



HAL
open science

Extending trastuzumab-coated immunoliposome to HER2 negative breast cancer models: a proof of concept study

Anne Rodallec, Guillaume Sicard, Sarah Giacometti, Stéphane Robert,
Florian Correard, Fanny Bouquet, Ariel Savina, Joseph Ciccolini, Raphaëlle
Fanciullino

► To cite this version:

Anne Rodallec, Guillaume Sicard, Sarah Giacometti, Stéphane Robert, Florian Correard, et al.. Extending trastuzumab-coated immunoliposome to HER2 negative breast cancer models: a proof of concept study. Journées GPCO (Le Groupe de Pharmacologie Clinique Oncologique), Nov 2018, Villejuif, France. hal-04727223

HAL Id: hal-04727223

<https://hal.science/hal-04727223v1>

Submitted on 9 Oct 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

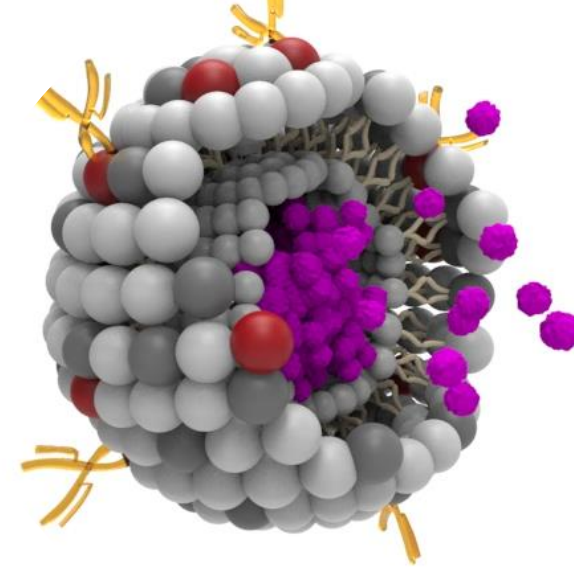
L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



A Rodallec¹, G Sicard¹, S Giacometti¹, S Robert², F Correard³, F Bouquet⁴, A Savina⁴, J Ciccolini¹ and R Fanciullino¹
1: SMARTc Unit, CRCM, AMU; 2: AMUTICYT, VRCM, AMU; 3: IMP, AMU; 4: Institut Roche, Boulogne Billancourt

