LBA3 - IMbrave150: Efficacy and safety results from a ph III study evaluating atezolizumab▼ plus bevacizumab vs sorafenib as first treatment for patients with unresectable hepatocellular carcinoma (HCC)

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Background:

The Phase Ib data has shown promising efficacy and safety for atezolizumab plus bevacizumab in unresectable HCC patients who have not received prior systemic therapy. Here, we report the primary analysis data from the Ph III IMbrave150 trial comparing atezolizumab plus bevacizumab vs sorafenib in this patient population.

Methods:

IMbrave150 enrolled systemic treatment naïve patients with unresectable HCC. Patients were randomised 2:1 to receive either atezolizumab 1200 mg plus bevacizumab 15 mg/kg intravenously on day 1 of each 21-day cycle or sorafenib 400 mg per os two times per day until unacceptable toxicity or loss of clinical benefit per investigator. Coprimary endpoints were overall survival (OS) and progression free survival (PFS) by independent review facility (IRF)-assessed RECIST 1.1. The key secondary endpoints IRF-overall response rate (ORR) per RECIST 1.1 and IRF-overall response rate (ORR) per HCC mRECIST were also part of the study statistical testing hierarchy.

Results:

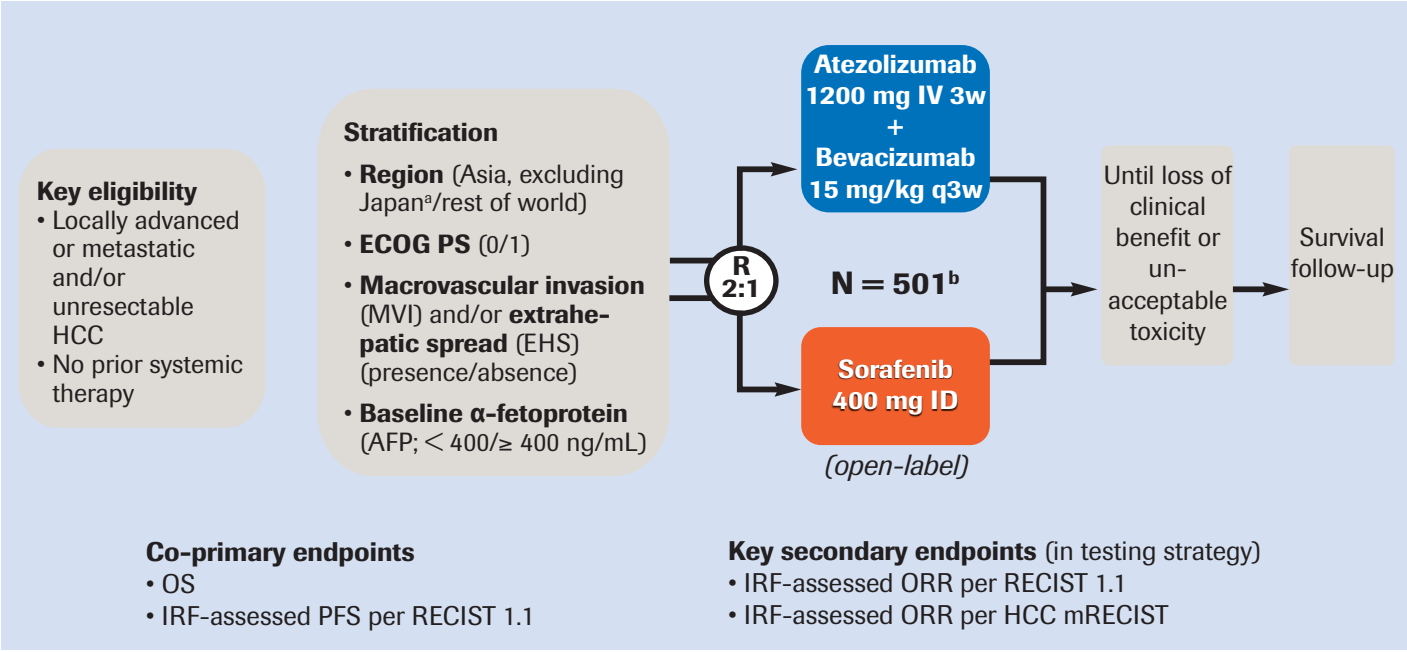
The ITT population included 336 patients randomised to atezolizumab plus bevacizumab and 165 randomised to sorafenib. Baseline demographics were well balanced between arms. With a median follow up of 8.6 months, OS HR was 0.58 (95% CI, 0.42, 0.79; $P = 0.0006$) and PFS HR was 0.59 (95% CI, 0.47, 0.76; $P < 0.0001$; see table) for atezolizumab plus bevacizumab vs sorafenib. ORR was 27% vs 12% ($P < 0.0001$) per IRF RECIST 1.1 and 33% vs 13% ($P < 0.0001$) per IRF HCC mRECIST for atezolizumab plus bevacizumab vs sorafenib, respectively. Results were generally consistent across clinical subgroups. Atezolizumab plus bevacizumab delayed deterioration of quality of life vs sorafenib [11.2 vs 3.6 months, HR, 0.63 (95% CI: 0.46, 0.85)]. Median therapy duration was 7.4 months for atezolizumab, 6.9 months for bevacizumab and 2.8 months for sorafenib. Grade 3-4 AEs occurred in 57% of patients receiving atezolizumab plus bevacizumab and 55% of patients receiving sorafenib. Grade 5 AEs were seen in 5% and 6% of patients, respectively.

