

Final height and body mass index in English and Italian adult survivors of childhood acute lymphoblastic leukemia (ALL) treated without cranial radiotherapy.

P. Bruzzi¹, A. Albanese², S. Nussey³, B. Predieri⁴, L. Iughetti⁴, A. Leiper⁵

¹Azienda Ospedaliera-Universitaria Policlinico, Paediatric Department, Modena, Italy; ²Royal Marsden Hospital, Paediatric Oncology Unit, Sutton, UK; ³St Georges Hospital, Endocrine Unit, London, UK; ⁴University of Modena & Reggio Emilia, Department of Medical and Surgical Sciences of Mothers, Children and Adults, Paediatric Unit, Modena, Italy; ⁵Great Ormond Street Hospital for Children, Haematology Unit, London, UK

INTRODUCTION

Adult survivors of childhood ALL treated with protocols including cranial radiotherapy (CRT) demonstrated a persistent increased body mass index (BMI) and a reduced final height (FH). To date, long-term data on growth in survivors exposed only to chemotherapy (CT) are only available from small numbers.

AIM OF THE STUDY

- To investigate the effect of CT alone on BMI and FH in an international and wide cohort of childhood ALL survivors.

Figure 1. Study Population



No differences were detected between excluded and included patients.

STUDY DESIGN, PATIENTS AND METHODS



- Collection of data:
 - Age
 - Height-SDS
 - BMI-SDS
 - WBC (first white blood cells) at: diagnosis of ALL (dT), at the end of treatment (eT) and FH

- Inclusion criteria:
 - Successful completion of CT (Italy: AIEOP ALL 87, 88, 91, 95 and 2000 protocols, UK: UKALL XI protocol)
 - Being in first remission
 - Achievement of FH

- Exclusion criteria:
 - Relapse
 - Exposure to CRT and/or bone marrow transplant
 - Presence of other diseases or therapies that could influence growth
 - Lack of data

- Height- and BMI-SDS were calculated for each value using age- and sex-matched population standards (www.who.org).
- Data were summarized using standard statistics (STATISTICA™ software, StatSoft Inc., Tulsa, OK, USA).
- Local Ethical Committees approved the protocol study.

RESULTS

1a. Demographic data of participants (see Figure 1)

	Ethnicity	Age dT (median ys; range)	Age eT (median ys; range)	Age FH (median ys; range)	Follow-up (mean ys; range)	MTX high dose iv / Dex
Females (F)	100% Caucasian (C)	5.1 (1.2 - 13.7)	7.1 (3 - 15.9)	17.1 (14 - 23.7)	12.0 (4.2 - 18.4)	100 / 100%
Males (M)	100% C	5.8 (1.3 - 12.8)	7.9 (3.2 - 14.9)	17.9 (14 - 23.9)	11.7 (4.6 - 16.6)	100 / 98%

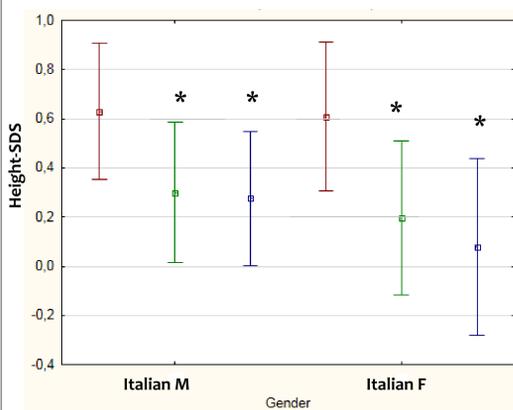
Legend: Dex: Dexamethasone exposure ≥ 250 mg/m²

1b. Demographic data of participants (see Figure 1)

	Ethnicity	Age dT (median ys; range)	Age eT (median ys; range)	Age FH (median ys; range)	Follow-up (mean ys; range)	MTX high dose iv / Dex
Females (F)	84% C 14% A 2% AA	3.8 (1.2 - 9.4)	5.8 (3 - 11.4)	17.1 (14.4 - 28)	13.3 (5.9 - 19.6)	54 / 45%
Males (M)	86% C 11% A 3% AA	3.69 (1.3 - 10.1)	5.6 (3.2 - 12.1)	17.6 (14.2 - 23.1)	13.4 (6 - 17.1)	39 / 38%

Legend: A: Asian; AA: Afro-Caribbean; Dex: Dexamethasone exposure 100 mg/m²

2a. Changes in Height-SDS over time



Albeit in an older cohort (than UK), the Italian data show:

- a reduction of Height-SDS in both sexes
- an increase in BMI-SDS during CT in both genders, but only girls maintain the increase at FH.

