Systemic and Locoregional Synergy: Transarterial Chemoembolization Combined with TKIs and Immunotherapy



COLLEGE OF MEDICINE

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INTRODUCTION

- Hepatocellular carcinoma (HCC) is a leading cause of cancer-related mortality, and its incidence is increasing.
- For unresectable HCC, double therapies with transarterial chemoembolization (TACE), tyrosine kinase inhibitors (TKIs), and immunotherapies are becoming increasingly common.
- Triple therapy with all three methods is relatively novel

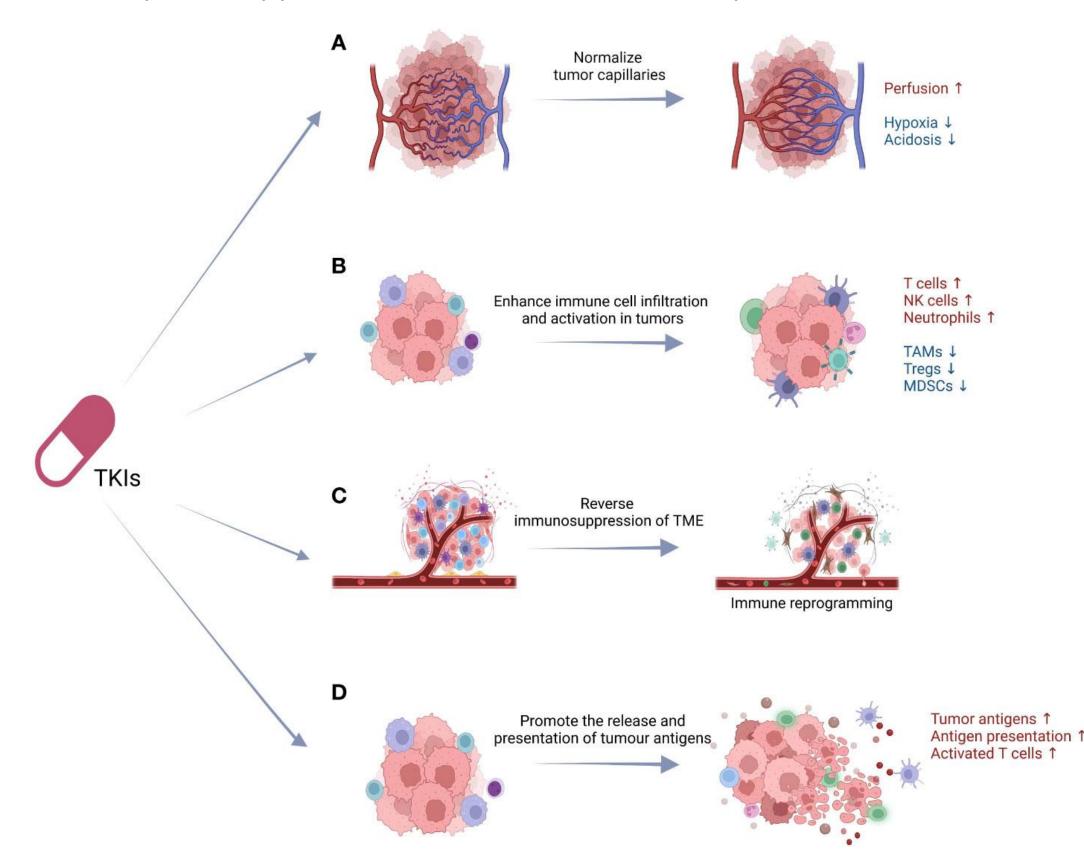


Figure 1: TKIs Impact on the Tumor Microenvironment, adapted from Liang et al.8

RESULTS

Retrospective trials have consistently demonstrated the increased effectiveness of triple therapy over double therapy¹⁻⁷. The safety profiles were analyzed, and one 87 patient trial specifically examining adverse effects in triple therapy noticed zero deaths or serious adverse effects resulting from this treatment regimen⁵.

