Preclinical efficacy of novel anti-oxMIF/HSG bispecific antibody for pretargeted radioimmunotherapy

EPS-214

Alejandro Puchol Tarazona, Irina Mirkina, Michael Thiele, Alexander Schinagl
OncoOne Research & Development GmbH, Karl-Farkas-Gasse 22, A-1030 Vienna, Austria

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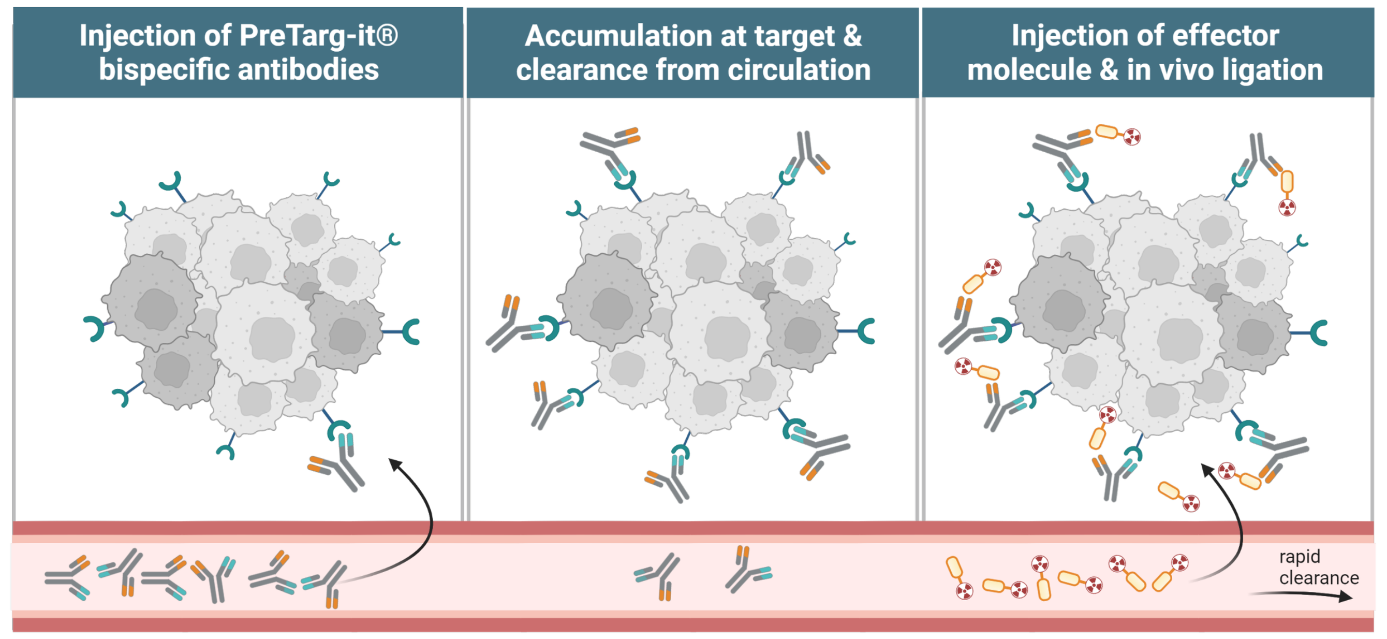
1 Introduction

Pre-Targeted Radioimmunotherapy (PRIT)

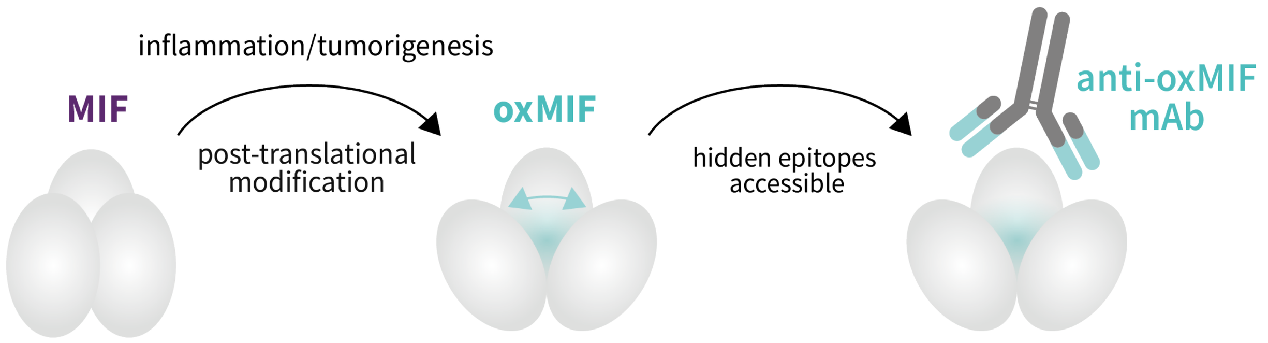
Radiolabeled antibodies have proven effective in patients with hematological malignancies, but adaptation of radioimmunotherapy (**RIT**) in solid tumors has been challenging. The slow clearance and delayed tumor uptake of directly radio-labeled antibodies can cause high non-target tissue irradiation, and related toxicity.



