Online Supplementary Table S1. Clinical and cytogenetic features of the 20 t-HeH cases.

Case no.	*Fusion gene*	*Sex/age (years)*	*WBC ($x10^9$/l)*	*Survival (months)*	*Karyotype*[1]
1	*TCF3/PBX1*	M/5.2	2.4	38+	52,XY,+X,+4,+6,del(12)(q21),+der(14)t(12;14)(q14;q32)ins(14;?)(q32;?),+18,der(19)t(1;19)(q23;p13),+21
2	*TCF3/PBX1*	M/6.6	7.0	123+	53-57,XY,+X,+4,+6,+10,+14,+17,+18,der(19)t(1;19)(q23;p13),+21,+21
3	*TCF3/PBX1*	F/6.5	2.1	125+	56-57,XX,+6,+10,+14,+17,+18,der(19)t(1;19)(q23;p13),+21,+21,+mar,inc
4	*TCF3/PBX1*	M/7.5	2.4	54+	63-65,XY,+X,+Y,t(1;19)(q23;p13),+5,+6,+8,+9,+10,+11,+11,+14,+16,+der(17)t(1;17)(q21;p11),+21,+21,+22,+mar
5	*BCR/ABL1*	M/12.7	22	19	52,XY,+X,+Y,t(9;22)(q34;q11),+14,+21,+21,+der(22)t(9;22)
6	*BCR/ABL1*	F/11.0	2.6	146+	57,XX,+X,+2,+6,t(9;22)(q34;q11),+10,+13,+14,+18,+20,+21,+21,+der(22)t(9;22)
7	*BCR/ABL1*	M/14.2	106	127+	51-58,XY,+?X,+?4,+21,+21,der(22)t(9;22)(q34;q11),inc
8	*BCR/ABL1*	F/5.6	2.0	156+	51-53,XX,t(9;22)(q34;q11),inc
9	*BCR/ABL1*	F/12.1	61	172+	52-56,XX,t(9;22)(q34;q11),+der(22)t(9;22),inc
10	*BCR/ABL1*	M/5.4	65	125+	54-59,X?,t(9;22)(q34;q11),inc
11	*MLL/AFF1*	F/3.9	31	16	51,XX,+X,+1,+2,t(4;11)(q21;q23),+20,+21
12	*MLL+*	M/4.0	11	50+	48-54,X,-Y,+X,+8,-11,der(11)t(11;11)(p15;q23)dup(11)(q21q13)dup(11)(q23q21),+21,+1-2mar,inc
13	*MLL+*	M/3.7	4.1	121+	60,XY,+X,+Y,add(1)(q32),+3,+4,+8,+9,+10,add(11)(q23),+14,+17,+18,+21,+21,+21,inc
14	*ETV6/RUNX1*	M/2.9	4.0	104+	51,XY,+X,+Y,+1,del(1)(p11)x2,+4,der(9)t(1;9)(p11;p13),+10,der(12)t(9;12)(p13;p12),t(12;21)(p13;q22)
15	*ETV6/RUNX1*	M/2.9	4.0	98+	51-53,XY,+5,+6,+10,t(12;21)(p13;q22),+15,+21
16	*ETV6/RUNX1*	M/3.8	6.1	143+	51,XY,+X,+4,+6,+10,t(12;21)(p13;q22),+21
17	*ETV6/RUNX1*	F/7.3	6.1	50+	51,XX,+4,+10,t(12;21)(p13;q22),+18,+der(21)t(12;21),inc
18	*ETV6/RUNX1*	F/6.3	1.5	75+	56-57,XX,+X,+4,+del(6)(q?),+8,+9,+10,der(12)t(6;12)(?;p?),t(12;21)(p13;q22),+14,+17,+18,+21,+21
19	*ETV6/RUNX1*	F/4.7	10	92+	49-52,XX,+4,+12,t(12;21)(p13;q22),+21,+der(21)t(12;21),+22,inc
20	*ETV6/RUNX1*	M/13.2	2.9	81+	52,XY,+der(3)t(3;21)(?;q?),+5,t(12;21)(p13;q22),+14,+16,inc

[1]*The t(12;21)(p13;q22) in cases 14-20 and the involvement of chromosomes 6 and 3 in cases 18 and 20, respectively, were identified by fluorescence in situ hybridization analysis. F: female; M: male; t-HeH: high hyperdiploidy with t(1;19)(q21;q23), t(9;22)(q34;q11), der(11q23), or t(12;21)(p13;q22); WBC: white blood cell count; +: alive.*

Online Supplementary Table S2. Clinical data in relation to modal chromosome number in 670 HeH cases treated according to the NOPHO ALL 1992/2000 protocols.