Triple Therapy vs TKI + Immunotherapy

Objective Response Rate (ORR)	Progression Free Survival (months)	Objective Survival (months)	Study Design
63.0 % vs. 29.6%, p < 0.001 ¹	8.4 vs 6.6, p = 0.115 ¹	26.9 vs. 24.2, p = 0.670 ¹	Retrospective, 54 patients ¹
56.7 % vs. 21.1%, p = 0.002 ²	8.4 vs. 4.0, p = 0.0016 ²	14.5 vs. 10.0 p < 0.0001 ²	Retrospective, 286 patients ²
50.9 % vs. 28.4%, p < 0.001 ⁴	9.1 vs. 5.0, p = 0.005 ⁴	19.1 vs 12.7, p = 0.002 ⁴	Retrospective, 104 patients ⁴

Table 1, Outcomes from Studies Comparing Triple Therapy vs TKI and Immunotherapy

Triple Therapy vs TKI + TACE³

- Retrospective Study, 87 patients
- Median OS: 24.00 vs. 21.40 months, p = 0.007
- Median PFS: 9.70 *vs.* 7.00 months, p = 0.017

Triple Therapy vs TACE + ICI

No studies have directly compared these treatment combinations

CONCLUSIONS

Triple therapy in HCC is associated with a significantly higher tumor response rate and lower disease progression while maintaining a similar safety profile as double therapies. Additional prospective studies are warranted to inform future clinical guidelines and become adapted into treatment regimens.

REFERENCES

- Zhang JX, Hua HJ, Cheng Y, Liu S, Shi HB, Zu QQ. Role of Transarterial Chemoembolization in the Era of Tyrosine Kinase Inhibitor and Immune Checkpoint Inhibitor Combination Therapy for Unresectable Hepatocellular Carcinoma: A Retrospective Propensity Score Matched Analysis. Acad Radiol. 2024;31(4):1304-1311. doi:10.1016/j.acra.2023.09.001
- 2. Lei Y, Bai Y, Bai X, et al. TACE Empowers Immune Checkpoint Inhibitors and Tyrosine Kinase Inhibitors in Unresectable HCC: A Multicenter Retrospective Study. *J Cancer*. 2025;16(8):2750-2761. Published 2025 Jun 12. doi:10.7150/jca.112706
- Jiang N, Zhong B, Huang J, et al. Transarterial chemoembolization combined with molecularly targeted agents plus immune checkpoint inhibitors for unresectable hepatocellular carcinoma: a retrospective cohort study. Front Immunol. 2023;14:1205636. Published 2023 Jul 31. doi:10.3389/fimmu.2023.1205636
- Zhang JX, Cheng Y, Wei J, et al. Transarterial Chemoembolization Combined with Tyrosine Kinase Inhibitors Plus Immune Checkpoint Inhibitors Versus Tyrosine Kinase Inhibitors Plus Immune Checkpoint Inhibitors in Unresectable Hepatocellular Carcinoma with First- or Lower-Order Portal Vein Tumor Thrombosis. Cardiovasc Intervent Radiol. 2024;47(6):751-761. doi:10.1007/s00270-024-03724-x
- 5. Li J, Kong M, Yu G, et al. Safety and efficacy of transarterial chemoembolization combined with tyrosine kinase inhibitors and camrelizumab in the treatment of patients with advanced unresectable hepatocellular carcinoma. *Front Immunol*. 2023;14:1188308. Published 2023 Jul 21. doi:10.3389/fimmu.2023.1188308
- 6. Pang B, Zuo B, Huang L, et al. Real-world efficacy and safety of TACE-HAIC combined with TKIs and PD-1 inhibitors in initially unresectable hepatocellular carcinoma. *Int Immunopharmacol*. 2024;137:112492. doi:10.1016/j.intimp.2024.112492
- 7. Yang F, Xu GL, Huang JT, et al. Transarterial Chemoembolization Combined With Immune Checkpoint Inhibitors and Tyrosine Kinase Inhibitors for Unresectable Hepatocellular Carcinoma: Efficacy and Systemic Immune Response. *Front Immunol.* 2022;13:847601. Published 2022 Feb 18. doi:10.3389/fimmu.2022.847601
- 8. Liang L, Wang X, Huang S, Chen Y, Zhang P, Li L and Cui Y (2023) Tyrosine kinase inhibitors as potential sensitizers of adoptive T cell therapy for hepatocellular carcinoma. *Front. Immunol.* 14:1046771. doi: 10.3389/fimmu.2023.1046771

