Clinical Summary: A Retrospective Analysis of DEM-TACE Delivered via Traditional Microcatheter vs Pressure-Enabled Drug Delivery™ in Patients with HCC

Titano JJ, Fischman AM, Cherian A, et al. End-hole Versus Microvalve Infusion Catheters in Patients Undergoing Drug-Eluting Microspheres-TACE for Solitary Hepatocellular Carcinoma Tumors: A Retrospective Analysis. *Cardiovasc Intervent Radiol.* 2019;42(4):560-568. doi:10.1007/s00270-018-2150-6.

SUMMARY:

A retrospective, single-center study included 88 treatment-naive patients with solitary HCC tumors <6.5 cm who underwent treatment using either Pressure-Enabled Drug Delivery (PEDD™) (n = 18) or a traditional microcatheter (TMC) (n = 70). Blinded radiological and histopathological evaluation showed that PEDD achieved:

- **A significantly higher objective response rate vs the TMC (100% vs 76.5%)**, Figure 1
- **Improved pathological response vs the TMC (88.8% vs 33.8%),** Figure 2
- **A significantly higher concentration of therapy in the tumor vs the TMC (88.7% vs 55.3%),** Figure 3

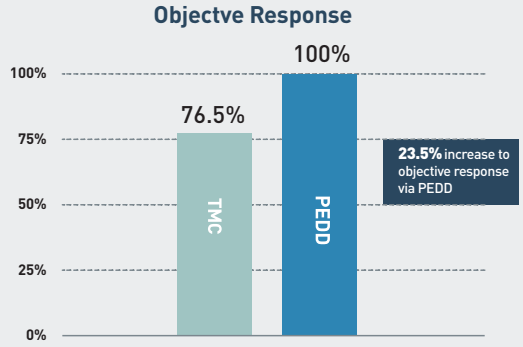

Figure 1. *PEDD achieved a significantly higher objective response rate vs the TMC (p=0.019)*

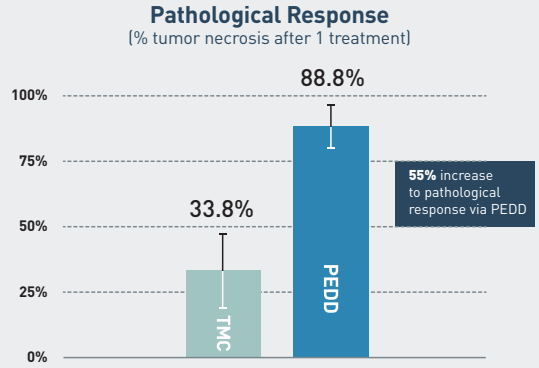

Figure 2.*PEDD achieved an improved pathological response rate vs the TMC (p=0.026)*

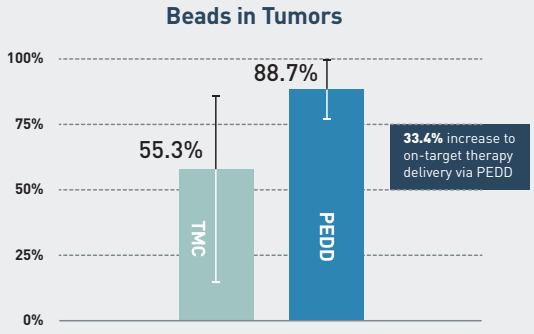

Figure 3. *PEDD achieved a significantly higher concentration of therapy in the tumor vs the TMC (p=0.002)*

The lower variation in both the percent tumor necrosis and percentage of microspheres in the tumor that was seen in the PEDD group compared to the TMC (2.5% vs 41.1% and 2.2% vs 44.5% respectively, **Figures 2 and 3**) suggests improved consistency in therapeutic delivery when using PEDD.

Analysis of explanted liver specimens suggests that the greater tumor necrosis rates observed in the PEDD group were associated with improved distal penetration and on-target distribution of microspheres delivered to the tumor.

STUDY DESIGN:

A retrospective, single-center study included 88 treatment-naive patients with solitary HCC tumors <6.5 cm who underwent DEM-TACE treatment using either PEDD (n = 18) or TMC (n = 70). 23 patients (5 PEDD, 18 TMC) received a liver transplant during the study, with one PEDD and six TMC patients excluded from the tumor necrosis analysis for receiving subsequent therapies prior to transplant.

Between 4- and 8-weeks post-treatment and then at 3-month intervals thereafter, patients underwent follow-up imaging with either contrast-enhanced, multiphase CT or MRI. Board-certified radiologists conducted blinded review of follow-up imaging by applying Modified Response Evaluation Criteria in Solid Tumors (mRECIST). Following liver explant, a board-certified pathologist performed a blinded review of the liver specimens to assess tumor necrosis and therapeutic distribution.

