EFFECTS OF CHEMOTHERAPY DOSE REDUCTIONS IN OVERWEIGHT AND OBESE PATIENTS WITH ACUTE MYELOID LEUKEMIA – A DANISH NATIONWIDE COHORT STUDY

Daniel Kristensen [1,2], Lars Børty Nielsen [1,2], Lasse Hjort Jakobsen [1,3], Tove-Christina Choe Kristensen [1], Tarec Christoffer El-Galaly [1,2], Anne Stidsholt Roug [1,2,4], Marianne Tang Severinsen [1,2]

1) Department of Hematology, Clinical Cancer Research Center, Aalborg University Hospital, 2) Department of Clinical Medicine, Aalborg University, 3) Department of Mathematical Sciences, Aalborg University, 4) Department of Hematology, Aarhus University Hospital

CLINDA

REGION NORDJYLLAND
– i gode hænder

Acute Myeloid Leukemia (AML)

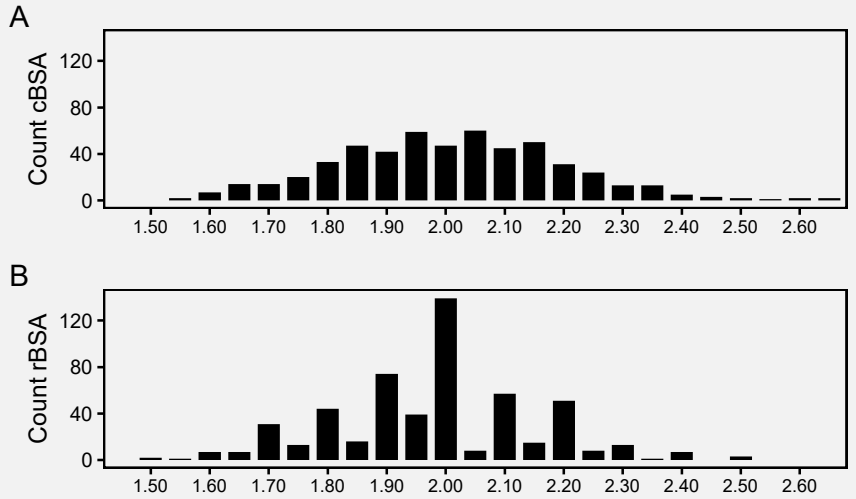
- Aggressive hematological malignancy
- Achieving complete remission and potentially long-term cure rely on the ability to tolerate toxic intensive induction therapy
- Overweight patients frequently receive dose reduction (DR) of chemotherapy, relative to weight-based doses
- Evidence regarding dose reduction in AML is limited

We utilized the Danish National Acute Leukemia Registry to conduct a retrospective cohort study

Overweight (BMI ≥ 25) AML patients aged 18 - 75 years and treated between 2000 - 2012 were included

We defined dose-reduction as ≤ 95% of actual BSA-based induction chemotherapy dose

Complete remission rates, and 30/90-day mortality were modeled, and OS and RFS were compared using 5-year restricted mean survival time difference (Δ5y-RMST)



$$BSA_{DuBois} = \sqrt{\frac{cm \cdot kg}{3600}}$$

Variable	Stratification	N	Relative risk of DR	Estimate (95%CI)	P-value
Sex	Female	227		Reference	
	Male	309		1.74 (0.97, 3.13)	0.062
Age	18-59	281		Reference	
	60-75	255		1.02 (0.60, 1.75)	0.933
Body Mass Index	25-29.9	369		Reference	
	30-34.9	113		2.52 (1.34, 4.75)	0.004
	>= 35	54		4.66 (2.42, 8.98)	<0.001
Body Surface Area	< 2.0	264		Reference	
	2.0-2.2	191		4.61 (1.85, 11.47)	0.001
	>= 2.2	81		15.21 (6.30, 36.73)	<0.001
WHO performance	0-1	445		Reference	
	2-4	91		0.85 (0.40, 1.80)	0.672
Smoking status	Never-smoker	200		Reference	
	Ever-smoker	250		1.08 (0.61, 1.93)	0.794
No. of Comorbidities	0	308		Reference	
	1	114		1.54 (0.84, 2.85)	0.166
	2+	79		1.39 (0.68, 2.87)	0.369
AML subtype	De novo AML	433		Reference	
	sAML	83		1.51 (0.77, 2.95)	0.229
	tAML	20		2.85 (1.12, 7.24)	0.028
Cytogenetic	Intermediate risk	355		Reference	
	Adverse risk	80		1.15 (0.53, 2.49)	0.732
	Favorable risk	52		2.20 (1.08, 4.49)	0.030

