LT patients, respectively. Patients prioritized by GEMA-Na were more often women, had higher prevalence of ascites and showed triple risk of the primary outcome compared to patients prioritized by MELD-Na. One in 15 deaths would be avoided by using GEMA instead of MELD, and 1 in 21 deaths would be avoided by using GEMA-Na instead of MELD-Na. Among women, 1 in 8 deaths would be avoided in either situation.

Conclusion: GEMA-Na predicts mortality or delisting due to clinical deterioration in patients awaiting LT more accurately than MELD-Na and its implementation may amend gender disparities.

COHORT	N	MELD	GEMA	MELD-Na	GEMA-Na
Training (overall)	5,762	0.753 (0.723–0.783)	0.780 (0.751–0.808) p <0.001	0.783 (0.755–0.810)	0.796 (0.769–0.823) p = 0.022
Training (women)	1,955	0.743 (0.690–0.795)	0.795 (0.748–0.842) p <0.001	0.784 (0.739–0.829)	0.821 (0.781–0.860) p < 0.001
Internal validation (overall)	1,920	0.712 (0.656–0.769)	0.752 (0.700–0.804) p = 0.001	0.742 (0.686–0.797)	0.766 (0.715–0.818) p = 0.006
Internal validation (women)	623	0.751 (0.658–0.844)	0.786 (0.698–0.874) p = 0.085	0.779 (0.688–0.871)	0.802 (0.716–0.888) p = 0.087
External validation (overall)	1,638	0.739 (0.682–0.796)	0.761 (0.703–0.819) p = 0.036	0.745 (0.690–0.800)	0.774 (0.720–0.827) p = 0.014
External validation (women)	432	0.736 (0.628–0.844)	0.789 (0.686–0.892) p = 0.004	0.714 (0.592–0.835)	0.796 (0.698–0.895) p = 0.009

GS006

Efficacy and safety of bulevirtide monotherapy given at 2 mg or 10 mg dose level once daily for treatment of chronic hepatitis delta: week 48 primary end point results from a phase 3 randomized, multicenter, parallel design study

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Background and aims: Bulevirtide (BLV) is a novel first-in-class entry inhibitor for the treatment of chronic HDV infection (CHD) that was conditionally approved in the EU in July 2020 based on Phase 2 data. In a pre-specified, alpha-controlled, interim 24 week analysis of a phase 3 study (MYR301; NCT03852719) it was demonstrated that monotherapy with BLV at 2 mg or 10 mg once daily had a significantly greater combined virologic/biochemical response compared with control with no active anti-HDV treatment and had a favorable safety profile. Here, we present findings for the Week 48 primary end point analysis of Study MYR301.

Method: 150 patients with CHD were randomized to 3 treatment groups and stratified based on the absence or presence of compensated cirrhosis: Arm A (control): no active anti-HDV treatment for 48 weeks followed by BLV 10 mg/d for 96 weeks (n = 51), and Arms B or C: immediate treatment with BLV at 2 mg/d (n = 49) or 10 mg/d (n = 50), respectively, each for 144 weeks, after which all arms enter treatment-free follow-up for additional 96 weeks. The primary end point of combined response was defined as undetectable HDV RNA or decrease by $\geq 2\log_{10}$ IU/ml from baseline and ALT normalization at Week 48; other end points included viral response (undetectable HDV RNA or decrease by $\geq 2\log_{10}$ IU/ml from baseline), ALT normalization, change in HDV RNA levels and change in liver stiffness measured by elastography.

Table. Efficacy and safety results at week 48.

