**Table S1.** Summary of Patients with biallelic ALPK3-cardiomyopathy (cases with adult-onset presentation are marked in grey)

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Individual** | **Sex** | **Origin** | **Age at Diagnosis** | **Cardiac Phenotype at Presentation** | **Cardiac Outcome** | **Zygosity/Variants** | **Nucleotide and protein changes** | **Location** | **Ref.** |
| 1 | A-IX:2F1P1 | M | Dutch | At birth | Severe biventricular dilatation | 5 day of post-partum: Death | Ho/Trunc | NM\_020778.4:c.4736-1G>A:p.Val1579Glyfs\*30 | Intron 9 | [12] [18] |
| 2 | B-IV:1F2P1 | F | Moroccan | 33 weeks of gestation | Cardiomegaly | 35 weeks of gestation: Death | Ho/Trunc | NM\_020778.4:c.3781C>T:p.Arg1261\* | Exon 6 | [12] [18] |
| 3 | B-IV:2F2P2 | F | Moroccan | 20 weeks of gestation | Severe biventricular hypertrophy and dilation | 2h post-partum: Death | Ho/Trunc | NM\_020778.4:c.3781C>T:p.Arg1261\* | Exon 6 | [12] [18] |
| 4 | B-IV:3F2P3 | F | Moroccan | At birth | Severe concentric LVH (13mm (z-score +6.0)) | 11y: Status quo; 13y: LVH 23mm, LVFS 27%, PVCs | Ho/Trunc | NM\_020778.4:c.3781C>T:p.Arg1261\* | Exon 6 | [12] [18] |
| 5 | C-V:2F3P1 | M | Turkish | 4y | Severe concentric LVH, RVH | 7y: VF, ICD; 14y: increased LVH, LVFS 26% | Ho/Trunc | NM\_020778.4:c.5294G>A:p.Trp1765\* | Exon 12 | [12] [18] |
| 6 | IV-1F4P1 | F | Pakistani | 6m | DCM+LVNC with rapid transformation into significant LVH, prolonged QT | 18y: ICD;30y: severe LVH, mild systolic dysfunction | Ho/Trunc  | NM\_020778.4:c.3792G.A:p.Trp1264\* | Exon 6 | [13][18] |
| 7 | IV-5F4P2 | M | Pakistani | 7weeks after birth | DCM with transformation into severe HCM at 8m, prolonged QT | 17y: LVH 27mm19y: mild systolic dysfunction, NSVT | Ho/Trunc  | NM\_020778.4:c.3792G.A:p.Trp1264\* | Exon 6 | [13][18] |
| 8 | F5P1 | M | Turkish | 21 weeks of gestation | DCM progressed to diffuse HCM at 4m, prolonged QT | 5y: ICD | Ho/Trunc | NM\_020778.4:c.2023delC:p.Gln675SerfsX30 | Exon 5 | [14][18] |
| 9 | F6P1 | M | Tunisian | 1week after birth | HCM/DCM; LVEF 35% at 3m | 6m: LVEF 50%11m: biventricular HCM, LV EF 74%3y: alive | Ho/Trunc | NM\_020778.4:c.1531\_1532delAA:p.Lys511Argfs\*12 | Exon 5 | [15][18] |
| 10 | F7P1 | M | ND | At birth | DCM, LV EF 12%; progressed to LVH +LVNC+RVH at 6m | 5y: PH6y: SCD | Comp Het/ Trunc+Mis | NM\_020778.4:c.1018C>T:p.Gln340\*c.2434G>A:p.Val812Met | Exon 4Exon 6 | [18] |
| 11 | F7P2 | M | ND | Fetal | Biventricular dysfunction; LV EF 37% at post-partum; DCM at 6m; severe LVH at 12m | 3,5y: severe HCM with normal LV EF;4,5y: RVH, HTx | Comp Het/ Trunc+Mis | NM\_020778.4:c.1018C>T:p.Gln340\*c.2434G>A:p.Val812Met | Exon 4Exon 6 | [18] |
| 12 | F7P3 | M | ND | 4m | HCM | 11y: VF, ICD;28y: biventricular hypertrophy and dilatation, HTx | Comp Het/Trunc+trunc | NM\_020778.4:c.1018C>T:p.Gln340\*c.4332delC:p.Lys1445Argfs\*29 | Exon 4Exon 6 | [18] |
| 13 | F8P1 |  | Cape Verde | 31y | Biventricular dilation, preserved EF, 2nd degree AV-block | 35y: IVS 11mm | Comp Het/ Trunc+Mis | NM\_020778.4:c.541delG:p.Ala181Profs\*130c.3439C>T:p.Arg1147Trp | Exon 1Exon 6 | [18] |
| 14 | F9P1 | M | ND | 53y | HCM, LV EF 65%, no LVOTO | ND | Comp Het/ Trunc+Mis  | NM\_020778.4:c.4997delA:p.Asn1666Thrfs\*14c.4091G>C:p.Gly1364Ala | Exon 10Exon 6 | [18] |
