PCN524

European Real-World Treatment Patterns of Systemic Therapies for Second Line (2L) Hepatocellular Carcinoma (HCC) Patients who Previously Received Sorafenib

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OBJECTIVES

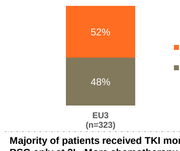
- Liver cancer is the fifth most common cancer worldwide[1], with HCC comprising 80% of all liver cancer cases. Alpha-fetoprotein (AFP) is used as a HCC tumour marker. Once detected in HCC patients, AFP levels usually increase with disease progression. Currently it is accepted that elevated AFP is a negative prognostic marker in advanced HCC[2].
- Historically, systemic drug treatment options for advanced HCC have been very limited however, more novel treatments have become available in the past several years. Ramucirumab is the first drug approved for a biomarker-selected patient population (2L treatment of patients with high baseline AFP [≥400 ng/mL])[3].
- This study examined real-world characteristics and treatment patterns of patients previously treated with sorafenib with AFP levels <400 ng/mL vs. ≥400 ng/mL at initiation of 2L treatment across EU3 (Germany, Italy and Spain).

METHODS

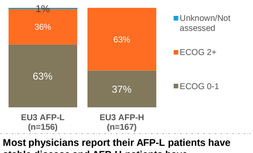
- Real world data were drawn from the HCC Disease Specific Programme™ (DSP) - a point in time survey administered to oncologists, hepatologists and gastroenterologists who completed patient record forms for the next 8 HCC patients with whom they consulted between Q4 2018 and Q1 2019 across EU3. The DSP methodology has been published and validated previously[4-6].
- Physician inclusion criteria for the DSP were: certified as specialist, aged between 5 and 35 years, currently responsible for treatment decisions for HCC patients and see a minimum of 5 HCC patients per month.
- For this analysis, patient inclusion criteria were: age ≥18 years; a physician-confirmed diagnosis of HCC; not currently enrolled in a clinical trial; and currently receiving 2L systemic drug treatment or best supportive care (BSC) only (not receiving systemic drug treatment) who were previously treated with sorafenib. Patients were stratified by AFP-Low (AFP-L [<400ng/mL]) and AFP-High (AFP-H [≥400 ng/mL]) status at initiation of 2L treatment. Study variables included patient demographics, background clinical information and treatment patterns.
- Statistical methods included descriptive statistics: count and percentage for qualitative variables; mean, median, minimum, maximum and standard deviation (SD) for quantitative variables.

KEY RESULT

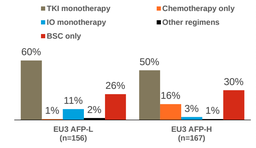
Over half of EU3 2L patients previously treated with sorafenib were AFP-H at initiation of 2L treatment.



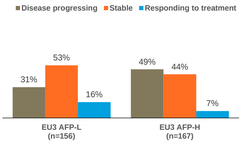
Compared to AFP-L patients, more AFP-H patients, but not all, had poorer ECOG.



Majority of patients received TKI monotherapy or BSC only at 2L. More chemotherapy use among AFP-H patients.



Most physicians report their AFP-L patients have stable disease and AFP-H patients have progressive disease.



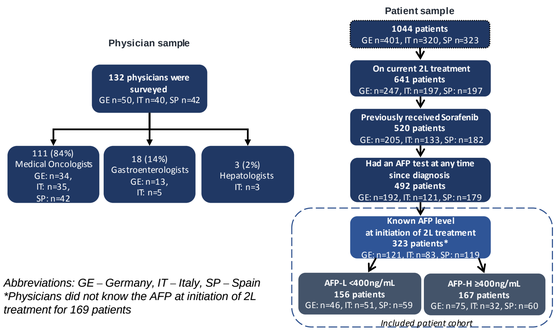
Abbreviations: TKI – Tyrosine kinase inhibitor; IO – Immuno-oncology, BSC – Best supportive care
Base: 2L patients previously treated with sorafenib with known AFP level at initiation of 2L treatment

Results

Sample

- 132 physicians, mostly medical oncologists, provided data on 1044 patients. Figure 1 shows the physician composition and patient cohorts included in this analysis.

