171P Transarterial chemoembolization (TACE) with or without anti-PD1/PD-L1 systemic therapy in unresectable hepatocellular carcinoma: A meta-analysis of randomized clinical trials

H.J.S. Kim[1], A.L. Júnior[1], T.C. Felismino[2], A.B. Carvalho De Brito[1]

[1]Clinical Oncology, A.C. Camargo Cancer Center - Unidade Antonio Prudente, Sao Paulo, Brazil; [2]Medical Oncology, A.C. Camargo Cancer Center - Unidade Antonio Prudente, Sao Paulo, Brazil

Background: Transarterial chemoembolization (TACE) is the standard treatment for unresectable hepatocellular carcinoma (HCC). However, many patients experience disease progression despite this approach. Recent randomized clinical trials (RCTs) have demonstrated significant benefits with the addition of systemic therapies, such as anti-PD1/PD-L1 agents and anti-angiogenic therapies. This systematic review and meta-analysis aimed to evaluate the safety and efficacy of TACE combined with immunotherapy in this patient population.

Methods: We conducted a systematic search on March 24, 2025, in PubMed, Embase, Cochrane databases, and the ASCO and ESMO websites for RCTs evaluating TACE with or without anti-PD1/PD-L1 therapies in unresectable HCC. The primary outcomes assessed were objective response rate (ORR), progression-free survival (PFS), and safety. Analyses were performed using R software (v.4.2.2) with random-effects models.

Results: Three RCTs (CAP-ACE, EMERALD-1, and LEAP-012) were included, involving 1,296 patients (748 received TACE plus immunotherapy and 548 received TACE alone). PD1/PD-L1 agents (camrelizumab, durvalumab, or pembrolizumab) arms included anti-angiogenic agents (TKIs or bevacizumab) in combination with immunotherapy. The combination therapy resulted in a 41% reduction in the risk of disease progression or death (hazard ratio [HR] 0.59, 95% CI 0.41-0.87, p=0.007). The combined therapy also showed an increased risk of achieving ORR (OR 2.31, 95% CI 1.43-3.72, p=0.0006) and disease control rate (OR 2.0, 95% CI 1.09-3.67, p=0.03). However, higher rates of treatment discontinuation (OR 5.22, 95% CI 2.98-9.17, $p < 0.00001$) and serious adverse events (OR 4.62, 95% CI 1.98-10.71, p=0.0004) were observed in the TACE + immunotherapy arm.

Conclusions: This meta-analysis demonstrates the significant efficacy of TACE combined with immunotherapy in patients with unresectable HCC. Further data from ongoing studies with extended follow-up are necessary to assess the long-term benefits and safety of this combination approach.

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172P Final analysis of a randomized, double blind, phase II study of sorafenib with or without YIV-906 in patients with advanced HCC

G.K. Abou-Alfa[1], Y. Yen[2], J.J. Harding[3], J. Whang-Peng[4], Y-K. Shi[5], M.F. Yuen[6], X. Li[7], S. Gu[8], C. Liu[9], L-B. Jeng[10], C.J. Yen[11], C. Pan[12], S-C. Chen[13], J.C-H. Hsieh[14], W.M. Saif[15], S-H. Liu[16], F. Li[17], W. Lam[17], E. Chu[18], Y-C. Cheng[17]

[1]Department of Medicine, MSKCC - Memorial Sloan Kettering Cancer Center, New York, United States of America; [2]Graduate Institute of Oncology, Taipei Medical University, Taipei City, Taiwan; [3]Medicine, Memorial Sloan Kettering Evelyn H. Lauder Breast Center, New York, United States of America; [4]Department of Medicine, Taipei Medical University - Municipal Wan Fang Hospital, Taipei City, Taiwan; [5]Medical Oncology Dept., Chinese Academy of Medical Sciences and Peking Union Medical College - National Cancer Center, Cancer Hospital, Beijing, China; [6]Medical Oncology Dept., Queen Mary Hospital, Hong Kong SAR, China; [7]Medical Oncology Dept., Beijing Youan Hospital, Capital Medical University, Beijing, China; [8]Medical Oncology Dept., Hunan Cancer Hospital, Changsha, China; [9]Medical Oncology Dept., Shanghai University of Traditional Chinese Medicine Shuguang Hospital, Shanghai, China; [10]Medical Oncology Dept., China Medical University Hospital, Taichung City, Taiwan; [11]Oncology, NCKUH - National Cheng Kung University Hospital, Tainan City, Taiwan; [12]Medical Oncology Dept., Calvin Pan. MD Gastroenterology & Hepatology Clinic, New York, United States of America; [13]Medical Oncology Dept., Taipei Veterans General Hospital, Taipei City, Taiwan; [14]Devision of Oncology, Department of Internal Medicine, Chang Gung Medical Foundation - Linkou Chang Gung Memorial Hospital, Taoyuan City, Taiwan; [15]Cancer Institute, The Barbara Ann Karmanos Cancer Institute, Wayne State University, Detroit, United States of America; [16]R&D, Yivia Inc., New York, United States of America; [17]Department of Medicine, Yale University School of Medicine, New Heaven, United States of America; [18]Medical Oncology Dept., Albert Einstein College of Medicine, Bronx, United States of America

Background: In multiple early-phase clinical trials in GI cancers (CRC, HCC, LAPC, LARC), YIV-906 (aka PHY906/KD018) was studied as an adjuvant to anti-cancer treatments (chemotherapy/chemoradiation). More than 250 GI cancer pts treated have demonstrated efficacy and safety. Preclinical studies illustrate YIV-906 immunomodulation in the tumor microenvironment and antitumor activity by enhancing innate and adaptive immunity. Additionally, YIV-906 reduces non-hematological toxicities by reducing GI inflammation (TNFa, NFkB, IL6, COX2, iNOS), promoting damaged tissue repair (Wnt pathway), and reducing pain (NK1).