Mode	*No. of cases (%)*	*Sex (M/F)*	*Median age (range)*	*Median WBC x 10^9/l (range)*	*pEFS (SE) at 5 years*	*pEFS (SE) at 10 years*	*pOS (SE) at 5 years*	*pOS (SE) at 10 years*
51	15 (2.2)	8/7 (1.1)	4.34 (1.75 – 14.0)	17.2 (3.6 – 131)	0.73 (0.12)	0.73 (0.12)	0.87 (0.09)	0.87 (0.09)
52	38 (5.7)	23/15 (1.5)	3.63 (1.31 – 13.2)	6.7 (1.0 – 91)	0.74 (0.07)	0.74 (0.07)	0.92 (0.05)	0.92 (0.05)
53	54 (8.1)	29/25 (1.2)	3.46 (1.39 – 14.1)	7.8 (0.7 – 129)	0.73 (0.06)	0.73 (0.06)	0.81 (0.05)	0.81 (0.05)
54	100 (15)	43/57 (0.8)	3.60 (1.03 – 14.8)	7.3 (0.6 – 169)	0.82 (0.04)	0.79 (0.04)	0.96 (0.02)	0.93 (0.03)
55	151 (23)	82/69 (1.2)	3.71 (1.06 – 15.0)	6.2 (0.4 – 170)	0.81 (0.03)	0.79 (0.03)	0.91 (0.02)	0.89 (0.03)
56	83 (12)	38/45 (0.8)	3.23 (1.22 – 14.4)	7.9 (0.5 – 90)	0.85 (0.04)	0.82 (0.04)	0.91 (0.03)	0.88 (0.04)
57	66 (9.9)	26/40 (0.7)	4.25 (1.22 – 14.2)	5.8 (1.0 – 65)	0.86 (0.04)	0.86 (0.04)	0.91 (0.04)	0.89 (0.04)
58	52 (7.8)	27/25 (1.1)	3.96 (1.39 – 12.5)	7.4 (0.8 – 92)	0.88 (0.05)	0.88 (0.05)	0.94 (0.03)	0.94 (0.03)
59	41 (6.1)	22/19 (1.2)	3.71 (1.03 – 14.2)	6.0 (0.5 – 291)	0.85 (0.06)	0.79 (0.07)	0.95 (0.03)	0.90 (0.05)
60	25 (3.7)	12/13 (0.9)	4.04 (1.94 – 14.6)	3.4 (1.3 – 60)	0.80 (0.08)	0.74 (0.09)	0.92 (0.05)	0.92 (0.05)
61	12 (1.8)	6/6 (1.0)	4.77 (2.04 – 10.4)	3.8 (0.9 – 14)	1.0	1.0	1.0	1.0
62	11 (1.6)	6/5 (1.2)	4.31 (1.48 – 14.4)	6.2 (2.1 – 52)	0.91 (0.09)	0.91 (0.09)	0.90 (0.10)	0.90 (0.10)
63	9 (1.3)	7/2 (3.5)	4.08 (1.88 – 7.33)	5.7 (1.0 – 30)	1.0	0.83 (0.15)	1.0	1.0
64	4 (0.6)	3/1 (3.0)	2.90 (2.73 – 3.14)	10.4 (3.4 – 18)	0.75 (0.22)	0.75 (0.22)	0.75 (0.22)	0.75 (0.22)
65	5 (0.7)	2/3 (0.7)	4.69 (3.31 – 10.5)	6.8 (2.3 – 25)	1.0	1.0	1.0	1.0
66	3 (0.4)	2/1 (2.0)	4.21 (3.36 – 10.0)	5.5 (1.2 – 21)	0.33 (0.27)	0.33 (0.27)	0.33 (0.27)	0.33 (0.27)
67	1 (0.1)	0/1	4.01	20	1.0	1.0	1.0	1.0

ALL: acute lymphoblastic leukemia; F: female; HeH: high hyperdiploidy without t(1;19)(q21;q23), t(9;22)(q34;q11),

der(11q23), or t(12;21)(p13;q22); M: male; pEFS: probability of event-free survival; pOS: probability of overall survival; SE: standard error; WBC: white blood cell count.

