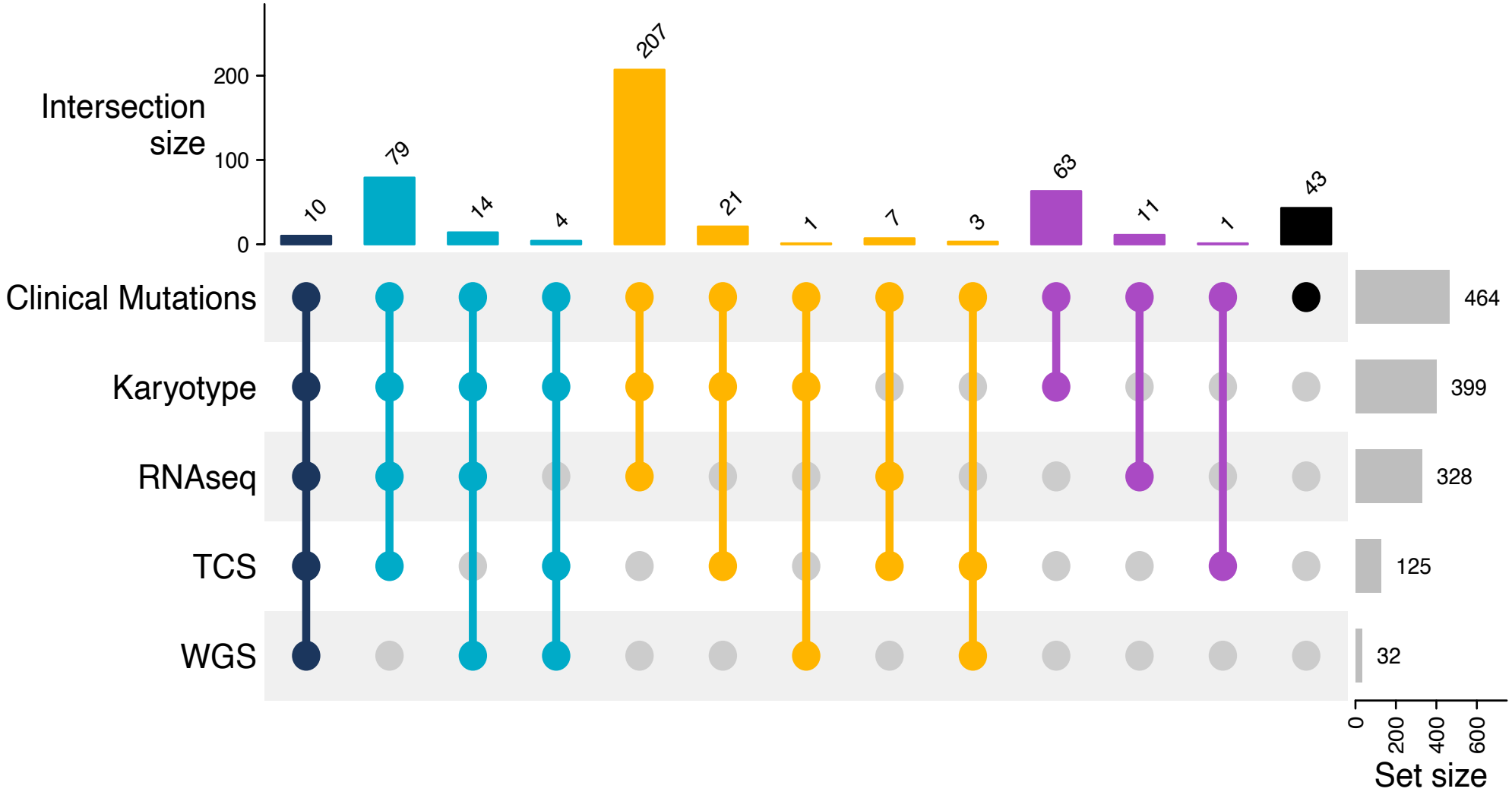
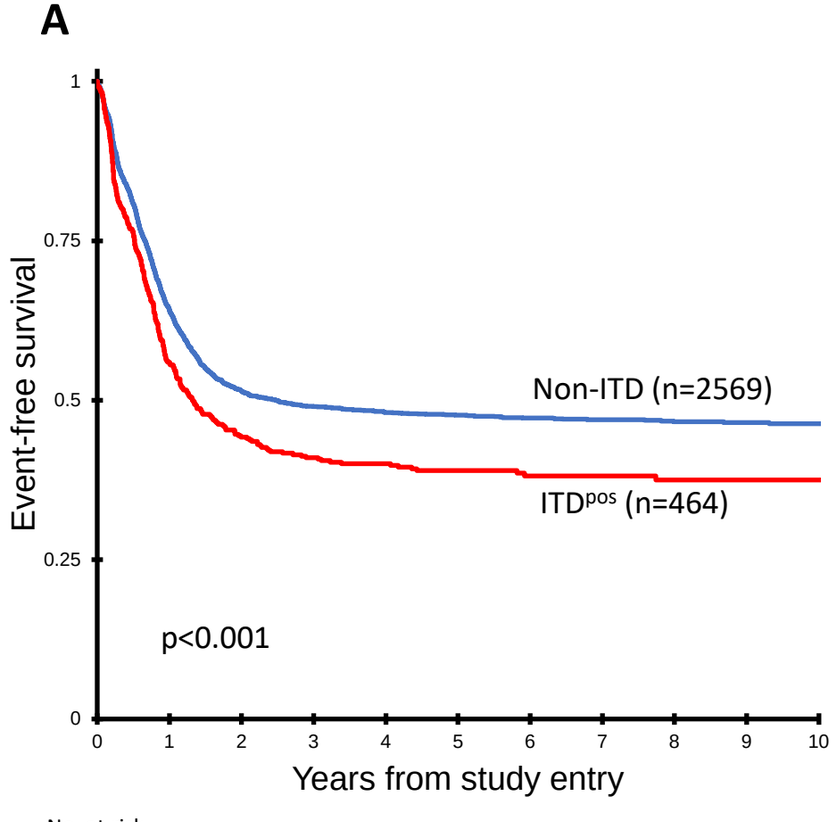
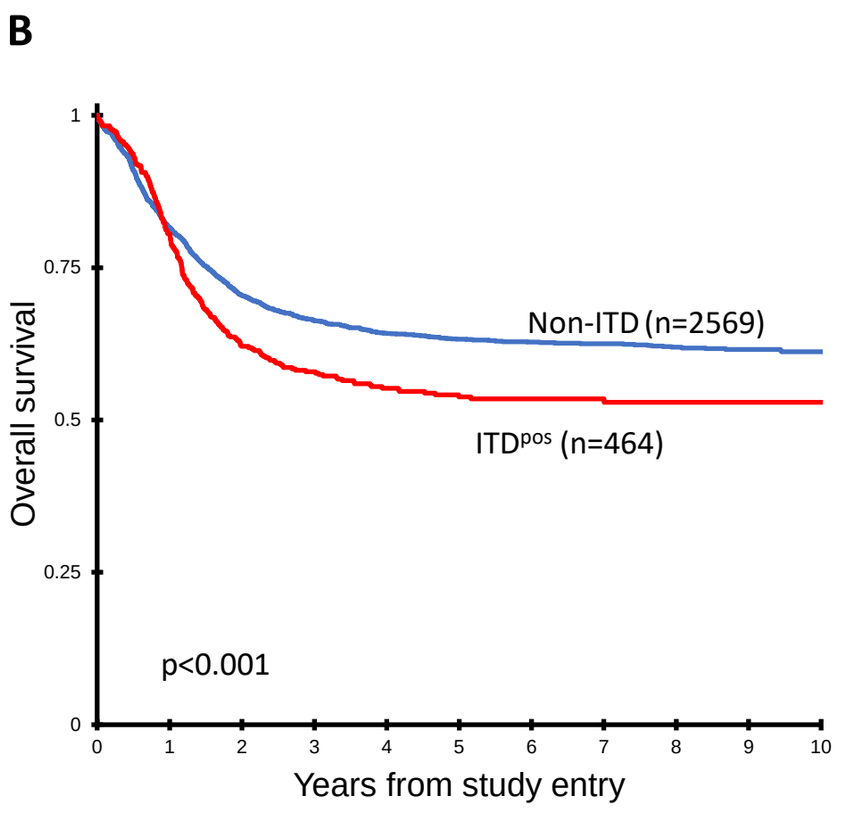
Supplemental Figure S1. UpSet plot of types of cytomolecular analyses utilized in characterizing the genomic landscape of FLT3-ITD positive cohort. Clinical mutations: single gene analysis used for clinical allocation in trials or performed retrospectively (*FLT3*-ITD, *NPM1, CEBPA, WT1, NUP98-NSD1, UBTF*), Karyotype: full karyotype, RNAseq: RNA sequencing, TCS: targeted capture sequencing, WGS: whole genome sequencing.



