Supplemental material for:

Hsi-Che Liu et al. **Children With Chronic Myeloid Leukemia Treated With Front-Line Imatinib Have A Slower Molecular Response And Comparable Survival Compared With Adults: A Multicenter Experience in Taiwan**

Supplemental Table 1. Molecular response at the time of 2nd generation tyrosine kinase inhibitors switch and the best molecular responses after 2nd generation tyrosine kinase inhibitors

	Molecular response at the time of 2G TKI switch		**Best molecular responses after2G TKI**		
Pediatric cohort	**IM response**	**No.**	**MMR**	**$MR^{4.0}$**	**$MR^{4.5}$**
	Failure	18	16 (89%)	11 (61%)	3 (17%)
	Warning	3	3 (100%)	1 (33%)	1 (33%)
	Optimal	3	3 (100%)	2 (67%)	2 (67%)
Adult cohort	**IM response**	**No.**	**MMR**	**$MR^{4.0}$**	**$MR^{4.5}$**
	Failure	209	145 (69%)	92 (44%)	66 (32%)
	Warning	28	28 (100%)	28 (100%)	10 (36%)
	Optimal	35	35 (100%)	33 (94%)	29 (83%)

2G, 2nd generation; IM, imatinib; MMR, major molecular response; $MR^{4.0}$, IS <0.01%; $MR^{4.5}$, IS <0.0032%; TKI, tyrosine kinase inhibitor.

Supplemental Table 2. Molecular responses according to *BCR::ABL1*^{IS} levels at 3 months after front-line imatinib

BCR::ABL1^{IS} at 3 months		No. (%)	IS <1% by 12 months % (95% CI)	MMR by 12 months % (95% CI)
Adult cohort*	≤10%	362 (48)	79.1 (74.5-83.7)	39.2 (35.4-43.0)
	>10%	389 (52)	40.4 (35.6-45.2)	14.5 (10.7-18.3)
	P		<0.0001	<0.0001
Pediatric cohort*	≤10%	27 (52)	65.4 (46.8-84.0)	30.8 (13.1-48.5)
	>10%	25 (48)	18.2 (2.1-34.3)	4.3 (0.0-12.6)
	P		0.002	0.008

CI, confident interval; MMR, major molecular response; IS, International Scale; OS, overall survival; PFS, progression-free survival.
*Patients who did not have data were not included in the analysis.

Supplemental Table 3. Molecular responses of Adult CML-CP treated with front-line imatinib according to Sokal score classification. (N =565*)

	***BCR::ABL1*^{IS} level at 3 months**			**Molecular response**		
	<1%	**1-10%**	**>10%**	**MMR**	**MR$^{4.0}$**	**MR$^{4.5}$**
LR, N =227 (40%)	54 (24%)	93 (41%)	80 (37%)	150 (66%)	107 (47%)	85 (37%)
IR, N =186 (33%)	35 (19%)	56 (30%)	95 (51%)	97 (52%)	76 (41%)	62 (33%)
HR, N =152 (27%)	20 (13%)	40 (26%)	92 (61%)	57 (38%)	44 (29%)	37 (24%)
P	0.036	0.006	<0.001	<0.001	0.002	0.027

HR, high risk; IM, imatinib; IR, intermediate risk; IS, International Scale; LR, low risk; MMR, major molecular response; MR$^{4.0}$, IS <0.01%; MR$^{4.5}$, IS <0.0032%.
*Patients who did not have data were excluded in the analysis.

Supplemental Table 4. Comparison of published multicenter studies of pediatric CML treated with front-line imatinib

