2022 ASCO® ANNUAL MEETING

Abstract No. 2501

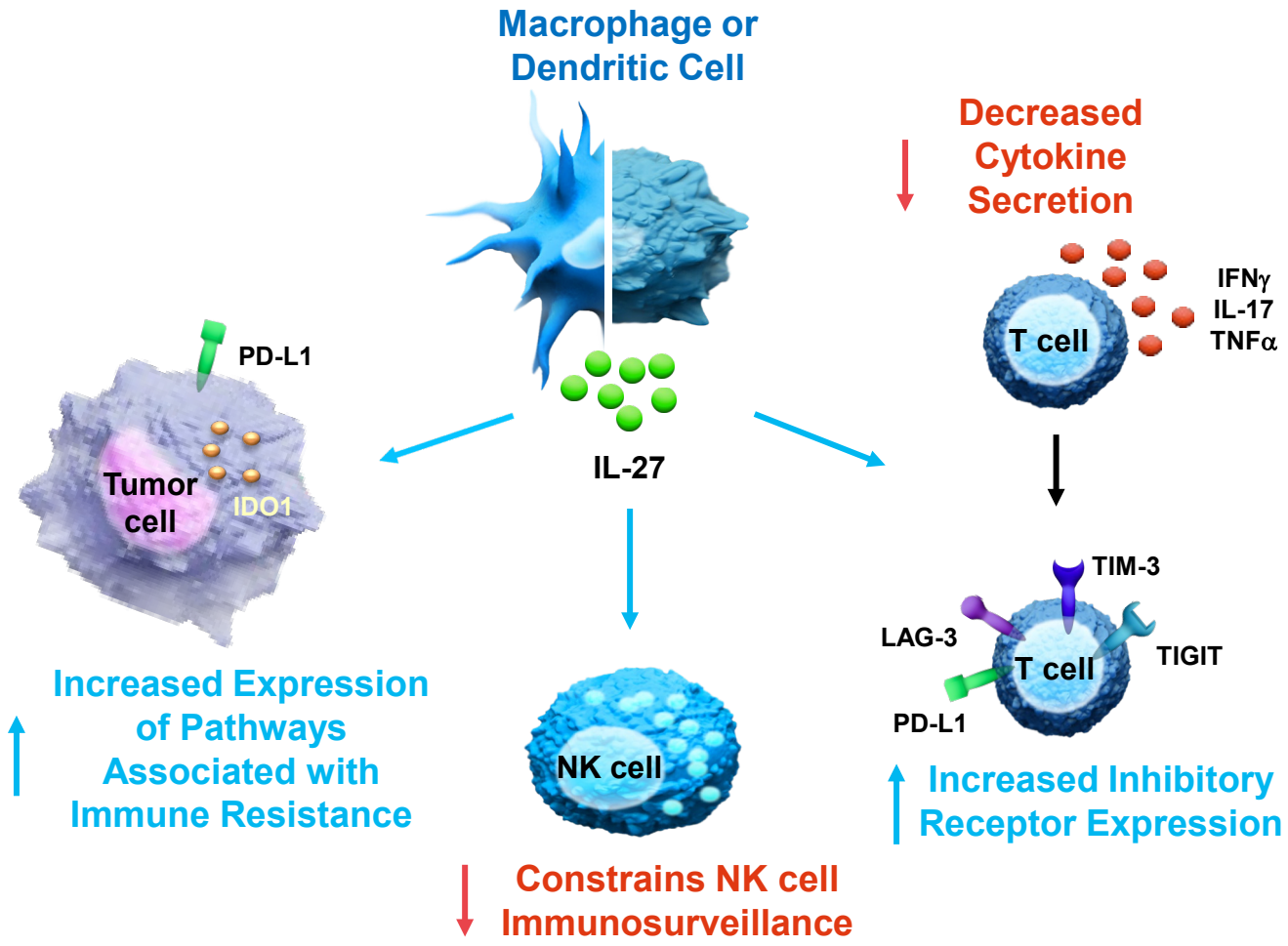
First-in-human study of SRF388, a first-in-class IL-27 targeting antibody, as monotherapy and in combination with pembrolizumab in patients with advanced solid tumors

Aung Naing,[1] Charlene Mantia,[2] Daniel Morgensztern,[3] Tae-Yong Kim,[4] Daneng Li,[5] Yoon-Koo Kang,[6] Thomas Marron,[7] Abhishek Tripathi,[8] Saby George,[9] Brian Rini,[10] Anthony El-Khoueiry,[11] Ulka Vaishampayan,[12] R. Kate Kelley,[13] Moshe Ornstein,[14] Leonard J. Appleman,[15] Lauren C. Harshman,[16] Benjamin Lee,[16] Nizar M. Tannir,[1] Hans Hammers,[17] Amita Patnaik,[18]

1. The University of Texas MD Anderson Cancer Center, Houston, TX, USA; 2. Dana-Farber Cancer Institute, Boston, MA; 3. Washington University School of Medicine, St. Louis, MO; 4. Seoul National University Hospital, Seoul, Korea; 5. City of Hope Comprehensive Cancer Center, Duarte, CA, USA; 6. Asan Medical Center, University of Uslan College of Medicine, Seoul, Korea; 7. The Mount Sinai Hospital, Icahn School of Medicine at Mount Sinai, New York, NY, USA; 8. Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA; 9. Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; 10. Vanderbilt University Medical Center; Nashville, TN, USA; 11. Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA, USA; 12. University of Michigan, Ann Arbor, MI, USA; 13. Helen Diller Family Comprehensive Cancer Center, UCSF Medical Center, San Francisco, CA, USA; 14. Cleveland Clinic, Cleveland, OH, USA; 15. Hillman Cancer Center, University of Pittsburgh Medical Center, Pittsburgh, PA, USA; 16. Surface Oncology, Cambridge, MA, USA; 17. Harold C. Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, Dallas, TX, USA; 18. South Texas Accelerated Research Therapeutics, San Antonio, TX, USA

