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MEETING SUMMARY
ESMO 2019, Barcelona, Spain

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HCC UPDATE

ESMO, European Society for Medical Oncology; HCC, hepatocellular carcinoma

DISCLAIMER

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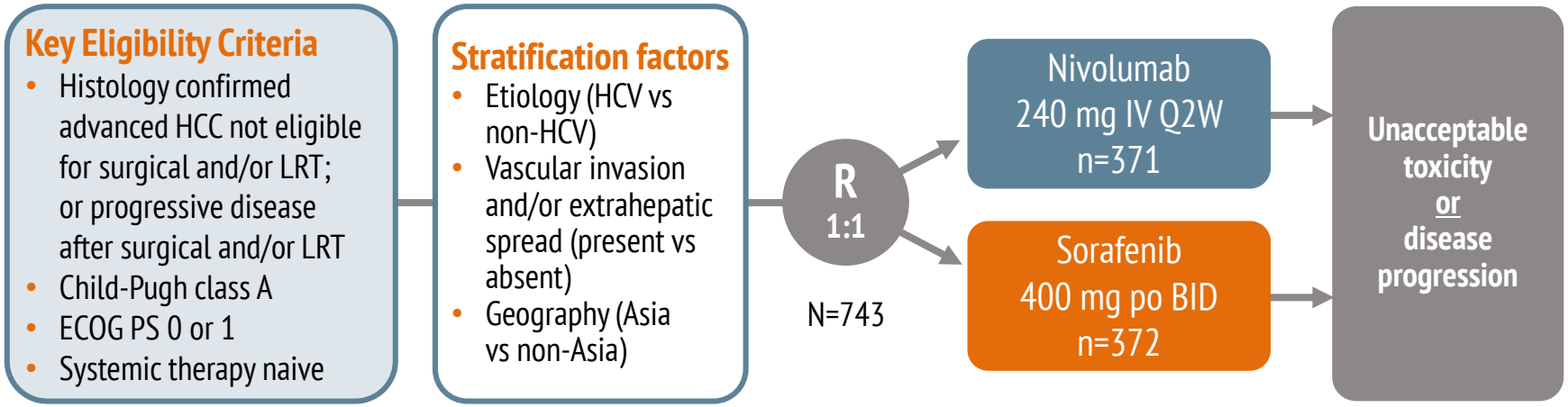
CHECKMATE 459: A RANDOMIZED, MULTI-CENTER PHASE 3 STUDY OF NIVOLUMAB VS SORAFENIB AS FIRST-LINE TREATMENT IN PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA

Yau, et al. ESMO 2019 Abstract #LBA38

CHECKMATE 459
STUDY DESIGN

- CheckMate 459 is a **randomised phase 3** study of **nivolumab vs sorafenib** in patients with advanced HCC[1]
  - **Background**: in the phase 1/2 study CheckMate 040 nivolumab demonstrated promising efficacy and safety data in advanced HCC, regardless of prior sorafenib treatment[2]



Objectives
- Primary – OS
- Secondary – ORR, PFS, efficacy by PD-L1 status
- Exploratory – HRQoL using FACT-Hep

- **Patient randomisation:** January 2016–May 2017
- **Database lock:** June 2019

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; LRT, loco-regional therapy; ORR, overall response rate; OS, overall survival; PD-L1, programmed death ligand 1; PFS, progression-free survival; po, oral; Q2W, once every two weeks; R, randomisation

1. Yau, et al. ESMO 2019 Abstract #LBA38; 2. El-Khoueiry A, et al. Lancet 2017;389:2492–502

CHECKMATE 459
PRIMARY ENDPOINT: OVERALL SURVIVAL (OS)