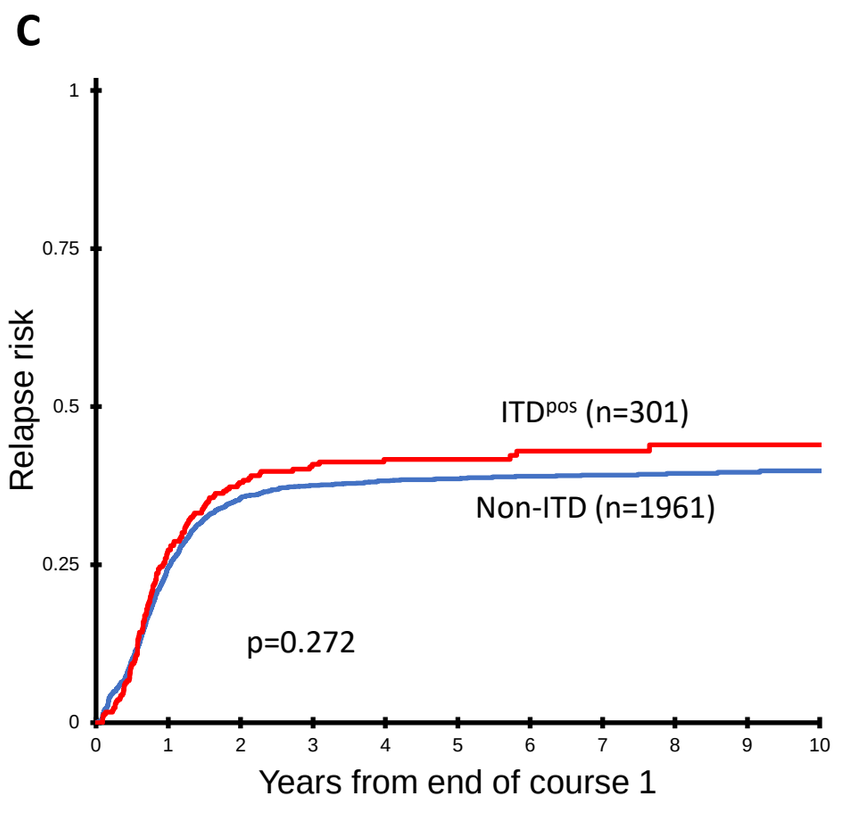
Supplemental Figure S2. Outcomes of ITD^{pos} vs non-ITD patients. (A) 5-year event-free survival, (B) overall survival, (C) relapse risk