Online Supplementary Table S3. Survival of the 688 HeH and 20 t-HeH patients treated according the ALL 1992/2000 protocols.

Cytogenetic group	*No. of cases*	*pEFS at 5 years (SE)*	*pEFS at 10 years (SE)*	*pOS at 5 years (SE)*	*pOS at 10 years (SE)*
HeH	688	0.82 (0.02)	0.80 (0.02)	0.91 (0.01)	0.89 (0.01)
t(1;19)	4	1.00	nd	1.00	nd
t(9;22)	6	0.67 (0.19)	0.67 (0.19)	0.83 (0.15)	0.83 (0.15)
der(11q23)	3	0.67 (0.27)	nd	0.67 (0.27)	nd
t(12;21)	7	1.00	1.00	1.00	1.00
Total	708	0.82 (0.02)	0.80 (0.02)	0.91 (0.01)	0.89 (0.01)

ALL: acute lymphoblastic leukemia; HeH: high hyperdiploidy without t(1;19) (q21;q23), t(9;22)(q34;q11), der(11q23), or t(12;21)(p13;q22); nd: not determined; pEFS: probability of event-free survival; pOS: probability of overall survival; SE: standard error; t-HeH: high hyperdiploidy with t(1;19), t(9;22), der(11q23), or t(12;21).

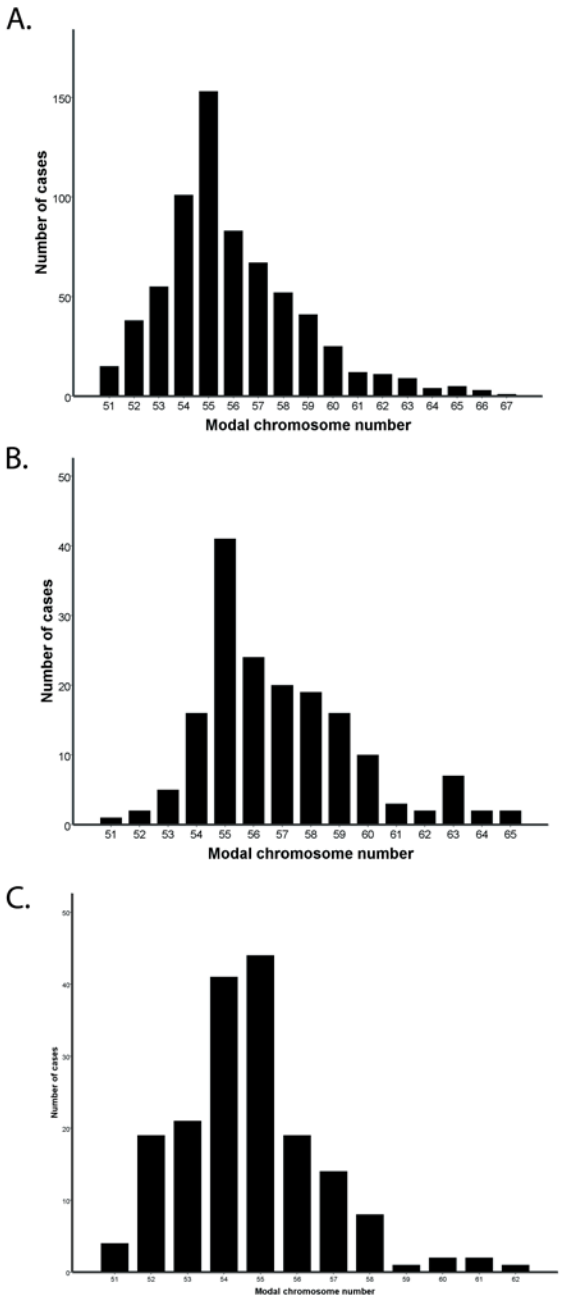
Online Supplementary Table S4. Survival of the HeH cases treated according to the NOPHO ALL 1992/2000 protocols and informative as regards specific chromosomal changes and karyotypic patterns.

