

## Survival outcomes for extranodal natural-killer T-cell lymphoma

Christopher P Fox and colleagues<sup>1</sup> report the results of their cohort study concerning extranodal natural-killer T-cell lymphoma (ENKTL) and found that overall survival at 5 years was 54% (95% CI 44–63) in 98 patients with nasal disease and 34% (27–46) in 68 patients with extranasal disease. It should be noted that ENKTL is often accompanied by hemophagocytic syndrome. In China, a study involving 28 patients with ENKTL-associated hemophagocytic syndrome reported that 13 (46%) of 28 patients died within 2 weeks after the diagnosis, and higher serum lactic dehydrogenase concentrations (>1000 U/L), hypofibrinogenemia, and splenomegaly were statistically significantly associated with poor survival.<sup>2</sup>

We speculate that hemophagocytic syndrome has a considerable prognostic impact on the survival of patients with ENKTL. We would be grateful if the authors could provide the details of patients with hemophagocytic syndrome in this study, including the frequency, remission rate, and impact on survival.

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- 1 Fox CP, Civallero M, Ko YH, et al. Survival outcomes of patients with extranodal natural-killer T-cell lymphoma: a prospective cohort study from the international T-cell Project. *Lancet Haematol* 2020; **7**: 284–94.
- 2 Liu YZ, Bi LQ, Chang GL, Guo Y, Sun S. Clinical characteristics of extranodal NK/T-cell lymphoma-associated hemophagocytic lymphohistiocytosis. *Cancer Manag Res* 2019; **11**: 997–1002.

## Authors' reply

Motoharu Shibusawa and Tetsuya Tanimoto highlight an important complication of extranodal natural-killer T-cell lymphoma (ENKTL); that of haemophagocytic lymphohistiocytosis. Two large retrospective datasets have shown that this complication developed in 21 (7.1%) of 295 and 23 (11.4%) of 202 patients with ENKTL.<sup>1,2</sup> Similarly, in a cohort of 80 ENKTL cases from January, 2017, to January, 2020, from the Samsung Medical Centre lymphoma registry, ten (12.5%) had the condition (Kim WS, unpublished).

Our ENKTL dataset from the international T-cell project study cohort<sup>3</sup> did not, unfortunately, capture haemophagocytic lymphohistiocytosis data within the case report forms. At study registration, serum lactate dehydrogenase was elevated in 56 (38.1%) of 147 evaluable patients and thrombocytopenia (platelet counts of <150 000/mm<sup>3</sup>) was identified in 19 (11.9%) of 160 evaluable patients. However, we recognise that neither serum lactate dehydrogenase nor thrombocytopenia is sufficiently specific for a diagnosis of haemophagocytic lymphohistiocytosis. Importantly, as Shibusawa and Tanimoto note, ENKTL-associated haemophagocytic lymphohistiocytosis is often associated with poor survival. From the Samsung Medical Centre lymphoma registry, the median overall survival of patients with ENKTL and haemophagocytic lymphohistiocytosis was 3.4 months (95% CI 0.0–7.4) compared with a median of 82.6 months (95% CI 37.6–127.64) for patients without this complication (Kim WS, unpublished). In the international T-cell project cohort of ENKTL, there was only one death in the first 2 weeks following registration and a further four deaths in week 4.

We agree that haemophagocytic lymphohistiocytosis, as a complication of ENKTL, represents an area of unmet clinical need in which new therapies are urgently needed. The pathophysiology

of this disease is characterised by a deregulated immune response and hypercytokinaemia leading to life-threatening organ dysfunction and impaired performance status. Thus, we suggest that an initial treatment approach for targeted suppression of the cytokine storm (with agents such as the anti-IL-6 receptor monoclonal antibody tocilizumab, or the IL-1 receptor antagonist anakinra), before initiation of cytotoxic chemotherapy, is a potentially effective strategy that warrants evaluation in prospective studies.

We declare no competing interests.

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- 2 Jia J, Song Y, Lin N, et al. Clinical features and survival of extranodal natural killer/T cell lymphoma with and without hemophagocytic syndrome. *Ann Hematol* 2016; **95**: 2023–31.
- 3 Fox CP, Civallero M, Ko YH, et al. Survival outcomes of patients with extranodal natural-killer T-cell lymphoma: a prospective cohort study from the international T-cell Project. *Lancet Haematol* 2020; **7**: 284–94.