Non-Hodgkin’s Lymphoma - Biology, excluding Therapy| November 16, 2008

**Circulating Antibodies to ALK Inversely Correlat with Relapse Risk and Circulating Tumor Cells in Children and Adolescents with ALK-Positive Anaplastic Large Cell Lymphoma**

Karen Pulford,

Christine Damm-Welk,

Birgit Burkhardt,

Martin Zimmerman,

Alfred Reiter,

Kamel Ait-Tahar,

Wilhelm Woessmann

*Blood* (2008) 112 (11): 2831.

<https://doi.org/10.1182/blood.V112.11.2831.2831>

* [Split-Screen](https://ashpublications.org/blood/article-split/112/11/2831/59426/Circulating-Antibodies-to-ALK-Inversely-Correlat)
* *Share Icon* Share
* *Tools Icon* Tools

**Abstract**

Tumour-associated antigens (TAAs) recognised by patients’ immune systems may be of prognostic relevance and also represent new immunotherapeutic targets. Circulating antibodies and T-cell responses to the TAA anaplastic lymphoma kinase (ALK) have been detected in patients with ALK-positive anaplastic large cell lymphoma (ALCL) (

Pulford et al.

Blood

2000

,

96

:

1605

–7

;

Ait-Tahar et al.

Int J Cancer

2006

,

118

:

688

–95

;

Cancer Res

2007

,

65

:

1891

–901

). Their exact significance with regard to prognosis is, however, unclear at present. In contrast, and unusually for non-Hodgkin’s lymphoma, low numbers of circulating tumor cells (CTCs) expressing nucleophosmin (NPM)-ALK-transcripts at diagnosis in bone marrow or blood confers an unfavourable prognosis (

Damm-Welk et al.

Blood

2007

,

110

:

670

–7

). The current study was performed to address whether there was any correlation between the magnitude of the autoantibody response to ALK with

* prognosis and
* the levels of CTCs at diagnosis in a cohort of uniformly treated children and adolescents with ALK-positive ALCL for whom full clinical data was available.

The anti-ALK-antibody titers were analyzed in initial serum or plasma samples from 86 patients and copies of NPM-ALK in initial bone marrow (n=61) and/or blood samples (n=53). The children were treated according to the NHL-BFM95 and ALCL99 trials carried out between 1996 and 2006. Antibody titers against ALK and copies of NPM-ALK were measured using ALK transfectants and quantitative RT-PCR as previously described (

Pulford et al.

Blood

2000

,

96

:

1605

–7

;

Damm-Welk et a

670

–7

). Circulating antibodies to ALK were detected in 80/86 (93%) of patients studied. The titers ranged between 1/50 and ≥1/60750. The median follow-up of the patients was 4.6 years (range 1.4–10.4 years). Antibody titers <1/60750, detected in 61 patients (71%), significantly correlated with advanced stage, mediastinal or visceral involvement. The 5 year event free survival rate (pEFS) of 25 patients with antibody titres ≥1/60750 was 88+/− 0.06% compared to 51+/−0.07% for 61 patients with titres less than 1/60750 (p<.003). Among those patients mounting an antibody response, higher antibody titers were significantly associated with lower cumulative incidence of relapses (CI-R): 17 patients with a titer between 1/50 and <1/2025 had a CI-R of 74±12% compared to a CI-R of 32±8% for 38 patients with titers between 1/2025 and <1/60750 and a CI-R of 12±7% for 25 patients with titers ≥1/60750 (p<.001). There was a significant inverse correlation between the magnitude of antibody titers and CTCs in 61 patients studied for the presence of both autoantibodies and CTC in bone marrow. None of the 20 patients with a high antibody titer (≥1/60750) had more than 10 copies NPM-ALK/104 copies ABL in bone marrow compared to 13 of 41 patients with lower antibody titers (p=.003). Comparison of antibody titers with CTCs in peripheral blood led to a similar grouping. In conclusion, the current study shows, for the first time, that the magnitude of the autoantibody response to ALK is inversely correlated with the relapse risk and disease dissemination in ALK-positive ALCL. Our results, therefore, provide clinical evidence that a strong immune response to ALK may control the progression of ALCL supporting the possibility that CTCs are a secondary phenomenon due to a limited anti-tumor immune response. These results also support the use of ALK as an immunotherapeutic target in ALCL.