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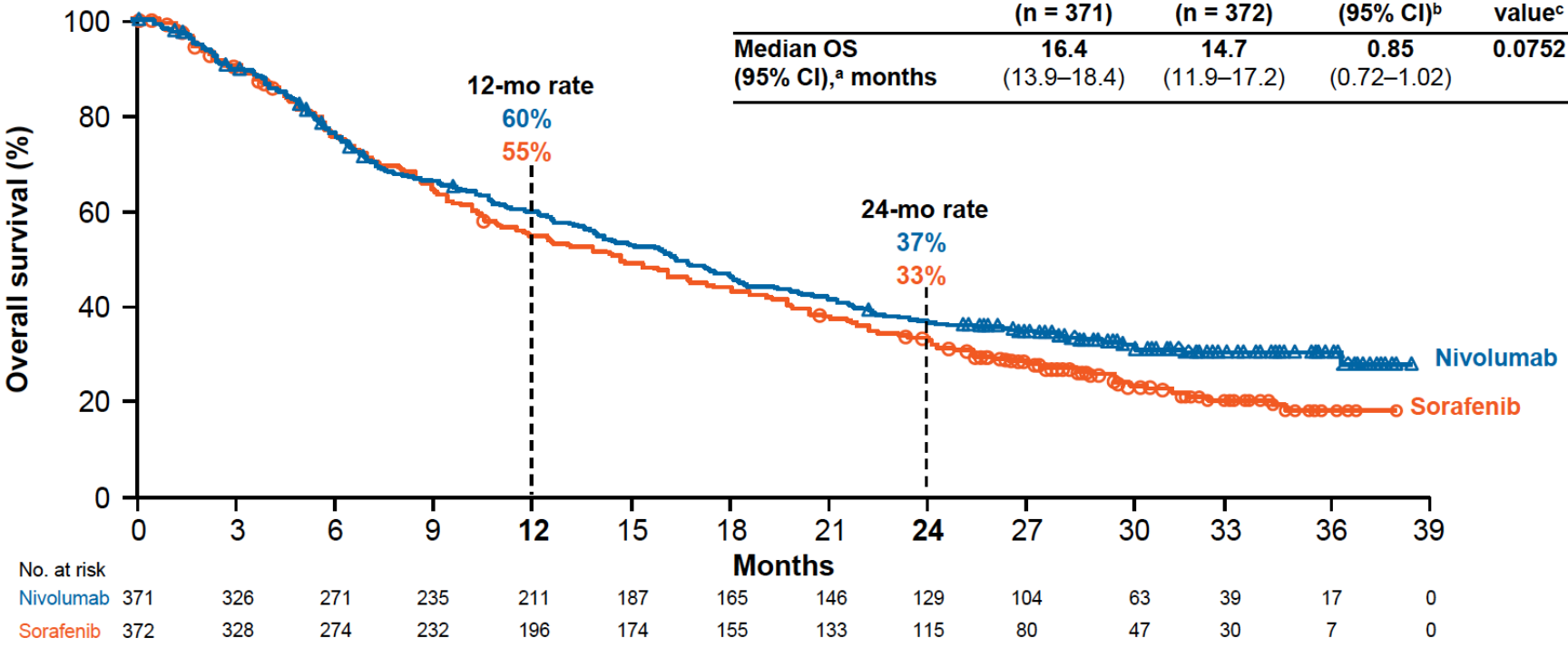
- Threshold for statistical **significance for OS was not met**
  - Nivolumab did demonstrate clinical benefit

	Nivolumab (n = 371)	Sorafenib (n = 372)	HR (95% CI)[b]	P value[c]
Median OS (95% CI),[a] months	**16.4** (13.9–18.4)	**14.7** (11.9–17.2)	**0.85** (0.72–1.02)	**0.0752**



[a]Based on Kaplan–Meier estimates; [b]Stratified Cox proportional hazards model. HR is nivolumab over sorafenib; [c]Pvalue from log-rank test
CI, confidence interval; HR, hazard ratio; OS, overall survival
Yau, et al. ESMO 2019 Abstract #LBA38

CHECKMATE 459
SECONDARY ENDPOINTS

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- Nivolumab **improved** the overall response rate (**ORR**) compared with sorafenib (15% vs 7%, odds ratio 2.41 [95% CI 1.48–3.92])
  - The complete response (CR) rate was higher in the nivolumab arm (4% vs 1%)
  - The disease control rate (DCR) was similar (55% vs 58%)
- There was **no difference** in progression-free survival (**PFS**, HR 0.93)
- 38% of patients in the nivolumab arm and 46% in the sorafenib arm received **subsequent systemic therapy**
  - Including immunotherapy in 20% and an investigational agent in 11% of patients in the sorafenib arm
- Nivolumab showed clinically meaningful **benefit in quality of life** (FACT-Hep) versus sorafenib
- **Safety**
  - Nivolumab was better tolerated than sorafenib
  - In the nivolumab arm, there were fewer grade 3/4 treatment-related adverse events (TRAEs) than in the sorafenib arm (22% vs 49%)

CI, confidence interval; CR, complete response; DCR, disease control rate; FACT-Hep, Functional Assessment of Cancer Therapy-Hepatobiliary questionnaire; HR, hazard ratio; ORR, overall response rate; PFS, progression-free survival; TRAEs, treatment-related adverse events

Yau, et al. ESMO 2019 Abstract #LBA38

CHECKMATE 459
CONCLUSIONS AND INTERPRETATION

- CheckMate 459 did **not meet the primary endpoint** of a significant improvement of OS
- However, this study **confirms the activity of nivolumab** in advanced HCC, with clinically meaningful improvements in OS and ORR
- The **median OS** of 16.4 months with nivolumab is the **longest ever seen** in a phase 3 trial in advanced HCC
  - The median OS of 14.7 months for sorafenib is the longest median OS seen in phase 3 trials with sorafenib in HCC
  - Long OS rates could be related to the subsequent treatment received by many patients

HCC, hepatocellular carcinoma; ORR, overall response rate; OS, overall survival
Yau, et al. ESMO 2019 Abstract #LBA38

