

14th Annual Congress of the European Haematology Association

GOOD GENERAL MEDICAL CONDITION IN LONG TERM SURVIVORS OF ADULT ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) BUT MORE HEALTH IMPAIRMENT IN OLDER PATIENTS AND PATIENTS AFTER STEM CELL TRANSPLANTATION (SCT): RESULTS OF A SYSTEMATIC ANALYSIS OF GMALL STUDIES

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Since 1981 the majority of adult pts with ALL in Germany was treated in 7 consecutive trials of the German Multicenter Study Group for Adult ALL (GMALL). Survival was step-wise improved to 50% in the most recent trial with an increasing number of long-term survivors. However so far there is no published evidence about health status and/or late effects in survivors of adult ALL. Therefore the GMALL initiated a retrospective analysis of pts from studies 2/84 - 6/99 alive more than 5 yrs after diagnosis. The questionnaire covered 8 organ systems and 1 category of "specific syndromes", known as potential late-effects of chemotherapy and was directed to treating physicians. It was intended to assess all diseases, appearing after end of therapy. 402 questionnaires were evaluable. Median age at diagnosis was 29 (15-64) years; median observation time was 10 yrs. Pts were included in GMALL-study 2/84 (10%), 3/87 (4%), 4/89 (15%), 5/93 (46%) and 6/99 (25%). 24% had received SCT (4% auto, 20% allo). In 94% of the pts the ECOG status was 0/1 (72/22%); 6% had ECOG 2-4. In 33% of the pts no disease was reported (table 1). 67% presented a disease in \geq one organ system; most frequently endocrinium (e.g. infertility, diabetes, osteoporosis), neurologic system (e.g. mood alteration, polyneuropathy, concentration) and skin (e.g. alopecia, erythema); cardiovascular diseases consisted mainly of hypertension; only 2 pts had heart failure. The most frequently documented category was "specific syndromes" in 39%. Infections, fatigue and osteonecrosis were the most frequent ones. GVHD/sicca syndrome was observed in 10% of all pts and in 44% of SCT pts. Favourable ECOG (0-1) was significantly more often observed in chemo vs SCT pts (97% vs 86%; $p=0.0003$). More pts with chemo had no disease compared to SCT pts (40% vs 9%; $p<0.0001$). All organ systems were more often involved in SCT pts. They also had more fatigue ($p=0.01$), and infections ($p<0.0001$). Age was associated with poorer ECOG too. 97% of the pts with diagnosis in adolescent age (15-25 yrs) had ECOG 0-1 compared to 81% in pts > 55 yrs. Fertility was evaluated by a patient-questionnaire (N=487). 58% of the pts (70% of chemo vs 21% of SCT pts; $p<0.0001$) with desire to have children could realise this wish (medical intervention in 21%). This so far largest data set of medical conditions and late effects of long-term survivors after adult ALL shows favourable results. The observed diseases had only in part a potential correlation to previous ALL therapy (e.g. GVHD, sec. malignancies, osteonecrosis, neurologic diseases). Compared to childhood ALL, the rate of late effects is remarkably low. The impaired health status in pts with SCT compared to chemo underlines that indications for SCT should be made carefully in high-risk patients only. Aftercare should consider specifically the most frequent late-effects i.e. osteonecrosis, fatigue, endocrinology and fertility. These may be cumbersome in individual pts. There is a trend towards more pronounced late effects in the most recent trial with intensified therapy. Therefore the analysis will be carried on. Supported by Deutsche-José-Carreras-Stiftung DJCLS-R05/09.

Table1: Most frequently involved organs/syndromes in long-term survivors of adult ALL

Patients	N=402	%
No diseases	132	33
Organ systems with pathologic findings	270	67
Neurologic system	110	27
Endocrinium (male)	56	22
Endocrinium (female)	45	30
Skin and mukosa	59	15
Lung	22	5
Kidney and liver	36	9
Cardiovascular system	61	15
Stomach and gut	21	5
Eye	37	9
Specific Syndromes	158	39
Infections within last 12 months	51	13
Fatigue	45	11
Graft versus host disease / sicca syndrome	42	10
Osteonecrosis	32	9
Secondary malignancies	19	5
Hyperthyreosis	14	4
Hypothyreosis	5	1