

ATEZOLIZUMAB + BEVACIZUMAB VS SORAFENIB IN HCC PATIENTS WITH PRIOR LOCOREGIONAL THERAPY: EXPLORATORY DATA FROM IMBRAVE150

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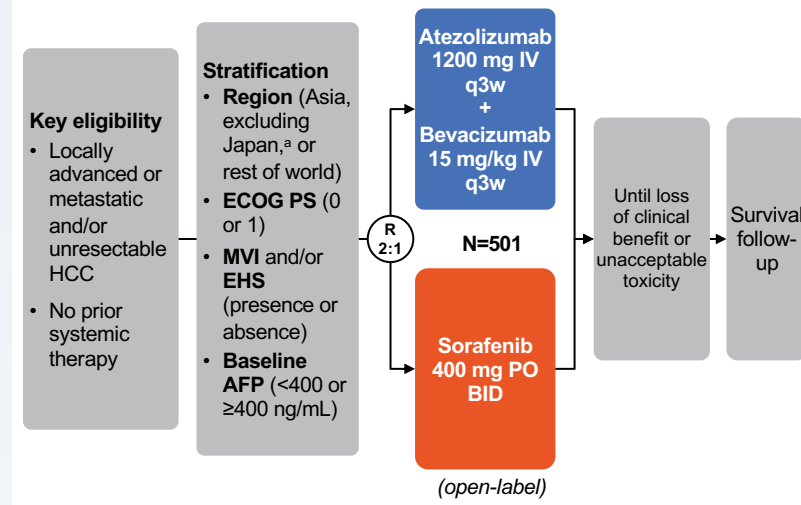
INTRODUCTION

- Atezolizumab + bevacizumab has been approved in >85 countries for the treatment of patients with unresectable HCC who have not received prior systemic therapy¹⁻³
- In the primary analysis from the Phase III IMbrave150 study (NCT03434379), both coprimary endpoints (OS and IRF-assessed PFS per RECIST 1.1) were met⁴
- With an additional 12 months of follow-up from the primary analysis (median, 15.6 months) atezolizumab + bevacizumab showed statistically significant and clinically meaningful treatment benefit and safety⁵
- Here, using updated data from IMbrave150, we report an exploratory analysis of the efficacy and safety of atezolizumab + bevacizumab in patients who had prior LRT

IRF, independent review facility; LRT, locoregional therapy.

PATIENTS AND METHODS

Figure 1. Study design and prior LRT at baseline⁴



- Primary endpoints**
- OS
 - IRF-assessed PFS per RECIST 1.1
- Key secondary efficacy endpoints**
- IRF-assessed ORR per RECIST 1.1
 - IRF-assessed DOR per RECIST 1.1

AFP, a-fetoprotein; BID, twice a day; EHS, extrahepatic spread; HCC mRECIST, modified RECIST for HCC; IV, intravenous; MVI, macrovascular invasion; PEI, percutaneous ethanol injection; PO, oral; R, randomized; q3w, every 3 weeks; RFA, radiofrequency ablation; TACE, transarterial chemoembolization; TAE, transarterial embolization.
^a Japan is included in rest of world.

Table 1: Prior LRT at baseline

	Atezo + Bev (n=336)	Sorafenib (n=165)
Prior LRT, n (%)	161 (48)	85 (52)
Median no. (range)	2 (1-26)	2 (1-18)
TACE, n (%)	131 (39)	71 (43)
Median no. (range)	2 (1-11)	2 (1-17)
RFA, n (%)	47 (14)	24 (15)
Median no. (range)	2 (1-10)	1 (1-6)
TAE, n (%)	12 (4)	8 (5)
Median no. (range)	1 (1-2)	1 (1-2)
PEI, n (%)	12 (4)	3 (2)
Median no. (range)	1 (1-3)	1 (1-4)