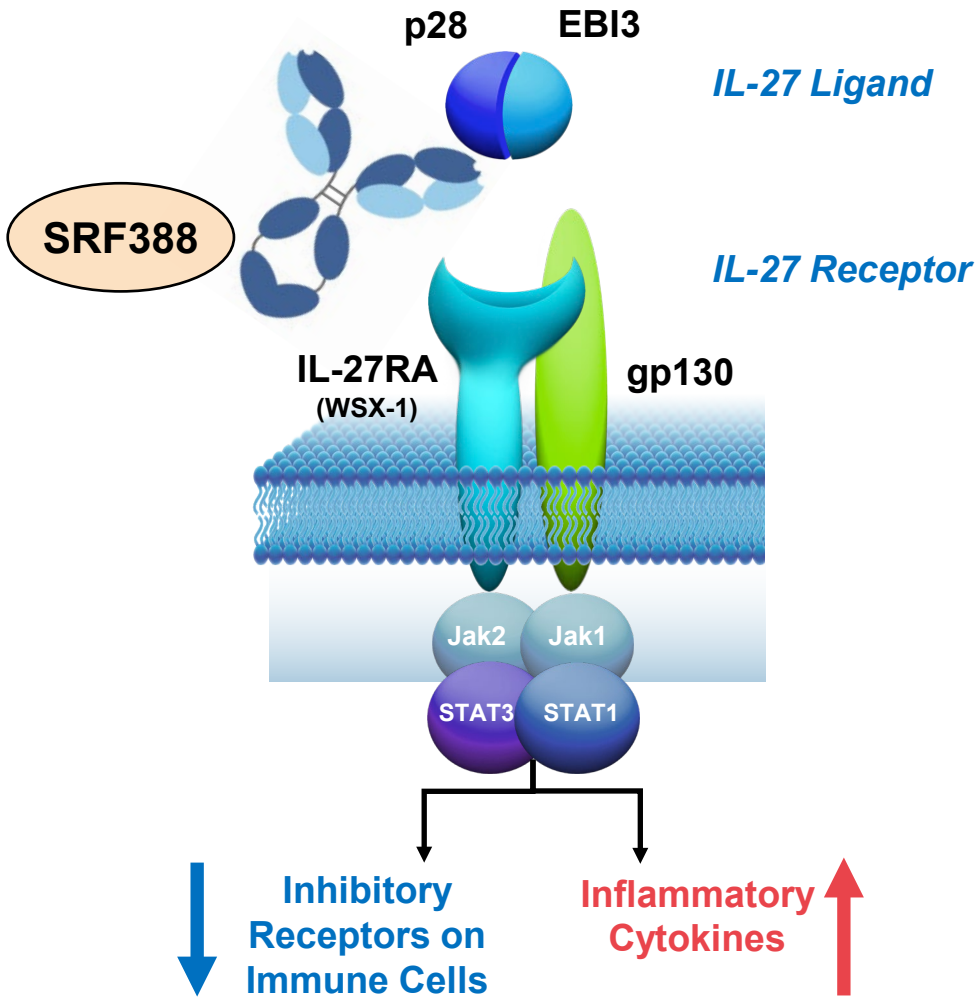
PRESENTED BY: Aung Naing, MD

IL-27 is an Immunoregulatory Cytokine That Inhibits Antitumor Responses

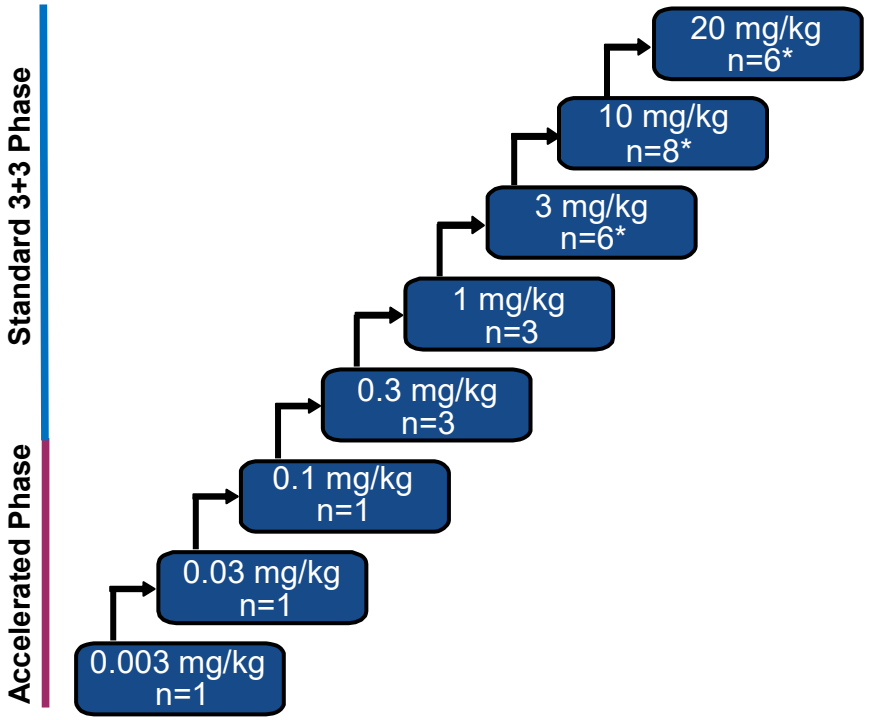


Villarino, et al. *Immunity*. 2003; Saur, et al. *J Immunol*. 2008; Carbotti, et al. *Oncotarget*. 2015; Chihara, et al. *Nature*. 2018; DeLong, et al. *Immunohorizons*. 2019; Aghayev, et al. *bioRxiv*. 2020

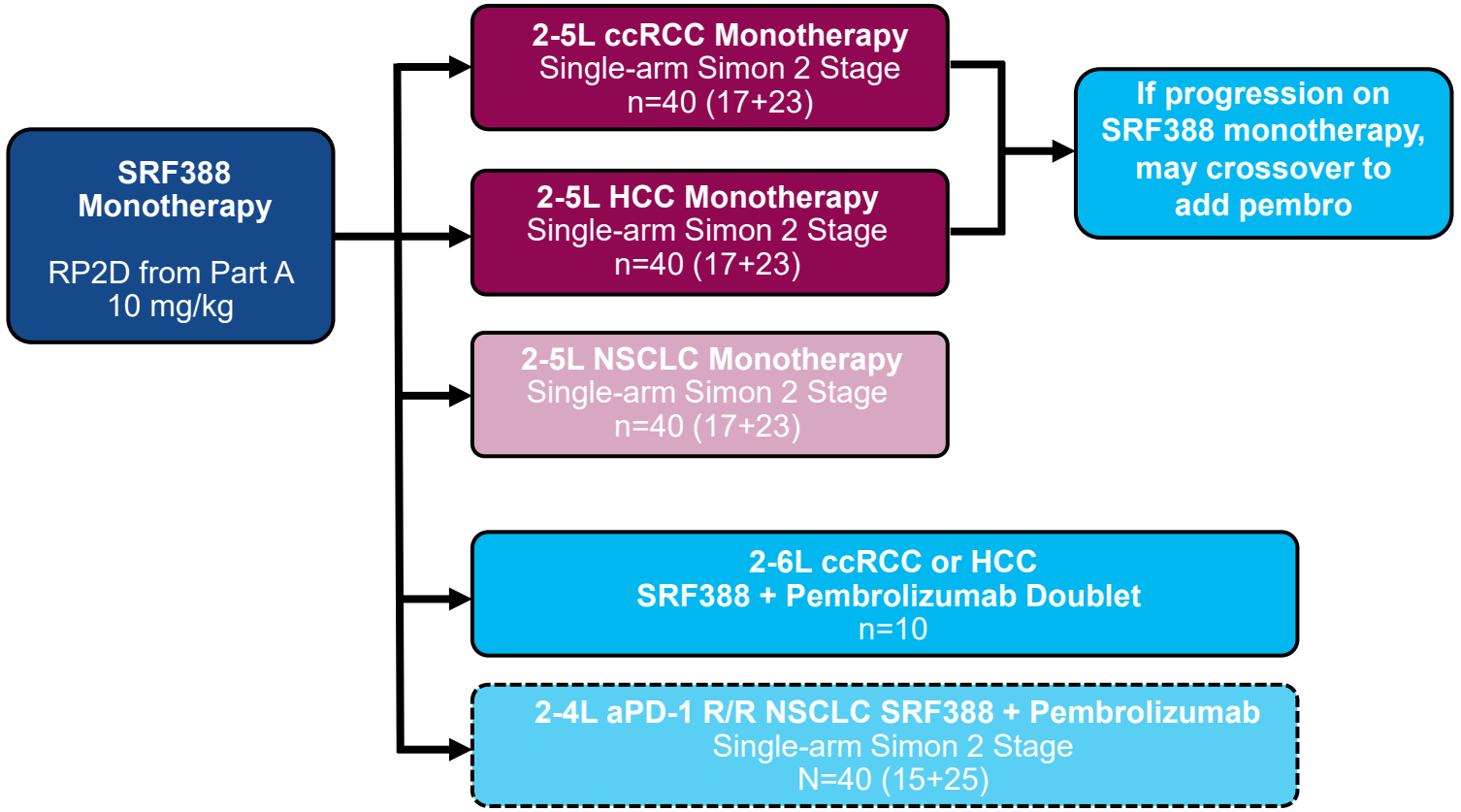
SRF388: First-in-Class Anti-IL-27 Antibody with a Unique I-O Rationale



SRF388-101: Phase 1, First-in-Human Study Design



*No DLTs, additional slots per cohort to increase experience at this dose



SRF388 is given IV every 4 weeks as a monotherapy and every 3 weeks with pembrolizumab