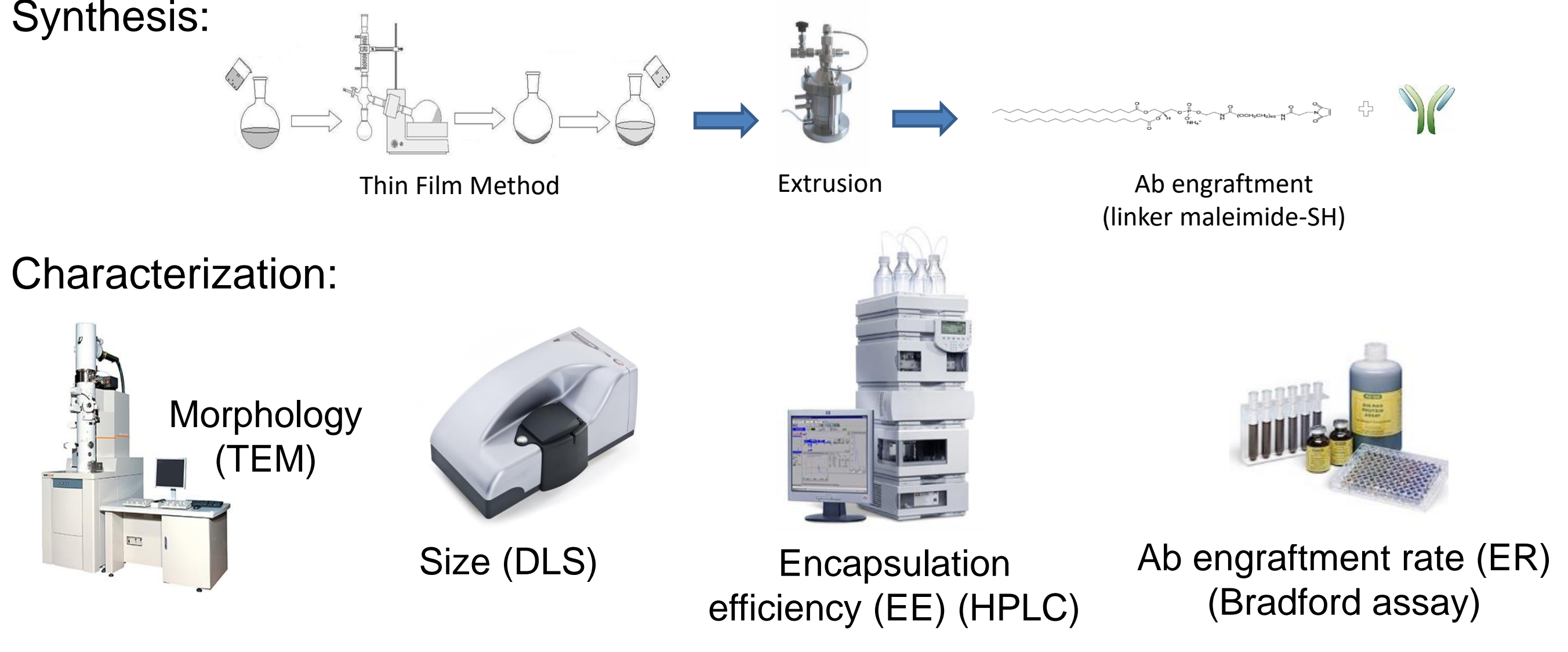
BACKGROUND

Since its first approval in 1998, the anti-Her2 monoclonal antibody (Ab) trastuzumab has considerably improved the clinical outcome of women with Her2+ breast cancer. However, only 25 % of breast cancer patients display amplification of Her2 gene and benefit from this therapy. Expanding trastuzumab indication to a wider group of patients with lower levels of Her2 has then largely been studied but was never conclusive. To potentialize trastuzumab tumor uptake and maybe overcome this limitation, we developed a docetaxel immunoliposome coated with trastuzumab.