RESULTS

Table 2: Baseline characteristics and demographics

	No prior LRT		1-2 prior LRT		≥3 prior LRT	
	Atezo + Bev (n=175)	Sorafenib (n=80)	Atezo + Bev (n=84)	Sorafenib (n=44)	Atezo + Bev (n=77)	Sorafenib (n=41)
Age, median (range), y	63.0 (26-88)	65.5 (34-87)	63.5 (34-88)	66.0 (38-84)	65.0 (27-85)	67.0 (33-83)
Male, n (%)	144 (82)	71 (89)	65 (77)	36 (82)	68 (88)	30 (73)
ECOG PS 1, n (%) ^a	67 (38)	35 (44)	35 (42)	14 (32)	25 (32)	13 (32)
Child-Pugh class, n (%)						
A5 / A6	125 (71) / 47 (27) ^b	57 (71) / 23 (29)	58 (69) / 26 (31)	35 (80) / 9 (20)	56 (73) / 21 (27)	29 (71) / 12 (29)
BCLC stage, n (%)						
A / B / C	1 (1) / 26 (15) / 148 (85)	2 (3) / 9 (11) / 69 (86)	3 (4) / 9 (11) / 72 (86)	3 (7) / 7 (16) / 34 (77)	4 (5) / 16 (21) / 57 (74)	1 (2) / 9 (22) / 31 (76)
AFP ≥400 ng/mL, n (%) ^a	72 (41)	33 (41)	29 (35)	14 (32)	25 (32)	14 (34)
Modified ALBI grade						
1 / 2a / 2b	92 (53) / 40 (23) / 42 (24) ^c	38 (48) / 17 (21) / 25 (31)	49 (58) / 19 (23) / 16 (19)	24 (55) / 12 (27) / 8 (18)	50 (65) / 13 (17) / 14 (18)	25 (61) / 8 (20) / 8 (20)
EHS, n (%) ^a	106 (61)	44 (55)	60 (71)	26 (59)	46 (60)	23 (56)
MVI, n (%) ^a	87 (50)	44 (55)	23 (27)	14 (32)	19 (25)	13 (32)
EHS and/or MVI, n (%) ^a	140 (80)	63 (79)	66 (79)	29 (66)	52 (68)	28 (68)
Varices, n (%)	45 (26)	20 (25)	25 (30)	13 (30)	19 (25)	10 (24)
HCC etiology, n (%) ^d						
HBV / HCV / non-viral	73 (42) / 42 (24) / 60 (34)	32 (40) / 16 (20) / 32 (40)	45 (54) / 15 (18) / 24 (29)	22 (50) / 7 (16) / 15 (34)	46 (60) / 15 (19) / 16 (21)	22 (54) / 13 (32) / 6 (15)

Clinical cutoff: 31 August 2020; median follow-up: 15.6 mo. ^a Per electronic case report form, not interactive voice/web response system. ^b Data are not included for 1 patient in the atezo + bev arm whose classification was B7 and 2 patients with missing data. ^c Baseline ALBI grade was missing for 1 patient. ^d For patients whose cause of HCC was multifactorial as assessed by the investigator, the viral cause was prioritized over non-viral causes to define the primary etiology of the patient.

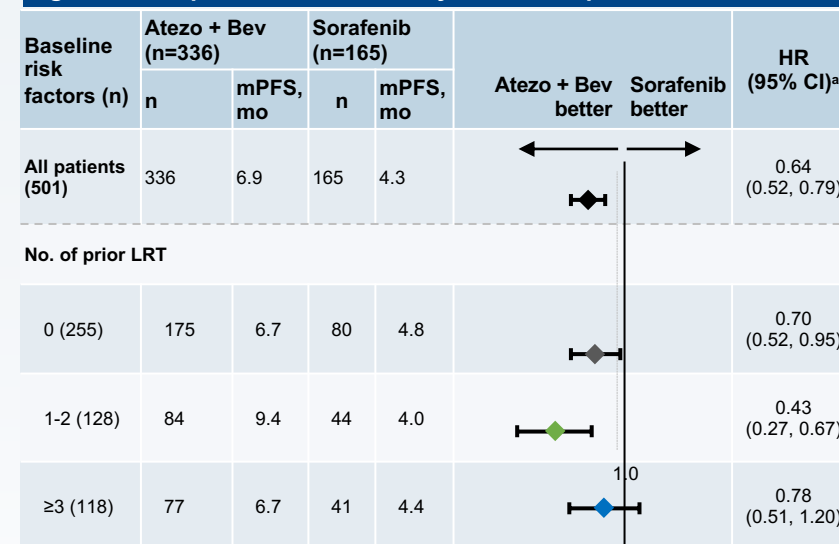
Figure 2. OS by number of prior LRT



	No prior LRT		1-2 prior LRT		≥3 prior LRT	
	Atezo + Bev (n=175)	Sorafenib (n=80)	Atezo + Bev (n=84)	Sorafenib (n=44)	Atezo + Bev (n=77)	Sorafenib (n=41)
Patients at risk at 12 months, n	107	36	58	16	49	26
Event-free rate, % (95% CI)	64.1 (56.9, 71.3)	51.7 (40.3, 63.1)	72.0 (62.2, 81.7)	48.8 (32.1, 65.6)	67.8 (57.2, 78.4)	71.5 (57.2, 85.7)

Clinical cutoff: 31 August 2020; median follow-up: 15.6 mo. mOS, median overall survival. ^a Unstratified HR shown for all characteristics except for "All patients."