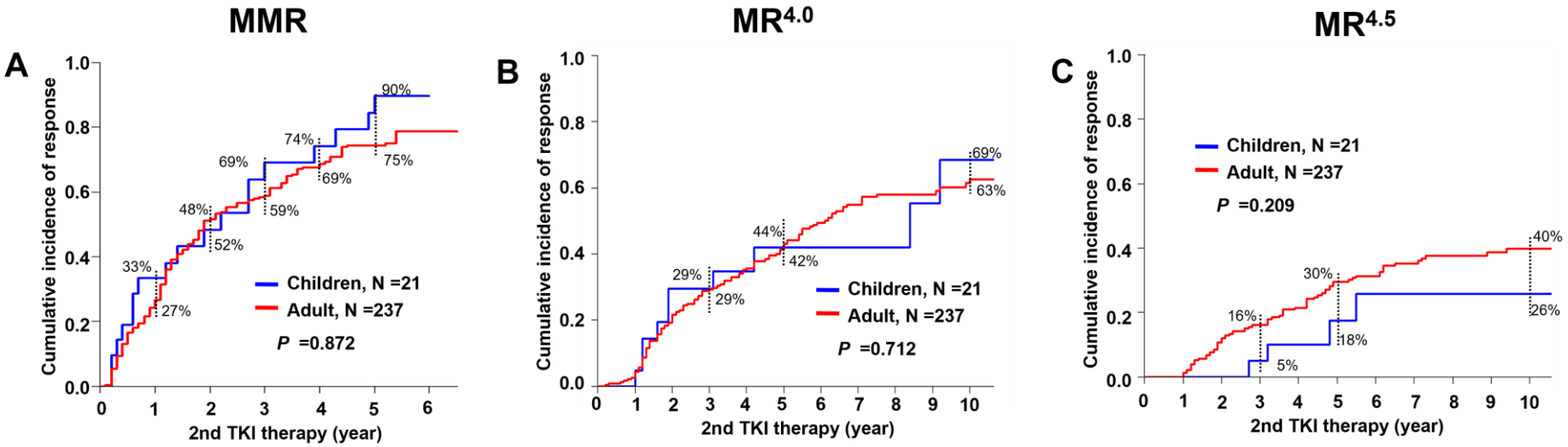
Author/Ref.	Study/ Country	Recruiting period	No. of patients	Median age (range)(y)	IM dosage (mg/m^2)	Median F/U duration (range)(mo)	Transcript e14/e13/e14 & e13/ND
Millot et al. [1]	France	2004-2008	44[a]	11.5 (0.8-17)	260 (188-403)	31 (11-64)	27/15/1/1
Giona et al. [2]	CML-Petit-01/Italy	2001-2013	47[b]	11.8 (2.8-17.9)	340	52 (3-146)	33/13/1/0
Janeczko-Czarnecka et al. [3]	Poland	2006-2016	57[c]	13.6 (1.2-17.9)	300 (220-468)	23.4 (ND)	ND
Suttorp et al. [4]	CML-PAED-II/ Germany, Czech, Netherlands, Italy, Denmark, Austria, Slovakia, Norway	2004-2015	140	13.2 (1.2-18)	260-300	25 (1-120)	68/52/14/6
Liu et al. [this study]	Taiwan	2004-2020	55	13.5 (1.4-17.9)	340 (205-340)	70.2 (3-166)	34/20/1/0

F/U, follow-up; IM, imatinib; ND, no available data.
[a]29 patients had previously received hydroxyurea.
[b]8 patients had previously received interferon.
[c]3 patients of accelerated phase were enrolled.

Supplementa1 Table 4. Comparison of published multicenter studies of pediatric CML treated with front-line imatinib (continued)

Author/Ref.	CCyR (%)		MMR (%)			OS	PFS
	6 mo	12 mo	12 mo	18 mo	24 mo		
Millot et al.[1]	46	61	31	55[d]	60[d]	ND	98% at 3 y
Giona et al.[2]	93	96	67	82[d]	82[d]	100%	60% at 8 y[e]
Janeczko-Czarnecka et al.[3]	ND	69	ND	61	ND	96%	ND
Suttorp et al.[4]	26	63	46	59	68	94% at 5 y	97% at 5 y
Liu et al. [this study]	17[f]	41[f]	19	26	34	100% at 5y	95% at 5 y