n (%)	Arm A Control (N = 51)	Arm B BLV 2 mg (N = 49)	Arm C BLV 10 mg (N = 50)
Combined Response[1]: Responder at Week 48	1 (2.0%)	22 (44.9%)	24 (48.0%)
95% CI	(0.0%, 10.4%)	(30.7%, 59.8%)	(33.7%, 62.6%)
p-value[2]	-	<.0001	<.0001
Viral Response[3]: Responder at Week 48	2 (3.9%)	35 (71.4%)	39 (78.0%)
95% CI	(0.5%, 13.5%)	(56.7%, 83.4%)	(64.0%, 88.5%)
p-value[4]	-	<.0001	<.0001
Biochemical Response[5]: Responder at Week 48	6 (11.8%)	25 (51.0%)	28 (56.0%)
95% CI	(4.4%, 23.9%)	(36.3%, 65.6%)	(41.3%, 70.0%)
p-value[4]	-	<.0001	<.0001
Change from BL in HDV RNA levels (log-10 scale): LS means (95% CI)	-0.019 (-0.391, 0.352)	-2.551 (-2.933, -2.169)	-3.101 (-3.482, -2.719)
p-value	-	<.0001	<.0001
Change from BL in liver stiffness (Fibroscan, kPa): LS means (95% CI)	0.88 (-0.80, 2.56)	-3.08 (-4.70, -1.46)	-3.17 (-4.90, -1.44)
p-value	-	0.001	0.001
Adverse Events Number (%) of participants with any:			
AE	39 (77%)	40 (82%)	44 (88%)
AE with Grade 3-4	3 (6%)	5 (10%)	4 (8%)
AE Related to BLV	0	24 (49)	36 (72%)
SAE[6]	1 (2%)	2 (4%)	1 (2%)

AE: adverse event, BL: baseline, BLV: bulevirtide, CI: confidence interval; LS: least squares, SAE: serious adverse event.
Undetectable HDV RNA defined as below limit of detection (6 IU/mL). ALT normalization defined as: ≤31 U/L for females and ≤41 U/L for males (Russian sites); or ≤34 U/L for females and ≤49 U/L for males (all other sites). Confidence intervals were calculated using Clopper-Pearson (exact) for proportions.
[1] Undetectable HDV RNA or decrease by $\geq 2\log_{10}$ IU/ml from baseline and ALT normalization.
[2] Fisher's exact tests used for each comparison of Bulevirtide 2mg and 10mg vs. Control using a significance level of 0.04 at week 48.
[3] Undetectable HDV RNA or decrease by $\geq 2\log_{10}$ IU/ml from baseline.
[4] Fisher's exact tests used for each comparison of Bulevirtide 2mg and 10mg vs. Control using a significance level of 0.05.
[5] ALT normalization.
[6] No SAEs assessed as related to BLV treatment

Results: Baseline characteristics included: mean (SD) age 41.8 (8.4) years, 57.3% males, 82.7% White, 47.3% with compensated cirrhosis, 60% were on nucleos (t)ide analogues therapy; mean (SD) HDV RNA 5.05 (1.35) $\log_{10}$ IU/ml and mean (SD) ALT 110.9 (69.0) U/L. At Week 48, similar combined responses were seen in the two BLV arms which were significantly greater than in the control arm (Table). Viral and biochemical responses were also similar in the BLV arms and significantly greater than control (p < 0.0001). BLV was safe and well tolerated during the 48-week treatment period. Asymptomatic elevations in total serum bile salts and injection site reactions occurred at a greater frequency at the higher BLV dose level. There

were no participants having an adverse event (AE) leading to discontinuation of BLV and no serious AEs attributed to BLV treatment.
Conclusion: Results at Week 48 demonstrate that treatment with BLV resulted in a significantly greater combined response compared to control. Monotherapy with BLV was safe and well tolerated.

Friday 24 June

General Session II

GS007

Transcatheter arterial chemoembolization (TACE) followed by conformal radiotherapy versus TACE alone for hepatocellular carcinoma: a western controlled trial

