

BACKGROUND

- Osteosarcoma is the most common primary bone cancer. Treatment consists of chemotherapy comprising of multiple cycles of methotrexate, cisplatin and doxorubicin (MAP) with intercalated surgery
- MAP protocol is associated with side effects and a five-year survival rate of 50% among 30-40% of the poor responders
- Our previous studies demonstrate that LIT1001 (doxorubicin-loaded hydroxyapatite) inhibits the growth of aggressive osteosarcoma in both subcutaneous and orthotopic bone models, with systemically administered doxorubicin (DOX) as the positive control.

AIMS

This study was aimed to evaluate:

LIT1001 as an add-on local therapy to standard MAP treatment, assessing its ability to improve tumor growth inhibition and tolerability in a preclinical osteosarcoma model.

RESULTS

Tumor activity: G3 and G5 demonstrated significantly lower tracer uptake than both G1 and G2.

All MAP+LIT1001 groups containing DOX (G3-G5) had significantly lower tracer uptake with respect to MAP+LIT1001 excipients.

METHODS

Tumor inoculation

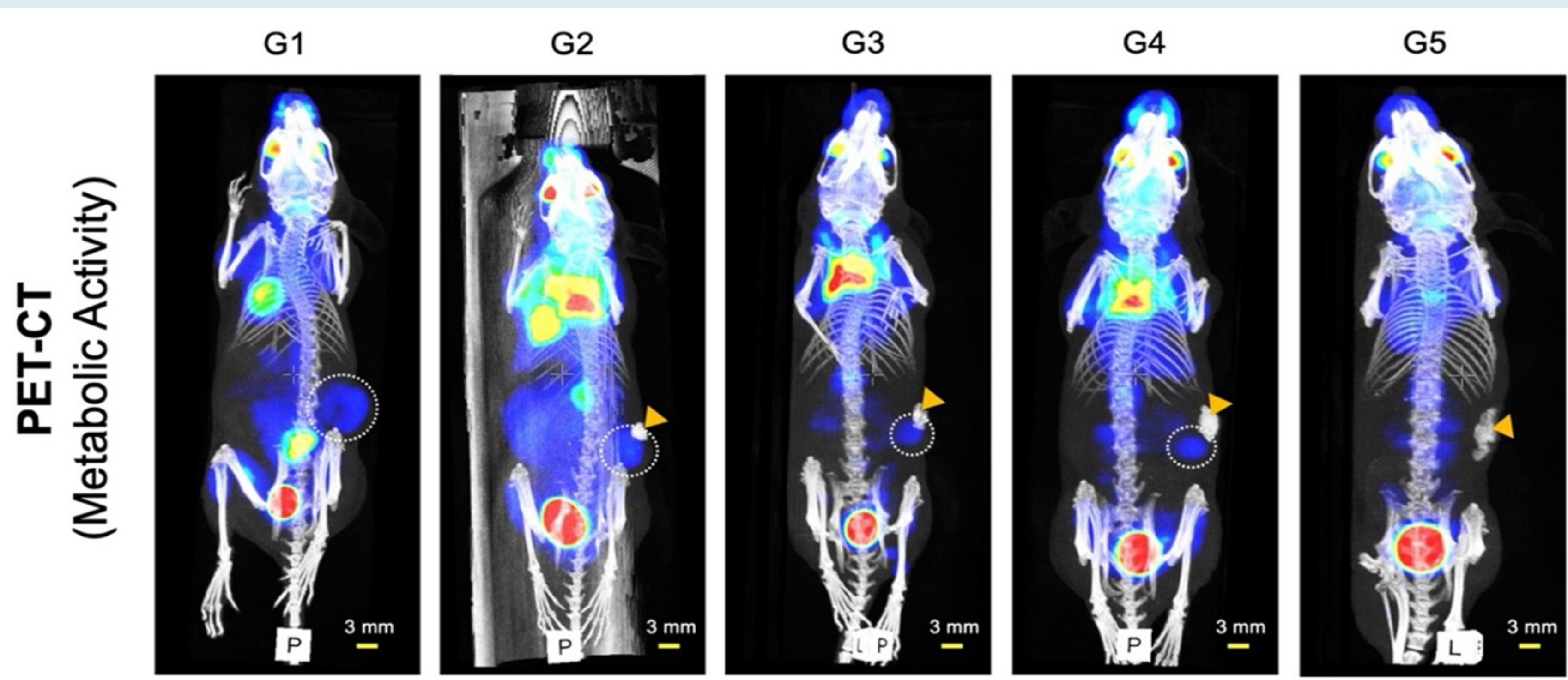
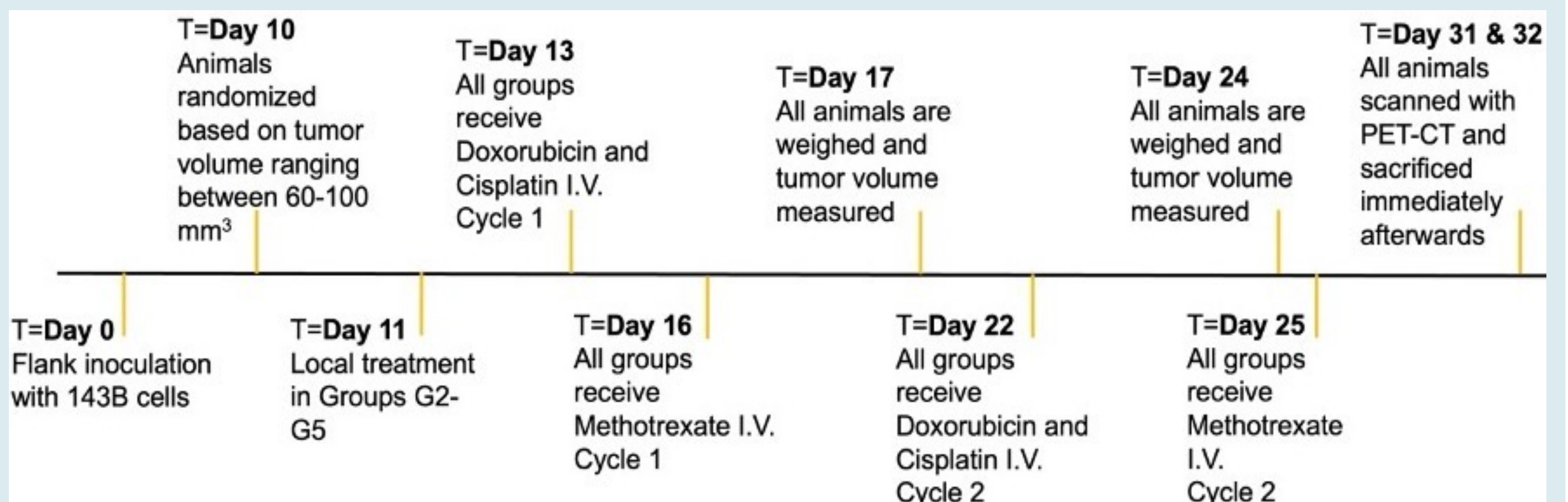
- 143B cells seeded on a collagen scaffold
- Subcutaneous flank implantation in nude mice
- 45 mice divided in 5 groups

Groups

- G1: MAP (administered systemically)
- G2: MAP+LIT1001 excipients
- G3: MAP+LIT1001 26 µg DOX
- G4: MAP+LIT1001 79 µg DOX
- G5: MAP+LIT1001 199 µg DOX

PET-CT:

PET_CT was performed to quantify metabolic activity of the tumor tissue after treatment using ¹⁸F-FDG



DISCUSSION

- Standard MAP therapy alone(G1) was not significantly enough to inhibit tumor growth or halt the metabolic tumor activity in this study, whereas a dose-dependent anti-tumoral response was observed when MAP was combined with LIT1001.
- Even when combined with two systemic MAP cycles and high local DOX, LIT1001 was well tolerated, with no obvious adverse effects on animal health, including at the highest dose (199 µg DOX).
- Using a ≥90% reduction in PET-CT metabolic activity as a surrogate for good histological response (≥90% tumor necrosis), the estimated response rate in this study was about 87%, compared with 53% reported for standard neoadjuvant chemotherapy in the EURAMOS-1 study.

