Scan QRCode to receive the poster!

Translational pharmacology supporting biologics development in Oncology

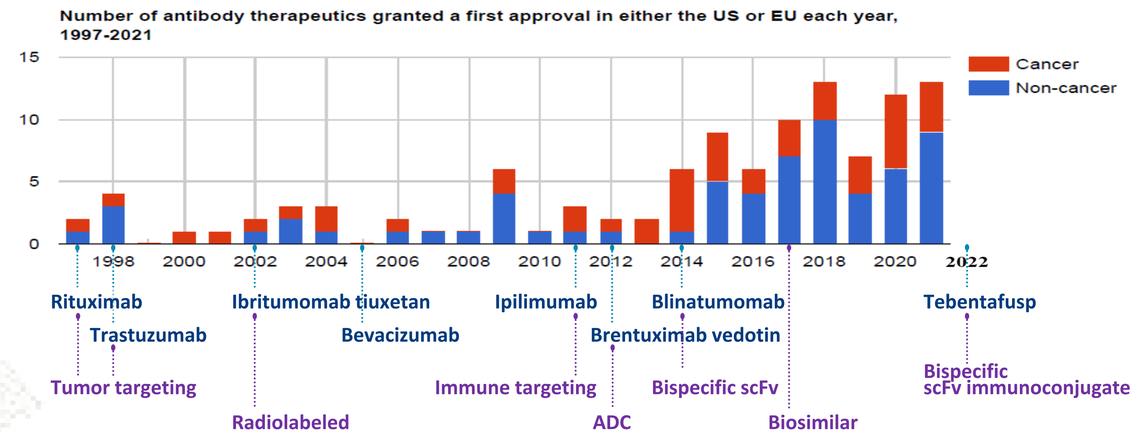
Caroline Mignard, Didier Grillot, Nicolas Ancellin, Sylvie Maubant, Olivier Duchamp, Fabrice Viviani – Oncodesign Services, 20 rue Jean Mazen, 21000 Dijon, France.

1 INTRODUCTION

New biological entities or biological therapeutic products (namely Biologics) include a huge diversity of products such as vaccines, gene and cellular therapies, recombinant therapeutic proteins, naked or conjugated monoclonal antibodies, bispecific antibody-like structure and others. Biologics can be composed of sugars, proteins, nucleic acids or complex combinations of these substances, or may even be living entities.

Biologics made a first revolution in cancer treatment with approval of rituximab and trastuzumab in late 1990's (two monoclonal antibodies targeting antigens expressed on tumor cells). A second major revolution was brought in the early 2010's with the approval of antibodies that target immune checkpoint on immune cells (i.e. ipilimumab targeting CTLA-4 positive regulatory CD4 T cells and nivolumab or pembrolizumab, both targeting PD-1 on T cells) rather than tumor cells.

Since 2017, there have been about 10 to 15 biologics approved each year, and many much more in clinical development, which represents a rapidly growing market in various therapeutic areas such as oncology, autoimmune diseases, inflammation, infectious diseases and others.



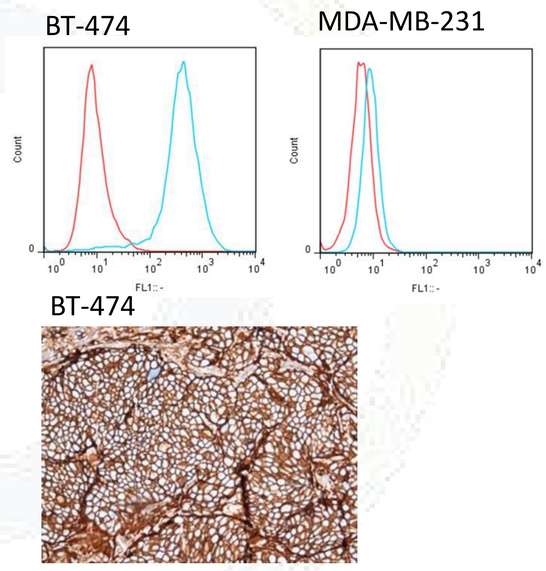
2 RESULTS

In vitro assays, targeting Her2

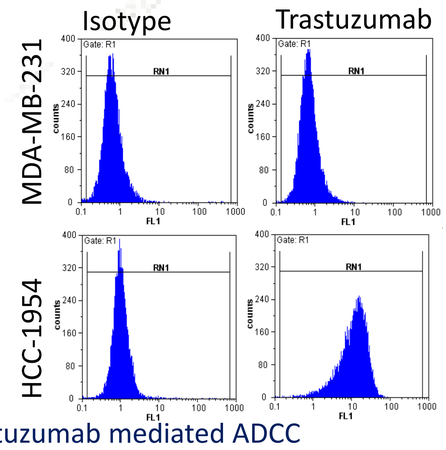
Target expression

Cell line	qPCR
	Erbb2 (Normalized value-arbitrary unit)
BT-474	5.63
MDA-MB-231	0.10

