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MEETING SUMMARY
WCGIC 2020, VIRTUAL MEETING

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HIGHLIGHTS FROM HCC CONNECT
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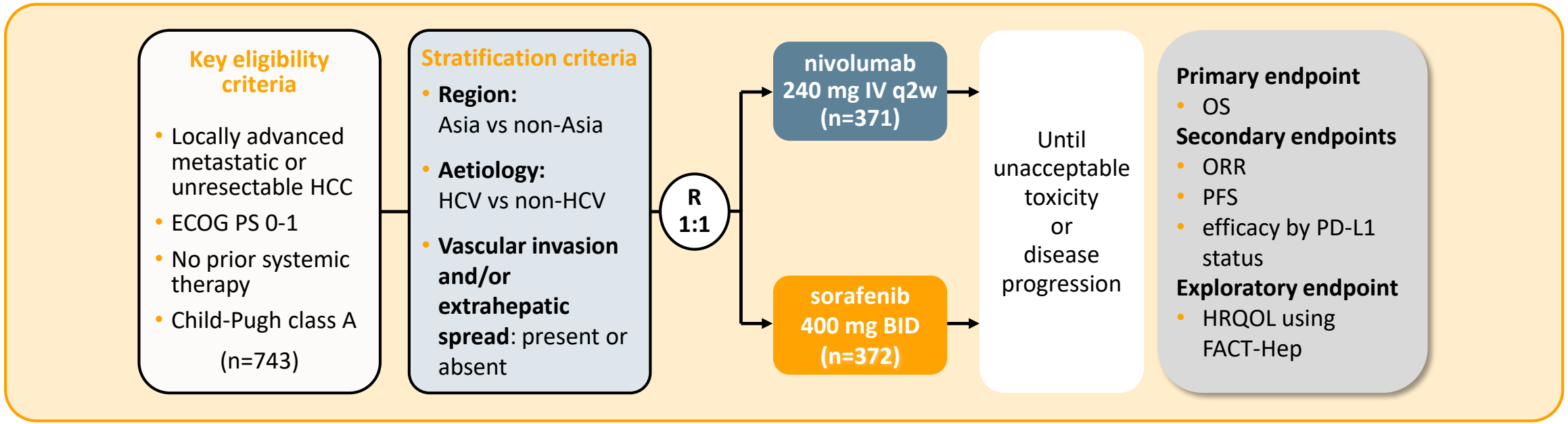
CHECKMATE 459: LONG-TERM SURVIVAL OUTCOMES WITH NIVOLUMAB VERSUS SORAFENIB AS FIRST-LINE TREATMENT IN PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA

Sangro B, et al.
WCGIC 2020. Abstract #LBA-3. Oral presentation

BACKGROUND

CheckMate 459 (NCT02576509): randomised, stratified, multi-centre phase 3 study assessing nivolumab versus standard-of-care sorafenib in first line for advanced HCC



Primary analysis (database lock: **June 2019**): Median OS = 16.4 months for nivolumab vs 14.7 months for sorafenib with favourable and manageable safty profile[1]

The abstract presents long-term follow-up survival and safety data from CheckMate 459 (database lock: **April 2020**) with a minimum follow-up of 33.6 months

BID, twice daily; ECOG PS, Eastern cooperative oncology group performance status; FACT-Hep, functional assessment of cancer therapy- hepatobiliary cancer; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HRQOL; health-related quality of life; IV, intravenous; ORR, objective response rate; OS, overall survival; PD-L1, programmed death ligand 1; PFS, progression-free survival; q2w, every 2 weeks

