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Overall vs. Tumour-related Survival in Multiple Myeloma

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IN THIS journal we have published results of a prospective randomised trial testing MP vs. VCMP induction therapy, and chemotherapy maintenance vs. no maintenance in multiple myeloma (MM) [1]. The admittance of patients has been stopped in 1986, after 320 stage II and III MM patients were collected. Now follow-up data enable us to verify previous results and to analyse prognostic factors for survival.

The survival of stage II and III patients was 60% at 48 months and was significantly better in MP-treated than in VCMP-treated patients ($P<0.02$). This previous analysis [1] was based on tumour related survival (TRS); at that point, death had occurred in 22 cases of the MP group and in 37 cases of the VCMP group. Although this definition of survival permitted us to calculate the correct risk of MM, a comparison with other trials has been difficult, as in most other studies overall survival (OAS) was estimated, i.e. tumour related and tumour unrelated deaths were not counted separately.

By 1990, 115 deaths had occurred. 84 causes of death (group A) were related to MM, i.e. infection ($n=18$), hypercalcaemia (11), bleeding due to thrombopenia (5), kidney failure (13), hyperviscosity (2), perforation of the gut due to amyloidosis (1), secondary leukaemia (1), suicide (1) or other tumour related reasons (32). 22 patients (group B) have clearly died from disorders other than MM, i.e. heart disease (10), seizures (2), carcinoma (2), pulmonary embolism (1), accident (1) or other non-MM related diseases (6). In 9 further patients (group C) no definite information was available about cause of death.

These data permit the calculation of 3 different types of survival. Applying the Kaplan–Meier method [2] data from all 320 patients were used to estimate OAS. For measuring TRS, data from all except group C patients were used for analysis, and the survival times of group B patients were handled as censored data. For measuring natural survival (NS) probability in the trial's population (median age 62 years) data from all except group C patients were used, and the survival data of group A patients were handled as censored data.

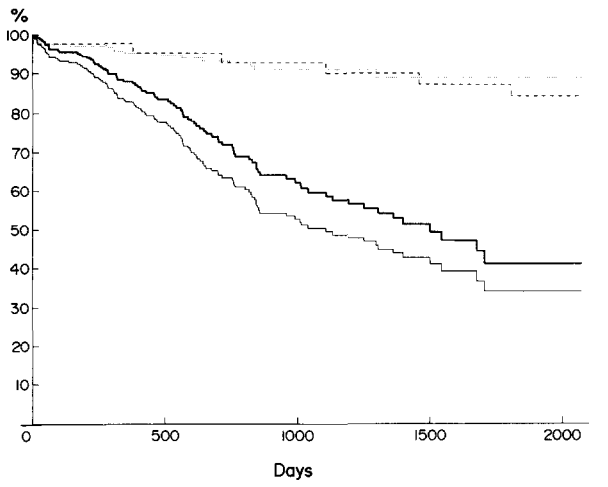

Fig. 1. Overall survival (OAS,——), tumour related survival (TRS,—), non-tumour related (natural) survival (NS, ·····) estimated in 320 multiple myeloma patients compared to survival of an age and sex matched control group (NS control, ------).

Results are shown in Fig. 1. The 50% OAS probability (1120 days) was found to be 1 year shorter than the 50% TRS probability (1500 days). The NS probability (90% at 1450 days) equalled the ageing public. This was proved by calculating the survival of an age and sex matched control group (NS control) using epidemiological data for Germany [3]; NS and NS control curves are congruent (Fig. 1).

Additional support for the reliability of these data comes from a statistical analysis of prognostic factors, where univariate analysis revealed age at diagnosis to be a significant prognostic factor (i.e. older patients have a shorter survival time) if OAS was used as the end point. However, age became irrelevant when OAS was replaced by TRS.

OAS has been demonstrated to be a useful indicator for prognosis in tumours and other diseases of younger and middle-aged patients. However, its significance appears to be limited in malignant diseases of ageing people, where OAS is influenced by the natural mortality rate. Therefore, unless a careful analysis of the causes of death is performed for each case, in trials studying older patients an adjustment for age appears necessary in order to obtain a realistic estimate of disease-related risk, which is an indispensable basis for planning of individual therapy strategies.

1. Peest D, Deicher H, Coldewey R, Schmoll H-J, Schedel I. Induction and maintenance therapy in multiple myeloma: a multicenter trial MP versus VCMP. *Eur J Cancer Clin Oncol* 1988, **24**, 1061–1067.
2. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Statist Assoc* 1958, **53**, 457–481.
3. Statistisches Bundesamt, Wiesbaden, ed. *Statistisches Jahrbuch 1990 für die Bundesrepublik Deutschland.* Stuttgard, Metzler-Poeschel, 1990, 68.

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