Comparison of efficacy between hepatic arterial infusion chemotherapy and sorafenib in advanced hepatocellular carcinoma with portal vein tumor thrombosis

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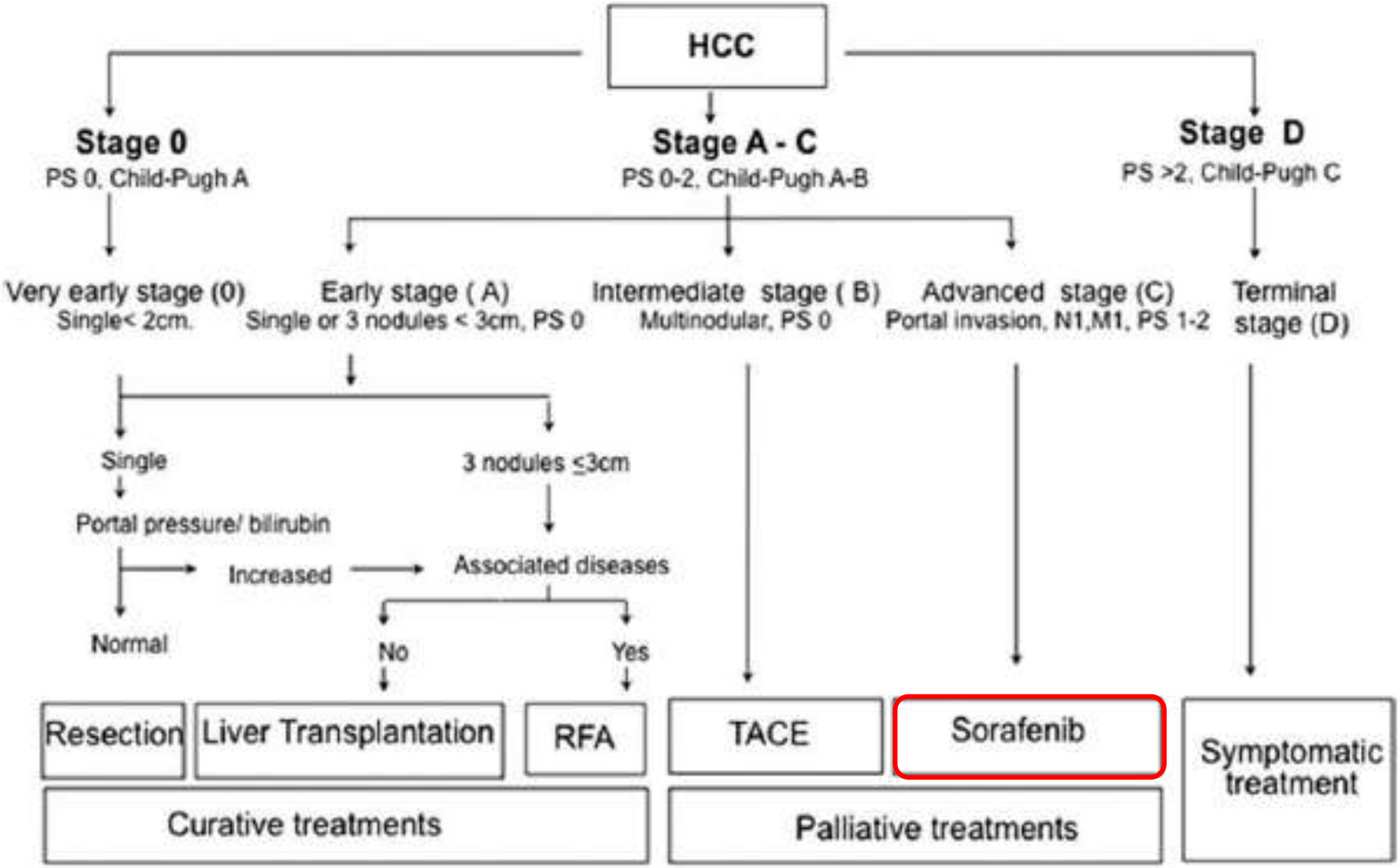
Introduction