1Yau T, et al. Ann Oncol 2019,30(suppl_5):v851-v934

RESULTS: EFFICACY

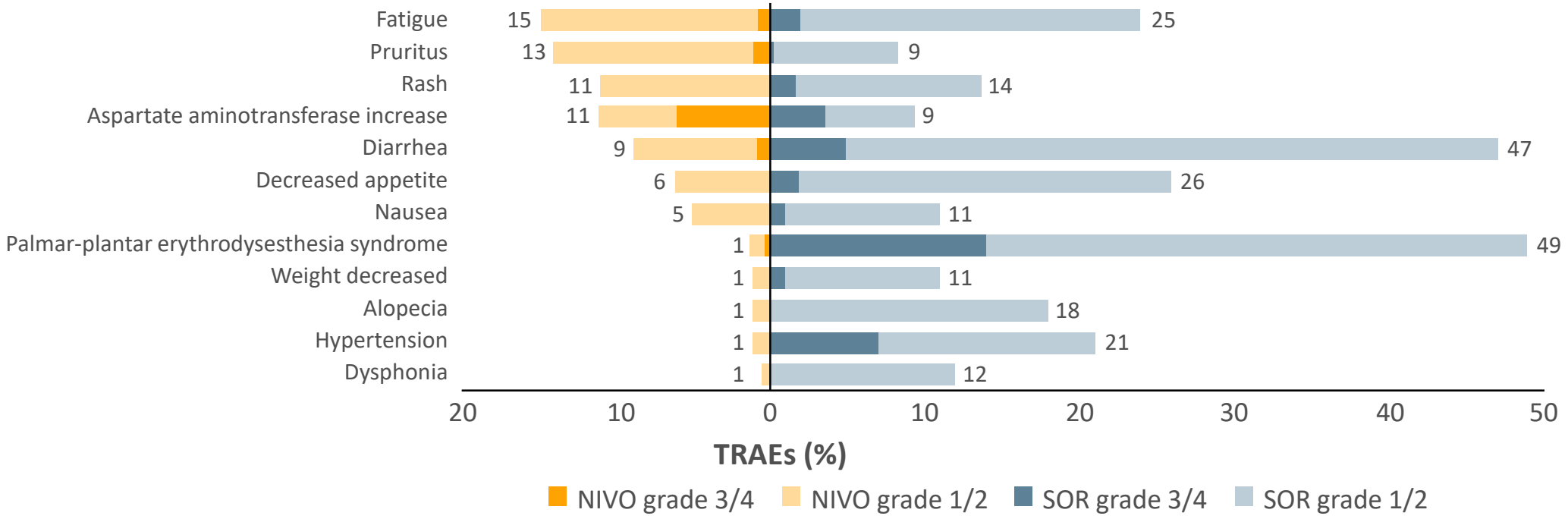
Overall survival	nivolumab (n=371)	sorafenib (n=372)
Median OS, months (95% CI)	**16.4 (14.0-18.5)**	14.8 (12.1-17.3)
HR (95% CI)	0.85 (0.72-1.00); p=0.0522	
Overall survival by PD-L1 expression		
Median OS in tumour cell PD-L1 ≥ 1%, months (95% CI)	**16.1 (8.4-22.3)**	8.6 (5.7-16.3)
HR (95% CI)	0.80 (0.54-1.17)	
Median OS in tumour cell PD-L1 < 1%, months (95% CI)	16.7 (13.9-19.4)	15.2 (12.7-18.1)
HR (95% CI)	0.84 (0.70-1.01)	
Overall survival by aetiology		
Median OS in HCV patients, months (95% CI)	**17.5 (13.9-21.9)**	12.7 (9.9-16.2)
HR (95% CI)	0.72 (0.51-1.02)	
Median OS in HBV patients, months (95% CI)	**16.1 (12.5-21.3)**	10.4 (8.5-17.3)
HR (95% CI)	0.79 (0.59-1.07)	
Median OS in uninfected patients, months (95% CI)	16.0 (10.8-20.2)	17.4 (13.7-21.3)
HR (95% CI)	0.91 (0.72-1.16)	

CI, confidence interval; HR, hazard ratio; HBC, hepatitis B virus; HCV, hepatitis C virus; OS, overall survival; PD-L1, programmed death ligand 1