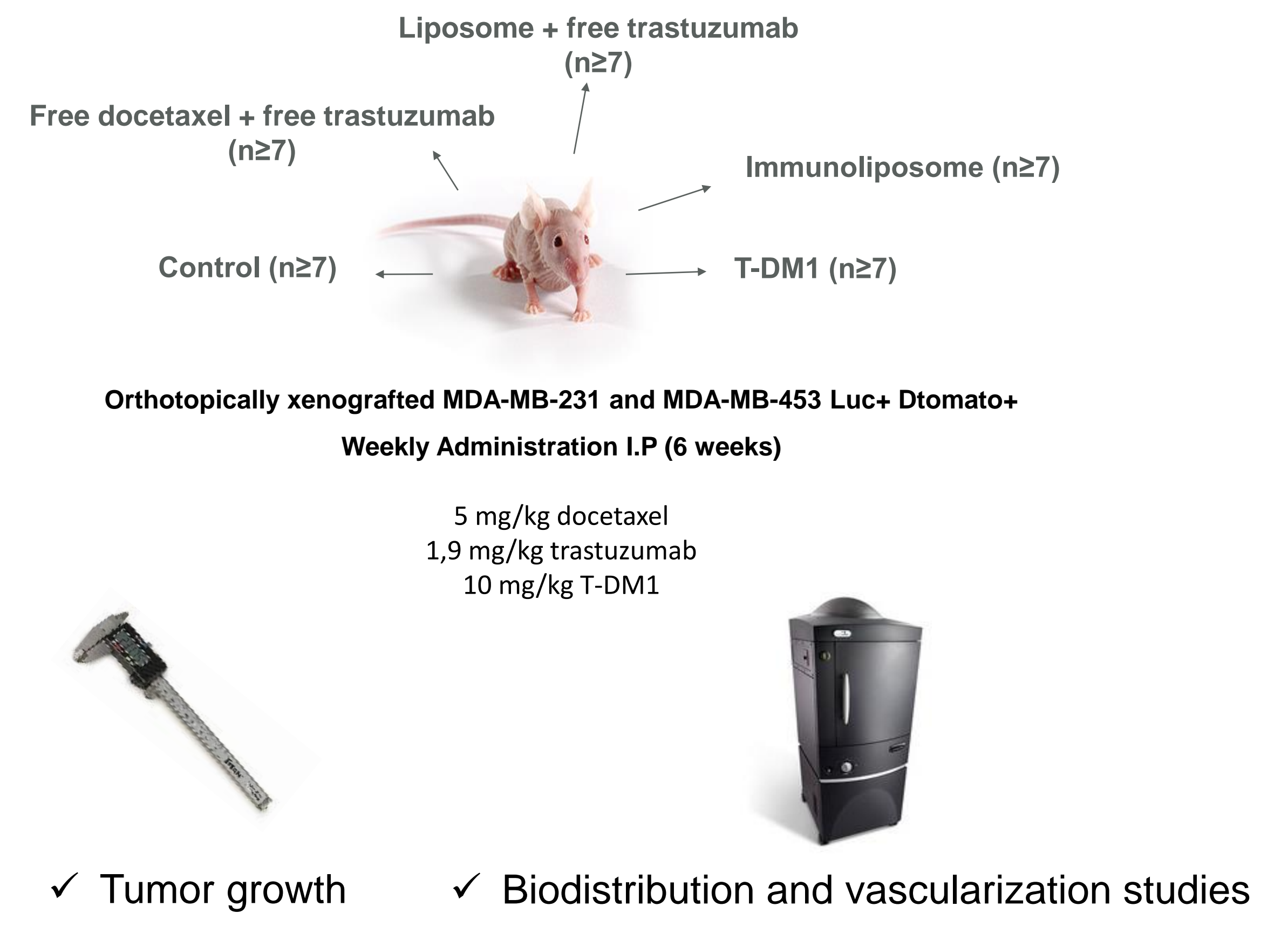


MATERIAL & METHODS

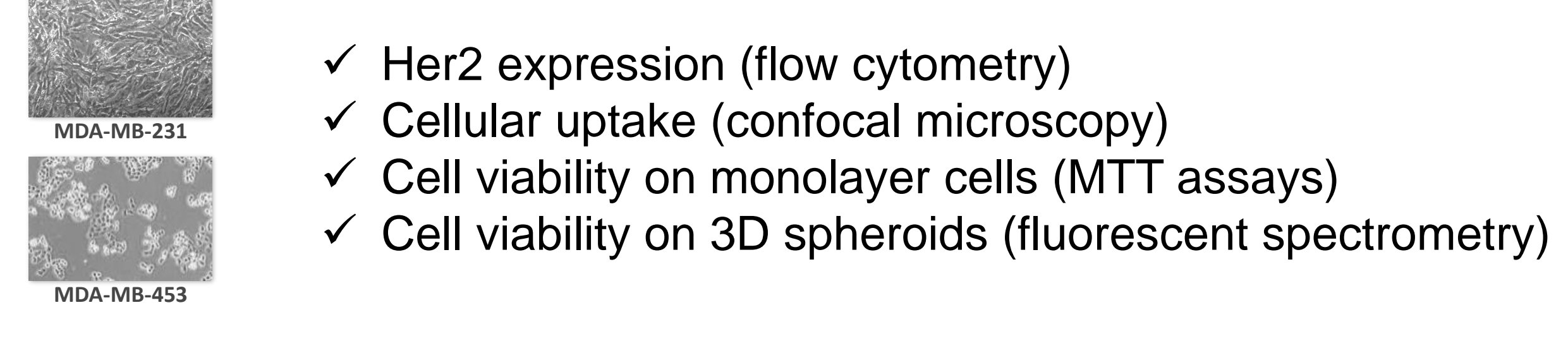
Step 1: Biopharmaceutical development of immunoliposomes