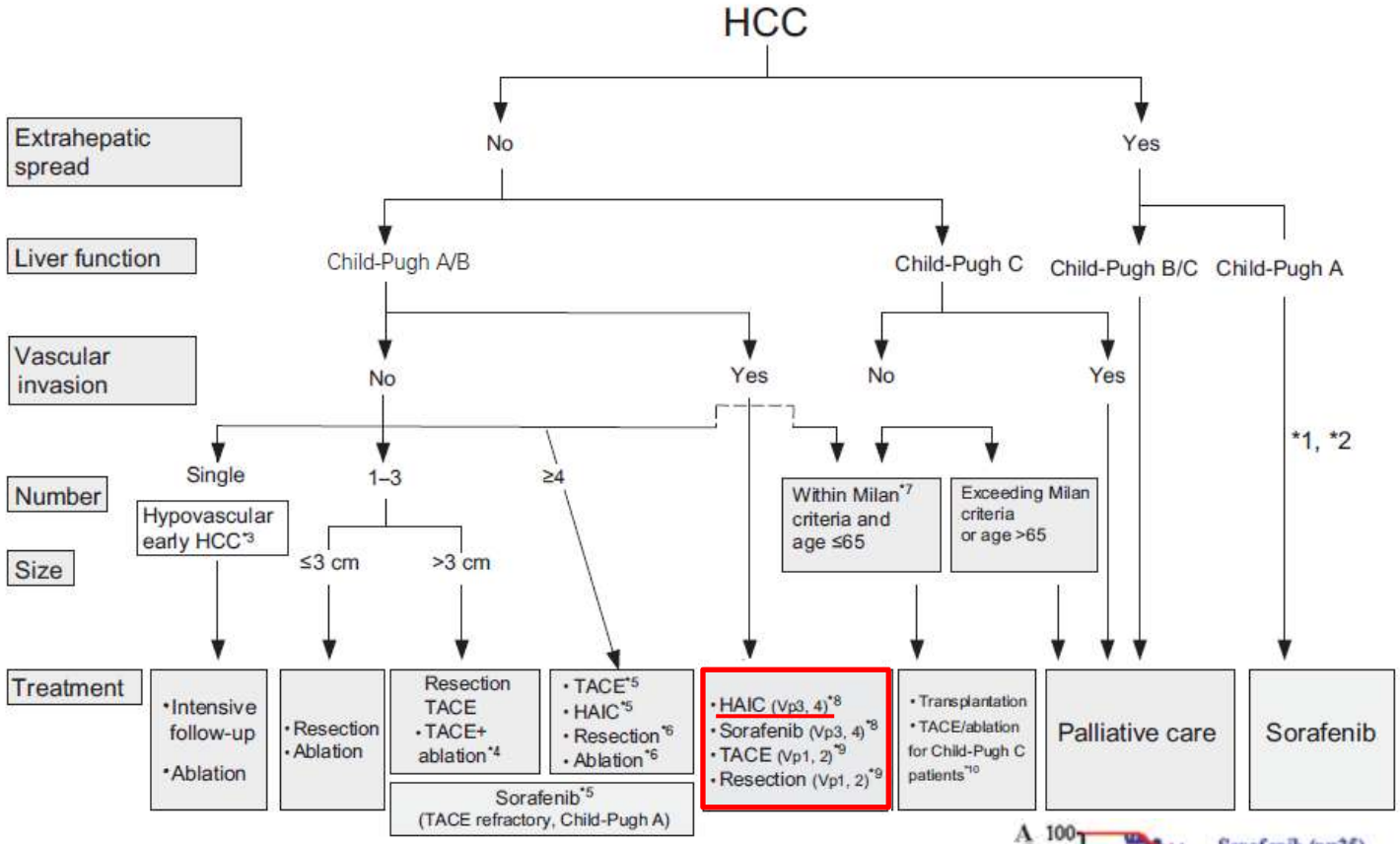


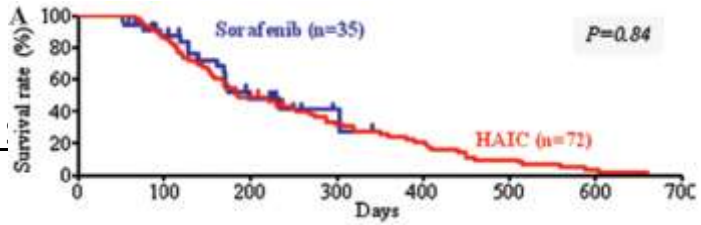
Introduction

- Hepatic arterial infusion chemotherapy (HAIC)
  - Used for the treatment of HCC for decades
  - Theoretically more effective against HCC than systemic chemotherapy
    - Increased local concentration
    - Lower systemic toxicity
  - Lack of randomized studies
    - Not standard practice in many countries for patients with advanced HCC

Introduction

1.





2. Treatment with sorafenib may achieve a similar [illegible] to that achieved by HAIC in advanced HCC

Hiramine et al. Experimental and Therapeutic Medicine 2011

Aim

- To compare the efficacy of HAIC and sorafenib in advanced HCC with portal vein tumor thrombosis

Patients

- Advanced HCC patients (n=110)
  - HAIC treatment group : 50 patients
  - Sorafenib treatment group : 60 patients
- From Feb 2008 to Jan 2013, 7 Korean centers, retrospectively

- HAIC regimen
  - 60 mg/m^2 cisplatin for 2 h on day 2
  - 500 mg/m^2 5-FU for 5 hours on days 1–3
  - with or without 35mg/m^2 epirubicin on day 1
- Sorafenib (Nexavar®, Bayer HealthCare, Leverkusen, Germany)
  - 400mg, twice a day

- Inclusion criteria

  1) Advanced HCC with portal vein tumor thrombosis
  2) Child Pugh score 5-7
  3) ECOG performance status 0-1
  4) WBC ≥ 3,000 cells/mm^3 or ANC ≥ 1,000 cells/mm^3
  5) Platelet count ≥ 50,000 cells/mm^3

Endpoint

- Primary endpoint
  - Overall survival (OS) and time to progression (TTP)
- Secondary endpoint
  - Treatment response
    - Objective response : CR + PR
    - Disease control : CR + PR + SD

