

CS1 is expressed on myeloma cells from early stage, late stage, and drug-treated multiple myeloma patients, and is selectively targeted by the HuLuc63 antibody

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Disclosures for Frits van Rhee, MD, PhD

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Honoraria	No relevant conflicts of interest to declare
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Presentation includes the following off-label use of a drug or medical device: N/A



CS1 is a potential target for MM therapy

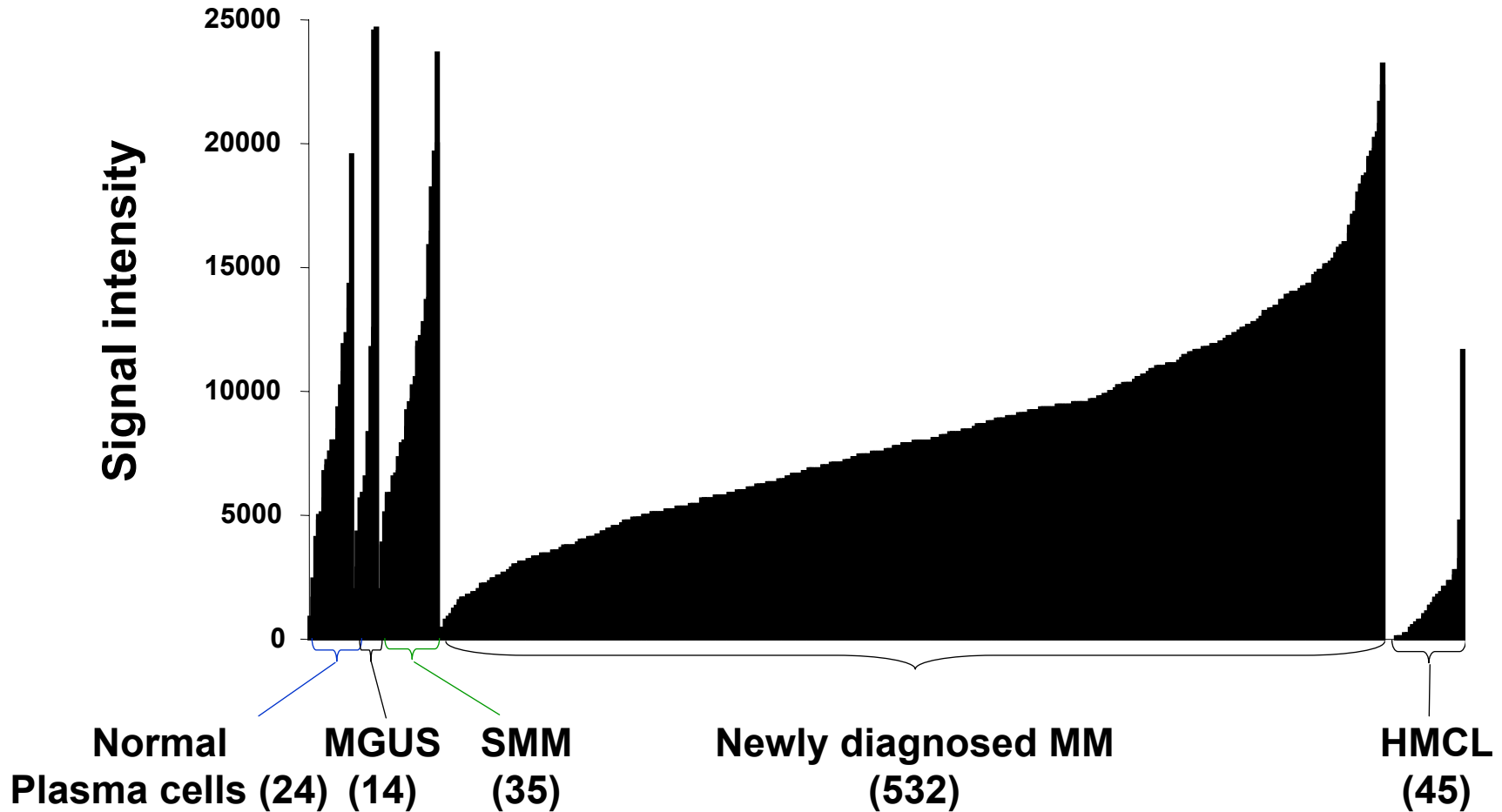
- CS1 is a member of the CD2 family of cell surface glycoproteins
 - CD2 subset 1, CD2-like receptor activating cytotoxic cells (CRACC), SLAM family member 7
- CS1 is highly expressed on primary myeloma
 - Previously reported to be expressed on NKs, NKTs, cytotoxic T cells and activated B cells
- CS1 is not expressed on normal tissues nor on CD34⁺ stem cells