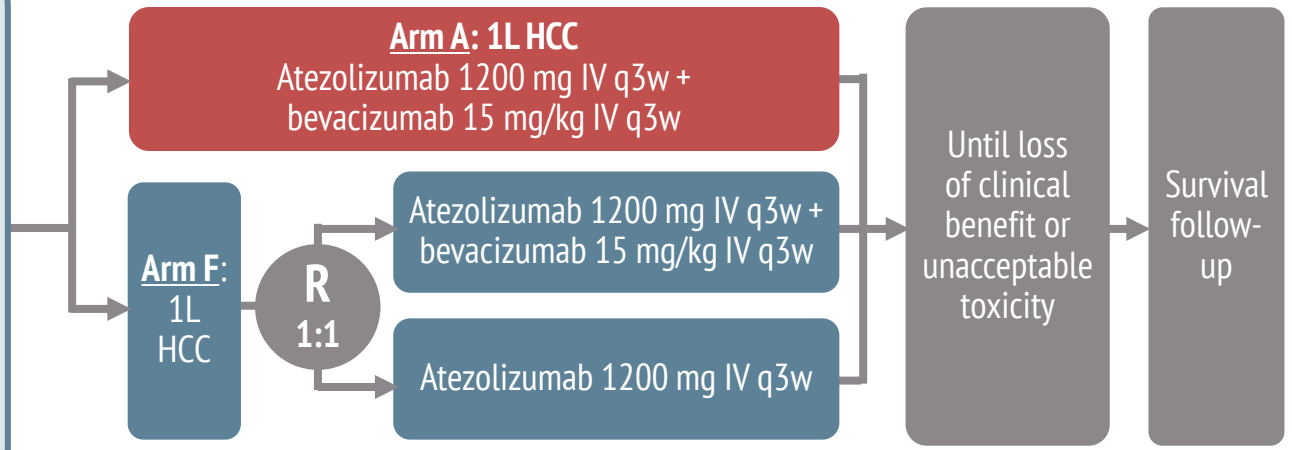
RANDOMISED EFFICACY AND SAFETY RESULTS FOR ATEZOLIZUMAB + BEVACIZUMAB IN PATIENTS WITH PREVIOUSLY UNTREATED, UNRESECTABLE HEPATOCELLULAR CARCINOMA

Lee, et al. ESMO 2019 Abstract #LBA39

GO30140
STUDY DESIGN

- GO30140 is a phase 1b study evaluating the combination of **atezolizumab + bevacizumab versus atezolizumab monotherapy** as **first-line** treatment for patients with unresectable HCC
- **Primary endpoints**
  - Arm A (atezolizumab + bevacizumab): ORR and safety
  - Arm F (atezolizumab + bevacizumab vs atezolizumab): PFS and safety

Eligibility Criteria
- Measurable disease per RECIST 1:1
- ECOG PS 0/1
- Adequate haematologic and organ function
- Child-Pugh score up to B7 for Arm A and Child-Pugh A for Arm F
- No prior systemic therapy
- No prior treatment with anti–CTLA-4, anti–PD-1 or anti–PD-L1 antibodies



1L, first-line; CTLA-4, cytotoxic T-lymphocyte-associated protein 4; ECOG PS, Eastern Cooperative Oncology Group performance status; HCC, hepatocellular carcinoma; IV, intravenous; ORR, overall response rate; PD-1, programmed death 1; PD-L1, programmed death ligand 1; PFS, progression-free survival; q3w, once every three weeks; RECIST, Response Evaluation Criteria In Solid Tumours

Lee, et al. ESMO 2019 Abstract #LBA39

GO30140
RESULTS

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Arm A
atezolizumab + bevacizumab
(n=104)

Median duration of follow up
- 12.4 months

ORR
- 36% (95% CI 26-46)

Safety
- Grade 3-4 TRAEs: 39%
- 3 grade 5 TRAEs (3%)

Arm F
atezolizumab + bevacizumab
(n=60)
vs atezolizumab (n=59)

Median duration of follow up
- 6.6 months

Median PFS
- 5.6 vs 3.4 months (HR 0.55, P=0.0108)

Safety
- Grade 3-4 TRAEs: 20% vs 5%
- No grade 5 TRAEs

CI, confidence interval; ORR, overall response rate; PFS, progression-free survival; TRAEs, treatment-related adverse events
Lee, et al. ESMO 2019 Abstract #LBA39

GO30140
CONCLUSIONS AND INTERPRETATION

- Arm A showed **promising responses and response durations** with atezolizumab + bevacizumab
- Data from Arm F indicate single-agent contribution of atezolizumab and bevacizumab to the overall treatment, although the duration of follow up is still limited
- The data from the phase 3 **IMBRAVE150 trial** will need to be awaited to confirm these results (Clinicaltrials.gov NCT03434379)

Lee, et al. ESMO 2019 Abstract #LBA39

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