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Supported by an Independent Educational Grant from BAYER

MEETING SUMMARY

AASLD 2016, BOSTON USA
NOVEMBER 11TH TO 15TH 2016

DR CATHERINE FRENETTE, SCRIPPS CENTER FOR ORGAN TRANSPLANTATION, LA JOLLA, CA, USA

THE CHANGING LANDSCAPE IN THE TREATMENT OF HCC

LONG-TERM FOLLOW-UP OF PATIENTS WITH CHRONIC HCV INFECTION AND COMPENSATED OR DECOMPENSATED CIRRHOSIS FOLLOWING TREATMENT WITH SOFOSBUVIR-BASED REGIMENS

MUIR ET AL

POSTER #880

CPT B OR C CIRRHOSIS PRIOR TO TREATMENT WITH SOF-BASED REGIMEN BY CPT CLASS AT BASELINE

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Number (%) of patients with CPT B or C cirrhosis prior to treatment with SOF- based regimen by CPT class at baseline of registry study				
		CPT Class at Registry Study Baseline		
		CPT A	CPT B	CPT C
Pretreatment CPT Class	CPT B (N=133)	83 (62)	50 (38)	0
	CPT C (N=15)	6 (40)	8 (53)	1 (7)

CONCLUSION

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- At baseline of this registry study, SVR was maintained in 99.9% of patients with cirrhosis post-treatment with a SOF-based regimen
- In patients with decompensated cirrhosis pretreatment, CPT class improved at entry into the registry study (from CPT B to A or from CPT C to B or A) in 65% and was unchanged in 35%
- This ongoing study will provide information on whether achieving SVR following treatment with an HCV DAA regimen will improve longer term liver function and reduce the rate of liver-related complications, including HCC

HEPATOCELLULAR CARCINOMA DEVELOPMENT IN HEPATITIS C VIRUS PATIENTS WHO ACHIEVED SUSTAINED VIRAL RESPONSE BY INTERFERON THERAPY AND DIRECT ANTI-VIRAL AGENTS THERAPY

NAGAOKI ET AL

POSTER #860

CONCLUSION

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- The rate of HCC development was reduced in patients infected with HCV genotype 1b, after achieving SVR with DAA based regimen
- The impact of DAA-based treatment was similar to that of IFN-based treatment with regard to HCC risk reduction in patients who achieved SVR
- The AFP level gradually decreased in both groups after anti-viral therapy and was similar at 1 and 2 years after the start of anti-viral therapy

