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MEETING SUMMARY
AASLD 2018, San Francisco, USA

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THE CHANGING LANDSCAPE IN THE TREATMENT OF HEPATOCELLULAR CARCINOMA

DISCLAIMER

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Please note:

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SAFETY AND EFFECTIVENESS OF REGORAFENIB IN SORAFENIB TREATED PATIENTS WITH RECURRENT HEPATOCELLULAR CARCINOMA AFTER LIVER TRANSPLANTATION: AN INTERNATIONAL MULTICENTER STUDY

Iavarone M et al. AASLD 2018.
Abstract #LB-17

PATIENT CHARACTERISTICS

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- Between May 2015 and June 2018 **28 LT patients** from 14 centres in Europe and Latin America were included
- **Patients characteristics**
  - 57 years old
  - 68% male
  - 50% HCV
  - 54% performance status 1
  - 93% had ⩾ 1 extrahepatic lesion
- **Immunosuppressive regimens**
  - mTOR-inhibitor-based therapy (54%)
  - CNI monotherapy (25%)
  - Mycophenolate monotherapy (14%)
  - Mycophenolate + CNI (6%)
- Median **time on sorafenib** was 11.3 months (range 0.7-76.4)

Iavarone M et al. AASLD 2018. Abstract #LB-17
CNI, calcineurin inhibitor; HCV, hepatitis C virus; LT, liver transplant; mTOR, mammalian target of rapamycin

SAFETY AND TOLERABILITY

- Regorafenib was started at full dose in all patients
- The median **treatment duration** was 6.5 months (0.1-23.1)
- **Most common grade ⩾ 3 AEs**
  - Fatigue (25%)
  - Dermatological AEs (18%)
- **Prevalent dosage of regorafenib**
  - 160 mg/day (39%)
  - 120 mg/day (25%)
  - ⩽ 80 mg/day (36%)

Iavarone M et al. AASLD 2018. Abstract #LB-17
AEs, adverse events

EFFICACY

- **Best response**
  - Partial response in 3 patients (11%)
  - Disease control in 12 patients (43%)
- 24 patients developed **radiological progression** during treatment
  - Growth of existing extra-hepatic lesions (9/24, 38%)
  - New extra-hepatic lesions/vascular invasion (8/24, 33%)
- **Median OS**
  - From regorafenib initiation: 12.9 months (95% CI 6.7-19.1)
  - For sorafenib + regorafenib sequential treatment: 38.4 months (95% CI 18.5-58.4)

Iavarone M et al. AASLD 2018. Abstract #LB-17
CI, confidence interval; OS, overall survival

CONCLUSION

- This is the first evidence that regorafenib is **safe in patients with recurrent HCC after LT**
- The impact of sequential sorafenib and regorafenib treatment on **OS** in this population seems **similar to that reported in no-LT patients**

Iavarone M et al. AASLD 2018. Abstract #LB-17
HCC, hepatocellular carcinoma; LT, liver transplant; OS, overall survival

NEWS:
FDA GRANTS ACCELERATED APPROVAL TO PEMBROLIZUMAB FOR THE TREATMENT OF PATIENTS WITH HEPATOCELLULAR CARCINOMA WHO HAVE PREVIOUSLY RECEIVED SORAFENIB