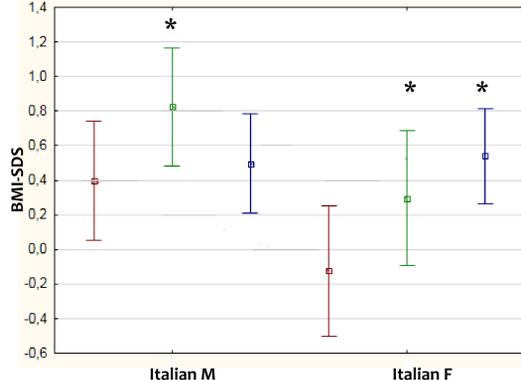
*Significant p-values versus dT.

4a. Significant Correlations

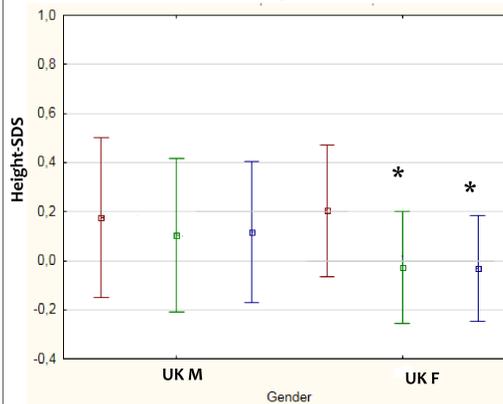
FH-SDS	r	p
Height-SDS dT	0.55	<0.0001
Height-SDS eT	0.49	<0.0001

Final BMI-SDS	r	p
BMI-SDS dT	0.41	<0.0001
BMI-SDS eT	0.47	<0.0001

3a. Changes in BMI-SDS over time



2b. Changes in Height-SDS over time



UK data show:

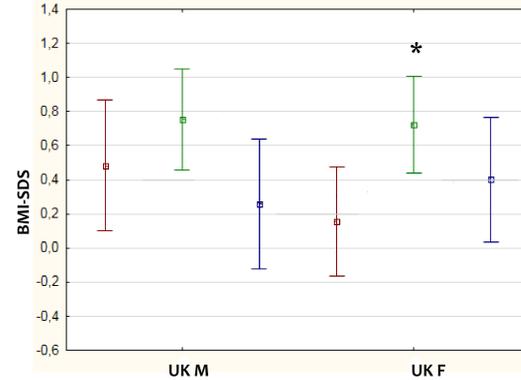
- an enduring effect on Height-SDS in girls but the effect on BMI-SDS during CT is lost by the time FH is reached.
- In boys, there is no effect on either Height-SDS or BMI-SDS.

4b. Significant Correlations

FH-SDS	r	p
Age dT	0.18	0.045
Height-SDS dT	0.62	<0.0001
Height-SDS eT	0.77	<0.001

Final BMI-SDS	r	p
BMI-SDS dT	0.40	<0.0001
BMI-SDS eT	0.62	<0.0001
WBC dT	0.21	0.022

3b. Changes in BMI-SDS over time



CONCLUSIONS

- Italian AIEOP protocols reduce Height-SDS in both sexes. They are associated with an increase in BMI-SDS at the end of CT. Only Italian girls show an increased final BMI-SDS.
- UKALL XI reduces Height-SDS in girls but not in boys. It has no effect on BMI-SDS in either sex at FH.
- Previous data on UKALL 97 (no CRT) showed an adverse effect on BMI-SDS of girls but not boys at FH (Harper RLC et al. BJH 2013; 163:510-513). UKALL 97 differs from UKALL XI in randomizing dexamethasone at induction (with mercaptopurine/thioguanine). As the Italian protocols all contain more dexamethasone than UKALL XI, exposure to high doses of this glucocorticoid might contribute to changes in BMI of female survivors of childhood ALL. However, the effect of high-dose methotrexate cannot be excluded.