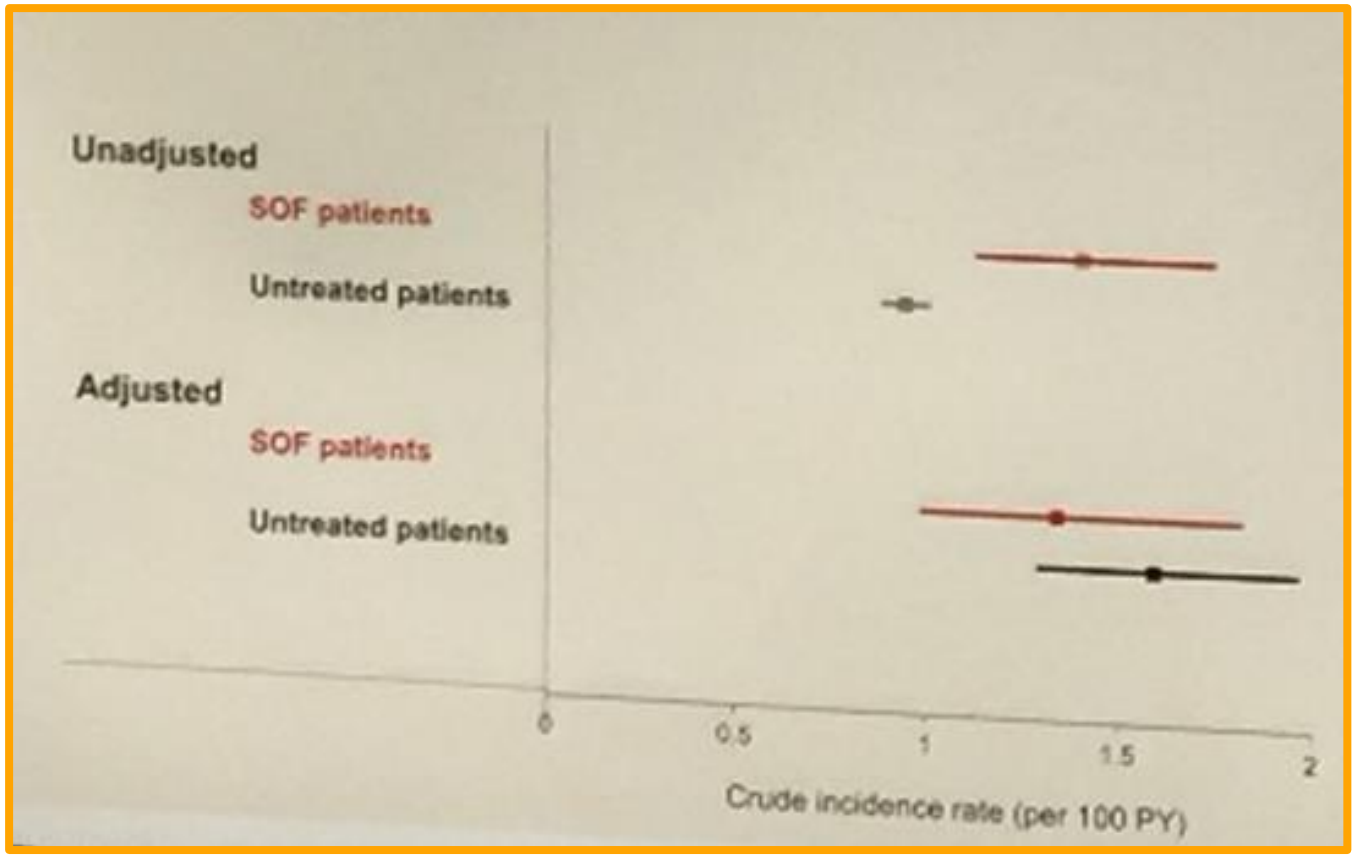
RISK OF INCIDENT LIVER CANCER FOLLOWING HCV TREATMENT WITH SOFOSBUVIR-CONTAINING REGIMENS

CHOKKALINGAM ET AL

POSTER #739

RESULTS

Cumulative incidence rates of liver cancer in each cohort before and after adjustment for covariates



SUMMARY

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- Before adjustment for significant covariates, liver cancer incidence appears higher in SOF treated patients vs untreated patients

- After adjustment for significant covariates, results in SOF-treated patients are not higher, indeed, they are nominally lower than rates among untreated patients, though not significantly so

- Age, gender, baseline cirrhosis status and baseline portal hypertension are important covariates that must be considered

NIVOLUMAB IN PATIENTS WITH ADVANCED HCC THE CHECKMATE 040 STUDY

MELERO ET AL

ABSTRACT #LB10

RESULTS NIVOLUMAB IN UNRESECTABLE HCC

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	Uninfected (n=135)	HCV infected (n=61)	HBV infected (n=66)	All patients (n=262)
ORR, n (%) [95% CI]	25 (19) [12, 26]	10 (16) [8, 28]	7 (11) [4, 21]	42 (16) [12, 21]
Complete response	4 (3)	1 (2)	0	5 (2)
Partial response	21 (16)	9 (15)	7 (11)	37 (14)
Stable disease	72 (53)	34 (56)	29 (44)	135 (52)
Progressive disease	35 (26)	14 (23)	29 (44)	78 (30)
Not evaluable	3 (2)	3 (5)	1 (2)	7 (3)

EFFICACY AND SAFETY OF REGORAFENIB VERSUS PLACEBO IN PATIENTS WITH HCC PROGRESSING ON SORAFENIB: RESULTS OF THE INTERNATIONAL, RANDOMIZED PHASE 3 RESORCE TRIAL