RP2D selected as 10 mg/kg based on safety, tolerability, PK, peripheral pSTAT1 inhibition, and preliminary efficacy observed in escalation[1]

[1]Hill et al AACR 2022

SRF388-101 Baseline Patient & Disease Characteristics

Demographics n (%)		SRF388 Escalation (n=29)	SRF388 HCC (n=17)	SRF388 ccRCC (n=21)	SRF388 + Pembro (n=10)
Age	Median years (range)	64 (46, 83)	64 (39, 77)	61 (48, 78)	69 (58, 74)
Gender	Female	18 (62.1)	4 (23.5)	2 (9.5)	1 (10.0)
	Male	11 (37.9)	13 (76.5)	19 (90.5)	9 (90.0)
Race	Asian	1 (3.4)	11 (64.7)	4 (19.0)	6 (60.0)
	Black or African American	1 (3.4)	1 (5.9)	1 (4.8)	1 (10.0)
	White	25 (86.2)	4 (23.5)	15 (71.4)	3 (30.0)
	Unknown	2 (6.9)	0 (0.0)	0 (0.0)	0 (0.0)
	Not Reported	0 (0.0)	1 (5.9)	1 (4.8)	0 (0.0)
ECOG PS	0	7 (24.1)	1 (5.9)	10 (47.6)	2 (20.0)
	1	22 (75.9)	16 (94.1)	11 (52.4)	8 (80.0)

Demographics n (%)		SRF388 Escalation (n=29)	SRF388 HCC (n=17)	SRF388 ccRCC (n=21)	SRF388 + Pembro (n=10)
Median time since initial diagnosis, months (range)		43 (6, 235)	27 (1, 137)	55 (26, 119)	58 (24, 132)
Lines of Prior Systemic Therapy	1	7 (24.1)	1 (5.9)	0 (0.0)	0 (0.0)
	2	4 (13.8)	7 (41.2)	5 (23.8)	5 (50.0)
	3-4	7 (24.1)	9 (52.9)	16 (76.2)	3 (30.0)
	≥ 5	11 (37.9)	0 (0.0)	0 (0.0)	2 (20.0)
Prior aPD-1/aPD-L1	Yes	23 (79.3)	12 (70.6)	21 (100.0)	6 (60.0)
	No	6 (20.7)	5 (29.4)	0 (0.0)	4 (40.0)
IMDC* (ccRCC patients only)	Favorable	1 (14.3)	-	4 (19.0)	1 (33.3)
	Intermediate	4 (57.1)	-	12 (57.1)	1 (33.3)
	Poor	0 (0.0)	-	2 (9.5)	0 (0.0)

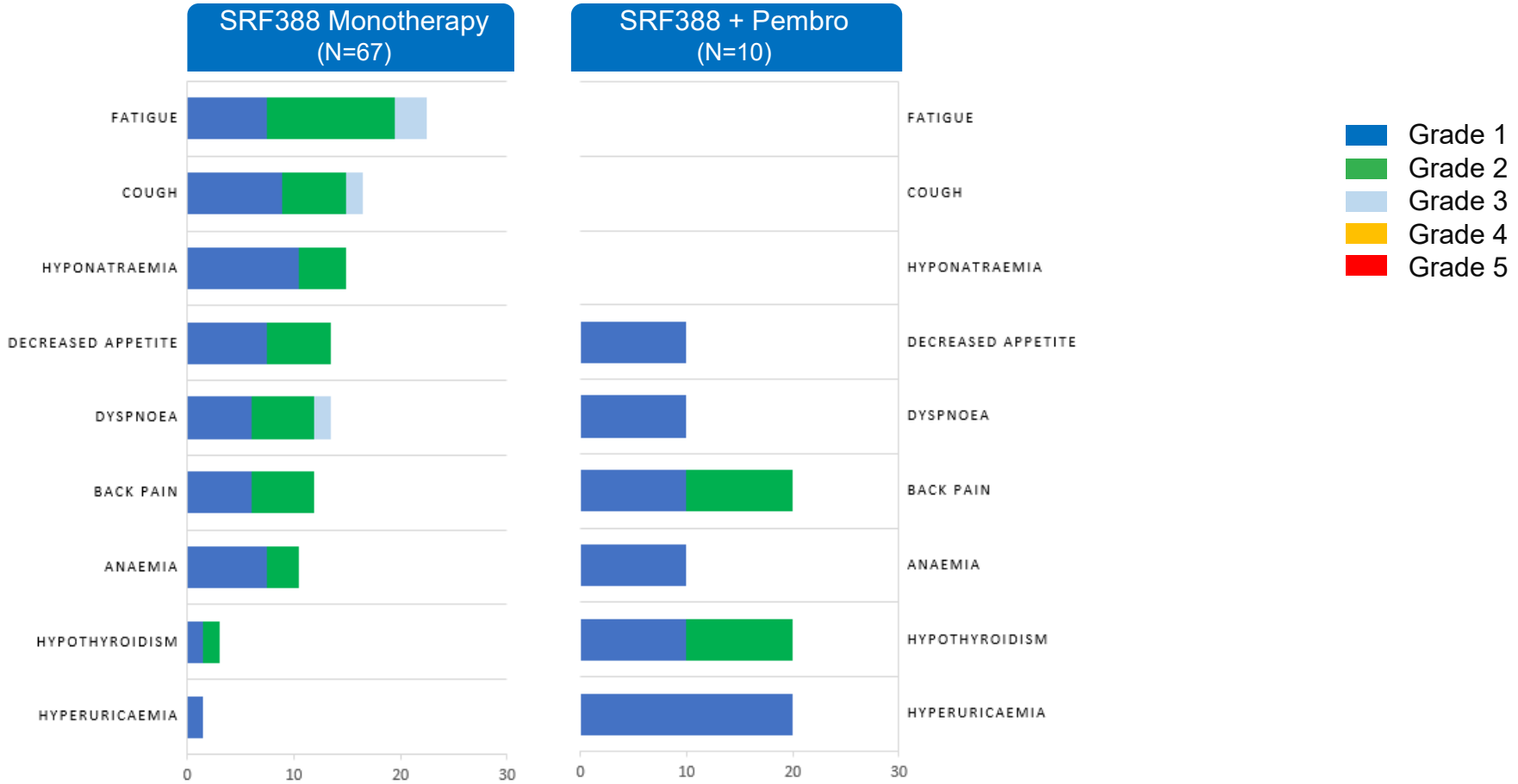
*One or more patients are missing data
IMDC, International Metastatic RCC Database Consortium (risk model for metastatic RCC)

*Data from 21 patients with ccRCC were included for demographics, safety, and PK: 17 Stage 1 patients, 4 Stage 2 patients. Of these, only 13 were response evaluable at the time of data cut.

