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CASE REPORT

Intratumoral Para-Toluenesulfonamide (PTS) Injection for Recurrent Hepatocellular Carcinoma Adjacent to the Heart: A Case Report

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Abstract: Recurrent hepatocellular carcinoma (HCC) adjacent to the heart is difficult to treat when surgery and conventional locoregional therapies are no longer feasible. We report an 87-year-old man with recurrent segment VIII HCC that remained viable after radiofrequency ablation, six sessions of transarterial embolization (TAE), and stereotactic body radiation therapy (SBRT). Following multidisciplinary review and regulatory approval for compassionate-use, the patient underwent CT-guided intratumoral para-toluenesulfonamide (PTS) injection. PTS (330 mg/mL) was administered as 5.0 mL on 13 March 2025 and 6.0 mL on 17 March 2025. A small residual enhancing focus was subsequently treated with an additional 0.5 mL on 24 June 2025, giving a total cumulative volume of 11.5 mL. Serial contrast-enhanced computed tomography showed progressive loss of arterial enhancement. Complete response according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST) was documented in September 2025 and was sustained on follow-up CT obtained on 15 April 2026, with no evidence of local recurrence. Serum alpha-fetoprotein remained below 3.0 ng/mL and liver function was preserved. A small pneumothorax and transient post-procedural pain resolved with conservative management; no severe or life-threatening treatment-related adverse events were documented. This case suggests that CT-guided intratumoral PTS injection may represent a feasible salvage local treatment strategy for carefully selected patients with anatomically challenging recurrent HCC when established locoregional options are no longer feasible.

Keywords: hepatocellular carcinoma, para-toluenesulfonamide, intratumoral injection, non-thermal tumor ablation, salvage local treatment, compassionate-use

Introduction

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy and remains a leading cause of cancer-related mortality worldwide.[1–7] Although surgical resection, liver transplantation, and image-guided locoregional therapies can achieve favorable outcomes in selected patients, recurrence is common and management becomes increasingly difficult after repeated treatment. Lesions adjacent to critical structures, including the heart, may preclude further surgery or thermal ablation because an adequate treatment margin cannot be achieved safely.

Para-toluenesulfonamide (PTS) is a small-molecule anticancer agent administered by direct intratumoral injection. Preclinical studies suggest that PTS disrupts tumor-cell membrane and lysosomal integrity and interferes with prosurvival signaling pathways, resulting in selective non-thermal tumor ablation.[8–12] Because its local antitumor effect does not depend on heat generation, PTS may be considered for anatomically challenging tumors in which thermal injury is a major concern. Limited clinical experience has been reported in several solid tumors,[13–15] but evidence in HCC is limited. One previous report described intratumoral PTS combined with chemoembolization after an inadequate response to transarterial chemoembolization (TACE).[16] Its use as standalone salvage intratumoral treatment for recurrent HCC adjacent to a vital structure has not been well described.

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We report an 87-year-old man with recurrent HCC adjacent to the heart and persistent viable tumor despite radiofrequency ablation, six sessions of TAE, and SBRT. The patient subsequently underwent compassionate-use CT-guided intratumoral PTS injection. This report describes the clinical rationale, treatment procedure, radiological response, safety, and follow-up outcome of PTS monotherapy when no further established locoregional treatment was considered feasible.

Case Presentation

Patient History and Disease Course

An 87-year-old man with treated chronic hepatitis B, non-insulin-dependent diabetes mellitus, benign prostatic hyperplasia, gout, and hypertension was initially diagnosed with hepatocellular carcinoma (HCC) in 2016. The primary tumor was successfully treated with radiofrequency ablation (RFA), with no evidence of local recurrence until April 2023.

Surveillance contrast-enhanced computed tomography (CT) performed in April 2023 demonstrated recurrent HCC in hepatic segment VIII at the hepatic dome. The lesion measured 5.11×3.87 cm and was located immediately adjacent to the diaphragm, pericardium, and heart (Figure 1).

Between April 2023 and December 2024, the patient underwent six sessions of transarterial embolization (TAE), followed by stereotactic body radiation therapy (SBRT) (60 Gy in five fractions). The procedures were documented in the medical record as TAE rather than TACE; the specific rationale for omission of a chemotherapeutic agent was not available in the retrospective record. Despite these treatments, serial contrast-enhanced CT continued to demonstrate persistent arterial enhancement, indicating residual viable tumor. Selective hepatic angiography demonstrated both hepatic artery-portal vein and hepatic arteriovenous shunts.