Conclusions:

IMbrave150 demonstrated statistically significant and clinically meaningful improvement in both OS and PFS for atezolizumab plus bevacizumab vs sorafenib in patients with unresectable HCC who have not received prior systemic therapy. The safety of atezolizumab plus bevacizumab is consistent with the known safety profile of each agent, and no new safety signals were identified. Atezolizumab plus bevacizumab has the potential to be a practice changing treatment in HCC.

Adapted from: Cheng A-L. et al. (2019) LBA3, Annals of Oncology, Volume 30, Supplement 9.

IMbrave150 study design



[a]Japan is included in rest of world.
[b]An additional 57 Chinese patients in the China extension cohort were not included in the global population/analysis.

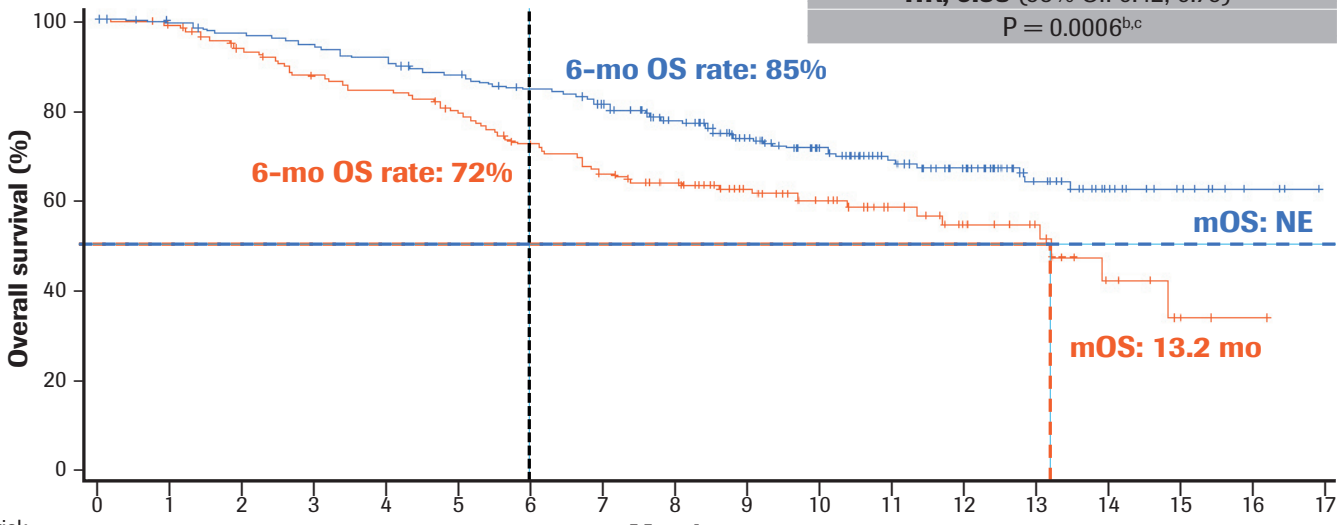
IMbrave150 baseline characteristics (ITT)