Data cut as of 24 Mar 2022, subject to change

SRF388 TEAEs Regardless of Relationship to Study Drugs

Majority of TEAEs consistent with advanced disease; No dose-limiting toxicities or ≥ Grade 3 related toxicities



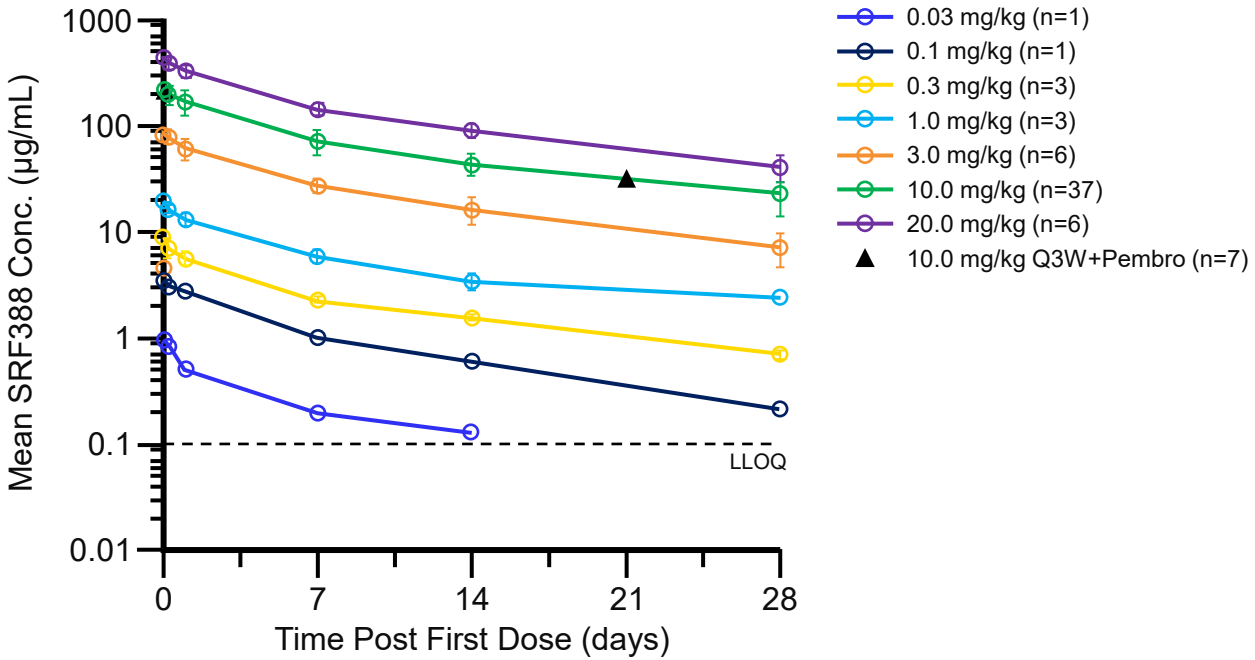
Percentage of Patients With TEAEs ≥10% on monotherapy and >10% in pembrolizumab combination

TEAE defined as an AE that emerges or worsens in the period from the first dose of SRF388 to 30 days after the last dose

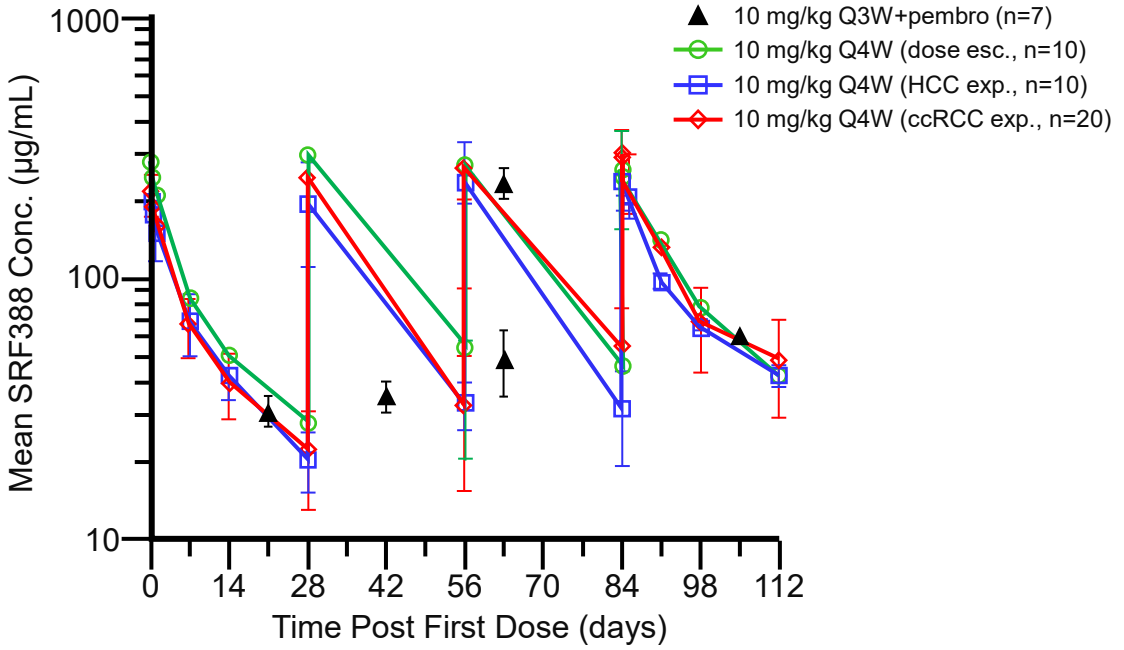
Data cut as of 24 Mar 2022, subject to change

SRF388 Pharmacokinetic Profile

PK linear at doses up to 20 mg, exposures comparable in RCC, HCC, and in combo with pembrolizumab



Note: 0.003 mg/kg Cycle 1 samples below limit of quantitation

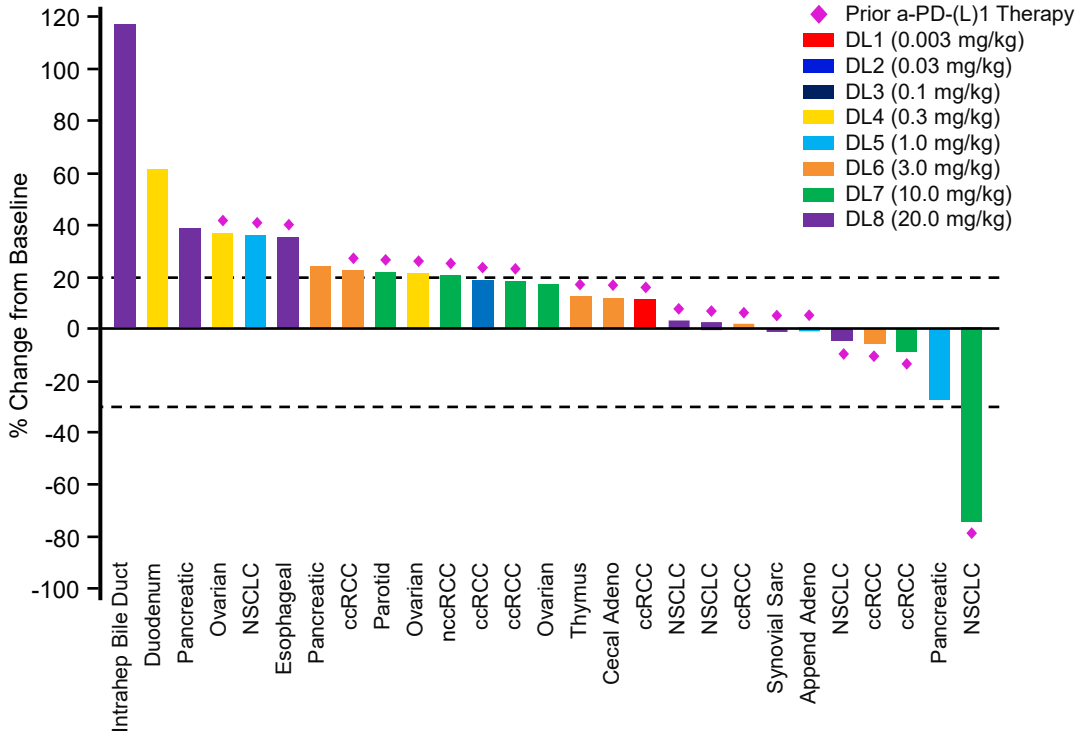


- SRF388 elimination appears linear across the doses investigated
- Comparable PK irrespective of tumor type when given as a monotherapy and in combination with pembrolizumab
- Overlapping SRF388 concentration ranges when given every 3- or 4-weeks supporting administration flexibility & convenience
- Estimated $T_{1/2}$ of SRF388 ~10 days

