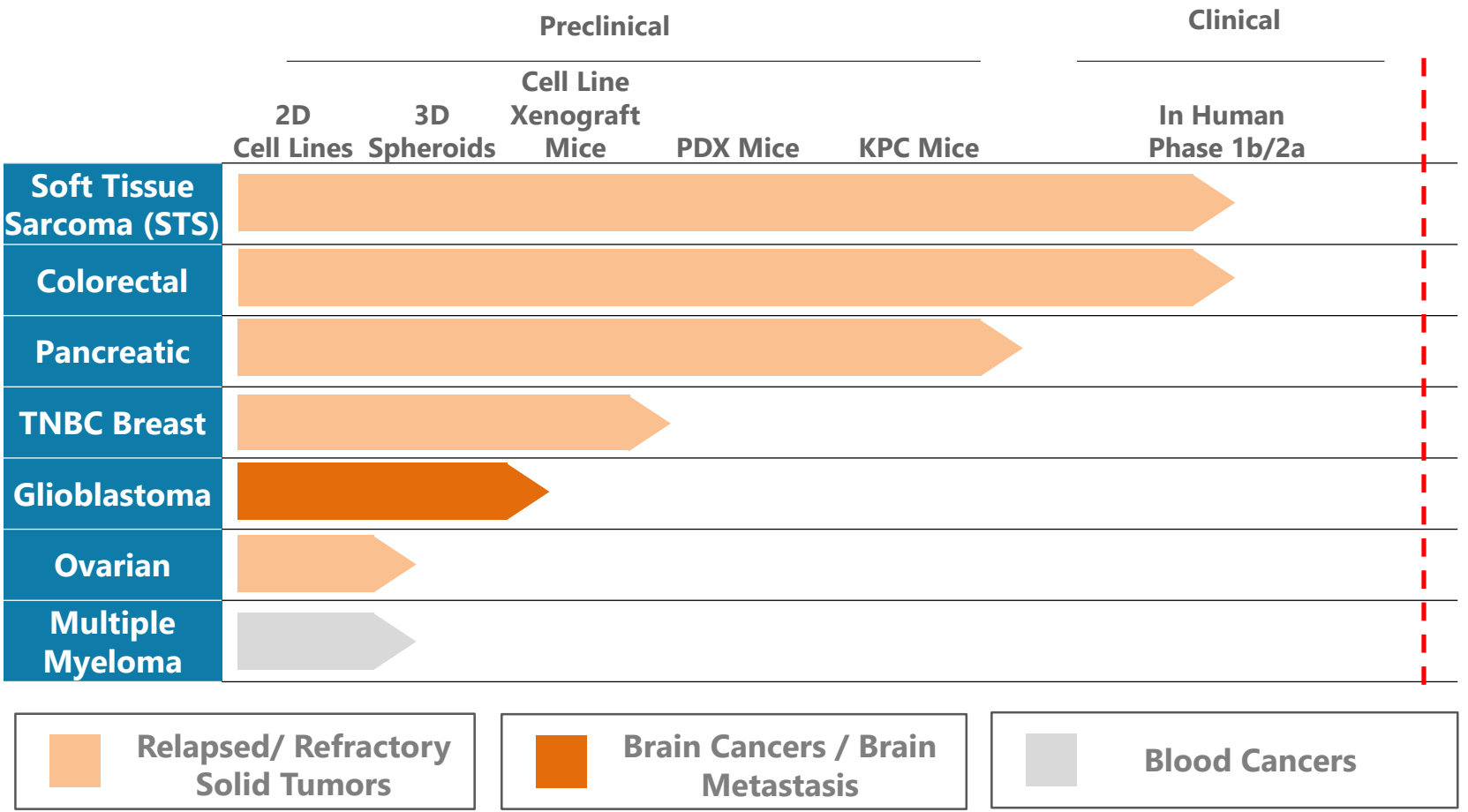
IMMiX

iMX-110: Tumor Killing Across A Wide Range of Indications

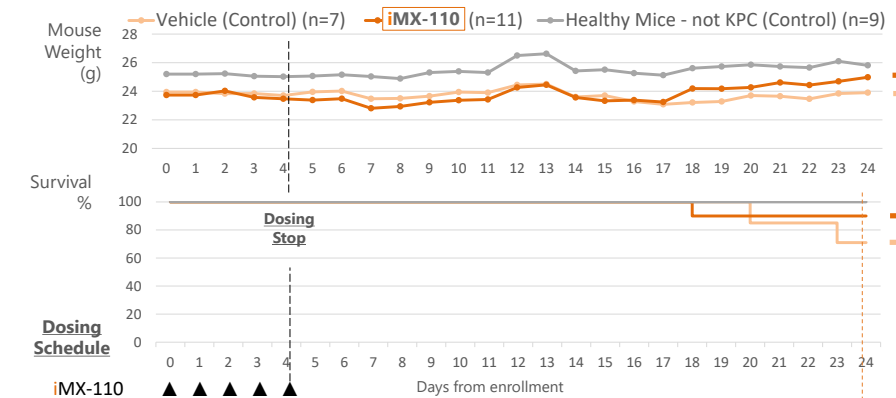


Source: Immix Biopharma Management.