Methods: A double-blinded, placebo-controlled, randomized phase II study combining sorafenib (SORA) with YIV-906 was conducted on advanced, naïve HCC pts (NCT04000737): primary endpoint was PFS; secondary endpoints were TTP, ORR, DCR, OS, QoL and safety. CPA cirrhotic pts were randomized and stratified by metastatic and ECOG. Tumor assessments were performed at every other cycle. Translational correlatives included PK and biomarker analysis.

Results: From 107 CPA, BCLC-B or C, HBV(+) HCC pts screened: 60 per protocol set pts received at least one study treatment dose. Investigator evaluated YIV-906 arm (N=41) mPFS was 4.1 months, the placebo arm (N=19) was 2.3 months (HR=0.50 and p=0.063) with RECIST 1.1. The YIV-906 arm mOS was 14.3 months vs. placebo 7.5 months, with HR=0.92 and p=0.81. Further sub-analysis in pts completing at least 2 cycles (N=49, 1 cycle = 28 days) was statistically significant. In the YIV-906 arm mPFS was 5.6 months vs. placebo arm 2.3 months; with a 69% risk reduction in disease progression or death (HR=0.31 [95% CI: 0.13, 0.72]; p=0.004). The median duration of SORA exposure was 108 days in the YIV-906 arm and 58.5 days in the placebo arm. Compared to SORA monotherapy no new safety signals were identified.

Conclusions: Despite early closure of this study due to shifting treatment landscapes, and running concurrently during pandemic lockdowns, the trial's recruitment satisfied its statistical power requirement, meriting further HCC studies of YIV-906.

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173P Dose escalation STRATegy of regorafenib in Advanced HepatoCellular Carcinoma: Phase II STRATA-HCC trial

L.G.D. Fonseca[1], M.C. Pacheco De Mello[2], L. Gomes[3], J.V. Gregorio[1], G.M. Bariani[2], E. Brandao[1], L.T. Ikeoka[4], H. Pereira[1], P.M. Hoff[1], J. Sabbaga[1]

[1]Department of Medical Oncology, ICESP - Instituto do Cancer do Estado de Sao Paulo, Sao Paulo, Brazil; [2]Clinical Oncology Department, ICESP - Instituto do Cancer do Estado de Sao Paulo, Sao Paulo, Brazil; [3]Radiology, ICESP - Instituto do Cancer do Estado de Sao Paulo, Sao Paulo, Brazil; [4]Hospital das Clínicas da Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo, Brazil

Background: Regorafenib prolonged overall survival (OS) after progression on sorafenib in the phase 3 RESOURCE trial with the standard-dose strategy (160 mg/day orally for 21 days of a 28-day cycle). In the RESOURCE study, the median treatment duration was 3.6 months, and 25% of patients were discontinued due to treatment-related adverse events. Despite limited supportive evidence, various dosing schedules are used to alleviate toxicities. This trial aims to evaluate the safety and activity of an escalated regorafenib dosing schedule.

Methods: STRATA-HCC is a phase II single-arm study that included previously treated HCC patients with Child-Pugh A-B7 and PS 0-1. Regorafenib was given in a dose-escalation strategy starting 80 mg/d with weekly escalation, per 40 mg increments, to 160 mg/d if no significant drug-related adverse events occurred during cycles 1-2. The maximum tolerated dose (MTD) was administered from cycle 3 on. The primary endpoint was the proportion of patients completing cycle 4 with no progression or intolerance. OS, response rate, and quality of life are secondary endpoints. The primary endpoint was achieved if 65% of patients completed cycle 4 ($p = 0.10$, $\beta = 20\%$).

Results: 25 patients were included (median age 64 yrs, 80% viral etiology, 80% prior locoregional therapies). Eight (32%) patients had received prior immunotherapy, and 20% had received ≥2 lines of systemic treatment. Most were BCLC-C (72%), performance status 1 (56%), and Child-Pugh A (92%). The primary endpoint was met, with 72% of participants completing 4 cycles (8% did not complete due to intolerance, and 20% due to disease progression). MTD was 120 mg/d in 52% and 80 mg/d in 44%. Most common grade ≥2 events were fatigue (20%), hand-foot skin reaction (12%), and hypertension (12%). The 1-year survival rate for patients treated with regorafenib in the 2nd line (n=20) was 66.9% (95%CI: 32.4-86.7%), and the median OS of the entire cohort was 9.9 months (95%CI: 6.9-NA). Disease control was achieved in 88%.

Conclusions: This single-arm trial demonstrated that a dose-escalation strategy of regorafenib provided treatment benefits with a favorable safety profile, representing an alternative approach after 1st-line therapy.