RX3117, An Oral Antimetabolite Nucleoside Shows Activity in Subjects with Pancreatic Cancer. Preliminary Results of Stage 1 of the Phase 1a/2b Study

Drew W. Rasco[1], Christine Peterson[2], Ely Benaim[2] and Jaime R. Merchan[3]. [1]South Texas Accelerated Research Therapeutics, San Antonio, TX, [2]Rexahn Pharmaceuticals Inc., Rockville, MD, [3]Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, FL

Abstract #445

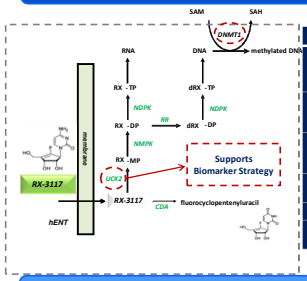
Background: RX-3117 is an oral small molecule antimetabolite, cyclopentyl pyrimidyl nucleoside that is activated by uridine cytidine kinase 2. RX-3117 has shown efficacy in xenograft models of gemcitabine resistant pancreatic, bladder and colorectal cancer. Data from stage 1 of the Phase 1b/2a clinical study of RX3117 as a single agent in subjects with metastatic pancreatic cancer is described below.

Methods: Stage 1 of the Phase 1b/2a study (NCT02030067) is designed to evaluate safety, tolerability and efficacy following treatment with 700 mg administered orally once-daily for 5 consecutive days with 2 days off per week for 3 weeks with 1 week off in each 4 week cycle in a 2-stage Simon design. Eligible subjects (aged ≥ 18 years) were those with relapsed/refractory metastatic pancreatic cancer. The primary endpoint is a ≥ 20% (2 out of 10 subjects) rate of progression free survival (PFS) benefit (i.e., proportion of subjects with stable disease for at least 4 months) and/or a 10% (1 of 10 subjects) with a partial response rate or better.

Results: As of Sep 2016, 8 out of 10 subjects have been enrolled (4 females, 4 males), the mean age was 70 years, ECOG performance status was 1 and 5 subjects had received more than 4 prior therapies. Two subjects met the primary endpoint of stable disease with a duration of 140-168 days at the time of this submission. The most frequent adverse events were moderate to severe anemia, mild to moderate fatigue, abdominal pain and diarrhea.

Conclusions: This ongoing trial shows an early efficacy signal where RX-3117 is active against advanced pancreatic cancer. As the primary endpoint has been achieved, the study will now move to stage 2 where an additional 40 subjects with advanced pancreatic cancer will be enrolled.

RX-3117 Proposed Mechanism



	Gemcitabine	RX-3117
1. Phosphorylation (activation) Enzyme	Deoxycytidine kinase (dCK)	Uridine-cytidine kinase 2 (UCK2)
2. Degradation by Cytidine Deaminase	Fast deamination	Slow deamination
3. DNA Methyl–transferase 1 Activity	Yes	Yes: DNA Hypomethylation
4. Membrane Transport	hENT - dependent	hENT - dependent
5. Incorporation	DNA & RNA	DNA & RNA
6. Synthesis Inhibition	DNA & RNA	DNA & RNA

Study Design

The Phase 1 study was amended to allow a 2-stage phase 1b/2a study design to treat subjects with metastatic pancreatic or bladder cancer with single agent RX-3117 at the dose and schedule identified in Phase 1.

Stage 1 was planned to treat 10 evaluable subjects with metastatic pancreatic cancer. Advancement to stage 2 was predefined as 20% or more subjects with progression free survival of ≥ 4 months or a partial/ complete response in at least 10% of subjects. Preliminary data as of January 7, 2017, is presented from subjects with metastatic pancreatic cancer subjects.

Stage 1 Pancreatic Phase 2 Demographics*

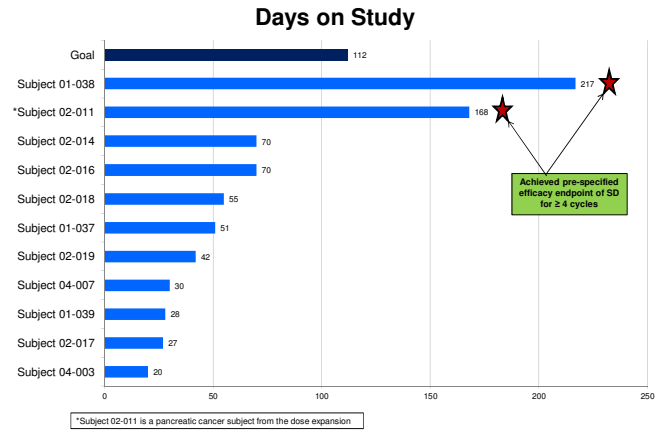
Category		Category	
		ECOG score	n (%)
Gender	n (%)	0	1 (9%)
Female	6 (55%)	1	10 (91%)
Male	5 (45%)		
		Median age (range)	72 (56-78)
Race	n (%)	Prior anticancer treatments	n (%)
White	9 (82%)	1	3 (27%)
Black	1 (9%)	2	2 (18%)
Asian	1 (9%)	3	0 (0%)
		4+	6 (55%)

* Includes 1 subject in the dose expansion who also met the criteria

Phase 1b/2a Pancreatic Safety Profile

Adverse Event	Number of subject(s) per grade			
	Grade 1	Grade 2	Grade 3/4	Overall
Anemia	0	3	4/0	7
Fatigue	2	1	1/0	4
Diarrhea	3	0	0	3
Leucopenia	0	1	1/0	2
ALT Increased	0	1	0	1
Anorexia	0	0	1/0	1
AST Increased	0	1	0	1
Constipation	1	0	0	1
Decreased appetite	1	0	0	1
Elevated Alk Phosphatase	1	0	0	1
Epigastric pain	1	0	0	1
GI pain	1	0	0	1
Hypophosphatemia	0	0	1/0	1
Light headed	1	0	0	1
Neutropenia	0	1	0	1
Thrombocytopenia	0	1	0	1
Vomiting	1	0	0	1

Treatment (Days)



Conclusions

- RX-3117 is safe and well tolerated when administered at the recommended Phase 2 Dose of 700 mg administered for 5 consecutive days with 2 days off for 3 weeks with 1 week off.
- Subjects enrolled into stage 1 of the clinical trial had active progressive disease, with 54% of them having failed ≥ 3 prior cancer therapies (including 5-FU and gemcitabine-based therapies). Data also includes 1 subject from the dose expansion who met the response criteria
- Two subjects met the predefined protocol efficacy criteria by having stable disease for more than 4 months.
- Forty additional subjects are now being recruited in stage 2 of the Phase 1b/2a.
- Future clinical studies include combining RX-3117 with other agents for the treatment of pancreatic and bladder cancer.

Author Disclosures

Christine Peterson, PhD, and Ely Benaim, MD – Rexahn Pharmaceuticals

For further information about RX-3117 and Rexahn Pharmaceuticals please contact Dr. Ely Benaim: benaime@rexahn.com, (240) 268-5300 x 304