iMX-110 Pancreatic Preclinical KPC Mouse Model (1/2): Shrinks Tumors Far Beyond SOC & Evidence of Tumor-Immune System Interaction Reset

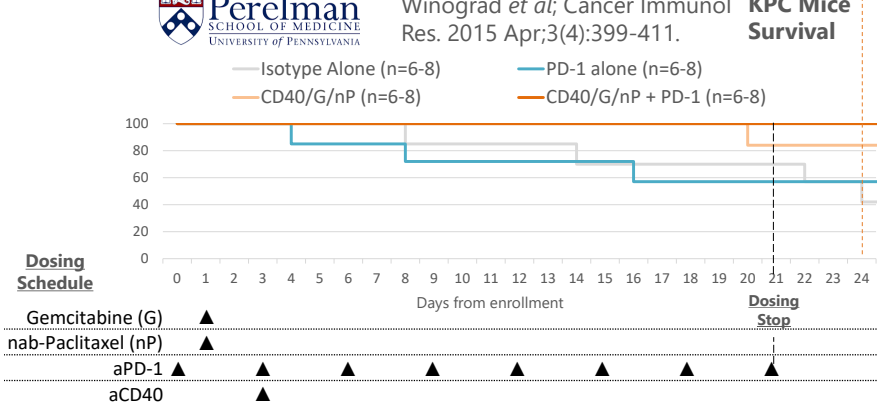
Pancreatic Pdx1-Cre (KPC mice) Model – iMX-110 Monotherapy - IMMiX Biopharma Unpublished Data

IMMiX Biopharma **Mouse Weight (Top) & Survival (Bottom)**



Perelman School of Medicine University of Pennsylvania

Winograd *et al*; Cancer Immunol Res. 2015 Apr;3(4):399-411. **KPC Mice Survival**



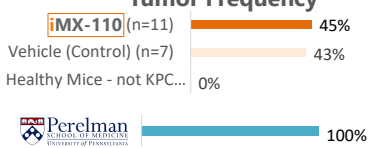
Post- iMX-110 Treatment Tumor Size (cm)

Mouse A (Vehicle) – Tumor @ Death (Day 23)

VS.

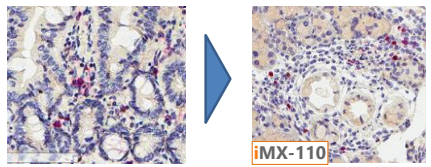
Mouse B (iMX-110) Tumor @ Sacrifice (Day 24)

Tumor Frequency

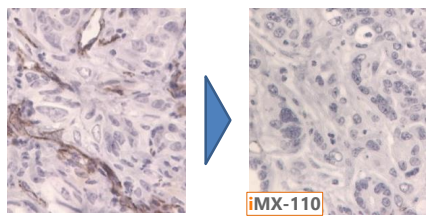


Pre & Post iMX-110 Treatment Histology

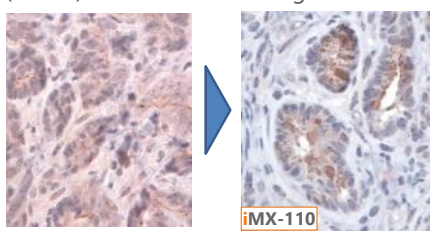
Inhibiting T-regulatory (FoxP3+) cells (stained in bright red-blue); activating anti-tumor immune attack



CD31 (stained) Endothelial cells throughout tumor



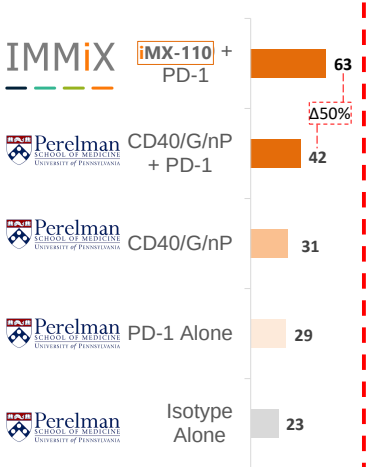
CD8 (stained) T cell distribution throughout tumor