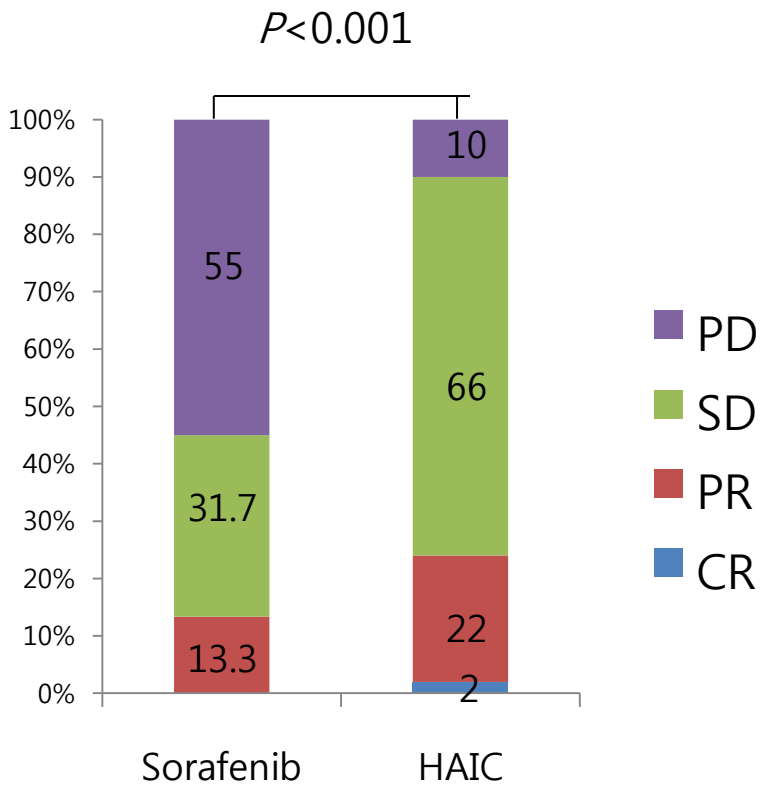
Baseline characteristics

	Total (n=110)	Sorafenib (n=60)	HAIC (n=50)	*P* value
Mean age ± SD (yr)	55.1 ± 9.4	55.8 ± 9.0	54.3 ± 9.9	0.401
Sex				
Male	82 (74.5)	44 (73.3)	38 (76)	0.828
Femal	28 (25.5)	16 (26.7)	12 (24)	
Etiology				
HBV/HCV/Alcohol/Others	85/7/11/7	41/5/8/6	44/2/3/1	0.095
Tumor maximal diameter (cm)				
<10cm	52	30	22	0.565
>10cm	29	28	57	
Child-Pugh class				
A/B	92/18	47/13	45/5	0.124
Portal vein thrombosis				
Vp2/Vp3/Vp4	12/30/68	5/16/39	7/14/29	0.595
Extrahepatic metastasis				
Yes/No	33/77	21/39	12/38	0.296
Stage				
AJCC (III/IV)	60/50	34/26	35/15	0.170
Previous treatment				
Yes/No	40/70	21/39	19/31	0.843
Combined locoregional treatment				
Yes/No	27/83	9/51	18/32	0.014
Serum AFP (ng/dl)				
<200/≥200	35/73	20/38	15/35	0.683

Treatment response

mRECIST

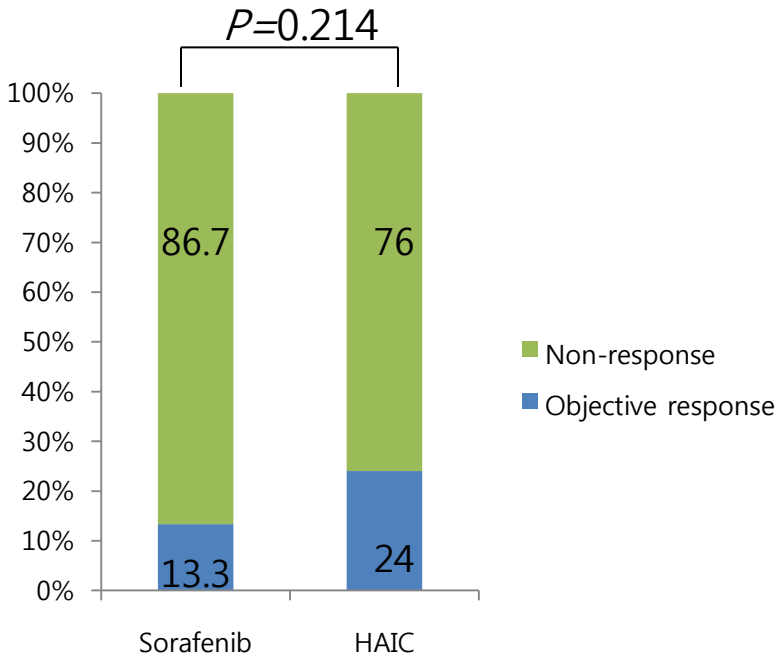
	CR	PR	SD	PD	p-value
Sorafenib	0	8	19	33	<0.001
HAIC	1	11	33	5	