Pre-targeting techniques overcome limitations of RIT by decoupling the radioactive payload from the tumor-targeting vector

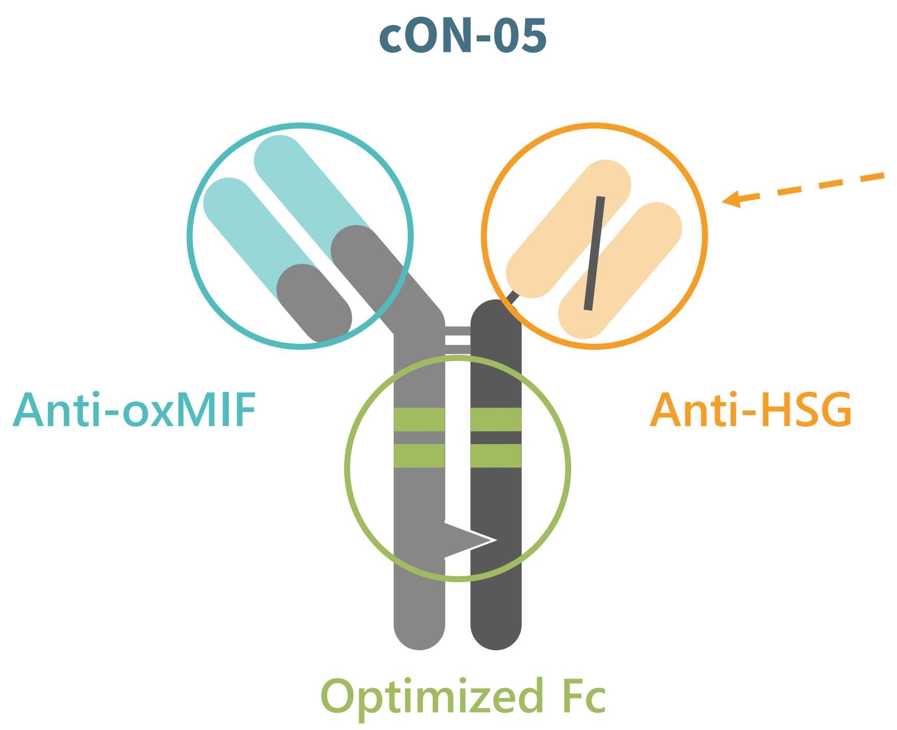
The tumor target: oxMIF

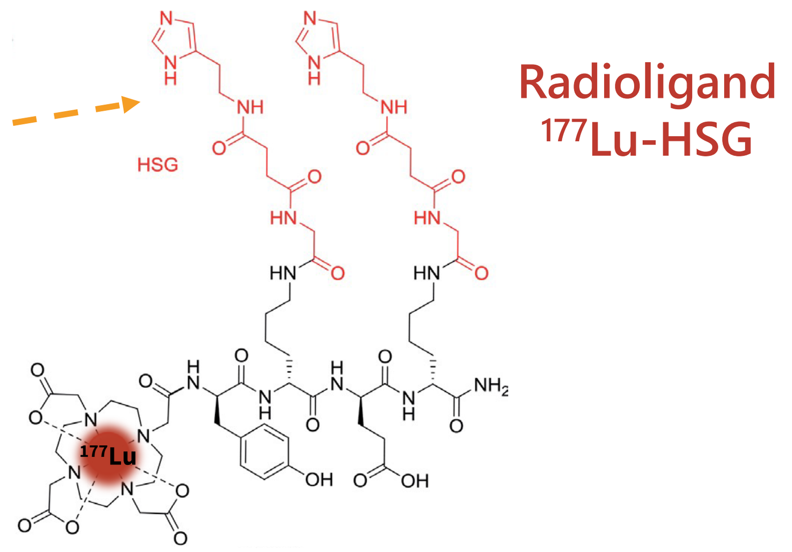
The founders of OncoOne discovered the disease-related and druggable isoform [1,2] of one of the most important drivers of innate and adaptive immunity: the macrophage migration inhibitory factor (MIF) [3]. Because it is generated in the pro-oxidative tumor microenvironment it was named "**oxMIF**" (oxidized MIF) [1,2,4]. In contrast to MIF, which is abundantly expressed in healthy and diseased tissues [3], oxMIF is formed by a post-translational modification which leads to a structural transformation that exposes epitopes in the MIF homotrimer that are otherwise inaccessible to antibodies in the center of the trimer [5,6].