Source: Immix Biopharma Management. Winograd et al. Induction of T-cell Immunity Overcomes Complete Resistance to PD-1 and CTLA-4 Blockade and Improves Survival in Pancreatic Carcinoma. Cancer Immunol Res..2015 Apr;3(4):399-411. doi: 10.1158/2326-6066.CIR-14-0215. Epub 2015 Feb 12. Note: Immix Biopharma data - on days 12-13, for 10 of the 27 total mice weight measurements were not obtained. Immix Biopharma Dosing: IMX-110 dosed based on doxorubicin at 1.4 mg/kg. Winograd, et al Dosing: gemcitabine (Eli Lilly) 120 mg/kg, nab-paclitaxel (Sigma) 108 mg/kg, aCD40 (FGK45; BioXcell) 100µg/dose, aPD-1 (RMP1-14; BioXcell) 200µg/dose

iMX-110 Pancreatic Preclinical KPC Mouse Model (2/2): (iMX-110 + PD-1) Outperforms (Gem + Pac + PD-1 + CD-40)

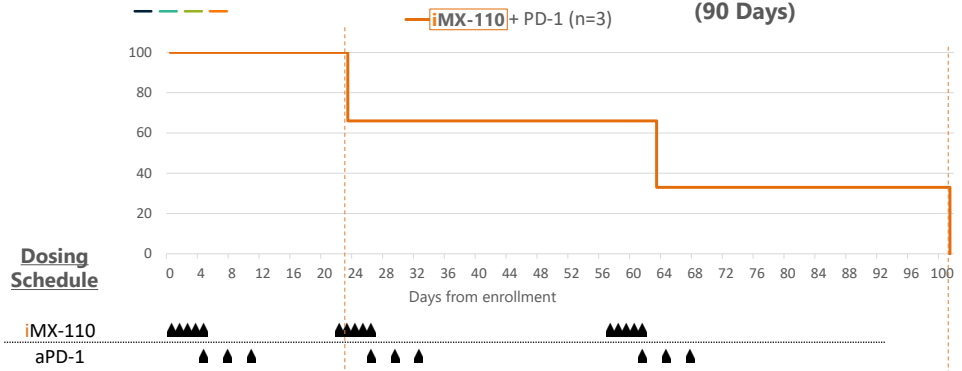
Median Survival Comparison Pdx1-Cre (KPC mice) Panc Model



Pancreatic Pdx1-Cre (KPC mice) Model – iMX-110 + PD-1 Combination

IMMiX Biopharma Unpublished Data

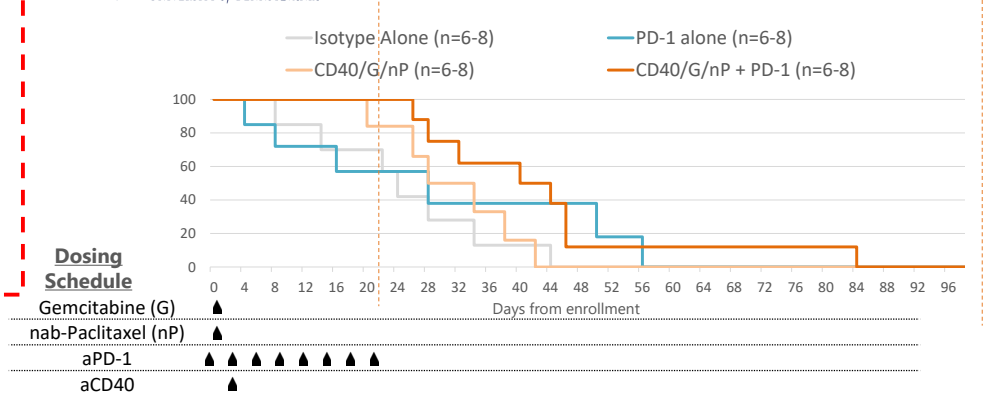
KPC Mice Survival (90 Days)



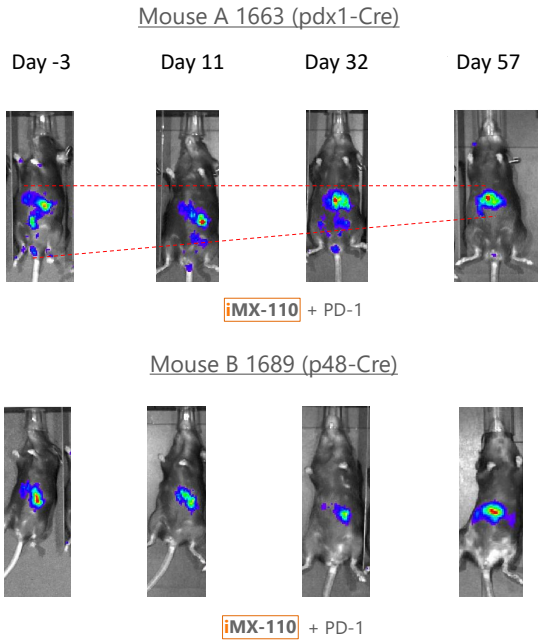
Perelman School of Medicine University of Pennsylvania

Winograd *et al*; Cancer Immunol Res. 2015 Apr;3(4):399-411.