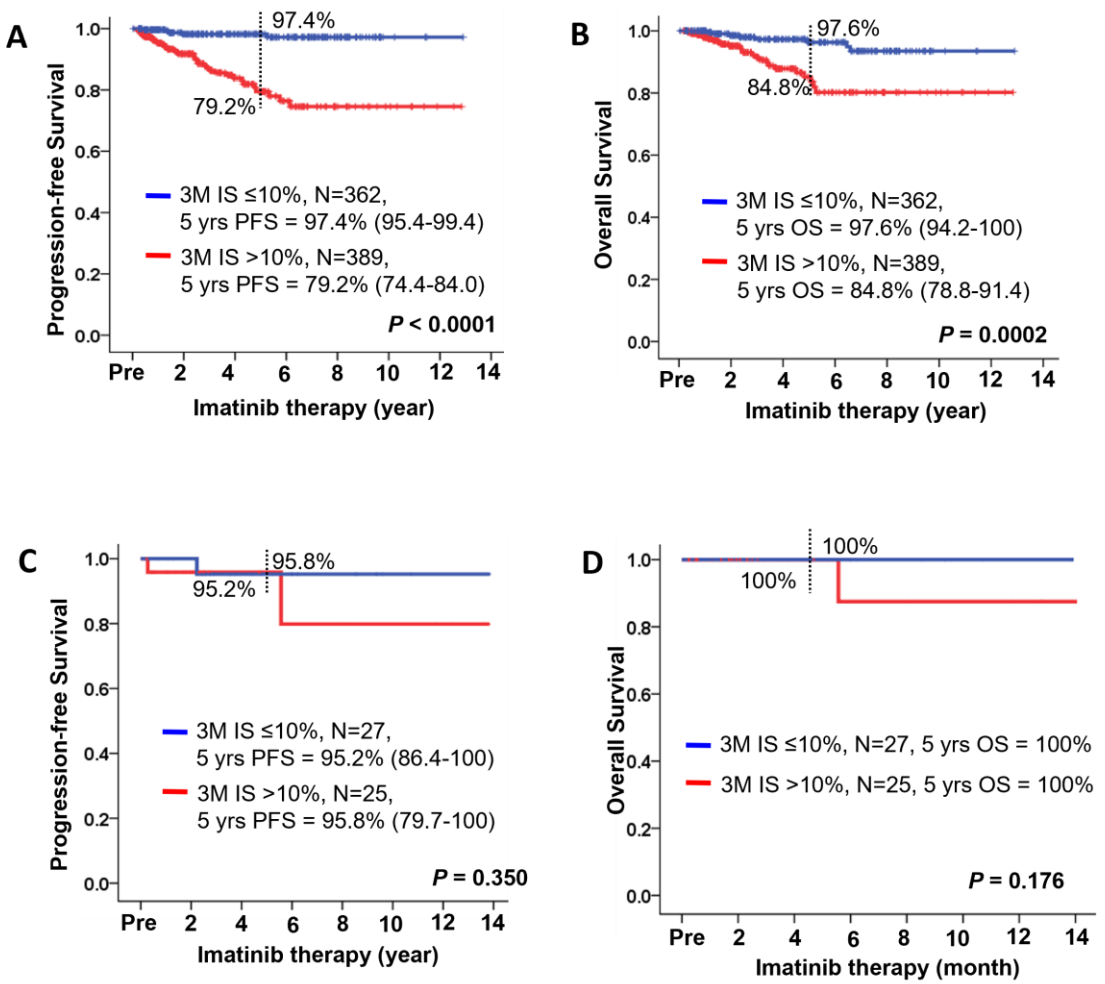
CCyR, complete cytogenetic response; IM, imatinib; MMR, major molecular response; ND, no available data; OS, overall survival; PFS, progression-free survival.
[d]Not indicated in the text of the paper, but interpolated from a figure presented.
[e]The data is for responding patients who continued IM.
[f]IS <1% in the current study.



Supplemental Figure 1. Cumulative incidences of MMR, $MR^{4.0}$ and $MR^{4.5}$ in pediatric (N =21*) and adult (N =237*) CML patients who switched to 2G TKI therapy. A). MMR; B). $MR^{4.0}$; C). $MR^{4.5}$.

