

## Serum Soluble CD25 and CD30 Levels as a Biomarker in Adult T-Cell Leukemia/Lymphoma Patients Undergoing Allogeneic Hematopoietic Stem Cell Transplantation

Shigeki Takemoto<sup>1,2\*</sup>

<sup>1</sup>Department of International Cooperation, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan

<sup>2</sup>Clinical Laboratory, National Hospital Organization Kumamoto Medical Center, Kumamoto, Japan

\*Corresponding author: Dr. Shigeki Takemoto, M.D., Ph.D., Chief of Clinical laboratory, National Hospital Organization Kumamoto Medical Center, 1-5 Ninomaru, Kumamoto 860-0008, Japan, Tel: +81-(0)96-353-6501; Fax: +81-(0)96-325-2519; E-mail: [takemots@kumamed.jp](mailto:takemots@kumamed.jp)

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### Abstract

Adult T-cell leukemia/lymphoma (ATL) is one of the incurable mature T-cell malignancies. Recently, younger survivors after chemotherapy are candidates for allogeneic hematopoietic stem cell transplantation (HSCT). We compared the clinical value of soluble CD30 (sCD30) levels with soluble interleukin 2 receptor  $\alpha$  chain (sCD25) levels in 24 ATL patients underwent HSCT at National Hospital Organization Kumamoto Medical Center. In univariate analysis of prognostic factor in patients underwent HSCT, both sCD25 ( $p=0.041$ ) and sCD30 levels ( $p=0.0003$ ) levels were significant predictor of overall survival in HSCT. Furthermore, sCD30 levels before the conditioning therapy turns out to predict more patients with early death (7 of 11) than were predicted by sCD25 levels (4 of 11). In addition, regarding graft-versus-host disease (GVHD), no acute GVHD or severe acute GVHD (grade III or IV) ( $n=10$ ) was associated with unfavorable prognosis in contrast to the favorable prognosis associated with grade I and II ( $n=14$ ) (hazard ratios=8.2, 95% confidence intervals 2.4–28,  $p=0.0007$ ). It is thought that sCD30 is a useful biomarker to predict the risks involved with HSCT.

**Keywords:** Soluble CD30 (sCD30); Adult T-cell leukemia/lymphoma (ATL); Allogeneic hematopoietic stem cell transplantation (HSCT); Graft-versus-host disease (GVHD)

### Short Commentary

Adult T-cell leukemia / lymphoma (ATL) is one of the incurable mature T-cell malignancies [1]. ATL patients are usually first treated with chemotherapy [2]. Recently, younger survivors after chemotherapy are candidates for allogeneic hematopoietic stem cell transplantation (HSCT) [3]. We compared the clinical value of soluble CD30 (sCD30) levels with soluble interleukin 2 receptor  $\alpha$  chain (sCD25) levels in 24 ATL patients underwent HSCT at National Hospital Organization Kumamoto Medical Center [4]. The sera of the patients before conditioning therapy were preserved and levels of sCD30 and sCD25 were subsequently measured using sandwich enzyme-linked immunosorbent assay. In some patients, serial blood samples were taken during the course of treatment if they consented to the procedures. CD30 is a member of the tumor necrosis factor receptor superfamily [5]. The soluble form, sCD30, is cleaved by a disintegrin and metalloproteinase (ADAM)10 and/or ADAM17, while shedding of CD25 is dependent on matrix metalloproteinase-9 [6]. The levels of sCD30 as well as sCD25 are elevated in HTLV-1 carriers and highly elevated in ATL [5]. In univariate analysis of prognostic factor in patients underwent HSCT, both sCD25 ( $p=0.041$ ) and sCD30 levels ( $p=0.0003$ ) levels were significant predictor of overall survival in HSCT. Furthermore, sCD30 levels before the conditioning therapy turns out to predict more patients with early death (7 of 11) than were predicted by sCD25 levels (4 of 11) [4].

Regarding graft-versus-host disease (GVHD), Kanda et al. reported that the development of grade I-II acute GVHD was significantly

associated with higher overall survival compared with the absence of acute GVHD [7]. Furthermore, occurrence of either grade I-II or grade III-IV acute GVHD was associated with lower disease-associated mortality compared with the absence of acute GVHD [7]. In our study, no acute GVHD or severe acute GVHD (grade III or IV) ( $n=10$ ) was associated with unfavorable prognosis in contrast to the favorable prognosis associated with grade I and II ( $n=14$ ) (hazard ratios=8.2, 95% confidence intervals 2.4–28,  $p=0.0007$ ) [4]. Chen et al. compared the expression of CD30 on specific peripheral blood T-cell subsets and levels of sCD30 from patients with acute GVHD after HSCT and also analyzed the expression of CD30 in the biopsies of affected tissues from patients with intestinal acute GVHD [8]. Usually, both levels of soluble cytokine receptors are elevated temporally, suggesting successful treatment of GVHD [8]. However, in our two patients with severe acute GVHD, the sCD30 levels were elevated to 8 and 49 times at the peak of GVHD from the basal value after transplantation. Levels of sIL-2 were 4 and 7 times, respectively. In those cases, sCD30 levels were shown to surge rather than sCD25 after bone marrow transplantation. However, further analysis is required to reach the conclusion.

So far there is no application of sCD30 measurement to any diseases covered by insurance in Japan. However, it is thought that sCD30 is a useful biomarker to predict the risks involved with HSCT. This is the reason why the serial examination of sCD30 might be required for the success of ATL treatment.

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