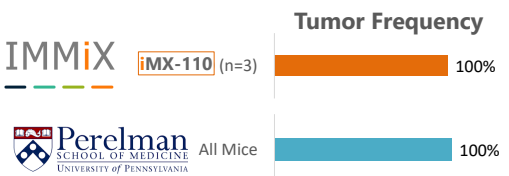
KPC Mice Survival (90 Days)



IMMiX Individual Mice – Luciferase activity (tumor growth) activity



Tumor Frequency



Source: Immix Biopharma Management, Winograd et al. Induction of T-cell Immunity Overcomes Complete Resistance to PD-1 and CTLA-4 Blockade and Improves Survival in Pancreatic Carcinoma. Cancer Immunol Res..2015 Apr;3(4):399-411. doi: 10.1158/2326-6066.CIR-14-0215. Epub 2015 Feb 12.

Immix Biopharma Dosing: IMX-110 dosed based on doxorubicin at 1.5 mg/kg, aPD-1 (RMP1-14; BioXcell) 100µg/dose

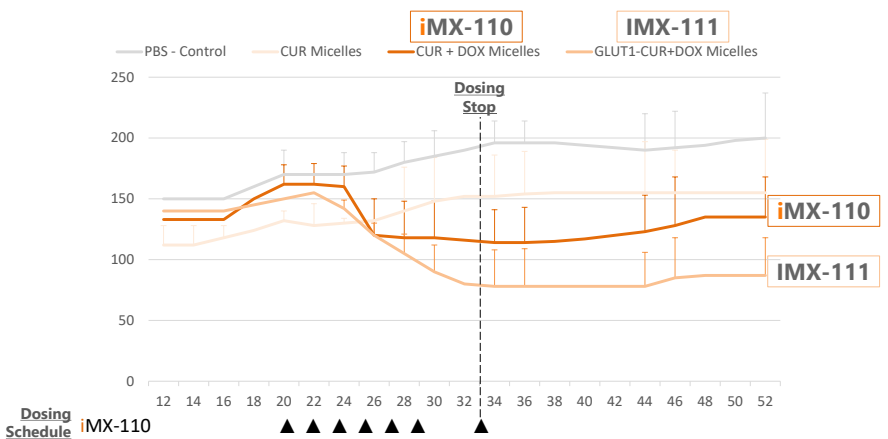
Winograd, et al Dosing: gemcitabine (Eli Lilly) 120 mg/kg, nab-paclitaxel (Sigma) 108 mg/kg, aCD40 (FGK45; BioXcell) 100µg/dose, aPD-1 (RMP1-14; BioXcell) 200µg/dose

IMMiX

iMX-110 TNBC Breast & Colorectal Preclinical Xenograft Mouse Model: Immix Biopharma Therapies Produce Rare Tumor Shrinkage/Stability

1 Kills Tumors in Doxorubicin resistant MDA-MB-231 TNBC Breast Cancer Cell Line ...

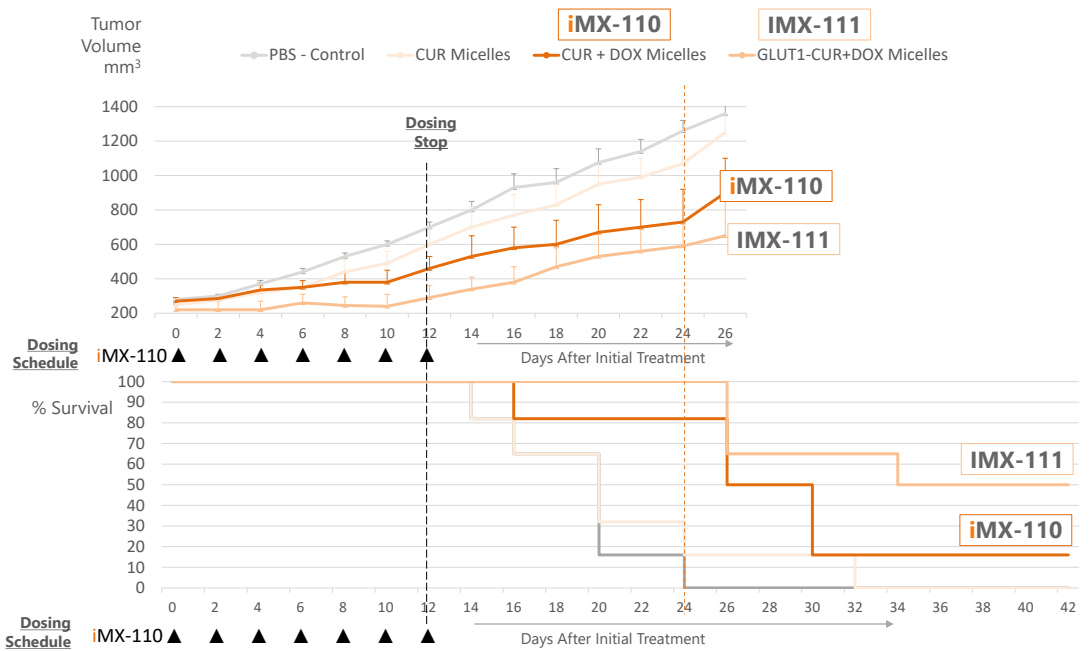
MDA-MB-231 Xenograft Model: Tumor Volume After 7 injections