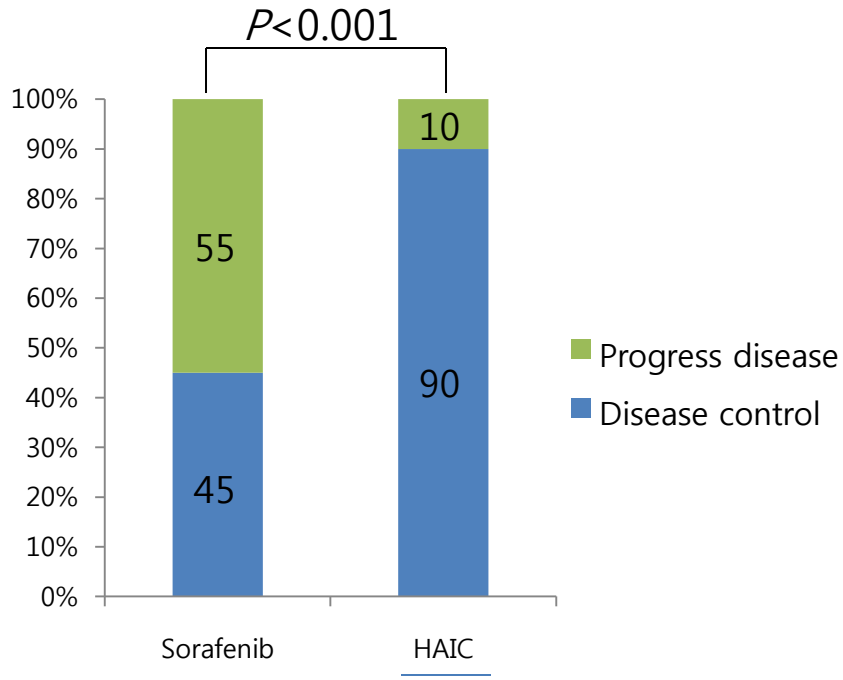
By χ^2-test

Response rate

	Objective response	Non-response	Disease control	Progressive disease
Sorafenib	8	52	27	33
HAIC	12	38	45	5
p-value	0.214		<0.001	



