Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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715P The safety and efficacy of lenvatinib combined with TACE and PD-1 inhibitors (Len-TAP) versus TACE alone in the conversion resection for initially unresectable hepatocellular carcinoma: Interim results from a multicenter prospective cohort study

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Background: Surgical resection is the main treatment for hepatocellular carcinoma (HCC) in China. While more than 70% of HCC are in the intermediate or advanced stages at diagnosis and are unresectable; For those patients, transarterial chemoembolization (TACE) is the main conversion therapy to improve the resectability rate and to diminish postoperative relapse. But its success rate is only about 10%; Both Lenvatinib and PD-1 inhibitors (immune checkpoint inhibitors) are indicated for unresectable HCC (uHCC); The purpose of this study was to assess the safety and efficacy of Lenvatinib combined with TACE and PD-1 inhibitors (Len-TAP) versus TACE alone as conversion therapy for patients with initially uHCC.

Table: 715P

	Len-TAP, n (%)	TACE, n (%)	*P* value
Baseline			
Age, years	54.4±11.0	58.8±8.6	0.163
Gender-male	68(95.8)	62(87.3)	0.070
Etiology			
HBV	60(84.5)	56(78.9)	0.419
HCV	1(1.4)	3(4.2)	
ECOG PS			
0	64(90.1)	66(93.0)	0.546
1	7(9.9)	5(7.0)	
BCLC stage			
B	30(42.3)	31(43.7)	0.865
C	41(57.7)	40(56.3)	
AEs			
Grade 3 AEs	38(53.5)	13(18.3)	<0.001
Outcomes			
Median PFS, days	531±81.2	224±33.3	<0.001
Conversion resection rate	36(50.7)	11(15.5)	<0.001
mRECIST			
ORR	56(78.9)	12(16.9)	<0.001
DCR	67(94.4)	31(43.7)	<0.001
RECIST 1.1			
ORR	27(38.0)	5(7.0)	<0.001
DCR	61(93.0)	20(28.1)	<0.001

Methods: This is a multicenter, prospective, cohort study. Key Eligibility Criteria:18-70 years old; HCC confirmed by radiographic or histology; No systemic treatment history; BCLC stage B/C. The conversion therapy includes Len-TAP (Lenvatinib followed by TACE and Camrelizumab/Sintilimab) and TACE alone. Their adverse events (AEs), response rate, conversion-resection rate, and survival outcome were compared.

Results: From October 2020 to March 2022, 71 patients were enrolled in both groups. Until April 2022, the Len-TAP group had a higher rate of Grade 3 AEs (P<0.001), there were no level 4 or 5 TRAEs in both groups. At 16±1 weeks, the ORR based on mRECIST was 78.9% and 16.9% in the Len-TAP and TACE groups (P<0.001). The Len-TAP group had a better conversion resection rate (50.7% vs 15.5%,P<0,001) than TACE group. The median PFS were 531±81.2 and 224±33.3 days(P<0.001), and the 1 year OS rate was 93.3% and 64.3%(P=0.002) in the Len-TAP and TACE groups.

Conclusions: Lenvatinib combined with TACE and PD-1 inhibitors was safe and effective, which can improve resectability rate and prolong overall survival for patient with uHCC.

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716P Impact of COVID-19 pandemic on clinical outcomes in hepatocellular carcinoma: A multicentre cohort study

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Background: Hepatocellular carcinoma (HCC) accounts for 90% of all liver cancer cases and is the fifth most common form of cancer. HCC remains the second most common cause of cancer-related death. Patients with early-stage disease may be treated surgically with resection, liver transplantation, or percutaneous ablation with curative intent. COVID-19 pandemic has caused severe disruption of healthcare services worldwide and has interrupted patients' access to essential services. During the first wave, many healthcare services were shut to all but emergencies. However, the immediate and long-term impact of COVID-19 on clinical outcomes in HCC are unknown. In this study, we aimed to determine the indirect impact of COVID-19 health service utilisation on HCC outcomes.

Methods: A prospective cohort study was conducted from March 15 until June 30 2020. Patients were enrolled from 8 tertiary hospitals in the UK and Germany with dedicated HCC management services. All patients with current or past HCC who were discussed at a multidisciplinary meeting (MDT) were identified. Hospital medical records, HCC MDT notes and hospital HCC databases were used to gather patient demographic and HCC related clinical data. Presence of the COVID-19 pandemic was operationalised as the time period during which the first wave of COVID-19 pandemic was present in the UK. Any delay to treatment (DTT) and the effect on survival at 1 year were reported. Any delay to treatment (DTT) and the effect on survival at 1 year were reported.

Results: The median time from MDM discussion to commencement of treatment was 49 days (IQR 26-83), with 70.1% of patients commencing treatment after 31 days of MDM discussion (n=171). Patients with BCLC stages-A/B disease were more likely to experience DTT. Significant delays across all treatments for HCC were observed but delay was most marked for those undergoing curative therapies. Even though severe delays were observed in curative HCC treatments, this did not translate in reduced survival in patients.

Conclusions: Interruption of routine healthcare services because of the COVID-19 pandemic caused severe delays in HCC treatment. However, DTT did not translate to reduced survival. Longer follow is important given the delay to therapy in those receiving curative therapy.

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717P Phase II study of transhepatic artery chemoembolization (TACE) combined with tislelizumab (TIS) and lenvatinib (LEN) in patients with unresectable hepatocellular carcinoma(uHCC)

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Background: In the treatment of advanced uHCC, combination therapy of anti-angiogenic targeted drugs combined with immune checkpoint inhibitors has become a hot topic , but efficacy still does not meet clinical needs, and the objective response rate (ORR) is only 27%-36%. TACE is widely used in the treatment of advanced uHCC. The aim of this study was to evaluate the efficacy and safety of TACE in combination with TIS and LEN in patients with uHCC.