| 15 | F10P1 (twin of F10P2) | F | ND | 3m | DCM, LV FS 9,4% | 5m: dilated LV with FS 27%6m: concentric LVH, LV FS 41%9y: LVH 23mm, PH, short PQ, prolonged QT | Comp Het/ Trunc+Mis | NM\_020778.4:c.5105+5G>C:p?c.597G>T:p.Glu199Asp | Intron 11Exon 1 | [18] |
| 16 | F10P2(twin of F10P1) | F | ND | 3m | DCM, LV FS 14% | 3,5y: concentric LVH, LV FS 33% 9y: moderate LVH, LV FS 36%, PH, prolonged QT | Comp Het/ Trunc+Mis | NM\_020778.4:c.5105+5G>C:p?c.597G>T:p.Glu199Asp | Intron 11Exon 1 | [18] |
| 17 | F11P1 | F | ND | 14y | Severe concentric HCM | 15y: ICD | Comp Het/ Trunc+Mis | NM\_020778.4:c.2023delC:p.Gln675Serfs\*30c.4888G>T:p.Val1630Phe | Exon 5Exon 10 | [18] |
| 18 | F12P1 | F | Turkish | 10y | Concentric HCM with trabeculation | 44y: LVNC | Ho/Trunc | NM\_020778.4:c.3418C>T:p.Gln1140\* | Exon 6 | [18] |
| 19 | F13P1 | F | Turkish | 35 weeks of gestation | Mild LVH; biventricular HCM with slightly decreased LV function at birth | 2d: poor biventricular function7d: HCM+DCM2y: moderate concentric LVH | Ho/Mis | NM\_020778.4c.5155G>C:p.Ala1719Pro | Exon 12 | [18] |
| 20 | IV-4 | M | ND | 31 weeks of gestation | LVNC, mild ventricular disfunction; biventricular dilatation and hypertrophy, LVEF 40%, LVNC at birth | 30m: apical LVNC, LVH, no dilatation, LVEF 62% | Ho/Trunc | NM\_020778.4:c.639G>A:p.Trp213\* | Exon 1 | [16] |
| 21 | IV-1 | M | ND | At birth | DCM, LVEF 30% | 12y: HCM, LVEF 57% | Ho/Trunc | NM\_020778.4:c.639G>A:p.Trp213\* | Exon 1 | [16] |
| 22 | IV-2 | F | ND | At birth | LV trabeculation, VSD | 10y: HCM, LVEF 70%, no VSD | Ho/Trunc | NM\_020778.4:c.639G>A:p.Trp213\* | Exon 1 | [16] |
| 23 | III-2 | M | ND | 38y | HCM, LVEF 60%, asymptomatic | ND | Ho/Trunc | NM\_020778.4:c.639G>A:p.Trp213\* | Exon 1 | [16] |
| 24 | III-1 | M | ND | 28y | HCM, LVEF 58%, asymptomatic | ND | Ho/Trunc | NM\_020778.4:c.639G>A:p.Trp213\* | Exon 1 | [16] |
| 25 | IV-6 | F | ND | At birth | LVH, LV dilatation, LVNC, LVEF 26% | 42m: HCM, LVEF 49% | Ho/Trunc | NM\_020778.4:c.639G>A:p.Trp213\* | Exon 1 | [16] |
| 26 | Patient 1 | M | Russian | At birth | Severe HCM | 4y: marked LVH, LVEF 49%, LV trabeculation 9y: IVS 33mm, no LVOTO; prolonged QT 12y: SCD | Comp Het/Trunc+Trunc | NM\_020778: c.2033delG: p.R687fsc.3558delG: p.V1186fs | Exon 5Exon 6 | [17] |
| 27 | Patient 2 | F | Russian | 21y | HCM, LVEF 78%, asymptomatic | 25y: HCM, no LVOTO, LVEF 38%, LV trabeculation, NSVT30y: prolonged QT, syncope, ICD33y: HTx | Ho/Mis | NM\_020778:c.G4897A:p.G1633R | Exon10 | [17] |
| 28 | Presented case | M | Turkic | 38y | LVEF 30%; LVH 16mm; no LVOTO; restrictive diastole, LV trabeculation;  | ND | Comp Het/Trunc+Mis | NM\_020778.5: c.1958C>G:p.Ser653\*c.3491G>A:p.Arg1164Gln | Exon 6Exon 6 | Present study |

Trunc: protein-truncated variant; Mis: missense variant; LVH: left ventricular hypertrophy; RVH: right ventricular hypertrophy; LVFS: left ventricular fractional shortening; PVCs: premature ventricular contractions; VF: ventricular fibrillation; ICD: implantable cardioverter defibrillator; DCM: dilated cardiomyopathy; LVNC: left ventricular non-compaction; NSVT: non-sustained ventricular tachycardia; LVEF: left ventricular ejection fraction; ND: not done; PH: pulmonary hypertension; SCD: sudden cardiac death; HTx: heart transplant; IVS: interventricular septum; LVOTO: left ventricular outflow tract obstruction; VSD: ventricular septal defect.