Multidisciplinary Assessment and Ethical Approval

The case was reviewed by a multidisciplinary team comprising hepatologists, interventional radiologists, radiation oncologists, and hepatobiliary surgeons. Repeat hepatic resection was considered inappropriate because of the patient's advanced age, multiple comorbidities, and high operative risk. Thermal ablation, including radiofrequency ablation (RFA) and microwave ablation (MWA), was considered unsuitable because the tumor directly abutted the heart, precluding an adequate ablative margin while increasing the risk of collateral injury. As repeated TAE and SBRT failed to achieve durable local tumor control, no established locoregional treatment was considered both technically feasible and clinically appropriate.

After discussion of the investigational nature of treatment, its potential benefits, foreseeable risks, and available alternatives, the patient elected to undergo compassionate-use intratumoral para-toluenesulfonamide (PTS) therapy. Written informed consent was obtained for treatment and publication of this case and the accompanying clinical images. The treatment protocol was approved by the Institutional Review Board of Kaohsiung Veterans General Hospital (KSVGH IRB No. 1141001494) and authorized by the Taiwan Food and Drug Administration (TFDA Drugs No. 1149014240).

Treatment Procedure and Response Assessment

PTS was supplied as a sterile injectable solution containing 330 mg/mL para-toluenesulfonamide. Tumor response was assessed by serial multiphasic contrast-enhanced CT according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST). Clinical status, liver function, serum alpha-fetoprotein (AFP), and procedure-related adverse events were evaluated during follow-up. Because this was a compassionate-use case rather than a prospective clinical trial, follow-up intervals were determined according to clinical need and were not governed by a prespecified study schedule.

Under local anesthesia and intermittent CT guidance, a 21-gauge Chiba needle was advanced through a transpulmonary approach into the viable enhancing portion of the tumor. Needle-tip position was confirmed by CT before injection. PTS was delivered slowly at multiple intratumoral sites while the patient was clinically monitored. Immediate post-procedural CT was performed to assess intratumoral distribution and identify complications.