Step 3: In vivo proof of concept studies



Step 2: In vitro proof of concept studies



RESULTS

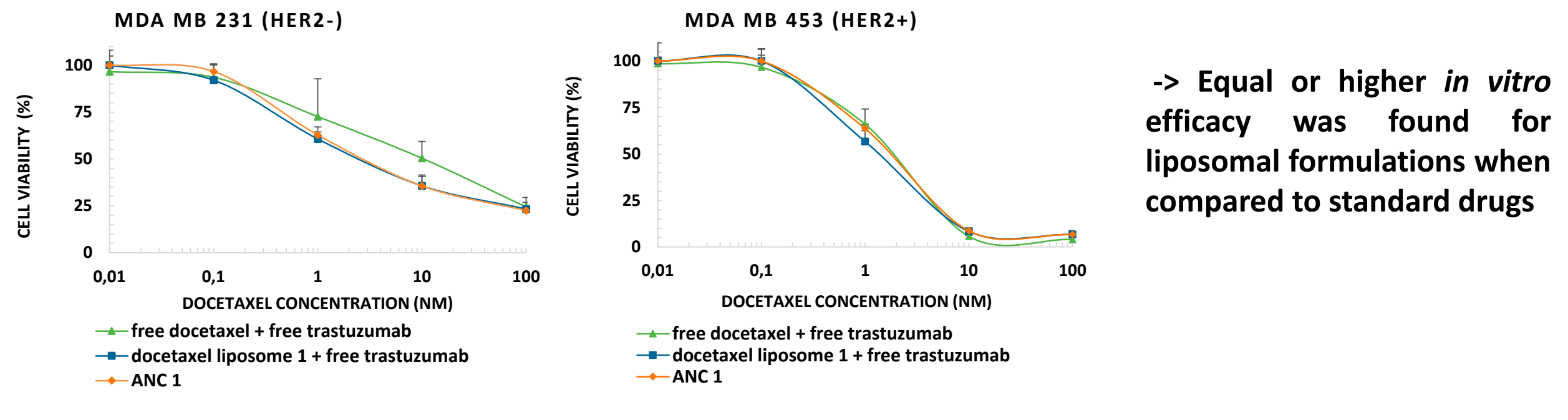
Step 1: Characterization of immunoliposomes

Size (nm)	PDI	Docetaxel EE (%)	Morphology	Ab ER (%)	Stability
140 ± 3	< 0.2	> 90		30 ± 6	One week

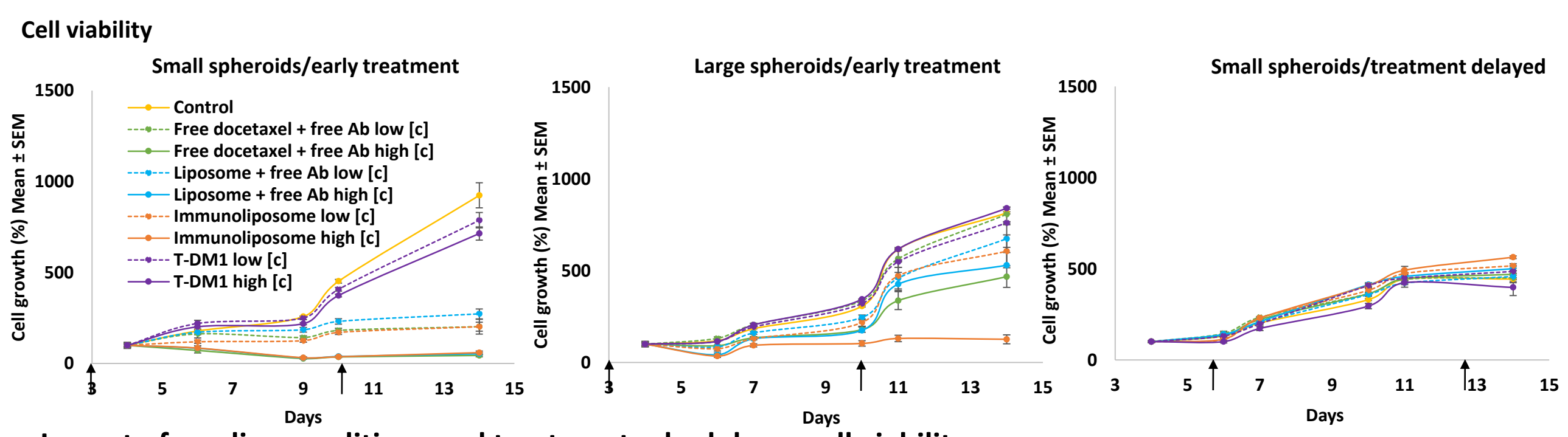
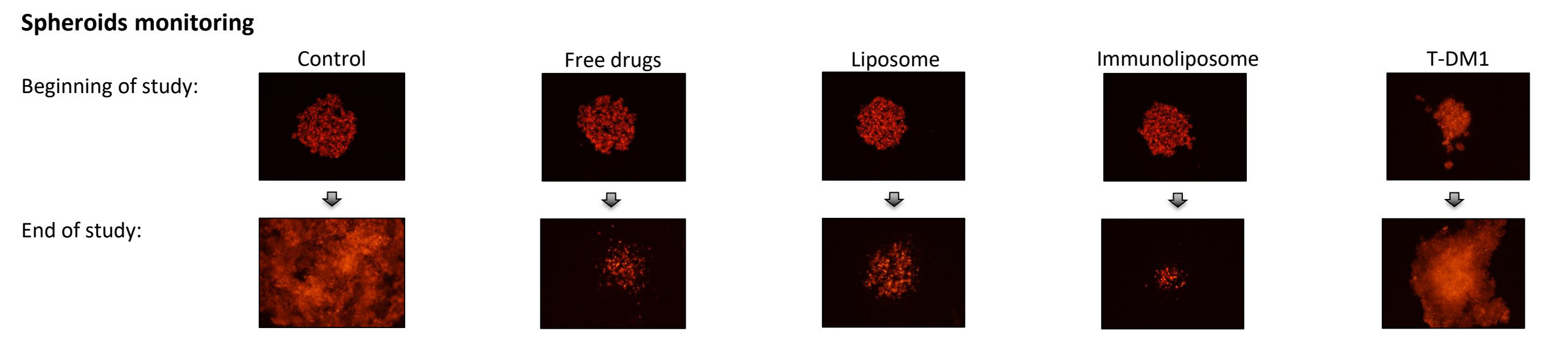
Step 2: In vitro proof of concept studies