Aberration	*pEFS at 5 years (SE)*	*pEFS at 10 years (SE)*	*P*[a]	*pOS at 5 years (SE)*	*pOS at 10 years (SE)*	*P*[1]
1						
Disomy	0.85 (0.02)	0.82 (0.02)	0.283	0.92 (0.02)	0.91 (0.02)	0.451
Gain	1.00	1.00		1.00	1.00	
2						
Disomy	0.85 (0.02)	0.83 (0.02)	0.670	0.93 (0.02)	0.91 (0.02)	0.794
Gain	0.89 (0.11)	0.89 (0.11)		0.89 (0.11)	0.89 (0.11)	
3						
Disomy	0.85 (0.02)	0.82 (0.02)	0.337	0.92 (0.02)	0.91 (0.02)	0.256
Gain	0.93 (0.07)	0.93 (0.07)		1.00	1.00	
4						
Disomy	0.70 (0.06)	0.68 (0.06)	**<0.0001**	0.88 (0.04)	0.88 (0.04)	0.426
Gain	0.90 (0.02)	0.87 (0.02)		0.93 (0.02)	0.92 (0.02)	
5						
Disomy	0.86 (0.02)	0.83 (0.03)	0.879	0.92 (0.02)	0.92 (0.02)	0.442
Gain	0.86 (0.05)	0.82 (0.05)		0.92 (0.03)	0.88 (0.04)	
6						
Disomy	0.71 (0.07)	0.68 (0.07)	**0.003**	0.88 (0.05)	0.88 (0.05)	0.498
Gain	0.88 (0.02)	0.85 (0.02)		0.93 (0.02)	0.91 (0.02)	
7						
Disomy	0.85 (0.02)	0.83 (0.02)	0.465	0.92 (0.02)	0.90 (0.02)	0.381
Gain	0.87 (0.07)	0.87 (0.07)		0.96 (0.04)	0.96 (0.04)	
8						
Disomy	0.83 (0.03)	0.82 (0.03)	0.438	0.91 (0.02)	0.90 (0.02)	0.512
Gain	0.89 (0.03)	0.84 (0.04)		0.94 (0.02)	0.92 (0.03)	
9						
Disomy	0.86 (0.02)	0.84 (0.03)	0.263	0.93 (0.02)	0.92 (0.02)	0.211
Gain	0.81 (0.06)	0.78 (0.06)		0.87 (0.05)	0.87 (0.05)	
10						
Disomy	0.81 (0.04)	0.76 (0.05)	0.052	0.88 (0.04)	0.86 (0.04)	0.062
Gain	0.87 (0.02)	0.85 (0.03)		0.94 (0.02)	0.93 (0.02)	

