Experimental Agents and Outcomes in Chemical Ablation for Unresectable Hepatocellular Carcinoma

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PURPOSE

- Hepatocellular carcinoma (HCC) is a common cause of cancer-related deaths worldwide [1].
- Neoadjuvant locoregional therapies (LRTs) are a fundamental treatment approach for unresectable HCC [1-3].
- Chemoablation is indicated for select patients who are not candidates for other LRTs due to lesion location or anatomical restrictions [1-3].
- This review summarizes the therapeutic potential and clinical outcomes of various chemical agents in chemoablation for unresectable HCC.

METHODS

- Using PubMed, a comprehensive review of prospective trials and meta-analyses published between 2013-2025, focusing on chemoablation approaches for HCC.
- Data were collected regarding tumor response, survival outcomes, and toxicity profiles to evaluate efficacy for each chemoablative agent.

RESULTS

- Aside from standard chemoablation agents, including percutaneous ethanol injection (PEI) and percutaneous acetic acid injection (PAI), other experimental agents have been investigated within the context of cancerous lesions.

RESULTS CONT.

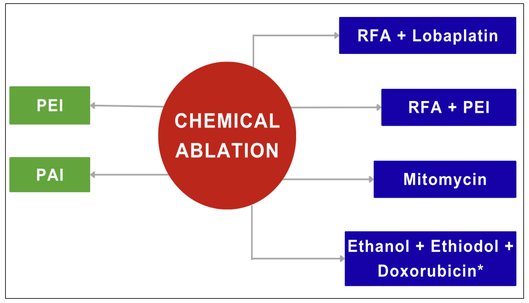

Figure 1. Established Agents for Chemical Ablation and Experimental Agents. PEI and PAI are established agents (left), while the other agents have been investigated in studies (right). Not yet applied experimentally to HCC (*).

Clinical Status	Therapeutic Intervention	Agent	Study
Established	SCA	PEI	[4-9]
		PAI	[4,6-9]
Experimental	RFA + CIA	Lobaplatin	[10]
	RFA + SCA	PEI	[10]
	CIA	Mitomycin	[11]
	SCA + CIA*	Ethanol + Ethiodol + Doxorubicin	[12]

Table 1. Established Chemical Ablation Agents and Experimental Agents Studied in Clinical Trials for Unresectable Hepatocellular Carcinoma. Standard Chemical Ablation (SCA); Radiofrequency Agent (RFA); Chemoimmunoablation (CIA). Not yet applied experimentally to HCC (*).

- PEI and PAI are the most established chemoablation agents with favorable safety profiles, but generally lower response rates compared to other LRTs, such as RFA.
- Combination treatment of chemoablation with RFA, using PEI or lobaplatin, have demonstrated improved outcomes compared to chemoablation or RFA monotherapy.
- Recent investigation in CIA have proposed chemotherapeutic treatments as alternative chemoablation agents.
- Mitomycin displayed efficacy regarding clinical outcomes.
- An emulsion of ethanol, ethiodol, and doxorubicin has displayed promising tumor response with no toxicity concerns, though it has not yet been investigated in HCC.

Agent	Tumor Response (Ablation Rate, Response Rate)	Survival Outcomes	Toxicity Profile
PEI	87%	26%⁺	Transient fever, nausea, vomiting, abdominal pain
PAI	91%	43%⁺	Transient fever, nausea, vomiting, abdominal pain, gross haematuria
Lobaplatin (with RFA)	93.3%, 20%*	~60%⁺	Transaminsase elevation, abdominal pain
Ethanol (with RFA)	90.5%, 19%*	~50%⁺	Transaminsase elevation, abdominal pain
Mitomycin	NDA, 88%^	26.6 months#	Bradycardia, seizure, pneumothorax, acute bleeding
Ethanol + Ethiodol + Doxorubicin	100%^	NDA	None

Table 2. Tumor Response, Survival Outcomes, and Toxicity Profile of Established and Investigational Chemical Ablation Agents. 2-year local tumor response rate (*). No data available (NDA). Objective response (Partial response + Complete Response) (^). 5-year estimated survival (+). Medial survival (#).

CONCLUSION

- Although chemoablation is second line compared to other LRTs, it offers a safe and viable option in patients with anatomical limitations.
- Standard chemoablation agents, such as PEI and PAI, remain effective.
- Advancements in cancer pharmacology and chemoablation have inspired investigations into alternative chemoablation approaches to improving tumor response and patient outcomes.
- There is developing evidence that shows combination therapy involving chemoablation improves tumor response and overall survival for unresectable HCC.
- Combination therapies, particularly chemoablation with RFA or novel CIA regimens, warrant further investigation for their potential to improve treatment outcomes for unresectable HCC.

REFERENCES