Tumor inhibition studies of various micellar formulations. Nude mice bearing ~150 mm³ MDA-MB-231 tumors were treated every 2 days starting at Day 20 except last injection administered at day 33 (7 total IV injections) at a dose of 6 mg/kg CUR and 1 mg/kg DOX. N≥6 with SEM (Sourced from Abouzeid et al, 2014).

2 ... And Kills Tumors in HCT-116 Colorectal Cancer Cell Line Which Is Not Typically Treated With Doxorubicin

HCT-116 Xenograft Model: Tumor Volume & Survival Curve After 14 day treatment (7 injections)



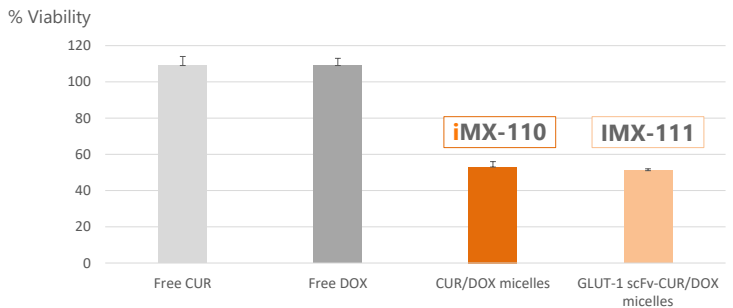
Tumor inhibition studies of various micellar formulations. Female nude (NU/NU) mice bearing 250mm³ HCT-116 tumors were treated every 2 d starting at day 0 (7 total tail vein injections, arrows correspond to injection days) at a dose of 4 mg/kg CUR and 0.4 mg/kg DOX. N = 6 with SEM. Empty micelle dose was equivalent to the amount of lipid from the drug-loaded micelle groups. A – Tumor volume. B – Survival curve, survival was determined when the tumor reached 1000mm³ (Sourced From Abouzeid et al, 2013)

Source: Immix Biopharma Management. Abouzeid, et. al. Anti-cancer activity of anti-GLUT1 antibody targeted polymeric micelles co-loaded with curcumin and doxorubicin (2013 - https://doi.org/10.3109/1061186x.2013.840639); Abouzeid et al, Nanotechnology-based treatment for chemotherapy-resistant breast cancer. SPIE 9166, Biosensing and Nanomedicine VII, 916606 (27 August 2014); doi: 10.1117/12.2064660. Measurements ± SD.

IMMiX

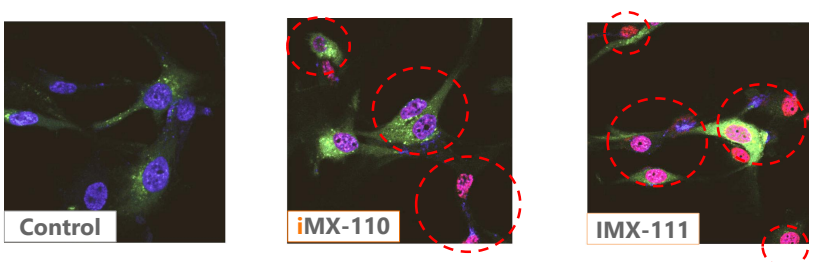
iMX-110 Glioblastoma Preclinical 3D Spheroids (Doxorubicin Resistant): Tumor Killing, Spheroid Penetration & Nucleus-Seeking

GBM U87MG 3D Spheroids Model: Cell viability (%) vs. control (Free CUR or Free DOX) of doxorubicin-resistant U87MG cells after 48 h



