

Criterion	Applicability/Assessment in data
Clustering of breakpoints	Applicable. Statistical evidence for breakpoint clustering in 5/9 of chromosomes 21 and 2/4 of chromosomes 15 of rob(15;21) iAMP21 samples (Supplementary Figure 2).
Regularity of oscillating copy-number states	Applicable. As opposed to 'conventional chromothripsis', copy numbers oscillate over multiple copy number states since chromothripsis takes place on amplified chromosomes (by BFBs in sporadic iAMP21 and by whole-chromosome duplication in rob(15;21) iAMP21). Copy number profiles are shown in Figure 1A, Figure 2A, Figure 3 and Extended Data Figure 6.
Interspersed loss and retention of heterozygosity	Applicable. Sporadic iAMP21 and der(15;21) show interspersed loss and retention of LOH in multiple samples (Supplementary Figure 3). Segments of LOH are expected to occur less frequently as chromothripsis takes place on amplified chromosomes (by BFBs in sporadic iAMP21 and by whole-chromosome duplication in rob(15;21) iAMP21).
Prevalence of rearrangements affecting a specific haplotype	Applicable. FISH and cytogenetic analysis demonstrated that gross chromosomal rearrangements only affected one of the two chromosomes 21 in sporadic cases, and only the rob(15;21) chromosome in the Robertsonian cases (Figure 1D, Figure 2D-E, Supplementary Figures 12E, 16E, 18E, 20D-E, 21D-E, 23D-E).
Randomness of DNA segment order and fragment joins	Applicable. Rearrangement join orientations in iAMP21 and der(15;21) chromosomes are consistent with random draws from a uniform multinomial distribution. However aggregated data of all other chromosomes show a significant departure from this null distribution, where deletion-type rearrangements seem to dominate the rearrangement landscape (Extended Data Figure 2). We also evaluated randomness of DNA segment orders, but found that as noted earlier ¹⁴ , DNA segment orders were non-random even in chromosomes presumed to have undergone chromothripsis (data not shown).
Ability to walk the derivative chromosome	Not applicable , as in both sporadic and rob(15;21) associated iAMP21, chromothripsis takes place on chromosomes with preceding or synchronous duplication (by BFBs in sporadic iAMP21 and by whole-chromosome duplication in rob(15;21) iAMP21). In this scenario, it would be impossible to walk the derivative chromosome as outlined in the criteria.