No. at risk											
Year	0	1	2	3	4	5	6	7	8	9	10
Non-ITD	2569	1616	1263	1157	1088	960	768	591	426	297	226
FLT3-ITD	464	257	196	175	153	123	90	71	54	35	24

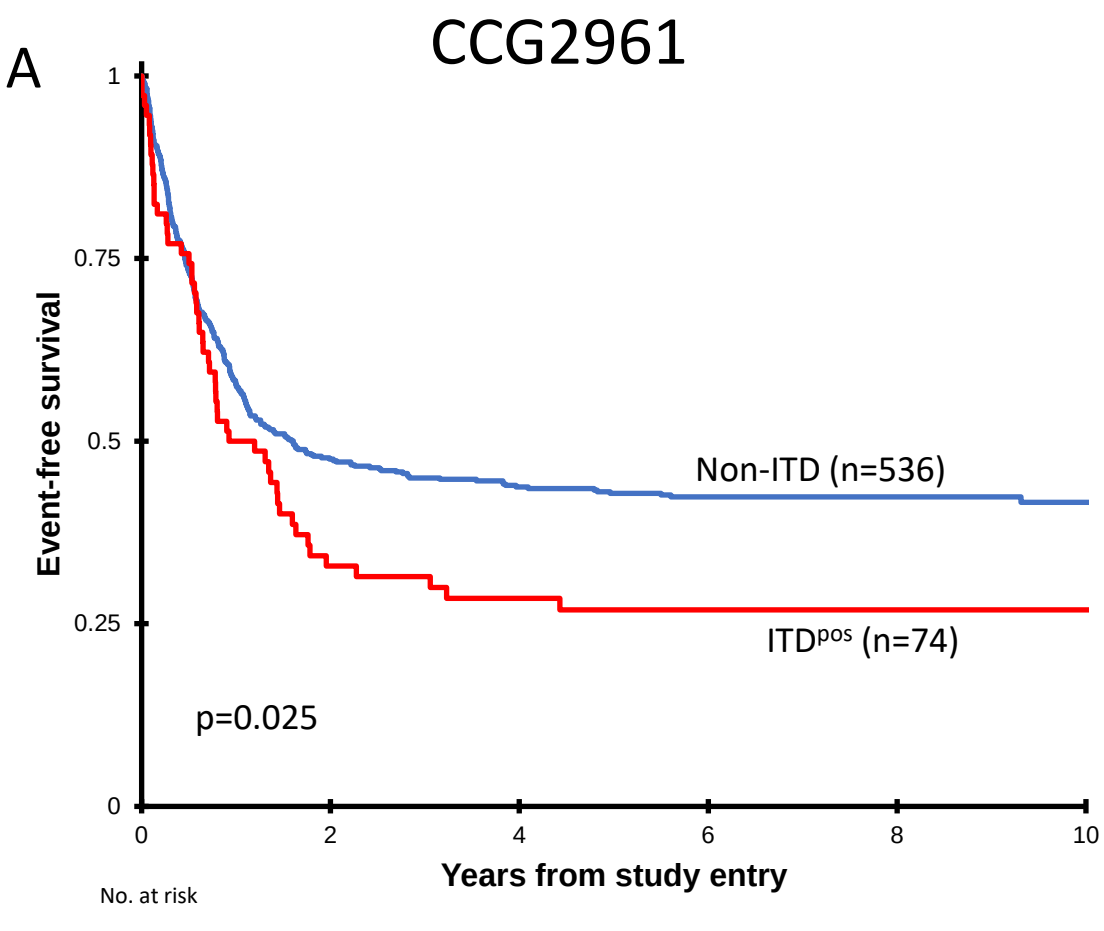


No. at risk											
Year	0	1	2	3	4	5	6	7	8	9	10
Non-ITD	2569	2045	1720	1558	1455	1282	1025	790	566	383	288
FLT3-ITD	464	367	273	245	212	169	125	99	78	51	35

