Use of a real-world data registry to rapidly generate outcomes data following a case study of a novel treatment combination in pancreatic adenocarcinoma

Rahib, L.[1]; Shapiro, M.[2]; Shrager, J.[2]; Hoos, W. [2]; Federowicz, B. [2]; Kinsey, C.[3]

[1]Cancer Commons, Los Altos, CA ; [2]xCures, Los Altos, CA ; [3]Huntsman Cancer Center, University of Utah, Salt Lake City, UT

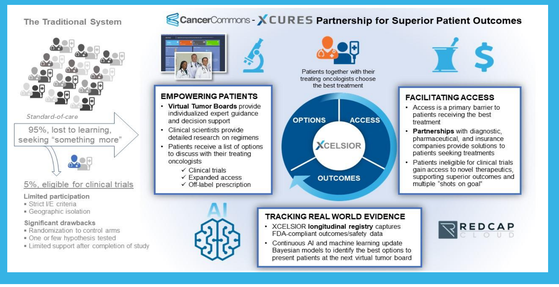
Background:

XCELSIOR is an IRB approved, patient-centric, real-world data and outcomes registry for developing operational and analytic methods in precision oncology. Kinsey et al. reported on an exceptional response in a heavily pre-treated pancreatic adenocarcinoma patient using combined MEK inhibition with autophagy inhibition (Nature Medicine, 2019), off-label trametinib plus hydroxychloroquine (Tram/HCQ). We sought to understand the utilization of this regimen in clinical practice and analyze safety and outcomes information from patients in XCELSIOR identified as being treated with this combination. Searching the XCELSIOR database, we identified 6 patients that received this regimen as part of their clinical care for pancreatic adenocarcinoma. As part of their participation in XCELSIOR, these patients shared access to their full medical records, which were collected, processed, and abstracted into a 21 CFR 11 compliant database for analysis. We report on these patients and six additional patients (including the exceptional responder previously reported in Nature Medicine, 2019) treated with this combination at the Huntsman Cancer Center.

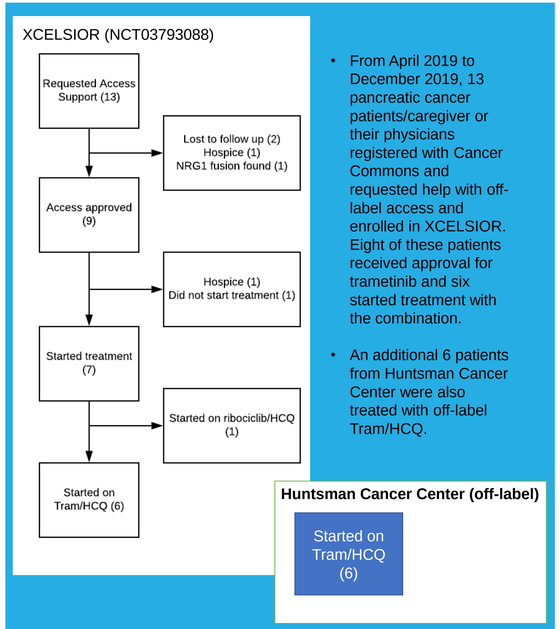
Methods and Process:

XCELSIOR: Patients/caregivers registered with Cancer Commons and indicated they were interested in information about treatment options for their late-stage, metastatic disease and/or had Cancer Commons' Virtual Tumor Board review their case and provide information about potential treatment options to share with their oncologist. Patients who were eligible for the XCELSIOR registry provided informed consent and access to their medical records related to their care, which were collected and abstracted into the registry database. Patients who requested assistance navigating their care received assistance throughout the process from a nurse navigator, including help obtaining coverage for trametinib. Longitudinal follow-up included ongoing collection of medical records and direct contact with patients/caregivers and their physicians. All patients received 2 mg trametinib and 1200 mg HCQ daily. All patients who received this combination had exhausted standard of care options and their prior scan showed progression.

Huntsman Cancer Center: From March 2018 to September 2019, six patients were treated with off-label trametinib/HCQ at the Huntsman cancer center. All patients had exhausted standard of care options and were progressing prior to treatment. Patients received 2 mg Trametinib and 1200 mg HCQ daily, two patients started on 800 mg HCQ for a week and then escalated to 1200 mg of HCQ.



Patient Cohorts



- From April 2019 to December 2019, 13 pancreatic cancer patients/caregiver or their physicians registered with Cancer Commons and requested help with off-label access and enrolled in XCELSIOR. Eight of these patients received approval for trametinib and six started treatment with the combination.
- An additional 6 patients from Huntsman Cancer Center were also treated with off-label Tram/HCQ.

