MEETING SUMMARY
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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
  - **Background**: in the phase 1/2 study CheckMate 040 nivolumab demonstrated promising efficacy and safety data in advanced HCC, regardless of prior sorafenib treatment

**Key Eligibility Criteria**
- Histology confirmed advanced HCC not eligible for surgical and/or LRT; or progressive disease after surgical and/or LRT
- Child-Pugh class A
- ECOG PS 0 or 1
- Systemic therapy naive

**Stratification factors**
- Etiology (HCV vs non-HCV)
- Vascular invasion and/or extrahepatic spread (present vs absent)
- Geography (Asia vs non-Asia)

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

**CheckMate 459 Study Design**

- **Randomisation**: 1:1
- **Database lock**: June 2019
- **Nivolumab**: 240 mg IV Q2W, n=371
- **Sorafenib**: 400 mg po BID, n=372

**Patient randomisation**: January 2016–May 2017
**Unacceptable toxicity or disease progression**

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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

CHECKMATE 459

PRIMARY ENDPOINT: OVERALL SURVIVAL (OS)

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

<table>
<thead>
<tr>
<th></th>
<th>Nivolumab (n = 371)</th>
<th>Sorafenib (n = 372)</th>
<th>HR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median OS</td>
<td>16.4 (13.9–18.4)</td>
<td>14.7 (11.9–17.2)</td>
<td>0.85 (0.72–1.02)</td>
<td>0.0752</td>
</tr>
</tbody>
</table>

CI, confidence interval; HR, hazard ratio; OS, overall survival

*aBased on Kaplan–Meier estimates; bStratified Cox proportional hazards model. HR is nivolumab over sorafenib; cP-value from log-rank test

Yau, et al. ESMO 2019 Abstract #LBA38
CHECKMATE 459

SECONDARY ENDPOINTS

• 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 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.

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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

Arm A: 1L HCC
Atezolizumab 1200 mg IV q3w + bevacizumab 15 mg/kg IV q3w

Arm F: 1L HCC
Atezolizumab 1200 mg IV q3w + bevacizumab 15 mg/kg IV q3w

R 1:1
Atezolizumab 1200 mg IV q3w

Until loss of clinical benefit or unacceptable toxicity
Survival follow-up

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**

**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

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CI, confidence interval; ORR, overall response rate; PFS, progression-free survival; TRAEs, treatment-related adverse events

Lee, et al. ESMO 2019 Abstract #LBA39
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)
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