Aim

To develop an [redacted] antibody to be used in local immunotherapy of cancer based on a fully human antibody [redacted] by increasing the affinity/potency [redacted] from 1.7 nM to below 0.1 nM.

1 Summary

A [redacted] high affinity antibody for local immunotherapy of cancer was developed [redacted], a [redacted] antibody originating from a human antibody library [redacted]

Five molecular libraries were designed based on the sequence and structure [redacted]. These libraries contained restricted variability at specific positions or random variability covering the entire variable sequence. From these libraries, an initial selection round using phage display was made to enrich [redacted] binders with moderate and high affinity.
The enriched molecular libraries were then recombined using FIND™. The resulting FIND-library contained recombined sequences from [redacted] binders originating from all the starting libraries. This FIND-library was subjected to several rounds of phage selection with increasing stringency. From these selection rounds approximately 10,000 individual clones were screened in a concentration independent affinity ELISA. The top 100 clones were selected and screened in Biacore and in an in vitro functional assay and ranked based on protein behavior. The top 10 clones went further to hit-to-lead, where protein behavior, affinity, in vitro efficacy and potency were analyzed in more detail. ADC-1013 [redacted] was chosen based on the results from this process. Finally, different Fc-format was evaluated, and it was decided to use the common gamma heavy chain for ADC-1013.

In conclusion the lead optimization using FIND resulted in a drug candidate exceeding the established goals for the project

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