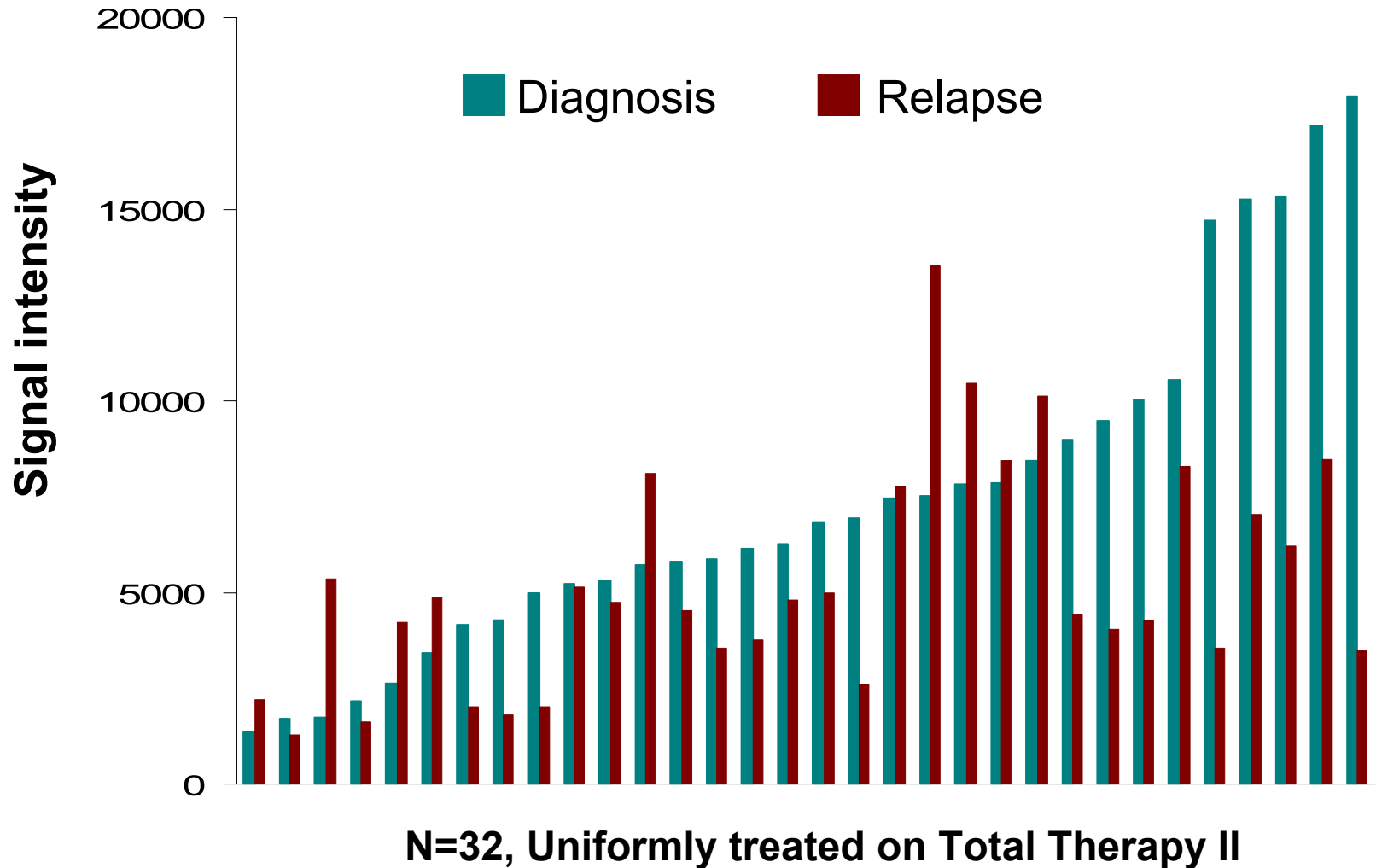
Objectives

- Evaluate CS1 as a potential target for myeloma therapy
- CS1 expression in myeloma
- Test the ability of HuLuc63, a humanized CS1 antibody to induce NK cell mediated myeloma cell death

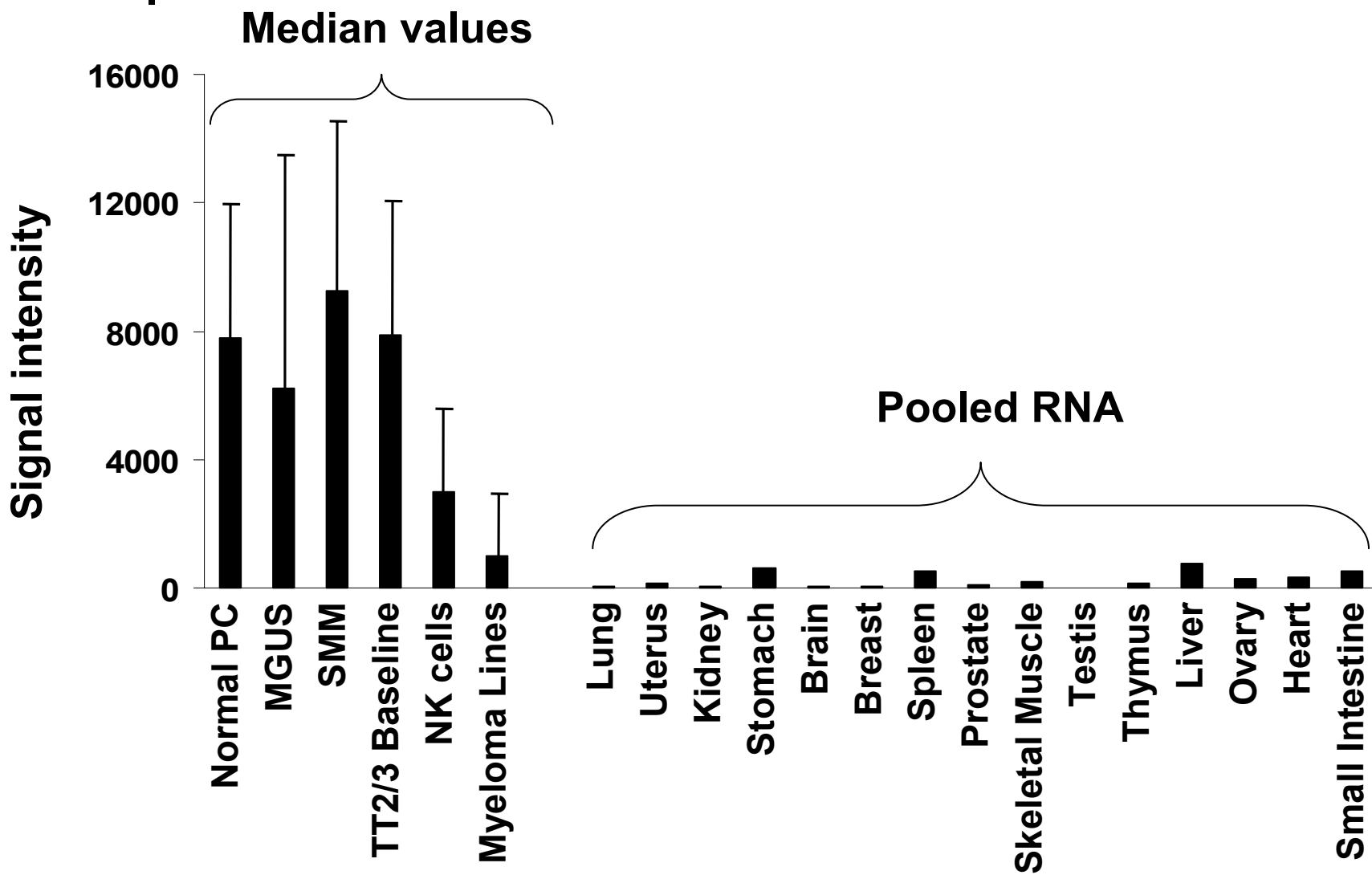
● ● ● | **CS1 is expressed by purified PC from healthy donors and patients with MGUS, smoldering and newly diagnosed MM**