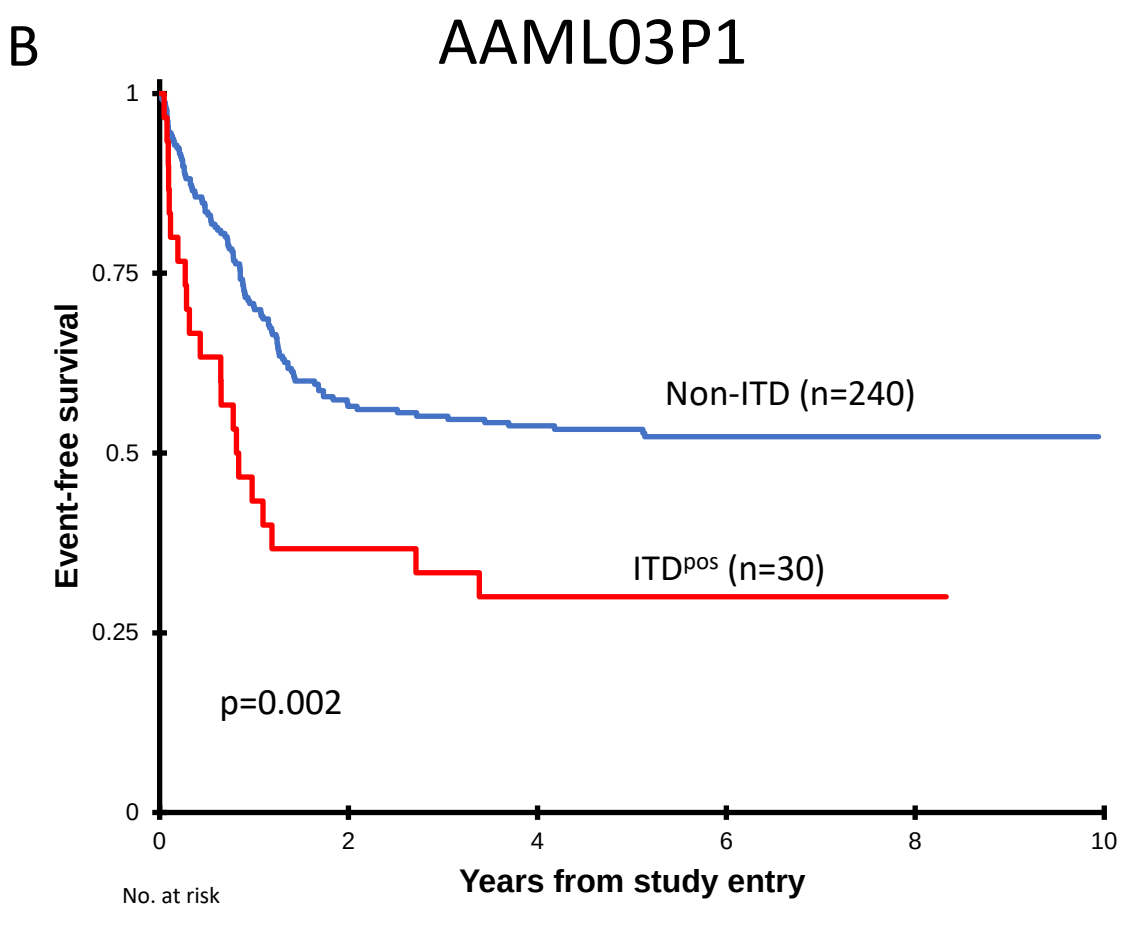


No. at risk											
Year	0	1	2	3	4	5	6	7	8	9	10
Non-ITD	1961	1323	1074	992	932	814	648	498	346	238	176
FLT3-ITD	301	197	155	140	123	99	71	58	43	29	20