Methods: This study was single-center, single-arm, open-label phase II exploratory clinical study (NCT05131698). Eligible patients were BCLC-C and not candidates for surgical resection or liver transplantation, at least one lesion evaluable by RECIST 1.1 criteria, an Eastern Cooperative Oncology Group performance status of 0 or 1, and Child-pugh grade A. Enrolled patients received TACE treatment (loplatin + raltitrexed + iodine oil) at the beginning, and then were treated with TIS (200 mg, IV, on Day 1 of a 21-day cycle) and LEN (body weight $\geq$ 60 kg: 12 mg/day; $<$ 60 kg: 8 mg/day) daily. The primary endpoint of this study was safety and ORR by RECISTv1.1. The secondary endpoints included overall survival (OS), disease control rate (DCR), and progression-free survival (PFS).

Results: As of March 18, 2022, a total of 18 patients were enrolled and had TIS in combination with LEN after TACE treatment. Patients had BCLC stage C, Child-Pugh scores of 5 (n = 8) or 6 (n = 10). The median follow-up time is 6.0 months. The overall ORR and DCR were 50% and 66.7%, respectively (1 CR, 5.5%; 8 PR, 44.5%; 3 SD, 16.7%). All 18 patients remained on study. Any grade treatment-emergent adverse events (TEAEs) occurred in 44.5% (n=8). The most common TEAEs were abnormal liver function (n=7, 38.8%), thrombocytopenia (n=5, 27.7%), and leukopenia (n=5, 27.7%). Only one patient experienced grade 3 TEAE (pneumonia); seven patients experienced grade 1 TEAEs.

Conclusions: Preliminary analysis showed that TACE combined with TIS and LEN showed a considerable efficiency with relatively high ORR and a tolerable safety profile in uHCC treatment.

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718P Prognosis-related molecular subtypes and immune features associated with hepatocellular carcinoma

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Background: Bioinformatics tools were used to identify prognosis-related molecular subtypes and biomarkers of hepatocellular carcinoma (HCC).

Methods: The TCGA datasets and GEO datasets (GSE14520, GSE76427, and GSE25097) were screened for differentially expressed genes (DEGs) between HCC and normal tissues. DEGs in the same direction across the four datasets were analyzed for enrichment. Non-negative matrix decomposition to identify subtypes of HCC with different prognosis. Cox regression and Kaplan-Meier curve analyses were performed to identify overlapping DEGs associated with survival defined as prognosis-related genes. An area under the curve $>$ 0.80 of genes used to construct random survival forest and least absolute shrinkage and selection operator (LASSO) models to identify feature genes. We constructed a Gaussian mixture model (GMM) to identify feature genes with ability to diagnose HCC recurrence. Key gene associated with OS were determined by univariate Cox regression analysis. Nomograms mode was used to evaluate the predictive power. The mutation and methylation of key gene were analyzed in TCGA. The relative levels of immune cell infiltration were determined by single-sample gene set enrichment.

Results: Four datasets identified 3,330 DEGs in the same direction that were involved in cell cycle, and FOXO signaling pathway. Subtype C2 showing better overall survival than subtype C1. Seven feature genes (SORBS2, DHRS1, SLC16A2, RCL1, IGFALS, GNA14, and FANCI) that may be involved in HCC occurrence and prognosis. A univariate Cox model identified FANCI as a key gene involved mainly in the cell cycle, and mismatch repair. FANCI had two mutation sites and may undergo methylation. ssGSEA showed that Th2 and Th cells are significantly high-infiltrated in HCC patients.

Conclusions: We defined two molecular subtypes of HCC that are associated with different prognosis, and we identified FANCI as a good prognostic indicator in HCC.

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719P Tyrosine kinase inhibitors and/or immune checkpoint inhibitors is required for improving efficacy of transarterial chemoembolization for hepatocellular carcinoma: A large-scale multicenter real-world study of 582 patients

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Background: Data on elucidating the efficacy and safety of transarterial chemoembolization (TACE) based systemic therapy in patients with hepatocellular carcinoma (HCC) are lacking.

Methods: In this multicenter retrospective study, 582 HCC patients receiving TACE based therapy were enrolled between Apr 2015 and Dec 2021. Patients were assigned either with TACE monotherapy (n=317), TACE plus tyrosine kinase inhibitors (TKIs) (n=66), TACE plus immune checkpoint inhibitors (ICIs) (n=33), or TACE plus TKIs and ICIs (n=139). The efficacy and safety of four treatment regimens were compared.

Results: There were no significant differences among the four study groups in baseline characteristics, including BCLC stage, tumor number, tumor size and embolus (all $P>0.05$). The mean follow-up period was 17.6 (95% CI: 15.7-19.5) months and the mean number of TACE sessions were 3 (range 1-13) for all patients. The objective response rate (ORR) was 28.7%, 39.4%, 42.4%, and 57.6%, respectively ($P=0.024$), while the disease control rate (DCR) was 54.6%, 72.7%, 69.7%, and 87.1%, respectively ($P=0.037$) (mRECIST). The TACE plus TKIs and ICIs group achieved the longest median progression-free survival (PFS) and overall survival (OS) compared to the other 3 groups, especially to the TACE alone group (PFS: 6.4 vs. 7.1 vs. 7.3 vs. 8.7 months, $P=0.046$; and OS: 15.1 vs. 17.6 vs. 18.5 vs. 21.9 months, $P=0.030$). There were no unexpected toxicities.

Conclusions: TACE plus TKIs and ICIs appeared to deliver the longest PFS and OS in HCC patients receiving TACE based regimens. Adverse events were consistent with those of previous TACE combination trials.

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