RESULTS: EFFICACY (CON'T) AND SAFETY

OS rate (%)	nivolumab	sorafenib
12-month	60%	55%
24-month	37%	33%
33-month	29%	21%

- Events occurring in > 10% of patients in either treatment arm are presented:



OS, overall survival; NIVO, nivolumab; SOR, sorafenib; TRAE, treatment-related adverse event

CONCLUSIONS

CheckMate 459 study did not meet its primary endpoint; however, in this long-term analysis, the authors showed that:

- Median OS : 16.4 months for nivolumab vs 14.8 months for sorafenib
- Median OS longer with nivolumab vs sorafenib in HCV and HBV groups
- Median OS is consistently beneficial with nivolumab regardless of PD-L1 expression

- **Nivolumab has a more favourable safety profile than sorafenib** with:
  - Grade 3-4 TRAEs: 22% for nivolumab vs 50% for sorafenib
  - TRAEs leading to discontinuation: 8% with nivolumab vs 11% with sorafenib
  - Liver function preservation over time in the nivolumab arm compared with sorafenib arm

HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; OS, overall survival; PD-L1, programmed death ligand 1; TRAEs, treatment-related adverse events

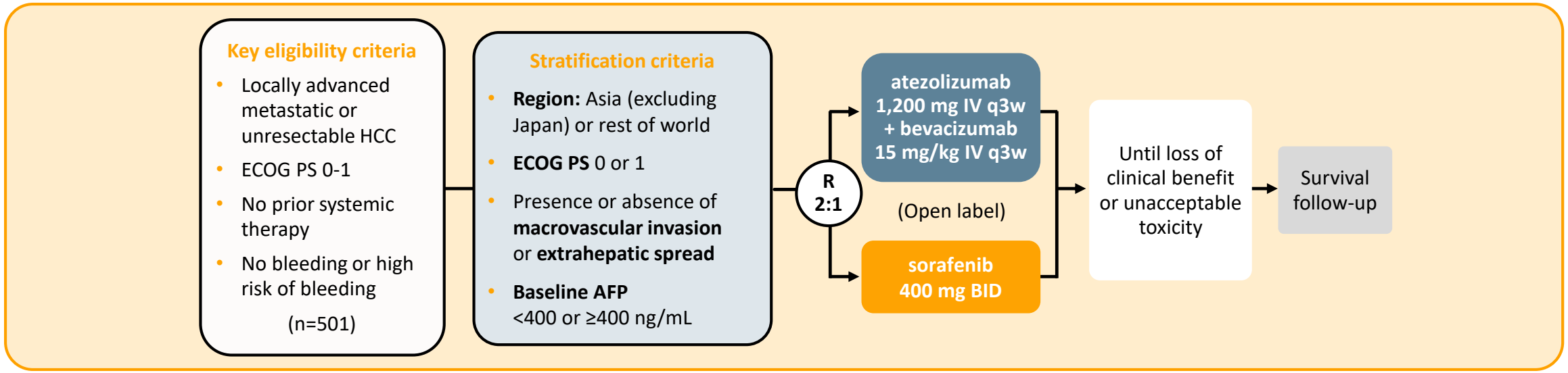
ATEZOLIZUMAB + BEVACIZUMAB VS SORAFENIB FOR UNRESECTABLE HEPATOCELLULAR CARCINOMA (HCC): RESULTS FROM OLDER ADULTS ENROLLED IN IMBRAVE150

Li D, et al.

WCGIC 2020. Abstract #O-8. Oral presentation

TRIAL DESIGN

IMbrave150 (NCT03434379): Randomised phase 3 trial assessing combination therapy with the PD-L1 inhibitor atezolizumab and the VEGF inhibitor bevacizumab versus standard-of-care sorafenib in first line for advanced HCC



The abstract presents exploratory analysis of **results from older adults (≥65 years) enrolled in IMbrave150**