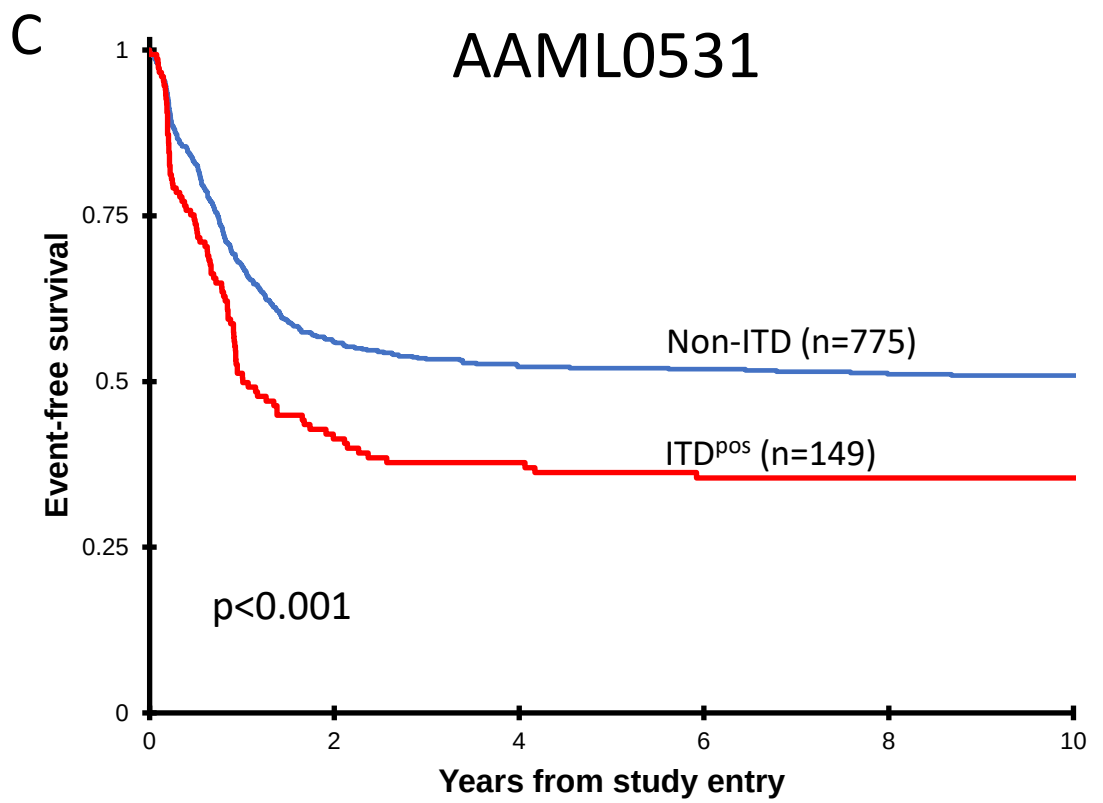
Supplemental Figure S3. Event-free survival of ITD^{pos} patients compared to non-ITD patients according to treatment trial. (A) CCG-2961, (B) AAML03P1, (C) AAML0531, (D) AAML1031.



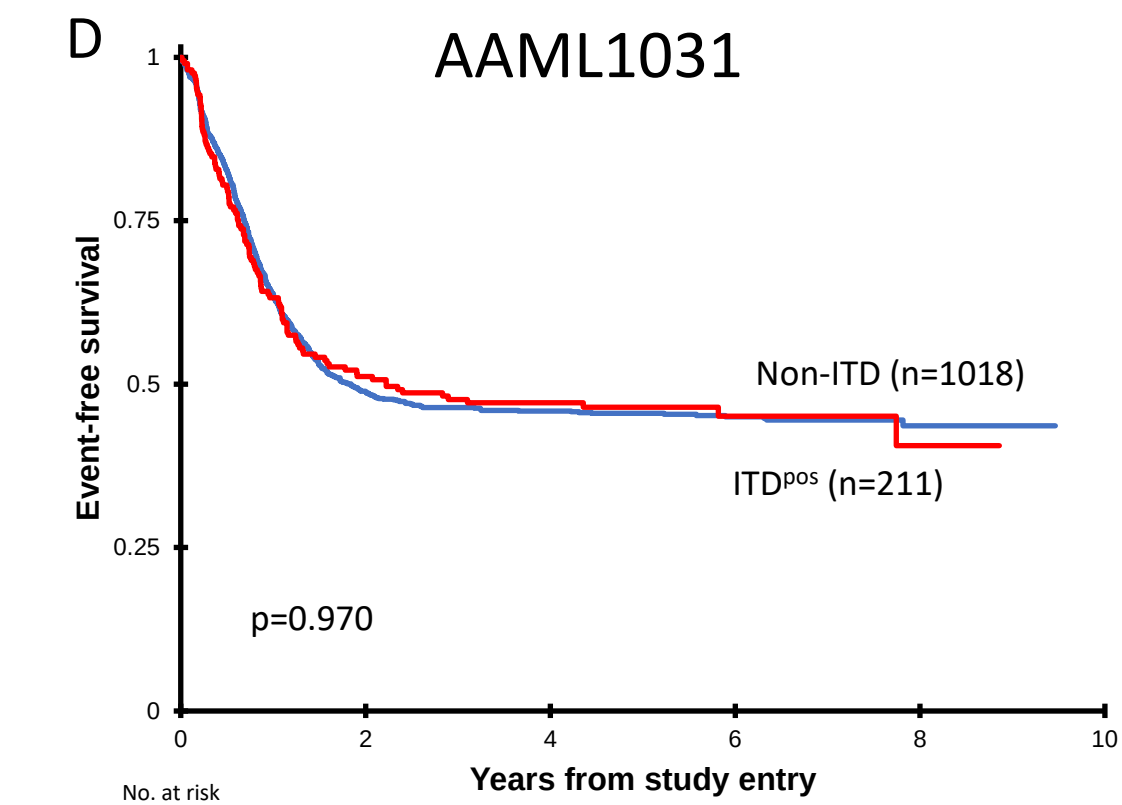
No. at risk											
Year	0	1	2	3	4	5	6	7	8	9	10
Non-ITD	536	306	246	223	210	192	167	122	84	61	38
ITD^{pos}	74	37	23	21	18	15	11	11	10	6	5