CS1 is expressed in newly diagnosed and relapsed MM



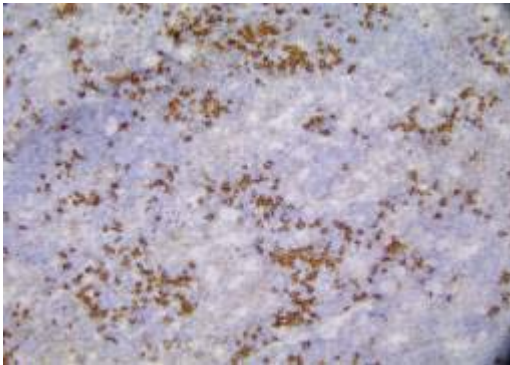
CS1 is not expressed in normal tissues



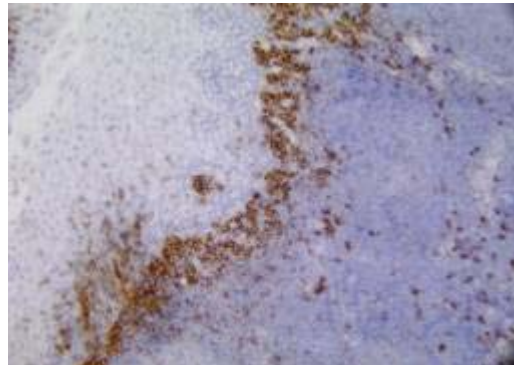
Normal human tissue reactivity of MuLuc63 (IHC) is restricted to plasma cells

- No MuLuc63 binding detected in epithelia, muscles or major organs
- Binding detected in plasma cells of tonsil, gut, bladder, cervix, lymph node and other tissues

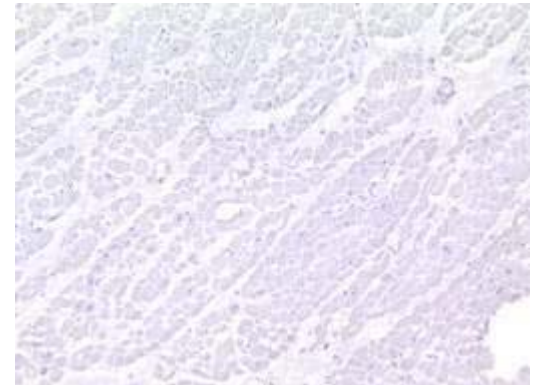
Lymph Node



Tonsil



Heart Atrium





HuLuc63

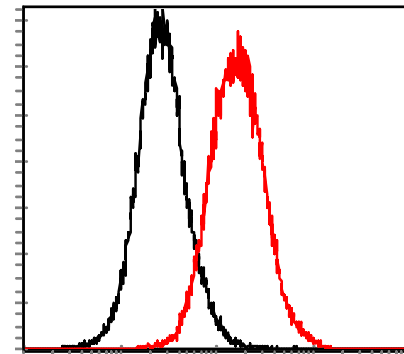
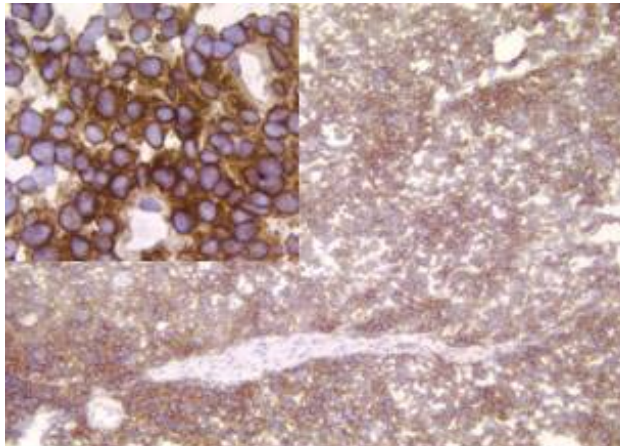
- Humanized IgG1 derived from MuLuc63, an anti-human CS1 antibody
- Recognizes CS1 by flow cytometry and fresh-frozen immunohistochemistry

HuLuc63 stains malignant plasma cells by IHC and flow cytometry

IHC of solitary plasmacytomas
(9/9 were positive)