Characteristic	Atezolizumab + Bevacizumab n = 336	Sorafenib n = 165
Median age (range), years	64 (26-88)	66 (33-87)
Sex, male, n (%)	277 (82)	137 (83)
Region, n (%)		
Asia (excluding Japan[a])	133 (40)	68 (41)
Rest of world	203 (60)	97 (59)
ECOG PS 1, n (%)	127 (38)	62 (38)
Child-Pugh class, n (%)		
A | B	333 (99) | 1 (< 1)	165 (100) | 0
BCLC staging at study entry, n (%) A | B | C	8 (2) | 52 (15) | 276 (82)	6 (4) | 26 (16) | 133 (81)
Aetiology of HCC, n (%)		
HBV | HCV | Non-viral	164 (49) | 72 (21) | 100 (30)	76 (46) | 36 (22) | 53 (32)
AFP ≥ 400 ng/mL, n (%)	126 (38)	61 (37)
EHS, n (%)	212 (63)	93 (56)
MVI, n (%)	129 (38)	71 (43)
EHS and/or MVI, n (%)	258 (77)	120 (73)
Prior TACE, n (%)	130 (39)	70 (42)
Prior radiotherapy, n (%)	34 (10)	17 (10)

[a] Japan is included in rest of world.

OS: co-primary endpoint

Median OS (95% CI), mo[a]	
Atezolizumab + Bevacizumab	NE
Sorafenib	13.2 (10.4, NE)
HR, 0.58 (95% CI: 0.42, 0.79)[b]	
P = 0.0006[b,c]	

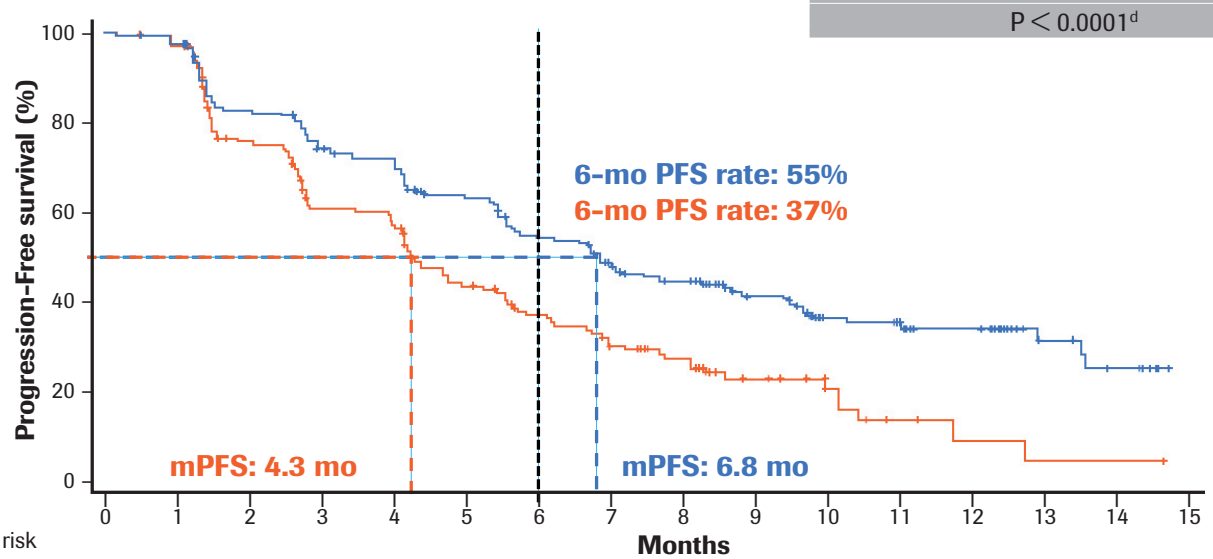


No. at risk																	
Sorafenib	165	157	143	132	127	118	105	94	86	60	45	33	24	16	7	3	1	NE
Atezolizumab + Bevacizumab	336	329	320	312	302	288	275	255	222	165	118	87	64	40	20	11	3	NE

NE, not estimable. [a] 96 patients (29%) in the Atezo + Bev arm vs 65 (39%) in the sorafenib arm had an event. [b] HR and P value were from Cox model and logrank test and were stratified by geographic region (Asia vs rest of world, including Japan), AFP level (< 400 vs ≥ 400 ng/mL) at baseline and MVI and/or EHS (yes vs no) per IxRS. [c] The 2-sided P value boundary based on 161 events is 0.0033. Data cutoff, 29 Aug 2019; median survival follow-up, 8.6 mo.