No. at risk											
Year	0	1	2	3	4	5	6	7	8	9	10
Non-ITD	240	164	128	120	117	103	86	80	53	8	0
ITD^{pos}	30	13	11	10	8	6	5	5	1	0	0

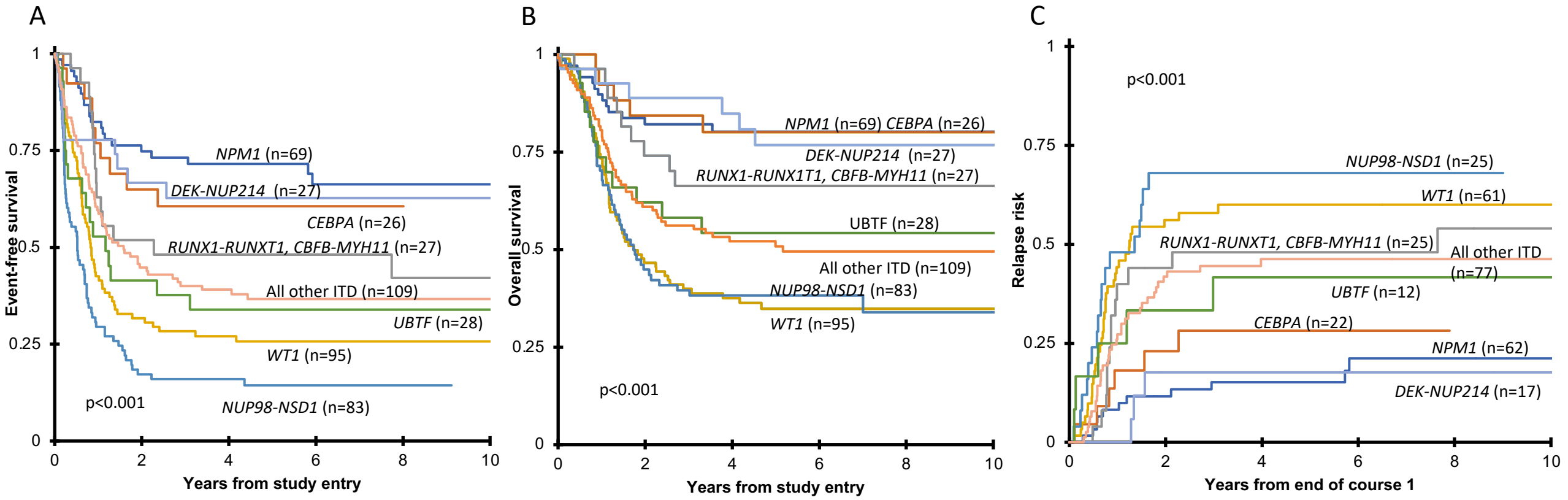


No. at risk											
Year	0	1	2	3	4	5	6	7	8	9	10
Non-ITD	775	510	419	382	351	332	303	271	249	224	188
ITD^{pos}	149	75	58	52	50	48	45	39	35	29	19

