Technology from Kyoto University

Anti-OX40L Antibody to Prevent Bendamustine-Induced T Cell Reduction

We are looking to out-license the technology for its commercialization.

Preventing the reduction of T cells associated with bendamustine for the effective suppression of its side effects

◆Background

Bendamustine is one of the widely used anticancer drugs with high therapeutic efficacy against B-cell lymphoma and it has the effect of modifying signals from various tumor necrosis factor (TNF) receptors. However, it is also known to cause a reduction in CD4-positive T cells over an extended period, starting from the initiation of treatment and lasting for several months after its conclusion, which increases the risk of opportunistic infections and severe cases of coronavirus infections.

◆Description and Advantages

Kyoto University researchers found that the signal for T cell survival from OX40, one of TNF receptors, is converted into a cell death signal by bendamustine, leading to a decrease in CD4-positive T cells. Consequently, it was discovered that by inhibiting the signaling between OX40 and its ligand (OX40L) using anti-OX40L antibodies during bendamustine administration, the number of T cells could be maintained without compromising the therapeutic effect on B-cell lymphoma (Fig.1).

- **Suppression of CD4-positive T cell reduction by bendamustine (Fig. 2)**
- **Safety of anti-OX40L antibodies**

  The basic safety of anti-OX40L antibody is confirmed in clinical trials for other indications.

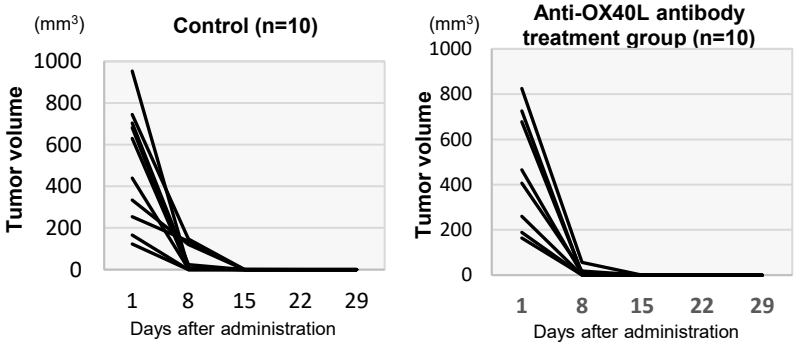

Fig.1 The effect of anti-OX40L antibody on the antitumor effect of bendamustine in mouse B-cell lymphoma

Both the group administered control antibody followed by bendamustine and the group administered anti-OX40L antibody followed by bendamustine showed complete lymphoma disappearance after 15 days, demonstrating comparable therapeutic effects, confirming that the anti-OX40L antibody does not interfere with the efficacy of bendamustine on B-cell lymphoma.

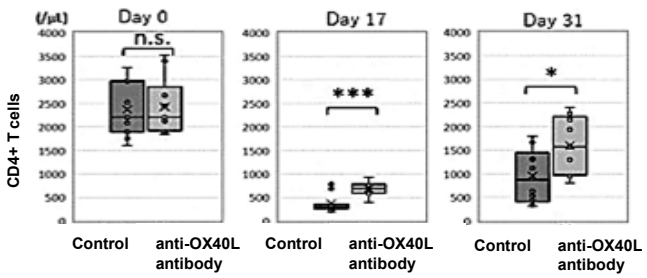

Fig.2 The effect on CD4+ T cells and CD8+ T cells

Initially, 100 μg of anti-OX40L antibody or control antibody were intraperitoneally administered to wild-type mice, followed by intravenous administration of bendamustine at 40 mg/kg 3 hours later (day 1). The same was performed 4 days later (day 5) and peripheral blood sampling was conducted on day 17 and day 31. The comparison of the cell counts of CD4+ T cells and CD8+ T cells in peripheral blood revealed that the anti-OX40L antibody effectively suppresses the reduction of T cells induced by bendamustine, confirming its efficacy in maintaining T cell levels.

◆Development Status

TRL: Level 3*

*Preliminary efficacy tests completed using mouse models of diffuse large B cell lymphoma after target identification

◆Applications

- Combination drug for bendamustine
- Novel T-cell depletion inhibitor targeting OX40

◆Offerings

- Patent License
- Option for License
- Collaborative Research (mechanism elucidation, animal testing)

◆Contact

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IAC Institutional Advancement and Communications

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