Figure 1: Sample composition



Abbreviations: GE – Germany, IT – Italy, SP – Spain
**Physicians did not know the AFP at initiation of 2L treatment for 169 patients*

Patient demographics and clinical characteristics

- Overall, EU3 patients with a known AFP at initiation of 2L treatment have a median age of 67 years and most are male (73%). Small differences in age and gender were observed between AFP-L and AFP-H patients [Table 1].
- Most EU3 AFP-L and AFP-H patients are Barcelona Clinic Liver Cancer (BCLC) stage C (53% and 41%, respectively), followed by BCLC stage B (24% vs. 31%, respectively). In Spain and Italy, AFP-H patients are more often BCLC stage B than BCLC stage C, while in Germany, AFP-H patients in the analysis are more often BCLC stage C. More of the BCLC stage D patients are AFP-H than AFP-L [Table 1].

Table 1: Patient demographics and clinical characteristics

		AFP-L				AFP-H			
	EU3 (n=323)	EU3 (n=156)	Germany (n=46)	Italy (n=51)	Spain (n=59)	EU3 (n=167)	Germany (n=75)	Italy (n=32)	Spain (n=60)
Mean age, years (SD)	66.1 (8.82)	65.4 (9.73)	64.2 (9.87)	69.3 (8.06)	62.9 (10.05)	66.8 (7.83)	66.2 (8.56)	68.8 (6.77)	66.4 (7.34)
Median age, years	67.0	67.0	66.0	70.0	64.0	67.0	67.0	68.0	67.0
Male	73%	74%	76%	73%	73%	72%	71%	59%	80%
Current BCLC staging									
Stage 0	<1%	1%	0%	2%	0%	0%	0%	0%	0%
Stage A	3%	4%	2%	10%	2%	1%	0%	6%	0%
Stage B	28%	24%	26%	31%	17%	31%	24%	44%	32%
Stage C	46%	53%	46%	47%	63%	41%	52%	38%	28%
Stage D	19%	12%	11%	8%	17%	25%	20%	13%	37%
Unknown / not assessed	4%	6%	15%	2%	2%	3%	4%	0%	3%
Hepatitis B or C diagnosed prior to HCC diagnosis	47%	49%	26%	59%	59%	46%	43%	50%	47%
Receiving supportive therapy									
Yes	64%	53%	59%	57%	44%	75%	73%	69%	80%
No	*36%*	*47%*	*41%*	*43%*	*56%*	*25%*	*27%*	*31%*	*20%*
Type of supportive therapy received									
Base	n=207	n=82	n=27	n=29	n=26	n=125	n=55	n=22	n=48
Analgesics (any)	92%	87%	89%	83%	88%	95%	91%	95%	100%
Non-opioid analgesics	*43%*	*39%*	*33%*	*34%*	*50%*	*45%*	*51%*	*45%*	*38%*
Opioid analgesics	*61%*	*57%*	*67%*	*48%*	*58%*	*63%*	*53%*	*64%*	*75%*
Anti-emetic medication	*41%*	*40%*	*41%*	*41%*	*38%*	*42%*	*51%*	*77%*	*15%*
Prednisolone	*24%*	*21%*	*7%*	*24%*	*31%*	*26%*	*13%*	*59%*	*25%*
Anti-viral therapy	*6%*	*2%*	*7%*	*0%*	*0%*	*8%*	*16%*	*0%*	*2%*
Antibiotics	*11%*	*9%*	*7%*	*17%*	*0%*	*13%*	*18%*	*18%*	*4%*
TACE	*3%*	*2%*	*0%*	*7%*	*0%*	*4%*	*5%*	*9%*	*0%*
Other	*2%*	*5%*	*4%*	*0%*	*12%*	*0%*	*0%*	*0%*	*0%*

Figure 2: Current Child-Pugh score

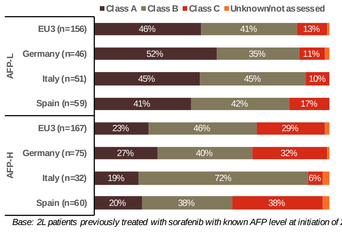
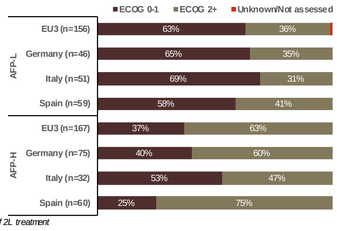
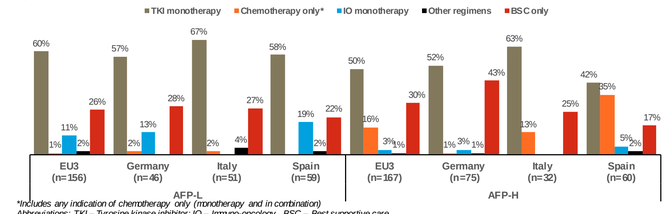