Evaluation of 48 h cytotoxicity on U87MG spheroids in vitro. The spheroids were treated with 40 µM CUR and 0.8 µM DOX, alone or in combination. The viability values obtained by CellTiter-Glo assay following 48 h treatment of the spheroids. Five spheroids were used as one replicate and results indicate n = 3, one-way ANOVA with Tukey's multiple comparison test (Sarisozen et al, 2016)

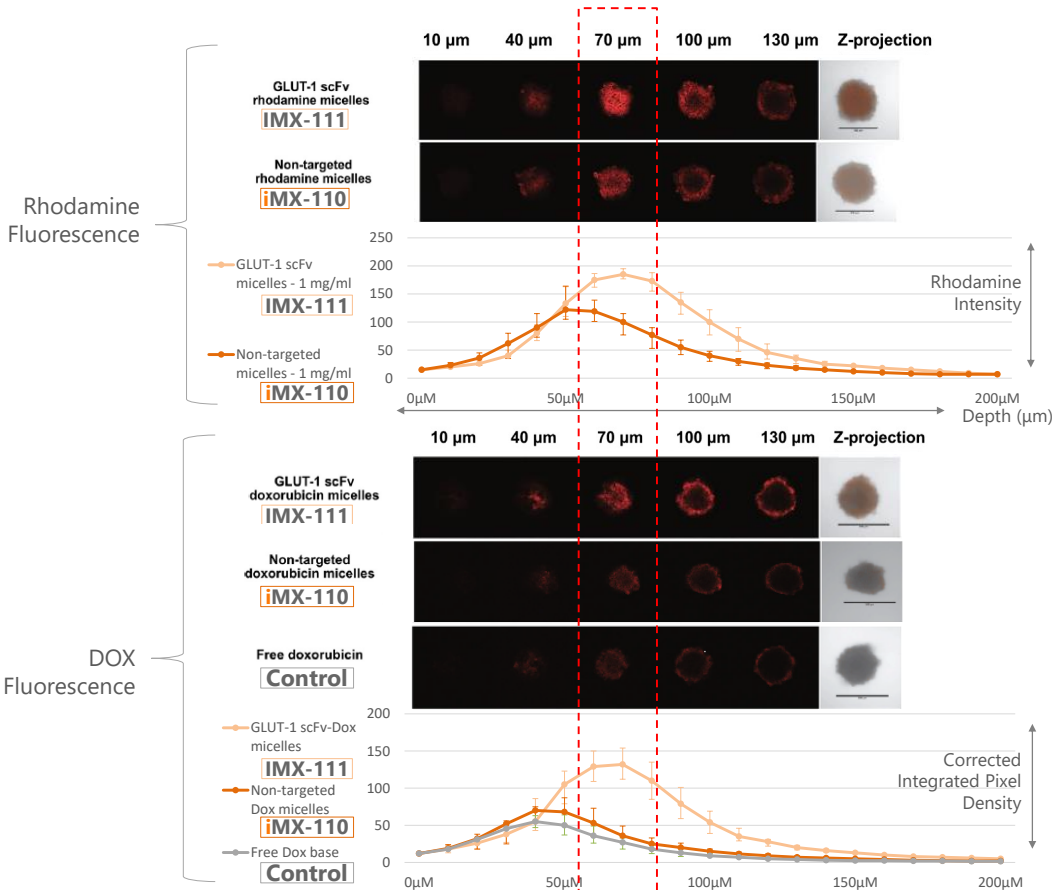
Penetration Into Doxorubicin resistant U87MG 3D Spheroids Cell Nuclei (Pink/Red Color)



Colocalization (magenta) of DOX (red) in the nuclei (blue) with the early-endosomal marker (green) by confocal microscopy. (A) Control, (B) non-targeted DOX micelles, (C) GLUT-1 scFv-targeted DOX micelles, 63x, 1.4-numerical aperture plan-apochromat oil immersion objective, ROI: 40x40 µM (Sarisozen et al, 2016)

Source: Immix Biopharma Management. Sarisozen et. al. (2016 - https://doi.org/10.1016/j.ejpb.2016.08.013).
Note: Measurements ± SD.