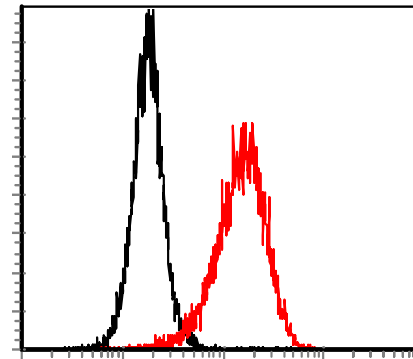
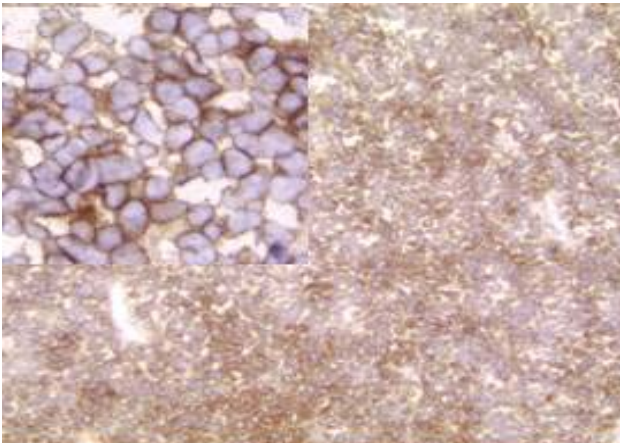
Flow cytometry of CD138+ plasma cells
(7/7 were positive)

Case#1



BM derived
myeloma

Case#2

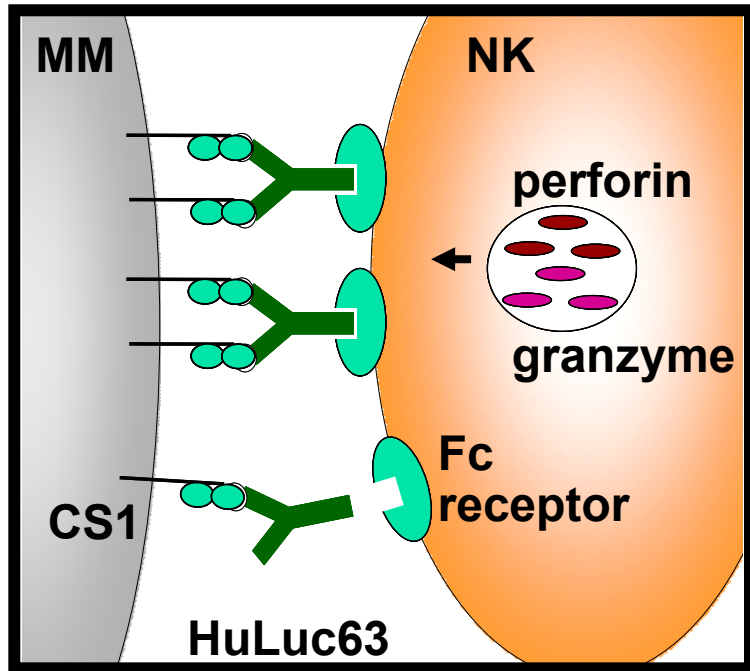


Pleural effusion
derived myeloma

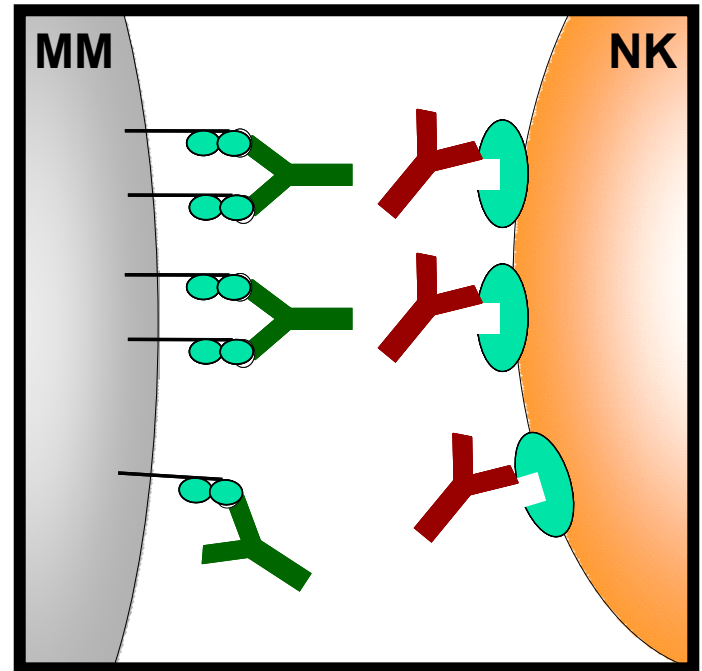
Isotype **HuLuc63**

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HuLuc63 induces killing of myeloma cells by antibody dependant NK cell cell mediated cytotoxicity (ADCC)

