Contribution ID: **27** Type: **not specified**

212Pb-NNV003 as a novel targeted alpha therapy for CD37 positive B-cell chronic lymphocytic leukemia (CLL) and non-Hodgkin lymphoma (NHL)

Background

Chronic lymphocytic leukemia (CLL) is the most common leukemia in adults in western countries, accounting for approximately one quarter of all leukemias and Non-Hodgkin lymphoma (NHL) caused an estimated 200,000 cancer deaths worldwide in 2014. More than 90,000 cases of chronic lymphocytic leukemia (CLL) and non-Hodgkin lymphoma (NHL) are expected in the US each year.
Immuno-chemotherapy using anti-CD20 monoclonal antibodies (mAb) in combination with DNA alkylating agents is the front-line therapy of CLL and NHL. Despite promising initial results, relapses after repeated administration of immuno-chemotherapy are frequent and relapsed/refractory patients show poor prognosis. As CD37 is strongly and selectively expressed on the surface of mature B lymphocytes and B-cell malignancies, the development of new therapies targeting CD37 expressing cells may prove useful for relapsed or refractory patients as an alternative to CD20 targeting agents. We have developed a targeted alpha therapy (TAT) where the CD37-specific antibody NNV003 is coupled to the *in-vivo* alpha-particle-generator, 212Pb. When treated with alpha radiation, targeted cancer cells are exposed to high linear energy transfer (LET). LET acts over a short range (50–100 μm), causing double strand breaks in the DNA of targeted cells while sparing adjacent normal tissues

Materials and Methods

The efficacy of a single escalating 212Pb-NNV003 administration was evaluated on disseminated models of human Burkitt's lymphoma (Daudi) and CLL (MEC-2). 10 million Daudi cells or 2.5 million MEC-2 cells were intravenously injected in CB17-SCID or R2G2 mice and 212Pb-NNV003 was given two days later. Unspecific, 212Pb-labeled antibody was used as control. Dose range finding and tolerability studies were performed in CB17-SCID and R2G2 tumor-free mice to define the maximum tolerated dose prior to the efficacy studies.

Results

212Pb-NNV003 displays a favorable toxicity profile after a single intravenous injection in tumor-free mice. No acute hematological toxicity was observed, and animals presented only a slight initial reduction in their platelets (PLT) counts which was fully recovered 4-weeks after injection.
A single intravenous dose of 10, 15 or 20 μCi of 212Pb-NNV003 led to 70 %, 90 % and 100 % of mice injected with MEC-2 cells being tumor free 20 weeks post cell injection. Control animals that received saline, cold antibody or 212Pb-cetuximab presented a median survival of 4.9, 5.4 and 9.3 weeks, respectively.
A single intravenous dose of 2.5, 5 and 7.5 μCi 212Pb-NNV003 led to over 80% tumor-free mice injected with Daudi cells 15 weeks post cell injection. Control animals that received saline, cold antibody or 212Pb-cetuximab presented a median survival of 7, 7.8 and 7.7 weeks, respectively.

Conclusion

The results of preclinical studies suggest that TAT using 212Pb-NNV003 may have positive clinical implication for the treatment of CD37 positive CLL and NHL.

Email Address

amal.saidi@oranomed.com

Presentation Type

Contributed Oral

Primary author: Dr SAIDI, Amal (Orano Med)

Co-authors: Dr MAALAND, Astri (Nordic Nanovector); Dr HEYERDAHL, Helen (Nordic Nanovector); Dr DAHLE, Jostein (Nordic Nanovector); Dr TORGUE, Julien (Orano Med)

Presenter: Dr SAIDI, Amal (Orano Med)

Track Classification: Preclinical