AFP, alpha-fetoprotein; BID, twice a day; ECOG PS; Eastern Cooperative Oncology Group performance status; HCC, hepatocellular carcinoma; IRF, independent review facility; IV, intravenous; (m)RECIST, (modified) Response Evaluation Criteria In Solid Tumours; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PRO, patient-reported outcome; q3w, every 3 weeks; QoL, quality of life; R, randomisation; VEGF, vascular endothelial growth factor

Finn RS, et al. N Engl J Med 2020;382:1894-905

RESULTS: EFFICACY

- Data cut-off date: 29 August 2019; median survival follow-up: 8.6 months

	<65 years		≥65 years	
	atezolizumab + bevacizumab (n=175)	sorafenib (n=74)	atezolizumab + bevacizumab (n=161)	sorafenib (n=91)
Median OS, months	NE	11.4	NE	14.9
OS, HR (95% CI)	0.59 (0.38-0.91)		0.58 (0.36-0.92)	
Median PFS per IRF RECIST v1.1, months	6.7	2.9	7.7	4.8
PFS, HR (95% CI)	0.50 (0.36-0.71)		0.63 (0.45-0.89)	
Response-evaluable population, n	171	70	155	89
ORR per IRF RECIST v1.1, n (%)	49 (29)	7 (10)	40 (26)	12 (13)
CR, n (%)	11 (6)	0	7 (5)	0

CI, confidence interval; CR, complete response; HR, hazard ratio; IRF, independent review facility; NE, not evaluable; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours

RESULTS: SAFETY

	atezolizumab + bevacizumab	
	<65 years (n=171)	≥65 years (n=158)
Grade 3-4 AEs, n (%)	92 (54)	94 (59)
Treatment-related grade 3-4 AEs, n (%)	55 (32)	62 (39)
Grade 5 AEs, n (%)	7 (4)	8 (5)
Treatment-related grade 5 AEs, n (%)	2 (1)	4 (3)
AEs leading to withdrawal from any components, n (%)	21 (12)	30 (19)
AEs leading to withdrawal from both components, n (%)	9 (5)	14 (9)

AEs, adverse events

CONCLUSIONS

ATEZOLIZUMAB + BEVACIZUMAB: APPROVED BY US FDA ON 29 MAY 2020 AS FIRST-LINE SYSTEMIC THERAPY FOR ADVANCED HCC

- Analysis of older patients (≥65 years) from IMbrave150 demonstrated that:
  - OS, PFS and ORR benefits are consistent across ages
  - Safety profile is consistent across age groups with no significant additional toxicities. However due to the specific eligibility criteria for the trial population, safety in a broader population warrants further study

- These data show that older patients (≥65 years) with advanced HCC could benefit from the combination treatment in 1L setting

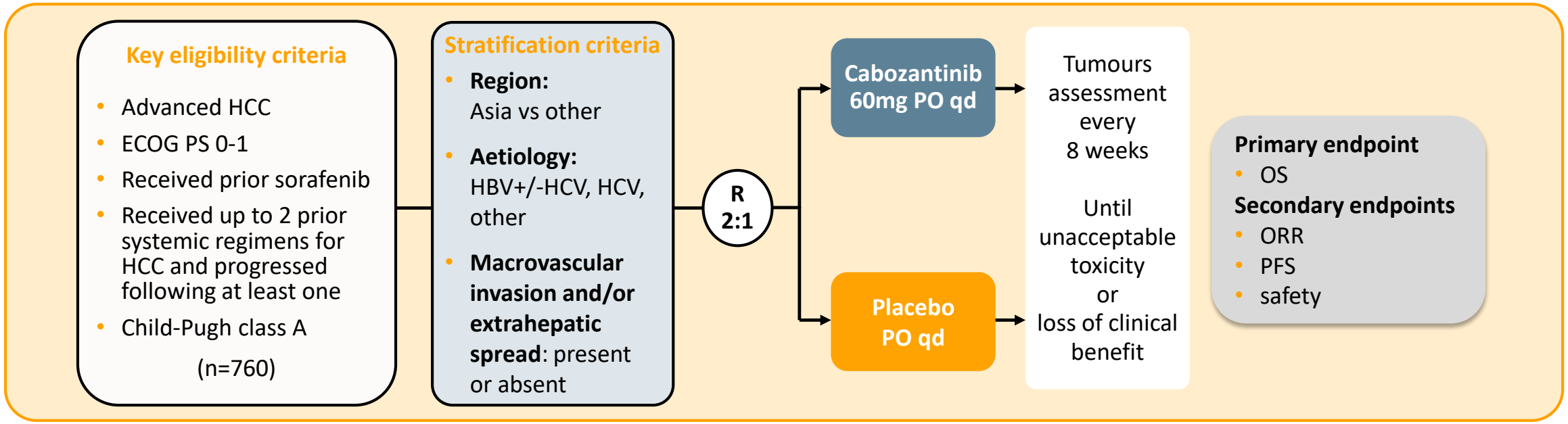
1L, first-line; FDA, Food and Drug Administration; HCC; hepatocellular carcinoma; ORR; objective response rate; OS, overall survival; PFS, progression-free survival