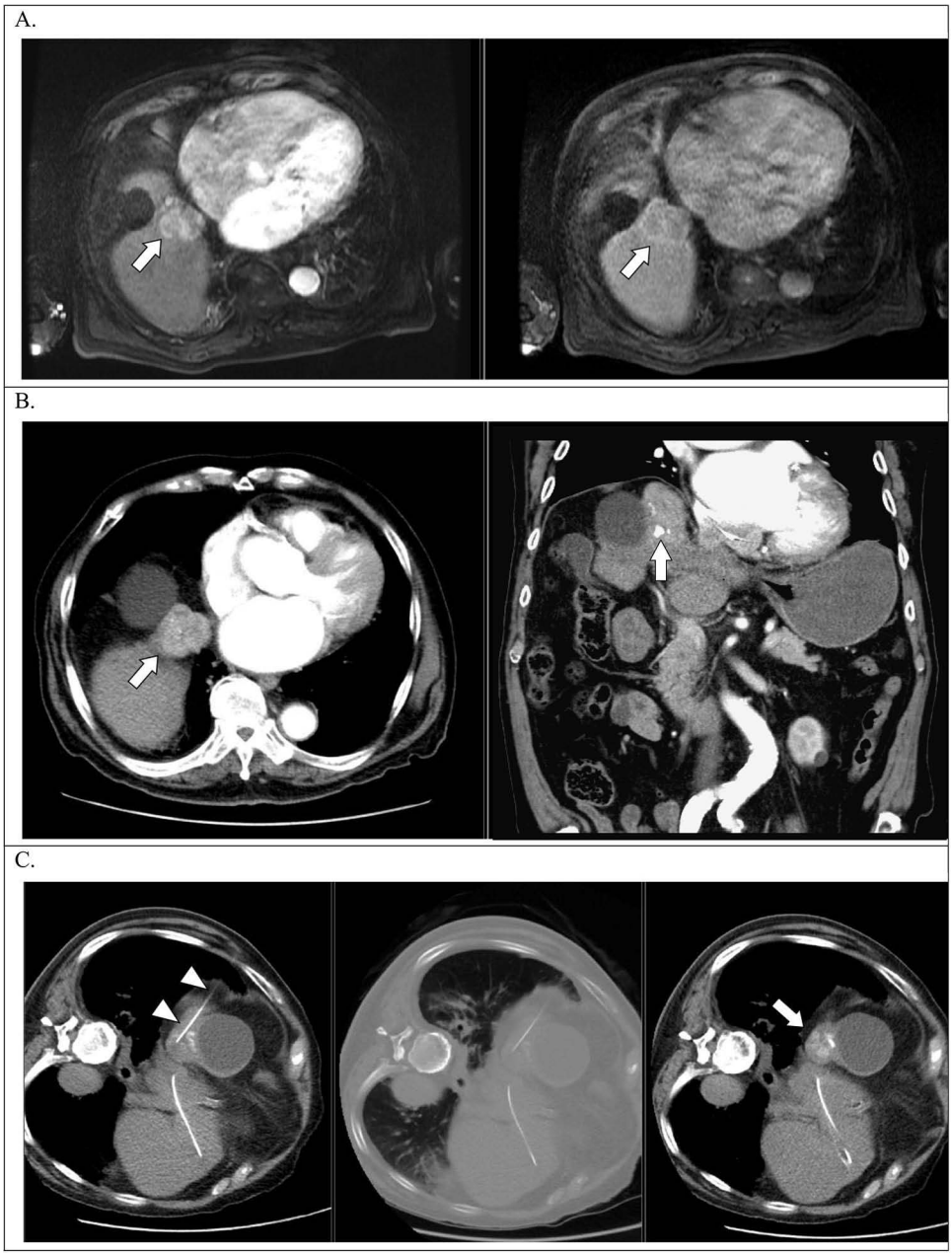


Figure 1 Baseline imaging, persistent viable tumor after locoregional therapy, and CT-guided intratumoral PTS treatment. (**A**) Contrast-enhanced CT obtained in April 2023 shows a 5.11×3.87 cm hypervascular recurrent HCC in segment VIII at the hepatic dome, immediately adjacent to the diaphragm, pericardium, and heart (arrow). (**B**) Contrast-enhanced CT after six TAE sessions and SBRT shows persistent arterial-phase enhancement, indicating residual viable tumor according to mRECIST (arrow). (**C**) CT-guided transpulmonary puncture with a 21-gauge Chiba needle (arrowheads); post-injection CT demonstrates multipoint intratumoral distribution of PTS (arrow). Arrows and arrowheads identify the tumor, residual enhancing tumor, and puncture needle as specified in each panel.

The patient received 5.0 mL of PTS on 13 March 2025 and 6.0 mL on 17 March 2025, for an initial cumulative volume of 11.0 mL. The exact numerical injection rate was not prospectively recorded. Immediate post-procedural CT demonstrated satisfactory intratumoral distribution without major hemorrhage or other acute procedure-related complication.

Radiological Response and Follow-Up

Contrast-enhanced CT obtained approximately four weeks after the second PTS session showed a marked reduction in arterial enhancement and extensive non-enhancing change consistent with tumor necrosis, with a small residual enhancing focus at the tumor margin (Figure 2). The residual focus remained localized on subsequent imaging and was considered technically accessible for targeted treatment.