BRUIX ET AL ON BEHALF OF THE RESORCE INVESTIGATORS

RESORCE TRIAL DESIGN

Clinicaltrials.gov 01774344

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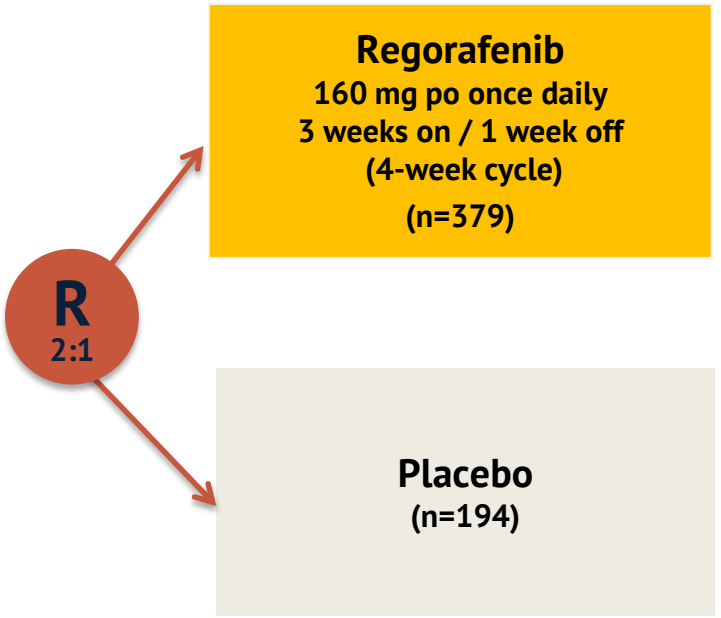
- Patients with HCC with documented radiological progression during sorafenib treatment

- Stratified by:
  - Geographic region (Asia vs ROW)
  - Macrovascular invasion
  - Extrahepatic disease
  - ECOG PS (0 vs 1)
  - AFP (<400 ng/mL vs ≥400 ng/mL)



- 152 centers in 21 countries in North and South America, Europe, Australia, Asia
- All patients received best supportive care
- Treat until progression, unacceptable toxicity, or withdrawal

ROW, rest of the world; ECOG PS, Eastern Cooperative Oncology Group performance status; AFP, alpha-fetoprotein

KEY INCLUSION CRITERIA

- HCC confirmed by histological or cytological analysis, or diagnosed by non-invasive assessment per AASLD criteria in a patient with confirmed cirrhosis
- BCLC stage B or C patients who could not benefit from resection, local ablation, or chemoembolization
- Documented radiological progression during sorafenib
- Randomization within 10 weeks after the last sorafenib dose
- Tolerability of prior sorafenib, defined as receiving sorafenib ⩾400 mg daily for at least 20 of the last 28 days of treatment
- ECOG PS 0/1
- Child-Pugh A liver function

BCLC, Barcelona Clinic Liver Cancer; ECOG PS, Eastern Cooperative Oncology Group performance status

BASELINE CHARACTERISTICS (1)

	Regorafenib (n=379)	Placebo (n=194)
Male	88%	88%
Age, median years (range)	64 (19–85)	62 (23–83)
Race		
White	36%	35%
Asian	41%	40%
Black	2%	1%
Other/ not reported	21%	24%
Geographic region Asia*	38%	38%
ECOG performance status, 0/1	65% / 35%	67% / 33%
Etiology of HCC†		
Alcohol use	24%	28%
Hepatitis B	38%	38%
Hepatitis C	21%	21%
NASH	7%	7%
Other	7%	5%
Unknown	17%	16%

*China, Japan, Korea, Singapore, Taiwan; †Patients may have had more than one etiology
NASH, nonalcoholic steatohepatitis

BASELINE CHARACTERISTICS (2)

