Supplementary Online Content

Ladas EJ, Sheng H, Athale UH, et al. Overweight or obesity and outcomes in children with acute lymphoblastic leukemia. *JAMA Netw Open.* 2025;8(X):e259952. doi:10.1001/jamanetworkopen.2025.9952

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. DFCI 05-001 Treatment Protocol[1]

Phase	Induction	Consolidation I	CNS	Consolidation II	Continuation
	All patients	**All patients**	**SR**	**SR#**	**All patients**
Treatment Details	*Steroid Prophase (Days 1-3):* Methlyprednisone 32 mg/m^2 IV divided three times daily, days 1-3 *Remission Induction Therapy (Days 4-32):* - Vincristine (VCR) 1·5 mg/m^2 IV once per week (maximum 2 mg), days 4, 11, 18, and 25 - Prednisone 40 mg/m^2 PO divided three times daily, days 4 to 32 - Doxorubicin (DOX) 30 mg/m^2 IV, days 4 and 5 - Methotrexate (MTX) 40 mg/m^2 IV push, day 6 - Pegasparaginase (IV-PEG) 2,500 IU/m^2 IV, day 7 *Intrathecals:* IT cytarabine dosed by age on day 0†; IT methotrexate/cytarabine/hydrocortisone (IT-MAH) dosed by age on day 18; IT-methotrexate (ITM) dosed by age on day 32	- VCR 2 mg/m^2 (maximum 2 mg) IV, day 1 - 6-mercaptopurine (6-MP) 50 mg/m^2 PO daily at bedtime, days 1-14 - ITM dosed by age, day 1‡ - High dose MTX 5 grams/m^2 IV over 24 hours on day 1, followed by Leucovorin rescue	- VCR 2 mg/m^2 (maximum 2 mg) IV, day 1 - 6-MP 50 mg/m^2 PO daily at bedtime, days 1-14 - DEX 18 mg/m^2 PO divided twice daily, days 1-5 - Start ASP according to randomization starting on day 1‡‡	Every 3-week cycles: - VCR 2 mg/m^2 (maximum 2 mg) IV, day 1 - 6-MP 50 mg/m^2 PO daily at bedtime, days 1-14 - DEX 6 mg/m^2 PO divided twice daily, days 1-5 - MTX 30 mg/m^2 IV push or IM weekly, days 1, 8, and 15 (Week 1 MTX omitted if IT-MAH given) - IT-MAH dosed by age every nine weeks for six doses and then every 18 weeks - ASP continued according to randomization‡‡	Every 3-week cycles: - VCR 2 mg/m^2 (maximum 2 mg) IV, day R - 6-MP 50 mg/m^2 PO daily at bedtime, days 1-14 - DEX 6 mg/m^2 PO divided twice daily, days 1-5 - MTX 30 mg/m^2 IV push or IM weekly, days 1, 8, and 15 (Week 1 MTX omitted if IT-MAH given) - IT-MAH dosed by age every 18 weeks
	Ph + ALL ††	**HR and VHR**	**HR and VHR**	**HR and VHR**	
Treatment Details	Imatinib 340 mg/m PO (maximum 600 mg) daily starting on day 18	Same as SR patients with the addition of: DOX 30 mg/m^2 IV on day 1 with dexrazoxane 300 mg/m^2 IV	Same as SR, except: - DOX 30 mg/m^2 IV on day 1 with dexrazoxane 300 mg/m^2 IV - DEX 18 mg/m^2 PO divided twice daily, days 1-5 - HR patients: Start ASP according to randomization starting on day 1‡‡	Every 3-week cycles, same as SR, except: - No weekly MTX - DOX 30 mg/m^2 IV on day 1 with dexrazoxane 300 mg/m^2 IV - Once cumulative DOX reaches 300 mg/m^2 IV, weekly MTX given as in the SR arm - DEX 18 mg/m^2 PO divided twice daily, days 1-5	

