#172P

Final Analysis of A Randomized, Double Blind, Phase 2 Study of Sorafenib With or Without YIV-906 in Patients With Advanced HCC

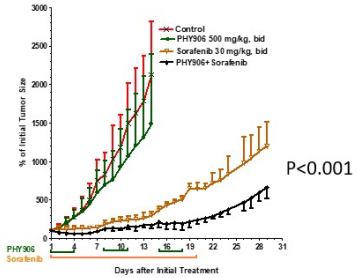
Ghassan K. Abou-Alfa[1,2,3], Yun Yen[4], James J. Harding[1,2], Jacqueline Whang-Peng[5], Yuankai Shi[6], Man Fung Yuen[7], Xuihui Li[8], Shanzhi Gu[9], Chenghai Liu[10], Long-Bin Jeng[11], Chia Jui Yen[12], Calvin Q. Pan[13], San-Chi Chen[14], Jason Chia-Hsun Hsieh[15], Wasif M. Saif[16], Shwu-Huey Liu[17], Fangyong Li[18], Wing Lam[18], Edward Chu[19], and Yung-Chi Cheng[18]

[1] Memorial Sloan Kettering Cancer Center, New York, NY; [2] Weill Medical College at Cornell University, New York, NY; [3] Trinity Medical College, Dublin, Ireland; [4] Taipei Medical University, Taipei, Taiwan; [5] Taipei Municipal Wanfang Hospital, Taipei, Taiwan; [6] Cancer Hospital Chinese Academy of Medical Sciences, Beijing; [7] Queen Mary Hospital, The University of Hong Kong, Hong Kong; [8] Beijing Youan Hospital, Capital Medical University, Beijing; [9] Hunan Cancer Hospital, Changsha, Hunan; [10] Shanghai University of Traditional Chinese Medicine Shuguang Hospital, Shanghai; [11] China Medical University Hospital, Taichung, Taiwan; [12] National Cheng Kung University Hospital, Tainan, Taiwan; [13] Calvin Pan. MD Gastroenterology & Hepatology Clinic, New York, NY[14] Taipei Veterans General Hospital, Taipei, Taiwan; [15] Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan; [16] Karmanos Cancer Institute, Detroit, MI[17]. Yiviva Inc., New York, NY; [18] Yale University School of Medicine, New Haven, CT; [19] Montefiore-Einstein Cancer Center: Albert Einstein College of Medicine, Bronx, NY

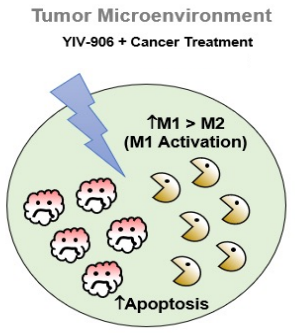
Sponsored by Yiviva Inc.

Background

YIV-906 is a botanically derived formulation, Its polychemical composition potentiates several immune and inflammation pathways. Preclinical studies illustrate YIV-906 immunomodulation in the tumor microenvironment and antitumor activity by priming innate and adaptive immunity while reducing Sorafenib toxicity.

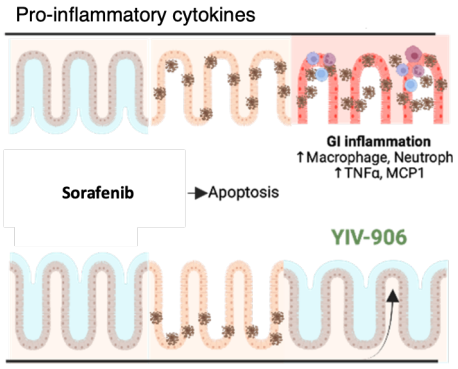


More than 250 GI cancer pts treated have demonstrated efficacy and safety. Additionally, YIV-906 reduces non-hematological toxicities by reducing GI inflammation (TNFa, NFkB, IL6, COX2, iNOS), promoting damaged tissue repair (Wnt pathway), and reducing pain (NK1).



YIV-906 Increases Therapeutic Index by Increasing and Polarizing Macrophages and modulating the immune system

- Convert chronic to acute Inflammation of tumor micro-environment
- Increase M1 like macrophage infiltration
- Enhances Apoptosis



YIV-906 Increases Safety by Reducing Inflammation in GI And Speeding Up Tissue Recovery

- Suppresses inflammation via inhibiting NF-kB, COX2, iNOS, IL-6
- Promotes damaged tissue recovery by enhancing the re-population of intestinal stem/progenitor cell via potentiation of WNT signaling.