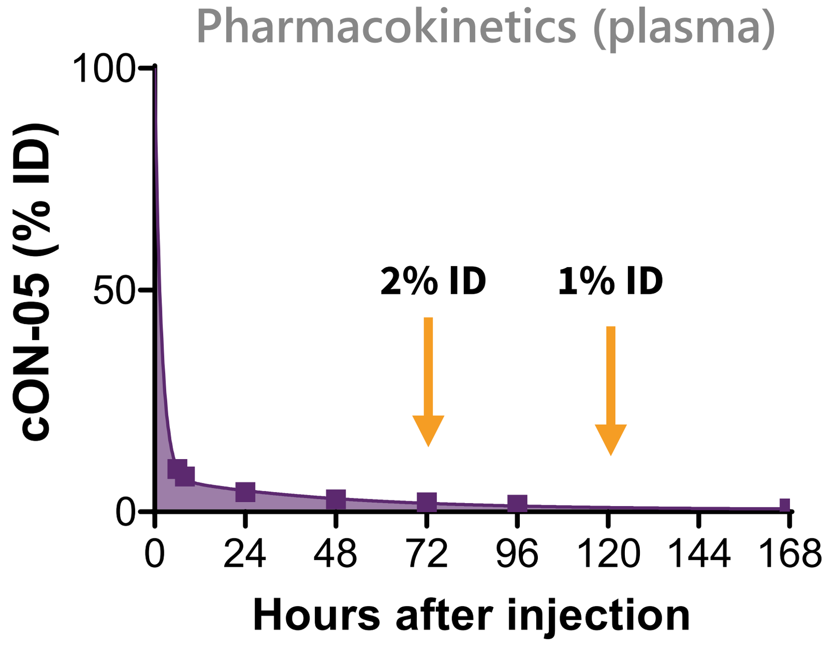


Targeting oxMIF as the disease related isoform of MIF overcomes the previous significant challenges associated with targeting MIF

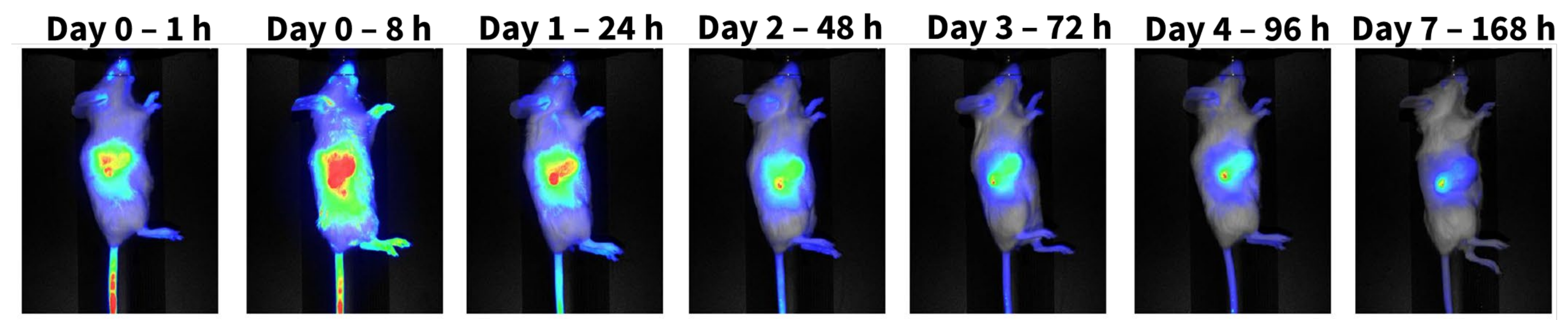
2 Biodistribution and PK of PreTarg-it ® bsmAb cON-05 & radioligand ^{177}Lu-HSG