Topics:

[adolescent](https://ashpublications.org/blood/search-results?f_SemanticFilterTopics=adolescent), [antibodies](https://ashpublications.org/blood/search-results?f_SemanticFilterTopics=antibodies), [child](https://ashpublications.org/blood/search-results?f_SemanticFilterTopics=child), [circulating tumor cells](https://ashpublications.org/blood/search-results?f_SemanticFilterTopics=circulating%20tumor%20cells), [ki-1+ anaplastic large cell lymphoma](https://ashpublications.org/blood/search-results?f_SemanticFilterTopics=ki-1+%20anaplastic%20large%20cell%20lymphoma), [recurrence risk](https://ashpublications.org/blood/search-results?f_SemanticFilterTopics=recurrence%20risk), [antibody titer](https://ashpublications.org/blood/search-results?f_SemanticFilterTopics=antibody%20titer), [anaplastic lymphoma kinase](https://ashpublications.org/blood/search-results?f_SemanticFilterTopics=anaplastic%20lymphoma%20kinase), [autoantibodies](https://ashpublications.org/blood/search-results?f_SemanticFilterTopics=autoantibodies), [cancer](https://ashpublications.org/blood/search-results?f_SemanticFilterTopics=cancer)

**Disclosures:** No relevant conflicts of interest to declare.

**Author notes**

Corresponding author

2008, The American Society of Hematology

[Volume 112, Issue 11](https://ashpublications.org/blood/issue/112/11)

November 16 2008

* [Previous Article](https://ashpublications.org/blood/article/112/11/2830/59416/Relapsed-MALT-Lymphomas-Are-Associated-with-a)
* [Next Article](https://ashpublications.org/blood/article/112/11/2832/59436/FLIPI-and-F2-Index-Prognostic-Indices-in-Advanced)

Advertisement

**Potential Articles of Interest**

1. [Correlation of the autoantibody response to the ALK oncoantigen in pediatric anaplastic lymphoma kinase–positive anaplastic large cell lymphoma with tumor dissemination and relapse risk](https://ashpublications.org/blood/article/115/16/3314/27057/Correlation-of-the-autoantibody-response-to-the?utm_source=TrendMD&utm_medium=cpc&utm_campaign=Blood_TrendMD_0)

Ait-Tahar et al., Blood, 2010

1. [The Autoantibody Response to ALK In Pediatric Anaplastic Large Cell Lymphoma: A Children's Oncology Group Report](https://ashpublications.org/blood/article/116/21/4130/67810/The-Autoantibody-Response-to-ALK-In-Pediatric?utm_source=TrendMD&utm_medium=cpc&utm_campaign=Blood_TrendMD_0)

Megan S. Lim et al., Blood

1. [Immune response to the ALK oncogenic tyrosine kinase in patients with anaplastic large-cell lymphoma](https://ashpublications.org/blood/article/96/4/1605/258442/Immune-response-to-the-ALK-oncogenic-tyrosine?utm_source=TrendMD&utm_medium=cpc&utm_campaign=Blood_TrendMD_0)

Pulford et al., Blood, 2000

1. [4: The Receptor Tyrosine Kinase ALK — Its Fusion Partners and Their Implication in Various Cancers](https://www.worldscientific.com/doi/abs/10.1142/9789813200944_0004?utm_source=TrendMD&utm_medium=cpc&utm_campaign=World_Scientific_TrendMD_1)

World Scientific

1. [FDA Accepts Pfizer's sNDA for Xalkori in Rare ALK-Positive Pediatric Leukemia Indication](https://www.precisiononcologynews.com/regulatory-news-fda-approvals/fda-accepts-pfizers-snda-xalkori-rare-alk-positive-pediatric-leukemia?utm_source=TrendMD&utm_medium=TrendMD&utm_campaign=TMD_PON#.X2thLmhKg2w)

Precision Oncology News, 2020

1. [Reproductive performance of pandemic influenza A virus infected sow herds before and after implementation of a vaccine against the influenza A (H1N1)pdm09 virus](https://porcinehealthmanagement.biomedcentral.com/articles/10.1186/s40813-019-0141-x?utm_campaign=BSLB_AWA_SK01_GL_40813_HP_TrendMDQ420&utm_content=null&utm_medium=cpc&utm_source=trendmd)

Sophie Gumbert et al., Porcine health management., 2020

[Powered by](https://www.trendmd.com/how-it-works-readers)

View Metrics

**Cited By**

[Google Scholar](http://scholar.google.com/scholar?q=link:https%3A%2F%2Fashpublications.org%2Fblood%2Farticle%2F112%2F11%2F2831%2F59426)

**Email alerts**

Article Activity Alert

Latest Issue Alert