Figure 4. PFS per IRF RECIST 1.1 by number of prior LRT



	No prior LRT		1-2 prior LRT		≥3 prior LRT	
	Atezo + Bev (n=175)	Sorafenib (n=80)	Atezo + Bev (n=84)	Sorafenib (n=44)	Atezo + Bev (n=77)	Sorafenib (n=41)
Patients at risk at 12 months, n	52	13	29	2	21	9
Event-free rate, % (95% CI)	34.3 (27.1, 41.6)	20.4 (11.1, 29.8)	39.3 (28.5, 50.1)	8.1 (0.0, 18.5)	32.8 (21.7, 43.9)	32.2 (16.7, 47.7)

Clinical cutoff: 31 August 2020; median follow-up: 15.6 mo. mPFS, median progression-free survival. ^a Unstratified HR shown for all characteristics except for "All patients."

Table 3: Response and duration of response

	No prior LRT		1-2 prior LRT		≥3 prior LRT	
	Atezo + Bev (n=172)	Sorafenib (n=78)	Atezo + Bev (n=79)	Sorafenib (n=41)	Atezo + Bev (n=75)	Sorafenib (n=40)
Confirmed ORR, % (95% CI) ^{a,b}	29 (22.4, 36.5)	15 (8.2, 25.3)	35 (25.0, 47.0)	5 (0.6, 16.5)	25 (16.0, 36.7)	10 (2.8, 23.7)
Odds ratio (95% CI) ^c	2.3 (1.1, 4.5)		10.7 (2.4, 47.7)		3.1 (1.0, 9.7)	
CR, n (%)	8 (5)	1 (1)	11 (14)	0	6 (8)	0
PR, n (%)	42 (24)	11 (14)	17 (22)	2 (5)	13 (17)	4 (10)
SD, n (%)	76 (44)	33 (42)	31 (39)	15 (37)	37 (49)	21 (53)
DCR, n (%)	126 (73)	45 (58)	59 (75)	17 (41)	56 (75)	25 (63)
PD, n (%)	34 (20)	19 (24)	15 (19)	12 (29)	14 (19)	9 (23)
NE, n (%)	3 (2)	7 (9)	4 (5)	4 (10)	1 (1)	3 (8)
Missing, n (%)	9 (5)	7 (9)	1 (1)	8 (20)	4 (5)	3 (8)
Median DOR ^b (95% CI), mo	21.4 (12.6, NE)	10.6 (4.7, 16.5)	15.6 (13.5, NE)	17.0 (NE, NE)	16.3 (13.8, NE)	12.6 (12.4, 21.8)

Clinical cutoff: 31 August 2020; median follow-up: 15.6 mo. DCR, disease control rate; NE, not evaluable. ^a Only patients with measurable disease at baseline were included in the analysis of ORR. ^b Only confirmed responders were included in the analysis of ORR and DOR. ^c Odds ratios are unstratified.

Table 4: Safety summary

	No prior LRT ^a		1-2 prior LRT ^a		≥3 prior LRT ^a	
	Atezo + Bev (n=170)	Sorafenib (n=77)	Atezo + Bev (n=84)	Sorafenib (n=41)	Atezo + Bev (n=75)	Sorafenib (n=38)
Treatment duration, median (range), mo	Atezo=8.7 (0-28); Bev=7.6 (0-28)	3.0 (0-25)	Atezo=8.7 (0-27); Bev=6.7 (0-27)	1.6 (0-19)	Atezo=7.6 (0-28); Bev=6.3 (0-26)	2.8 (0-17)
All-grade AE, any cause, n (%)	167 (98)	77 (100)	82 (98)	40 (98)	73 (97)	37 (97)
Treatment-related all-grade AE	146 (86)	73 (95)	75 (89)	39 (95)	63 (84)	36 (95)
Grade 3-4 AE, n (%) ^b	107 (63)	43 (56)	54 (64)	22 (54)	46 (61)	24 (63)
Treatment-related Grade 3-4 AE ^b	79 (46)	30 (39)	33 (39)	20 (49)	31 (41)	22 (58)
Serious AE, n (%)	88 (52)	31 (40)	38 (45)	12 (29)	34 (45)	8 (21)
Treatment-related serious AE	46 (27)	9 (12)	13 (15)	10 (24)	17 (23)	6 (16)
Grade 5 AE, n (%)	13 (8)	7 (9)	6 (7)	1 (2)	4 (5)	1 (3)
Treatment-related Grade 5 AE	3 (2)	1 (1)	2 (2)	0	1 (1)	0
AE leading to withdrawal from any component, n (%)	39 (23)	8 (10)	15 (18)	4 (10)	18 (24)	6 (16)
AE leading to withdrawal from both components	19 (11)	0	7 (8)	0	8 (11)	0
AE leading to dose interruption of any study treatment, n (%)	106 (62)	39 (51)	46 (55)	16 (39)	43 (57)	24 (63)
AE leading to dose reduction of sorafenib, n (%) ^c	0	31 (40)	0	13 (32)	0	14 (37)

Clinical cutoff: 31 August 2020; median follow-up: 15.6 mo. AE, adverse events. ^a Safety-evaluable population (defined as patients who received study treatment). ^b Highest grade experienced. ^c No dose modification allowed for atezo + bev arm.

