

Supplementary data

Supplementary Table 1 Class 3 variant positive samples in cohort 1 and 2 and their ultrasound findings

Case	Gene	Genomic change	Protein change	NGS panel	De novo	Pathogenicity	NT (mm)	Persistent NT	JLS	Hydrops fetalis	Pleural effusion	Ascites	Cardiac anomalies	Renal anomalies	Polyhydramnios	Other anomalies	Pregnancy outcome
41	RAF1	c.1928C>T	Pro643Leu	-	-	VUS	8.1	+	-	-	-	-	-	-	-	-	ToP at 14 weeks
42	RIT1	c.646C>T	Pro216Ser	+	-	VUS	not measured	-	-	-	-	-	VSD, dysplastic pulmonary valve, tricuspid valve stenosis, seen at 16 weeks	-	-	-	ToP>16 weeks
43	HRAS	c.488_507del	Ile163fs	+	?	VUS	7.2	n/a	-	-	-	-	-	-	-	-	ToP at 12 weeks
44	SOS1	c.3709C>G	Pro1237Ala	+	-	VUS	nuchal fold at 19 weeks	+	-	-	-	-	subaortal VSD	-	-	-	Live birth, healthy

NT, nuchal translucency; JLS, jugular lymph sacs; VUS, variant of unknown significance; mat, maternal; pat, paternal; ToP, termination of pregnancy; VSD, ventricular septum defect; n/a, not applicable

Supplementary Figure 1 Correlation between increase in NT and mutation present

		NT_plain	Mutation_present
NT_plain	Pearson Correlation	1	-.486**
	Sig. (2-tailed)		.000
	N	110	110
Mutation_prese nt	Pearson Correlation	-.486**	1
	Sig. (2-tailed)	.000	
	N	110	110

** . Correlation is significant at the 0.01 level (2-tailed).