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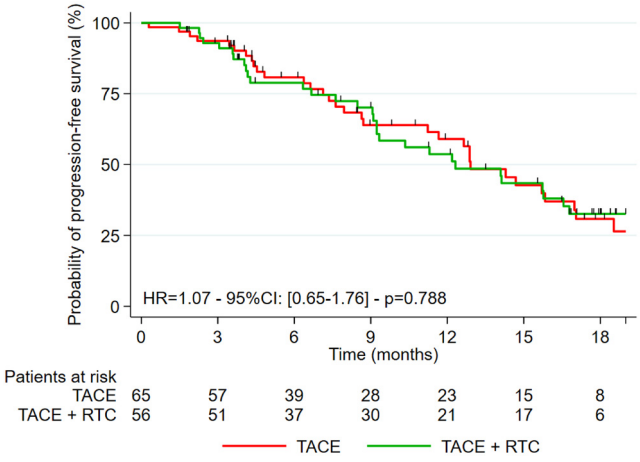
Background: Transarterial chemoembolization (TACE) is a recommended treatment for patients with hepatocellular carcinoma and no possible ablative therapy. We aimed to compare the efficacy and safety of a combination of one TACE followed by external conformal radiotherapy (CRT) to the two TACE procedure.
Methods: TACERTE was an open-labelled randomized controlled trial with a 1:1 allocation rate. Patients had a mean age of 70 y, were male in 86 %. Etiology was HCV in 13%, HBV in 2% and alcohol for the others. The primary end point was progression-free survival (PFS; Kaplan-Meier analysis) in the intention-to-treat population. The typical schedule of CRT was 54 gy in 18 sessions. DC beads were used for TACE in 82/120 (68%). Study registered in clinical trial.gov (NCT01300143).
Results: Among the 120 randomized patients, 64 were in the arm TACE alone and 56 in the TACE-CRT arm. 91/120 (76%) did not have received any previous therapy. Eight patients (4 in each arm) had a rapid tumoral progression and did not received the planned therapy. The PFS at 12 and 18 months was 53% and 32 % in the TACE and CRT group and 59% and 30 % in TACE alone group (HR = 1.07; 95% CI: [0.65–1.76]-p = 0.78). A centralized blinded review of imaging was possible in 95 patients (79%) and confirmed the absence of significant differences between the two arms. The overall survival (OS) at 12, 18 and 60 months was 69%, 57% and 15% in the TACE and CRT group and 81%, 75% and 17% in the TACE alone group (HR = 1.23–95%CI: [0.83–1.82]-p = 0.297). The median OS was 22 months (95%CI:[15.7–26.2]) in the TACE-CRT arm and 30 months (95% IC:[23–35]) in the other. The cumulated number of grade III–IV adverse events (AE) was 83 in the TACE and CRT group and 59 in the TACE alone group. A propensity score analysis demonstrated that exposure to TACE and CRT was associated to more AE.



Conclusion: In contrast with the results of previous eastern randomized trials, this first western randomized controlled trial demonstrates that compared to the conventional TACE, the combination of TACE followed by CRT procedure has no positive effect on the PFS or the OS in patients with unresectable HCC.
Funding: Programme Hospitalier de Recherche Clinique" (PHRC) in 2009 (Institut National du Cancer).

GS008

The global burden of liver cancer (LC) and chronic liver diseases (CLD) is driven by non-alcoholic steatohepatitis (NASH) and alcohol liver disease (ALD)

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Background and aims: Although chronic viral hepatitis B and C (CHB and CHC) and ALD have been the main drivers of burden of chronic liver disease (CLD) and liver cancer (LC), NASH has recently become more prominent. **Aim:** To assess changes in the global prevalence, incidence, mortality and morbidity [disability-adjusted life-years (DALYs)] related to LC and CLD according to the etiology of CLD and 21 GBD regions of the world.
Method: The data was obtained from the Global Burden of Disease Study 2019 (GBD 2019). Incidence, prevalence, mortality and DALYs were calculated. Annual percent change (APC) was calculated by using Joinpoint regression program, National Cancer Institute.
Results: In 2019 globally, the prevalence, incidence, mortality and DALYs from liver disease was 1.69 billion (LC 0.04% and CLD 99.96%), 2.59 million (LC 20.7% and CLD 79.3%); 1.95 million (LC 24.8% and CLD 75.3%) and 58.7 million (LC 21.3% and CLD 78.7%). Over the last decade (2009 to 2019), there was +33.7% increase in prevalence of LC and +22.7% in the prevalence of CLD. Furthermore, there was +30.0% increase in the incidence of LC and +14.8% increase in the incidence of CLD. Finally, both deaths [LC (+27.2%) and CLD (+10.6%)] as well as DALYs [LC (+21.9%) and CLD (+5.1%)] increased.
During the past decade (2009–2019), the observed increases (APC = +1.33%) in global LC death rate (per 100, 000) were driven by NAFLD (from 0.36 to 0.45, APC = +2.47%), ALD (from 0.97 to 1.17, APC = +1.91%), HBV (from 2.25 to 2.48, APC = +0.21%) and HCV (from 1.64 to 1.83, APC = +1.12%) (Figure).
In contrast, between 2009 and 2019, the observed decreases (APC = –0.18%) in the global CLD death rate (per 100, 000) were driven by decrease in HBV (from 5.07 to 4.28, APC = –1.83%); while HCV (from