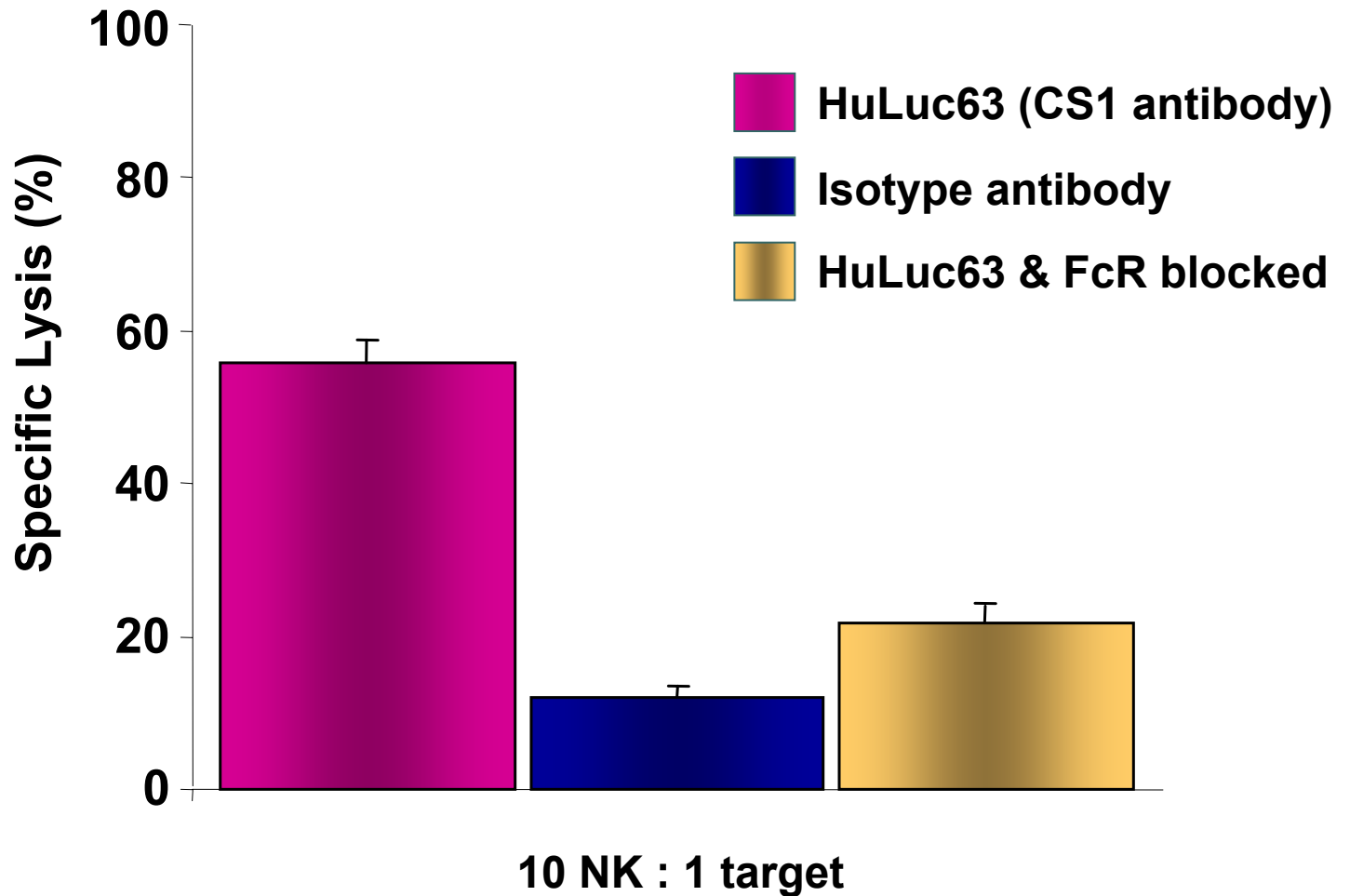


Lysis

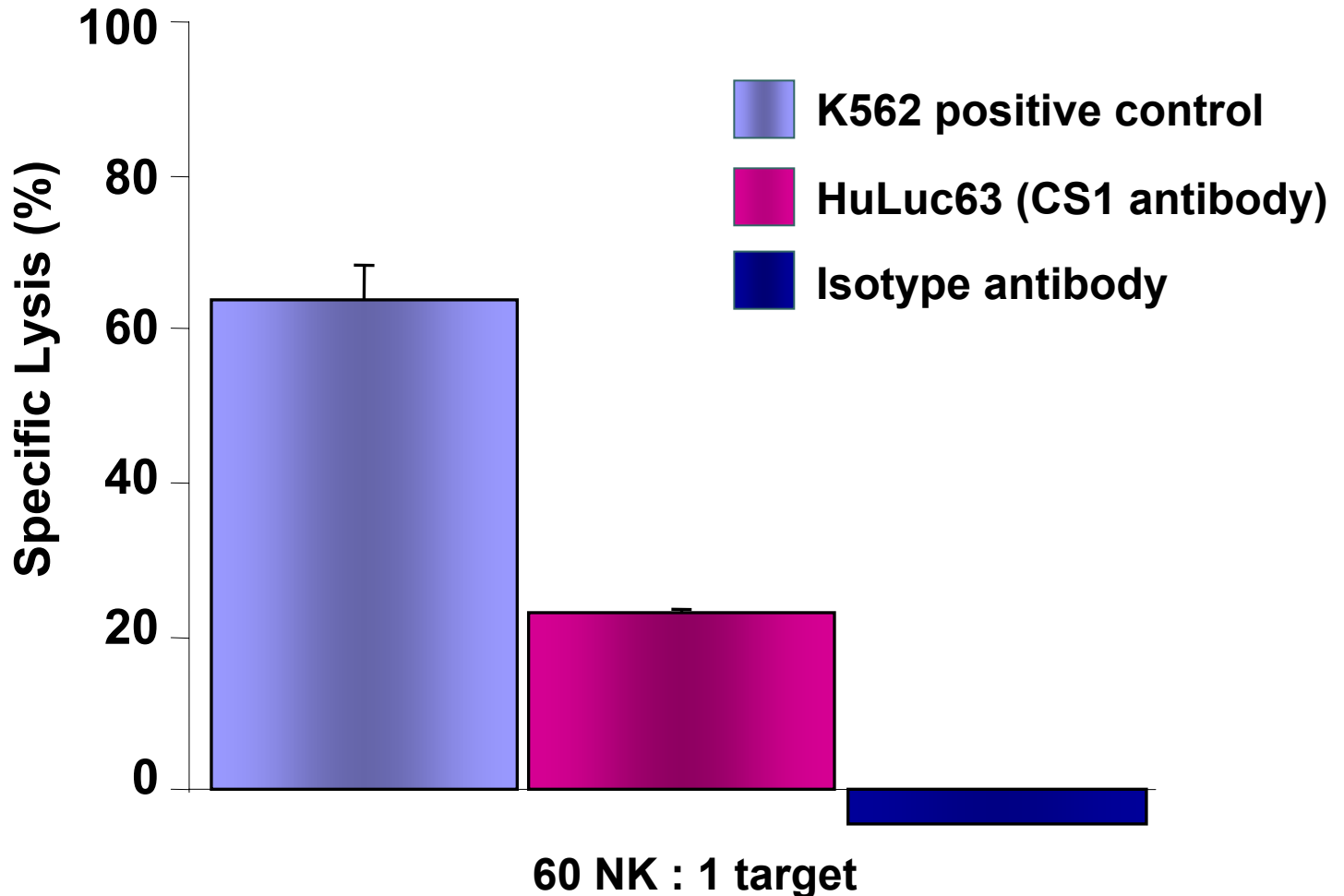


No Lysis

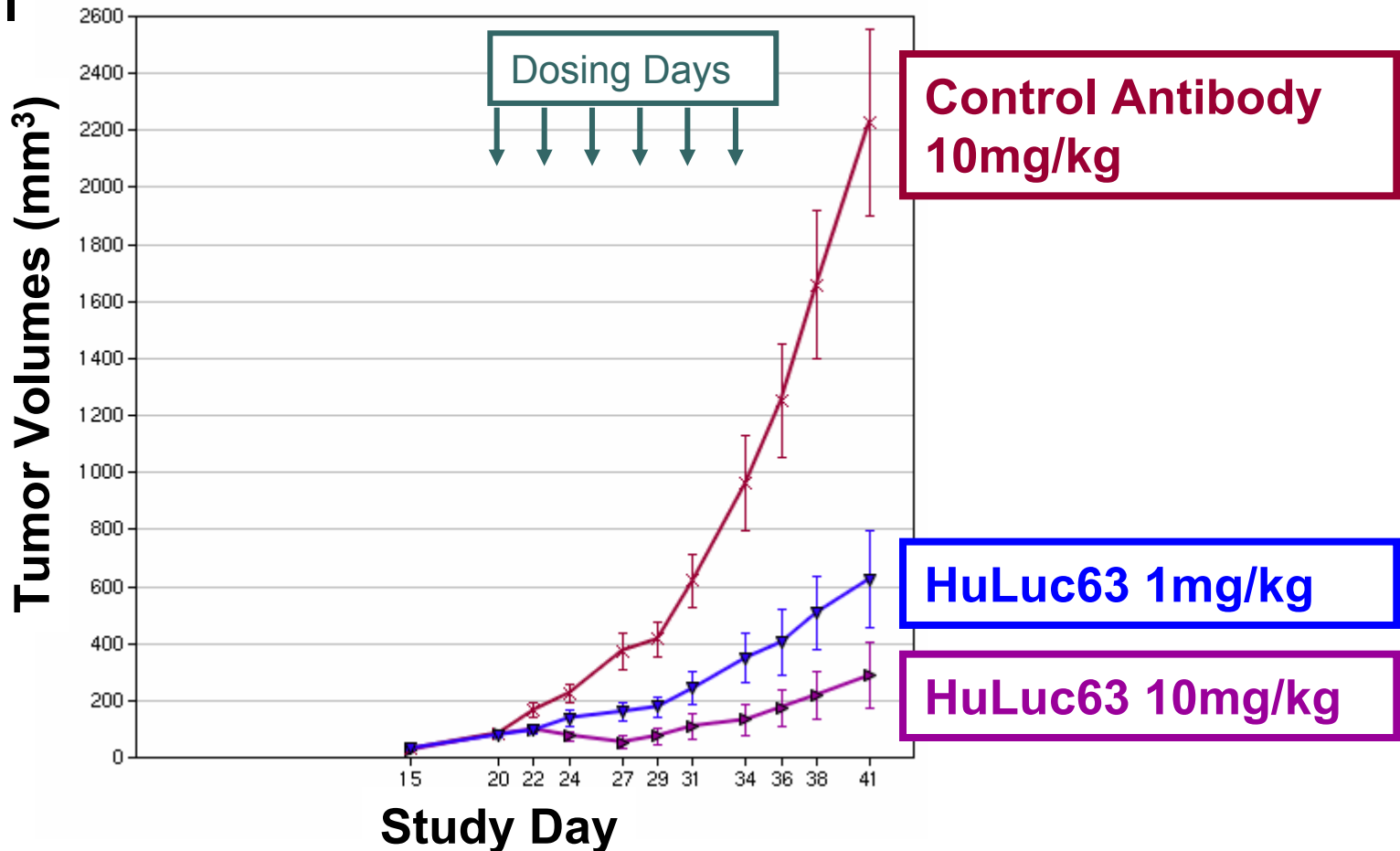
HuLuc63 induces killing of primary myeloma cells in an **allogeneic** system



HuLuc63 induces killing of primary myeloma cells in an **autologous** system



HuLuc63 inhibits tumor growth in the OPM2 xenograft model *in vivo*



*For more details, see Rice et al., abstract #3503 Poster Session III-732

ERADICATION OF TUMORS IN PRE-CLINICAL MODELS OF MULTIPLE MYELOMA BY ANTI-CS1 MONOCLONAL ANTIBODY HULUC63: MECHANISM OF ACTION STUDIES.