Patient Characteristic

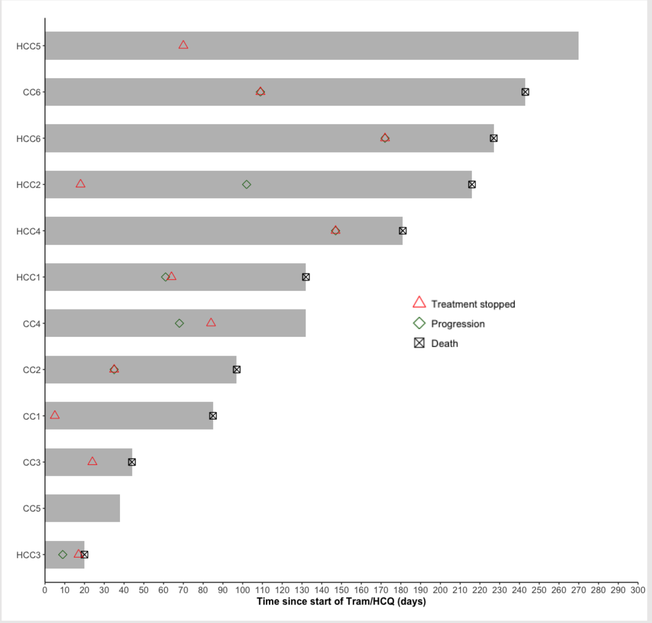
	Both Cohorts (n=12)	XCELSIOR (n=6)	HCC (n=6)
Male	7 (58%)	4 (67%)	3 (50%)
Female	5 (42%)	2 (33%)	3 (50%)
Median age at diagnosis (range)	61 (45-74)	65 (55-74)	60 (45-67)
Stage at Diagnosis			
Resectable	5 (42%)	1 (17%)	4 (67%)
Locally advanced	4 (33%)	2 (33%)	2 (33%)
Metastatic	3 (25%)	3 (50%)	
Prior Systemic Therapy (excluding neoadj/adj)			
1	2 (17%)		2 (33%)
2	6 (50%)	4 (67%)	2 (33%)
3	2 (17%)	1 (17%)	1 (17%)
4+	2 (17%)	1 (17%)	1 (17%)
Previous therapy			
Resection	7 (58%)	1 (17%)	6 (100%)
Radiotherapy	4 (33%)	2 (33%)	2 (33%)
Chemotherapy	12 (100%)	6 (100%)	6 (100%)
Other	4 (33%)	1 (17%)	3 (50%)
Genomics (n=10)			
Site of biopsy			
Pancreas	6 (60%)	2 (40%)	4 (80%)
Liver	1 (10%)	1 (20%)	(0%)
Lung	1 (10%)		1 (20%)
Peritoneum	1 (10%)	1 (20%)	
Blood	1 (10%)	1 (20%)	
KRAS mutation			
G12D	6 (60%)	2 (40%)	4 (80%)
G12R	3 (30%)	2 (40%)	1 (20%)
Q16L	1 (10%)	1 (20%)	

HCC, Huntsman Cancer Center

Patient Status:

- 9 patients deceased, 3 alive
- 8 (67%) patients were treated with Tram/HCQ for > 30 days
  - 6 patients evaluable for PFS
  - 8 patients evaluable for OS
- XCELSIOR: 4 patients deceased, 2 alive; 1 still on Tx (as of December 2019)
- HCC Cohort: 5 patients deceased, 1 alive (as of January 2020)

Patient outcomes



PFS, OS, and time on therapy

	Both Cohorts (n=12)	(XCELSIOR (n=6)	HCC (n=6)
Median time on treatment >30 days	8 (67%)	4 (67%)	4 (67%)
Median PFS (Months), n=6	2.9		
Median OS since start of Tram/HCQ (Months), n=8	7.4		
Response (n=7)			
Partial Response	1 (14%)		1 (25%)
Stable Disease (at least 8 weeks)	3 (43%)	1 (25%)	2 (67%)
Progression	3 (43%)	2 (50%)	1 (33%)
All Patients			
Median PFS (Months), n=8	2.8		
Median OS since start of Tram/HCQ (Months), n=12	5.9		
Post Tram/HCQ therapy	4 (67%)	2 (33%)	2 (33%)
Median time on treatment in days (range)	35 (5-172)	36.5 (5-109)	67 (17-172)
Reason for discontinuation (n=11)			
Progression	5 (50%)	3 (60%)	2 (40%)
Intolerable side effects	3 (30%)		3 (60%)
Stopped because of other health reasons	3 (30%)	2 (40%)	1 (20%)

HCC, Huntsman Cancer Center

Summary Results:

- Twelve late-stage, metastatic pancreatic adenocarcinoma patients were treated with Tram/HCQ
- Median time on treatment was 35 days
- Eight patients were treated with the combination for at least 30 days. For this cohort of patients, the median PFS was 2.9 months and median OS was 7.4 months
- Of 7 evaluable patients, 3 patients had stable disease, 1 had a partial response, and 3 progressed
- Two patients with stable disease had >50% decrease in CA 19-9
- One patient with a partial response had > 90% decrease in CA 19-9
- The most common side effects were Grade 1 fatigue and Grade 1/2 rash

Conclusions:

- Tram/HCQ was well tolerated in heavily treated metastatic pancreatic cancer patients and demonstrates clinical benefit for this group.
- We demonstrate the feasibility of utilizing real-world data in precision oncology.
- Collection and reporting of the XCELSIOR cohort with median follow-up of 4.3 months occurred in only 8 months by leveraging the XCELSIOR infrastructure.
- Updates on current alive patients and future patients who enroll in XCELSIOR will be reported at a later time.

Acknowledgment:

The authors would like to thank the patients and their families for participating in this study.