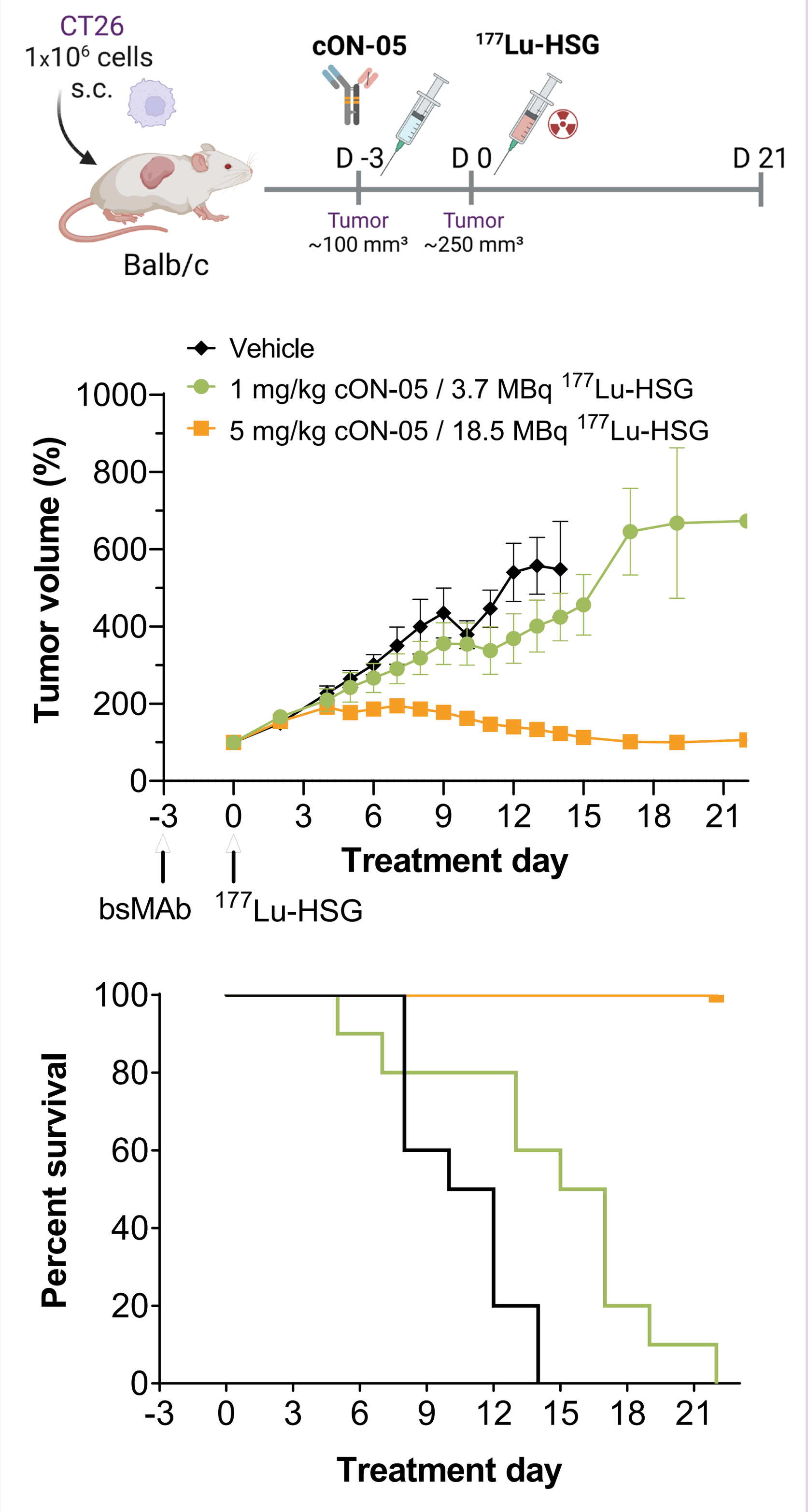
Biodistribution



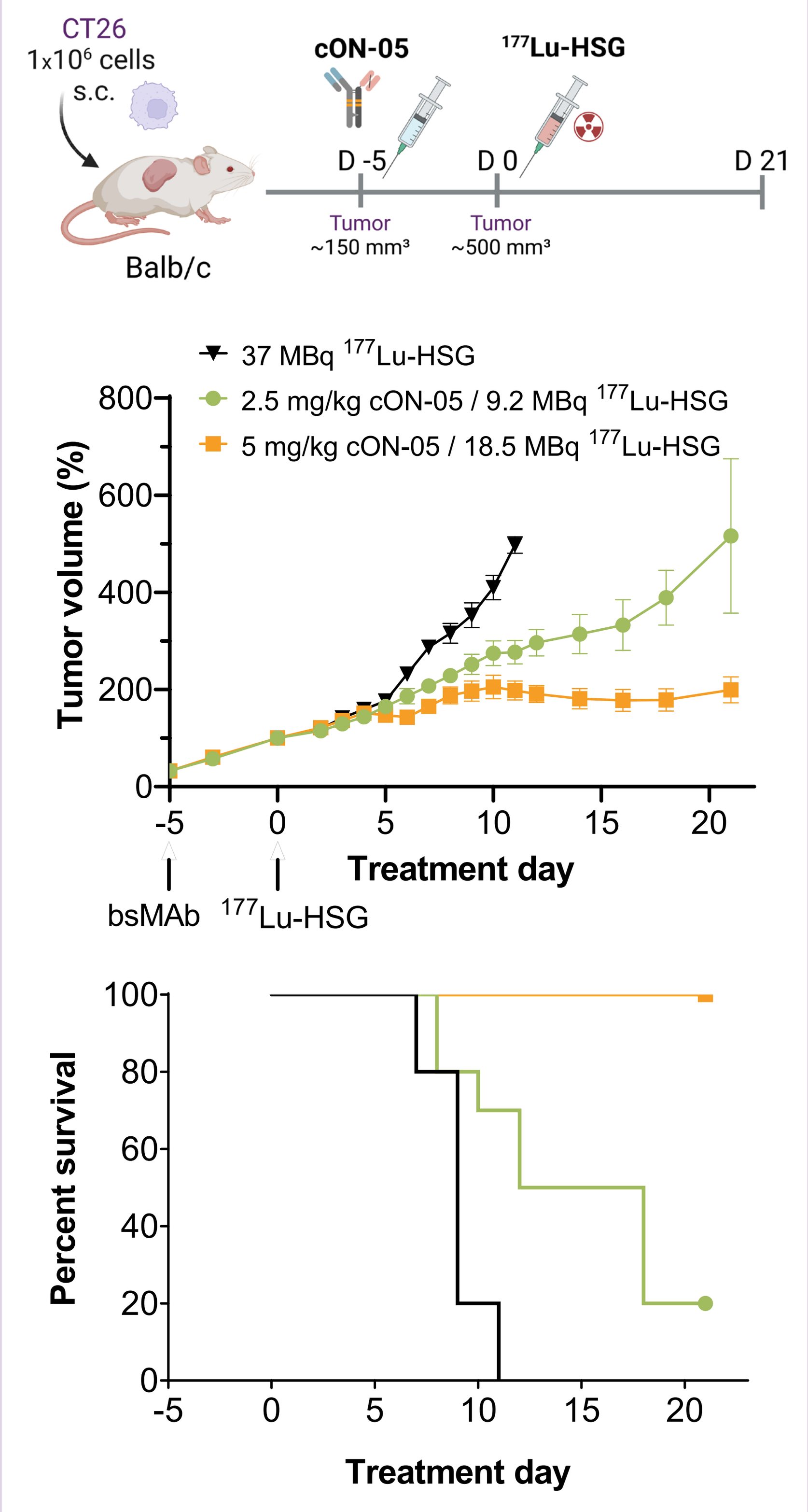
Optimal tumor-to-non-tumor ratio is reached at 3-5 days post injection, with 1-2% of cON-05 remaining in circulation