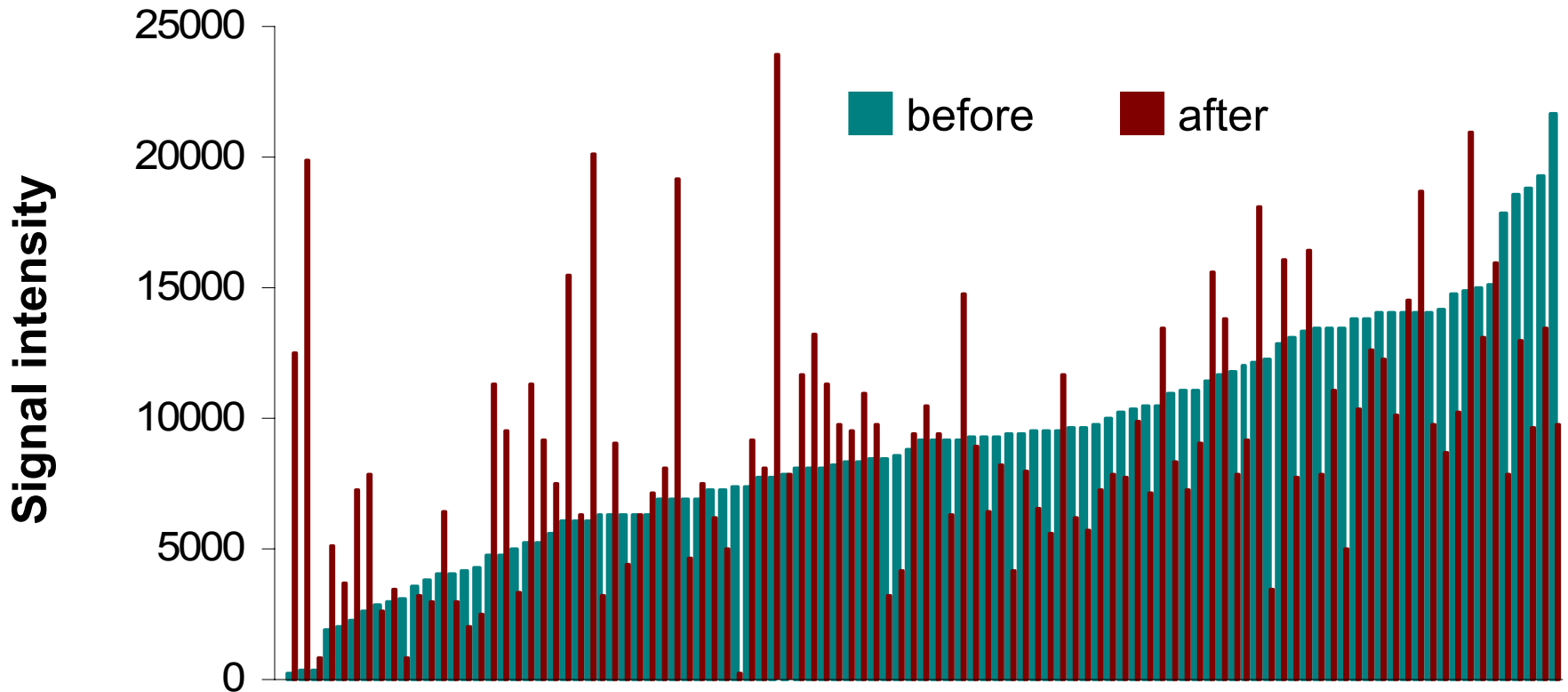
HuLuc63 and bortezomib

- Bortezomib can enhance recognition and killing of myeloma by NK cells*
- Will the combination of HuLuc63 and bortezomib further enhance NK-cell mediated lysis of myeloma cells?

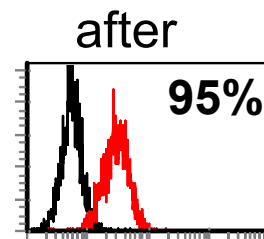
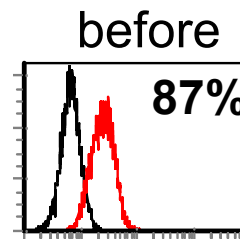
*For more details, see Shi et al., abstract #727 Poster Session III-727