Cell viability on monolayer cells



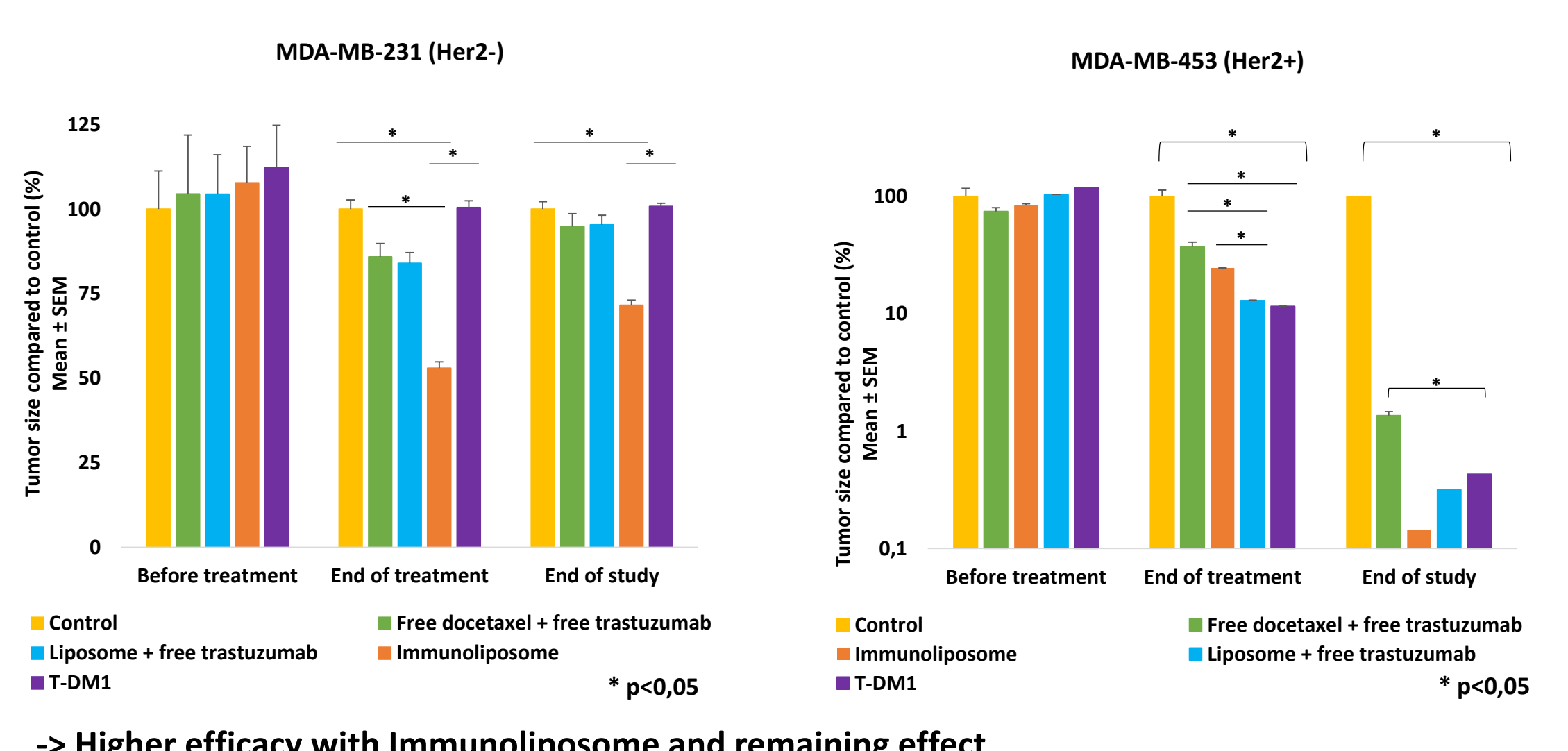
Cell viability on 3D spheroids: MDA-MB-453 (similar results on MDA-MB-231)