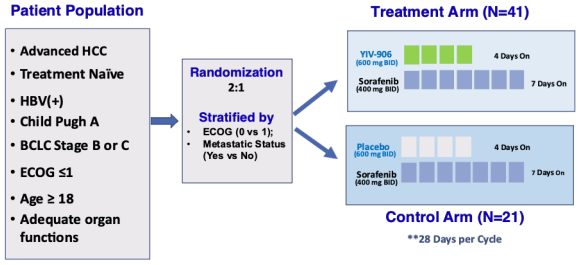
Conclusions

- YIV-906 is a novel modality that sets it apart from the conventional single molecule – single target approach.
- This double blind RCT trial studied the efficacy of combination YIV-906 + sorafenib (SORA) versus sorafenib monotherapy.
- The primary endpoint was PFS. There is numerical improvement in: mPFS 4.1 mo vs 2.3 mo, mTTP 5.59 mo vs 2.33 mo , OS 14.3 vs 7.5 mo, ORR 2.4% vs 0%, and DCR 58.5% vs 47.4%.
- YIV-906 + SORA arm patients demonstrated greater treatment exposure duration and continuation, thus remaining on treatment longer.
- Considering fulfilling the efficacy objective, and safety results, YIV-906 + sorafenib provides a potential benefit for HBV(+) HCC patients and merits further exploration.

Methods

Study Design

- **International, Double Blinded Randomized Placebo Control**

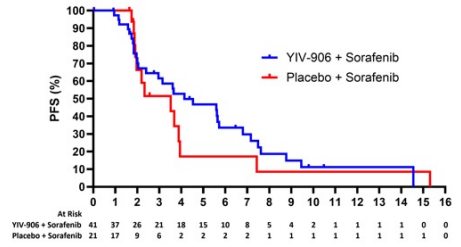


- **Primary Endpoint:** PFS
- **Secondary Endpoints:** TTP, OS, ORR, DCR, Safety and Tolerability, QoL, PK (CN sites only)
- **Exploratory Study:** biomarkers

Results

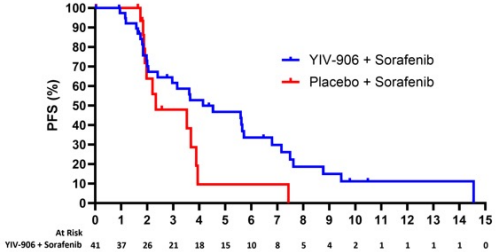
PFS (RECIST 1.1)

ITT Analysis Set



Parameter	YIV-906 arm (n=41)	Placebo arm (n=21)
Events, n (%)	30 (73)	13 (62)
mPFS, mo (95% CI)	**4.1**(2.0 – 5.7)	**3.5**(1.9 – 3.9)
Stratified HR (95% CI)	**0.72** (95% CI: 0.35 - 1.48) **p-value 0.371**	

PPS Analysis Set



Parameter	YIV-906 arm (n=41)	Placebo arm (n=19)
Events, n (%)	30 (73)	12 (63)
mPFS, mo (95% CI)	**4.1**(2.0 – 5.7)	**2.3**(1.9 – 3.9)
Stratified HR (95% CI)	**0.50** (95% CI: 0.24 - 1.05) **p-value 0.063**	

Baseline Characteristics

	Statistic	YIV-906 + Sorafenib (N=41)	Placebo + Sorafenib (N=21)	Total (N=62)
Age (years)	n	41	21	62
	Mean (SD)	60.1 (13.7)	60.9 (9.8)	60.4 (12.5)
	Median	57.0	62.0	62.0
	Min	28	38	28
	Max	85	75	85
Sex				
Male	n (%)	32 (78.0)	15 (71.4)	47 (75.8)
Female	n (%)	9 (22.0)	6 (28.6)	15 (24.2)
Ethnicity				
Asian	n (%)	41 (100.0)	21 (100.0)	62 (100.0)
Non-Asian	n (%)	0	0	0
BCLC Stage				
B	n (%)	13 (31.7)	6 (28.6)	19 (30.6)
C	n (%)	27 (65.9)	15 (71.4)	42 (67.7)
Child-Pugh Score				
CLASS A (5-6)	n (%)	41 (100.0)	21 (100.0)	62 (100.0)
5	n (%)	29 (70.7)	14 (66.7)	43 (69.4)
6	n (%)	12 (29.3)	6 (28.6)	18 (29.0)
α-fetoprotein (ng/ml)				
<400	n (%)	23 (56.1)	12 (57.1)	35 (56.5)
≥400	n (%)	18 (43.9)	9 (42.9)	27 (43.5)