Penetration Into Doxorubicin resistant U87MG GBM U87MG 3D Spheroids Model



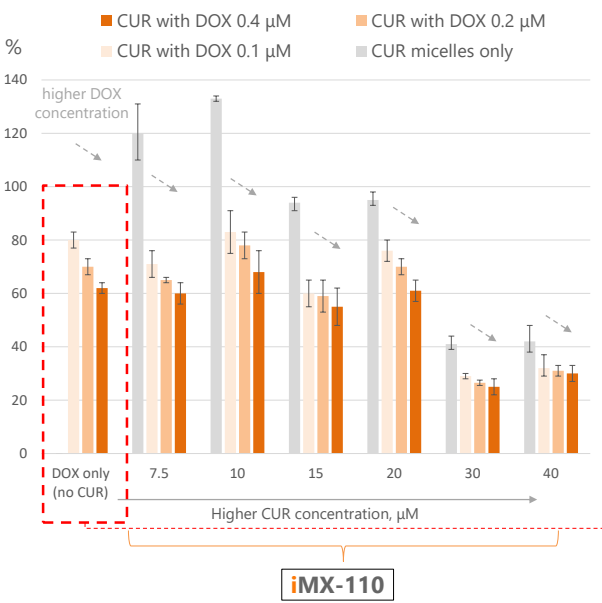
Confocal scanning laser microscopy analysis of rhodamine- or DOX-loaded micelles fluorescence in U87MG spheroids. Spheroids were incubated for 4 h with the formulations in serum complete medium. (PICTURES) Rhodamine or DOX distribution throughout the spheroids at different layers of depth. Z-projection images were obtained using average intensity and represent the average rhodamine or DOX fluorescent signal collected from each layer of the spheroid. (GRAPHS) (TOP) Corrected integrated pixel density as a representation of rhodamine intensity vs. distance from the apex of the spheroids, at 1 mg/ml lipid concentration. n = 5, mean ± SD, two-way ANOVA with Sidak' s multiple comparisons. (BOTTOM) DOX intensity profiles of DOX-loaded micelles in the spheroids. n = 5, mean ± SD.

IMMiX

iMX-110 TNBC Breast & Colorectal in Preclinical 2D Cell Lines - Tumor Killing

1 .. Kills Cancer Cells in Doxorubicin resistant MDA-MB-231 TNBC Breast Cancer Cell Line

Cell viability (%) vs. control (empty micelle) of doxorubicin-resistant TNBC MDAMB-231 cells after 48 h

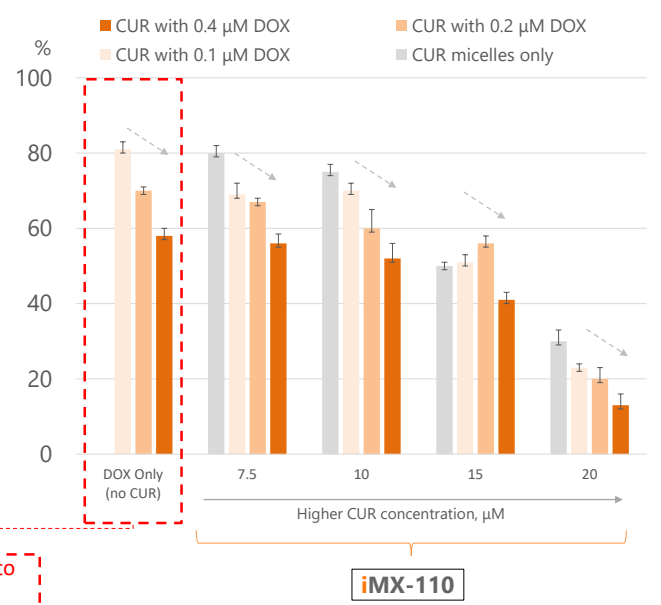


Viability of doxorubicin-resistant MDAMB-231 breast cancer cells following 48 h of continuous incubation with combination treatment at various concentrations of CUR and DOX. Cell viability was determined using CellTiter Blue cell viability assay. Data shown are representative of three independent experiments performed in triplicate (Abouzeid et al, 2014)

Resistance Level to Doxorubicin

2 Kills Cancer Cells in HCT-116 Colon Cancer Cell Line Which Is Not Typically Treated With Doxorubicin...

Cell viability (%) vs. control (empty micelle) of doxorubicin-resistant HCT-116 cells after 48 h



Viability of doxorubicin-resistant HCT-116 colon cancer cells after 48 h of continuous incubation with combination micelles at various concentrations of CUR and DOX. Cell viability was determined using CellTiter Blue cell viability assay. Data shown are representative of three independent experiments performed in triplicate (Abouzeid et al, 2013)