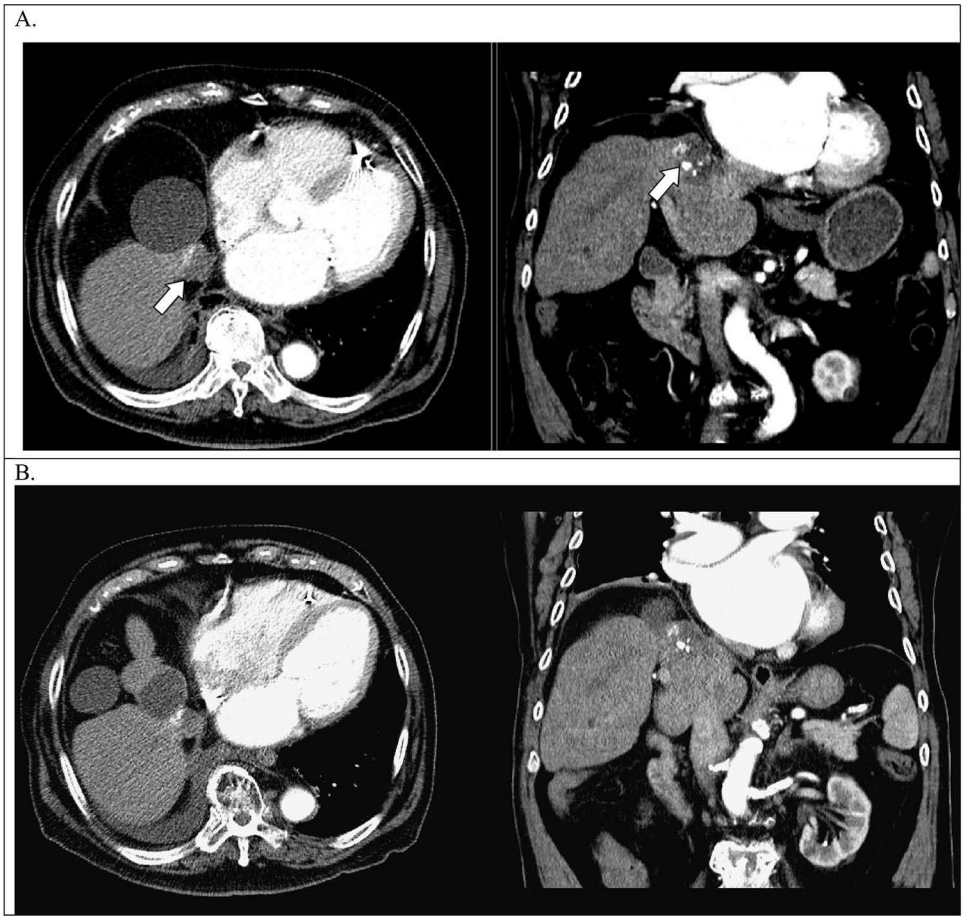


Figure 2 Radiological response after CT-guided intratumoral PTS treatment. (**A**) Contrast-enhanced CT obtained approximately four weeks after PTS injections of 5.0 mL and 6.0 mL shows marked loss of arterial enhancement, extensive non-enhancing change consistent with tumor necrosis, and a small residual enhancing focus at the tumor margin (arrow). (**B**) Contrast-enhanced CT obtained on 15 April 2026 confirms sustained complete response with complete disappearance of arterial enhancement according to mRECIST. The arrow indicates the residual viable focus in (**A**).

After multidisciplinary reassessment, an additional CT-guided intratumoral injection of 0.5 mL PTS was administered on 24 June 2025 specifically to treat the residual enhancing focus. This decision was based on persistent viable enhancement on follow-up CT and was performed under the same compassionate-use protocol. The total cumulative injected volume was 11.5 mL.

Follow-up contrast-enhanced CT in September 2025 showed complete disappearance of arterial enhancement, consistent with complete response according to mRECIST. CT on 15 April 2026 confirmed sustained complete response without local recurrence. During follow-up, serum AFP remained below 3.0 ng/mL and liver function remained within the normal range. The overall clinical course, treatment sequence, and radiological response are summarized in Figure 3.

Safety

Treatment was well tolerated. A small pneumothorax related to the transpulmonary puncture route was identified on post-procedural CT and resolved with supplemental oxygen and observation, without chest tube placement. Transient post-procedural pain resolved within several hours after oral analgesic treatment. No treatment-related hepatic failure, major hemorrhage, infection, systemic toxicity, or severe or life-threatening adverse event was documented. All observed adverse events resolved with conservative management, and no invasive intervention was required.