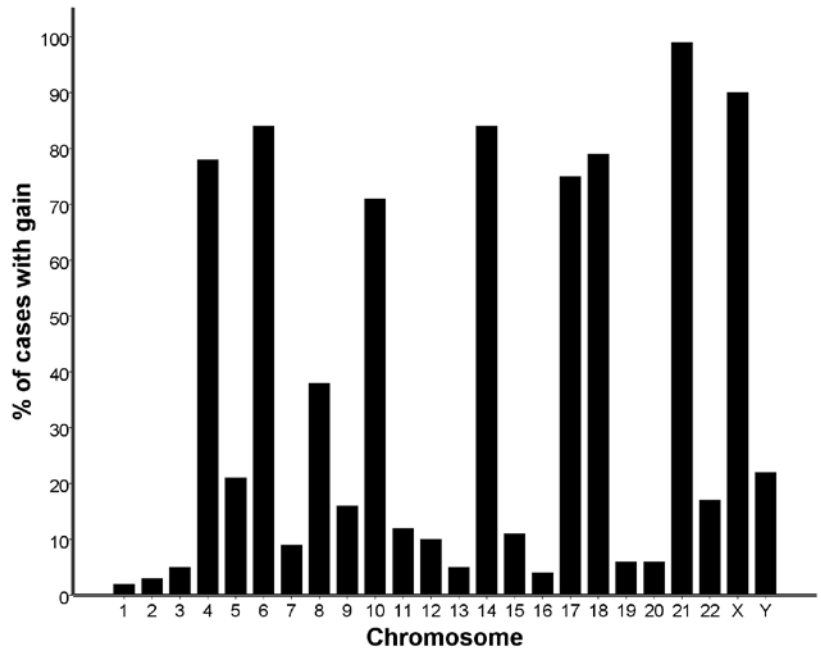
11						
Disomy	0.84 (0.02)	0.82 (0.03)	0.148	0.92 (0.02)	0.91 (0.02)	0.473
Gain	0.95 (0.04)	0.91 (0.05)		0.97 (0.03)	0.94 (0.05)	
12						
Disomy	0.84 (0.02)	0.81 (0.03)	0.067	0.92 (0.02)	0.90 (0.02)	0.102
Gain	0.96 (0.04)	0.96 (0.04)		1.00	1.00	
13						
Disomy	0.85 (0.02)	0.82 (0.02)	0.676	0.93 (0.02)	0.91 (0.02)	0.582
Gain	0.88 (0.08)	0.88 (0.08)		0.88 (0.08)	0.88 (0.08)	
14						
Disomy	0.82 (0.06)	0.79 (0.06)	0.592	0.95 (0.03)	0.95 (0.03)	0.267
Gain	0.86 (0.02)	0.83 (0.03)		0.92 (0.02)	0.90 (0.02)	
15						
Disomy	0.84 (0.02)	0.82 (0.03)	0.270	0.92 (0.02)	0.91 (0.02)	0.883
Gain	0.94 (0.04)	0.90 (0.06)		0.93 (0.05)	0.89 (0.06)	
16						
Disomy	0.86 (0.02)	0.83 (0.02)	0.775	0.92 (0.02)	0.91 (0.02)	0.888
Gain	0.82 (0.12)	0.82 (0.12)		0.91 (0.09)	0.91 (0.09)	
17						
Disomy	0.76 (0.05)	0.74 (0.05)	**0.010**	0.86 (0.04)	0.86 (0.04)	0.080
Gain	0.89 (0.02)	0.86 (0.03)		0.94 (0.02)	0.93 (0.02)	
18						
Disomy	0.80 (0.05)	0.73 (0.06)	**0.049**	0.88 (0.04)	0.86 (0.05)	0.143
Gain	0.87 (0.02)	0.85 (0.02)		0.93 (0.02)	0.92 (0.02)	
19						
Disomy	0.86 (0.02)	0.83 (0.02)	0.146	0.92 (0.02)	0.91 (0.02)	0.658
Gain	0.72 (0.11)	0.72 (0.11)		0.94 (0.05)	0.94 (0.05)	
20						
Disomy	0.86 (0.02)	0.83 (0.02)	0.966	0.92 (0.02)	0.91 (0.02)	0.196
Gain	0.83 (0.09)	0.83 (0.09)		1.00	1.00	
21						
Disomy	1.00	1.00	0.380	1.00	1.00	0.535
Gain	0.85 (0.02)	0.82 (0.02)		0.92 (0.02)	0.91 (0.02)	
22						
Disomy	0.83 (0.02)	0.81 (0.03)	**0.040**	0.92 (0.02)	0.91 (0.02)	0.508
Gain	0.96 (0.03)	0.93 (0.04)		0.96 (0.03)	0.93 (0.04)	

X						
Disomy	0.79 (0.08)	0.79 (0.08)	0.526	0.90 (0.06)	0.90 (0.06)	0.702
Gain	0.86 (0.02)	0.83 (0.02)		0.93 (0.02)	0.91 (0.02)	
Y						
Disomy	0.84 (0.04)	0.80 (0.04)	0.751	0.91 (0.03)	0.91 (0.03)	0.247
Gain	0.79 (0.07)	0.79 (0.07)		0.85 (0.06)	0.85 (0.06)	
Triple trisomies						
No	0.80 (0.03)	0.77 (0.03)	**0.002**	0.89 (0.02)	0.88 (0.03)	0.066
Yes	0.92 (0.02)	0.89 (0.03)		0.95 (0.02)	0.94 (0.02)	
Modal numbers						
51-53	0.73 (0.04)	0.73 (0.04)	**0.020**	0.86 (0.03)	0.86 (0.03)	0.091
>53	0.84 (0.02)	0.82 (0.02)		0.93 (0.01)	0.90 (0.01)	
51-55	0.79 (0.02)	0.77 (0.02)	**0.024**	0.91 (0.02)	0.89 (0.02)	0.615
>55	0.86 (0.02)	0.84 (0.02)		0.92 (0.02)	0.90 (0.02)	
Structural changes						
No	0.84 (0.03)	0.81 (0.03)	0.844	0.92 (0.02)	0.89 (0.02)	0.592
Yes	0.82 (0.03)	0.80 (0.03)		0.90 (0.02)	0.88 (0.02)	
Gain of 1q						
No	0.85 (0.02)	0.82 (0.03)	0.450	0.92 (0.02)	0.90 (0.02)	0.605
Yes	0.87 (0.04)	0.87 (0.04)		0.93 (0.03)	0.93 (0.03)	
Deletion of 6q						
No	0.85 (0.02)	0.83 (0.02)	0.860	0.92 (0.02)	0.90 (0.02)	0.788
Yes	0.86 (0.09)	0.86 (0.09)		0.91 (0.09)	0.91 (0.09)	
Gain of 17q						
No	0.85 (0.02)	0.83 (0.02)	0.565	0.92 (0.02)	0.90 (0.02)	0.957
Yes	0.91 (0.09)	0.91 (0.09)		0.91 (0.09)	0.91 (0.09)	

