Supplementary table 1. Primary indication of invasive testing for 130 prenatal cases

|                              | Chorionic villi | Amniotic fluid | Total |
|------------------------------|-----------------|----------------|-------|
| DS screening positive only   | 32              | 21             | 53    |
| Fetal ultrasound abnormality |                 |                |       |
| Number of fetal anomalies    |                 |                |       |
| One                          | 4               | 16             | 35    |
| Two                          | 6               | 8              | 14    |
| Three                        | 2               | 3              | 5     |
| More than three              | 4               | 3              | 7     |
| Increased NT >= 3.5 mm or cystic hygroma | 21 | 1 | 22 |
| Family history of chromosomal abnormality | 2 | - | 2 |
| Others                       | 2\(^a\)         | -              | 2     |
| Total                        | 73              | 57             | 130   |

\(^a\)One non-invasive prenatal test (NIPT) positive; dichorionic diamniotic twin 1 with scan abnormality and twin 2 (this twin) normal

DS: Down syndrome; NT: nuchal translucency
## Supplementary table 2. Abnormal aCGH results and outcome (n=11)

| Case number | Gestation | Sample type | aCGH result (ISCN 2016) | Referring indication | Karyotype result | CNV size and type/classification, gene(s) or syndrome | Outcome / remarks |
|-------------|-----------|-------------|--------------------------|---------------------|-----------------|------------------------------------------------------|------------------|
| 1           | 13+1      | uncultured CV | arr[GRCh37] 13q31.2q34(89022234_15083595)x2~3 | 1st trimester DS screening risk 1:2; USS: Absent nasal bone, ? AVSD, exomphalos, bilateral talipes | 47,XX,+mar dn[4]/46,XX[46] | • 26.06 Mb mosaic copy gain in 13q31.2-q34 / Pathogenic, mosaic partial trisomy 13q | TOP. No postmortem. |
| 2           | 13+4      | uncultured CV | arr[GRCh37] 21q22.11(34169002_35051732)x3 dn,21q22.3(45066431_48091216)x1 dn | 1st trimester DS screening risk 1 in 210. | 46,XY,r(21)(p11.2q22.3)dn | • 882.73kb copy gain in 21q22.11 / uncertain clinical significance • 3.02Mb copy loss in 21q22.3 / Pathogenic, ring chromosome 21 | Post test counselling by clinical geneticist. Livebirth. OFC <3rd at 13 months. |
| 3           | 13+6      | uncultured CV | arr[GRCh37] 18p11.32q3(146484_78013620)x2~3,22q11.1q13.33(17528442_51178150)x3 | 1st trimester DS screening risk 1 in 11, low PAPP-A 0.09 MoM | 47,XX,+22 | • Mosaic 77.87 Mb copy gain in 18p11.32-q23 / Pathogenic mosaic trisomy 18 • 33.65 Mb copy gain in 22q11.1-q13.33 / Pathogenic, trisomy 22 | TOP. Abortus: no gross abnormality. |
| 4           | 17+5      | uncultured AF | arr[GRCh37] 8p23.3p12(202133_291477)x1 | USS: Oligohydramnios, LV < RV, LVOT not well seen, pericardial effusion, echogenic bowel, increased nuchal translucency (6mm at 11 weeks). NIPT: reduction in the amount of DNA from chromosome 8p. | 46,XY,del(8)(p12)dn[16]/46,XY[15] | • 28.99Mb copy loss in 8p23.3-p12 (mosaic loss in cultured cells) / Pathogenic, terminal 8p deletion | TOP. No postmortem. |
| 5           | 20+5      | uncultured AF | arr[GRCh37] 1q43q44(239841348_249208146)x3,4q34.3q35.2(182344275_190896675)x1 | USS: Fetal diaphragmatic hernia | 46,XY,ish der(4)(D4Z1+,D4S2930−,VIJyRM2123+) | • 9.37 Mb copy gain in 1q43-q44 • 8.55 Mb copy loss in 4q34.3-q35.2 / Pathogenic unbalanced translocation (metaphase FISH confirmed the unbalanced translocation. | Decided to keep pregnancy. Joint counselling with paediatric surgeon. Defaulted follow up since 25 weeks. Declined parental karyotype. |
| Case | Week | Cell Type | Caller | Caller | Description | karyotype | Notes |
|------|------|----------|--------|--------|-------------|----------|-------|
| 6    | 19+3 | uncultured AF | arr[GRCh37] Xp21.2p21.1(31464899_31522762)x0 mat | 1st trimester DS screening risk 1:230. | 46,XY | • 57.86 kb deletion in Xp21.2-p21.1, involving DMD gene / Pathogenic, Dystrophinopathy | Post-test counselling with neurologist. Livebirth. BMD. Borderline global delay at 19 months. |
| 7    | 23+4 | uncultured AF | arr[GRCh37] 16p13.11(15125829_16287900)x3 pat | USS: Fetal intracranial tumor | 46,XX | • 1.16 Mb copy gain in 16p13.11 / Pathogenic, 16p13.11 duplication syndrome | TOP. No postmortem. Post-TOP counselling by clinical geneticist. Normal paternal phenotype. |
| 8    | 13+4 | uncultured CV | arr[GRCh37] 16p11.2(29657192_30188269)x1 dn | 1st trimester DS screening risk 1:90 | 46,XX | • 531.08 kb copy loss in 16p11.2 / Pathogenic, 16p11.2 microdeletion syndrome | Post-test counselling by clinical geneticist. TOP. No postmortem. |
| 9    | 20   | uncultured AF | arr[GRCh37] 16p11.2(29657192_30188269)x1 dn | NIPT low risk. USS: multiple level hemivertebra, 1A1V, right ventricle hypoplasia with tricuspid atresia. | 46,XX | • 531.08 kb copy loss in 16p11.2 / Pathogenic, 16p11.2 microdeletion syndrome | TOP. Postmortem: right ventricular hypoplasia, tricuspid atresia, ASD, hemivertebrae. Maternal aCGH showed mosaic 9p13.2 deletion confirmed on FISH. Post TOP counselling by clinical geneticist. Normal maternal phenotype. |
| 10   | 22+4 | uncultured AF | arr[GRCh37] 16p11.2(29657192_30188269)x1 dn | USS: TOF, possibility of transposition of great artery. | 46,XY | • 531.08 kb copy loss in 16p11.2 / Pathogenic, 16p11.2 microdeletion syndrome | TOP. Postmortem: Tetralogy of Fallot, right sided aortic arch, atretic ductus arteriosus, cerebellar hypoplasia. |
| 11   | 20+1 | uncultured AF | arr[GRCh37] 2q34(212660463_213736135)x3 pat | NIPT low risk. USS: spine abnormality, Right club foot. | 46,XX | • 1.08 Mb copy gain in 2q34 / Uncertain clinical significance | TOP. No postmortem. Babygram: hemivertebra, non-segmentation defect, 11 pairs of ribs, bilateral clubfeet. Normal paternal phenotype. |

aCGH: array comparative genomic hybridization; AF: amniotic fluid; AVSD: atrioventricular septal defect; BMD: Becker muscular dystrophy; CNV: copy number variant; CV: chorionic villi; DS: Down syndrome; BMD: Becker muscular dystrophy; FISH: fluorescence in-situ hybridization; MoM: multiples of median; NIPT: non-invasive prenatal testing; PAPP-A pregnancy associated plasma protein-A; TOF: Tetralogy of Fallot; TOP: termination of pregnancy; USS: ultrasound scan.