OUTCOMES FOR PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA (HCC) AND CHILD-PUGH B LIVER FUNCTION IN THE PHASE 3 CELESTIAL STUDY OF CABOZANTINIB VS PLACEBO

El-Khoueiry A, et al.
WCGIC 2020, Abstract #SO-9. Oral presentation

TRIAL DESIGN

CELESTIAL (NCT01908426): Randomised double-blind controlled phase 3 trial assessing cabozantinib vs placebo in previously treated patients with advanced HCC



The abstract presents a retrospective analysis of data from patients with Child-Pugh B by week 8 from the CELESTIAL study

ECOG PS; Eastern Cooperative Oncology Group performance status; HBV, hepatitis B virus; HCC; hepatocellular carcinoma; HCV, hepatitis C virus; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, per os; qd, once a day; R, randomisation

RESULTS: EFFICACY

- At Week 8, 51/470 patients in the cabozantinib arm and 22/237 patients in the placebo arm had investigator-assessed Child-Pugh B cirrhosis

	Child-Pugh B subgroup		Overall	
	cabozantinib (n=51)	placebo (n=22)	cabozantinib (n=470)	placebo (n=237)
Median OS, months (95% CI)	8.5 (7.7-12.2)	3.8 (3.3-4.8)	10.2 (9.1-12.0)	8.0 (6.8-9.4)
OS, HR (95% CI)	0.32 (0.18-0.58)		0.76 (0.63-0.92); p=0.005	
Median PFS, months (95% CI)	3.7 (1.9-5.2)	1.9 (1.7-2.1)	5.2 (4.0-5.5)	1.9 (1.9-1.9)
PFS, HR (95% CI)	0.44 (0.25-0.76)		0.44 (0.36-0.52); p<0.001	

CI, confidence interval; HR, hazard ratio; OS, overall survival; PFS, progression-free survival

RESULTS: SAFETY

	cabozantinib arm*	
	Child-Pugh B subgroup (n=51)	Overall (n=467)
Median duration of exposure (range), months	3.7 (1.4-12.9)	3.8 (0.1-37.3)
Dose reduction, %	61	62
Discontinuation due to treatment-related AE, %	18	16
All causality Grade 3-4 AEs, %	71	68
Fatigue	20	10
Ascites	14	4
Aspartate aminotransferase increase	14	12
Thrombocytopenia	12	3
Palmar-plantar erythrodysesthesia	8	17
Hypertension	8	16

*safety population
AE, adverse event

CONCLUSIONS

- Retrospective exploratory analysis of patients with Child-Pugh B by week 8 from CELESTIAL study showed that:
  - cabozantinib has a manageable safety profile in this subgroup
  - efficacy data for OS and PFS suggest clinical benefit in this subgroup

- These data show that further clinical trials investigations are needed in Child-Pugh B patients with HCC to fill the high unmet medical need for this population

HCC; hepatocellular carcinoma; OS, overall survival; PFS, progression-free survival