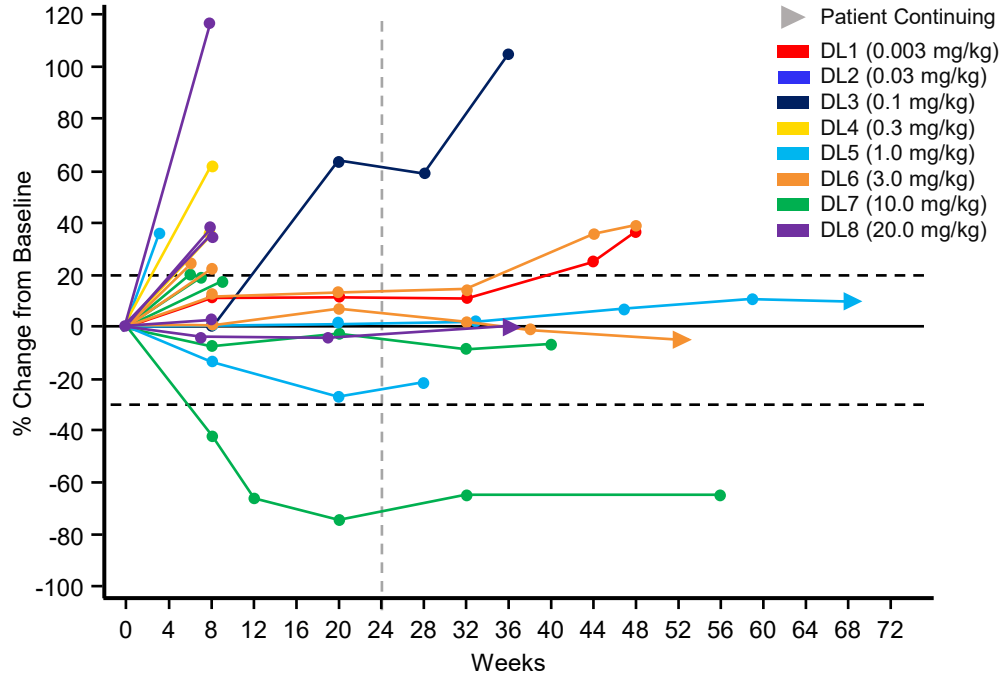
SRF388 Monotherapy Dose Escalation Response Summary

Confirmed PR observed in a patient with NSCLC

Best Percent Change from Baseline in Sum of Target Lesions (n=27)



Target Lesion Change Over Time (n=27)



- Confirmed PR deepened to -74% with resolution of baseline dyspnea in a patient with squamous cell NSCLC, whose disease was primarily resistant to three prior regimens, including chemotherapy and PD-1 blockade
- 64% of the 11 patients with response or disease stabilization had durable control at 6 months or beyond

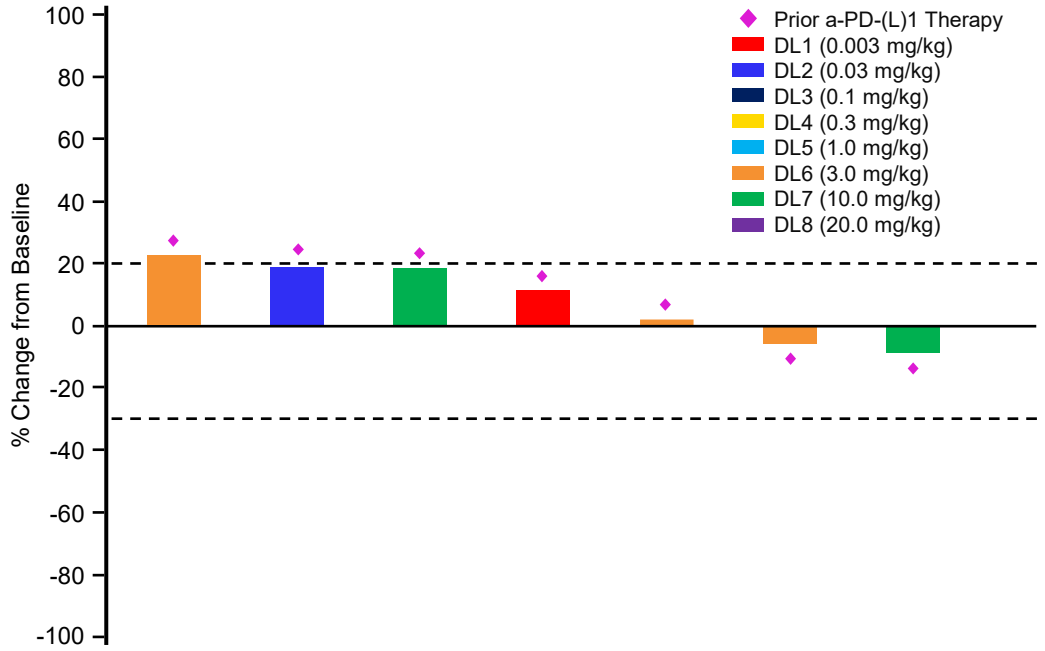
Imaging Assessments at 8 weeks and then every 12 weeks, investigator assessed using RECIST1.1

Data cut as of 24 Mar 2022, subject to change

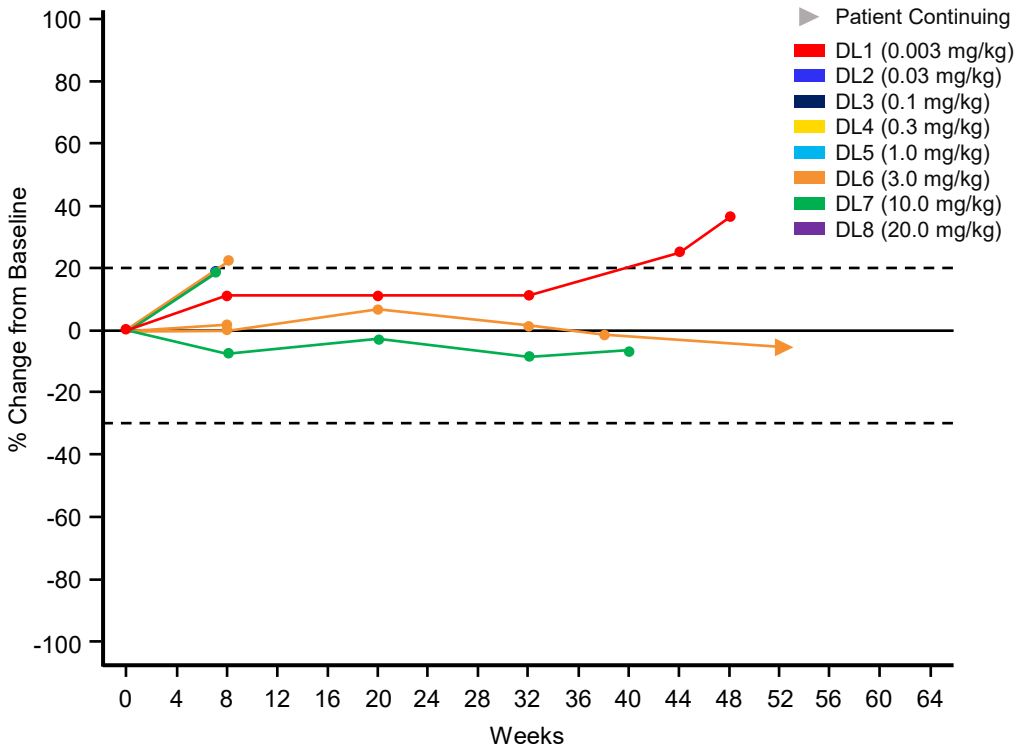
SRF388 Monotherapy Dose Escalation: ccRCC Subset Response Summary