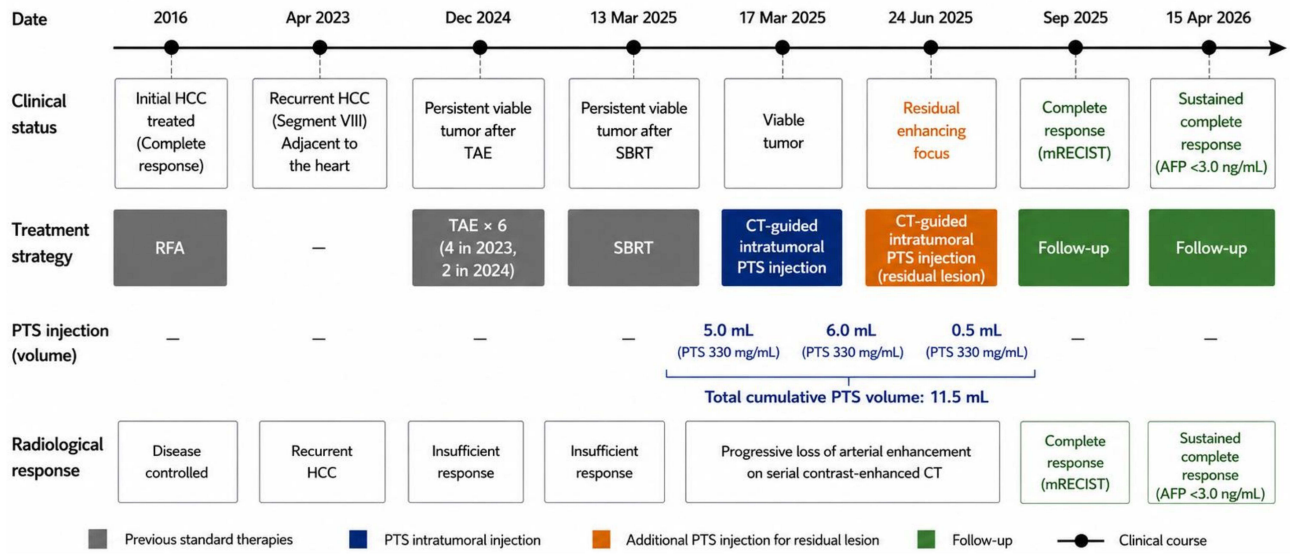


Figure 3 Clinical course and treatment strategy leading to complete response after CT-guided intratumoral PTS injection. Timeline illustrating the clinical course of recurrent hepatocellular carcinoma, including previous locoregional therapies, CT-guided intratumoral para-toluenesulfonamide (PTS) injections (5.0 mL, 6.0 mL, and 0.5 mL; total cumulative volume 11.5 mL), radiological response according to mRECIST, and sustained complete response confirmed on 15 April 2026.
Abbreviations: AFP, alpha-fetoprotein; CT, computed tomography; HCC, hepatocellular carcinoma; mRECIST, modified Response Evaluation Criteria, in Solid Tumors; PTS, para-toluenesulfonamide; RFA, radiofrequency ablation; SBRT, stereotactic body radiation therapy; TAE, transarterial embolization.

Discussion

Recurrent HCC adjacent to the heart presents a substantial therapeutic challenge, particularly after failure of multiple locoregional treatments. In this patient, persistent viable tumor remained after six TAE sessions and SBRT. Repeat resection was inappropriate because of advanced age, comorbidities, and operative risk, while RFA and microwave ablation were considered unsafe because the tumor directly abutted the heart and an adequate thermal margin could not be achieved. Hepatic artery-portal vein and hepatic arteriovenous shunts further reduced the predictability of additional transarterial treatment and raised concern regarding non-target embolic passage. CT-guided intratumoral PTS was therefore selected, after multidisciplinary review, as a compassionate-use salvage local treatment.

PTS produces a local, non-thermal antitumor effect after direct intratumoral administration.[8–12] This distinguishes it from thermal ablation, for which treatment efficacy and safety depend on heat distribution and an adequate ablative margin. For a tumor immediately adjacent to the heart, avoidance of thermal injury was the principal theoretical advantage of PTS. CT guidance permitted direct visualization of the transpulmonary puncture route, confirmation of needle-tip position, and multipoint delivery into the enhancing tumor while allowing immediate assessment for pneumothorax or hemorrhage.

The observed response may have reflected high local drug exposure and multipoint distribution within the viable tumor. Serial imaging before PTS consistently showed persistent arterial enhancement despite TAE and SBRT. After the initial 11.0 mL PTS treatment, enhancement markedly decreased, and the remaining focal enhancement was treated with a targeted 0.5 mL injection. Complete response was then documented and sustained through 15 April 2026. This temporal sequence supports a clinically meaningful contribution from PTS, although a delayed effect of prior TAE or SBRT cannot be excluded.