		VHR	**Cranial radiation**	**Cranial radiation**	
Treatment Details		In addition to above: Consolidation IB - Cyclophosphamide 1000 mg/m^2 IV over 1 hour, day 1 - Cytarabine 75 mg/m^2 IV push daily, days 2-5 and 9-12 - 6-MP 50 mg/m^2 PO daily at bedtime, days 1-14 - ITM dose by age, day 1 Consolidation IC - Cytarabine 2 grams/m^2 IV every 12 hours for a total of four doses starting on day 1 - Etoposide 100 mg/m^2 IV daily, days 3-5 - Dexamethasone (DEX) 18 mg/m^2 PO divided twice daily, days 1-5 (10 doses total) - Asparaginase (ASP) according to randomization, beginning on day 8‡‡	- None: All SR, HR B-ALL with presenting WBC < 100K/□1 and absence of CNS-3 - 12 Gy: CNS-1 or CNS-2 with any of the following: T-ALL, VHR group, or B-ALL with WBC ≥ 100K/□1 - 18 Gy: CNS-3 at diagnosis	- None: IT-MAH dosed by age every nine weeks for six doses, and then every 18 weeks - Prior cranial radiation: IT-MAH every 18 weeks	
				Consolidation II ends after 30 weeks of asparaginase therapy and cumulative DOX dose of 300 mg/m^2.	Treatment completed after 104 weeks of continuous complete remission.

[1]Adapted from Place AE, et al. *Lancet Oncology* November 6, 2015.
Abbreviation: IV: intravenous; PO: by mouth
† Patients with CNS leukemia at diagnosis (CNS-2 and CNS-3) received IT cytarabine two times per week until CSF clear of blast cells on three consecutive examinations.
†† Patients with Ph+ ALL continued to receive imatinib in combination with HR chemotherapy until they proceeded to stem cell transplant. These patients did not participate in asparaginase randomization and received IM-EC during post-induction therapy.
‡ ITM not administered if Day 32 ITM given within previous 72 hours
‡‡ IM-EC 25,000 IU/m^2/ dose IM x every week (30 consecutive doses total) or IV-PEG 2,500 IU/m^2/ dose IV every two weeks (15 consecutive doses total).
# SR patients who received fewer than 10 weeks of post-induction asparaginase due to toxicity were treated with three cycles of "HR" Consolidation II therapy, including additional doxorubicin (to cumulative dose 150 mg/m^2) and higher dose dexamethasone. No changes to treatment were made for HR/VHR patients who tolerated fewer than 10 weeks of post-induction asparaginase.

eTable 2. Prevalence of Weight Classification (BMI *z* Score) by Time Point*

	BMIz Status Study Entry (N/%)	**BMIz Status EOI (N/%)**	**BMIz Status CON (N/%)**	**BMIz Status EOT (N/%)**
Underweight/Normal	559 (70.5%)	367 (66.2%)[a]	452 (63.5%)[a]	369 (51.6%)[a]
Overweight	124 (15.6%)	84 (15.2%)[b]	126 (17.7%)[c]	160 (22.4%)
Obese	110 (13.9%)	103 (18.6)	134 (18.8%)[a]	186 (26.0%)[d]
Total	793	554	712	715

*Paired t-test were carried out to compare the mean BMIz scores at study entry with each of the following 3 time points. [a]$P < 0.001$; [b]$P < 0.01$; [c]$P < 0.03$; [d]$P < 0.02$

eTable 3. Association of Treatment-Related Toxicity With BMI *z* Score Classification at Diagnosis*

Outcome	**BMI Classification at Diagnosis***			
	Underweight/Normal N=559	Overweight N=124	Obese N=110	*P* value
Treatment-Related Toxicities**	322 (58%)	73 (59%)	67 (61%)	0.80

*Chi-squre tests for contingency table. **TRT includes children who developed either infection, pancreatitis, or thrombosis by EOT.