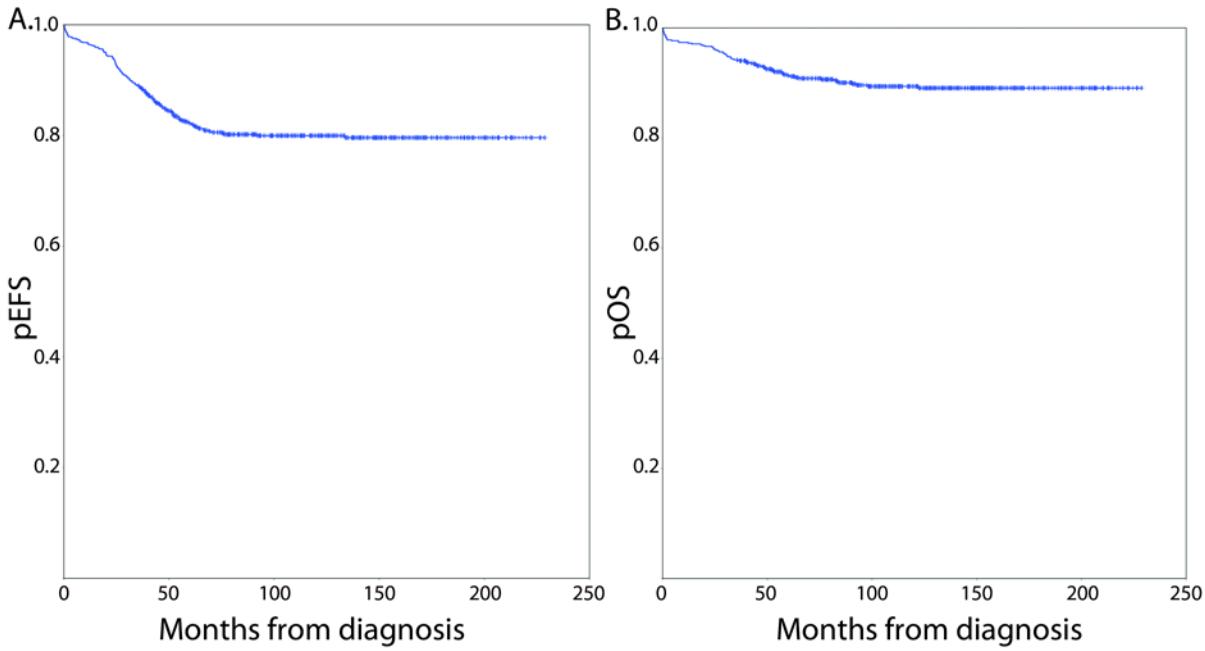
[1]*Significant P values are in bold type. HeH: high hyperdiploidy without t(1;19)(q21;q23), t(9;22)(q34;q11), der(11q23), or t(12;21)(p13;q22); NA: not applicable; pEFS: probability of event-free survival; pOS: probability of overall survival; SE: standard error.*



Online Supplementary Figure S1. Modal chromosome number distribution of the HeH cases. (A) Among the 675 HeH cases with known modal numbers, the median mode was 55 chromosomes, with a range of 51-67 chromosomes. (B) Among the HeH cases with triple trisomies (+4, +10, +17), the median mode was 56 chromosomes (range, 51-65). (C) Among the HeH cases without triple trisomies, the median mode was 55 chromosomes (range, 51-62). The modal number distributions differed significantly (P<0.0001) between the triple trisomy-positive and -negative HeH cases.



Online Supplementary Figure S2. Frequencies of chromosome gains among the 298 informative HeH cases. Chromosomes X, 4, 6, 8, 10, 14, 17, 18, and 21 were all gained (trisomies, tetrasomies, and pentasomies combined) in more than 25% of cases.



Online Supplementary Figure S3. Event-free (A) and overall survival (B) of 688 consecutive HeH cases diagnosed in the Nordic countries 1992-2008 and treated according to the NOPHO ALL 1992/2000 protocols.