Cell line	IHC/FISH			
	IHC (4B5 antibody)	HER2 gene copy number	Chromosome 17 number of centromers	HER2/CNE17 ratio
BT-474	3+	>20	3.1	>6.4
MDA-MB-231	0	3.2	3.1	1.03

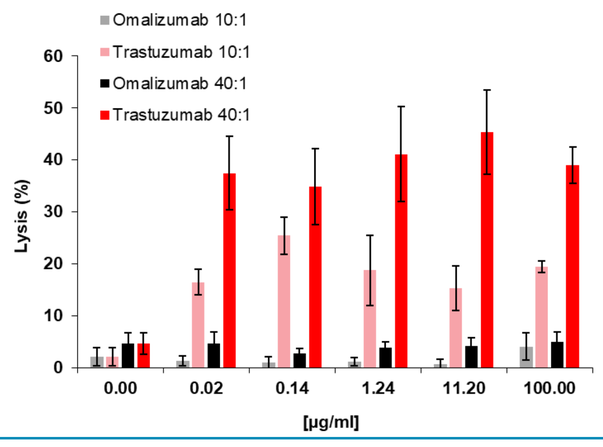


Trastuzumab binding



Trastuzumab mediated ADCC

SK-BR-3 + trastuzumab + activated hPBMCs

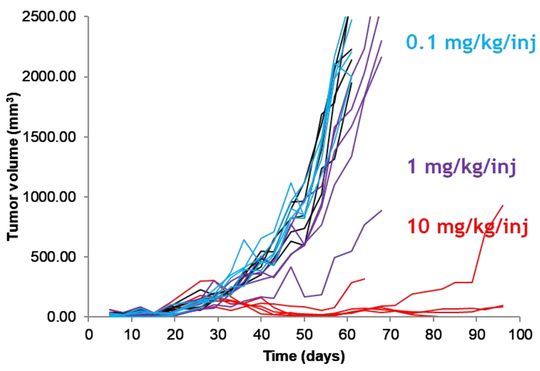


In vivo studies, targeting Her2

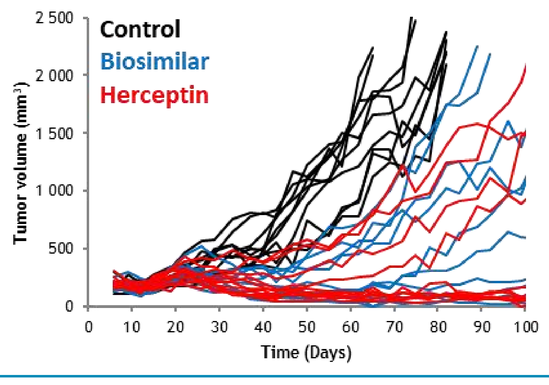
In vivo pharmacology

SC BT-474 human breast carcinoma

IP trastuzumab, TWx3



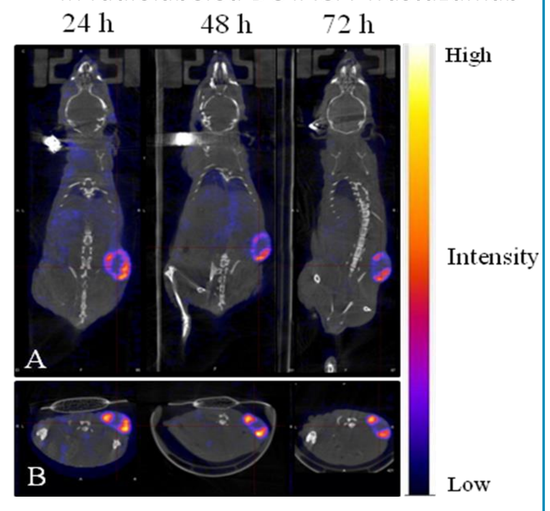
Trastuzumab biosimilar, Q1Dx1



In vivo SPECT imaging

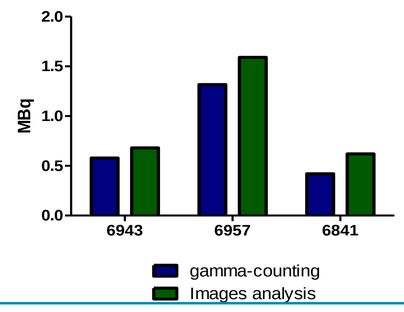
SC BT-474 human breast tumor

^{111}In radiolabeled DOTAGA-Trastuzumab



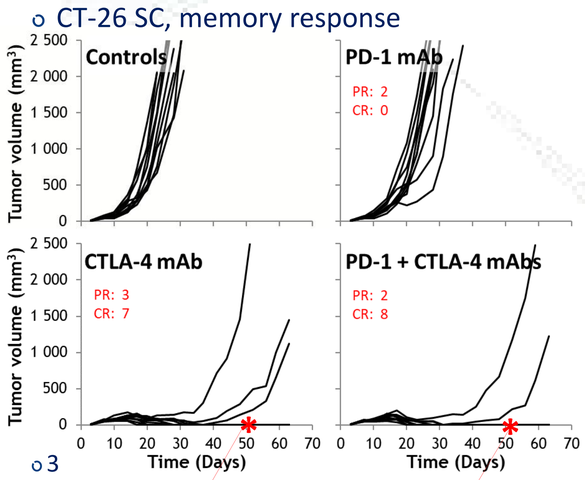
Radioactivity uptake in tumors

γ-counting compared to images analysis

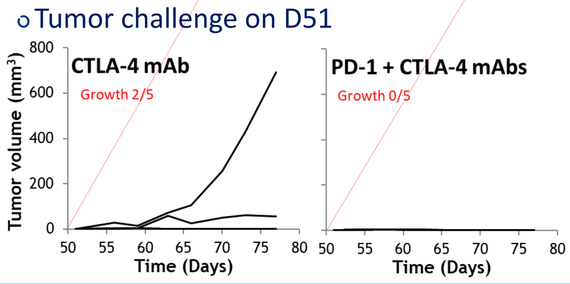


In vivo syngeneic studies, targeting PD-1

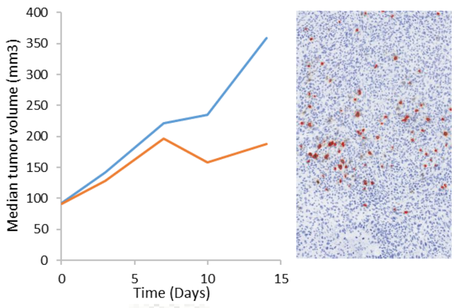
CT-26 SC, memory response



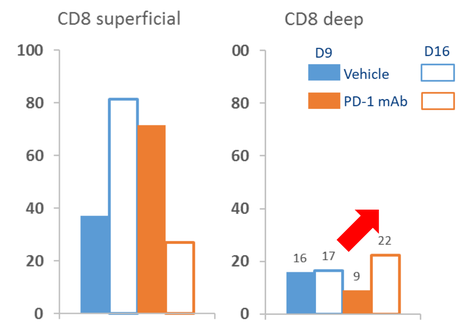
3 Tumor challenge on D51



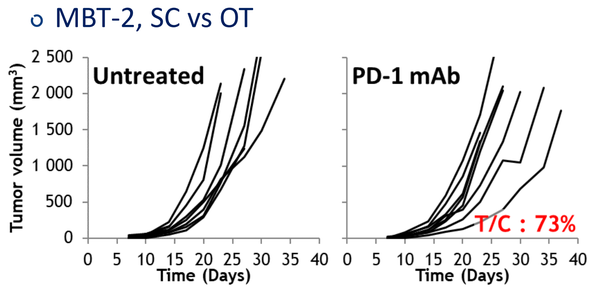
EMT-6 SC, CD8 infiltrate



Migration of CD8

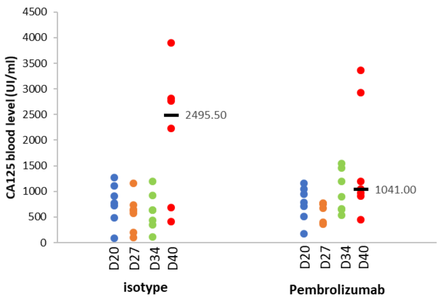