RESULTS:

Comparison of imaging response at initial follow-up revealed that the incidence of mRECIST objective response was significantly greater in the PEDD group (100%) relative to the TMC group (76.5%) (p = 0.019), **(Figure 1)**. At 1-month, the complete response in the PEDD group was 66.6% and in the TMC group was 50.0% (p = 0.200). At 6-months, 35.4% of patients in the TMC group demonstrated local progression of disease on follow-up imaging vs. 14.3% in the PEDD group, with no statistically significant difference between the groups (p = 0.413).

The percentage necrosis was defined as the volume of necrotic areas divided by the total tumor volume. The average tumor necrosis rate in the PEDD explants was 88.8 ± 2.5% vs. 33.8 ± 41.1% in the TMC explants (p = 0.026), **(Figure 2)**. The higher variation of percent tumor necrosis seen in the TMC group (41.1% vs 2.5% for the PEDD group) suggests improved consistency in therapeutic delivery when using PEDD.

Percentage of on-target microsphere distribution in the tumor was defined as the number of microspheres present within the boundaries of the tumor divided by the total number of microspheres in the slides with tumor, **(Figure 4)**. Explant analysis showed that a greater on-target distribution of microspheres was found in the PEDD explant specimens, with an average of 88.7 ± 10.6% of the microspheres found in the tumor vs. surrounding tissue, compared to 55.3 ± 32.7% in the TMC group (p = 0.002), **(Figure 3)**. Target tumor necrosis percentage was also greater in the PEDD liver specimens (89.0 ± 2.2%) relative to the TMC liver specimens (56.1 ± 44.5%) (p = 0.006). The higher variation in the percentage of microspheres in the tumor seen in the TMC group (44.5% vs 2.2% for the PEDD group) suggests improved consistency in therapeutic delivery when using PEDD.

Traditional Microcatheter Explant Specimen

PEDD Explant Specimen

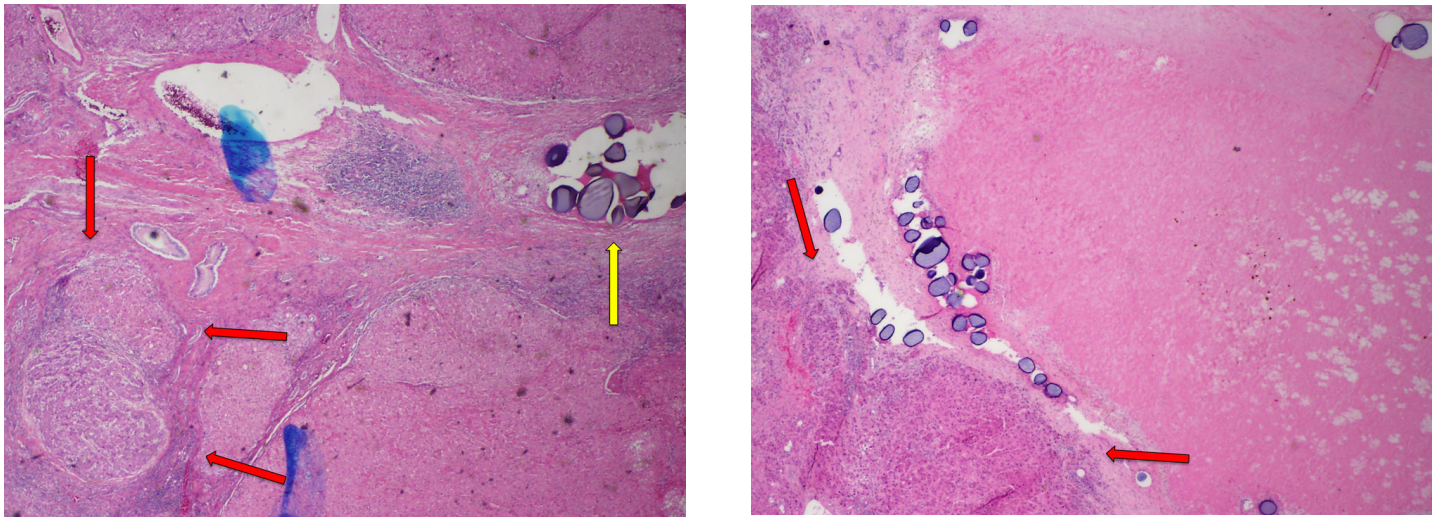

Figure 4. ***(left)*** *TMC explant specimen with red arrows indicating viable tumor tissue with no visible tumor necrosis. Yellow arrows show a cluster of microspheres distant from the tumor bed, indicating off-target delivery.* ***(right)*** *PEDD explant specimen with extensive fibrotic tissue identified. This is compatible with necrotic tumor with a small region of viable tumor tissue (red arrows) still present, demonstrating 90% tumor necrosis. Several groups of microspheres are noted within the tumor.*

CONCLUSION:

DEM-TACE procedures performed using PEDD in this single-center, retrospective study were safe and associated with improved tumor response at initial follow-up, with higher percentage tumor necrosis at explant, and with increased deposition of microspheres relative to those performed using TMC catheters.