BORTEZOMIB DOWN-REGULATES HLA CLASS I AND ENHANCES NATURAL KILLER CELL MEDIATED LYSIS OF MYELOMA

CS1 expression persists *in patients* 48 hrs after bortezomib administration

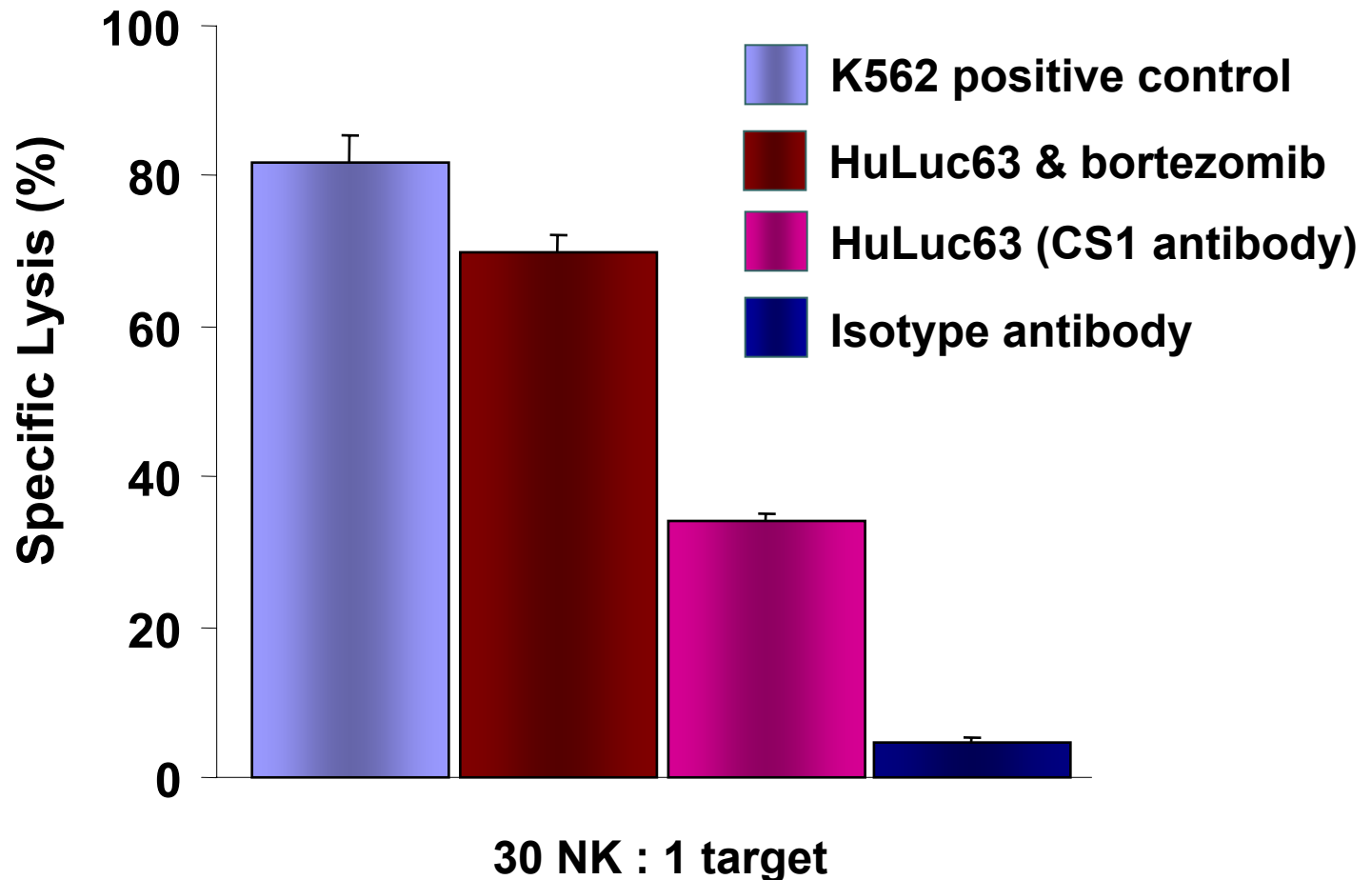


Cell surface CS1 expression persists after *In vitro* bortezomib (100nM, 18h)



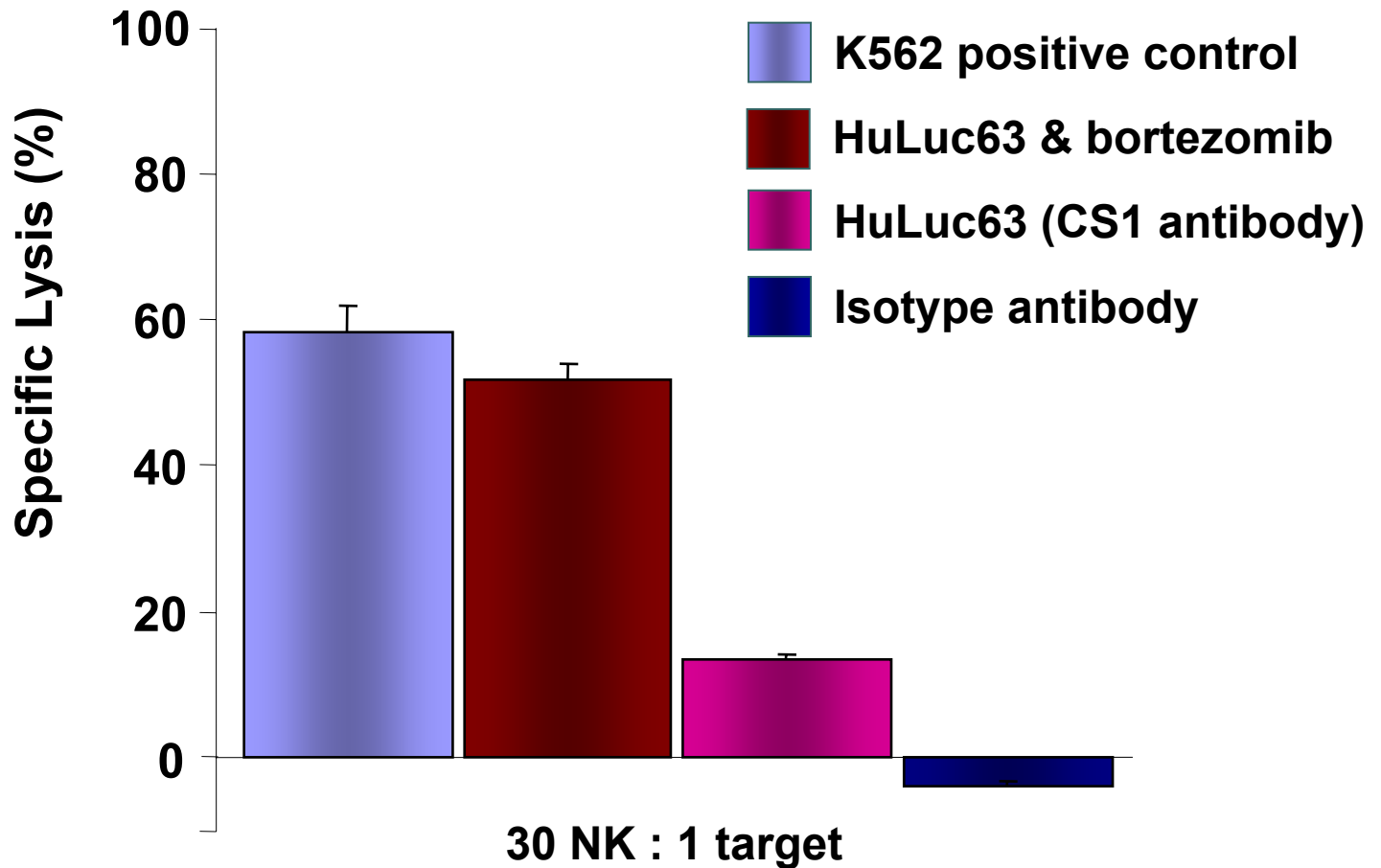
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Combination of HuLuc63 with bortezomib results in enhanced **allogeneic** NK cell mediated ADCC of primary myeloma



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Combination of HuLuc63 with bortezomib results in enhanced **autologous** NK cell mediated ADCC of primary myeloma





Conclusions

- CS1 is highly expressed in MM but not in normal tissues
- HuLuc63 can induce killing of MM cells *in vitro* and *in vivo*
- Preliminary data suggest that bortezomib may enhance HuLuc63 efficacy
- Our data support the clinical utility of CS1 targeted therapy
- HuLuc63 has entered a phase I study for the treatment of relapsed/refractory myeloma



Acknowledgements

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