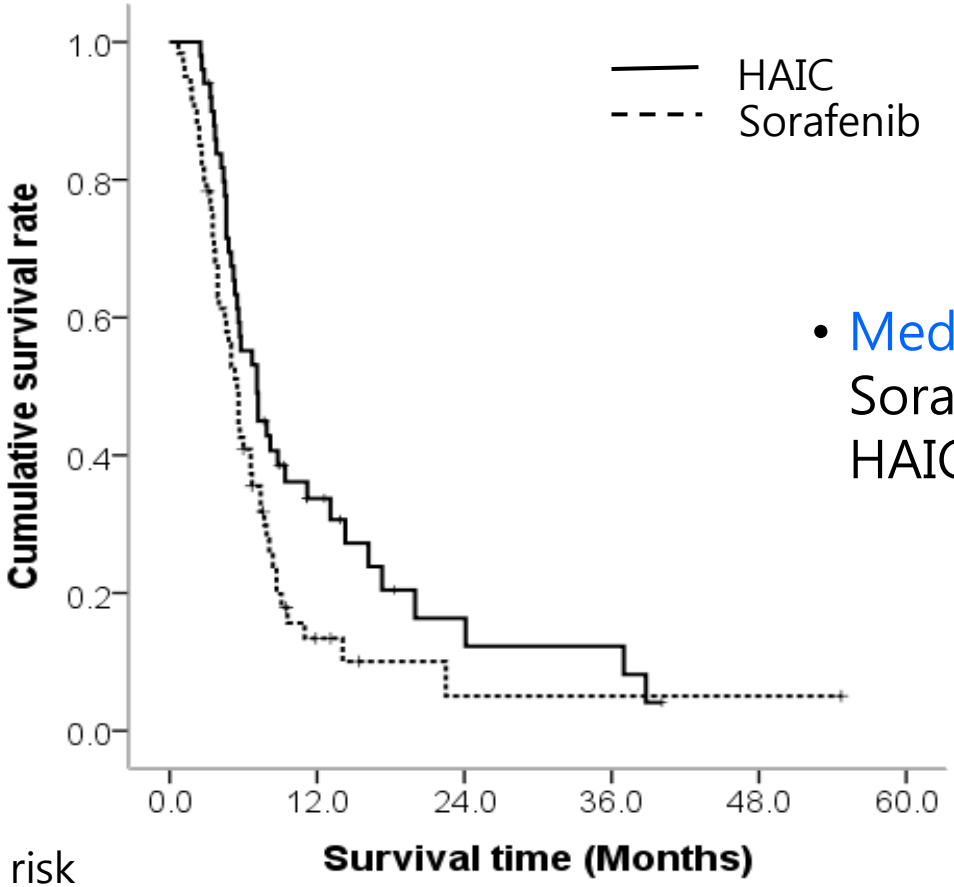
Objective response



Disease control rate

By χ^2-test

Overall survival

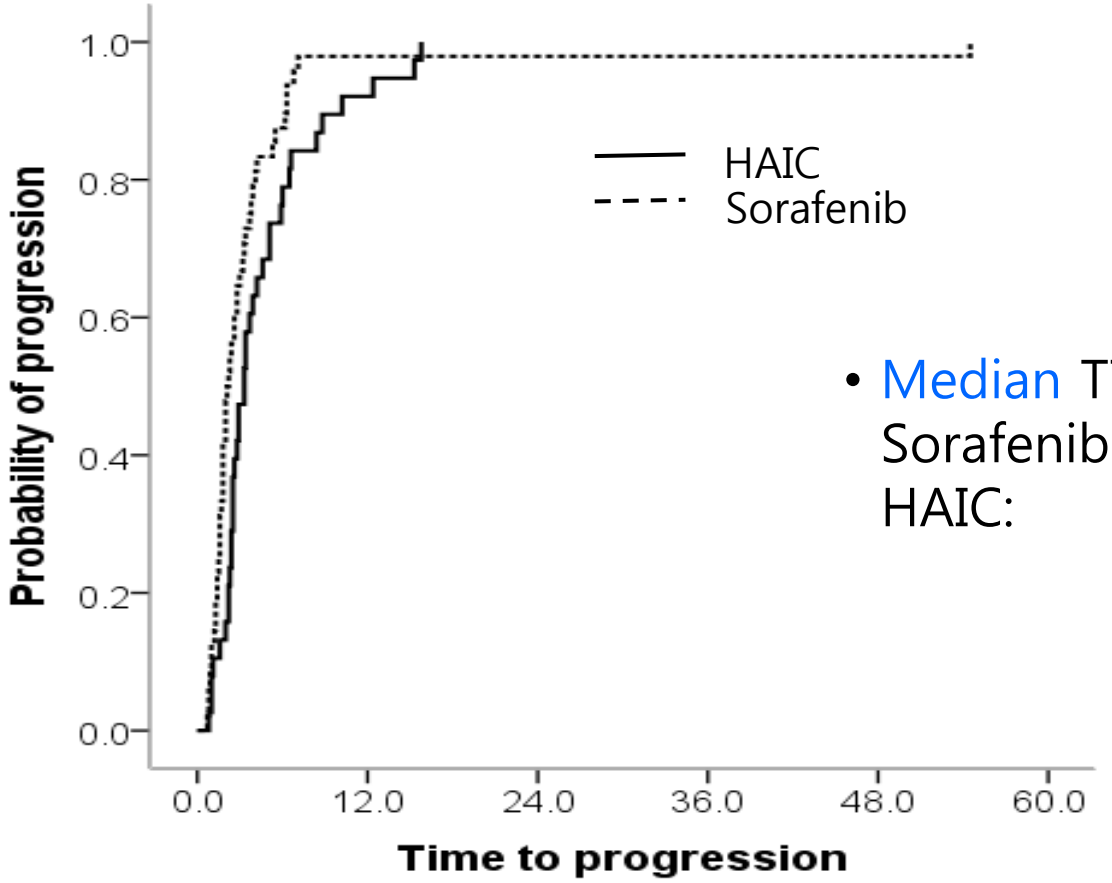


- Median survival (*P*=0.011)
  Sorafenib: 5.5 months
  HAIC: 7.1 months

No. at risk						
Sorafenib	60	5	1	1	1	0
HAIC	50	12	4	4	0	0

By Kaplan-Meier method

Time to progression



- Median TTP (*P*=0.034)
  Sorafenib: 2.1 months
  HAIC: 3.3 months

No. at risk						
Sorafenib	60	1	1	1	1	0
HAIC	50	5	0	0	0	0

By Kaplan-Meier method

Prognostic factor (Survival and TTP)

Variables	Overall survival				Tumor progression			
	Univariate (p-value)	Multivariate (p-value)	HR	95% CI	Univariate (p-value)	Multivariate (p-value)	HR	95% CI
Age <50/≥50	0.322				0.159			
Gender Male/Female	0.117				0.397			
Tumor diameter <10cm/≥10cm	<0.001	0.002	2.07	1.29 - 3.33	0.008	0.017	1.79	1.11 - 2.89
Child-Pugh A/B	0.463				0.36			
Portal vein thrombosis Vp2/Vp3/Vp4	0.759				0.234			
Extrahepatic spread Yes/No	0.01	0.061	0.63	0.39 - 1.02	0.048	0.064	0.60	0.35 - 1.03
Treatment group Sorafenib/HAIC	0.029	0.052	1.56	0.99 - 2.43	0.038	0.121	1.42	0.91 - 2.21
Previous treatment Yes/No	0.826				0.634			
Combined locoregional treatment Yes/No	0.014	0.010	1.97	1.18 - 3.30	0.011	0.006	2.05	1.28 - 2.43