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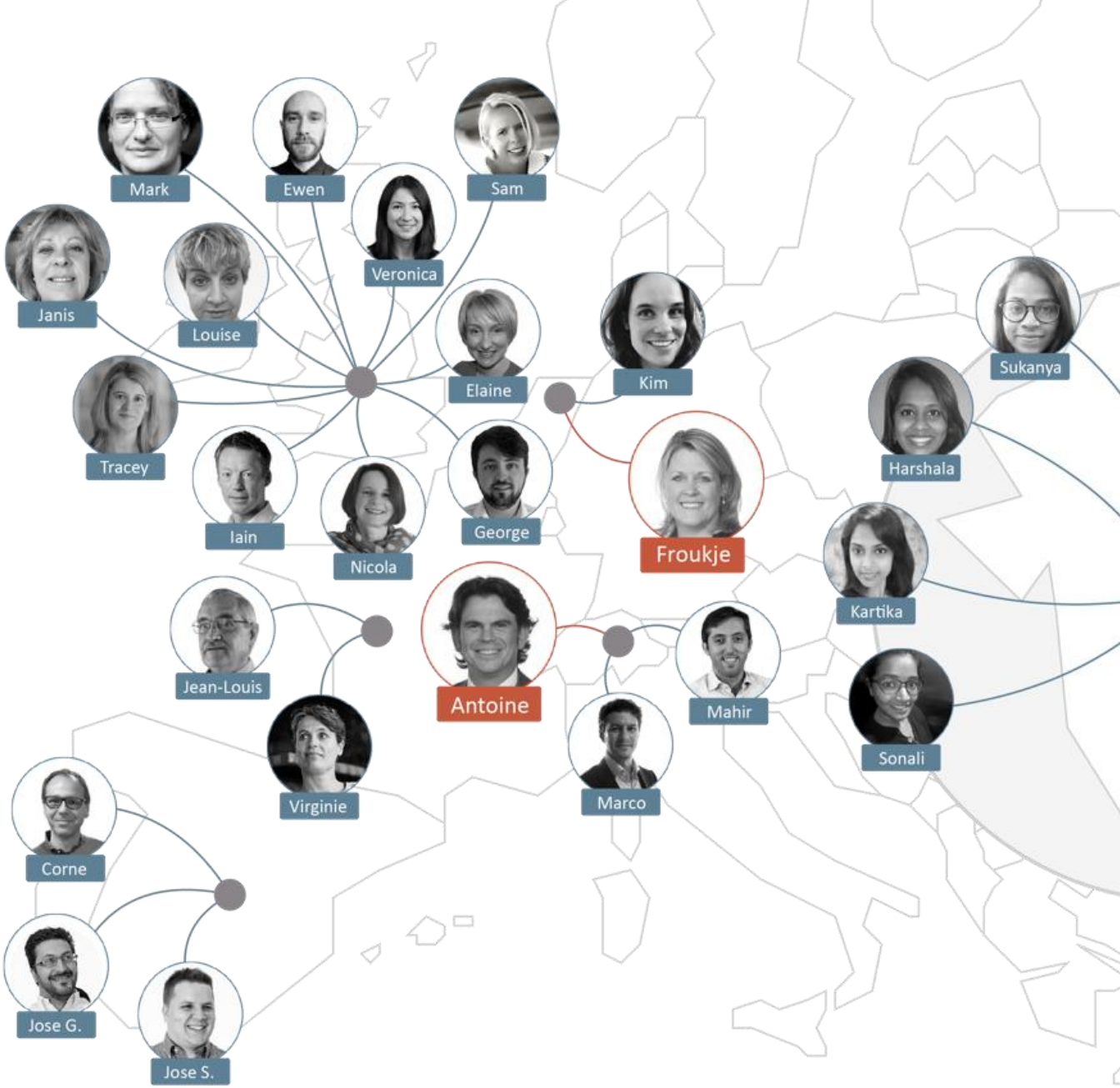

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