Confirmed PFS[a]: co-primary endpoint

Median PFS (95% CI), mo[b]	
Atezolizumab + Bevacizumab	6.8 (5.7, 8.3)
Sorafenib	4.3 (4.0, 5.6)
HR, 0.59 (95% CI: 0.47, 0.76)[c,d]	
P < 0.0001[d]	

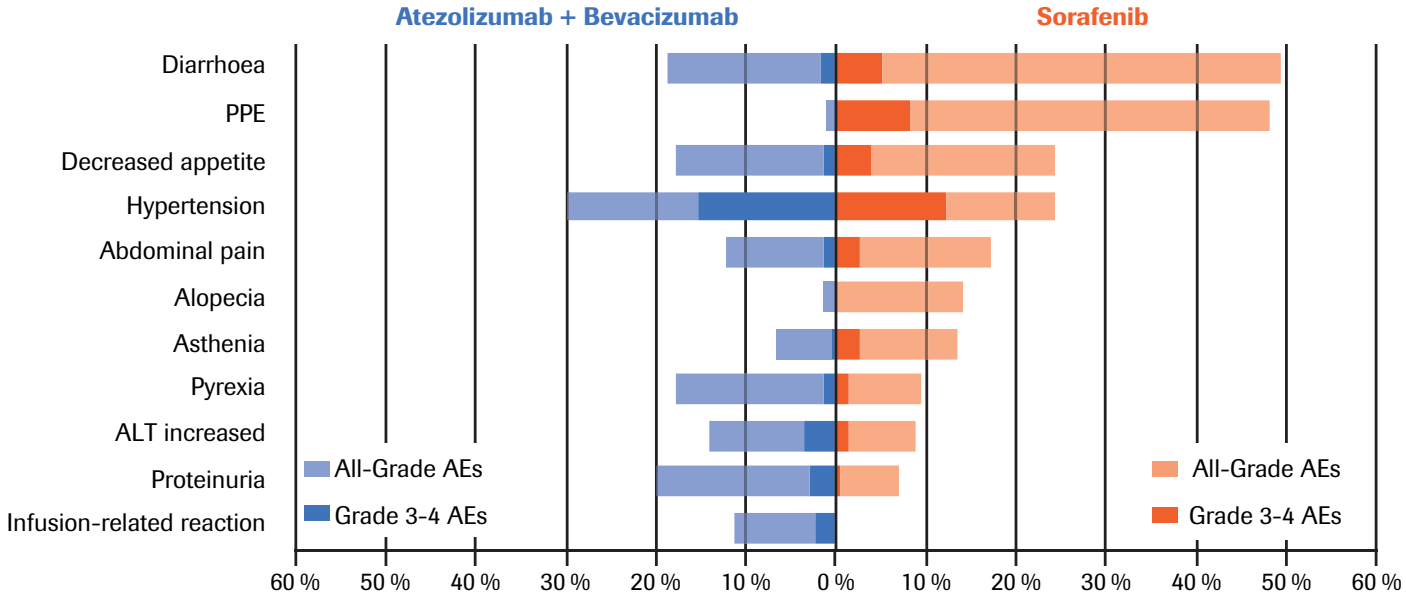


No. at risk																
Sorafenib	165	148	109	84	80	57	44	34	27	15	9	4	2	1	1	NE
Atezolizumab + Bevacizumab	336	322	270	243	232	201	169	137	120	74	50	46	34	11	7	NE

[a] Assessed by IRF per RECIST 1.1. [b] 197 patients (59%) in the Atezo + Bev arm vs 109 (66%) in the sorafenib arm had an event. [c] HR and P value were from Cox model and log-rank test and were stratified by geographic region (Asia vs rest of world, including Japan), AFP level (< 400 vs ≥ 400 ng/mL) at baseline and MVI and/or EHS (yes vs no) per IxRS. [d] The 2-sided P value boundary is 0.002.Data cutoff, 29 Aug 2019; median survival follow-up, 8.6 mo.

Safety[a]