Disease control rate of 57%, with 43% of patients experiencing stabilization ≥20 weeks

Best Percent Change from Baseline in Sum of Target Lesions (n=7)



Target Lesion Change Over Time (n=7)



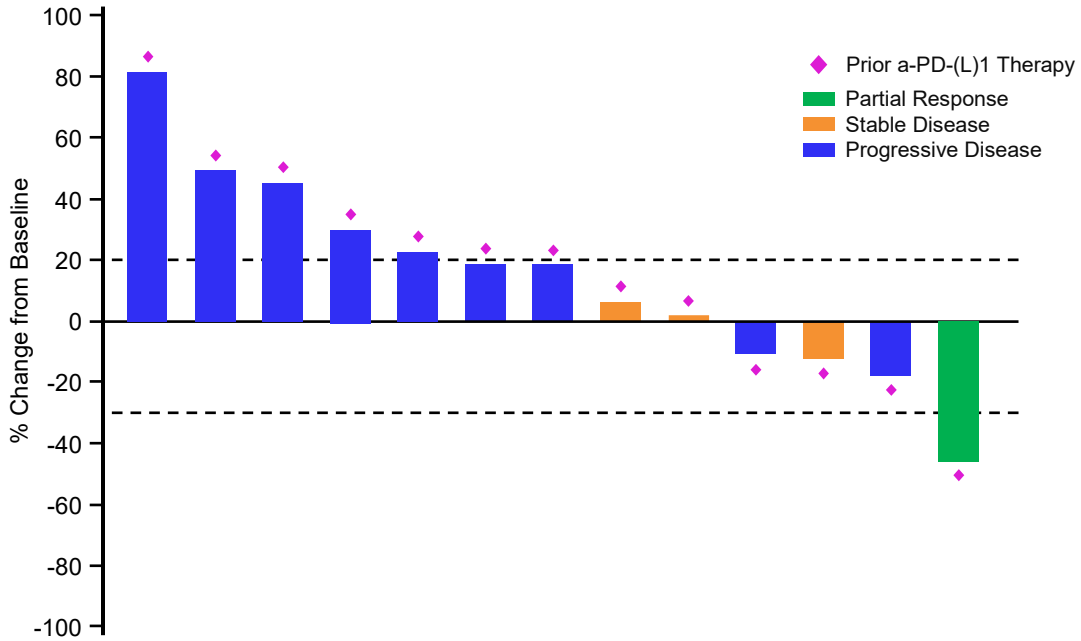
- Heavily pre-treated patients: 43% ≥5 lines of prior treatment; all aPD-(L)1 experienced

Data cut as of 24 Mar 2022, subject to change

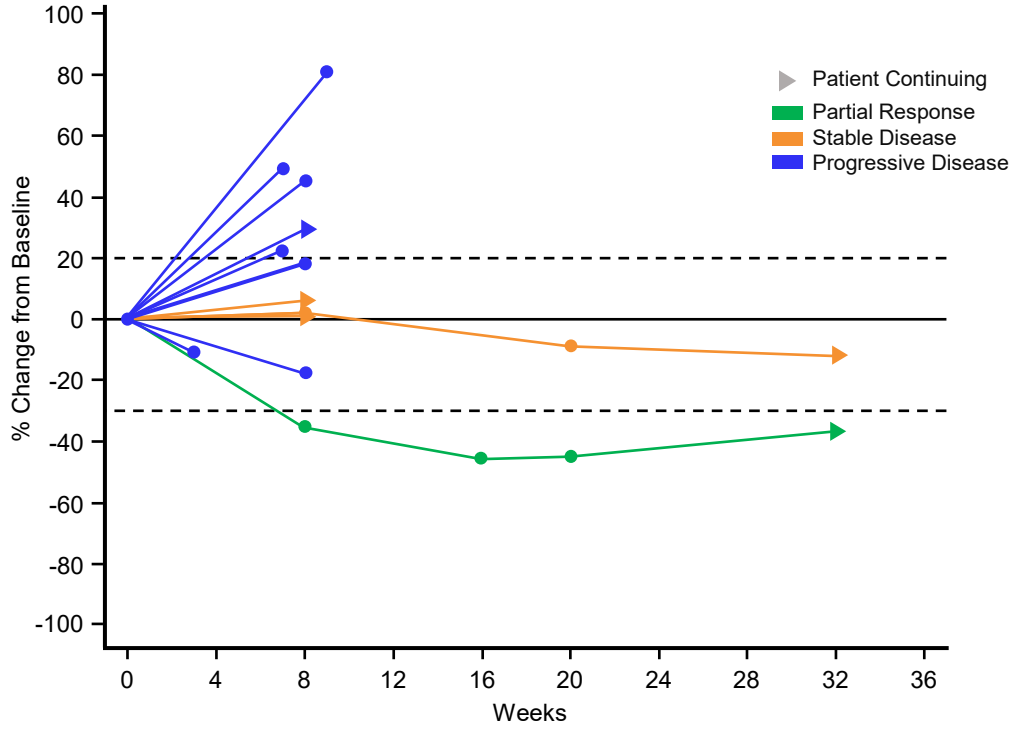
SRF388 ccRCC Monotherapy Dose Expansion Response Summary

Confirmed PR in a patient with ccRCC; 31% disease control rate

Best Percent Change from Baseline in Sum of Target Lesions (n=13)



Target Lesion Change Over Time (n=13)



- 57% intermediate-risk disease by IDMC, 100% prior aPD-(L)1 and VEGF(R) targeted therapy alone or in combination
- Patient with intermediate-risk, aPD-1 refractory disease experienced a durable, confirmed PR (ongoing C9)
- Criteria met to expand the ccRCC monotherapy cohort to Stage 2 (additional 23 patients)

Data cut as of 24 Mar 2022, subject to change

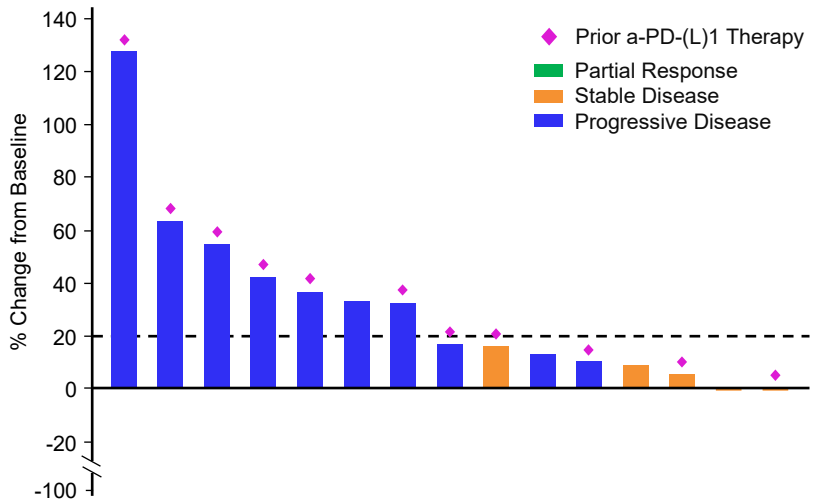
SRF388 HCC Monotherapy Expansion Disease Characteristics & Response Summary

Advanced treatment-refractory population with 94% receiving SRF388 as 3rd-line or greater