November 9th 2018

FDA APPROVAL PEMBROLIZUMAB BASED ON KEYNOTE-224

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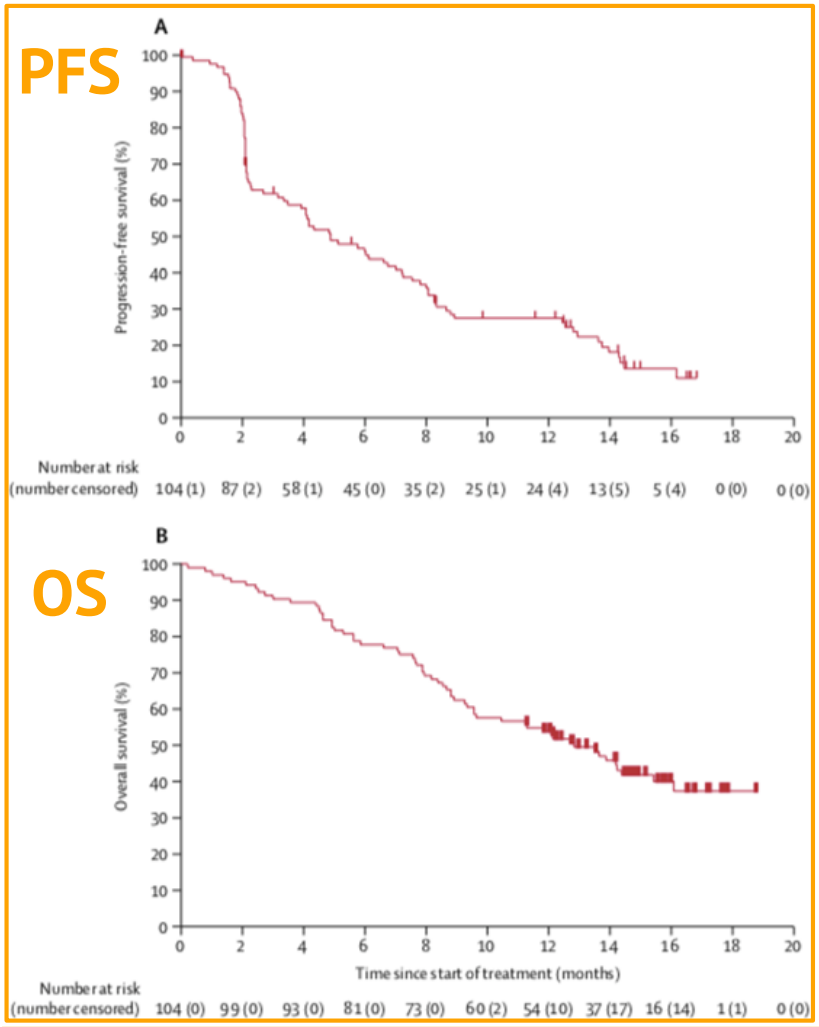
- On November 9th the **FDA granted accelerated approval** to **pembrolizumab** for the treatment of patients with HCC who have previously received sorafenib[1]
- The KEYNOTE-224 study showed an **ORR** of 17% (95% CI, 11-26) among 104 patients with advanced HCC previously treated with sorafenib[2]
  - 18 patients responded
    - 1 complete response
    - 17 partial responses
  - 46 stable disease
  - 34 progressive disease
  - 6 were not assessable

1. FDA Press Release. Available from: https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm625705.htm. Accessed 15 Nov 2018.
2. Zhu AX et al. Lancet Oncology. 2018;19:940-952
CI, confidence interval; FDA; US Food and Drug Administration; HCC, hepatocellular carcinoma; ORR, overall response rate

EFFICACY AND SAFETY KEYNOTE-224



- **PFS**
  - Median PFS: 4.9 months (95% CI, 3.4-7.2)
  - 12-month PFS rate: 28% (95% CI, 19-37)
- **OS**
  - Median OS: 12.9 months (95% CI, 9.7-15.5)
  - 12-month OS rate: 54% (95% CI, 44-63)
- **Safety**
  - 24% (n=25) of patients experienced grade 3 treatment-related AEs:
    - Increased AST (7%)
    - Increased ALT (4%)
    - Fatigue (4%)
  - 1 patient had grade 4 treatment-related hyperbilirubinemia
  - 1 death, associated with ulcerative esophagitis, was linked to treatment
  - 3 patients had immune-mediated hepatitis, but no viral flares were reported

Zhu AX et al. Lancet Oncology. 2018;19:940-952

AEs, adverse events; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; OS, overall survival; PFS, progression free survival

IN CLINICAL PRACTICE

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- Full data from randomized phase 3 studies that support daily use of immune checkpoint inhibitors are required
  - **Nivolumab** and **pembrolizumab** have recently been conditionally approved in the US
- At present, only **sorafenib** and **lenvatinib** are the first-line systemic treatments for patients with unresectable HCC
- **Regorafenib** is the only systemic agent approved worldwide for second-line treatment
  - **Ramucirumab** in patients progressed to sorafenib with AFP levels ⩾ 400 ng/ml and **cabozantinib** are awaiting approval for this indication
- Sequential treatment carried out in time will lead to improved treatment of patients with unresectable HCC

AFP, alpha fetoprotein; HCC, hepatocellular carcinoma

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