Figure 3: Current performance status (ECOG)



Base: 2L patients previously treated with sorafenib with known AFP level at initiation of 2L treatment

Figure 4: 2L treatment received



**Includes any indication of chemotherapy only (monotherapy and in combination)*
Abbreviations: TKI – Tyrosine kinase inhibitor; IO – Immuno-oncology, BSC – Best supportive care
Base: 2L patients previously treated with sorafenib with known AFP level at initiation of 2L treatment

- In EU3, there was only a minor difference in the proportion of patients diagnosed with hepatitis B or C prior to their HCC diagnosis, between AFP-L and AFP-H (49% vs. 46%, respectively). In Germany, smaller proportion of patients were diagnosed with hepatitis B or C in AFP-L than in AFP-H group, while in Italy and Spain the opposite trend was observed [Table 1].
- According to current Child Pugh score, AFP-L patients are more likely to have Class A, representing a well-functioning liver than AFP-H patients (46% vs. 23%). This trend was also observed across all EU3 countries [Figure 2].
- According to current patient performance status (Eastern Cooperative Oncology Group (ECOG) score), AFP-H patients are more likely to have a worse performance status than AFP-L patients (ECOG 2+: 63% vs. 36%). This trend was also observed across all EU3 countries [Figure 3].

2L treatment patterns

- In EU3, median time between first line (1L) initiation and 2L initiation was slightly shorter for AFP-H patients than AFP-L patients 8.1 months (95% confidence interval (CI) 8.3-9.8) vs. 9.0 months (95% CI 7.5-8.7)).
- The majority of both AFP-L and AFP-H patients received systemic drug treatment after 1L sorafenib. The most common 2L treatment received by AFP-L and AFP-H patients was TKI monotherapy. Across all EU3 countries, more AFP-L patients than AFP-H patients received TKI monotherapy (60% and 50%, respectively) [Figure 4].
- Similarly, for both AFP-L and AFP-H EU3 patients, the second most common treatment received at 2L was BSC only (26% and 30%, respectively) [Figure 4].
- A chemotherapy-containing regimen was more common in AFP-H than in AFP-L patients mainly driven by high use in Italy and Spain [Figure 4].

Current HCC disease status

- AFP-H patients were more likely to have a progressive disease compared to AFP-L patients (49% vs. 31%). This was consistent across EU3 [See key result].

Use of supportive therapies

- AFP-H patients were more likely to have received a supportive therapy than AFP-L patients (75% vs. 53%). This was observed across countries. Regardless of AFP level and country, analgesics were the most common supportive therapy prescribed [Table 1].
- Higher anti-viral use was observed among AFP-H BSC only patients than AFP-L BSC only patients (19% vs. 3%), driven mainly by Germany. In Italy, no anti-viral use was observed among systemic therapy only or BSC only patients. In Spain, limited use of anti-viral was observed among AFP-H systemic therapy only patients and no use was observed among AFP-L systemic therapy only patients or BSC only patients – data not shown.

Limitations

- The data analysed were physician-reported. Thus, no measures were clinically or independently validated. Data were not adjusted for age, stage of disease and other possible confounders. Sample size for subgroups also constitutes a limitation when interpreting the data.

CONCLUSIONS

- In the real word setting, patients previously treated with sorafenib who presented with AFP-H at initiation of 2L treatment had shorter time from 1L Sorafenib treatment to current 2L treatment, higher occurrence of progressive disease and greater utilisation of supportive therapies compared to AFP-L patients.
- These findings suggest that patients who have high AFP levels at initiation of 2L treatment are more difficult to treat and have a poor prognosis.

References: [1]Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM (2010) GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10, International Agency for Research on Cancer, Lyon, France. Available from: http://globocan.iarc.fr; [2]Von Felden, J., Schulze, K., Gil-Ibanez, I., Werner, T. and Wege, H., 2016. First-and second-line targeted systemic therapy in hepatocellular carcinoma—An update on patient selection and response evaluation. Diagnostics, 6(4), p.44; [3]Rimassa, L., 2018. Drugs in Development for Hepatocellular Carcinoma. Gastroenterology & hepatology, 14(9), p.542; [4]Anderson P, et al. Curr Med Res Opin. 2008;24(11):3063-3072; [5]Babineaux SM, et al. BMJ Open. 2016;6(8):e010352; [6]Higgins V, et al. Diabetes Metab Syndr Obes. 2016;9:371-380.

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