≥ 10% frequency of AEs in either arm and > 5% difference between arms



PPE, palmar-plantar erythrodysaesthesia.
[a] Safety-evaluable population

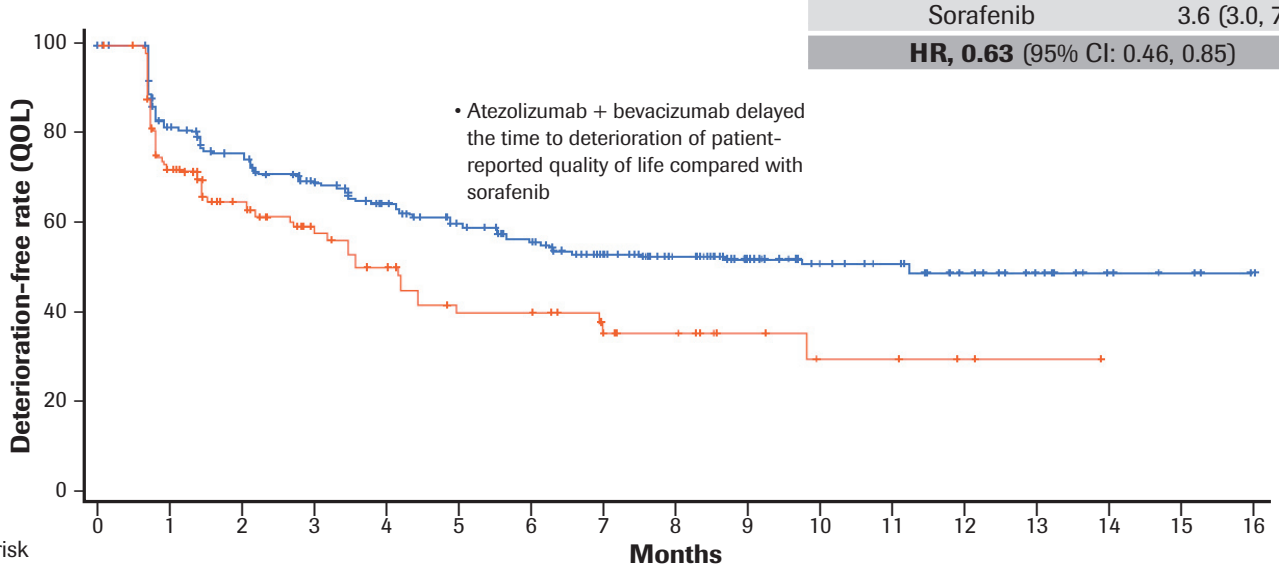
Safety summary[a]

Characteristic	Atezolizumab + Bevacizumab n = 329	Sorafenib n = 156
Treatment duration, median, mo	Atezolizumab = 7.4; Bevacizumab = 6.9	2.8
All-Grade AEs, any cause, n (%)	323 (98)	154 (99)
Treatment-related all-Grade AEs	276 (84)	147 (94)
Grade 3-4 AE , n (%)[b]	186 (57)	86 (55)
Treatment-related Grade 3-4 AE[b]	117 (36)	71 (46)
ECOG PS 1, n (%)	127 (38)	62 (38)
Child-Pugh class, n (%)		
A | B	333 (99) | 1 (< 1)	165 (100) | 0
Serious adverse event, n (%)	125 (38)	48 (31)
Treatment-related SAE	56 (17)	24 (15)
Grade 5 AE, n (%)	15 (5)	9 (6)
Treatment-related Grade 5 AE	6 (2)	1 (< 1)
AE leading to withdrawal from any component, n (%)	51 (16)	16 (10)
AE leading to withdrawal from both components	23 (7)	16 (10)
AE leading to dose interruption of any study treatment, n (%)	163 (50)	64 (41)
AE leading to dose modification of sorafenib, n (%)[c]	0	58 (37)

[a] Safety-evaluable population. [b] Highest grade experienced.
[c] No dose modification allowed for Atezo + Bev arm.

Patient-reported outcomes[a]

Quality of life (QOL) Median TTD (95% CI), mo[b]	
Atezolizumab + Bevacizumab	11.2 (6.0, NE)
Sorafenib	3.6 (3.0, 7.0)
HR, 0.63 (95% CI: 0.46, 0.85)	



No. at risk																	
Sorafenib	165	93	60	39	31	22	105	14	12	7	4	4	2	1	NE	NE	NE
Atezolizumab + Bevacizumab	336	239	208	181	157	134	275	99	78	58	40	32	20	14	7	5	NE

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire for Cancer; TTD, time to deterioration.
[a] Pre-specified secondary endpoint that was not formally tested; EORTC QLQ-C30 administered every 3 weeks on treatment and every 3 months after treatment discontinuation or progression. [b] Time to deterioration defined as first decrease from baseline of ≥ 10 points1 in the patient-reported health-related global health status/quality of life (GHS/QoL) scale of the EORTC QLQ-C30 maintained for 2 consecutive assessments or 1 assessment followed by death from any cause within 3 weeks.
1. Osoba D, et al. J Clin Oncol. 1998. Data cutoff, 29 Aug 2019; median survival follow-up, 8.6 mo.

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