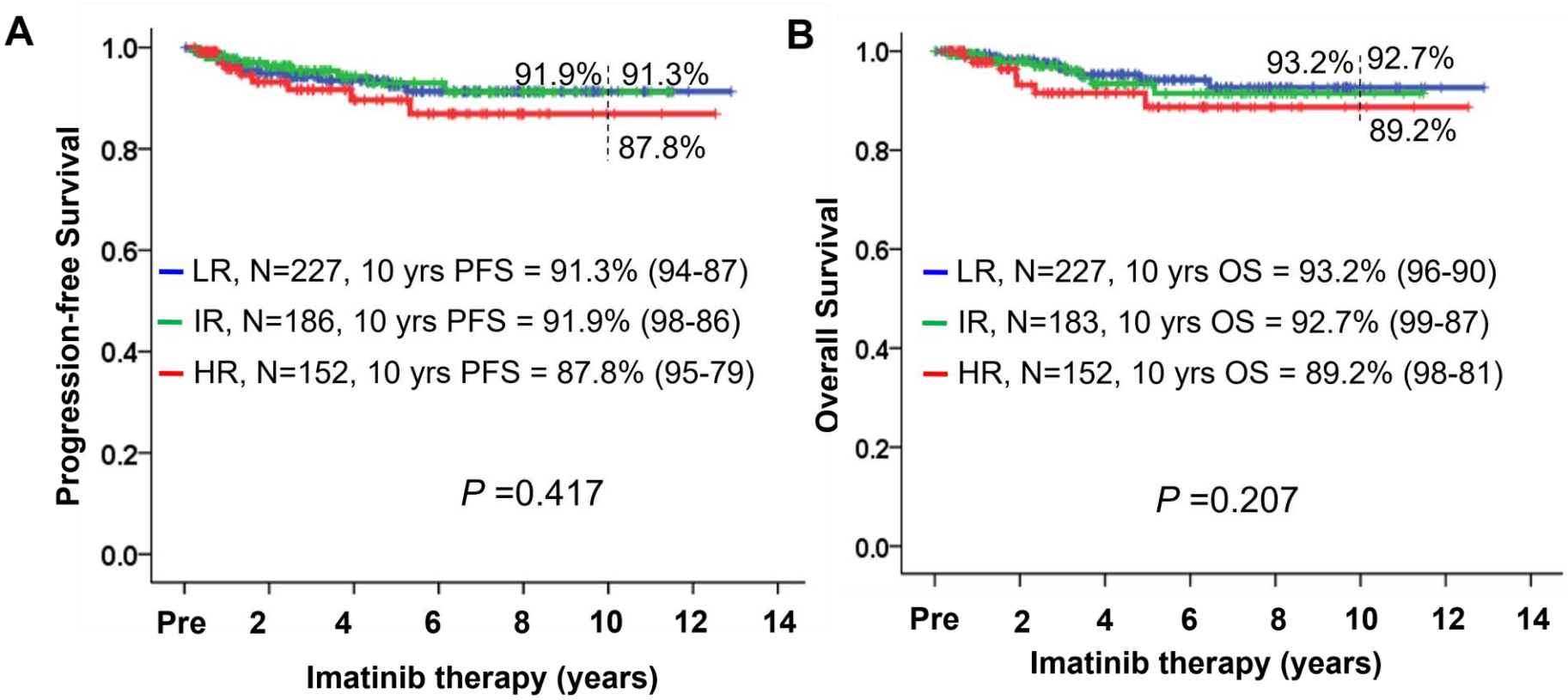
2G, 2nd generation; MMR, major molecular response; $MR^{4.0}$, International Scale (IS) <0.01%; $MR^{4.5}$, IS <0.0032%; TKI, tyrosine kinase inhibitor.

*Patients switched to 2G TKI due to failure or waring response of imatinib.



Supplemental Figure 2. Survivals according to *BCR::ABL1*^{IS} levels at 3 months after front-line imatinib
A and B: adult cohort (N =751*); C and D: pediatric cohort (N =52*)

The survivals are shown as mean (95% CI).
CI, confident interval; IS, International Scale; OS, overall survival; PFS, progression-free survival.
*Patients who did not have data were not included in the analysis.



Supplemental Figure 3. Survivals of Adult CML-CP treated with front-line imatinib according to Sokal score classification. (N =565*)

The survivals are shown as mean (95% CI).

CP, chronic phase; HR, high risk; IM, imatinib; IR, intermediate risk; IS, International Scale; LR, low risk; OS, overall survival; PFS, progression-free survival.

*Patients who did not have data were excluded in the analysis.

References

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3. Janeczko-Czarnecka M, Krawczuk-Rybak M, Karpinska-Derda I, Niedzwiecki M, Musiol K, Cwiklinska M, et al. Imatinib in the treatment of chronic myeloid leukemia in children and adolescents is effective and well tolerated: Report of the Polish Pediatric Study Group for the Treatment of Leukemias and Lymphomas. Adv Clin Exp Med. 2018;27(1):91-8.
4. Suttorp M, Schulze P, Glauche I, Gohring G, von Neuhoff N, Metzler M, et al. Front-line imatinib treatment in children and adolescents with chronic myeloid leukemia: results from a phase III trial. Leukemia. 2018;32(7):1657-69.