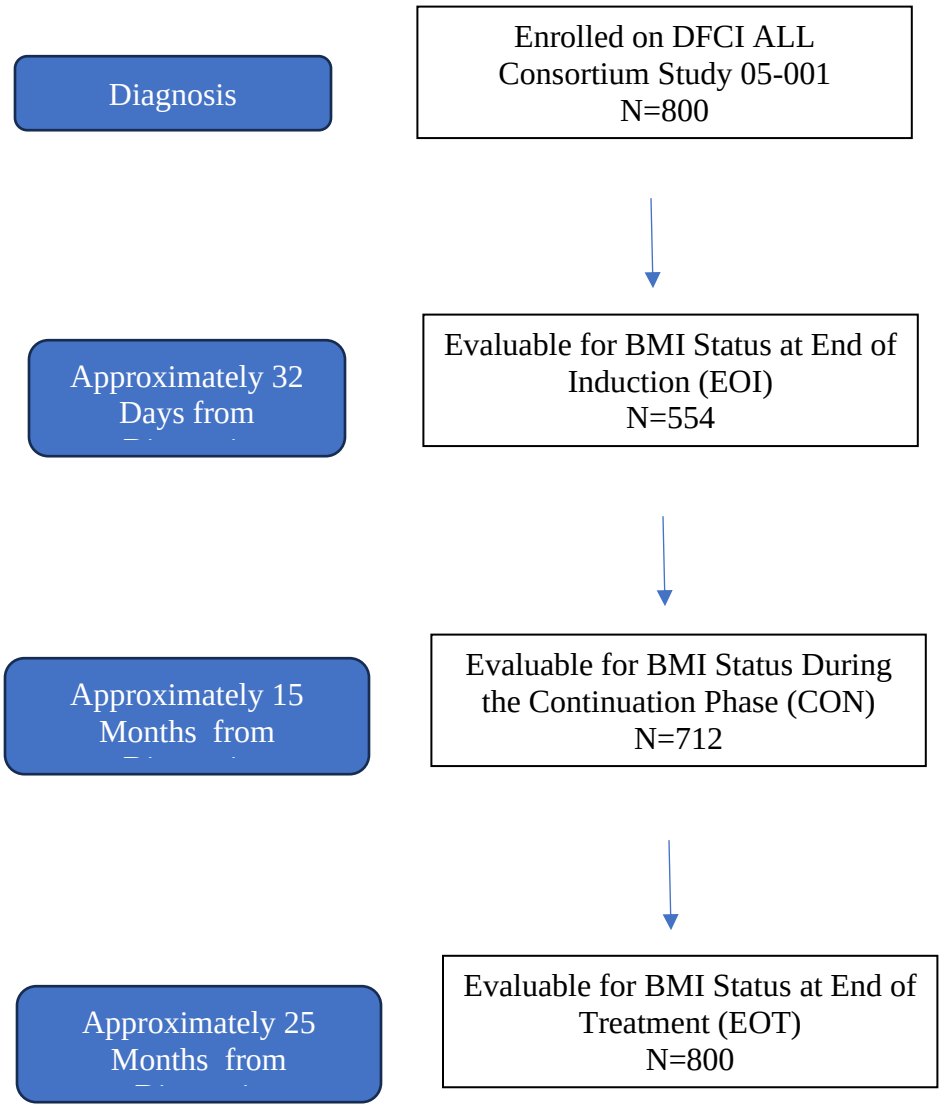
eTable 4. Overall Survival, Relapse-Free Survival, and Event-Free Survival Among Children With OW or OB on 2 or More Time Points From Diagnosis to EOT

Outcome	Hazard Ratio, 95% CI*	*P* value	Hazard Ratio, 95% CI**	*P* value
Overall survival	3.49 (1.28, 9.51)	0.01	3.42 (0.79-14.86)	0.10
Relapse-free survival	1.92 (1.07, 3.46)	0.03	2.15 (0.93-4.96)	0.07
Event-free survival	1.92 (1.08, 3.41)	0.03	2.42 (1.08-5.39)	0.03