Secondary Endpoints

Outcome	ITT		PPS	
	YIV-906 arm (n=41)	Placebo arm (n=21)	YIV-906 arm (n=41)	Placebo arm (n=19)
OS, mo (95% CI)	**14.3** (8.2, 18.8)	**8.0** (4.6, 32.1)	**14.3** (6.5-25.7)	**7.5** (4.6-32.1)
Stratified HR (95% CI)	0.97 (0.51 – 1.84) p-value 0.917		0.92 (0.48 – 1.79) p-value 0.814	
TTP, mo (95% CI)	**5.59** (3.15 – 7.49)	**2.33** (1.97 – NA)	**5.59** (3.15 – 7.49)	**2.33** (1.97 – NA)
Stratified HR (95% CI)	0.709 (0.333 - 1.507) p-value 0.3701		0.464 (0.208 – 1.031) p-value 0.054	
ORR(%) • ORR, n (%) • 95% CI • Difference in ORR, 95% CI, p Value	**1 (2.4)** (0.1, 12.9)	**0** (0.0, 16.1)	**1 (2.4)** (0.1, 12.9)	**0** (0.0, 17.6)
	2.4* (-2.3, 7.2), p value 0.513		**2.4** (-2.3, 7.2), p value 0.513	
DCR(%) • DCR, n (%) • 95% CI • Difference in DCR, 95% CI, p Value	**24 (58.5)** (42.1, 73.7)	**10(47.6)** (25.7, 70.2)	**24 (58.5)** (42.1, 73.7)	**9 (47.4)** (24.4, 71.1)
	10.9 (-15.2, 37.1), p value 0.363		**11.2** (-15.9, 38.2), p value 0.336	

*after improvement in IRRC-assessed per mRECIST, with the difference between the YIV-906 arm and the placebo arm of 19.6% (95% CI: 3.6%, 35.6%), (p=0.053)

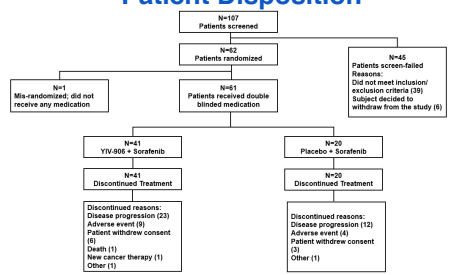
Adverse Events

Duration of Treatment	YIV-906 arm (n=41)	Placebo arm (n=20)
Median Duration of Study Treatment (Days, range)	63 (4-251)	33.5 (10-267)
Median Duration of Sorafenib Treatment (Days, range)	108 (5-438)	58.5 (16-465)

AEs, %	YIV-906 arm (n=41)	Placebo arm (n=20)
TEAEs • Any • Grade≥3 • Serious • Leading to tx discontinuation • Leading to dose reduction	97.6 73.2 39 24.4 46.3	100 65 30 20 55.0
TRAEs related to study drug • Related • Not related	51.2 46.3	30 70
TRAEs related to sorafenib • Related • Not related	92.7 4.9	95 5

TEAEs in ≥15% of Patients in Either Group, %	YIV-906 arm (n=41)		Placebo arm (n=20)	
	Any	Gr 3/4	Any	Gr 3/4
PPE	58.5	17.1	55.0	15
Diarrhea	51.2	12.2	25	5
Blood bilirubin increased	34.1	2.4	15	0
Fatigue	26.8	4.9	15	5
ALT increased	24.4	0	5	0
Hypertension	24.4	14.6	20	20
Weight decreased	24.4	0	20	5
Anaemia	22.0	7.3	5	0
AST increased	19.5	7.3	15	0
ALP increased	19.5	4.9	15	5
Platelet count decreased	17.1	2.4	5	5
Pyrexia	17.1	0	0	0
Decreased appetite	14.6	0	25	5
Rash	14.6	2.4	20	0
Vomiting	2.4	0	15	0

Patient Disposition



- 2025 ESMO GI Presenter Dr. Ghassan Abou-Alfa doesn't have any conflict of interests on this study. Contact email: abou-alg@mskcc.org.
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