Results

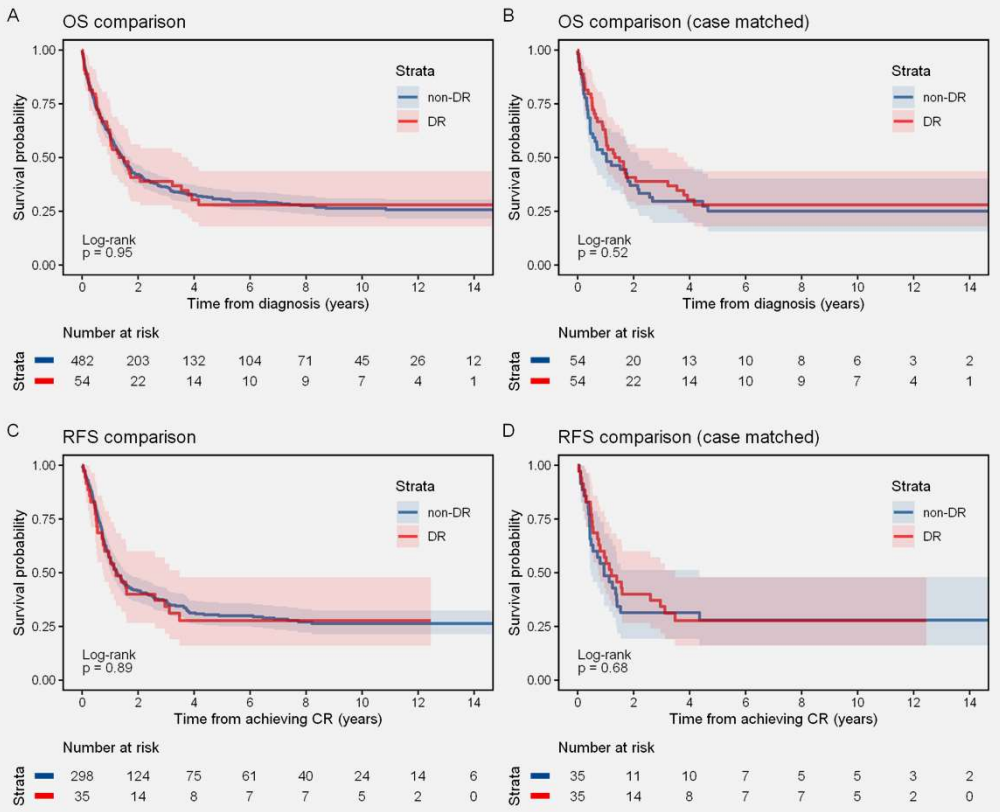
- The study cohort included 536 overweight AML-patients of whom 54 patients (10.1%) were categorized as DR (mean reduction 11.2%)
- We found no significant differences for rates of CR, 30- and 90-day mortality between patients receiving DR and non-DR chemotherapy
- Dose reduction did not affect:

median OS	DR	17.0 [11.9-45.5] months
	non-DR	17.5 [14.8-20.5] months
median RFS	DR	14.5 [9.0-41.7] months
	non-DR	15.0 [12.3-19.3] months

- Sensitivity analyses using a case-matched cohort and ≤90% cut-off to define DR led to the same conclusions

Discussion

- Our results suggest that IC dose reduction (using ≤ 95/90% threshold) does not adversely impact AML outcomes including 30- and 90-day mortality, rates of CR, RFS and OS
- What degree of reductions worsens outcomes? Difficult question as detecting small differences require many patients



		Total cohort (n = 536)						Case-matched cohort (n = 108)		
Outcome	**Strata**	**n/events/%**	**RR (95% CI)**	**P**	**n/events/%**	**aRR#**	**P**	**n/events/%**	**RR**	**P**
30-day mortality	Non-DR	482/43/8.9	ref.	-	401/37/9.2	ref.	-	54/6/11.1	ref.	-
	DR	54/7/13.0	1.45 (0.60-3.03)	.36	47/6/12.8	1.24 (0.42-3.11)	.67	54/7/13.0	1.17 (0.39-3.62)	.78
90-day mortality	Non-DR	482/77/16.0	ref.	-	401/66/16.5	ref.	-	54/11/20.4	ref.	-
	DR	54/11/20.4	1.28 (0.64-2.29)	.45	47/9/19.1	1.11 (0.48-2.28)	.79	54/11/20.4	1.00 (0.43-2.33)	1.0
CR*	Non-DR	482/298/61.8	ref.	-	401/254/63.3	ref.	-	54/34/63.0	ref.	-
	DR	54/35/64.8	1.05 (0.73-1.47)	.79	47/30/63.8	1.04 (0.68-1.55)	.84	54/35/64.8	1.03 (0.64-1.65)	.90

Acknowledgements

Everyone who has participated in forming and collecting data for The Danish Acute Leukemia Registry (DNLR) and this study