MBT-2, SC vs OT

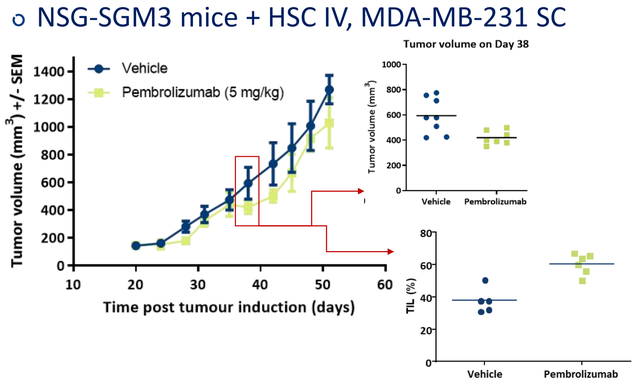


In vivo humanized mouse studies

NOG mice + NIH-OVCAR-3 IP, PBMC IV



NSG-SGM3 mice + HSC IV, MDA-MB-231 SC



3 CONCLUSION

Attempting to support biologics development cycle, Oncodesign Services has established a fully integrated offering from early discovery through preclinical testing as well as support to clinical studies. Various study cases can be shared covering the following:

- **Custom cellular model development for discovery and potency analysis,**
- ***In vitro* screen, target engagement or mechanism of action related studies whether effects are direct or mediated. Cellular models ranging from tumor cell lines, immune cells or primary materials.**
- ***In vivo* efficacy and safety studies using refined and highly characterized syngeneic, xenogeneic, PDX or humanized mouse models up to non-human primates,**
- **DMPK department can develop and validate LBA bioanalytical methods as well as qPCR/RT-qPCR bioanalytical (including GLP compliancy) and also assess immunogenicity,**
- **Biodistribution and tumor specificity analysis of in-house conjugated and radiolabeled biologics.**

oncodesign-services.com