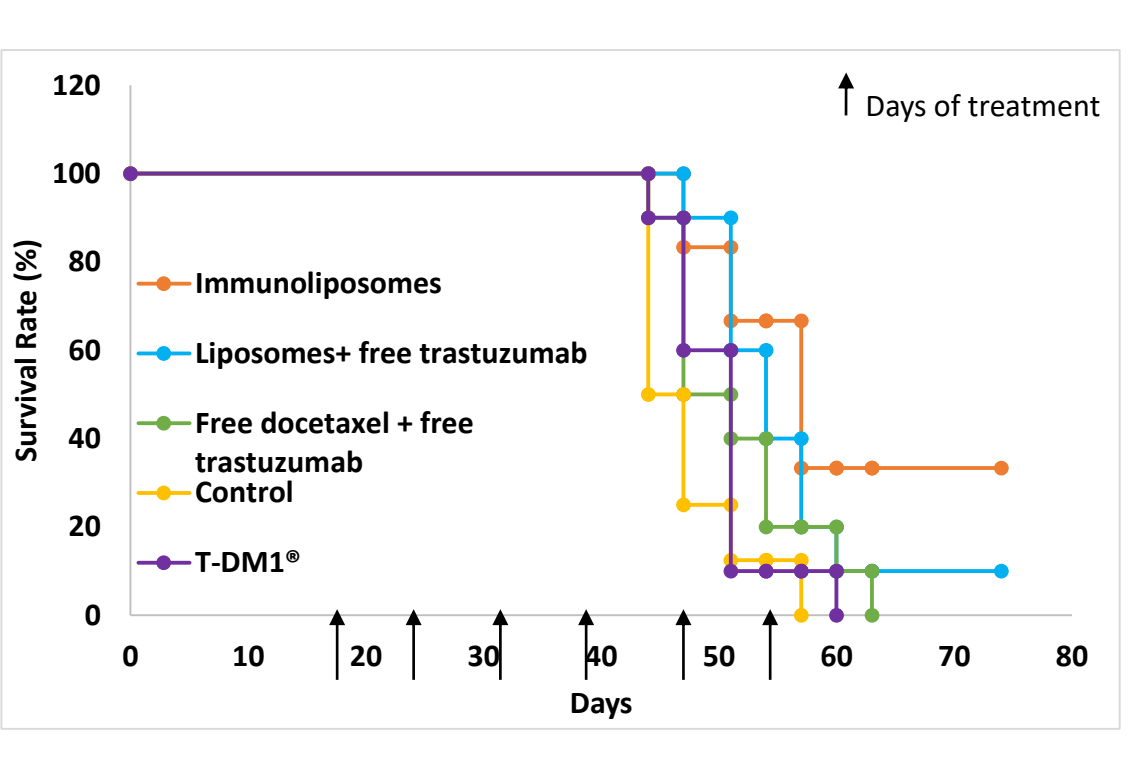
-> Impact of seeding conditions and treatment schedule on cell viability
-> No effect of T-DM1
-> Higher antiproliferative effect with Immunoliposome