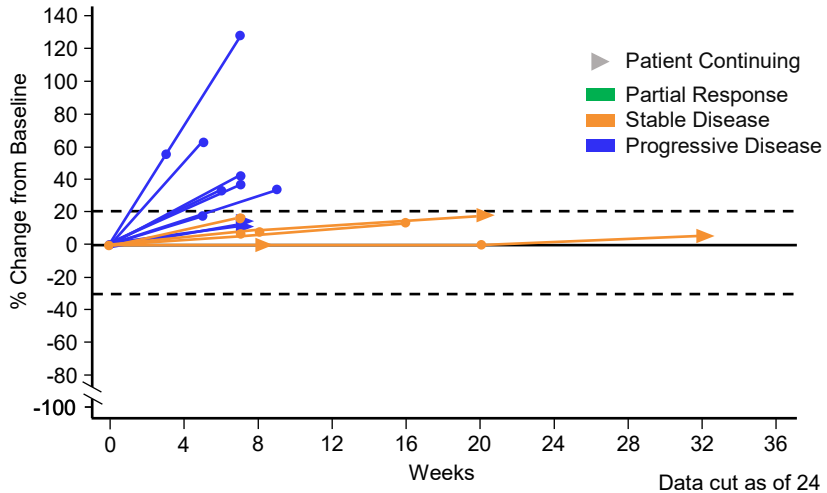
Patient and Disease Characteristics		N = 17
Age, years	Median (range)	64 (39, 77)
Sex	Male	13 (76.5)
	Female	4 (23.5)
Region	Asia excluding Japan	9 (52.9)
	United States	8 (47.1)
ECOG PS	0	1 (5.9)
	1	16 (94.1)
Child-Pugh score*	A5 & A6	11 (64.7)
	B7	3 (17.6)
BCLC stage*	B	2 (11.8)
	C	13 (76.5)
Viral Status*	HBV	10 (58.9)
	HCV	3 (17.6)
	Uninfected	4 (23.5)
Lines of prior anti-cancer therapy	1	1 (5.9)
	2	7 (41.2)
	3	6 (35.3)
	4	3 (17.6)
Prior aPD-(L)1 treatment		12 (70.6)
Prior VEGF(R) targeted therapy		17 (100)
Extrahepatic disease		13 (76.5)
Macrovascular involvement*		2 (11.8)
Baseline AFP (ng/mL)	< 400	7 (41.2)
	≥ 400	10 (58.8)

*One or more subjects are missing data.
AFP, Alpha-fetoprotein; BCLC, Barcelona Clinic Liver Cancer (BCLC) staging system

Best Percent Change from Baseline in Sum of Target Lesions (n=15)



Target Lesion Change Over Time (n=15)

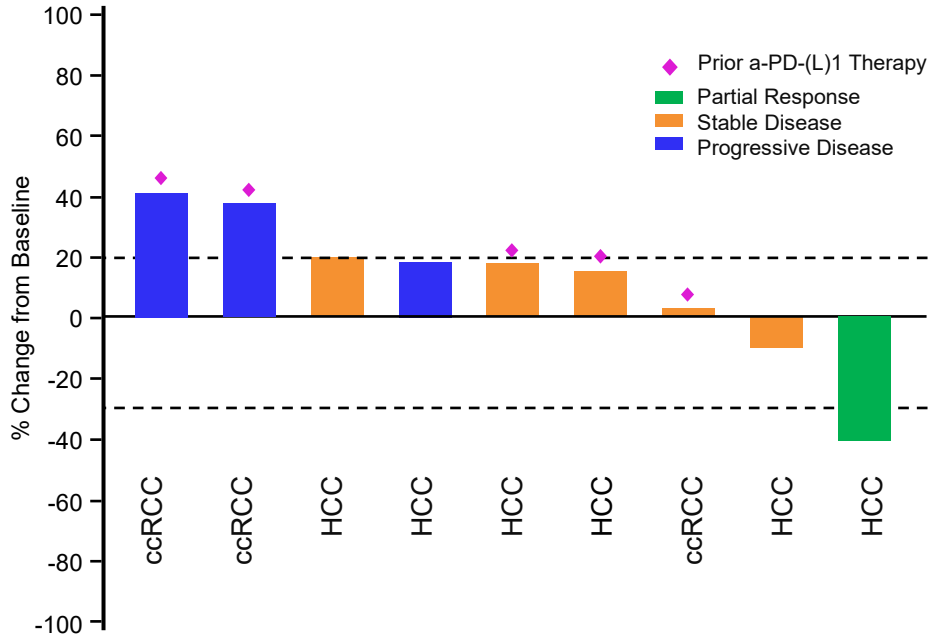


Data cut as of 24 Mar 2022, subject to change

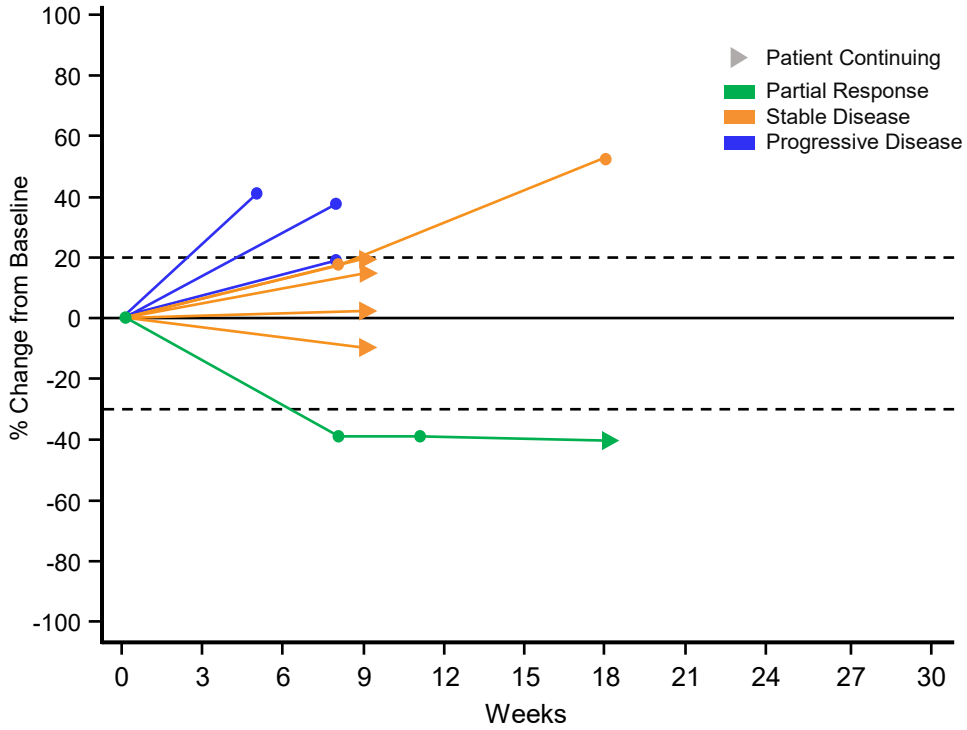
SRF388 Combination with Pembrolizumab Response Summary

Confirmed PR in a patient with HCC; 67% disease control rate

Best Percent Change from Baseline in Sum of Target Lesions (n=9)



Target Lesion Change Over Time (n=9)



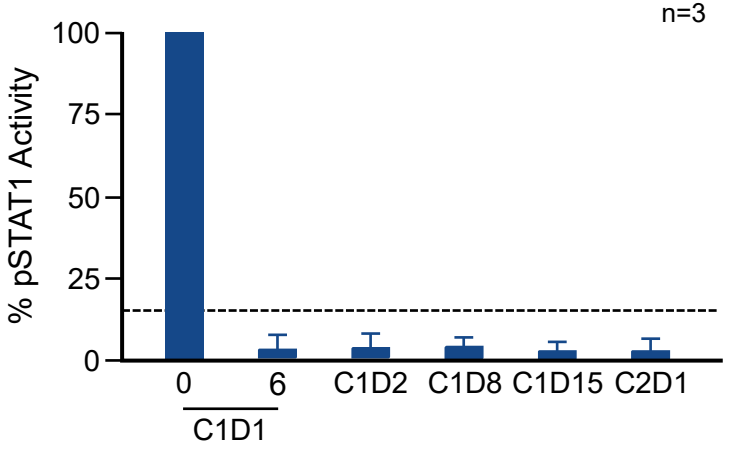
- No DLTs or additive immune-related AEs
- Full doses of both agents have been selected as the RP2D of the combination
- One patient with IO-naïve HCC refractory to two prior VEGFR TKIs experienced a confirmed PR