Serum AFP level (ng/dl) <200/≥200	0.022	0.062	1.61	0.98 - 2.67	0.302			

By Cox-proportional hazard model

Adverse effect

%	Adverse effect	Any grade	Grade 1	Grade 2	Grade 3	Grade 4
HAIC	Leukopenia	62	26	28	8	
(Overall AE	Neutropenia	68	14	22	24	8
: 100%)	Anemia	98	26	46	26	
	Thrombocytopenia	84	28	16	40	
	Bilirubin	74	30	36	8	
	ALT	72	38	16	16	2
	GI toxicity	62	44	18		
Sorafenib	HFSR	45	20	18.3	6.7	
(Overall AE	Alopecia	6.7	6.7	0	0	
:83.3%)	Rash	23.3	10	10	3.3	
	Diarrhea	38.3	15	10	13.3	
	Fatigue	36.7	10	18.3	8.3	
	Hypertension	3.3	0	3.3	0	

	(%)	Grade 1	Grade 2	Grade 3	Grade 4
Pre-HAIC	Leukopenia	12	4		
	Neutropenia	8	14		
	Anemia	42	10	2	
	Thrombocytopenia	48	8		
	Bilirubin	10			
	ALT	44			

Assessed by CTCAE v. 4.0

Conclusion

- HAIC treatment is comparable with sorafenib treatment in terms of overall survival and time to progression in advanced HCC patients with PVTT.
- HAIC showed higher response rate than sorafenib treatment.
- Therfore, HAIC treatment can be an alternative to sorafenib treatment in advanced HCC with PVTT.

Thank you for your attention !

Option of Treatment (Catholic Univ.)
- HCC stage C or refractory to TACE-