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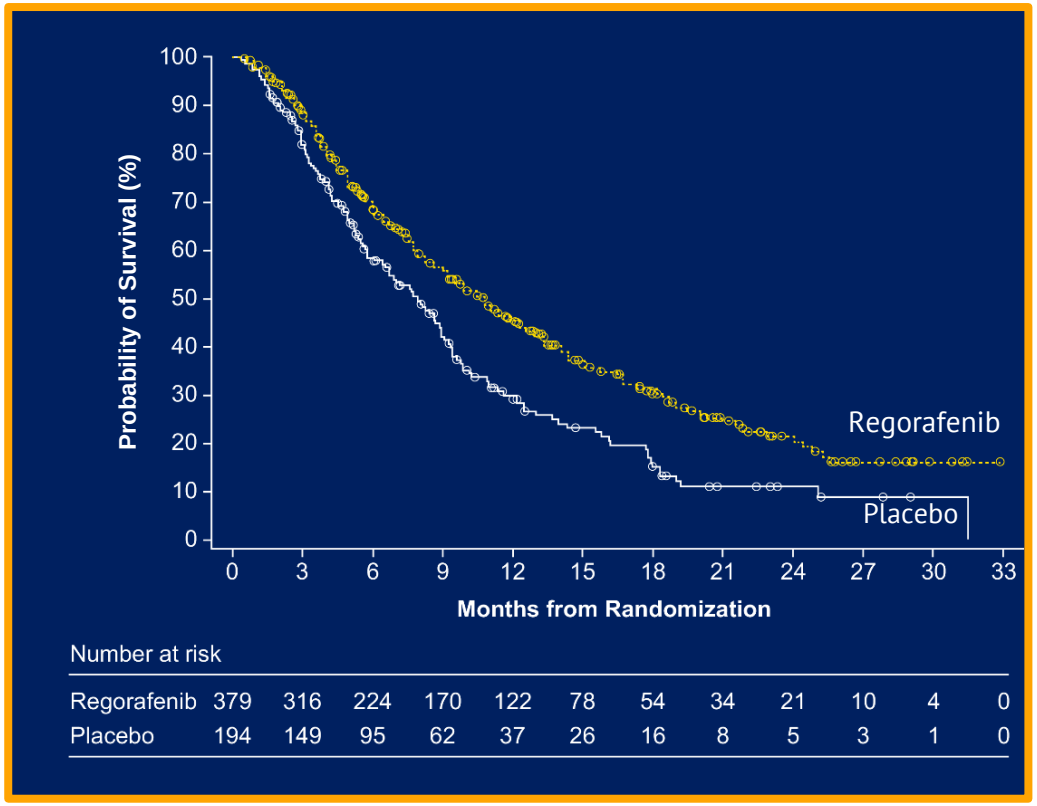
	Regorafenib (n=379)	Placebo (n=194)
BCLC stage, A / B / C	0.3% / 14% / 86%	0% / 11% / 89%
Child-Pugh class*		
A	98%	97%
B	1%	3%
Macrovascular invasion (MVI)	29%	28%
Extrahepatic disease (EHD)	70%	76%
MVI and/or EHD	80%	84%
Alpha-fetoprotein ≥400 ng/mL	43%	45%
Cirrhosis present†	75%	74%

*Child-Pugh class was missing in 1 patient (0.3%) in the regorafenib group
†Investigator assessment based on medical history. BCLC, Barcelona Clinic Liver Cancer

OVERALL SURVIVAL (OS)

PRIMARY ENDPOINT



	Regorafenib n=379	**Placebo** n=194
Events	232 (61%)	140 (72%)
Censored	147 (39%)	54 (28%)
Median OS (95% CI)	10.6 months (9.1, 12.1)	7.8 months (6.3, 8.8)
HR 0.62 (95% CI: 0.50, 0.78)		
P<0.001 (2-sided)		

BEST OVERALL TUMOR RESPONSE

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	mRECIST		RECIST 1.1	
	Regorafenib n=379	**Placebo** n=194	**Regorafenib** n=379	**Placebo** n=194
Response rate	10.6%	4.1%	6.6%	2.6%
	P=0.01 (2-sided)		*P*=0.04 (2-sided)	
Disease control rate	65.2%	36.1%	65.7%	34.5%
	P<0.001 (2-sided)		*P*<0.001 (2-sided)	
Complete response	0.5%	0	0	0
Partial response	10.0%	4.1%	6.6%	2.6%
Stable disease	54.4%	32.0%	58.8%	32.0%
Non CR/Non PD	0.3%	0	0.3%	0
PD	22.7%	55.7%	22.4%	57.2%
Not evaluable	5.0%	4.1%	5.0%	4.6%
Not assessed	7.1%	4.1%	6.9%	3.6%
Clinical progression*	22.7%	20.6%	22.7%	20.6%

*Worsening of ECOG PS≥3 or symptomatic deterioration including increase in liver function tests
PD, progressive disease

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