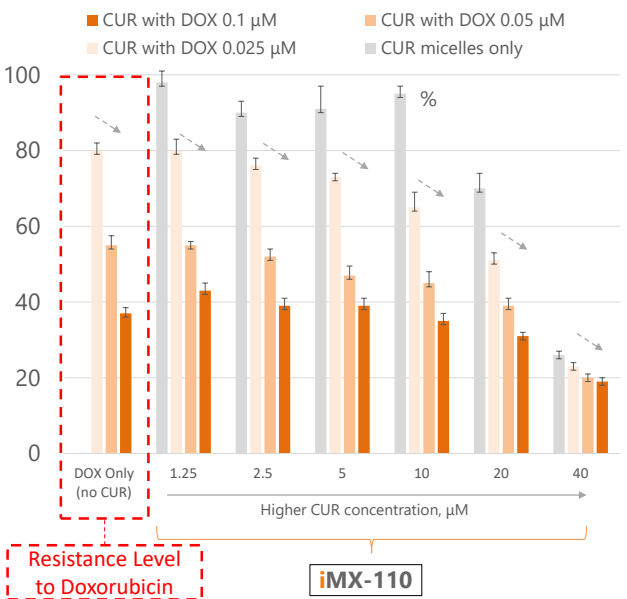
Source: Immix Biopharma Management. Abouzeid, et. al. Nanotechnology-based treatment for chemotherapy-resistant breast cancer. SPIE NanoScience + Engineering, 2014 Proceedings Volume 9166, Biosensing and Nanomedicine VII; 916606 (2014). https://doi.org/10.1117/12.2064660. Abouzeid, et. al. Anti-cancer activity of anti-GLUT1 antibody targeted polymeric micelles co-loaded with curcumin and doxorubicin (2013 - https://doi.org/10.3109/1061186x.2013.840639). Note: Measurements ± SD.

IMMiX

iMX-110 Cross-Indication 2D Cell Lines Tumor Killing Across Colorectal, TNBC Breast, Glioblastoma, Ovarian, & Multiple Myeloma (2/2)

3 .. Kills Cancer Cells in Doxorubicin resistant U87MG Glioblastoma Cancer Cell Line

Cell viability (%) vs. control (empty micelle) of doxorubicin-resistant U87MG cells after 48 h



Viability of doxorubicin-resistant U87MG glioblastoma cells following 48 h of continuous incubation with combination treatment at various concentrations of CUR and DOX. Cell viability was determined using CellTiter Blue cell viability assay. Data shown are representative of three independent experiments performed in triplicate (Sarisozen et al, 2016)

Source: Immix Biopharma Management, Sarisozen et. al. (2016 - https://doi.org/10.1016/j.ejpb.2016.08.013); Note: Measurements ± SD.

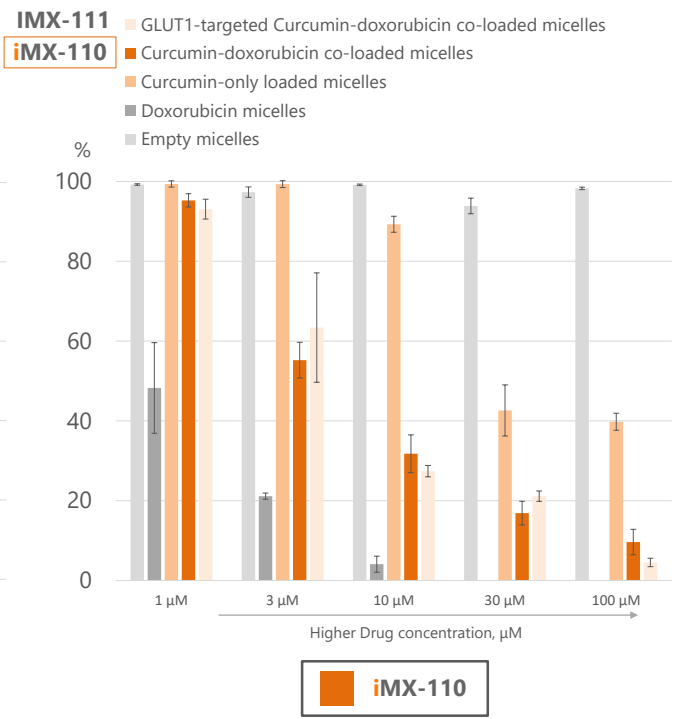
4 Kills Cancer Cells in Chemotherapy-resistant ovarian carcinoma (A2780/Adr) in vitro ..

Cell viability (%) vs. control (empty micelle) of doxorubicin-resistant A2780/Adr cells after 48 h

[Viability of doxorubicin-resistant A2780/Adr ovarian carconima cancer cells after 48 h of continuous incubation with combination micelles at various concentrations of CUR and DOX. Cell viability was determined using CellTiter Blue cell viability assay. Data shown are representative of three independent experiments performed in triplicate (Immix Biopharma Management)]

5 ... Kills Cancer Cells In Multiple Myeloma RPMI8226 ...

Cell viability (%) vs. control (empty micelle) of RPMI8226 cells after 48 h



[Viability of RPMI8226 multiple myeloma cells following 48 h of continuous incubation with combination treatment at various concentrations of CUR and DOX. Cell viability was determined using CellTiter Blue cell viability assay. Data shown are representative of three independent experiments performed in triplicate (Immix Biopharma Management)]