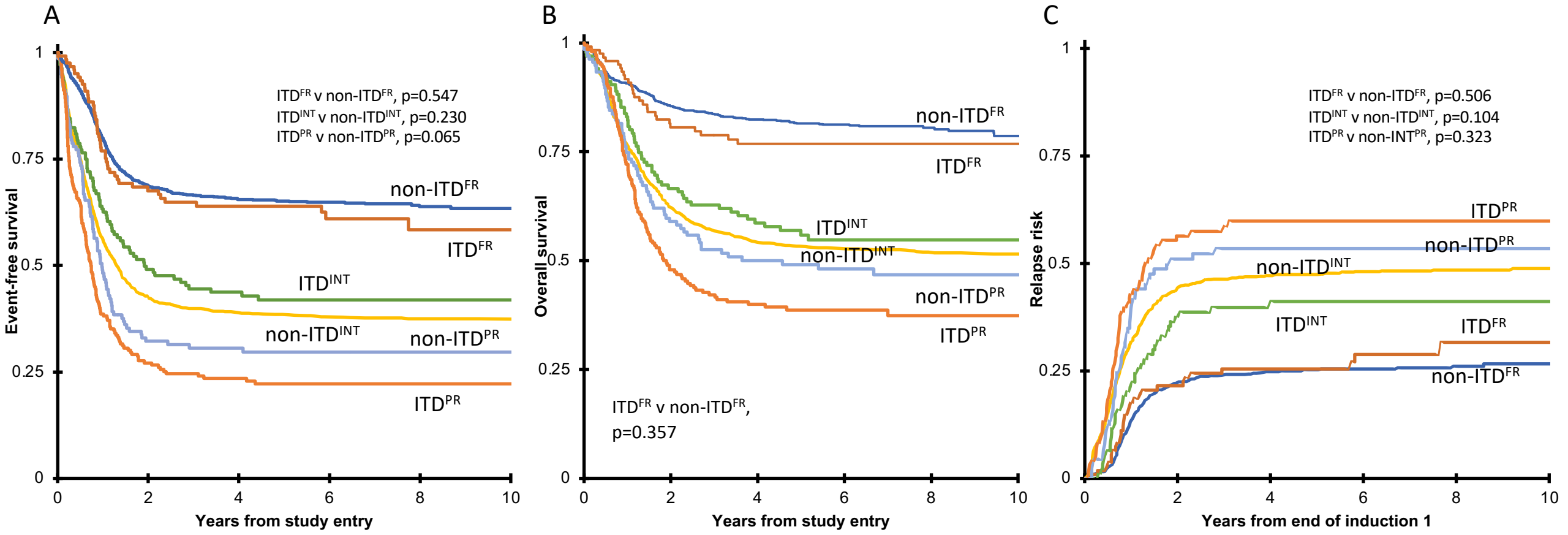


No. at risk											
Year	0	1	2	3	4	5	6	7	8	9	10
Non-ITD	1018	636	470	432	410	333	212	118	40	4	0
ITD^{pos}	211	132	104	92	77	54	29	16	8	0	0

Supplemental Figure S4. Outcomes of ITD^{pos} patients stratified by presence of co-occurring mutations. (A) 5-year event-free survival, (B) 5-year overall survival, (C) 5-year relapse risk.



Supplemental Figure S5. Outcomes for FLT3-ITD and non-FLT3-ITD patients according to co-occurring mutational risk groups, favorable (NPM1, CEBPA, RUNX1-RUNX1T1, CBFB-MYH11), intermediate (non favorable or poor), and poor (WT1, UBTF, NUP98-NSD1). (A) 5-year event-free survival, (B) 5-year overall survival, (C) 5-year relapse risk.



Supplemental Figure S6. Outcomes for ITD^{pos} patients treated Arm C of AAML1031 with sorafenib and HCT in CR1 according to co-occurring risk groups (FR, INT, and PR) and those with PR mutations further stratified according to presence of *NUP98::NSD1* fusion. (A) overall survival, (B) relapse risk.