6. Brusamolino E et al. The risk of acute leukemia in patients treated for Hodgkin's disease is significantly higher after combined modality programs than after chemotherapy alone and is correlated with the extent of radiotherapy and the type and duration of chemotherapy: a case-control study. *Haematologica* 1998;**83**:812–23.
7. Coleman CN et al. Non-Hodgkin's lymphomas and solid tumors in patients treated for Hodgkin's disease. *Cancer Surv* 1982;**1**:733–44.
8. Hoppe RT. Secondary leukemia and myelodysplastic syndrome after treatment for Hodgkin's disease. *Leukemia* 1992;**6**(Suppl. 4P):155–7.
9. Valagussa P et al. Absence of treatment-induced second neoplasm after ABVD in Hodgkin's disease. *Blood* 1982;**59**: 488–94.
10. Van Leeuwen FE et al. Leukemia risk following Hodgkin's disease: relation to cumulative dose of alkylating agents, treatment with teniposide combinations, number of episodes of chemotherapy, and bone marrow damage. *JCO* 1994;**12**:1063–73.
11. Amadori S et al. Acute promyelocytic leukemia following ABVD (doxorubicin, vinblastine, and dacarbazine) and radiotherapy for Hodgkin's disease. *Cancer Treat Rep* 1983;**67**:603–4.
12. Van Leeuwen FE et al. Splenectomy in Hodgkin's disease and second leukemia. *Lancet* 1987;**2**:210–1.

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SECOND SOLID CANCER AFTER HODGKIN'S DISEASE: ANALYSIS OF THE RISK AND REVISION OF THE LITERATURE

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At present time, patients with Hodgkin's disease (HD) have a high probability of cure. However, the late sequelae treatment-related have a remarkable clinical importance. An increased of second primary cancers (SPC) has been observed among long-term survivors of HD: particularly, acute non-lymphoid leukemia (ANLL), non-Hodgkin' lymphoma (NHL) and secondary solid tumours (ST).[1–5] The increase of ANLL risk has been correlated with host-related factors and the type of treatment procedures.[1,5] Several authors have demonstrated that secondary ANLL was likely with chemotherapy-treatment. NHL has been correlated with the radiochemotherapy treatment: the risk has concentrated in the first year following start of treatment and declined in the subsequent 5 years.[6] Recently, several studies have been focused attention on the incidence of ST: the appearance risk increases with the length of the follow-up (Fig. 1) and results correlated with the kind of treatment using RT alone or in combination with chemotherapy (CT).[1,4] The most frequent solid tumor are lung cancer, breast cancer, melanoma skin, gastrointestinal cancer and sarcoma of the bone.

On the occurrence of solid tumours in patients treated with CT alone, the results of BNLI[7] shows an increased risk of ST after CT alone: further study is required for a better examination of the increase in risk of ST after treatment with CT. Moreover, Maurizi et al.[4] show that additional therapy for relapsing patients with CT + RT after initial therapy with RT alone does not increase the risk of ST, while in a recent study[8] the addition of combined therapy for recurrent disease in patients previously treated with radiotherapy showed a significant increase in the relative risk of ST. In the authors' opinion, it is possible that either the cumulative dose of radiation received after secondary treatment with CT was responsible for a high occurrence of ST or that the increase in ST occurrence was due to initial radiation.

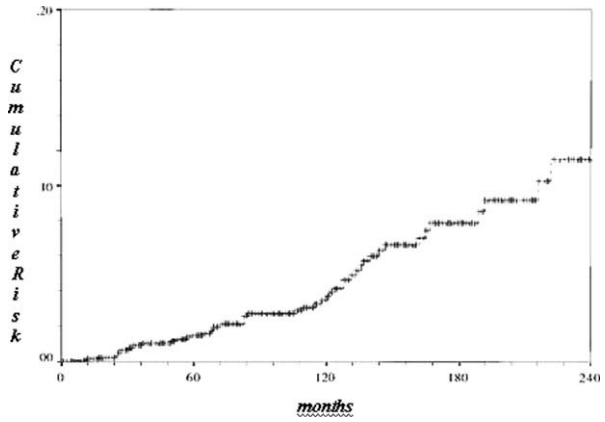

Fig. 1. Cumulative risk of solid tumour (ST).

Age is the major risk factor of solid tumours in the HD population, in the same way as age is a major risk factor of almost all solid cancer in the general population. It is uncertain whether this biological phenomenon is related to age or to the HD status of patients or whether it is an undifferentiated effect of treatment (RT or CT or CT + RT).

With respect to the location of ST, no definite relation could be made between the treatment received (radiotherapy alone and radiotherapy with chemotherapy) and the tumor tissue. For example, lung cancer was observed more often in patients who had received RT, but also in patients treated with CT alone. In their detailed analysis of various solid tumours, Kaldor et al.[9] have pointed out that the occurrence of lung cancer is higher in long-term HD survivors than in the general population. They conclude that this higher risk is due to the cancer-inducing effects of both CT and RT, compared with those produced by other risk factors, e.g. smoking for lung cancer. Van Leeuwen et al.[10]studied a cohort of 1939 patients treated for HD who developed 30 lung cancers and examined the relationship between the carcinogenic effect of smoking and radiation. They conclude that the appearance of lung cancer is related both to the radiation dose received by the lung and to smoking after radiation exposure.

Regarding the occurrence of breast cancer,Van Leeuwen et al.[11] and Yahalom et al.[12] reported an increased risk of breast cancer in women who have received radiation therapy for HD at a younger age. Moreover, Yahalom et al.[12] showed that breast cancer following the treatment for HD was bilateral and frequently involved the medial half of the breast,while the prognosis of the disease is similar to that of patients with primary cancer. In Hancock's experience,[13] the risk after 15 years is equivalent both in women treated with RT alone and in women receiving RT combined with MOPP. For other types of cancer such as cancer of the gastroenteric tract, of the soft tissue and of the nervous system, which have been observed in irradiation, there could be a

relation to the cancer-inducing effects of radiation after a relatively short time. In conclusion, a multifactorial etiology can be established. The appearance of ST in HD patients could be explained by immune deficiency caused by HD itself or by the treatment received to cure it. Genetic factors could also play a role, leading to the appearance of a neoplasm in a small percentage of patients exposed to environmental factors. These is also a higher risk, for patients who have had one tumour, of developing another. The increased risk of ST was connected with treatment received and with host-related and environmental factors. Since treatment-associated cancer continues beyond 15 years, the survivors of HD should be monitored in order to establish the treatment-related carcinogenic effects.

References:

1. Van Leeuwen FE et al. *JCO* 2000;**18**:487–97.
2. Maurizi-Enrici R et al. *Ann Hematol* 1997;**74**:103–10.
3. Maurizi-Enrici R et al. *Haematologica* 1998;**83**:636–44.
4. Maurizi-Enrici R et al. *Haematologica* 1997;**82**:57–63.
5. Brusamolino E et al. *Haematologica* 1998;**83**:812–23.
6. Krikorian JB et al. *NEJM* 1979;**300**:452–8.
7. Swerdlow AJ et al. *Brit Med J* 1992;**304**:1137–43.
8. Doria R et al. *JCO* 1995;**13**:2016–22.
9. Tucker MA. *Hematol Oncol Clin North Am* 1993;**7**:389–400.
10. Van Leeuwen FE et al. *JNCI* 1995;**87**:1530–7.
11. Van Leeuwen FE et al. *JCO* 1994;**12**:312–25.
12. Yahalom J et al. *JCO* 1992;**10**:1674–81.
13. Hancock SL et al. *JNCI* 1993;**85**:25–31.

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