3 *In vivo* efficacy of PreTarg-it ® bsmAb cON-05 & radioligand ^{177}Lu-HSG

Colorectal cancer syngraft

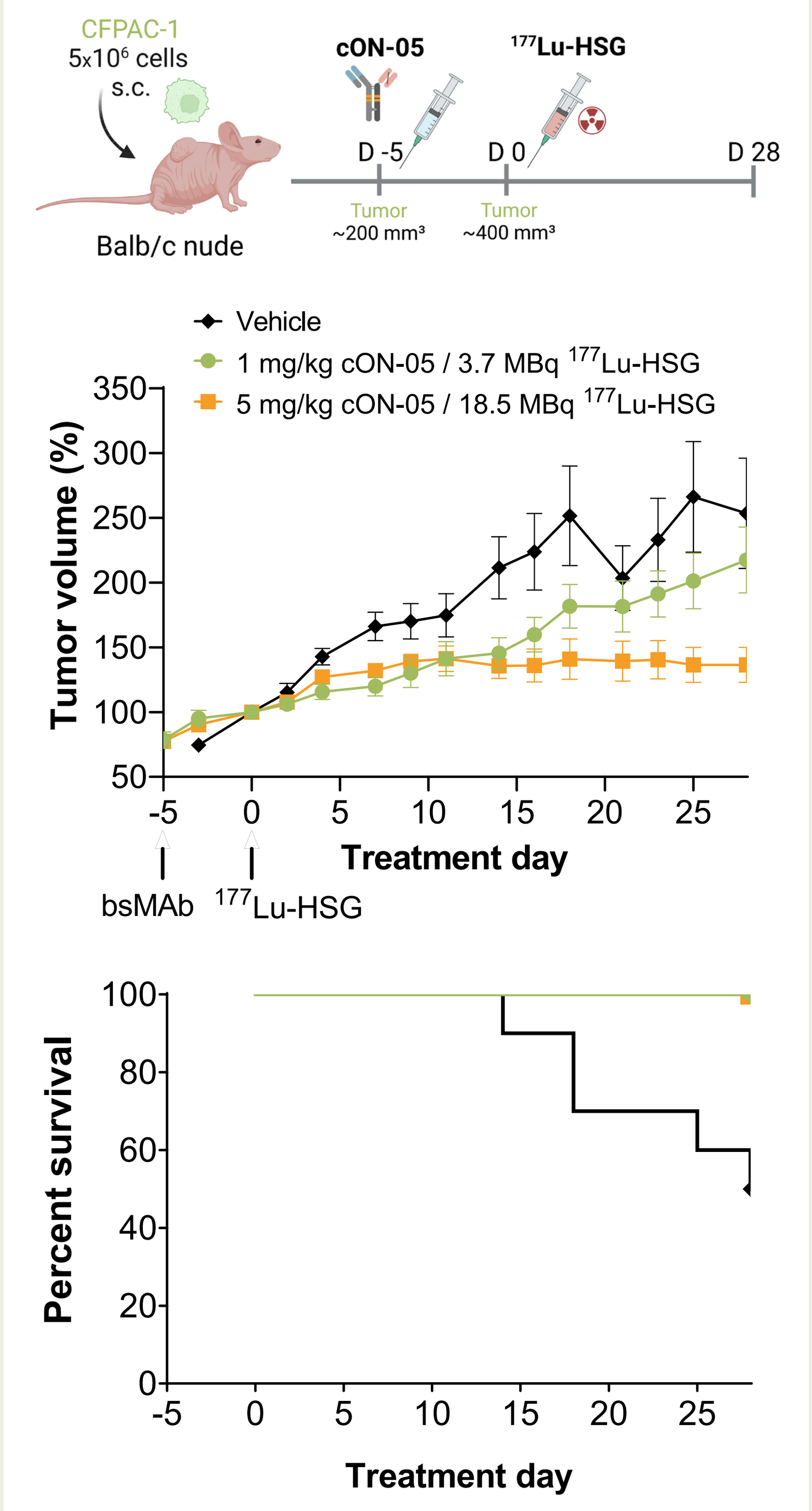


Highly significant tumor regression and survival benefit



Significant tumor growth inhibition and survival benefit

Pancreatic cancer xenograft



Significant tumor growth inhibition and survival benefit

4 Conclusions

- **cON-05 is a novel anti-oxMIF/HSG designed for pre-targeted radioimmunotherapy**
- **Pre-targeted radioimmunotherapy with cON-05 and ^{177}Lu-HSG has shown efficacy in murine models of cancer:**
  - ✓ **Highly significant tumor regression and survival benefit in colorectal syngraft model**
  - ✓ **Significant tumor growth inhibition in human pancreatic cancer xenograft model**

References

[1] Thiele et al., J Immunol. 2015 Sep 1;195(5):2343-52.
[2] Thiele et al. J Immunother Cancer 2022;10:e005475.
[3] Calandra & Roger, Nat Rev Immunol. 2003 Oct;3(10):791-800.
[4] Schinagl et al., Oncotarget. 2016 Nov 8;7(45):73486-73496.
[5] Schinagl et al., Biochemistry. 2018 Mar 6;57(9):1523-1532.
[6] Skeens et al., Structure. 2022 Mar 22;S0969-2126(22)00088-0.

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