Table 5: AESI with bevacizumab

	No prior LRT ^a		1-2 prior LRT ^a		≥3 prior LRT ^a	
	Atezo + Bev (n=170)	Sorafenib (n=77)	Atezo + Bev (n=84)	Sorafenib (n=41)	Atezo + Bev (n=75)	Sorafenib (n=38)
All-grade AESI, n (%)	117 (69)	34 (44)	56 (67)	22 (54)	50 (67)	22 (58)
Hypertension	58 (34)	15 (19)	32 (38)	13 (32)	32 (43)	13 (34)
Bleeding/hemorrhage	52 (31)	10 (13)	24 (29)	9 (22)	24 (32)	9 (24)
Proteinuria	49 (29)	8 (10)	30 (36)	4 (10)	23 (31)	3 (8)
Thromboembolic event—venous	7 (4)	3 (4)	3 (4)	2 (5)	4 (5)	0
Thromboembolic event—arterial	6 (4)	1 (1)	4 (5)	0	1 (1)	1 (3)
Congestive heart failure	1 (1)	1 (1)	0	1 (2)	1 (1)	0
Fistula/abscess (non-gastrointestinal)	1 (1)	1 (1)	0	0	0	0
Gastrointestinal perforation	1 (1)	0	1 (1)	0	1 (1)	0
Wound-healing complications	1 (1)	0	2 (2)	0	0	0

Clinical cutoff: 31 August 2020; median follow-up: 15.6 mo. AESI, adverse event of special interest. ^a Safety-evaluable population

Table 6: Grade 3-4 and Grade 5 AEs

	No prior LRT ^a		1-2 prior LRT ^a		≥3 prior LRT ^a	
	Atezo + Bev (n=170)	Sorafenib (n=77)	Atezo + Bev (n=84)	Sorafenib (n=41)	Atezo + Bev (n=75)	Sorafenib (n=38)
Grade 3-4 AEs occurring in ≥5% of patients with 0, 1-2 or ≥3 prior LRT, n (%)						
Hypertension	27 (16)	5 (6)	14 (17)	6 (15)	15 (20)	8 (21)
Aspartate aminotransferase increased	18 (11)	7 (9)	4 (5)	2 (5)	4 (5)	0
Diarrhea	8 (5)	5 (6)	2 (2)	2 (5)	1 (1)	1 (3)
Blood bilirubin increased	6 (4)	8 (10)	5 (6)	0	2 (3)	2 (5)
Grade 5 AEs occurring in ≥2 patients in any group, n (%)						
Gastrointestinal hemorrhage	2 (1) ^b	0	1 (1)	0	0	0
Multiple organ dysfunction syndrome	2 (1)	0	0	0	0	0
Hepatic cirrhosis	1 (1)	2 (3) ^c	0	0	0	0
Cardiac arrest	1 (1)	1 (1)	0	0	0	0
Death, not otherwise specified	0	2 (3)	0	0	1 (1)	0

Clinical cutoff: 31 August 2020; median follow-up: 15.6 mo. ^a Safety-evaluable population (defined as patients who received study treatment). ^b 1 patient who had no prior LRT in the atezo + bev arm had treatment-related Grade 5 gastrointestinal hemorrhage. ^c 1 patient who had no prior LRT in the sor arm had treatment-related Grade 5 hepatic cirrhosis.

CONCLUSIONS

- A survival benefit was seen with atezolizumab + bevacizumab vs sorafenib regardless of whether patients received prior LRT
- Atezolizumab + bevacizumab seemed to have more benefit in patients with 1-2 vs ≥3 prior LRTs, suggesting there is an optimal time for switching from LRT to systemic treatment
- The safety and tolerability profile of atezolizumab + bevacizumab remains consistent with the known safety profiles of each individual drug and the underlying disease
- Atezolizumab + bevacizumab provides the longest overall survival observed in a Phase III study in patients receiving systemic therapy for front-line unresectable HCC, confirming this combination as the standard of care for previously untreated, unresectable HCC, including in patients who received prior LRT

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DISCLOSURES

- Riad Salem, MD, is a consultant for AstraZeneca, Boston Scientific, Cook, Eisai, Genentech and Sirtex
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