Step 3: In vivo proof of concept studies

✓ Tumor growth

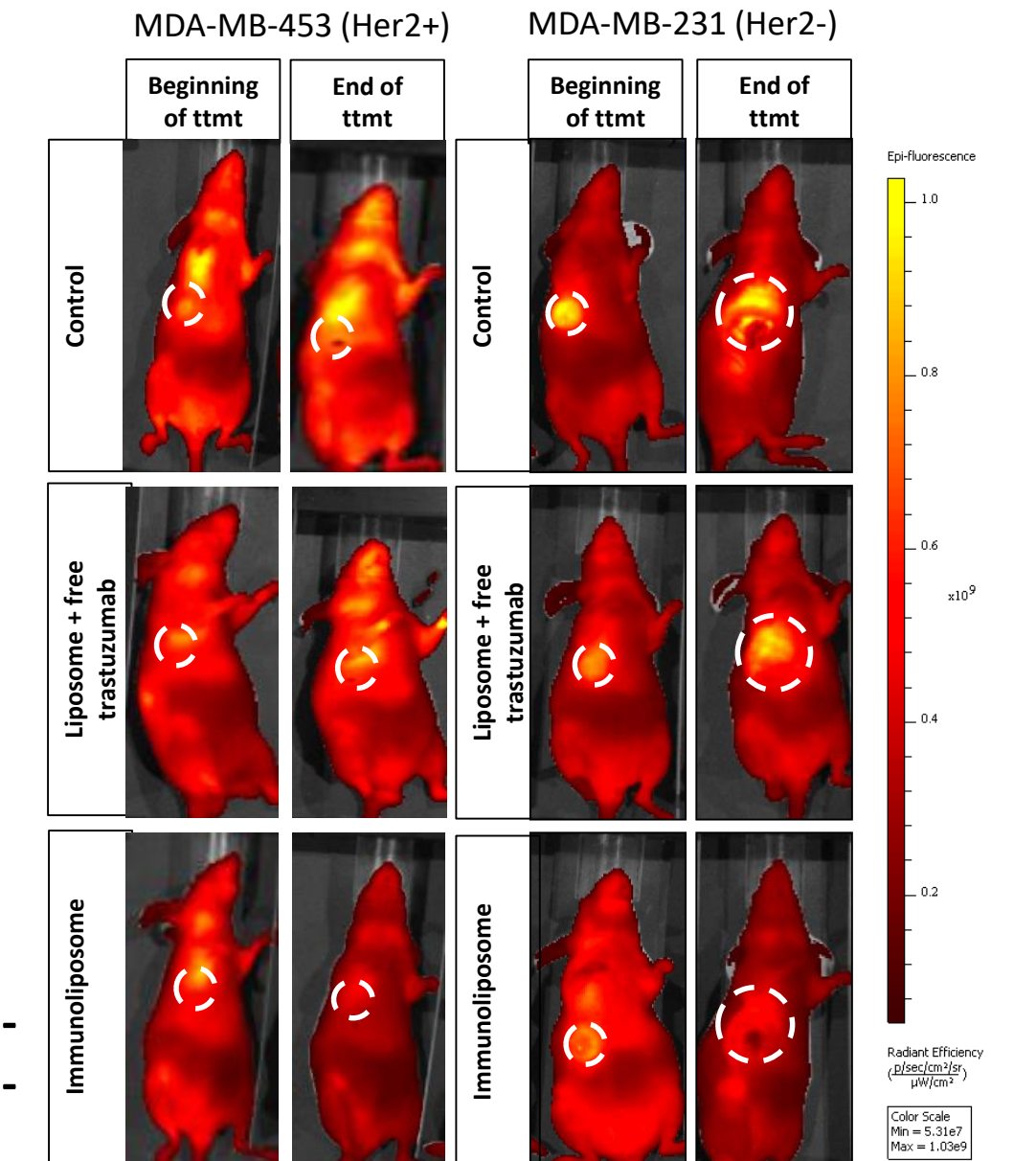


✓ Survival studies

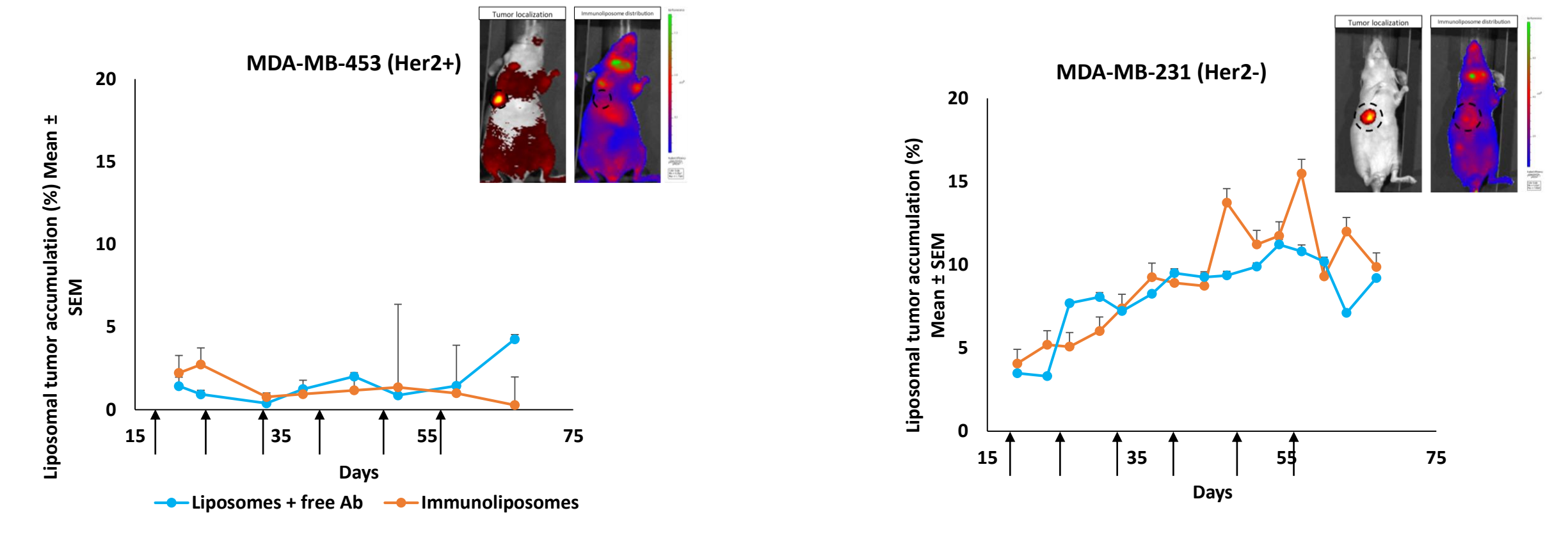


-> Mean survival was not reach for MDA-MB-453 xenografted mice
-> Survival was 22 % longer with Immunoliposome

✓ Vascularization studies



✓ Biodistribution studies



-> No difference in tumor uptake between Liposome and Immunoliposome
-> Intratumor accumulation was 3 % and 15 %
-> Intratumor accumulation was independent to Her2 expression

CONCLUSION & PERSPECTIVES

- ✓ **Conclusions**
 - Feasibility of making 3rd generation liposomes, fitting optimal characteristics.
 - Immunoliposome achieved higher antiproliferative effect on 2D and 3D cell models.
 - Optimized biodistribution profile, leading to higher in vivo efficacy with Immunoliposome.
 - Her2 expression and especially vascular density dependent tumor uptake, demonstrating the interest of such nanoparticle in triple negative breast cancer.

- ✓ **Perspectives**
 - Pharmacokinetic studies: plasmatic and intratumor docetaxel dosing
 - Optimization of in vitro models (co-cultured spheroids and organoids)
 - Confirmation of Immunoliposome advantages on a second Her2- model (MCF7)
- ✓ **References**
Rodallec et al. Int. J. Nanomedicine, 2018