Benign
179	c.244G>A	Exon 1	p.Asp82Asn	9.36e-4	Substitution	Missense	Benign/Likely benign/VUS	Likely benign/VUS	VUS	Benign
180	c.684C>G	Exon 3	p.Asn228Lys	4.55e-4	Substitution	Missense	Benign/Likely benign	Likely benign	Likely benign	Benign
181		Exon 4	p.His336Asp		Substitution	Missense	NA	VUS	VUS	Benign

[1]https://gnomad.broadinstitute.org/gene/ENSG00000275410?dataset=gnomad_r4 (db accessed April 04, 2024)

[2]https://www.ncbi.nlm.nih.gov/clinvar (db accessed July 11, 2023)

[3]https://databases.lovd.nl/shared/variants/HNF1B#object_id=VariantOnTranscript%2CVariantOnGenome&id=HNF1B&order=VariantOnTranscript%2FDNA%2CASC&search_transcriptid=00009498&search_VariantOnTranscript/DNA=c.738G%3ET&page_size=100&page=1 (db accessed November 15, 2023)

[4]https://hnf1b.uni-leipzig.de/ (db accessed July 11, 2023) and Vasileiou G & al, Prenat Diagn. 2019 Nov;39(12):1136-1147

NA: not available; VUS: variant of uncertain significance

Patients highlighted in grey are those with a benign *HNF1B* variant; they were excluded from the analysis.

Supplementary Table S2: Follow-up data of patients with *HNF1B* disease.

			HNF1B			
	N		***HNF1B* variants**	**17q12del**	**p.value[3]**	**q.value[4]**
All	508		168	340		
Number of visits	508	6 (4-9)	6 (3-9)	6 (4-8)	0.976	0.976
Duration of follow-up (y)	500	11 (7-17)[1]	12 (8-17)	11 (6-16)	0.143	0.166
Progression to CKD-stage 3	473	99 (21%)[2]	61 (39%)	38 (12%)	<0.001	<0.001
Progression to ESKF	472	37 (7.8%)	26 (16%)	11 (3.5%)	<0.001	<0.001
Hypomagnesemia	437	127 (29%)	27 (19%)	100 (34%)	0.002	0.005
Hyperuricemia	433	283 (65%)	106 (74%)	177 (61%)	0.011	0.019
Hyperglycemia	486	60 (12%)	26 (16%)	34 (10%)	0.067	0.094

[1]Median (25%-75%); [2]n (%); [3]Wilcoxon rank sum test; Pearson's Chi-squared test; [4]False discovery rate correction for multiple testing

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	11, Fig 1
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8-10
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	8,11
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n.a.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-10
Bias	9	Describe any efforts to address potential sources of bias	8-10
Study size	10	Explain how the study size was arrived at	n.a.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-10
		(*b*) Describe any methods used to examine subgroups and interactions	9-10
		(*c*) Explain how missing data were addressed	n.a
		(*d*) If applicable, explain how loss to follow-up was addressed	n.a
		(*e*) Describe any sensitivity analyses	n.a
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11, Fig 1, Table 1, Suppl Table S2
		(b) Give reasons for non-participation at each stage	n.a.
		(c) Consider use of a flow diagram	n.a.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11, Fig 1, Table 1, Suppl Table S2
		(b) Indicate number of participants with missing data for each variable of interest	Table 2
		(c) Summarise follow-up time (eg, average and total amount)	Suppl Table S2
Outcome data	15*	Report numbers of outcome events or summary measures over time	Suppl Table S2

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11-13 11-13 11-13
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11-13
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.