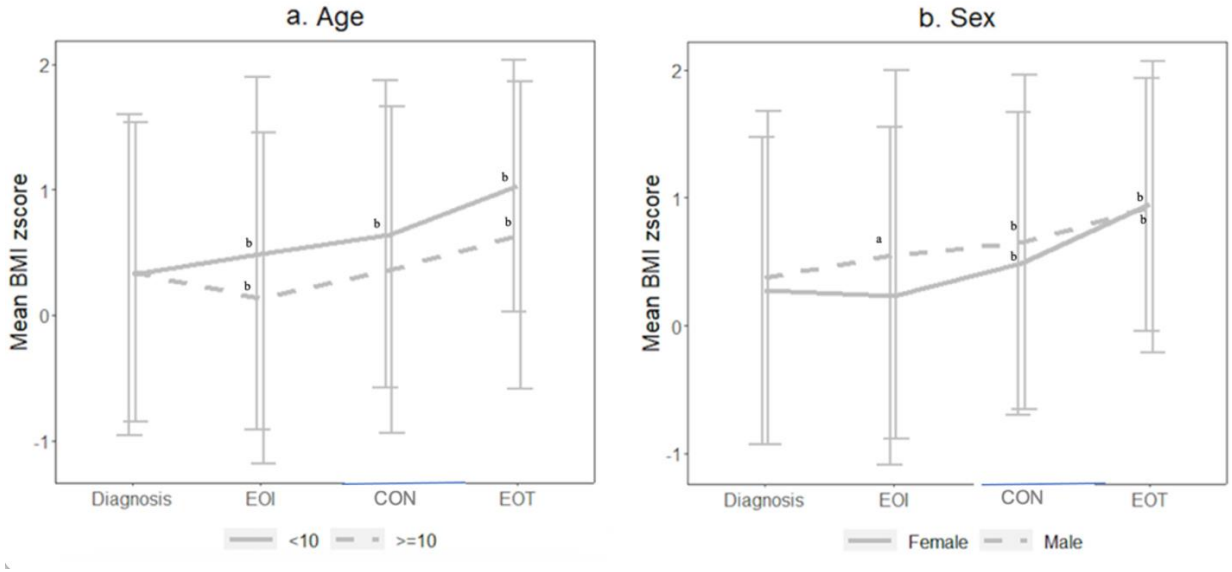
*Multivariable Cox model adjusted for final risk group, ethnicity, and sex; **Multivariable Cox model adjusted for final risk group, ethnicity, sex, and baseline BMI.

eFigure 1. STROBE Flow Chart

STROBE, Strengthening the Reporting of Observational Studies in Epidemiology.

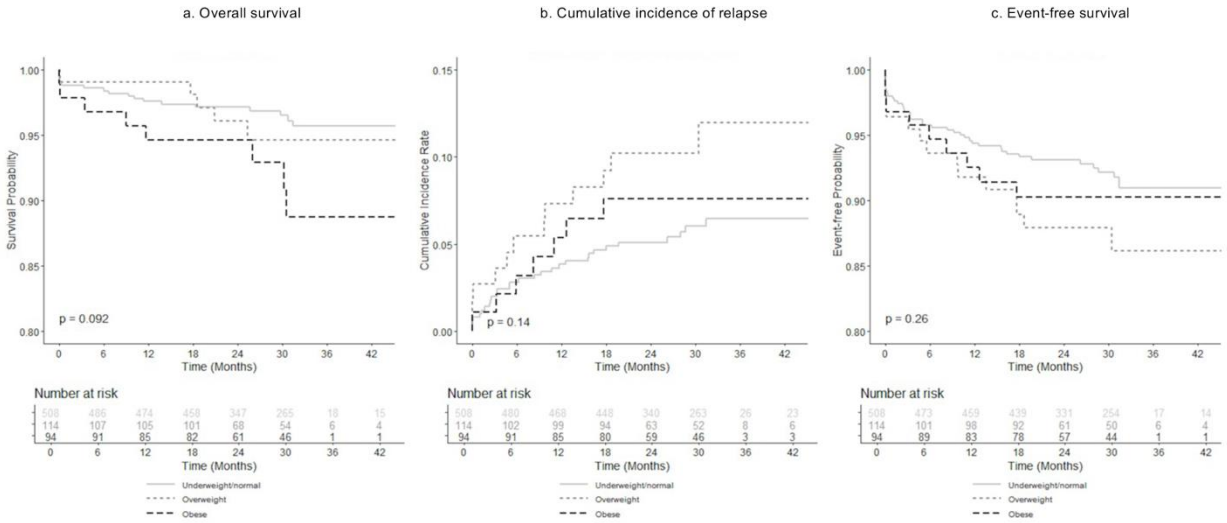


eFigure 2. Mean BMI *z* Score Trajectories From Diagnosis to EOT by Demographic and Clinical (ALL and Nutrition Status) Characteristics



*Paired t-test were carried out to compare the mean BMIz scores of dx with each of the following 3 timepoints, respectively. [a]$P \leq 0.05$; [b]$P < 0.001$

eFigure 3. Overall Survival, Cummulative Incidence of Relapse, and Event-Free Survival From EOT to Post Treatment by BMI *z* Score Classification at Diagnosis*



* Kaplan-Meier survival curves were generated comparing baseline BMI classification to overall survival, relapse, and event-free survival.