Published clinical experience with intratumoral PTS for HCC remains very limited. The previous report by He et al involved PTS combined with chemoembolization in advanced HCC[16] The present case differs because PTS was used as standalone salvage intratumoral treatment for recurrent HCC adjacent to the heart after repeated TAE and SBRT, when conventional thermal ablation was considered unsafe. The image-guided, multipoint technique and targeted treatment of a residual enhancing focus further illustrate a potential strategy for anatomically difficult tumors, but these observations remain hypothesis-generating.

Percutaneous ethanol injection is an established non-thermal local treatment for selected small HCCs, but uneven diffusion can limit tumor coverage, particularly in larger or structurally heterogeneous lesions, and leakage may cause pain

or injury to adjacent tissues.[2,3,5] This single case does not permit direct comparison between PTS and ethanol, RFA, TAE, or SBRT. PTS should therefore not be interpreted as a replacement for established therapies; rather, it may warrant investigation as a salvage option in carefully selected patients for whom standard local treatments are unsafe or no longer feasible.

This report has several limitations. First, it describes a single, highly selected patient treated under compassionate-use, and the findings cannot be generalized. Second, complete response was assessed radiologically by mRECIST without histopathological confirmation of complete tumor necrosis. Third, although complete response was sustained for approximately seven months after its first documentation and for more than one year after the initial PTS treatment, longer follow-up is needed to determine durability. Fourth, treatment dose, injection rate, injection-site distribution, retreatment criteria, and follow-up intervals were not prospectively standardized. Finally, prior TAE and SBRT may have contributed to tumor control, although viable tumor persisted before PTS treatment.

Despite these limitations, the case demonstrates the technical feasibility of CT-guided intratumoral PTS injection and documents sustained complete radiological response in an anatomically challenging recurrent HCC. Future prospective studies are warranted to evaluate safety, optimal dose, injection technique standardization, retreatment criteria, and efficacy in patients with anatomically challenging or locoregionally refractory HCC.

Conclusion

This case demonstrates the technical feasibility and favorable local tumor control achieved with CT-guided intratumoral PTS injection in a patient with recurrent HCC adjacent to the heart after failure of multiple conventional locoregional therapies. Although the findings from a single patient should be interpreted cautiously, this case suggests that CT-guided intratumoral PTS injection may represent a potential salvage treatment option for carefully selected patients with localized recurrent HCC when surgery, thermal ablation, transarterial therapy, or radiotherapy are no longer feasible because of anatomical constraints or persistent viable disease. Future prospective clinical studies are warranted to determine the safety, efficacy, optimal patient selection, and long-term oncologic outcomes of this image-guided non-thermal chemical ablation strategy.

Ethics Statement

The compassionate-use treatment protocol was reviewed and approved by the Institutional Review Board of Kaohsiung Veterans General Hospital (KSVGH IRB No. 1141001494). Authorization for compassionate clinical use of PTS was granted by the Taiwan Food and Drug Administration (TFDA Drugs No. 1149014240). All procedures were performed in accordance with the Declaration of Helsinki and applicable institutional and governmental regulations.

Informed Consent

Written informed consent was obtained from the patient for participation in the compassionate-use protocol, treatment, publication of this case report, and publication of the accompanying clinical images.

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Author Contributions

Chia-Ling Chiang: Conceptualization, patient management, interventional radiology procedures, data interpretation, manuscript review, and supervision. Chien-Yang Liao: Clinical data collection, radiological assessment, literature review, and manuscript revision. Mao-Yuan Lin: Drug information, technical consultation, literature review, and critical revision of the manuscript. Chuan-Ching Yang: Conceptualization, literature review, manuscript drafting and revision, and project coordination. All authors made a significant contribution to the work reported, whether that was in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Mao-Yuan Lin and Chuan-Ching Yang are employees of Gongwin Biopharm Co., Ltd., which supplied the investigational PTS used in this compassionate-use treatment. Chia-Ling Chiang for the manuscript was supported by the manufacturer from the injection ablation agent for free, during the conduct of the study; and reports honoraria from payment for oral presentation at TATA2025 held in Taipei., outside the submitted work . Gongwin Biopharm Co., Ltd. had no role in patient selection, clinical decision-making, performance of the procedure, radiological response assessment, interpretation of imaging findings, or determination of clinical outcomes. The remaining authors declare that they have no competing interests.

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