SRF388 10 mg/kg + Pembrolizumab 200 mg IV every 3 weeks, imaging assessments every 9 weeks

Data cut as of 24 Mar 2022, subject to change

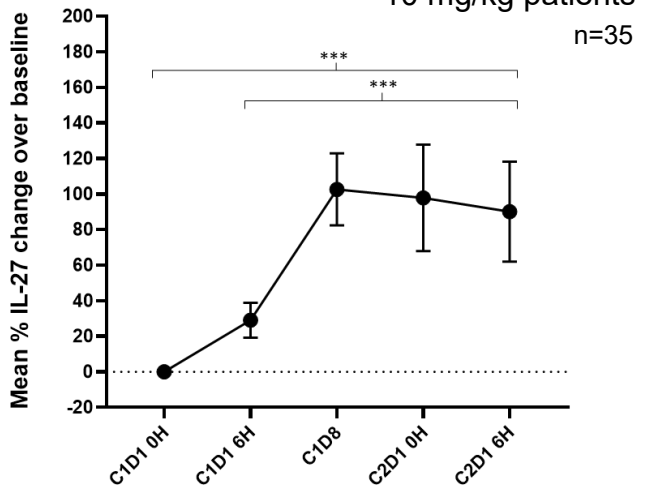
SRF388 Leads to Expected Pharmacodynamic Effects on IL-27 Signaling and Circulating IL-27 Levels and an Upregulation of IFNγ

pSTAT1



Patnaik, et al. ASCO 2021

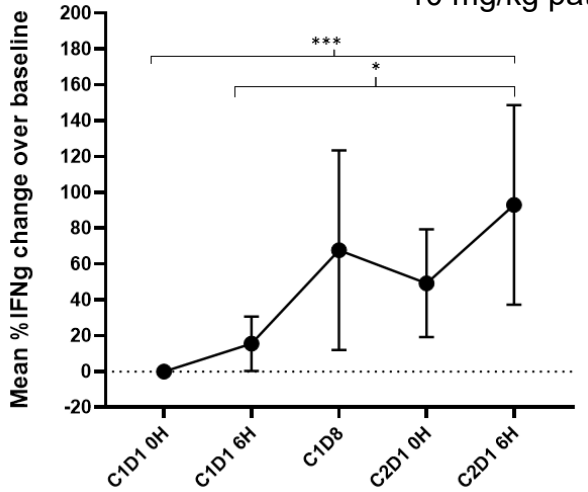
IL-27



***p<0.0001

Data updated and adapted from Hill, et al. AACR 2022

IFNγ



***p<0.0001; *p<0.05

- SRF388 inhibition of IL-27 induced pSTAT1 signaling in circulating T cells maintained through trough starting at 0.3 mg/kg

- Increased levels of IL-27 detected in serum after SRF388
- Phenomenon described for other therapeutic antibodies against cytokines[1] and attributed to decreased receptor-mediated clearance of bound cytokine

- Increased levels of IFNγ detected in serum after SRF388 consistent with its mechanism of action

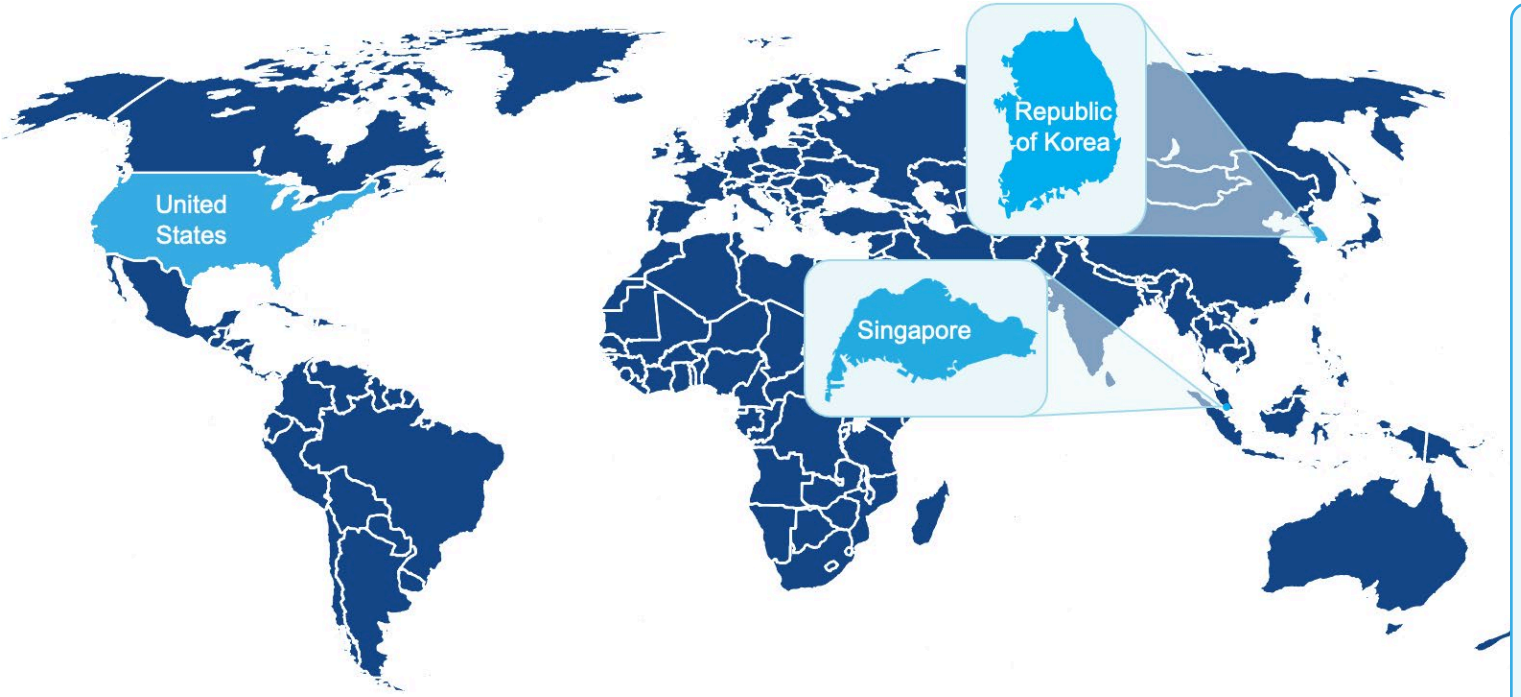
[1] e.g., Bevacizumab & VEGF: Yang, et al. *N Eng J Med*. 2003; Bocci, et al. *Can Res*. 2004

Summary

SRF388 first-in-class novel IO with promising antitumor activity & tolerability

- First-in-class immunomodulatory cytokine antagonist with a novel mechanism of action
- Encouraging monotherapy activity with favorable safety profile, tolerability, and convenient schedule
  - No dose-limiting toxicities or safety signals have been identified up to 20 mg/kg
  - 3 confirmed partial responses across different but biologically relevant solid tumor indications including one with primary aPD-1 refractory disease
  - Criteria met to expand the RCC monotherapy cohort to Stage 2 (additional 23 patients)
- SRF388's tolerability and distinct mechanism of action support combination potential
  - Compelling biology and preclinical data for complementary activity with PD-1 blockade
  - IL-27 blockade likely to complement a broad range of standard of care therapies in mechanism
- These results merit continued evaluation of SRF388 as a monotherapy and in combination

Acknowledgements



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Republic of Korea:
Seoul National University Hospital (Tae-Yong Kim)
Severance Hospital, Yonsei University Medical Center (Sun Young Rha)
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